> Tel: 91-80-6657995/6722563
> Fax (PP): 91-80-2274699
> Email: admin@leo.ilban.ernet.in
> esg@bgl.vsnl.net.in
> Website: http://www.altindia.net/esg/index.htm
>
> ---
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>

Health Minister.doc

Name: Health Minister.doc
Type: Winword File (application/msword)
Encoding: base64

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Environment Support Group
36, Reservoir Road
Basavanagudi
Bangalore 560 004. INDIA
Telefax: 91-80-6614855/6657995
Email: esg@bgl.vsnl.net.in admin@leo.ilban.ernet.in
Website: http://www.altindia.net/esg/index.htm

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4 of

TI: Hepatitis B vaccination and reduced risk of primary liver cancer among adults: A cohort study in Korea.
AU: Lee-M-S; Kim-D-H; Kim-H; Lee-H-S; Kim-C-Y; Park-T-S; Yoo-K-Y; Park-B-J; Ahn-Y-O
AD: Department of Preventive Medicine, University of Ulsan, College of Medicine, 388-1 Songpa-gu, Poongnap-dong, Seoul 138-040, South Korea
SO: INT-J-EPIDEMIOL. International-Journal-of-Epidemiology. 1998; 27/2 (316-319)
AB: Background. Primary liver cancer is an important health problem in Kore where hepatitis B virus (HBV) infection is prevalent. The authors conducted prospective cohort study to evaluate the protective effect of HBV vaccinati against liver cancer in adults. Methods. A total of 370,285 males aged \ 3(comprised the study population. They were clinically free of liver diseases and had not been vaccinated against HBV at enrolment. The results of HBV surface antigen (HBsAg) and antibody to HBsAg (anti-HBs) marker positivity those of the vaccination programme which took place during 1985 were used the construction of the cohort. About 5% (n = 18,914) were HBsAg positive, 78,094 were anti-HBs positive, and 273,277 were negative for both. Among t candidates for HBV vaccination (n = 273,277), 35,934 (13.2%) people had be vaccinated against HBV during 1985. Cases of liver cancer were ascertained record linkage and from medical records covering 1986-1989. A multivariate log-linear model was used to test statistical significance and to estimate relative risks (RR). Results. The total follow-up period was 1,404,566 person-years, with an average of 3 years and 10 months. A total of 302 inc cases were ascertained. The overall incidence rate of liver cancer was 21. 100,000 person-years. With reference to the incidence level among the unvaccinated and uninfected, the RR of primary liver cancer among the chronically infected and that of the unvaccinated and infected was 18.1 (9 : 14.2-22.9) and 0.34 (95% CI : 0.19-0.60), respectively. The RR among the vaccinated group was 0.58 (95% CI : 0.31-1.09). Conclusions. This study suggested that artificial immunization through HBV vaccination, even in adulthood, reduces the risk of liver cancer. It might also offer a practic means of primary prevention, especially in areas with hyperendemicity of H infection. (Abstract from CANCERLIT and EMBASE)

6 c

TI: Persistent nodules at sites of hepatitis B vaccination due to aluminiu sensitization.
AU: Skowron-F; Grezard-P; Berard-F; Balme-B; Perrot-H
AD: Department of Dermatology, Hopital de l'Antiquaille, 1 Rue de l'Antiquaille, 69321 Lyon Cedex 05, France
SO: CONTACT-DERMATITIS. Contact-Dermatitis. 1998; 39/3 (135-136)

8

TI: Liver cancer in Taiwan falls after universal hepatitis B vaccination
AU: Mayor-S
SO: BMJ. 315(7099):7 1997

12

TI: Hepatitis B vaccination and hepatocellular carcinoma in Taiwan.
AU: Lee-C-L; Ko-Y-C
AD: School of Public Health, Kaohsiung Medical College, Shih-Chuan 1st Ro

Kaohsiung, Taiwan
SO: PEDIATRICS. Pediatrics. 99/3 (351-353) 1997
AB: Objective. In 1984, Taiwan started a large-scale hepatitis B vaccina

program, enabling us to test the hypothesis that prevention of hepatiti
virus infection eventually decreases the incidence of hepatocellular car
Methods. Groups aged 0 to 9 years and 10 to 100 years in each calendar y
were defined as the study group and the reference group, respectively. T
percentage of children vaccinated in the study group increased during re
years. The study group and the reference group were divided into 5-year
strata (0 to 4, 5 to 9, ..., 80 to 84, and 85 and over). Poisson regress
used to estimate age- and gender-adjusted liver carcinoma mortality rate
for 1974 through 1993, relative to 1974. Results. The adjusted mortality
ratios of liver carcinoma in the study group decreased significantly for
and 1993, whereas in the reference group it did not show the same result
significantly declining trend of liver carcinoma mortality rate ratios
observed in the study group after 1984, whereas the same trend was not
the reference group. Conclusions. Our results support the hypothesis th
hepatitis B vaccination can decrease the incidence of hepatocellular ca
(Abstract from CANCERLIT and EMBASE)

1

TI: Universal hepatitis B vaccination in Taiwan and the incidence of
hepatocellular carcinoma in children.
AU: Chang-M-H; Chen-C-J; Lai-M-S; Hsu-H-M; Wu-T-C; Kong-M-S; Liang-D--C
Shau-W-Y; Chen-D-S

AD: Department of Pediatrics, National Taiwan University Hospital, Chung-Shan
South Rd., Taipei, Taiwan
SO: NEW-ENGL-J-MED. New-England-Journal-of-Medicine. 336/26 (1855-1859) 1997
AB: BACKGROUND: A nationwide hepatitis B vaccination program was implemented
Taiwan in July 1984. To assess the effect of the program on the development o
hepatocellular carcinoma, we studied the incidence of this cancer in children
in Taiwan from 1981 to 1994. METHODS: We collected data on liver cancer in
children from Taiwan's National Cancer Registry, which receives reports from
each of the country's 142 hospitals with more than 50 beds. Data on childhood
liver cancer were also obtained from Taiwan's 17 major medical centers. To
prevent the inclusion of cases of hepatoblastoma, the primary analysis was
confined to liver cancers in children six years of age or older. Data were a
obtained on mortality from liver cancer among children. RESULTS: The average
annual incidence of hepatocellular carcinoma in children 6 to 14 years of ag
declined from 0.70 per 100,000 children between 1981 and 1986 to 0.57 betwee
1986 and 1990, and to 0.36 between 1990 and 1994 (P<0.01). The corresponding
rates of mortality from hepatocellular carcinoma also decreased. The incider
of hepatocellular carcinoma in children 6 to 9 years of age declined from 0
for those born between 1974 and 1984 to 0.13 for those born between 1984 an
1986 (P<0.001). CONCLUSIONS: Since the institution of Taiwan's program of
universal hepatitis B vaccination, the incidence of hepatocellular carcinom
children has declined. Author (Abstract from CANCERLIT and EMBASE)

16 of

TI: [Hepatocellular carcinoma: a preventable cancer]
AU: Viviani-S; Jack-A; Bah-E; Montesano-R
AD: International Agency for Research on Cancer Banjul, Gambia.
SO: Epidemiol-Prev. 21(2):129-36 1997
AB: Hepatocellular carcinoma (HCC) is one of the most common cancers world
and a public health concern in many developing countries. The main risk fa
is the chronic carriage state of the hepatitis B virus which is found in a
20% of the adult population in many African and Asian countries. Other
important risk factors are HCV infection, aflatoxin exposure and alcohol
consumption. The Gambia Hepatitis Intervention Study was launched in 1986
the aim of evaluating the efficacy of the hepatitis B vaccination, given
early infancy, in preventing HBV infection, its chronic carriage status,

later, HCC. For this purpose, a randomised vaccine trial was designed an
carried out. Over a period of four years a total of 124.577 children wer
recruited, one half received the usual EPI vaccines (BCG, DTP, OPV, meas
yellow fever) and the other half the hepatitis B vaccine in addition to
ones. Hepatitis B vaccination has been successfully integrated into the
"Expanded Programme of Immunization" in The Gambia, since every new born
can receive this vaccination in addition to the EPI vaccine. The first m
point evaluation showed that in four-year-old children, hepatitis B vacc
efficacy was 84% in preventing infection and 94% in preventing chronic
status of HBV. Other mid point evaluations are still ongoing. A nationw
Cancer Registry was set up to detect HCC cases in the cohort under stud
Follow-up through the Cancer Registry is planned for the next 30 years.
Refs) Author

1 of
Marked Reco

TI: Hepatitis B virus infection [letter]
AU: Cherian-T; John-TJ
AD: Department of Pediatrics, Christian Medical College and Hospital, Vellor
Tamil Nadu.
SO: Indian-Pediatr. 1997 Aug; 34(8): 762-3
This source is Available in S.J.M.C Library
Call Number: From: 1969+
LA: ENGLISH

2 of
Marked Reco

TI: Antimalarial vaccine.
AU: Rajeshwari-K
AD: Department of Pediatrics, Hindu Rao Hospital, Delhi.
SO: Indian-Pediatr. 1997 Jul; 34(7): 657-8
This source is Available in S.J.M.C Library
Call Number: From: 1969+
LA: ENGLISH

3 of
Marked Reco

TI: No seroconversion after hepatitis B immunization.
AU: John-TJ
AD: Department of Clinical Virology, Christian Medical College, Vellore, Tam
Nadu.
SO: Indian-Pediatr. 1997 Jun; 34(6): 555-6
This source is Available in S.J.M.C Library
Call Number: From: 1969+
LA: ENGLISH

PC-SPIRS 3.40 MEDLINE (R) 1998/01-1998/10

1 of 7
Marked Record

TI: Global status of HB immunization, 1998.
AU: Kane-MA
AD: Expanded Programme on Immunization, Global Programme for Vaccines and Immunization, World Health Organization, Geneva.
SO: Acta-Gastroenterol-Belg. 1998 Apr-Jun; 61(2): 237
this source is not Available in S.J.M.C.Library
LA: ENGLISH

2 of 7
Marked Record

TI: The United Kingdom's hepatitis B immunisation strategy--where now?
AU: Goldberg-D; McMenamin-J
AD: Scottish Centre for Infection and Environmental Health, Glasgow.
SO: Commun-Dis-Public-Health. 1998 Jun; 1(2): 79-83
LA: ENGLISH
AB: The World Health Organization recommended in 1992 that all countries should introduce universal hepatitis B vaccination into their immunisation schedules by December 1997. Over 80 countries, many of them in western Europe, have complied with the recommendation, but, in the United Kingdom (UK), hepatitis B vaccine is offered to selected high risk population groups only. Vaccination uptake in many of these groups is poor and transmission of hepatitis B remains a problem. The current incidence of hepatitis B is lower in the UK than in countries that have adopted a universal approach. It is impossible, however, to predict the number of acute infections that might occur in an unvaccinated teenage population in the year 2015 if the UK's current strategy remains unaltered. Universal immunisation would guarantee that hundreds, if not thousands, of acute illnesses and an appreciable number of severe outcomes would be prevented each year. The authors believe that funding this intervention would be money well spent.

3 of 7
Marked Record

TI: [Vaccination against hepatitis B in Switzerland: towards a global strategy]
AU: Kammerlander-R; Vaudaux-B; Bourquin-C; Zimmermann-HP; Raeber-PA
AD: Office federal de la sante publique, Division epidemiologie et maladies infectieuses, Berne.
SO: Rev-Med-Suisse-Romande. 1998 Apr; 118(4): 335-9
this source is not Available in S.J.M.C.Library
LA: FRENCH; NON-ENGLISH

4 of 7
Marked Record

TI: Unsafe injections [comment]
AU: Kane-M
AD: Global Programme for Vaccines and Immunization, World Health Organization, Geneva, Switzerland.
SO: Bull-World-Health-Organ. 1998; 76(1): 99-100
this source is not Available in S.J.M.C.Library
LA: ENGLISH
AB: In many developing countries use of unsterilized or improperly sterilized needles and syringes is common and causes millions of cases of viral hepatitis

B and C as well as contributing to the spread of human immunodeficiency virus (HIV) and other bloodborne pathogens. To combat this problem, WHO has stimulated the development of the "auto-destruct" syringe and encourages all donors, international agencies, and health departments to include a supply of such syringes with all vaccines supplied for emergency purposes. In addition, health providers and the public need to be educated about the risk of inappropriate and unsterile injections.

5 of
Marked Recor

TI: We have a cancer vaccine--why don't we use it? [editorial]
AU: Hall-A
SO: Trop-Med-Int-Health. 1998 May; 3(5): 337-8
this source is not Available in S.J.M.C.Library
LA: ENGLISH

6 of
Marked Recor

TI: Plasma-derived and recombinant hepatitis B vaccines [letter]
AU: John-TJ
AD: IAP Committee on Immunization, Thekkakora.
SO: Indian-Pediatr. 1997 Aug; 34(8): 745-6
This source is Available in S.J.M.C Library
Call Number: From: 1969+
LA: ENGLISH

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from the Ref: get a copy of IAP recommendatio

7 of
Marked Recor

TI: Hepatitis B and breastfeeding.
SO: Indian-Pediatr. 1997 Jun; 34(6): 518-20
This source is Available in S.J.M.C Library
Call Number: From: 1969+
LA: ENGLISH

619-484-3197 (phone/voicemail)
619-484-1187 (fax)
via@access1.net (email)
http://www.909shot.com (NVIC website)
http://www.access1.net/via (VIA website)
****
We Must Have The Freedom To Choose & Respect Everyone's Choice
****
Any information obtained here is not to be construed as medical
OR legal advice. The decision to vaccinate and how you
implement that decision is yours and yours alone.
****

>From shotinfo@ozemail.com.au Sun Apr 4 13:31:10 1999
Received: from Waffle on leo by WafPeg 0.25, 93.04.04
for ADMIN on standalone PMail ; Mon, 5 Apr 1999 08:56:45 IST+5.30
Received: by leo (1.65/waf)
via UUCP; Mon, 05 Apr 99 08:56:37 IST
for leo.ilban.ernet.in!ADMIN
Received: from ozemail.com.au (uucp@localhost) by ilban.ernet.in (8.7.5/8.7.3) with UUCP id N
Received: from fep9.mail.ozemail.net (fep9.mail.ozemail.net [203.2.192.103])
by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA24125
for <ADMIN@leo.ilban.ernet.in>; Sun, 4 Apr 1999 12:37:02 +0530
Received: from avn (s1lis1p07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: TREATMENT FOR HEPATITIS B DISEASE
Date: Sun, 4 Apr 1999 17:03:52 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKAEGOEMAA.shotinfo@ozemail.com.au>
MIME-Version: 1.0
Content-Type: text/plain;
charset="iso-8859-1"
Content-Transfer-Encoding: 7bit
X-Priority: 3 (Normal)
X-MSMail-Priority: Normal
X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal

-----Original Message-----
From: karin schumacher [mailto:via@access1.net]
Sent: Saturday, 23 January 1999 5:58
To: via
Subject: TREATMENT FOR HEPATITIS B DISEASE

Issue Number 48 January 21, 1999

January 21, 1999
EPIVIR-HBV (LAMIVUDINE) IS APPROVED BY THE FDA AS ORAL TREATMENT FOR CHRONIC HEPATITIS B
On December 9, 1998, the FDA approved the first oral, anti-viral medication for the treatment of adults with chronic hepatitis B associated with evidence of hepatitis B viral replication and active liver inflammation. Epivir-HBV, a brand name for lamivudine, is available as a tablet and as an oral solution. Epivir-HBV is manufactured by Glaxo Wellcome, Inc., based in Research Triangle Park, North Carolina.

For additional information about Epivir-HBV, read the package insert.
letter to IAC EXPRESS RE: ABOVE NEWSLETTER.

Meeting on Hep B

January 22, 1999

Dear Sir/Madam:

I read your IAC Express #48 Newsletter which is promising for Hepatitis B sufferers.

My question is: If there is a treatment for this disease and the risk population is relatively small (5% of the total population), then why is there the need and push for immunizing the entire population.

Please answer at your convenience.

Thank you.

Karin Schumacher

****
Karin Schumacher
Vaccine Information & Awareness (VIA)
12799 La Tortola
San Diego, CA 92129
619-484-3197 (phone/voicemail)
619-484-1187 (fax)
via@access1.net (email)
http://www.909shot.com (NVIC website)
http://www.access1.net/via (VIA website)
****
We Must Have The Freedom To Choose & Respect Everyone's Choice
****
Any information obtained here is not to be construed as medical OR legal advice. The decision to vaccinate and how you implement that decision is yours and yours alone.
****

>From shotinfo@ozemail.com.au Sun Apr 4 13:31:11 1999
Received: from Waffle on leo by WafPeg 0.25, 93.04.04
for ADMIN on standalone PMail ; Mon, 5 Apr 1999 08:56:46 IST+5.30
Received: by leo (1.65/waf)
via UUCP; Mon, 05 Apr 99 08:56:37 IST
for leo.ilban.ernet.in!ADMIN
Received: from ozemail.com.au (uucp@localhost) by ilban.ernet.in (8.7.5/8.7.3) with UUCP id N
Received: from fep9.mail.ozemail.net (fep9.mail.ozemail.net [203.2.192.103])
by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA24126
for <ADMIN@leo.ilban.ernet.in>; Sun, 4 Apr 1999 12:37:02 +0530
Received: from avn (s1lis1p07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: MATHATMA GANDHI WAS ANTI-VACCINE
Date: Sun, 4 Apr 1999 17:03:50 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKOEGNEMAA.shotinfo@ozemail.com.au>
MIME-Version: 1.0
Content-Type: text/plain;
charset="iso-8859-1"
Content-Transfer-Encoding: 7bit
X-Priority: 3 (Normal)
X-MSMail-Priority: Normal
X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal

Hi I know this is off the subject but it might be interesting and useful

-----Original Message-----
From: karin schumacher [mailto:via@access1.net]
Sent: Saturday, 23 January 1999 7:16
To: via
Subject: MATHATMA GANDHI WAS ANTI-VACCINE

Sai Sanjeevini Foundation wrote:
Here are the quotes from Mahatma Gandhi:

".. I am and have been for years, a confirmed anti-vaccinationist. Anti Vaccination has no backing from the orthodox medical opinion. A medical man who expresses himself against vaccination loses caste. Tremendous pecuniary interests too have grown round vaccination."

On being asked to vaccinate the ashram (hermitage) inmates during the small pox epidemic.

"How can I go back on the principles I have held so dear all my life, when I find that it is these very principles that are being put to the test? I have not in the least doubt in my mind that vaccination is a filthy process, that is harmful in the end and that it is little short of taking beef*."

*Non-violence was the base on which Gandhiji stood everything he did. Besides, while some Hindus eat meat, they would usually draw the line at beef because we hold the cow holy since, like the mother, she gives us milk and for many other reasons which it would be difficult to enumerate here.

Sanathana Sai Sanjeevini.....healing fragrances - Healing with Prayers.....in loving surrender: http://www.uriel.net/~lakhani

Sai Sanjeevini Foundation
108/39, Silver Oaks
DLF City - Phase 1
Gurgaon - 122002
Haryana, India
Tel : 91-124-351030/351430

****
Karin Schumacher
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San Diego, CA 92129
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619-484-1187 (fax)
via@access1.net (email)
http://www.909shot.com (NVIC website)
http://www.access1.net/via (VIA website)
****
We Must Have The Freedom To Choose & Respect Everyone's Choice
****
Any information obtained here is not to be construed as medical OR legal advice. The decision to vaccinate and how you implement that decision is yours and yours alone.
****

>From shotinfo@ozemail.com.au Sun Apr 4 13:31:13 1999
Received: from Waffle on leo by WafPeg 0.25, 93.04.04
for ADMIN on standalone PMail ; Mon, 5 Apr 1999 08:56:46 IST+5.30
Received: by leo (1.65/waf)

via UUCP; Mon, 05 Apr 99 08:56:40 IST
for leo.ilban.ernet.in!ADMIN
Received: from ozemail.com.au (uucp@localhost) by ilban.ernet.in (8.7.5/8.7.3) with UUCP id N
Received: from fep9.mail.ozemail.net (fep9.mail.ozemail.net [203.2.192.103])
by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA24127
for <ADMIN@leo.ilban.ernet.in>; Sun, 4 Apr 1999 12:37:02 +0530
Received: from avn (s1lis1p07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: [AVML] Is Hepatitis B Vaccine Safe for Kids? 20/20 Story
Date: Sun, 4 Apr 1999 17:03:46 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKMEGNEMAA.shotinfo@ozemail.com.au>
MIME-Version: 1.0
Content-Type: text/plain;
charset="iso-8859-1"
Content-Transfer-Encoding: 8bit
X-Priority: 3 (Normal)
X-MSMail-Priority: Normal
X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal

-----Original Message-----
From: owner-avml@Majordomo.net [mailto:owner-avml@Majordomo.net]On Behalf Of Carolyn
Sent: Saturday, 23 January 1999 2:55
To: Sue; P.R.O.V.E.; P Campbell; Magerle; M Cessna; K NVIC; J. Johns; AVML; A:VacAware; A KVIA; C. Gerner
Subject: [AVML] Is Hepatitis B Vaccine Safe for Kids? 20/20 Story

Who's Calling the Shots?

Critics Say Required Hepatitis B Vaccine Not Safe for Everyone

Since a new policy requiring hepatitis B vaccinations took effect in 1991, 274 newborn deaths following vaccination have been reported. (ABCNEWS.com)

ABCNEWS.com
Two years ago, Ronnie Allen was your typical all-American, 4-year-old boy — vibrant, healthy, happy and strong.

But before he could start preschool in suburban St. Louis, he was required to have a vaccination against hepatitis B. He got his shot the day before Halloween. And he nearly didn't make it to Christmas.

He was diagnosed with a rare and life-threatening form of arthritis. He 's had chemotherapy 10 times and is in constant pain. Ronnie's parents, and his doctor, blame the hepatitis shot.

"We just thought it was like all the immunization shots," says his mother, Janet Allen. "We were doing it to protect our child."

Some scientists believe that in certain people the vaccine can be worse than the disease it prevents. Yet it's the law in most states that children can't attend school without first having the three-dose vaccination which prevents hepatitis B.

Who's At Risk?
Hepatitis B kills 4,000 to 5,000 people a year. Like AIDS, it's spread through blood or body fluids — sex with an infected partner, needle-sharing among infected drug users and passed by infected mothers to their children. Infected people may be symptom-free for years as the virus slowly assaults the liver. And liver failure is fatal.
In 36 states, schools require children to be vaccinated for hepatitis B

before they enter kindergarten or first grade. In some of those states, the laws take effect this year or in 2000 or later. (ABCNEWS.com)

"The only way that we know to prevent it is to have widespread vaccination," says Dr. Harold Margolis, director of infectious diseases at the Centers for Disease Control.

Dr. Bonnie Dunbar, a cellular biologist at Baylor College of Medicine, believes that in certain people, a genetic component sets off an explosive chain of events after they receive the vaccine.

"The only thing that happened is they took this vaccine," she says, "and within a month most of these people have had completely debilitating lifestyle changes."

Package inserts alert doctors that serious adverse experiences have been reported after vaccination, including multiple sclerosis, arthritis, Guillain-Barre Syndrome and lupus. But manufacturers don't believe there is a link between the vaccine and these illnesses.

Baby Deaths Attributed to SIDS

The CDC agrees. Since 1991, the agency has endorsed mandatory vaccination of newborns, even though the risk of hepatitis B infection is small in children.

"How is a baby possibly going to get hepatitis B? It's ridiculous to give this vaccine to a child," says Michael Belkin, whose daughter Lyla died last September. "I wish we'd known that before receiving the vaccine. No one told us."

Lyla Belkin's death was also attributed to SIDS, a broad category often used when a healthy baby dies. She had received her first hepatitis B shot at 6 days old, and a second one a month later.

On Sept. 16, 1998, Lorna Belkin nursed Lyla at 5:30 a.m. Not long after, she found her daughter pale and cold.

"She died early in the morning," Mrs. Belkin says, "about 16 hours after the vaccination."

Millions Vaccinated Safely

Since the CDC's policy took effect in 1991, 274 such newborn deaths following vaccination have been reported to the federal government. And 20/20 has learned that most of these newborn deaths were listed as SIDS. An additional 2,600 infants have had serious medical problems.

An analysis of federal vaccine statistics, however, shows that these numbers are barely measurable when compared to the 9 million babies vaccinated so far. That's evidence, say vaccine proponents, that there is no link between the vaccine and health problems.

Dr. Robert Sharrar of vaccine manufacturer Merck estimates that perhaps 20 million children and adults have been vaccinated safely.

"I don't truly believe that those illnesses were caused by the vaccine," he says, adding that "there's no doubt in my mind that people are much better off taking the vaccine than they are being exposed to the natural disease process."

But critics say the vaccination decision should be left to parents.

"I don't think the government has a role to come in and mandate for children that are clearly not at risk that they need to receive the hepatitis B vaccine," says Sue Blevins, director of the Institute for Health Freedom, a nonprofit patient's rights group.

As for Ronnie Allen, it's still touch and go. His arthritis stabilized enough to permit him to start kindergarten in September, but as long as he lives, he'll need medication. And his parents don't know if his deterioration has stopped for good.

His dad, Ron Allen, has this advice for other parents considering shots for their kids: "If they don't think it's necessary, let them make the choice and say no."

For More Information
Centers for Disease Control
National Immunization Program Hotline 1-800-232-2522 (English)

1-800-232-0233 (Spanish)
To report a problem after vaccination: Vaccine Adverse Event Reporting System (VAERS) 1-800-822-7967

Why Vaccinate Everybody?
One of the recurring questions with mandatory hepatitis B vaccination is, why not immunize only the people at high risk for infection?

When the vaccine was first approved in 1986, the first people to get it were health care workers at risk for being exposed to tainted blood. Some of the workers reported adverse reactions to the vaccine and won legal settlements against the manufacturer.

But overall, the vaccine was deemed safe and effective. So its use was expanded.

Worldwide, 200 million people are chronically infected with hepatitis B. And in the United States alone, there are more than 200,000 new cases yearly.

About 27,000 of those cases are children. Roughly 6,000 to 7,000 are infants who were infected by their mothers during pregnancy.

Dr. Harold Margolis of the Centers for Disease Control says another 20,000 children get infected in the first five years of life through close contact with someone else in their family. And there's no way to identify who that might be, so the policy has been to vaccinate all kids.

"That is a well accepted public health approach and policy," Margolis says.

Studies have also shown that about 30 percent of patients don't know where they acquired their infection, which would make it difficult to identify all people at risk.

Search for more on
S U M M A R Y

Schools in 36 states require kids to get shots for hepatitis B, but some believe the vaccination isn't always safe.
Why Vaccinate Everybody?

W E B L I N K S

CDC: Hepatitis B and the Vaccine that Protects You

Immunization Action Coalition

Hepatitis B Vaccine and Hepatitis B Immune Globulin

American Liver Foundation: Hepatitis B Vaccine

National Vaccine Information Center

"The decision ultimately needs to be in the parents' hands, the parents are going to be the ones living with the consequences."
Sue Blevins, Institute for Health Freedom

http://www.abcnews.go.com/sections/living/DailyNews/hepb2020.html

```
>From shotinfo@ozemail.com.au  Sun Apr  4 13:31:12 1999
Received: from Waffle on leo by WafPeg 0.25, 93.04.04
      for ADMIN on standalone PMail ; Mon, 5 Apr 1999 08:56:46 IST+5.30
Received: by leo (1.65/waf)
        via UUCP; Mon, 05 Apr 99 08:56:40 IST
        for leo.ilban.ernet.in!ADMIN
Received: from ozemail.com.au (uucp@localhost) by ilban.ernet.in (8.7.5/8.7.3) with UUCP id N
Received: from fep9.mail.ozemail.net (fep9.mail.ozemail.net [203.2.192.103])
        by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA23973
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Received: from avn (slils1p07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: INDIA PEDIATRICIANS AGAINS LOW-COST HEP B VACCINE
Date: Sun, 4 Apr 1999 16:58:06 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKGEGMEMAA.shotinfo@ozemail.com.au>
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X-Priority: 3 (Normal)
X-MSMail-Priority: Normal
X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal


-----Original Message-----
From: karin schumacher [mailto:via@access1.net]
Sent: Monday, 1 February 1999 3:08
To: via
Subject: INDIA PEDIATRICIANS AGAINS LOW-COST HEP B VACCINE


Michael Belkin wrote:
http://www.the-asian.com/news/jan99/30hepatitis.htm

The Asian
30 January 1999

Vaccine manufactures and the Karnataka govt lock horns over Hepatitis B
Priyadarshini Aji \ Bangalore

WHILE Acquired Immuno Deficiency Syndrome hogs all attention in the
media and the medical fraternity, an equally fatal disease like
Hepatitis B is being completely sidelined. Except in Karnataka where Non
Governmental Organisations and Hepatitis B
vaccine companies have been carrying out awareness campaigns for quite
some time now. But if the Karanataka government has its way, these
awareness campaigns will soon have to come to a halt.   The state
government is looking into allegations prominent pediatricians have
levied against NGOs and manufactures of the Hepatitis B vaccine.

The accusation is that of creating panic of an epidemic, and cashing in
on it for their own mercenary purposes. The Karnataka government on
Friday set up a high-level committee, comprising drugs controller Dr
Anand Rajashekar, director of Health and Family Welfare Services Dr D T
Hema Reddy and others, to look into the issue.  The Hepatitis B vaccine
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manufacturers and the NGOs conducting awareness and vaccination camps in and around Bangalore are aghast by the allegation. They claim that the government, instead of taking preventive measures, is attempting to stop them from creating awareness.

Quoting statistics from a survey conducted by Shanta Biotech Ltd which manufactures Hepatitis B vaccines, Dr U S R Karanth of the Ashwini clinic says: "One in every 20 persons in India is a carrier of Hepatitis B. At least 50 percent of these carriers are likely to develop serious liver problems. Of the adult population who have this disease, about 4.5 lakh people will die." Dr Karanth points out that the World Health Organisation has issued a directive to all countries to include the Hepatitis B vaccine in their immunisation schedule, and undertake mass immunisation programmes to prevent the spread of the disease. Like AIDS, Hepatitis B spreads through blood transfusion, open wounds, sexual transmission and used syringes. And is incurable. Victims suffer from cirrhosis of the liver and even cancer.

Eighty countries have already put the Hepatitis B vaccine into its immunisation schedule. Except India of course, which has yet to wake up to the immensity of the problem. People traveling to United States of America, United Kingdom and other developed countries have to be immunised against Hepatitis B, along with typhoid and leprosy, before visas are granted. Newborn children, medical and paramedical staff are the high-risk groups. The vaccine is given in three doses of 0.5 ml each to children, and 1 ml each to adults. Still H C Mahadevappa, the Karnataka health minister -- a medical student himself -- is skeptical. ``Until there is a national policy on the issue, I will not take any action in the state. I have asked the committee to report on the prevalence of the disease and its actual impact. The disease is said to cause cirrhosis of the liver, which can be treated. I am not convinced about the urgency of the immunisation programme. Especially when we have not even completed the other programmes for prevention of polio, whooping cough and tetanus," he says, almost defiantly.

In the urban centres of Karnataka, awareness about Hepatitis B has spread like wild fire. People queue up in hundreds at the camps conducted by charity organisations and other social welfare groups. Mahadevappa declares that this is because the drug manufacturers have managed to 'sensationalise' the issue. "I fear that vaccine manufacturers are trying to make money out of this. They are selling their drugs on mass basis, for lower rates at these camps." The manufacturers are aghast at the idea. "Earlier, people in this country had to depend on imported Hepatitis B vaccines manufactured by SmithKline Beecham and Cadila, which cost about Rs 500 to 600 for one dose of 0.5 ml, the recommended dose for children under 10 years of age. We are selling Shanvac at Rs 120 through retail outlets. In the camps, we supply the vaccine at Rs 90 for a paediatric dose. The one ml dose costs Rs 300 in the retail market, while at the camps it is supplied at Rs 180," says George Kurikose, business development manager of Shanta Biotech Ltd.

Interestingly, the company has sold 4 lakh doses of its Shavnac Hepatitis B vaccine, worth Rs 4.8 crore, in the last month. The company, which set up shop last year, Shanta Biotech, has a turnover of Rs 12 crore in the current financial year. According to Dr Karanth, the pediatricians in Karnataka, who are affected by the camps, have complained to the government. "If the patient goes to a pediatrician, he charges Rs 300 per one ml dose.

He also gets commission from the medical shop and the vaccine companies. The camps have taken away all that business," he adds. But at the same

time, Dr Karanth admits that some of the camps, organised by local charities in rural and semi-rural areas, might not have all the proper facilities to administer the injections. "I welcome the idea of a high level committee looking into the problems faced by the camps organised by the local charities. But it should look at all sides, not just the negative factors. Administration of the injections is very important, and the government by itself cannot afford to put it on the immunisation programme. The camps are fulfilling this lacunae." Till the impact is known in its totality, Hepatitis B will still continue on its killing spree.

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619-484-3197 (phone/voicemail)
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http://www.909shot.com (NVIC website)
http://www.access1.net/via (VIA website)
****
We Must Have The Freedom To Choose & Respect Everyone's Choice
****
Any information obtained here is not to be construed as medical OR legal advice. The decision to vaccinate and how you implement that decision is yours and yours alone.
****

>From shotinfo@ozemail.com.au Sun Apr 4 13:31:11 1999
Received: from Waffle on leo by WafPeg 0.25, 93.04.04
for ADMIN on standalone PMail ; Mon, 5 Apr 1999 08:56:46 IST+5.30
Received: by leo (1.65/waf)
via UUCP; Mon, 05 Apr 99 08:56:38 IST
for leo.ilban.ernet.in!ADMIN
Received: from ozemail.com.au (uucp@localhost) by ilban.ernet.in (8.7.5/8.7.3) with UUCP id N
Received: from fep9.mail.ozemail.net (fep9.mail.ozemail.net [203.2.192.103])
by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA23981
for <ADMIN@leo.ilban.ernet.in>; Sun, 4 Apr 1999 12:31:17 +0530
Received: from avn (s1lis1p07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: STANFORD MEDICAL SCHOOL ON HEP B VACCINE
Date: Sun, 4 Apr 1999 16:58:10 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKIEGMEMAA.shotinfo@ozemail.com.au>
MIME-Version: 1.0
Content-Type: text/plain;
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X-Priority: 3 (Normal)
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X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal

-----Original Message-----
From: karin schumacher [mailto:via@access1.net]
Sent: Thursday, 28 January 1999 6:12
To: via
Subject: STANFORD MEDICAL SCHOOL ON HEP B VACCINE

> > > For those of you who are interested in what Physicians are being taught
> > > about Vaccines there is a site on the internet
> > >
> > > http://www-med.stanford.edu/school/DGIM/teaching/modules/immunization.html
> > >
> > > Interestingly enough, one of the most prestigious medical
> > > schools, STANFORD UNIVERSITY,is NOT in agreement about vaccinating
> > > newborns against Hepatitis B. In his teaching module, Eliseo
> > > Perez-Stable, MD, says the following:
> > >
> > > "ACIP, the American Academy of Pediatrics and the American Academy of
> > > Family Practice recommend universal immunization of all infants against
> > > HBV, regardless of risk. Although this policy is moderately economically
> > > attractive, many have criticized the unneeded vaccinations and the added
> > > pain of more "baby shots". Bloom and colleagues completed a cost
> > > effectiveness study on HBV vaccination strategies and concluded that the
> > > strategy with the lowest cost per year of life saved was
> > >
> > > 1)Screen all pregnant women
> > >
> > > 2)If HBsAg positive: vaccinate infant against HBV and administer HBIG.
> > >
> > > 3)vaccinate all children at 10 years and re-vaccinate with a booster 10
> > > years later."
> > >
> > > I urge you to send this information on to others. I am committed to
> > > stopping the routine vaccine of newborns throughout N. America. Babies'
> > > immune systems are not developed enough to take this vaccine. I fear
> > > that this is a huge money-making scheme on the part of the pharmaceutical
> > > companies and that it is going to have huge health costs for the general
> > > public.
> > >
> > > Contact at least one public health official in your community today and
> > > let them know there is a campaign to end the vaccination of babies
> > > against Hepatitis B. When the people lead, the leaders follow.
> > >
> > > Yours in partnership to save one child's life,
> > >
> > > Gloria Lemay, Private Birth Attendant, Mother, Grandmother, Uppity Woman
> > > Vancouver, B.C., Canada >>
> > >
> > Patrice Bobier, Midwife in Michigan

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619-484-1187 (fax)
via@access1.net (email)
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http://www.access1.net/via (VIA website)
****
We Must Have The Freedom To Choose & Respect Everyone's Choice
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Any information obtained here is not to be construed as medical
OR legal advice. The decision to vaccinate and how you
implement that decision is yours and yours alone.
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>From shotinfo@ozemail.com.au Sun Apr 4 13:31:13 1999
Received: from Waffle on leo by WafPeg 0.25, 93.04.04
for ADMIN on standalone PMail ; Mon, 5 Apr 1999 08:56:46 IST+5.30
Received: by leo (1.65/waf)
via UUCP; Mon, 05 Apr 99 08:56:40 IST
for leo.ilban.ernet.in!ADMIN
Received: from ozemail.com.au (uucp@localhost) by ilban.ernet.in (8.7.5/8.7.3) with UUCP id N
Received: from fep9.mail.ozemail.net (fep9.mail.ozemail.net [203.2.192.103])
by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA23964
for <ADMIN@leo.ilban.ernet.in>; Sun, 4 Apr 1999 12:31:10 +0530
Received: from avn (s1lis1p07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: HEP B VACCINE EFFORT DRAWS FIRE
Date: Sun, 4 Apr 1999 16:58:00 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKCEGMEMAA.shotinfo@ozemail.com.au>
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Content-Type: text/plain;
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X-MSMail-Priority: Normal
X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal

-----Original Message-----
From: karin schumacher [mailto:via@access1.net]
Sent: Thursday, 4 February 1999 4:47
To: via
Subject: HEP B VACCINE EFFORT DRAWS FIRE

Michael Belkin wrote:
source:
http://search.washingtonpost.com/wp-srv/WPlate/1999-02/02/1071-020299-idx.ht
ml

Hepatitis B Vaccine Effort Draws Fire
Critics Cite Reports of Adverse Effects in Opposing Mandatory
Inoculations of Children
By Marc Kaufman
Washington Post Staff Writer
Tuesday, February 2, 1999; Page Z11

Public health campaigns to control hepatitis B through mandatory
childhood vaccination programs have created an increasingly vocal and
determined backlash from groups claiming the vaccine is harming more

people than health officials will acknowledge. Armed with federal statistics they say show the vaccine has resulted in thousands of "adverse reactions"--including conditions similar to rheumatoid arthritis and multiple sclerosis--these critics are demanding that parents be allowed more easily to choose not to give their children the hepatitis B vaccine. Health authorities in France, responding to similar concerns, ended their mandatory hepatitis B vaccination program for 11- and 12-year-olds in October.

American public health officials, however, have made clear that they see no reason to scale back their hepatitis B campaigns, saying the vaccine is one of the safest and most useful ever devised. Research, they say, has not found any correlation between the hepatitis B vaccine and any significant or unexpected reactions. "We take it very seriously when people use inappropriate information to undermine vaccine programs," said Barbara Reynolds, a spokeswoman for the CDC.

There is a real chance they can push us back to a pre-vaccine, developing-country level of health care in the US, she said. "Something similar is already happening in countries like Sweden, Japan and the United Kingdom." The CDC reports that the hepatitis B virus, which attacks the liver, infects about 200,000 Americans annually and sends 11,000 people to the hospital with deep fatigue, muscle pain and jaundice. Chronically infected people can develop liver cancer and other potentially fatal diseases. There is no cure.

Hepatitis B virus is spread through blood and other bodily fluids. It is widespread in some tropical nations, but in the United States is found most frequently in intravenous drug users and people who participate in high-risk sexual activities. Health care workers are also considered at high risk. While critics of the vaccine program say most young children don't need it because they are not at risk, public health officials say the best way to attack the disease is through vaccinations at birth or before school.

Since the early 1990s, hepatitis B inoculations have been given routinely to infants in the United States. At least 36 states--including Virginia and Maryland--and the District of Columbia require the full series of three shots before a child can register for school. While the stakes are always high in disputes about vaccinations, the hepatitis B controversy has an added importance: The vaccine is the first to use recombinant DNA technology. With other genetically engineered vaccines in the pipeline, the fate of the hepatitis B vaccine is being closely watched. Bonnie Loe Fisher, president of the National Vaccine Information Center in Vienna, has been at the center of calls to reassess the safety of the hepatitis B vaccine.

"This whole issue has become very, very polarized," she said. "Top authorities have committed themselves to a policy on the vaccine and insist there is no problem here. On the other side, people are suffering." While Fisher has been a critic of government policies on vaccines since she co-founded her group in 1982--although she insists she is not "anti-vaccine" and has given vaccines to her own children--others concerned about the hepatitis B vaccine have not been skeptics before.

Baylor College of Medicine molecular biologist Bonnie S. Dunbar, who has worked on vaccine development and autoimmune responses for two decades, has been raising some of the most pointed questions with researchers, at conferences and in the media. She came to her skepticism through experience. As she explains it, her brother Bohn Dunbar, then a healthy, active man of 46, got the hepatitis B vaccine five years ago. Soon

after,
she said, he developed rashes on his face and became deeply fatigued. "Basically, he never gets out of bed now," Bonnie Dunbar said. "He has gone to more than a dozen doctors, and they have told him they believe he had a reaction to the vaccine." After a
medical student in her lab also had a severe reaction, Dunbar began research on the vaccine.

What she found, she said, was that many people were complaining of apparently adverse reactions to the vaccine and that people of European descent seemed to be most likely to respond poorly to the vaccine. She said she grew increasingly concerned after learning that the vaccine's manufacturer, Merck & Co., had not tested for adverse reactions beyond five days. Merck spokeswoman Isabelle Claxton disagreed sharply with Dunbar's
conclusion and said Merck was constantly studying the safety and efficacy of its vaccines. She said Merck is sponsoring a "significant," long-term Harvard University study of nurses who have been required to take the hepatitis B vaccine. She said
results of the study are expected this summer.

According to Gina Mootrey, a medical epidemiologist with the CDC's National Immunization Program, there are several additional studies either planned or underway into reactions to the hepatitis B vaccine. Some of those studies, she said, will be looking at its long-term effects. "I don't think there is the evidence out there now that would make us change any of our policies," said Mootry. "At this point in time, we still believe the vaccine to be extremely safe." Critics of the vaccine point to the "adverse event" reports that have come in to the Vaccine Adverse Event Reporting System (VAERS) operated by the Food and Drug Administration. The reporting system was established in 1986 as part of the Vaccine Injury Act, which redirected all vaccine claims from the civil courts to the US Court of Claims.

According to the National Vaccine Information Center, between 1990 and 1998 the system received 24,775 reports of adverse reactions to inoculations that included the hepatitis B vaccine. More than two-thirds of the reports, the center said, were from patients who had received only the hepatitis B vaccine. Mootrey agreed that the number of VAERS reports "is fairly sizable," but said the large volume was predictable because more than 40 million people (an estimate based on the number of doses distributed) have been
vaccinated since the campaign began in the early 1990s.

CDC officials say that because the reporting system takes in unconfirmed information and often takes in many reports about the same person, it provides little more than a first
alert that something may be wrong with a vaccine. But CDC officials say a follow-up survey of VAERS reports regarding infants who received the vaccine from 1991 to 1994 concluded that there were "no unexpected events." In a recent press release, the CDC
wrote that "VAERS data can easily be misinterpreted or mis-analyzed. Because the VAERS data is available to the general public, this unfortunately is not uncommon."

****

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****
We Must Have The Freedom To Choose & Respect Everyone's Choice
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Any information obtained here is not to be construed as medical
OR legal advice. The decision to vaccinate and how you
implement that decision is yours and yours alone.
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for leo.ilban.ernet.in!ADMIN
Received: from ozemail.com.au (uucp@localhost) by ilban.ernet.in (8.7.5/8.7.3) with UUCP id N
Received: from mail-relay-blr.ernet.in (mail-relay-blr.ernet.in [202.141.1.18])
by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA24073
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Received: from avn (s1lis1p07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: HEP B TREATMENT AVAILABLE
Date: Sun, 4 Apr 1999 16:58:26 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKAEGNEMAA.shotinfo@ozemail.com.au>
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charset="iso-8859-1"
Content-Transfer-Encoding: 7bit
X-Priority: 3 (Normal)
X-MSMail-Priority: Normal
X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal

-----Original Message-----
From: karin schumacher [mailto:via@access1.net]
Sent: Wednesday, 2 December 1998 5:35
To: via
Subject: HEP B TREATMENT AVAILABLE

IF THERE IS A CURE FOR HEP B, WHY THE NEED FOR THE VACCINE?

Canadian discovery for the treatment of Chronic Hepatitis B is approved
in Canada... offers real hope to thousands of infected Canadians
Hundreds of millions of people infected worldwide

December 1, 1998
Glaxo Wellcome Inc. and BioChem Pharma Inc. announced today that
Heptovir(TM) (lamivudine), the first oral anti-viral medication for the
treatment of chronic hepatitis B, was approved by the Therapeutic
Products Program of Health Canada. Experts believe that Heptovir is set
to revolutionize the treatment of hepatitis B for millions of people
infected with the virus around the world.

Heptovir is a very significant development in the management of

hepatitis B infection,'' said Dr. Michael Levy, Senior Vice President, Research and Development and Chief Medical Officer at Glaxo Wellcome Inc. ``What's exciting about Heptovir is that unlike the current therapy, we now have a well tolerated and easy-to-use treatment most people
infected with chronic hepatitis B can benefit from.

Heptovir, taken as a once-a-day tablet, slows and can actually halt the progression of liver disease,'' said Dr. Sam Lee, President of the Canadian Association for the Study of the Liver and Associate Professor of Medicine at the University of Calgary. Heptovir is a very potent inhibitor of hepatitis B viral replication and has been shown to decrease the amount of virus to undetectable levels in up to 98 per cent of patients while on treatment(1). In the longer term, we hope that Heptovir will prevent progression to cirrhosis or liver cancer.

It is estimated that 250,000 Canadians are chronically infected with hepatitis B(2). Chronic hepatitis B infection can cause serious liver disease (cirrhosis) and can lead to liver failure, liver cancer and death. Worldwide, forty per cent of men and 15 per cent of women who become infected with hepatitis B in early childhood will die prematurely from hepatitis B complications.

We are proud that this Canadian discovery has the potential to positively impact this very significant medical need,'' said Dr. Gervais Dionne, Executive Vice President, Research and Development, BioChem Pharma. ``The only previously available therapy works in a minority of chronic hepatitis B patients. Heptovir, on the other hand, is effective in treating most patients and thus provides a new possibility for treating their
infection.

Heptovir helps control disease progression by allowing many patients to seroconvert, which means the virus stops replicating and immunity is achieved,'' said Dr. Lorne Tyrrell, an infectious disease specialist and professor of medicine at the University of Alberta who first showed lamivudine to be active against hepatitis B. ``Patients taking Heptovir have the added benefit of improvements in liver disease, regardless of whether
they develop immunity to the virus.'' Dr. Tyrrell screened lamivudine for use in hepatitis B at a lab in the Glaxo Heritage Research Institute located at the University of Alberta.

One of the first patients in the world to receive Heptovir was a patient of Dr. Tyrrell's. ``If it wasn't for Heptovir, I would not have even been a candidate for a liver transplant and there is a good chance that I wouldn't be here today,'' said Kit Li, who received Heptovir before and after his liver transplant in 1994. ``I'm happy to say that my new liver is still virus free and I have a normal life again.''

Lamivudine was discovered by BioChem Pharma and was developed throughout the world by Glaxo Wellcome Inc. Canada is one of the first countries in the world to approve Heptovir. ``Heptovir is a great Canadian success story that will help many of the more than 300 million people who are chronically infected with the hepatitis B virus worldwide,'' added Dr. Dionne.

According to the World Health Organization, hepatitis B is one of the most common infectious diseases in the world and the ninth most common cause of death. An estimated one to two million people per year, or as many as 4,500 people every day, die from hepatitis B-related complications. Under the terms of the BioChem-Glaxo Wellcome license agreement, BioChem will receive a royalty based on sales and Glaxo
Wellcome has the right to develop, manufacture and sell Heptovir

worldwide. An equally owned partnership will commercialize Heptovir in Canada.

Glaxo Wellcome Inc. is committed to improving the lives of Canadians by fighting disease. Based in Mississauga, Ontario, the company employs nearly 1,400 people. Glaxo Wellcome is one of the top 20 investors in Canadian research and development and one of the top 10 corporate donors in Canada. As a result of Glaxo Wellcome's investment, $770,000 annually, to the Glaxo Heritage Research Institute at the University of Alberta, Canadian researchers at the Institute played a key role in the development of Heptovir. Glaxo Wellcome is part of U.K. based Glaxo Wellcome plc.

BioChem Pharma Inc. is an international biopharmaceutical company dedicated to the research, development and commercialization of innovative products for the detection, prevention and treatment of human diseases. The company's shares are traded on the Montreal and Toronto Stock Exchanges (BCH) and on NASDAQ National Market (BCHE).

Lamivudine, the generic name for Heptovir, is currently indicated for the treatment of chronic hepatitis B in New Zealand and the Philippines. More than 30 regulatory product submissions have been filed worldwide and the product received a unanimous recommendation for approval from the Food and Drug Administration in the United States.

Heptovir(TM) is a trade-mark of Glaxo Group Limited, Glaxo Wellcome Inc., licensed use to Glaxo Wellcome BioChem. B-Roll available by satellite at 11:00 a.m. and 3:00 p.m. EST at ANIK E 2 C Band, transponder 2 B, audio 6.2 and 6.8.

Notes to Editors

- The liver is the largest and one of the most important internal organs in the body. It cleans the blood of toxic chemicals, produces important proteins for the blood, and regulates nutrients. Along with the kidneys, the liver clears the blood of drugs and poisonous substances that would otherwise accumulate in the bloodstream.

- Hepatitis B infection can lead to a gradual destruction of a person's liver. Experts believe that the damage caused by hepatitis B infection results from the body's own immune response to the presence of hepatitis B virus in the liver. Chronic hepatitis B infection leads to cirrhosis of the liver or long-term liver damage possibly leading to liver failure, liver cancer and death.

- Until now, there has been little or no effective treatment for people of Asian and Aboriginal decent, people who acquired their infection in childhood and patients harbouring a variant strain of the hepatitis B virus known as pre-core mutant. Heptovir is the first effective treatment for these patient populations.

REFERENCES

(1) Product Monograph of Heptovir(TM) (lamivudine), Glaxo Wellcome Inc. Nov. 1998.

(2) Management of Viral Hepatitis: Clinical and Public Health Perspectives - A Consensus Statement. Canadian Journal of Gastroenterology 1997; 11(5): 407-416.

SOURCE Glaxo Wellcome Inc.

CONTACT: Christine Lennon/MichleRoy, BioChem Pharma Inc., Ph: (450)978-7771/ (BCH. BCHE)

****

Karin Schumacher

Vaccine Information & Awareness (VIA)

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619-484-3197 (phone/voicemail)
619-484-1187 (fax)
via@access1.net (email)
http://www.909shot.com (NVIC website)
http://www.access1.net/via (VIA website)
****
We Must Have The Freedom To Choose & Respect Everyone's Choice
****
Any information obtained here is not to be construed as medical
OR legal advice. The decision to vaccinate and how you
implement that decision is yours and yours alone.
****

>From shotinfo@ozemail.com.au Sun Apr 4 13:31:13 1999
Received: from Waffle on leo by WafPeg 0.25, 93.04.04
for ADMIN on standalone PMail ; Mon, 5 Apr 1999 08:56:46 IST+5.30
Received: by leo (1.65/waf)
via UUCP; Mon, 05 Apr 99 08:56:41 IST
for leo.ilban.ernet.in!ADMIN
Received: from ozemail.com.au (uucp@localhost) by ilban.ernet.in (8.7.5/8.7.3) with UUCP id N
Received: from mail-relay-blr.ernet.in (mail-relay-blr.ernet.in [202.141.1.18])
by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA24039
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by mail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA02121
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Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: HEPATITIS B VACCINE: FRONT PAGE COVERAGE
Date: Sun, 4 Apr 1999 16:58:30 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKCEGNEMAA.shotinfo@ozemail.com.au>
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Content-Type: text/plain;
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X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal

-----Original Message-----
From: karin schumacher [mailto:via@access1.net]
Sent: Tuesday, 1 December 1998 6:06
To: via
Subject: HEPATITIS B VACCINE: FRONT PAGE COVERAGE

Dawn Richardson <prove@swbell.net> wrote:

DEAR PROVE MEMBERS,
FRONT PAGE COVERAGE! AFTER FRANCE WITHDREW HEP B VACCINE FOR TEENS, WE STARTED SENDING INFO TO DIFFERENT REPORTERS AND KEPT IN CONTACT WITH THEM. WE PROVIDED CONTACTS TO BE INTERVIEWED AND OTHER FACTS, AND HERE IS ONE ARTICLE THAT CAME OUT OF THESE EFFORTS - IT WAS PUBLISHED TODAY. IF YOU WANT TO THANK ANDREW FOR THE TIME HE SPENT ON THIS IMPORTANT STORY, HIS EMAIL IS apark@statesman.com IF YOU WANT TO WRITE A LETTER TO THE EDITOR OF THE AUSTIN AMERICAN STATESMAN THANKING THEM OR ADDING ANY

Dunbar also believes in universal immunizations and has worked for two decades developing vaccines to protect public health. But since watching two people suffer neurological failures after taking the hepatitis B vaccine, she has spoken out against its further use.

The vaccine, developed by drug companies Merck and Co. and SmithKline Beecham, was the first recombinant DNA vaccine put on the market in the United States. Unlike conventional vaccines for measles, mumps and polio, the genetically engineered hepatitis B shot does not contain a live form of the virus. Theoretically, the shot won't give you hepatitis B, as sometimes happens with vaccines that contain a live virus. But Dunbar is convinced that in some people, a protein in the recombinant mixture triggers an autoimmune reaction, provoking the body to attack its own nerves and tissue. She has cataloged more than 100 cases of autoimmune disorders found by other scientists, but she can recall two other cases from memory: her brother, whose rashes, joint pain and chronic fatigue have been determined to be side effects of the hepatitis B vaccine; and one of her students, who suffered temporary blindness in one eye and deteriorating eyesight in the other after taking the shot. The CDC and both drug companies acknowledge hearing of similar cases, but they call them extremely rare.

Dunbar worries that newborns who are given the vaccine are even more vulnerable to that risk because of their less formidable defenses. Under Merck guidelines, newborns and teen-agers receive the same dose of the vaccine. "We know from our animal lab experiments that the immune system of the neonate is very different from the adult," Dunbar said. "It has to be studied." The CDC says it's looking into the effects of the vaccine and will have results to report next year. Drug companies are also trying to determine how long the immune response to the vaccine lasts before booster shots are
needed. That has yet to be established.

In the meantime, a growing number of Texas parents are resisting the state's effort.
Some physicians worried about the effect on infants advise expectant mothers to decline the hepatitis B vaccine when they arrive at the hospital to give birth. Other physicians sign one-year medical exemptions that allow children of concerned parents to enter school without the shots. Many parents opt to apply for an exemption that allows a permanent out for children whose families believe in the anti-vaccine tenets of certain
religions. Others have joined a Cedar Park group, Parents Requesting Open Vaccine Education, that has lobbied the Legislature and the state Health Department for more information about the hepatitis B vaccine before its use is expanded. Still, pushing against the vaccine's momentum is not easy. "I just felt such pressure," said Terri McDermott, an Austin mother who refused to have her son vaccinated for hepatitis B when he was born in June. "I think had I not said, 'I'm following up with my own doctor,' if I didn't basically have some excuse, then I would have been pressured into doing it."

> *Dawn Richardson*
> *PROVE(Parents Requesting Open Vaccine Education)*
> *P.O. Box 1071*
> *Cedar Park, TX 78630-1071*
> *(512) 918-8760*
> *prove@swbell.net (email)*
> *http://home.swbell.net/prove (web site)*
> ---
>
> *PROVE provides information on vaccines, and*
> *immunization policies and practices that affect the*

ADDITIONAL COMMENTS, IT CAN BE DONE AT letters@statesman.com.

http://www.austin360.com/news/002state/11nov/30/30vaccines.htm

Hepatitis vaccine safety questioned
Some parents resist required B virus shot for infants, but health officials say risk slight
By Andrew Park
American-Statesman Staff
Published: Nov. 30, 1998

The statistics say Pamela Daviscourt is crazy to worry about the hepatitis B shot the State of Texas wants to give her 20-month-old son. Only about 22,000 of the 20 million people in the United States vaccinated against the virus have reported bad reactions to it, and no one knows whether those reactions were even caused by the shots. But Daviscourt doesn't think she's crazy to hold off. Infants have little chance of catching the virus except from their mothers, and she doesn't have hepatitis B.

Still, why not give the boy the vaccine, which he'll eventually need to enter public school here? The issue, she said, is safety. She said she fears the vaccine carries more risks than benefits. "My approach has been to feed my child as nutritionally as possible and keep his immune system up," said Daviscourt, who recently moved to Austin from Washington state. "I just believe if his immune system is strong, he is going to be resistant to anything out there." Unlike some opponents of immunization programs, Daviscourt harbors no religious or political objection to vaccinating her child, just concern about recent reports of bad reactions to the hepatitis B vaccine. A small number of people have developed arthritis, chronic fatigue, symptoms of multiple sclerosis and other conditions after taking the shot. Similar reports in France brought that country's hepatitis B immunization program to a halt last month.

In Texas, the state Health Department receives at least 50 to 60 reports each year from people who have suffered health problems after being immunized for hepatitis B, ranging in seriousness from headaches to deaths. Officials say they have no way of knowing whether those reactions were caused by, or even related to, the vaccine. "Though no vaccine is risk-free, the hepatitis B is one of the safest," said Sharon Duncan, hepatitis coordinator at the Texas Department of Health. "The benefits outweigh the risk. We do believe that it is safe."

The department recommends that all newborns and children up to the age of 12 be vaccinated against hepatitis B, which can lead to chronic liver diseases, including cancer. This year, all children entering public school in Texas had to be immunized against hepatitis B, and the shots were offered to seventh-graders in Austin public schools this month. The effort did not come about because hepatitis B poses great risks to children. The virus is primarily transmitted among adults who have unprotected sex, share drug needles or are exposed to contaminated blood. There is also evidence that it can be passed through saliva and tears and from a mother to a child in the womb. Locally, only a few cases of hepatitis B in children are reported each year.

Still, immunizing all infants is widely considered the only way to protect against an outbreak of the disease. Health departments complain that they cannot get teen-agers and adults to be vaccinated once they have begun risky behavior or other exposure to the virus. Better to immunize them while they're young and receiving other vaccines, the logic goes, and it's an argument supported by the American Academy of Pediatrics, the Centers for Disease Control and Prevention and the World Health Organization. Baylor College of Medicine immunologist Bonnie

> *children and adults of Texas. Our mission is to prevent*
> *vaccine injury and death and to promote and protect*
> *the right of every person to make informed independent*
> *vaccination decisions for themselves and their families.*
> ---
>
> *This information is not to be construed as medical*
> *OR legal advice. The decision to vaccinate and how*
> *you implement that decision is yours and yours alone.*
> ---
>
> *To subscribe to this list, send a note to prove@swbell.net*
> *with the word "subscribe" in the subject line.*

****
Karin Schumacher
Vaccine Information & Awareness (VIA)
12799 La Tortola
San Diego, CA 92129
619-484-3197 (phone/voicemail)
619-484-1167 (fax)
via@access1.net (email)
http://www.909shot.com (NVIC website)
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****
We Must Have The Freedom To Choose & Respect Everyone's Choice
****
Any information obtained here is not to be construed as medical
OR legal advice. The decision to vaccinate and how you
implement that decision is yours and yours alone.
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>From shotinfo@ozemail.com.au Sun Apr 4 13:31:13 1999
Received: from Waffle on leo by WafPeg 0.25, 93.04.04
for ADMIN on standalone PMail ; Mon, 5 Apr 1999 08:56:46 IST+5.30
Received: by leo (1.65/waf)
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for leo.ilban.ernet.in!ADMIN
Received: from ozemail.com.au (uucp@localhost) by ilban.ernet.in (8.7.5/8.7.3) with UUCP id N
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Received: from avn (s1lis1p07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: HEPATITIS B VACCINE AND DIABETES
Date: Sun, 4 Apr 1999 16:58:36 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKGEGNEMAA.shotinfo@ozemail.com.au>
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[illegible] MimeOLE V4.72.3155.0
Importance: Normal

-----Original Message-----
From: karin schumacher [mailto:via@access1.net]
Sent: Sunday, 13 September 1998 2:28

To: via
Subject: HEPATITIS B VACCINE AND DIABETES

Croft Woodruff <croft@cwhealth.com> wrote:

There is more to the "A-B-C of hepatitis" than what public health officials and the media are telling parents when scare tactics are used to motivate them into having their babies receive the hepatitis B shot (the Province, Sept. 10/98).

Epidemiological studies carried out in New Zealand by J. Barthelow Classen, MD, of Classen Immunotherapies Inc., Baltimore, Maryland, at the request of New Zealand authorities (New Zealand Medical Journal, May 24, 1996) found a 65 percent increase in the incidence of insulin dependent diabetes among juveniles who had received the hep B vaccination. Dr. Classen, formerly with the United States National Institutes of Health, is a strong supporter for the use of vaccines in preventing disease. His findings have since been published in a peer reviewed journal and confirmed by studies carried out elsewhere. It seems that certain proteins in the vaccine may initiate an auto-immune response in susceptible children that attacks and destroys the insulin producing cells in their pancreas. There is other evidence surfacing that other auto-immune diseases (such as lupus) may be triggered by the vaccine.

According to Health Canada there have been no reported children deaths from hepatitis B under the age of 15 in the last ten years. In 1996 there were 61 cases reported in this age group. These victims were either born to mothers who were infected or members of Asian communities where the disease is highly endemic. In light of the evidence, it is highly irresponsible for health authorities to suggest hepatitis B is such a wide spread health threat that justifies vaccinating thousands of babies not at risk for hepatitis B when the alarm has been sounded by a respected researcher that this vaccine has the
potential to place many of those infants at risk of becoming insulin dependent diabetics. The failure to warn parents that these vaccines put their babies at serious risk calls in to question the competence of these health bureaucrats.

The United States Congress instituted a taxpayer funded vaccine damage compensation program in 1986 when the vaccine manufacturers threatened to stop production because they could no longer afford liability costs and costly court awards. To date over $944,000,000 from this fund has been paid out.

If these vaccines are so safe, why is it that manufacturers of the vaccines cannot get liability insurance for their product?

Croft Woodruff,
6262 A Fraser Street
Vancouver BC V5W 3A1
324 2121

>From Pediatric News
Rise in Type 1 Diabetes Blamed on Late Vaccination
By: Miriam E. Tucker, Senior Writer
[Pediatric News 32(4):4, 1998. © 1998 International Medical News Group.]

The incidence of type 1 diabetes is rising dramatically in American and European children. There are many theories about why this is happening, but one in particular is receiving a lot of media attention lately--that the increase may be linked with the timing of childhood immunizations.

Experts agree that current data don't support that theory, although the possibility is being studied. In Allegheny County, Pa., which has the oldest type 1 diabetes registry in the United States, the incidence of the disease was at a stable 12 cases per 100,000 population aged 0-19 years from 1965 until the mid-1980s. Around 1985 the rate increased to about 18-19 per 100,000. Since 1994 it appears to have risen even more, according to Ronald LaPorte, Ph.D., who oversees the registry.

Especially worrisome is the "extraordinary" increase among African Americans, who in the past have had lower rates of type 1 diabetes than whites. During the 1970s and 1980s, about 7-8 per 100,000 blacks aged 0-19 years developed type 1 diabetes. In the mid-1980s, that incidence rose to 11 per 100,000. Now for the first time, the incidence among African Americans--males in particular--is slightly higher than for whites. But type 1 diabetes is rising among whites, too, Dr. LaPorte, professor of epidemiology at the University of Pittsburgh, told this newspaper. Other U.S. registries have been in existence for less than 15 years, but the same trend seems to be occurring nationwide.

Long-term European data show the same thing: In Finland, for example, which has the world's highest rate of type 1 diabetes, the incidence rose from 12 per 100,000 children aged 0-15 in 1953 to 38 in 1986, and to 45 in 1996. Throughout Europe the incidence of type 1 diabetes is rising about 2%-3% per year, while the United States is "probably a little higher," Dr. LaPorte noted. One "hot" theory among researchers to explain the increase is that the autoimmune destruction of pancreatic islet cells may be triggered by a "superantigen," possibly arising from a viral infection, a food, or a toxin. Some data support a link between type 1 diabetes and cow's milk. "We know it has to be something in the environment, since the gene pool can't change that rapidly," Dr. LaPorte said.

The media, however, has latched onto the theory of immunologist J. Barthelow Classen. He believes the immunization schedule, which begins immunizations at 2 months of age, is exacerbating the risk for type 1 diabetes and other autoimmune diseases. Giving these immunizations at birth could reduce the risk, he told this newspaper. He is president of Classen Immunotherapies Inc., a Baltimore company that is developing "immunization methods" and "methods of testing immunization schedules" to minimize the risk for development of type 1 diabetes. According to Dr. Classen, maternal viruses are passed on to the infant at birth and take hold within the first 6 weeks of life. Giving vaccines during this period would trigger the release of interferon, which would block the viral infections. When vaccines are given at 2 months of age, they exacerbate the virus-induced inflammation that is already occurring in the pancreatic islet cells. This is particularly true of the vaccines that contain killed components such as Haemophilus influenzae b (Hib), which activate macrophages, he said.

In type 1 diabetes-prone mice, Dr. Classen found that giving low doses of killed human vaccines at birth completely prevented the development of diabetes, while immunizing at 8 weeks either increased the risk or did not change it. He also cites human epidemiologic data to support his theory: In various parts of the US and Europe, the institution of new vaccines has been followed by a rise in type 1 diabetes incidence. For instance, the diabetes increases in both Pittsburgh and Finland followed the introduction of the Hib conjugate vaccine, according to Dr. Classen. (The Hib vaccine was licensed in the United States in 1987).

Immunization expert Dr. Michael Katz said Dr. Classen's theory "is not yet supported by data. "What worries me is that this will create anxiety about immunizations. At this moment there is no basis for revising the immunization schedule," said Dr. Katz, who has served on two Institute

of Medicine vaccine safety committees and is the Carpentier Professor of Pediatrics Emeritus at Columbia University in New York. Dr. LaPorte went a step further: "I think [Dr. Classen] is completely wrong." The increase in immunizations in the early 1960s did not affect diabetes incidence, and countries with good immunization coverage, like Japan and China, have not seen a rise in diabetes.

Everyone--even Dr. Classen--says more data are needed before anyone considers manipulating the immunization schedule. The National Institute of Allergy and Infectious Diseases began a study in collaboration with British public health officials to gather all the data relating to the topic. They will hold a meeting to look at the findings later this year. At least three other conferences looking at the relationship between infectious diseases and autoimmunity are planned. The Centers for Disease Control and Prevention is also studying the relationship in an already-established database population of more than 500,000 children in [illegible] HMOs. The agency will look at type 1 diabetes rates in children who received the Hib B vaccine at birth and those whose first dose was given at 2 months, and it also will look at diabetes rates after use of the Hib vaccine began.

Vaccine 1998 Feb;16(4):329-334

Major adverse reactions to yeast-derived hepatitis B vaccines--a review. Grotto I, Mandel Y, Ephros M, Ashkenazi I, Shemer J Israel Defense Force, Medical Corps, Israel.

Yeast-derived recombinant DNA hepatitis B vaccines usage became widely accepted since the early 1990s. Severe adverse events have been reported infrequently in adults and rarely in infants and children given hepatitis B vaccine in the ten years which have passed since the introduction of the vaccine. Some of the data were summarized in previous review articles. Our review of the literature revealed reports of serious adverse reactions which included immediate reactions (anaphylaxis and urticaria) as well as delayed reactions, including skin, rheumatic, vasculitic (including Systemic Lupus Erythematosus and glumerulonephritis), hematologic, ophthalmologic and neurologic reactions. These cases were summarized and a pathogenetic mechanism is offered.

PMID: 9607051, UI: 98269934

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12799 La Tortola
San Diego, CA 92129
619-484-3197 (phone/voicemail)
619-484-1187 (fax)
via@access1.net (email)
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****
We Must Have The Freedom To Choose & Respect Everyone's Choice
****
Any information obtained here is not to be construed as medical
OR legal advice. The decision to vaccinate and how you
implement that decision is yours and yours alone.
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>From shotinfo@ozemail.com.au Sun Apr 4 13:31:13 1999
Received: from Waffle on leo by WafPeg 0.25, 93.04.04
for ADMIN on standalone PMail ; Mon, 5 Apr 1999 08:56:46 IST+5.30
Received: by leo (1.65/waf)

via UUCP; Mon, 05 Apr 99 08:56:41 IST
for leo.ilban.ernet.in!ADMIN
Received: from ozemail.com.au (uucp@localhost) by ilban.ernet.in (8.7.5/8.7.3) with UUCP id N
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by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA24005
for <ADMIN@leo.ilban.ernet.in>; Sun, 4 Apr 1999 12:31:31 +0530
Received: from avn (s1lis1p07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: WHO AND THE FRENCH SUSPENSION OF HEP B VACCINE
Date: Sun, 4 Apr 1999 16:58:20 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKOEGMEMAA.shotinfo@ozemail.com.au>
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X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal

-----Original Message-----
From: karin schumacher [mailto:via@access1.net]
Sent: Sunday, 6 December 1998 2:56
To: via
Subject: WHO AND THE FRENCH SUSPENSION OF HEP B VACCINE

Todd Gastaldo <gastaldo@teleport.com> wrote:

World Health Organization:
CDC is spreading WHO's fraudulent claim that cancer prevention is a "demonstrated benefit" of hepatitis B vaccination. CDC Vaccination Czar Walter Orenstein, MD may be reached at wao1@cdc.gov.

WHO, please correct your information - and please ask Dr. Orenstein to make a note on the CDC web page that the WHO information has been corrected.

Thank you.

Todd D. Gastaldo, D.C.

(Copied to the e-mail addresses at the end of this post. I found them via Ron Slaughter's National Association for Chiropractic Medicine link to Julie Powell, DC, DABCN's web page (pediatrics)....)

From: Todd Gastaldo <gastaldo@gte.net>
To: Orenstein, Walt <wao1@cdc.gov>
Cc: Donald M. Petersen, Jr. <Don@DCMedia.com>; Dr. Terry Rondberg <worldall@ix.netcom.com>; ncehinfo@cdc.gov <ncehinfo@cdc.gov>; martine.aubry.ttt@wanadoo.fr <martine.aubry.ttt@wanadoo.fr>; Chiro List <chiro-list@silcom.com>; webmaster@sante.gouv.fr <webmaster@sante.gouv.fr>; schlafly@cruzio.com <schlafly@cruzio.com>; tetra@tetrahedron.org <tetra@tetrahedron.org>

Date: Tuesday, October 27, 1998 11:15 PM
Subject: Hep B vaccine might cause MS? English translation please...

Walter Orenstein, MD
Director
National Immunization Program
Centers for Disease Control

Dr. Orenstein,

This is a request for an English translation of the French government's October 1998 decision to suspend routine Hepatitis B vaccination of adolescents due to the possibility that Hepatitis B vaccine causes Multiple Sclerosis.

Dr. Orenstein, your website carries an October 2, 1998 press release from WHO titled,
NO SCIENTIFIC JUSTIFICATION TO SUSPEND HEPATITIS B IMMUNIZATION

According to WHO:
"On 1 October 1998, the French Ministry of Health announced a decision to suspend routine HB immunization of adolescents in French schools, while continuing the immunization of infants and high risk adults..."

In a separate article, WHO reports:
"A number of anecdotal reports have linked the administration of hepatitis B vaccine with the onset of multiple sclerosis (MS)...
http://www.who.int/gpv-safety/Diseases/hepatitis b vaccine and multiple.htm

But WHO doesn't think there is any real cause for the French government's action; and accordingly, WHO recommends continued Hepatitis B vaccination of adolescents, "based on demonstrated important benefits - including the prevention of cirrhosis and cancer..."
http://www.who.int/gpv-safety/Diseases/hepatitis b vaccine and multiple.htm

When did prevention of CANCER become a "demonstrated important benefit" of hepatitis B vaccination?? The lastest information I've found (see below), indicates that cancer prevention has NOT been demonstrated...

A little relevant history is in order...
As hundreds of millions of Third World children were being injected with hepatitis B vaccine, most of the world's physicians were refusing hepatitis B vaccine injections - for fear of catching AIDS.

...[O]ver the next 5 to 10 years...[Third World countries] will need 350 million doses a year...By the year 2000 we will have accomplished our task if we see hepatitis B incorporated as the seventh universal immunogen for infant immunization in the Expanded Program on Immunization that is sponsored by the World Health Organization." [James E. Maynard, M.D., executive director of a nine physician international task force run by the Seattle-based Program for Appropriate Technology and Health (PATH), discussing the hepatitis B vaccine produced by Alfred M. Prince, M.D. of the New York Blood Center. In Marwick C: JAMA, Sept.18, 1987;258(1):1439]

Dr. AM Prince, developer of the hepatitis B vaccine, wrote in 1991:
[M]any high-risk individuals...do not wish to be vaccinated. This applies surprisingly to about 50% of physicians and nurses in many countries, who despite all assurances remain unconvinced that HBV vaccine will not transmit unknown agents of disease." [Prince AM: Hepatitis B virus: active and passive immunization. In Cryz SJ (ed.): Vaccines and immunotherapy, 1991, New York: Pergamon Press.]

In one study MDs refused hepatitis B vaccination - even when it was offered free of charge: "...the majority of physicians...failed to be vaccinated even when offered
the hepatitis B vaccine free of charge." [Clancy CM, Cebul RD, Williams

SV. Guiding individual decisions: a randomized controlled trial of decision analysis. Am J Med, 1988;84(2):283-8]

Even stranger than doctors not taking their own hepatitis B vaccine is the fact that Hepatitis B vaccine researchers discovered early on that nearly all the African children on whom they were experimenting, were testing positive for hepatitis B virus [The Lancet, May12, 1989, p. 1057-60] - but were almost never expressing symptoms of the disease called hepatitis. [Cancer Res, 1987;47:5782-87]

And now a 1998 press release reports, in effect, that these same Hepatitis B vaccine researchers are indicating that unvaccinated infants WERE suffering from acute hepatitis - from infancy up to the age of ten years:

"The Gambia Hepatitis Intervention Study has clearly demonstrated that protection against persistent hepatitis B infection by infant vaccination continues up to the age of ten years. The study of this protection against...against acute hepatitis...should be continued into the adolescent years when new modes of exposure to the virus will occur."
http://www.iarc.fr/preleases/121e.htm

Whatever the case with acute hepatitis, the 1998 press release to which I am referring was titled, "Recommendations for the control of hepatitis B-related CANCER" [emphasis added] - but upon reading the press release, one finds that the Gambian study is being conducted because researchers DON'T KNOW whether Hep B vaccine prevents cancer...

According to the press release:
"GHIS should ensure that cancer registration in The Gambia and linkage of individuals with liver cancer to vaccine records is made as effective as possible, in order for the study to fulfill its *ORIGINAL AIM* of measuring vaccine efficacy against liver cancer." [emphasis added]
http://www.iarc.fr/preleases/121e.htm

Dr. Orenstein, most of the world public is unaware that millions billions?) are being spent to innoculate children to MAYBE prevent the adult cancer called hepatocellular carcinoma - as 50% of African children in some areas starve to death. [50% mortality rate is from Sachs MY and Martin AS (Eds.): Worldmark Encyclopedia of the Nations, Volume 2: Africa, 7th ed., 1988, New York: Worldmark Press, Ltd., John Wiley & Sons, Inc.]

Interesting side note: I am truly surprised that the 1998 press release about The Gambian experiment (see above) did not explicitly mention the woodchuck studies and the epidemiologic studies being used to claim that Hep B vaccine prevents cancer. Also interesting is Duesberg and Schwartz's 1992 claim that "there is no convincing evidence that hepatitis B viral DNA is functionally relevant for the initiation and maintenance of hepatomas." [Duesberg PH and Schwartz JR: Latent viruses and mutated oncogenes: no
evidence for pathogenicity. Progress in Nucleic Acid Research and Molecular Biology, 1992;43:135-204]

Back to the matter at hand...
Dr. Orenstein, your CDC web site contains ENGLISH-language press releases and articles that in effect pejorize the recent French action as unscientific and unnecessary. You link to French government health minister Bernard Kouchner, MD's "Point sur la vaccination contre l'Hépatite B jeudi 1er octobre 1998" - without any translation into English.
http://www.cdc.gov/nip/vacsafe/vaccinesafety/Hot%20Topics/hepb.htm

MS is a serious disease, Dr. Orenstein. *Any* evidence - even anecdotal - that Hepatitis B vaccine causes MS should be available in English. Americans should be FULLY informed. I certainly do not take lightly vaccination decisions of the country (France) that produced Prof. Claude Bernard, the father of experimental medicine...

Could you please have someone at CDC IMMEDIATELY translate the French government's explanation into English? Will you notify me when this is done? It is a long shot, but, in addition to copying the e-mail address of the webmaster@sante.gouv.fr , I have copied martine.aubry.ttt@wanadoo.fr . Hopefully, this latter e-mail address is the e-mail address of Madame Martine Aubry, Ministre de l'Emploi et de la Solidarité. If I have reached Madame Aubry, hopefully she will forward this e-mail to the above mentioned Bernard Kouchner, MD, Secrétaire d'Etat à la Santé. I would like Dr. Kouchner to know that at least one U.S. citizen is interested in reading his side of the story - in English... (My apologies to martine.aubry.ttt@wanadoo.fr if I have not reached the Ministre de l'Emploi et de la Solidarité.)

Thank you for replying Dr. Orenstein - and thanks also to nceninfo@cdc.gov for forwarding my e-mail to you...

I look forward to hearing back from you regarding the English translation requested above...

Todd D. Gastaldo, D.C.
P.S. Before you replied with your e-mail address, I found some other e-mail addresses of CDC employees. I will blind copy them. Perhaps one or more of them are fluent in French and can assist you in translating the words of Bernard Kouchner, MD, Secrétaire d'Etat à la Santé.

From: Orenstein, Walt <wao1@cdc.gov>
To: 'Gastaldo, Todd' <gastaldo@gte.net>
Date: Tuesday, October 27, 1998 12:55 PM
Subject: Your email request

Mr. Gastaldo,
Your email was forwarded to us, stating that you were looking for the email address of the Director of the National Immunization Program. You can reach me at:

Walter A. Orenstein, M.D.
wao1@cdc.gov

****

Karin Schumacher
Vaccine Information & Awareness (VIA)
12799 La Tortola
San Diego, CA 92129
619-484-3197 (phone/voicemail)
619-484-1187 (fax)
via@access1.net (email)
http://www.909shot.com (NVIC website)
http://www.access1.net/via (VIA website)

****
We Must Have The Freedom To Choose & Respect Everyone's Choice
****
Any information obtained here is not to be construed as medical OR legal advice. The decision to vaccinate and how you implement that decision is yours and yours alone.
****

>From shotinfo@ozemail.com.au Sun Apr 4 13:31:11 1999

Meeting on Hep B

Received: from Waffle on leo by WafPeg 0.25, 93.04.04
for ADMIN on standalone PMail ; Mon, 5 Apr 1999 08:56:46 IST+5.30
Received: by leo (1.65/waf)
via UUCP; Mon, 05 Apr 99 08:56:39 IST
for leo.ilban.ernet.in!ADMIN
Received: from ozemail.com.au (uucp@localhost) by ilban.ernet.in (8.7.5/8.7.3) with UUCP id N
Received: from fep9.mail.ozemail.net (fep9.mail.ozemail.net [203.2.192.103])
by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA24019
for <ADMIN@leo.ilban.ernet.in>; Sun, 4 Apr 1999 12:31:41 +0530
Received: from avn (sllis1p07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: HEP B VACCINE LINKED TO AUTOIMMUNE RHEUMATOID DISEASES
Date: Sun, 4 Apr 1999 16:58:34 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKEEGNEMAA.shotinfo@ozemail.com.au>
MIME-Version: 1.0
Content-Type: text/plain;
charset="iso-8859-1"
Content-Transfer-Encoding: 7bit
X-Priority: 3 (Normal)
X-MSMail-Priority: Normal
X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal

-----Original Message-----
From: karin schumacher [mailto:via@access1.net]
Sent: Wednesday, 11 November 1998 4:02
To: via
Subject: HEP B VACCINE LINKED TO AUTOIMMUNE RHEUMATOID DISEASES

Classen Immunotherapies: Hepatitis B Vaccine Linked to Autoimmune Rheumatoid Diseases
The following release was issued today from Classen Immunotherapies:

Data from France released at the 62nd Annual Meeting of the American College of Rheumatology, held November 8-12, 1998, in San Diego, California links immunization against hepatitis B to the development of autoimmune rheumatoid diseases such as lupus and rheumatoid arthritis. The rise of autoimmunity following hepatitis B immunization in school children and adults has become a major public health concern. In October, the Ministry of Health in France suspended routine hepatitis B immunization of school children while continuing hepatitis B immunization at birth. The reason for this decision was reportedly the increased risk of autoimmune diseases that has been associated with the vaccine when it is given starting at school age or later.

The data from France links hepatitis B immunization to both the development of newly diagnosed cases of autoimmune rheumatoid diseases as well as the exacerbation of previously diagnosed cases that were in remission. This finding is supported by data from Canada published in September which linked immunization against hepatitis B to the development of autoimmune rheumatoid diseases in firefighters.

John B. Classen, M.D. an immunologist at Classen Immunotherapies published papers linking the immunization against hepatitis B and other diseases to the development of insulin dependent diabetes, an autoimmune disease. Dr. Classen's work found that immunization starting after 2 months of life was associated with an increased risk of autoimmunity compared to starting at birth. Data from a small study published by the

US government appears to support his data and showed that when hepatitis B immunization was given starting after 2 months of life it was associated with an almost doubling of the risk of diabetes.

"The data from humans and animals is very clear, when you stimulate the immune system with vaccines you increase the risk of autoimmunity and exacerbate smoldering inflammatory conditions. Vaccine induced autoimmunity is a major public health problem because of the number of vaccine doses given and the large percentage of people with undiagnosed inflammatory conditions. We need to develop ways of giving vaccines without increasing the risk of autoimmune diseases" states Classen.

"The French decision to continue hepatitis B immunization at birth while discontinuing immunization starting at school age suggests the French Ministry of Health may believe that they can decrease vaccine induced autoimmunity by giving vaccines starting in the first month of life. They appear to be accepting our findings" adds Classen.

Dr. Classen's research has been published in numerous journals and featured in national news reports. For the latest information on the effects of vaccines on insulin dependent diabetes and other autoimmune diseases visit the Vaccine Safety Website (http://vaccines.net).

****
Karin Schumacher
Vaccine Information & Awareness (VIA)
12799 La Tortola
San Diego, CA 92129
619-484-3197 (phone/voicemail)
619-484-1187 (fax)
via@access1.net (email)
http://www.909shot.com (NVIC website)
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OR legal advice. The decision to vaccinate and how you
implement that decision is yours and yours alone.
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for ADMIN on standalone PMail ; Mon, 5 Apr 1999 08:56:46 IST+5.30
Received: by leo (1.65/waf)
via UUCP; Mon, 05 Apr 99 08:56:39 IST
for leo.ilban.ernet.in!ADMIN
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Received: from fep9.mail.ozemail.net (fep9.mail.ozemail.net [203.2.192.103])
by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA23987
for <ADMIN@leo.ilban.ernet.in>; Sun, 4 Apr 1999 12:31:23 +0530
Received: from avn (s1lis1p07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: HEPATITIS B PREVALENT IN US DEPSITE VACCINE
Date: Sun, 4 Apr 1999 16:58:12 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKKEGMEMAA.shotinfo@ozemail.com.au>
MIME-Version: 1.0
Content-Type: text/plain;
charset="iso-8859-1"
Content-Transfer-Encoding: 7bit
X-Priority: 3 (Normal)
X-MSMail-Priority: Normal

Meeting on Hep B

X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal

-----Original Message-----
From: karin schumacher [mailto:via@access1.net]
Sent: Friday, 1 January 1999 3:57
To: via
Subject: HEPATITIS B PREVALENT IN US DEPSITE VACCINE

Carolyn <noshotz@erie.net> wrote:
Wednesday December 30 5:18 PM ET
SOURCE: American Journal of Public Health 1999;89:14-18

Hepatitis B prevalent in US despite vaccine
NEW YORK, Dec 30 (Reuters Health) -- Although the hepatitis B vaccine has been available since 1981, hepatitis B infection remained as prevalent in the US in the early 1990s as it was in the early 1980s, according to a report in the January issue of the American Journal of Public Health, a journal of the American Public Health Association.

Dr. Geraldine M. McQuillan and colleagues with the Centers for Disease Control and Prevention (CDC) explain this finding by the fact that widespread vaccination programs were not launched until the early to mid-1990s. For the last two decades, an estimated 200,000 to 300,000 people in the US have contracted the hepatitis B virus annually. The virus is associated with inflammation of the liver and an increased risk of liver cancer. It can be transmitted via blood transfusions, sex, and contaminated needles.

The CDC researchers analyzed data from the National Health and Nutrition Examination Survey II (NHANES II), which was conducted between 1976 and 1980, and NHANES III conducted between 1988 and 1994. NHANES II included more than 28,000 people in the US, while NHANES III included an estimated 40,000. The survey design includes the results of blood tests for hepatitis B. The overall prevalence of hepatitis B infection did not change significantly between NHANES II, when it was 5.5%, and NHANES III, when the prevalence was 4.9%, the researchers determined.

In both surveys, the prevalence of hepatitis B was low until age 12, when it increased significantly. In addition, prevalence was higher than average among those who had multiple sex partners, those who began having sex at an early age, cocaine users, and men who had sex with men, McQuillan and colleagues report. ``In both surveys and in all racial/ethnic groups, the prevalence of hepatitis B virus infection did not begin to increase until puberty, suggesting that sexual transmission is the primary mode of spread in the United States,'' they explain.

In light of this finding, it is ``not surprising'' that the prevalence of hepatitis B infection did not decline between the early 1980s and the early 1990s, they add. Although a Hepatitis B vaccine was first licensed in the US in 1981, federal hepatitis B vaccination programs for infants did not begin until late 1992, and programs for adolescents did not start until 1995. Vaccination of healthcare workers and others with work-related risks of infection began in 1981, but did not become widespread until 1991,
according to the CDC researchers.

Data from NHANES demonstrate that children have a low but appreciable

adolescence, presumably with the onset of sexual activity and other high-risk behaviors; this supports the need to routinely vaccinate, McQuillan and co-authors conclude. Future NHANES should provide a means to evaluate the age-specific effect of hepatitis B immunization on infection prevalence.

****
Karin Schumacher
Vaccine Information & Awareness (VIA)
12799 La Tortola
San Diego, CA 92129
619-484-3197 (phone/voicemail)
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>From shotinfo@ozemail.com.au Sun Apr 4 13:31:12 1999
Received: from Waffle on leo by WafPeg 0.25, 93.04.04
for ADMIN on standalone PMail ; Mon, 5 Apr 1999 08:56:46 IST+5.30
Received: by leo (1.65/waf)
via UUCP; Mon, 05 Apr 99 08:56:39 IST
for leo.ilban.ernet.in!ADMIN
Received: from ozemail.com.au (uucp@localhost) by ilban.ernet.in (8.7.5/8.7.3) with UUCP id N
Received: from fep9.mail.ozemail.net (fep9.mail.ozemail.net [203.2.192.103])
by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA23994
for <ADMIN@leo.ilban.ernet.in>; Sun, 4 Apr 1999 12:31:24 +0530
Received: from avn (s1lis1p07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: [AVN] Hep B
Date: Sun, 4 Apr 1999 16:58:15 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKMEGMEMAA.shotinfo@ozemail.com.au>
MIME-Version: 1.0
Content-Type: text/plain;
charset="iso-8859-1"
Content-Transfer-Encoding: 7bit
X-Priority: 3 (Normal)
X-MSMail-Priority: Normal
X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal

-----Original Message-----
From: Sebastiana [mailto:pienaar@omen.net.au]
Sent: Thursday, 10 December 1998 5:11
To: avml@Majordomo.net; AVN@onelist.com
Subject: [AVN] Hep B

From: Sebastiana <pienaar@omen.net.au>

from URL: http://www.slackinc.com/general/idn/199804/hepb.htm

Meeting on Hep B

Alopecia linked to HepB immunizations, in rare cases

ACIP voted to add this adverse event to the hepatitis B recommendation statement.

[Incidence of alopecia]

[Your Turn]

April 1998

ATLANTA - A statement about alopecia will soon be added to the Advisory Committee on Immunization Practices' (ACIP) hepatitis B recommendation statement, based on a unanimous vote by the Centers for Disease Control and Prevention (CDC) committee.

This decision follows a report that appeared in October 1997 which reviewed the Vaccine Adverse Events Reporting System (VAERS) reports of hair loss after immunizations. This report indicated that of 60 patients with reported alopecia, 46 received hepatitis B vaccines. The cases ranged in age from 17 days to 56 years; 70% were adults and 83% were female.

Of the 60 reports, 16 had positive rechallenges for hair loss (recurrence following readministration of a suspect product), with nearly all (15) occurring after hepatitis B immunization.

"Although the association has not been proven, the VAERS rechallenge data are noteworthy and they raise some vaccine safety concerns," said Geoffrey S. Evans, MD, Division of Vaccine Injury Compensation, Health Resources and Services Administration. "It seems to me that we are obligated to provide some clarity."

Although the advisory committee voted to include a comment regarding alopecia following hepatitis B vaccination, they unanimously voted not to indicate causality.

"I think it's very important that we differentiate causality from association," said Samuel L. Katz, MD, Wilburt C. Davison professor and chairman emeritus of pediatrics, Duke University Medical School.

Robert T. Chen, MD, chief of Vaccine Safety and Development Activity, National Immunization Program, explained that when alopecia began appearing in VAERS, the CDC and the Food and Drug Administration (FDA) decided to search for the same adverse event in reports to the Vaccine Safety Data Link (VSD), a similar surveillance system.

Steven B. Black, MD, Northern California Kaiser Permanente, together with Henry Shinefield, MD, and Robert L. Davis, MD, headed the VSD analysis and used data from the VSD Center at Group Health Cooperative in Puget Sound (GHC) and Northern California Kaiser Permanente (NCKP).

Incidence of alopecia

Using automated data and linking it with outpatient diagnostic codes, the initial results identified several hundred cases of alopecia from automated data and did not show a significant association with receipt of hepatitis B vaccine, Black explained.

He then completed a retrospective matched case-control study. Patients with visits for hair loss were identified and five controls were assigned for each case. A total of 392 cases, ages 0-7 years, were identified in NCKP and 130 cases, ages 7-17 years, were identified in GHC.

"The majority of cases in each group were in females, and the predominant age group was 10-17 years," Black said.

During 1995, within the 10-17 year age group, 81,876 doses of hepatitis B were administered and two cases of alopecia occurred; all within 14 days of vaccination.

"Based on this information, we're 95% sure that if there is an excess risk associated with hepatitis B vaccine, that it is 8.2 per 100,000 or fewer. I want to emphasize that it could be a lot less. It could be zero," Black said.

"We conclude at this point that this study did not demonstrate a statistically significant elevated risk of alopecia following hepatitis B vaccination in children," he said.

Recovery occurred in all cases in which outcome is known. All FDA-approved hepatitis B vaccines and the plasma-driven products were represented in both studies of VAERS and VSDL reports.

"The bottom line is that we've got a clear signal from safety surveillance indicating that vaccines probably can cause hair loss, but maybe only rarely," said Robert P. Wise, MD, MPH, FDA Center for Biologics Evaluation and Research, lead author on the study of the VAERS reports.

For more information:

Wise RP, Kiminyo KP, Salive ME, et al. Hair loss after routine immunization. JAMA 1997;278:1176-78.

Your turn

You can express your views on this article, or other relevant themes, in the Infectious Disease News Specialty Forums.

Meeting on Hep B

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>From shotinfo@ozemail.com.au Sun Apr 4 13:31:10 1999
Received: from Waffle on leo by WafPeg 0.25, 93.04.04
for ADMIN on standalone PMail ; Mon, 5 Apr 1999 08:56:45 IST+5.30
Received: by leo (1.65/waf)
via UUCP; Mon, 05 Apr 99 08:56:36 IST
for leo.ilban.ernet.in!ADMIN
Received: from ozemail.com.au (uucp@localhost) by ilban.ernet.in (8.7.5/8.7.3) with UUCP id N
Received: from fep9.mail.ozemail.net (fep9.mail.ozemail.net [203.2.192.103])
by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA23936
for <ADMIN@leo.ilban.ernet.in>; Sun, 4 Apr 1999 12:30:52 +0530
Received: from avn (s1lis1p07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: [AVN] JA: Thromocytopenic purpura after Heb B.
Date: Sun, 4 Apr 1999 16:57:44 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKGEGLEMAA.shotinfo@ozemail.com.au>
MIME-Version: 1.0
Content-Type: text/plain;
charset="iso-8859-1"
Content-Transfer-Encoding: 7bit
X-Priority: 3 (Normal)
X-MSMail-Priority: Normal
X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal

-----Original Message-----
From: Sebastiana [mailto:pienaar@omen.net.au]
Sent: Monday, 15 March 1999 11:48
To: avml@Majordomo.net; AVN@onelist.com
Subject: [AVN] JA: Thromocytopenic purpura after Heb B.

From: Sebastiana <pienaar@omen.net.au>

>From URL:
http://www.ncbi.nlm.nih.gov/htbin-post/Entrez/query?uid=9613364&form=6&db=m&
Dopt=b

Arch Dis Child 1998 Mar;78(3):273-4

Thrombocytopenic purpura as adverse reaction to recombinant hepatitis B vaccine.

Ronchi F, Cecchi P, Falcioni F, Marsciani A, Minak G, Muratori G, Tazzari PL, Beverini S

Divisione Pediatrica-Ospedale Civile di Cattolica (RN), Cattolica (RN), Italy.

Three cases of immune thrombocytopenic purpura after the first dose of recombinant hepatitis B vaccine occurred in infants under 6 months of age.

Other possible causes of this condition were excluded. Antiplatelet antibodies were present. A defect in platelet production was excluded in two children. Corticosteroid treatment was effective. Subsequent administration of other vaccines (against polio, diphtheria, and tetanus) did not cause relapse of thrombocytopenia.

PMID: 9613364, UI: 98276312

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for <ADMIN@leo.ilban.ernet.in>; Sun, 4 Apr 1999 12:30:59 +0530
Received: from avn (sllis1p07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: HEP B BILL STALLED IN NEW JERSEY
Date: Sun, 4 Apr 1999 16:57:52 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKMEGLEMAA.shotinfo@ozemail.com.au>
MIME-Version: 1.0
Content-Type: text/plain;
charset="iso-8859-1"
Content-Transfer-Encoding: 7bit
X-Priority: 3 (Normal)
X-MSMail-Priority: Normal
X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal

-----Original Message-----
From: karin schumacher [mailto:via@access1.net]
Sent: Saturday, 27 February 1999 11:35
To: via
Subject: HEP B BILL STALLED IN NEW JERSEY

ZachNPep@aol.com wrote:
Hi all, We were able to postpone the hep. b vote. We found out the day before the bill was to be voted on. We made a flurry of last minute calls, and we did it! Her is an article that was in one of the papers. - Sue Collins

Vote is delayed on bill requiring hepatitis vaccine
Goup has fought measure that would have required shots for schoolage children.
By Larry Higgs

Staff Writer

LONG HILL - A township woman and other concerned parents convinced the state Legislature to delay voting on a bill that would have required hepatitis vaccinations for schoolage children. The state Senate postponed a vote Thursday on Bill A-1850, which would have required hepatitis B shots for admission to kindergarten, first or sixth grade.

Sue Collins, president of the Central Jersey Chapter of Parents for Freedom of Vaccination Choice, was one of several people who contacted legislators to express concerns about medical complications caused by hepatitis shots. She spoke Thursday to Senate President Donald DiFrancesco, R-Scotch Plains.

"I want to congratulate the Senate for the foresight to see it is not a black-and-white issue and looking into it more," Collins said. The Bill was introduced in March by Assemblyman John Wisniewski, D-Sayreville, and David Wolfe, R-Brick. Postponing the vote isn't unusual, said Rene Trabert, DiFrancesco's spokeswoman. "There simply wasn't enough information. There were enough questions to put off the vote," Trabert said.

The next voting session is scheduled for March 22, but she didn't know whether the Legislature would vote on the bill then. The bill was opposed by the parents' group, which contends that hepatitis is not a childhood disease and that children risk greater harm from the vaccination. "There has been growing opposition from parents of kids who've suffered seizures or been killed due to reactions to the vaccine," Collins said. "To mandate a vaccine with risks doesn't make sense. It should be a parent's choice."
Collins said she's aware of a case in New Jersey in which a child suffered epileptic seizures after being vaccinated.

****
Karin Schumacher
Vaccine Information & Awareness (VIA)
12799 La Tortola
San Diego, CA 92129
619-484-3197 (phone/voicemail)
619-484-1187 (fax)
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Received: from fep9.mail.ozemail.net (fep9.mail.ozemail.net [203.2.192.103])
by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA23962
for <ADMIN@leo.ilban.ernet.in>; Sun, 4 Apr 1999 12:31:09 +0530
Received: from avn (s1lis1p07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>

To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: HEP B EFFICACY STUDY
Date: Sun, 4 Apr 1999 16:57:58 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKAEGMEMAA.shotinfo@ozemail.com.au>
MIME-Version: 1.0
Content-Type: text/plain;
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Content-Transfer-Encoding: 7bit
X-Priority: 3 (Normal)
X-MSMail-Priority: Normal
X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal

-----Original Message-----
From: karin schumacher [mailto:via@access1.net]
Sent: Friday, 19 February 1999 3:50
To: via
Subject: HEP B EFFICACY STUDY

Hepatitis Vaccines; "Effects of a Supplementary Hepatitis B Vaccine Dose in
Children Aged 8 to 10 Years Unprotected after Primary Vaccination."
February 18, 1999

Vaccine Weekly: According to an abstract submitted by the authors to the 3rd Canadian National Immunization Conference entitled Partnerships for Health Through
Immunization, held December 6-9, 1998, in Calgary, Alberta, Canada,

"INTRODUCTION: In spite of the high antigenicity of vaccines against hepatitis B (HB) in children, those with no response or a weak response to the vaccination remain a problem. What is the best vaccination strategy for these children? This study presents the humoral response following a supplementary dose given to children who were unprotected after primary vaccination.

METHOD: In an earlier study, 2,255 children aged 8 to 10 years received either three doses of 10 (micro)g of Engerix-B (SmithKline Beecham) or three doses of 2.5 (micro)g of Recombivax (Merck Frosst Canada) in school according to the usual schedule (0, 1, 6). One month after the third dose, a blood sample was taken. Radioimmunoassay (AUSAB, Abbott) was used to measure the anti-HBs. In this study, 21 children had not reached the protective level of 10 IU/L. Eighteen children (10 non responsive: IU/L; 8 weakly responsive: 2 to 9 IU/L) accepted the supplementary dose of the same vaccine which was administered 20 months (Engerix-B) and 9 months (Recombivax) after the last of the primary vaccination doses. One month after the supplementary dose, a blood sample was
taken.

RESULTS: One month after the supplementary dose, all the children had developed antibodies. However, two of the initially non-responsive children had not reached the protective level. After the supplementary dose, the geometric average anti- HB level was higher in those children with an initially weak response as compared to initially non-responsive children (353 vs. 33 IU/L). This is not, however, a statistically significant difference. The vaccine used, the dose, the time interval between the
supplementary dose and the blood sample had no significant effect on the immune

response.

CONCLUSION: Although a single supplementary dose of the recommended dosage appears to be effective in protecting all the children with a weak response, a second supplementary dose may benefit some non-responsive children."

AUTHORS: N. Laflamme, B. Duval, N. Boulianne, G. De Serres, P. De Wals, R. Masse, G. Trudeau, G. Delage and L. DesJardins. Affiliation not provided.

****

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http://www.909shot.com (NVIC website)
http://www.access1.net/via (VIA website)

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We Must Have The Freedom To Choose & Respect Everyone's Choice
****
Any information obtained here is not to be construed as medical OR legal advice. The decision to vaccinate and how you implement that decision is yours and yours alone.
****

>From shotinfo@ozemail.com.au Sun Apr 4 13:31:13 1999
Received: from Waffle on leo by WafPeg 0.25, 93.04.04
for ADMIN on standalone PMail ; Mon, 5 Apr 1999 08:56:46 IST+5.30
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via UUCP; Mon, 05 Apr 99 08:56:40 IST
for leo.ilban.ernet.in!ADMIN
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by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA23919
for <ADMIN@leo.ilban.ernet.in>; Sun, 4 Apr 1999 12:30:31 +0530
Received: from avn (s1lis1p07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
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Message-ID: <NCBBJDFKEKEIGIHFLBEKMEGKEMAA.shotinfo@ozemail.com.au>
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Content-Transfer-Encoding: 7bit

X-Priority: 3 (Normal)
X-MSMail-Priority: Normal
X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal

-----Original Message-----
From: Bart Classen [mailto:Classen@worldnet.att.net]
Sent: Friday, 4 October 1996 1:21
To: Recipient list suppressed
Subject:

John B. Classen M.D., M.B.A.
President and CEO
Classen Immunotherapies, Inc.
6517 Montrose Avenue
Baltimore, MD 21212 U.S.A.
Tel: (410) 377-4549
Fax: (410) 377-8526
Email: Classen@worldnet.att.net

Dear Sir or Madam:

The American Society of Microbiology has chosen to highlight Classen Immunotherapies' presentation in their press room during the 36th ICAAC meeting held on September 15-18. The American Society of Microbiology choose to promote our presentation entitled The Timing of Immunization Alters Diabetes Risk because they feel it is one of the most interesting and possibly important presentations at the ICAAC meeting. ICAAC, The Interscience Conference on Antimicrobial Agents and Chemotherapy, is possibly the largest conference on infectious diseases.

Enclosed is the presentation summary that will be made available in the ICAAC press room. The American Society of Microbiology prohibits the publishing of references to the presentation until the date of the presentation (Monday September 16th, 1PM).

For more information regarding the ICAAC Conference and Press Room please contact

Barbara Hyde, Director of Communications
American Society of Microbiology
1325 Massachusetts Avenue, NW
Washington, DC 20005-4171
tel: 202-942-9206
fax: 202-942-9367
E-mail: bhyde@asmusa.org

You may contact me at any time for more information on Classen Immunotherapies and our data.

Sincerely

John Barthelow Classen, MD

New Immunization Schedules May Prevent 50% of Juvenile Diabetes (IDDM)

Extensive human and animal data indicates that starting immunization in the first week of life, as opposed to 6 weeks of life, is likely to prevent 50% or more cases of juvenile diabetes, also known as insulin dependent diabetes (IDDM). Insulin dependent diabetes may afflict 1% of US citizens during their life time and costs the US approximately $30 billion dollars annually. These discoveries may lead to a major reduction in diabetes and other autoimmune diseases, annual savings to the US economy of over $15 billion and allow potentially millions of people to receive compensation through the National Vaccine Injury Compensation Program. Safer immunization schedules where common pediatric vaccines such as the diphtheria, tetanus, acellular pertussis, hepatitis B, Hemophilus influenza and polio vaccines are started at birth could be implemented in just a few years if governments make vaccine safety a priority.

These revolutionary studies examine the long term affects of vaccines on

autoimmune diseases. Vaccines are typically approved for marketing based on clinical trials which asses adverse events occurring within 30-60 days of immunization in a population that may be less than 30,000 individuals. Post marketing surveillance of vaccines has generally only been able to detect adverse events occurring within days of immunization. The establishment of IDDM registries in the mid 1980s has allowed us to study the affect of vaccines on 100,000s of individuals followed for 10 years or more, creating patient follow ups in excess of 2 million patient years. This scientific breakthrough has allowed us to make the important discovery of the potential affect of vaccines on IDDM, which is verified in animal models of diabetes. Unfortunately there are few registries to allow the study of vaccines on other autoimmune diseases however animal models indicate the timing of immunization may have an equally important affect on other autoimmune diseases including lupus.

The data is being presented at the 36th ICAAC meeting, New Orleans, on Monday September 16th, 1996 at 1 PM, session 21, board G023. These studies were performed by J. Barthelow Classen, MD, MBA, CEO of Classen Immunotherapies, Inc. (Baltimore, MD) who is also affiliated with the Greater Baltimore Medical Center, and David Carey Classen MD, MS who is affiliated with University of Utah/LDS Hospital, Salt Lake City, Utah. Dr. Jaako Tuomilehto of the Finnish Public Health Service and several additional collaborators have also contributed.

The studies below include a large prospective randomized clinical trial, several epidemiological studies and animal toxicity studies. The studies show 2 phenomenon, immunization starting during the first few weeks of life prevents IDDM while immunization starting at 6 weeks or later is associated with an increased risk of IDDM. The data also shows the affects caused by different vaccines are additive. The proposed mechanism of action is interferon release. Interferon, released at birth by immunization, may prevent the newborn from becoming infected with diabetes inducing viruses from the mother's blood. When interferon is released following immunization after 6 weeks of life the interferon may exacerbate autoimmunity. Summaries of the data being presented are included below.

I. Immunization at birth prevents diabetes

1.Swedish BCG vaccine data (Diabetologia 39:500-502, 1996). Sweden routinely gave the BCG, tuberculosis, vaccine at birth to all children until mid 1975 when it was stopped. The cumulative incidence of IDDM in the children immunized at birth, born in 1974, was reduced by 48 cases/100,000 children compared to unimmunized children born in 1976 ($p = 0.0028$).

2.European BCG vaccine data. The cumulative incidence of IDDM in countries which give the BCG vaccine at birth is on average reduced 52 cases/100,000 children immunized (32% reduction) compared to countries that did not give BCG vaccine ($p = 0.02$). The result is nearly identical to the Swedish study.

3.Dutch smallpox vaccine data. The cumulative incidence of IDDM in children born during a smallpox epidemic, and thus likely to have received the smallpox vaccine early in life, was reduced by 90 cases/100,000 children (45% reduction) compared children born in non epidemic years ($p=0.05$).

4.New Zealand Hepatitis B data. The hepatitis B vaccine was routinely given at birth to all children born in New Zealand in 1988 and 1989, after which time immunization was started after 6 weeks. Dr. Russell Scott who runs a IDDM registry in NZ indicated those born in these years had a decreased risk of IDDM.

5.Animal data (Autoimmunity, in press). Mice immunized starting at birth with the DTP and polio vaccines did not develop diabetes compared to 46% of mice receiving saline ($p=.0001$). Additional studies showed an additive affect of the separate vaccines. Results have been confirmed in rats.

II. Immunization starting after 6 weeks increases risk of diabetes
1.Finnish Hemophilus influenza B vaccine Clinical Trial (Collaboration with Dr. Jaako Tuomilehto, Finnish Public Health Service). 114,000 children in Finland were randomized and one group received 4 doses of the HiB vaccine starting at 3 months of life while a second group received 1 dose at 2 years of life. The groups were followed for approximately 10 years and there were 20 more cases of IDDM in the group receiving the 4 doses (205 versus 185). This represents a rise in the cumulative incidence of IDDM of at least 23 cases/100,000 children immunized. Following wide spread use of the vaccine the incidence of diabetes rose in the US and appears to be rising in the UK.

3.New Zealand hepatitis B vaccine data (N. Z. Med. J. 109:195, 1996). All children under 16 began receiving the hepatitis B vaccine in New Zealand starting in 1988 with almost all receiving the vaccine starting after 6 weeks of life except those born in 1988 and 1989. Following the immunization the annual incidence of IDDM on average has been elevated 54% (17.2 cases/100,000 versus 11.2 cases/100,000) during a 6 year period compared to the prior 6 year period (p=0.0001).

4.European BCG vaccine data. The cumulative incidence of IDDM in countries which give the BCG vaccine at school age is on average increased by more than 50 cases/100,000 children immunized compared to countries that did not give BCG vaccine (p=0.005).

5.Live viral vaccine data (measles, mumps, rubella, polio, smallpox). Epidemics of IDDM have also consistently occurred following massive immunization with a number of live vaccines given to children older than 2 months. Examples will be included in the poster.

6.Animal data (Autoimmunity, in press) In mice at low risk for diabetes, 23% of a group receiving pertussis vaccine at week 8 developed diabetes compared to 7.7% in a group that did not (p=0.065).

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Received: from Waffle on leo by WafPeg 0.25, 93.04.04
for ADMIN on standalone PMail ; Mon, 5 Apr 1999 08:56:46 IST+5.30
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for <ADMIN@leo.ilban.ernet.in>; Sun, 4 Apr 1999 12:30:49 +0530
Received: from avn (sl1is1p07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: PARENTS TAKE COURT ACTION TO CHALLENGE HEPATITIS B VACCINE
Date: Sun, 4 Apr 1999 16:57:40 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKEEGLEMAA.shotinfo@ozemail.com.au>
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Content-Type: text/plain;
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X-Priority: 3 (Normal)
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X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal

-----Original Message-----
From: karin schumacher [mailto:via@access1.net]
Sent: Tuesday, 16 March 1999 5:20
To: via
Subject: PARENTS TAKE COURT ACTION TO CHALLENGE HEPATITIS B VACCINE

Sebastiana wrote:
PARENTS TAKE COURT ACTION TO CHALLENGE HEPATITIS B VACCINE

Winnipeg has recently become the epicentre for vaccine related issues. This past November(1998) a group of parents with the assistance of the Association for Vaccine Damaged Children challenged public health officials with a court injunction in an attempt to stop the hepatitis B vaccine campaign from being launched in public schools.

Historically, this is a First! It is the first time that a group of Canadians have appealed to the courts to stop the fraudulent and unethical actions of a provincial health bureaucracy from imposing a mass vaccination campaign aimed at all grade 4 children. The issue is informed consent. The consent form fails to disclose all the material risks of the vaccine, but proceeds to play up the fear of an epidemic arising if children aren't vaccinated, and implies that people who choose to defer from the vaccine are bad parents for not protecting their children. In some schools, only vaccinated children received rewards such as teddy bears or treat bags.

In October, 1998, the French courts ordered a halt to further vaccination of school children following reports of neurological illnesses being provoked by the hepatitis B vaccine. A large class action lawsuit is in the works in France, launched by 15,000 people claiming vaccine caused injuries which have resulted in chronic disabilities like multiple sclerosis and lupus. Medical doctors, researchers, and parents both in Europe and North America are expressing alarm at the ever increasing numbers of reports of vaccine associated health problems.

The Manitoba court was presented with compelling scientific evidence linking hepatitis B vaccine to a heightened risk of neurological injury. The court was told that the consent form designed by health officials failed to disclose serious vaccine risks, thereby disabling parents from making an informed decision on behalf of their children.

Predictably, the Court ruled in favour of the province, allowing it to proceed with its mass vaccination plan. Shockingly, it failed to uphold the biomedical/ethical standards derived from Canadian Case Law, that material risks, regardless of how insignificant they may be statistically, must be disclosed prior to any medical procedure. The Court's failure to order health officials to re-write the consent form to include the possibility of serious, adverse reactions, is a striking violation of the principle of informed consent, granted all Canadians. It is a compelling example of the dysfunction of our legal system in its failure to uphold the most fundamental ethical standards in the practice of medicine and public health. It is a testament to the degree that the current medical monopoly has the power to violate the individual's right to "security of the person", as provided in the Canadian Charter of Rights and Freedoms.

The precepts that have arisen out of case law and Supreme Court decisions to form the body of knowledge contained within Canadian medical law, uphold and grant "Every individual's right to information on material risks and the fundamental right of persons to be free from unwanted physical interference. Medical care is wrongful and a 'battery'

unless the patient has given consent to it." True consent cannot be obtained from people who have been denied knowledge of all material risks.

Although the parents lost the court case, they won a moral victory in that the media attention alerted parents across the province to seek more information prior to submitting their children to the vaccine. Representatives from the Association for Vaccine Damaged Children, the Eagle Foundation, and Parents for Informed Consent appeared on television shows and on radio programs across the province warning the public of the potential risks of this vaccine. Public health officials, in spite of requests from radio and television producers, refused to debate the issue with them on the air.

Public health officials were infuriated that Parents for Informed Consent showed up at some parent advisory committee meetings to share information they had received from respected scientists and doctors who have serious concerns about this vaccine. Principals were reprimanded for allowing this information into their schools. Even a community newspaper was chastised by health officials for quoting Dr. Bonnie Dunbar, a cell biologist, medical professor and vaccine developer who has blown the whistle on hepatitis B vaccine in the U.S. Yet despite parents' repeated requests for Public Health's scientific research on the safety of the vaccine, they have received only WHO's (World Health Organization) editorialized propaganda, without any hard, scientific data to back up safety claims.

In Manitoba, as in other provinces, health officials are still under the delusion that they can get away with their fraudulent, and coercive mass vaccination campaigns, based on disinformation and lies. In Manitoba, health nurses have been telling parents that of the billion doses of the [illegible] side effects, and that [illegible] ing and redness at the injection site.

These nurses, sent out to speak to the public, have failed to inform parents that the Centers for Disease Control in Atlanta has on one diskette alone 40,000 reactions to the hepatitis B vaccine ranging from fever, to blindness, to death. It is estimated that only 10% of adverse reactions get reported. Nor is the public told that Manitoba does not have a mandatory reporting system of adverse reactions without which there can be no true picture of the rate of vaccine injury. In addition, none of the nurses appeared knowledgeable about the health effects of the genetically engineered properties of this vaccine, one of the most critical areas of concern, not only because of the newness of this technology in injectable form, but also because of the discussion genetic engineering is generating in food technology.

The Association for Vaccine Damaged Children and Parents for Informed Consent have distributed information on this vaccine and its adverse side effects to Health Ministers, Education Ministers, MLA's, Senators, College of Physicians and Surgeons, Medical Association of Registered Nurses, Dentists, Pediatricians, Neurologists, Professors of Medical Ethics, Chiropractors and Naturopathic Doctors. Their goal in appealing to these various organizations is to raise awareness about the potential dangers of this genetically engineered vaccine and to initiate long-term, independent studies investigating the safety of hepatitis B vaccine. They are calling for the federal government to institute a mandatory reporting system to document adverse reactions to all vaccines.

Undoubtedly, the greatest obstacle to the public's understanding of the real risks posed by mass vaccination programs to children and the future health of our society, is the monopoly exerted by orthodox medicine and

its unholy alliance with the transnational pharmaceutical cartel. Together, they have aggressively spawned the unbridled expansion of a drug based ideology. Just as religious ideology was removed from public schools, so must we now depose the medical dictatorship and its drug based ideology from the public school system. Parents, teachers and concerned citizens should contact the Association for Vaccine Damaged Children as well as their school boards to demand that the school based vaccination programs be terminated. The health of our next generation depends on it !!!

The Association for Vaccine Damaged Children,
67 Shier Dr.
Winipeg MB R3R 2H2

(204)895-9192 or (204)896-0971

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12799 La Tortola
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619-484-1187 (fax)
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We Must Have The Freedom To Choose & Respect Everyone's Choice

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Any information obtained here is not to be construed as medical OR legal advice. The decision to vaccinate and how you implement that decision is yours and yours alone.

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Received: from Waffle on leo by WafPeg 0.25, 93.04.04
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Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: HEPATITIS B VACCINE
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X-Priority: 3 (Normal)
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X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal

-----Original Message-----

From: Karin Schumacher [mailto:via@ihot.com]
Sent: Tuesday, 31 December 1996 3:18
To: rickp@ramlink.net; Karin Schumacher
Subject: HEPATITIS B VACCINE

Bart Classen wrote:
The Baltimore Sun today, Monday December 30th had an article discussing vaccines as a cause of Gulf War Syndrome. The article mentions an immunologist by the name of Dr. Pam Asa in Memphis Tennessee who reportedly believes many of the gulf war veterans developed lupus from the vaccines they received. This would be consistent with my own research on vaccines and autoimmunity, particularly insulin dependent diabetes. The article was written by Jonathan Bor at the Baltimore Sun. You can also get information on the Hepatitis B vaccine by having the package insert sent to you or your doctor by the manufacturer, Merck or SmithKline Beecham. The same information is contained in the Physician's desk reference. The package inserts often list a number of autoimmune diseases associated with the vaccines but the information is almost useless since the risk is not quantified and is only based on follow up of 30 days or less.

Bart Classen, MD

Rick A. Presley wrote:
I think i have had a reaction to the Engerix B vaccine howevere i can't seem to get an answer from anyone i've been told my symptoms are due to the shot and then told from another there not. I don't know which one is right all I know is just after i recieved this vaccine booster i got sick and have not been the same this has been for a year now soon to be 2 in may. I was wondering if you have had any information on this vaccine and if it can cause Lupus type symptoms or Lupus its self. I'm only looking for comment I will not hold anyone to their opinion. Any info would be greatly appreciated.

Thank you
Robin--

****
Karin Schumacher
Vaccine Information & Awareness (VIA)
792 Pineview Drive
San Jose, CA 95117
408-397-4192 (voice mail/pager)
408-554-9053 (phone/fax)
via@ihot.com (email)
http://www.ihot.com/~via (website)
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We Must Have The Freedom To Choose &
Respect Everyone's Choice
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Received: from Waffle on leo by WafPeg 0.25, 93.04.04
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To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: OHIO AAP OPPOSES HEP B VACCINE
Date: Sun, 4 Apr 1999 16:57:47 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKIEGLEMAA.shotinfo@ozemail.com.au>
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X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal



-----Original Message-----
From: karin schumacher [mailto:via@access1.net]
Sent: Friday, 12 March 1999 4:18
To: via
Subject: OHIO AAP OPPOSES HEP B VACCINE


Sebastiana wrote:

Thursday March 11 3:14 PM ET
Medical Group Opposes Legislation - (COLUMBUS) -- The Ohio Chapter of
the American Academy of Pediatrics opposes legislation to repeal the
requirement that children be vaccinated against hepatitis ``B'' before
entering kindergarten. The group says the vaccine is safe and highly
effective in preventing the infection among susceptible children and
adults... and that serious side effects are extremely rare. Cincinnati
state Representative Dale Van Vyven (VY-ven) has introduced legislation
to put an end to the three-shot vaccine because of possible risks to
kids.

**********************************************************************
Karin Schumacher
Vaccine Information & Awareness (VIA)
12799 La Tortola
San Diego,  CA  92129
619-484-3197 (phone/voicemail)
619-484-1187 (fax)
via@access1.net (email)
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**********************************************************************
We Must Have The Freedom To Choose & Respect Everyone's Choice
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Any information obtained here is not to be construed as medical
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OR legal advice. The decision to vaccinate and how you
implement that decision is yours and yours alone.
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for leo.ilban.ernet.in!ADMIN
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From: Maureen Hickman [mailto:acii@ozemail.com.au]
Sent: Saturday, 6 March 1999 11:12
To: avn@onelist.com
Subject: [AVN] HEPATITIS 'B' COURT VICTORY

From: Maureen Hickman <acii@ozemail.com.au>

Another Court Victory for Hepatitis 'B' Victim
6.3.99

Heather A. is a woman in her mid forties and is a trained nurse who worked
for
Home Care from 1986 until 1991. Home Care suggested that Heather and other
members of Home Care staff be vaccinated against Hepatitis 'B' as they were
working in a risk profession. Heather had her first vaccination against
Hepatitis 'B' in August 1990. Approximately one week later she noticed
diffused aching in both the lateral and medial aspects of the right elbow.
In
September 1990 Heather received a second injection of the Hepatitis 'B'
vaccine. Within two days she developed recurrence of the pain in the right
elbow and this time was accompanied by pain in the right knee and right
wrist
as well.

Heather complained to her employer and also saw several medical
practitioners.
She underwent an injection of steroids but this gave no satisfactory pain
relief. X-ray results were normal. A medical diagnosis was made of tennis

elbow.

In February 1991 Heather had her third Hepatitis 'B' injection. Following this her health deteriorated and she developed constant pain in the left elbow and over the next seven to ten days she developed arthralgia in the wrist, right elbow, both ankles, knees, fingers and toes.

Approximately five months after her third injection of the Hepatitis 'B' vaccine Heather became pregnant. Ante-natal testing revealed Turner syndrome and she had a termination of her pregnancy. She was greatly distressed by this and was concerned that in fact the vaccination may have played a part in causing this chromosome abnormality of the fetus.

Following the vaccination of Hepatitis 'B' vaccine, Heather developed arthralgia and subsequently polyarthralgia, chronic fatigue syndrome and a psychiatric disorder known as an adjustment disorder. The essential feature of an adjustment disorder is the development of clinically significant emotional or behavioural symptoms in response to identifiable psychosocial stressor or stressors.

A medico/legal doctor for the Plaintiff said that her prognosis for recovery is poor and that she should now be considered totally and permanently disabled as a result of her illness and symptoms. He said 'I would also say, with the same degree of confidence, that Heather A. would be unlikely to have suffered the illness and symptoms she has suffered since the vaccinations, were it not for her vaccination with Engerix B in 1990/1991.

Heather A's case came before the Compensation Court of New South Wales on 18.2.99 and was settled by way of a Commutation on 23.2.99. Heather has received a significant lump sum settlement plus payment of medical expenses for treatment for an agreed sum. Heather is happy with the result although no amount of money could ever compensate a person for years of past or future ill-health, however, she can now look to the future.

Health workers, before following their employer's suggestions to undergo vaccination for Hepatitis 'B', should carefully consider whether the risks of suffering a severe adverse reaction to the vaccine, such as arthritis and/or chronic fatigue syndrome, is far worse than catching the disease itself.

If you know anybody in NSW suffering similar symptoms to Heather emanating from a Hepatitis 'B' vaccine, administered during the course of their employment, please let them know that Carters may be able to assist them. Carters have a further workers' compensation Hepatitis 'B' claim listed for hearing during the middle of 1999.

Thanks to the many individuals both local and from around the world who provided Hepatitis 'B' information to me. This information was invaluable. AVN can also be relied upon for assistance in legal matters.

Maureen Hickman/Carters Law Firm, Sydney, Australia,
e-mail: acii@ozemail.com.au Telephone: 02 9649-0233 Facsimile:
02
9649 5995
Address: 1 Harrow Road, Auburn NSW 2144

Any information obtained here is not to be construed as medical or legal advice. The decision to vaccinate and how you implement that decision is yours and yours alone.

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-----Original Message-----
From: via@ihot.com [mailto:via@ihot.com]
Sent: Sunday, 4 May 1997 11:04
To: Karin Schumacher
Subject: JAMA ON HEP B

Perspectives on Hepatitis B Vaccination

To the Editor.--I read with interest and appreciation the recent Landmark Perspective and the discussion regarding the hepatitis B vaccine by Dr Douglas.[1] However, I find it somewhat disturbing that Douglas did not mention the potential untoward results of viral vaccines, or those already reported as presumably being due to the hepatitis B vaccine. Douglas must be aware of the untoward results from the vaccine, not only because of lawsuits his company has settled in which demyelinating disease was involved, but also because of reports of

adverse reactions linked to vaccine use in the medical literature,[2-4] including multiple sclerosis-like diseases, Guillain-Barre syndrome, optic neuritis, and transverse myelitis.

Despite these reports, the strategy of universal vaccination in the United States has been promoted widely by Merck, the Centers for Disease Control and Prevention, and others.[5,6] Should not the parents of infants be made aware of the potential and reported dangers of the hepatitis B vaccine before they are asked to give permission for the vaccination? After all, infants in many areas of the United States are not at risk for infection with the hepatitis B virus. Furthermore, the much heralded strategy of eradicating hepatitis B disease by universal vaccination is just that--a strategy rather than a proven measure.[5,6] Should individuals who are at low risk for this disease forego this vaccination until the strategy is proven successful in areas of the country that have already mandated it, such as New York state? In no way do these remarks denigrate the use of the present vaccine in high-risk populations in both the United States and worldwide.

Burton A. Waisbren, Sr, MD
Milwaukee, Wis

References

1. Douglas RG Jr. The heritage of hepatitis B vaccine. JAMA. 1996;276:1796-1798.
2. Herroelen L, de Keyser J, Ebinger G. Central nervous system demyelination after immunization with recombinant hepatitis B vaccine. Lancet. 1991;338:1174-1175.
3. Nadler JP. Multiple sclerosis and hepatitis B vaccination. Clin Infect Dis. 1993;17:928-929.
4. Kaplanski G, Retornaz F, Durand J. Central nervous system demyelinization after vaccination against hepatitis B and HLA haplotype. J Neurol Neurosurg Psychiatry. 1995;25:758-759.
5. Centers for Disease Control. Hepatitis B virus, a comprehensive strategy for eliminating hepatitus B virus transmission in the United States through universal childhood vaccination: recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR CDC Surveill Summ. 1991;40(RR-13):1-25.
6. West DJ, Calandra GB, Hesley TM, Ioli V, Miller WJ. Control of hepatitis B through routine immunization of infants: the need for flexible schedules and new combination vaccine formulations. Vaccine. 1993;11:S21-S27. (JAMA. 1997;277:1124)

In Reply.--The Landmark Perspective article was written in response to a request from the editors of JAMA to provide a historical perspective on the Landmark Article by Buynak et al.[1] The purpose of the Perspective was to trace the development of hepatitis B vaccines and to show how they can be used to eliminate and eventually eradicate hepatitis B infection, and with it many cases of cirrhosis and cancer of the liver, from the human population. My article was not intended to provide complete information about hepatitis B vaccines.

Dr Waisbren must know that lawsuits and isolated case reports of adverse events occurring in temporal association with vaccination do not prove a causal relationship. In fact, the Vaccine Safety Committee of the Institute of Medicine examined 4 types of evidence to determine if a causal association exists between the administration of certain types of vaccines and selected adverse experiences. They considered biologic plausibility; case reports, case series, and uncontrolled observational studies; controlled observational studies; and controlled clinical trials. The committee concluded that the evidence is inadequate to accept or reject a causal relation between hepatitis B vaccine and

Guillain-Barre syndrome, optic neuritis, multiple sclerosis, or transverse myelitis.[2] Furthermore, I would like to point out that the comprehensive strategy for eliminating hepatitis B virus transmission through universal childhood vaccination is a recommendation of the Advisory Committee on Immunization Practices of the US Public Health Service.[3] This recommendation is also endorsed by the American Academy of Pediatrics.[4] This strategy was developed because the previous strategy of vaccinating persons in the major risk groups has had limited success in preventing the transmission of hepatitis B. This strategy recognizes that the reduction in hepatitis B disease and hepatitis B-associated liver disease from universal infant vaccination may not become apparent for a number of years.

I agree with Waisbren that parents should be advised by physicians of the risks and the benefits for all vaccines that their children receive; however, infrequent reports of adverse events with no demonstrated causal relationship to the vaccine hardly justify a retreat from the universal childhood hepatitis B vaccination strategy that has been so widely accepted. Public health policy must be based on known risks and benefits, not on theoretical possibilities.

R. Gordon Douglas, Jr, MD
Merck & Co Inc
Whitehouse Station, NJ

References

1. Buynak EB, Roehm RR, Tytell AA, Bertland AU II, Lampson GP, Hilleman MR. Vaccine against human hepatitis B. JAMA. 1976;235:2832-2834.
2. Institute of Medicine, Vaccine Safety Committee. Adverse Events Associated With Childhood Vaccines: Evidence Bearing on Causality. Washington, DC: National Academy Press; 1994.
3. Centers for Disease Control. Hepatitis B virus, a comprehensive strategy for eliminating hepatitis B virus transmission in the United States through universal childhood vaccination: recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR CDC Surveill Summ. 1991;40(RR-13):1-25.
4. American Academy of Pediatrics, Committee on Infectious Diseases. Policy statement: universal hepatitis B immunizations. Pediatrics. 1992;89:795-800. (JAMA. 1997;277:1124)

In Reply.--Numerous studies indicate that hepatitis B vaccines have an excellent safety profile and that adverse neurologic events following hepatitis B vaccination are exceedingly rare.[1-4] Population-based studies following large-scale hepatitis B immunization programs for infants in Alaska, New Zealand, and Taiwan have not established an association between hepatitis B vaccination and the occurrence of serious neurologic adverse events.[3-4]

In the United States, data on adverse events associated with vaccination are available through the national Vaccine Adverse Event Reporting System (VAERS), a passive surveillance system. In 1993, the Institute of Medicine (IOM) reviewed case reports in the medical literature and those reported to VAERS between November 1990 through July 1992 and concluded that the evidence to date was insufficient to assess a causal link between any serious neurologic event and hepatitis B vaccination.[1] A more recent review by the Food and Drug Administration of case reports in VAERS for 1991 through 1994 concluded that there have been no unexpected adverse events reported to occur in neonates and infants given hepatitis B vaccine, despite the use of at least 12 million doses of vaccine in these age groups.[2] The adverse events cited by Dr Waisbren that he concludes are caused by hepatitis B vaccination (eg, multiple sclerosis, Guillain-Barre syndrome) (1) are rare; (2) occur in the absence of

Meeting on Hep B

hepatitis B vaccinations; and (3) have their peak incidences in the older age groups recommended to receive hepatitis B vaccinations prior to the universal infant hepatitis B vaccination policy. Establishing or disproving a causal relation between hepatitis B vaccination and these adverse events is methodologically and logistically formidable. The evidence to date suggests that even if there is a causal relation between hepatitis B vaccination and adverse neurologic events, the occurrence is exceedingly rare and is far outweighed by the benefits of vaccination.

In contrast to possible rare adverse events, infection with hepatitis B virus (HBV) was a relatively common event prior to the implementation of hepatitis B vaccination programs. During the late 1980s, between 200,000 and 300,000 persons were infected each year and the lifetime risk of HBV infection was 5%. It is estimated that each year between 5000 and 6000 persons die from HBV-related chronic liver disease in the United States.[5] Recommendations to vaccinate all infants have been made by the American Academy of Pediatrics, the American Academy of Family Physicians, and the Advisory Committee on Immunization Practices.

We disagree with Waisbren that the current plan to eliminate HBV transmission in the United States is not a "proven strategy." In fact, within the same issue of JAMA as the article by Dr Douglas, there is a report on the remarkable success of routine infant immunization in eliminating HBV transmission in Taiwan and the Pacific.[6] There are numerous other reports to support the conclusion that the current strategy to eliminate HBV transmission in the United States is a well-conceived and reasonable public health policy.

Frank Mahoney, MD
Jennifer C. Lloyd, DVM, MSPH
Gary L. Euler, DrPH
Centers for Disease Control and Prevention
Atlanta, Ga

References

1. Stratton KR, Howe CJ, Johnston RB, eds. Adverse Events Associated With Childhood Vaccines: Evidence Bearing on Causality. Washington, DC: National Academy Press; 1994.
2. Niu MT, Davis DM, Ellenberg S. Recombinant hepatitis B vaccination of neonates and infants: emerging safety data from the Vaccine Adverse Event Reporting System. Pediatr Infect Dis J. 1996;15:71-76.
3. Centers for Disease Control and Prevention. Update, vaccine side effects, adverse events, contraindications, and precautions: recommendations of the Advisory Committee on Immunization Practices. MMWR CDC Surveil Summ. 1996;45(RR-12):7-8.
4. McMahon BJ, Helminiak C, Wainwright RB, Bulkow L, Trimble BA. Frequency of adverse reactions to hepatitis B vaccine in 43,618 persons. Am J Med. 1992;92:254-256.
5. Centers for Disease Control. Hepatitis B virus: a comprehensive strategy for elimination of transmission through universal childhood vaccination: recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR Morb Mortal Wkly Rep. 1991;40(RR-13):1-20.
6. Durand AM, Sabino H Jr, Mahoney F. Success of mass vaccination of infants against hepatitis B. JAMA. 1996;276;1802-1803.(JAMA. 1997;277:1124-1125)

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via@ihot.com (email)
http://www.909shot.com (NVIC website)
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**********************************************************
We Must Have The Freedom To Choose &
Respect Everyone's Choice
**********************************************************
Any information obtained here is not to be
construed as medical or legal advice.  The
decision to vaccinate is yours alone.

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Hepatitis B law under review
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Sent: Saturday, 27 March 1999 3:04
To: van@mypostbox.com
Subject: Hepatitis B law under review


        Ohio's Greatest Home Newspaper


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Hepatitis B law under review

March 24, 1999

By Mark D. Somerson
Dispatch Medical Reporter

c.. Legislation would suspend the law requiring children to be immunized for the disease while the issue is debated.

The state legislator who helped enact a law last year requiring Ohio children to be immunized against hepatitis B is trying to suspend it.

What began as a legislative effort to protect the public health has become a debate over parents' rights, big government and vaccination risks.

"What this means is we could have an unknown cohort of kids not protected against hepatitis B,'' said Joe Bronowski, senior adviser for immunization at the Ohio Department of Health, the agency responsible for coordinating vaccinations.

"This is a very serious disease.''

Opponents, however, said they never got the chance to voice their concerns.

By the age of 3, about 87 percent of children in Ohio are fully immunized against hepatitis B, a communicable disease that infects as many as 320,000 people nationwide each year and kills as many as 5,000.

To catch the 13 percent who fall through the cracks in Ohio, Sen. Grace Drake, R-Solon, introduced a bill in May to require children to be immunized against hepatitis B by the time they start kindergarten.

When the bill reached the House, Rep. Dale Van Vyven, R-Sharonville, said he was asked by a colleague to attach the measure to an infectious-waste bill approved by the Senate.

The amended bill passed 95-0, was signed by Gov. George V. Voinovich in July and took effect in September.

"It wasn't until late last year, quite some time after passage of the measure, that questions concerning the safety of the hepatitis B vaccine reached my office,'' Van Vyven said during House testimony three weeks ago.

Van Vyven, chairman of the House Health, Retirement and Aging Committee, sponsored House Bill 200, which would suspend the law indefinitely while the issue is debated.

"No one argues that measures to prevent the spread of hepatitis B

should be in place,'' he said. "The argument lies in requiring parents to have their children immunized as a condition of entering kindergarten.

"Is the hepatitis B vaccine truly beneficial to the pre-kindergarten group and whose decision should it really be . . . the state's, the pediatricians' or the parents?''

About 38 states require children to be fully immunized against hepati tis B before they enter kindergarten.

Hepatitis B, spread through blood and bodily fluids, causes liver disease. It is most commonly transmitted through sexual contact, intravenous drug use and needle sticks.

The vaccine was developed in the 1980s. By 1991, the U.S. Centers for Disease Control and Prevention in Atlanta recommended that children be immunized against the disease.

In Ohio, the law already requires children entering kindergarten to be fully immunized against polio, diphtheria, tetanus, pertussis, mumps, measles and rubella.

One of the first opponents to call Van Vyven was Kristine Severyn, a Dayton pharmacist and director of Ohio Parents for Vaccine Safety.

"This vaccination is not necessary for all Ohio children,'' Severyn said. "The only people at high risk are promiscuous adults, babies born to infected mothers and kids in chronic households.

"There are side effects, and the state is telling people to take a risk for a disease they will not likely catch.''

The Ohio Chapter of the American Academy of Pediatrics disagrees.

"I've given more than 10,000 vaccinations and have had no (side effects) reported,'' said Dr. Ann Rogers, a Columbus pediatrician. "In fact, the hepatitis B vaccine is the safest one we give.''

Rogers is scheduled to testify today at a hearing on the bill in the House Health, Retirement and Aging Committee, where she will represent both the Ohio State Medical Association and the academy of pediatrics.

"The thrust of my practice is prevention,'' Rogers said. "I want parents to raise healthy children.''

Drake said she doesn't mind the public discussing the law.

"I think it is always a good idea to open things for debate,'' she said. "But vaccinating these children is the right thing to do.''

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John B. Classen, MD

References

1. Classen JB. Diabetes epidemic follows hepatitis B immunization program. New Zealand Medical Journal 1996;109:195.

2. Classen JB. Method and composition for an early vaccine to protect against both infectious diseases and chronic immune mediated disorders or their sequela. PCT patent application 1994;PCT/US94/08825.

3. Classen JB. The timing of immunization affects the development of diabetes in rodents. Autoimmunity 1996;In press.

4. Capps R. Potential type I trigger, vaccination timing linked to diabetes. In: Diabetes Interview. v. 48. San Francisco, Ca: Kings Publishing, 1996:1,8-9.

5. Tuomilehto J, Virtala E, Karvonen M, et al. Increase in incidence of insulin-dependent diabetes mellitus among children in Finland. International Journal of Epidemiology 1995;24:984-92.

6. Eskola J, Kayhty H, Takala AK, et al. A randomized, prospective field trial of a conjugated vaccine in the protection of infants and young children against invasive Haemophilus influenzae type b disease. NEJM 1990;323:1381-7.

7. Classen JB, Classen DC. Vaccines modulate type I diabetes. Diabetologia 1996;39:500-2.

Ministry of Health Letter #2
New Zealand Medical Journal, October 11, 1996

Immunization and diabetes

Dr. Classen has suggested in his previous letter(NZ Med J 1996; 109:195) that immunisation causes IDDM. He now repeats this claim (NZ Med J 1996; 109:**) using analysis which again has not been subject to peer review. Such assertions can cause considerable anxiety, threaten the immunization programme and hence endager public health. Hence, the need for critical peer review before publishing such allegations.

Classen fails to explain why the Aukland diabetes registry did not show any increase following the the introduction of the Hepatitis B vaccine. Furthermore, and despite Dr. Classen's claims Dr. Scott does not consider the timing of the increase in Canterbury consistent with the Classen hypothesis.

It is also innacurate to suggest that the US Public Health Service have accepted his hypothesis. Dr. Klein has advised us that the only meetings held on this issue have been to meet Dr. Classen. They have not acknowledged there is evidence of risk, but as they are already looking at long term effects of immunisation as part of the trials on acellullular pertussi vaccine, they have decided to also look at IDDM in the long term follow up. Dr. Klein supports of the other international experts consulted by the Ministry of Health, there is no evidence of an association.

<P>"Is the hepatitis B vaccine truly beneficial to the =
pre-kindergarten=20
group and whose decision should it really be . . . the state's, =
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pediatricians' or the parents?''
<P><B></B>About 38 states require children to be fully immunized =
against=20
hepati<!--comphy--> tis B before they enter kindergarten.
<P>Hepatitis B, spread through blood and bodily fluids, causes =
liver=20
disease. It is most commonly transmitted through sexual contact,=20
intravenous drug use and needle sticks.
<P>The vaccine was developed in the 1980s. By 1991, the U.S. =
Centers for=20
Disease Control and Prevention in Atlanta recommended that =
children be=20
immunized against the disease.
<P>In Ohio, the law already requires children entering =
kindergarten to be=20
fully immunized against polio, diphtheria, tetanus, pertussis, =
mumps,=20
measles and rubella.
<P>One of the first opponents to call Van Vyven was Kristine =
Severyn, a=20
Dayton pharmacist and director of Ohio Parents for Vaccine Safety.
<P>"This vaccination is not necessary for all Ohio children,'' =
Severyn=20
said. "The only people at high risk are promiscuous adults, babies =
born to=20
infected mothers and kids in chronic households.
<P>"There are side effects, and the state is telling people to =
take a risk=20
for a disease they will not likely catch.''
<P>The Ohio Chapter of the American Academy of Pediatrics =
disagrees.
<P>"I've given more than 10,000 vaccinations and have had no (side =

effects) reported,'' said Dr. Ann Rogers, a Columbus pediatrician. =
"In=20
fact, the hepatitis B vaccine is the safest one we give.''
<P>Rogers is scheduled to testify today at a hearing on the bill =
in the=20
House Health, Retirement and Aging Committee, where she will =
represent=20
both the Ohio State Medical Association and the academy of =
pediatrics.
<P>"The thrust of my practice is prevention,'' Rogers said. "I =
want=20
parents to raise healthy children.''
<P>Drake said she doesn't mind the public discussing the law.
<P>"I think it is always a good idea to open things for debate,'' =
she=20
said. "But vaccinating these children is the right thing to do.''
<P>
<P>

<HR>

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Importance: Normal



-----Original Message-----
From: Bart Classen [mailto:Classen@worldnet.att.net]
Sent: Thursday, 10 October 1996 1:31
To: Recipient list suppressed
Subject:
```

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To whom it may concern:

Enclosed is an update of the ongoing communication I have been having with the New Zealand Ministry of Health regarding the Hepatitis B vaccine and the New Zealand diabetes epidemic.

Bart Classen, Letter #2
The Diabetes Epidemic and The Hepatitis B Vaccine
(letter to editor, New Zealand Medical Journal, 109: ?? 1996)

Dr. Poutasi replied to my letter (1) which noted a rapid rise in the incidence of insulin dependent diabetes (IDDM) following a hepatitis B immunization program in New Zealand. Her response contained several statements which should be addressed. She wrote " international experts who all agree there is no association between immunization and diabetes." Many experts in the US Public Health service have acknowledged my data (2,3) and have had several meetings to specifically review it (4). The outcome of these meetings is that the US government is studying the affect of the pertussis vaccine on IDDM in Sweden (National Vaccine Advisory Committee Meeting, Washington, DC, May 6-7, 1996, announced by Dr. David L Klein, National Institutes of Allergy and Infectious Diseases, tel: 301-496-5305). I recently presented data at an FDA meeting from a collaborating with Dr. Tuomilehto who runs the diabetes registry for the Finnish Public Health System (5). We studied the incidence of diabetes in 114,000 children randomized to receive 4 doses of the HiB or 1 dose of the HiB vaccine (6). The results revealed more cases of diabetes (205 versus 185) in the group receiving 4 doses versus 1 dose of vaccine (paper in preparation). This is equivalent to a minimum increase in IDDM of 23 cases/100,000 people immunized. The statement quoted above is clearly incorrect.

After reading my letter (1), Dr. Russell Scott who runs the diabetes registry in Christchurch has sent me data which shows that the incidence of IDDM has remained elevated during the 6 year interval, 1989-1994, on average by over 50% compared to the years 1982- 1987, as predicted based on my earlier data. This sustained rise is highly statistically significant and can not be readily explained by temporal variation as Dr. Poutasi suggests. She further added that the rise could not be do to the hepatitis B immunization since there was no rise after 1989, when the initiation of immunization was changed from birth to 6 weeks. Our data does show that immunization at birth reduces the risk of diabetes (7) however her reasoning is misleading since most of those immunized in 1988-1989 were immunized after 6 weeks of life as part of a catch up program.

The editors of the New Zealand Medical Journal should be commended for their willingness to publish letters which challenge established views. The Ministry of Health should try to get all data on this important topic made public as soon as possible so everyone can review it, even if the data is published as part of a letter. Dr. Scott has suggested that his cohort data may indicate that children born in 1988, and thus immunized at birth with the Hepatitis B vaccine, have a reduced risk of developing diabetes. If this is the case then the Ministry of Health's efforts in slowing dissemination of the data may result in needlessly causing individuals to develop IDDM.

John B. Classen, MD

References

1. Classen JB. Diabetes epidemic follows hepatitis B immunization program. New Zealand Medical Journal 1996;109:195.

2. Classen JB. Method and composition for an early vaccine to protect against both infectious diseases and chronic immune mediated disorders or their sequela. PCT patent application 1994;PCT/US94/08825.

3. Classen JB. The timing of immunization affects the development of diabetes in rodents. Autoimmunity 1996;In press.

4. Capps R. Potential type I trigger, vaccination timing linked to diabetes. In: Diabetes Interview. v. 48. San Francisco, Ca: Kings Publishing, 1996:1,8-9.

5. Tuomilehto J, Virtala E, Karvonen M, et al. Increase in incidence of insulin-dependent diabetes mellitus among children in Finland. International Journal of Epidemiology 1995;24:984-92.

6. Eskola J, Kayhty H, Takala AK, et al. A randomized, prospective field trial of a conjugated vaccine in the protection of infants and young children against invasive Haemophilus influenzae type b disease. NEJM 1990;323:1381-7.

7. Classen JB, Classen DC. Vaccines modulate type I diabetes. Diabetologia 1996;39:500-2.

Ministry of Health Letter #2
New Zealand Medical Journal, October 11, 1996

Immunization and diabetes

Dr. Classen has suggested in his previous letter(NZ Med J 1996; 109:195) that immunisation causes IDDM. He now repeats this claim (NZ Med J 1996; 109:**) using analysis which again has not been subject to peer review. Such assertions can cause considerable anxiety, threaten the immunization programme and hence endager public health. Hence, the need for critical peer review before publishing such allegations.

Classen fails to explain why the Aukland diabetes registry did not show any increase following the the introduction of the Hepatitis B vaccine. Furthermore, and despite Dr. Classen's claims Dr. Scott does not consider the timing of the increase in Canterbury consistent with the Classen hypothesis.

It is also innacurate to suggest that the US Public Health Service have accepted his hypothesis. Dr. Klein has advised us that the only meetings held on this issue have been to meet Dr. Classen. They have not acknowledged there is evidence of risk, but as they are already looking at long term effects of immunisation as part of the trials on acellullular pertussi vaccine, they have decided to also look at IDDM in the long term follow up. Dr. Klein supports of the other international experts consulted by the Ministry of Health, there is no evidence of an association.

Informal Consultation on Vaccines and Diabetes
Monday, January 30, Solar Building Room 1A4

9:00 Welcome Dr. John La Montagne

Introductions Dr. Regina Rabinovich

Background and Issues

9:15 Immunologic aspects of type I diabetes Dr Bart Classen

Animal Studies

Ecologic Studies

10:30 Break

10:45 Discussion

Questions to be addressed

Experiments in animal model systems

How faithfully do the NOD and the BB rat model systems reflect human disease? How does aging in these systems equate with humans?

What are the problems inherent in this experimental model?

Are dosages and route of administration appropriate?

What can be learned from these model systems that can be applied to the pathegenesis of human disease?

What are the mechanisms of pathogenesis in the model systems and in humans? What are the key determinants of observed chan~es in animals?

Are there other potential consequences of early presentation of antigens to the neonatal immune system in animals? In humans?

INFORMAL CONSULTATION ON VACCINES AND DIABETES
January 30, 1995

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NIAID Participants
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Dr. David Klein
Ms. Heidi Friedman
Ms. Deanna Kruszon-Moran

Incidence of Insulin Dependent Diabetes in Christchurch, New Zealand in 0-19 Year Olds.

(Mean yearly population 0-19 year olds: approximately 100,000)

Year	Incidence (cases/100,000 children)	
1970	5	Retrospective
1971	6	Average incidence 1970-1975: 8.6
1972	11.4	Approximate number of cases: 52
1973	7.3	
1974	9.5	
1975	12.5	
1976	9.8	Retrospective
1977	9.8	Average incidence 1976-1981:10.8
1978	15	Approximate number of cases:65
1979	9	
1980	7	
1981	14	
1982	12.5	Prospective
1983	12.5	Average incidence 1982-1987:11.2
1984	13.4	Approximate number of cases:73
1985	12.5	
1986	8.6	
1987	7.6	
1988	9.6	Hep B Immunization program begins
1989	16.4	Prospective
1990	21.4	Average incidence 1989-1994:17.2
1991	17.4	Approximate number of cases:103
1992	17.4	
1993	11.4	P=0.0001 (comparing 1982-1987 vs 1989-1994)
1994	19.4	P calculated using a normal approximation of a Poisson Distribution

>From shotinfo@ozemail.com.au Sun Apr 4 13:31:12 1999
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Importance: Normal

-----Original Message-----
From: karin schumacher [mailto:mandee@worldnet.att.net]
Sent: Monday, 29 July 1996 1:40
To: Vaccine Information & Awareness
Subject: HEPATITIS B VACCINE: DOCTORS NOT IN FAVOR

Doctors not sold on hepatitis B baby shots
ELISABETH ROSENTHAL
New York Times News Service
10-Mar-1993 Wednesday

More than a year after public health groups and medical societies recommended that every infant be vaccinated against hepatitis B, many pediatricians are defying this wisdom. Rebelling pediatricians point out that the hepatitis B virus, which causes a potentially fatal liver infection, is generally acquired in the late teens or early adulthood and no one knows whether immunity through a vaccine delivered in infancy will persist 15 to 20 years later. They say the recommended strategy will immunize children who are unlikely to be exposed to the disease. And they add that on top of all that, the vaccine, though safe, is relatively expensive. "I'm in general very strongly in favor of immunizations, but I'm not in favor of the hepatitis B vaccine being used in newborns," said Dr. Sydney Z. Spiesel, a pediatrician affiliated with Yale University who has done research in vaccine development.

"The current policy is based on getting kids when they are too young to fight back and hoping there will be enough residual immunity that many will be protected in later life," he said. "I don't know of a single immunologist who believes this to be true." A recent survey of all the pediatricians in North Carolina found only about half were giving the vaccine to infants and only about a third of family-practice doctors were doing so. "There are still a number of doctors who are giving all the other vaccines, but not this one," said Dr. Gary L. Freed, an assistant professor at the University of North Carolina, who conducted the survey and supports the use of the shots. In January, even among vaccine programs sponsored by the national Centers for Disease Control and Prevention, 11 out of 63 were not offering the vaccine. Some local governments felt the vaccine was not a priority, given their limited budgets.

CDC in favor
Hepatitis B virus is generally acquired through sexual intercourse or contact with an infected person's blood, through sharing needles, for

example, although young children living in extremely close contact with a person carrying the virus may acquire it as well. While acknowledging some problems with the current vaccination strategy, officials at the Centers for Disease Control and the American Academy of Pediatrics say the effort is justified and strongly recommend that the series of three shots be added as a routine infant vaccination.
They say there is evidence to suggest that at least some infants who receive the vaccine will remain protected into the teen-age years and that a single booster shot will probably be all that is necessary for those who do not. They add that 8 percent of hepatitis B infections are acquired before the age of 10, and that a child's chances of developing a deadly form of hepatitis B are three times as great as those of adults.

More to the point, these officials say that programs aimed at people at risk for hepatitis B -- infants of women with the infection, intravenous drug users, homosexual men, immigrants, health-care workers and people with multiple sexual partners -- have failed to stem the spread of the disease. About a third of people with hepatitis B have no risk factors. They believe that many pediatricians shy away from this particular vaccine because they do not witness the devastation caused by hepatitis B.
"Pediatricians say, 'I don't see this disease, so why should I immunize all my patients against it?' " said Dr. Caroline Breese Hall, a professor of pediatrics at the University of Rochester and chairman of the American Academy of Pediatrics Committee on Infectious Disease. "They don't understand how important this is."

Rare in children
Children rarely get hepatitis B, and even when they do, it generally does not cause them problems for decades. At all ages, the initial infection with the virus often produces minimal symptoms, and in most people the virus disappears without complications. But 10 percent of people will develop a chronic infection; these carriers, who may not know they are infected, can spread the disease and, over decades, the persistent presence of the virus can lead to liver failure, or in some cases cancer, that often cannot be effectively treated. Dr. Melvin Marks, medical director of Memorial Miller Children's Hospital in Long Beach, noted that hepatitis B was more common in the inner-city poor and in certain immigrant communities.
****

we must have the freedom to choose
and respect everyone's choice.

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****
any information obtained here is not to be
construed as medical advice. the decision
to vaccinate is yours and yours alone.

>From shotinfo@ozemail.com.au Sun Apr 4 13:31:11 1999
Received: from Waffle on leo by WafPeg 0.25, 93.04.04
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by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA23924
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Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: HEP B VACCINE: POOR PHYSICIAN COMPLIANCE
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Importance: Normal

-----Original Message-----
From: karin schumacher [mailto:mandee@worldnet.att.net]
Sent: Friday, 26 July 1996 7:50
To: Vaccine Information & Awareness
Subject: HEP B VACCINE: POOR PHYSICIAN COMPLIANCE

From: CYNTHIA GOLDENBERG <rabidbabe@earthlink.net>

Hepatitis B immunisation among invasive cardiologists: poor compliance with UK guidelines.
Author: Prendergast BD; Andrews NP; Thomas A; Davies L; McCabe M; Penny WJ
Address: University Hospital of Wales, Cardiff
Source: Br Heart J, 74: 6, 1995 Dec, 685-8

Abstract:
OBJECTIVES--To assess the compliance of invasive cardiologists in the United Kingdom with recently accepted national guidelines on the protection of health care workers and patients from hepatitis B. To determine levels of awareness of the infectivity and prevalence of the virus and current attitudes towards screening of patients before cardiac catheterisation and surgery.

DESIGN--Anonymous postal survey by questionnaire from the University Hospital of Wales, Cardiff. The questionnaire established the respondent's position, knowledge of hepatitis B, current immunological state, and policy towards the routine screening of patients for hepatitis B carriage.

PARTICIPANTS--All British cardiologists of consultant or senior registrar grade involved in invasive procedures.

RESULTS--The response rate was 78% (211/271). 20% of respondents had never been vaccinated against hepatitis B and about a third of those vaccinated had not complied correctly with the recommended immunisation regimen. There was little uniformity in practices for screening patients for hepatitis B carriage before invasive procedures, and the level of knowledge concerning the prevalence of hepatitis B and the risks of inoculation was poor.
CONCLUSIONS--Invasive cardiologists are at high risk of inoculation with hepatitis B. Nationally agreed guidelines are designed to protect both medical staff and patients against the risk of infection but currently they are ill heeded.

****
we must have the freedom to choose
and respect everyone's choice.

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****
any information obtained here is not to be
construed as medical advice. the decision
to vaccinate is yours and yours alone.

>From shotinfo@ozemail.com.au Sun Apr 4 13:31:11 1999
Received: from Waffle on leo by WafPeg 0.25, 93.04.04
for ADMIN on standalone PMail ; Mon, 5 Apr 1999 08:56:46 IST+5.30
Received: by leo (1.65/waf)
via UUCP; Mon, 05 Apr 99 08:56:38 IST
for leo.ilban.ernet.in!ADMIN
Received: from ozemail.com.au (uucp@localhost) by ilban.ernet.in (8.7.5/8.7.3) with UUCP id N
Received: from fep9.mail.ozemail.net (fep9.mail.ozemail.net [203.2.192.103])
by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA23965
for <ADMIN@leo.ilban.ernet.in>; Sun, 4 Apr 1999 12:31:11 +0530
Received: from avn (s1lisip07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: MICHAEL BELKIN: ACIP TESTIMONY ON HEP B
Date: Sun, 4 Apr 1999 16:57:55 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKOEGLEMAA.shotinfo@ozemail.com.au>
MIME-Version: 1.0
Content-Type: text/plain;
charset="iso-8859-1"
Content-Transfer-Encoding: 8bit
X-Priority: 3 (Normal)
X-MSMail-Priority: Normal
X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal

-----Original Message-----
From: karin schumacher [mailto:via@access1.net]
Sent: Saturday, 20 February 1999 6:58
To: via
Subject: MICHAEL BELKIN: ACIP TESTIMONY ON HEP B

Michael Belkin wrote:
>
> *SECOND TESTIMONY OF MICHAEL BELKIN BEFORE THE ADVISORY COMMITTEE ON*
> *IMMUNIZATION PRACTICES -- CENTERS FOR DISEASE CONTROL AND PREVENTION*
> *February 18, 1999 -- Atlanta Georgia*
>

> *Michael Belkin, NVIC*
>
> *The National Vaccine Information Center calls on the CDC to immediately make public all of the pre-licensure and post-licensure scientific data this Committee used to justify the safety of instituting a policy of universal vaccination of all newborn infants under two months of age with hepatitis B vaccine. We call on you to release to the public the scientific data, both basic science research into the biological mechanism of hepatitis B vaccine injury and death, and the case-controlled, long-term studies conducted on infants - including the location of the studies, the number and ages of infants enrolled and the time periods for follow-up for vaccine adverse events, including death, that you used to prove that this vaccine is safe to give to all newborns.*
>
> *We also call for the CDC and FDA to release to the public all scientific studies (if any) that were done to justify increasing the newborn dose of Merck Recombivax Hepatitis B vaccine from 2.5 mcg to 5 mcg in August 1998 -- after which my daughter died with the double dose.*
>
> *Finally, We request a detailed explanation of the statistical technique Dr. Chen from the CDC used to adjust the data in his Hepatitis B vaccine and Demyelination charts Results 1 and Results 2 in yesterday's presentation and handout, which reduced the rate from 10 times that of other vaccines to below -- including references from statistical textbooks showing that the method he used is a legitimate technique in the field of statistics.*
>
> *We expect to have the scientific data we requested no later than 30 days from today, a request we are also making under the Freedom of Information Act.*
>
> *Thank you very much*

--

****
Karin Schumacher
Vaccine Information & Awareness (VIA)
12799 La Tortola
San Diego, CA 92129
619-484-3197 (phone/voicemail)
619-484-1187 (fax)
via@access1.net (email)
http://www.909shot.com (NVIC website)
http://www.access1.net/via (VIA website)
****
We Must Have The Freedom To Choose & Respect Everyone's Choice
****

****

>From shotinfo@ozemail.com.au Sun Apr 4 13:31:14 1999
Received: from Waffle on leo by WafPeg 0.25, 93.04.04
for ADMIN on standalone PMail ; Mon, 5 Apr 1999 08:56:46 IST+5.30
Received: by leo (1.65/waf)
via UUCP; Mon, 05 Apr 99 08:56:42 IST
for leo.ilban.ernet.in!ADMIN
Received: from ozemail.com.au (uucp@localhost) by ilban.ernet.in (8.7.5/8.7.3) with UUCP id N
Received: from fep9.mail.ozemail.net (fep9.mail.ozemail.net [203.2.192.103])
by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA23710

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        for <ADMIN@leo.ilban.ernet.in>; Sun, 4 Apr 1999 12:25:28 +0530
Received: from avn  sllislp07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!ADMIN>
Subject: FW: VACCINE TAKES ITS SHOTS
Date: Sun, 4 Apr 1999 16:51:57 +1000
Message-ID: <NCBBJDFKEKEIGIHFLBEKCEGHEMAA.shotinfo@ozemail.com.au>
MIME-Version: 1.0
Content-Type: text/plain;
        charset="iso-8859-1"
Content-Transfer-Encoding: 7bit
X-Priority: 3 (Normal)
X-MSMail-Priority: Normal
X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
Importance: Normal
X-PMFLAGS: 34078848



-----Original Message-----
From: karin schumacher [mailto:via@access1.net]
Sent: Sunday, 28 March 1999 2:10
To: via
Subject: VACCINE TAKES ITS SHOTS


RAYMOND GALLUP wrote:
http://www.herald.com:80/liv art/docs/075479.htm

VACCINE TAKES ITS SHOTS
By KAREN RAFINSKI Herald Staff Writer
Lindsay Kirschner used to be an active teen. She loved tennis and
Rollerblading. Lately, though, she's been sidelined by a mysterious
illness that leaves her so tired she can't make it through the day
without a nap. She also has severe headaches and frequent nausea.

The cause? Her doctors believe the Coral Springs teen has been
debilitated by the hepatitis B vaccine administered in August 1997 --
one of the shots required for school attendance in Florida. ``Every time
you think you're getting better, something else
happens,'' says Lindsay, 15. ``I don't want my whole life to be like
this. I want to go to college in California. I want to be optimistic,
but I don't know if I have reason to be optimistic.''

But could the shot have done this to her?
Most scientists and doctors would say no. They give little credence to
accounts of disabling diseases stemming from the hepatitis B vaccine,
saying credible studies have failed to turn up any such link. Still,
there is a growing chorus of fears about the vaccine, fueled by parents
like Lindsay's mother Marilyn, whose children have gotten
sick and who want to stop making this vaccination mandatory. ``The risks
of this are just too high for the benefits,'' says Kirschner. Such fears
are drawing attention and, in two notable instances, government action.
France stopped requiring hepatitis B vaccinations for schoolchildren
last year (though not newborn vaccinations) because of public concerns,
even though a scientific study turned up no evidence of a problem. And
in New Jersey last year, the governor vetoed a bill to begin requiring
that schoolkids get the shot.

Now, because of the public's concerns, the U.S. Centers for Disease
Control and Prevention has begun a study of the safety of the vaccine,
expected to be finished in about a year. Scientists there say they acted
```

even though they still believe the vaccine is safe, that there is no evidence to support the fears and that the risks are small.
As with any vaccine, there are risks with the hepatitis B shot. Those that have been documented include allergic reactions in about one of every 600,000 vaccinations. Because of the way the vaccine is manufactured, it should not be taken by anyone with a known allergy to yeast. Other known side effects include soreness, fatigue, fever, headache, dizziness, rashes and flu-like symptoms. There is also some evidence linking it to hair loss.

Doctors want proof
But most doctors believe the risks are small, the benefits -- preventing 4,000 to 5,000 deaths a year in the United States alone -- far outweigh those risks and that the more serious side effects being attributed to the shot have not been proven. If there are serious consequences to the vaccine, these are so rare they can't be detected in studies, they say. ``The vaccine is safe,'' says Dr. James Cresanta, an epidemiologist with the Florida Department of Health in Broward County. ``It's been tested. It's been widely used for at least 10 years with few problems . . . If you can prevent 5,000 deaths a year, it seems like good public-health policy to me.''

A representative of SmithKline Beecham, which makes the vaccine, would not comment other than to point to studies and positions by mainstream medical organizations from the World Health Organization to the CDC that evaluated and supported the safety and need for the vaccine. Hepatitis B affects about one person in 200. Caused by a virus that attacks the liver, it can cause a chronic infection that leads to liver failure, cirrhosis and liver cancer. The virus is transmitted the same way that HIV, the AIDS virus, is: through contaminated blood and body fluids passed from person to person. It is spread through sexual contact, contaminated needles and from mother to child at birth. But hepatitis B is far more contagious than AIDS and much easier to get from just a single exposure. It can also live outside the body for up to a week, sometimes putting even those who don't engage in risky behavior at risk. And unlike AIDS, those who share a house with an infected person can catch hepatitis B even without sexual contact.

Kids more vulnerable
So while children are not members of the highest-risk groups -- people who have multiple sex partners or who are IV drug-users -- kids can still be exposed by an older sibling or by playing with a discarded needle, doctors say. Children are also more vulnerable to developing the chronic infection that leads to most deaths and disabilities caused by hepatitis B. Nine out of 10 adults can fight off the virus without lasting effects. But the younger children are, the more likely they are to develop chronic infections. Young children aren't immunized for the childhood risk, though, as much as they are to protect them in the future. Efforts to immunize the high-risk groups have failed, so mainstream medical organizations have endorsed a policy of immunizing babies to ensure that they are protected.

``If I knew I could get to the high-risk people, I don't think we would have to go further, but that was not accomplishable,'' says Dr. Jon Abramson, a pediatrician and chairman of pediatrics at Wake Forest University in Durham, N.C., who sits on the American Academy of Pediatrics committee on infectious diseases. ``This is a cost-effective way of making society, as a whole, healthier. You argue that vs. individual rights.''

A mother's side
That doesn't sit well with Gale Sikora of Cooper City, whose son Anthony had his first hepatitis B shot in 1994. Anthony, now 8, developed such a serious stiff neck that he was screaming in pain and had to be taken out

of day care. More than a month later, Sikora noticed that he had become clumsy, walking into walls. His day-care teacher called to say that Anthony was falling on the playground after even the slightest bump. Sikora, a registered nurse, didn't suspect the vaccine at first. She took Anthony to a series of neurologists and other doctors. They did tests to rule out a brain tumor and several rare conditions. But after harrowing months of tests that kept ruling out other causes, Sikora began to suspect the shot.

``Something did this -- this kid was a healthy kid,'' she says. ``The only thing different was the hepatitis B shot.'' Doctors treating Anthony were skeptical. They did more tests. Eventually, when they could find nothing, they filed a report with the federal government listing the incident as a possible adverse effect of the vaccine.
Sikora began to study the vaccine and found reports of other children who had developed symptoms similar to Anthony's in a telephone-book sized stack of ``adverse incidents'' reported to the federal government. Most of these were for the common, minor, well-known side effects of the vaccine. But she also found reports of stiff necks and children who had trouble walking.

She is frustrated that the government filed her report away without investigating -- that's common practice unless a troubling pattern jumps out. And she questions why the clinical trials to prove the vaccine's safety before it was put on the market followed those who got the shot for only a few days, which is standard practice. That isn't long enough, she says, to spot problems that might develop later, like her son's difficulties. Five years after taking the shot, Anthony is still getting physical
and occupational therapy, his mother says, and still suffers slights from other children on the playground, where he is unable to keep up with them.

Targets immune system
Despite the lack of proof, some doctors believe that problems suffered by Anthony Sikora and Lindsay Kirschner may indeed be the result of the hepatitis B vaccine. They suspect the shot could, in effect, confuse the body's immune system. Reports of serious adverse
effects of the vaccine vary greatly, but they have one thing in common: All are autoimmune diseases, like multiple sclerosis. ``When the body produces antibodies to protect patients against the virus, some of these antibodies are attacking components of the nervous tissue in the body,'' says Dr. Pancheta Wilson, a Coral Springs internist who has treated patients with complaints that followed their getting the shot. ``It's almost as if the body is turning against itself.''

Wilson says she hopes that tests to determine who might be susceptible to problems from the vaccine could someday be developed. For now, she cautions patients with autoimmune disorders or a family history of them to avoid the vaccine. Dr. Eric Rydland, a Coral Gables pediatrician, has wondered if there might be a link between some of his autism patients and the vaccines they received months earlier. But because of that time lag, he has never reported such a link because it would be too difficult to prove. ``There's nothing I can really put my finger on,'' says Rydland. ``The problem with vaccines is they study side effects for vaccines for relatively short periods of time. I'm curious myself about how long the effects can take place.''

A pattern or coincidence?
Rydland concedes that his is not a mainstream view. Indeed, researchers say that what appears to be a pattern in the incidents reported is probably little more than coincidence: Millions of children are vaccinated, and some of them are bound to develop some of these diseases on their own, from multiple sclerosis to chronic fatigue. If those

symptoms happen to develop around the time the shot is given, parents looking for a reason for their tragedy are apt to blame a vaccine, they say, and just because a vaccine precedes a symptom doesn't mean that it caused it.

Indeed, studies have found little evidence to point to a link between vaccines and chronic debilitating side effects. For example, studies have shown that those with MS are no more likely to have had the vaccine than those without the disease and those who were vaccinated seemed to have no higher incidence of the disease. Other studies have found no conclusive evidence of any link to arthritis, chronic fatigue or other autoimmune disorders.

That's not to say the possibility of serious side effects has been absolutely ruled out, though. ``If it's rare enough -- say, a one-in-a-100,000 or one-in-a-million chance -- it'd be hard to do a big enough study to find that,'' says Cresanta, the state Health Department doctor in Broward. ``I can't say the vaccine is 100 percent safe. Even if it's 99.9 percent safe, if you give it to 1 million people, some are going to have an adverse event. They can't say it doesn't happen at all. It just means it's so rare they can't find scientific evidence for it.'' Then, the weight of the anecdotal evidence ought to be considered, says Sikora, the Cooper City mom. ``Why are they giving this to kids?'' she asks. ``There are risks to everything, but this isn't a childhood disease. So why?'' e-mail krafinski@herald.com

****

Karin Schumacher
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http://www.909shot.com (NVIC website)
http://www.access1.net/via (VIA website)

****
We Must Have The Freedom To Choose & Respect Everyone's Choice
****
Any information obtained here is not to be construed as medical
OR legal advice. The decision to vaccinate and how you
implement that decision is yours and yours alone.
****

>From shotinfo@ozemail.com.au Sun Apr 4 13:31:14 1999
Received: from Waffle on leo by WafPeg 0.25, 93.04.04
for ADMIN on standalone PMail ; Mon, 5 Apr 1999 08:56:46 IST+5.30
Received: by leo (1.65/waf)
via UUCP; Mon, 05 Apr 99 08:56:42 IST
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by uumail-relay-blr.ernet.in (8.9.0/8.9.0) with ESMTP id MAA23709
for <admin@leo.ilban.ernet.in>; Sun, 4 Apr 1999 12:25:20 +0530
Received: from avn (s1lis1p07.ozemail.com.au [203.108.154.23]) by fep9.mail.ozemail.net (8.9.
Reply-To: <shotinfo@ozemail.com.au>
From: "Meryl Dorey" <shotinfo@ozemail.com.au>
To: <leo.ilban.ernet.in!admin>
Subject: RE: Hepatitis B Vaccination being misused in India:
Date: Sun, 4 Apr 1999 16:51:48 +1000
Message-ID: <[illegible].shotinfo@ozemail.com.au>
MIME-Version: 1.0
Content-Type: text/plain;

charset="iso-8859-1"
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X-Priority: 3 (Normal)
X-MSMail-Priority: Normal
X-Mailer: Microsoft Outlook IMO, Build 9.0.2212 (4.71.2419.0)
X-MimeOLE: Produced By Microsoft MimeOLE V4.72.3155.0
In-Reply-To: <199901231151.RAA30802@uumail-relay-blr.ernet.in>
Importance: Normal
X-CMFLAGS: 340788'8

Dear Dr.,

I must truly apologise for the long delay in getting back to you with information. I have been ill for the last several months and am just now trying to catch up on a huge backlog of email. I will forward you information that I have on the Hep B vaccine and if you need more, please let me know. I am much better now so should be able to reply in a lot less than 4 months next time! :-)

Please let me know what is happening in India. We only get the media view which we know is very jaundiced (no pun intended ;-) Polio and Hep B seem to be the two main vaccines being pushed there and we would be very interested to hear about the reporting of adverse reactions after these huge mandatory campaigns (we have heard that people have been vaccinated at gunpoint in villages though we don't know if that's true?)

Thanks again,
Meryl Dorey

Meryl W. Dorey,
President
The Australian Vaccination Network, Inc.
PO Box [illegible] 02 6687 1699 Phone
Bangalow NSW 2479 02 6687 2032 FAX
van@mypostbox.com http://www.ozemail.com.au/~shotinfo
"All truth goes through three stages. First it is ridiculed. Then it is violently opposed. Finally, it is accepted as self-evident."
(Schopenhauer)

Any information obtained here is not to be construed as medical OR legal advice. The decision to vaccinate and how you implement that decision is yours and yours alone.

> -----Original Message-----
> From: ADMIN@leo.ilban.ernet.in [mailto:ADMIN@leo.ilban.ernet.in]
> Sent: Saturday, 23 January 1999 5:49
> To: dilban.ernet.in; van@mypostbox.com
> Subject: Hepatitis B Vaccination being misused in India:
>
>
> Dear Van,
>
> Environment Support Group is non-profit research and advocacy network
> on environmental, health and social justice issues. We recently
> organised a coalition of Doctors and NGOs against the misuse of the
> Hepatitis B vaccination in Bangalore, a South Indian City.
>
> Despite the Press widely reporting our concerns, the
> Government has not initiated any action against commerical agencies
> who are exploiting the ignorance of the public by creating a fear
> psychosis of the disease. I am enclosing the Press Release made in
> this regard, and request you to provide us any recent research that
> we may use to lobby with our Government to take corrective action.

> Thank you for your response ASAP.
>
> With Best wishes for the New Year.
>
> Yours sincerely,
>
> Leo F. Saldanha
> Coordinator
> Environment Support Group
>
> ---
>
> Press Release
>
> Ongoing Vaccination Campaign against Hepatitis - B Unjustified
> Causing Needless Alarm
>
> 13 January 1998
>
> There is a major ongoing campaign initiated by some commercial agencies towards Hepatitis-B vaccination through vaccination camps, by providing injections of such vaccines as Engerix-B, Shanvac-B and Hepavac. These are being conducted along with very wide publicity by non-professional agencies exploiting the ignorance of well-meaning social organisations. The claims made by these agencies certainly do not present an accurate picture of the incidence of this disease, nor the imperative for such a massive vaccination programme.
>
> As such campaigns are continuing without any intervention whatsoever from the relevant Health agencies, and there have been reported instances of excessive indulgence in making money by exploiting the ignorance of the public, the undersigned wish to make the following statement in the wide public interest. We take strong objection to such developments and aim to awaken the relevant Health authorities, Local and State Governments, and public interest agencies and public-spirited individuals to join us in evolving a relevant and rational policy of immunisation.
>
> Hepatatis-B is only one form of Jaundice, and not the most widely communicable or of immediate public health importance. For instance, there are various other types of viruses that cause jaundice, spread through water and foodstuffs, which affect the public more, e.g., Hepatitis A, C, D, E and G. Other diseases of the liver also cause jaundice for instance when there is obstruction to bile flow. Hepatitis-B is transmitted in a manner very similar to AIDS transmission, i.e., through blood and blood products, injections, sexual activity, and from an infected mother to her child.
>
> Hence, the needless alarm created by the mass vaccination drive and associated information disseminated by the various agencies involved is wholly unjustified in its proportion and not relevant at all from the public health point of view. The ignorance of the people is being exploited, spreading fear and a wrong impression about the disease as well as the effectiveness of the vaccine.
>
> Unfortunately, people have been led to believe that the vaccine guarantees protection against all forms of "jaundice" and "cancer" of the liver. Dissemination of such misguided opinion gravely limits possibilities of effective community intervention for even more

> serious diseases prevalent in our society. For instance, TB,
> Malaria, Typhoid, Measles, Polio and other such diseases that take a
> heavier toll, are being ignored to the detriment of the public health.
>
> The introduction of these vaccines is highly questionable considering
> that there is no evidence based on community studies to justify the
> same on a mass scale in Indian conditions. Studies quoted in
> justification of the present campaign are extrapolations of very
> limited research based on hospital data, largely supported by drug
> companies with vested interests. Further, any documented evidence
> in our context has not proved the extraordinary claims that are being
> made about the effectiveness of the vaccine. On the contrary, small
> local studies negate the claims to efficacy of the vaccine.
>
> The Department of Health has been shockingly silent on the essential
> facts relating to the disease, quality of the vaccine, the cost of
> the product and the manner in which the vaccines are being promoted.
> This silence has been significantly exploited to the detriment of the
> public. In fact, people feel swindled by the varying costs of the
> different vaccines at different camps. Most dangerously, there is no
> legal and medical responsibility being taken in case the vaccines
> react adversely or if the vaccination is ineffective, as should be
> the case.
>
> Such gross mis-information which are half-truths, unwarranted,
> unscientific and unethical and which unnecessarily scare the general
> public into vaccination for all, is highly condemnable, and should be
> stopped immediately.
>
> Considering the gravity of the situation, we demand the following
> action with immediate effect:
>
> 1. Stop the mass vaccination that is being introduced in schools, at
> public camps and to non-risk groups.
> 2. The drug control authorities and relevant government agencies
> should immediately step in to take corrective action against the
> prevailing vaccination campaign and involve in a mass information
> dissemination exercise presenting the facts of the disease in
> arriving at a rational disease control approach.
> 3. The vaccination programme should only be conducted under proper
> medical supervision and not at all for profit, as is presently the
> case.
> 4. The Government must take the responsibility of constituting a
> committee of experts to prepare Guidelines for the prevention of the
> disease and introduce vaccination only where needed.
> 5. The Government should step in to subsidise the cost of the vaccine
> so that high risk groups such as health care workers, high-risk
> adults including sex workers, street children, pourakarmikas, fire-
> force and police personnel, house-hold contacts of Hepatitis B
> patients, those given to cultural rituals such as tatooing, etc., are
> protected from contracting this disease or spreading it to others.
>
> In short, this statement is being made in the public interest to
> prevent confusion in the public mind over the disease and the
> exaggerated need for vaccination. This is also a strong entreaty to
> the Government to end its ambivalent attitude to the ongoing
> campaigns, and prevent exploitation of the public by the vested
> interests. Finally, this is an initiative to inform the public to
> be guarded against the ongoing campaign and approach the relevant
> authorities and other sources for accurate information on the disease
> and its control.
>
> Statement issued in the public interest by:
>

> Dr. Shirdi Prasad Tekur, Consulting Child Health Specialist and
> Community Health Expert.
>
> Dr. C. Prakash Rao, Family Physician and Secretary, Drug Action Forum-
> Karnataka (A voluntary agency concerned about the social and
> scientific aspects of rational drug use).
> Tel: 3379016
>
> In consultation with:
>
> Community Health Cell, 367, Srinivasa Nilaya, Jakkasandra, 1st Main,
> 1st Block Koramangala, Bangalore 560 034 Tel: 5531518
>
> Dr. Harshad Devarbhavi, and Dr. Philip, Gastroenterologists, St.
> John's Medical College Hospital, Bangalore.
>
> Supporting organisations:
>
> Leo F. Saldanha, Coordinator, Environment Support Group, 36,
> Reservoir Road, Basavanagudi, Bangalore 560 004 (ESG is a non-profit
> research and advocacy agency working on various issues of public
> concern)
>
> Dharma Somashekar, President, Sanmathi, 1188, 3rd Cross, 26th Main,
> 1st Phase, J. P. Nagar, Bangalore 560 078. (Sanmathi is a group of
> mothers working towards creating safe and healthy neighbourhoods in
> Bangalore)
>
> ---
>
> Fact Sheet about Hepatitis-B and the Vaccine
>
> About the disease:
>
> Hepatitis B (HB) is caused by a virus and is only one form of
> Jaundice, others being A, C, D, E and G. HB is several times more
> infectious than AIDS, and very much like AIDS only prevention works
> as there is no cure.
>
> HB transmission is strikingly similar to the transmission of AIDS,
> i.e. through blood and blood products, injections, sexual activity
> and from an infected mother to her child. Transmission of HB
> infection through mosquito bites is unknown.
>
> Some estimates put the quantum of disease carriers in India at about
> 4 crores (40 million), though this evidence is not based on large-
> scale community studies. 90% of those infected will recover, whilst
> 10% may remain as highly infectious carriers. Only 1% of these
> develops Fulminant Hepatitis. Chances of an infection at birth are
> high and directly related to the number of injections received (as
> quoted from WHO report No WHO/EPI/GEN/88.5). The chances diminish
> such that at 12 months age, it is the same as in adults. The
> incidence of HB virus is highest in blood donors, frequent
> Intravenous users, health care workers, sexually promiscuous adults,
> and children born to infected mothers.
>
> HB is one of the top 10 causes of liver cancer (ibid.). 80% of liver
> cancers are attributable to HB infection. However, liver cancers
> form only 1.4% of all cancers.
>
> World Health Organisation recommends that "in countries with chronic
> carrier rates of hepatitis B of over 2%, HB immunisation should be
> introduced as an integral part of existing childhood immunisation
> programmes as quickly as resources permit. Efforts to use this
> vaccine in ways which do not strengthen existing programmes should

> not be encouraged."
>
> Though the cost of childhood immunisation in India against HB is only
> Rs. 100 crores, the Government has not yet included this vaccination
> in its immunisation programmes. On the contrary, the Government's
> ambivalent attitude in addressing the problem has given rise,
> unfortunately, to misuse of the public ignorance creating a scare
> amongst them and promoting unnecessary vaccination camps.
>
>
> About the vaccine:
>
> The Hepatitis B vaccine is among the best ever developed against any
> disease. It is seen is as the first and effective major cancer
> vaccine. The current price is the only major deterrent towards
> launching a mass immunisation programme.
>
> The vaccine is stable and effective only if kept at temperature
> ranging between 20 to 80 Centrigrade. It should not be frozen or
> exposed to higher ambient temperature ranges.
>
> The vaccine is most effective when first given within 48 hours of
> birth, and the scheduled repeat dosages are completed depending on
> the type of vaccine given. If the repeat dosages are not complete,
> then the immunity of the individual to the disease reduces
> significantly.
>
> The effectivity of the vaccination above 1 year of age is the same as
> for adults. Thereby, from a public health point of view childhood
> immunisation is extremely important and the adults who need this
> vaccination on a priority basis are only from high-risk groups. Such
> high-risk adults are medical personnel, rescue workers (police, fire
> force, military), Dourakarmikas (municipal waste collectors), street
> children, sex workers and people with multiple sex partners, patients
> on haemodialysis or those receiving blood and blood products,
> frequent intravenous (IV) users, house-hold contacts and sex partners
> of HB patients and international travelers.
>
> Vaccination must necessarily be given under medical supervision.
> Proper records of vaccination must be maintained for future
> reference.
>
> Very little is known about the long-term effects of the vaccine. In
> India very little evidence is available about the efficacy and any
> other effects of the vaccination programme as no community surveys
> have been conducted on a significantly large scale.
>
> Issued in the public interest by:
>
> Drug Action Forum Tel: 3570016
> Community Health Cell, 367, Srinivasa Nilaya, Jakkasandra, 1st Main,
> 1st Block Koramangala, Bangalore 560 034 Tel: 5531518
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Immunization Dialogue

Plasma-derived and Recombinant Hepatitis B Vaccines

Q. *At present many of us are using recombinant vaccine for hepatitis B immunization. However, this vaccine is costly and thus 90% of children can not avail it. In this context, I solicit comments on serum derived vaccine which is much cheaper and can be made available to a larger segment of population.*

Mukul Tiwari,
Child Specialist,
Apex Child-Mother General Hospital and Research Center,
University Road, Thatipur,
Gwalior.

Reply

Dr. Tiwari has requested for comments on the plasma-derived hepatitis B (HB) vaccine. Although not explicitly asked, the spirit of the request is for help in choosing between the two types of HB vaccines available on the market-the plasma-derived and the recombinant. In comparing the two products, safety and efficacy are the major elements, cost being a third important element. As Dr. Tiwari states, the plasma-derived vaccine is less costly than the recombinant vaccine. What about safety and efficacy?

The first HB vaccine licensed in the USA was plasma-derived, in the year 1981(1). The manufacturer used 3 purification processes (pepsin, urea, formalin) and each process would inactivate at least 10^5 chimpanzee infectious doses of HB virus per milliliter and all other classes of animal viruses including retroviruses (*e.g.*, HIV; HTLV 1 and 2). Although the manufacturer of that vaccine discontinued plasma-derived production and introduced recombinant vaccine, currently there are at least 4 major manufactures, 2 in Korea, one in China and one in Taiwan producing and marketting plasma-derived vaccine in Asian countries. The purification and inactivation processes of all manufacturers are equally good and no known extraneous virus can survive them. Thus, all licensed plasma-derived vaccines are completely safe from infection with HIV, HTLV, HBV or Hepatitis C virus, *etc.* Over 30 million subjects have been given this vaccine, and the safety record is impressive(2). The overall rates of post-immunization reactions, local and systemic were not more than in placebo recipients(2).

Recombinant vaccine is manufactured in yeast cells (5 major manufacturers) or CHO cells (1 manufacturer). Their safety record is equally impressive; the side-effects, are no more than for the plasma-derived vaccine. There have been instances of Guillain-Barre syndrome following either vaccine, but causative association remains unproven. Immediate hypersnsitivity reaction has been reported after the yeast-derived vaccine but it is extremely rare(2). In short, both vaccines, plasma-derived and recombinant are very safe; the World Health Organization has also stated so(3).

Both types of vaccines are also very highly immunogenic, hence effective. Over

the coming years, more recombinant vaccines will be used, as HB virus carrier pool is declining as source material for the plasma-derived vaccine. Meanwhile, either vaccine may be used-both are safe and effective.

T. Jacob John,
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Thekkakora, 2791,
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Vellore 632 002.

REFERENCES

1. Centers for Disease Control. Hepatitis B vaccine safety: Report of an inter-agency group. MMWR 1982; 31: 465-467.
2. Hollinger FB. Hepatitis B virus. *In*: Fields Virology, 3rd edn. Eds. Fields BN, Knipe DM, Howley PM. Philadelphia, Lippincot-Raven. 1996; pp 2739-2807.
3. World Health Organization. Expanded Program on Immunization for the 1990s. WHO Bull 1992; 70: 392-393.

NOTES AND NEWS

FIRST NATIONAL CONFERENCE OF PEDIATRIC HEMATOLOGY AND ONCOLOGY

The First National Conference of Pediatric Hematology and Oncology will be held on 8th and 9th November, 1997 at Mumbai, under the auspices of International Society of Pediatric Oncology (SIOP) and Indian Academy of Pediatrics (IAP) subspeciality chapter on Pediatric Hematology-Oncology (PHO Chapter of IAP).

Registration fees:	Before 31.8.97	Late fee after 31.8.97	Spot Registration
Regular Delegate	Rs. 300/-	Rs. 500/-	Rs. 750/-
Students	Rs. 150/-	Rs. 250/-	Rs. 300/-

Please send registration fees by Demand Draft only drawn in favour of "NATIONAL CONFERENCE PHO" payable at Mumbai. For further details contact: Dr. Bharat Agarwal/Dr. Rashmi Dalvi, Organizing Secretaries, Department of Pediatric Hematology, Oncology, B.J. Wadia Hospital for Children, Parel, Mumbai 400 012. Tel. No. 91-22-4129786 Extn. 344, Res: Dr. BA 6431901, Dr. RD 4443204. Telefax Clinic 91-22-6431901 or 6426846.

Readers' Forum

Hepatitis B Virus Infection

Q. I wish to seek a few clarification in relation to Hepatitis B virus infection: (i) It is claimed that Hepatitis B Virus (HBV) is transmitted via contact sports, minor abrasions, insects, mosquitoes and bedbug bites. If so, what are the chances?; (ii) Is any data available regarding HBsAg positivity in Indian children below 5 yrs and from 5-10 yrs of age?; and (iii) is there any change in schedule for HBV vaccination for babies of mothers completely vaccinated before?

S.P. Desai,
482/C Civil Court Road,
Karwar,
Karnataka 581 301.

A. Dr. Desai has raised several important issues about the epidemiology, transmission and prevention of HBV infection in children. We will address them one by one.

Horizontal transmission (*i.e.*, from person-to-person) of HBV in the school setting, and even more frequently within families, is an important mode of transmission in developing countries in Africa and Asia which have a moderate to high prevalence of infection. The exact mode(s) of transmission of HBV in these settings is not completely understood but they include contamination of open skin surfaces, including minor abrasions, with blood or infected body fluids from a HBV carrier. Similarly, HBV may be transmitted by contact sport if a person sustains an injury with a break in the skin surface which is then contaminated from blood or infected body fluid from another player. Therefore protection by HB immunization, even in older children who have not been vaccinated in infancy, is a good idea in countries (like India) where horizontal transmission via these modes is common.

HBV and hepatitis B surface antigen (HBsAg) are present in relatively high concentration in the blood of persons with chronic infection, HBsAg being present in much higher concentrations than HBV. Therefore, hematophagous insects including bedbugs and mosquitoes will have HBV and HBsAg in the stomach blood. Indeed, HBsAg has been detected in wild caught mosquitoes and from bedbugs. When the same insects bite another person they may inject saliva into the skin. Malaria sporozoites, and arthropod borne viruses such as dengue virus and Japanese encephalitis virus are found in the saliva due to replication cycles virus are found in the saliva due to replication cycles within the insect. On the other hand, HBV does not infect or replicate in insects and there is no virus in their saliva. Hence, virus transmission via an insect bite is not likely. If, on the other hand, an insect which lands on the skin after having fed on an infected carrier is smashed by slapping it and the site is then scratched, inoculation of infected blood into the skin resulting in infection is possible. The distribution of HBV is disproportionately low when compared to insect bites. Hence, this is not a mode of transmission, for all practical purposes.

The prevalence of HBsAg positivity in children less than 15 years in various parts of India has ranged from 1.3%-12.7% in different studies(1). In these studies, the prevalence in children 1-5 years and those 5-10 years were not significantly different. In India, a sizeable proportion of these children

are infected horizontally due to continued exposue. Therefore, all children, irrespective of their age would benefit from HB vaccination.

The antibody levels, following vaccination, in older infants and children are higher than in infants who are immunized at birth. This is likely to be due to the presence of passively acquired maternal antibody in young infants. However, the proportion of children who respond (*i.e.*, seroconversion rate) is similar in both age groups. Immunization at birth has the additional advantage of preventing vertical transmission from mother to infant. Since vertically acquired infection is an important mode of transmission of HBV and results in high rates of chronic carriage, it is more beneficial to start immunization at birth even though the antibody levels may be lower than when immunization is delayed. We, therefore, do not recommend a change in schedule for HBV vaccination of babies of mothers completely vaccinated before.

REFERENCE

1. Kant L, Arora NK. Transmission of hepatitis B virus in children: Indian scenario. *In*: Hepatitis B in India: Problems and Prevention. Eds. Sarin SK, Singhal AK. New Delhi, CBS Publishers and Distributors, 1996; pp 21-32.

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NOTES AND NEWS

XVI ANNUAL CONFERENCE OF IAP WEST BENGAL STATE BRANCH

The XVI Annual Conference of West Bengal State Branch of IAP is to be held on 21st December 1997 at Barasat. The Conference will be hosted by IAP North 24 Parganas District Branch. Last date of submission of Scientific Papers with Abstracts is 31st October, 1997. These should be accompanied with a Registration Fee of Rs. 150/- as Demand Draft in the name of "XVI Annual IAP West Bengal State Conference". For further details, please contact: Dr. D. Barman Roy, Organizing Secretary, IAP West Bengal State Conference, Pioneer Park, Barasat, North 24 Parganas, West Bengal.

16. Govt of India **CSSM review,** A Newsletter on the Child Survival and Safe Motherhood Programme, No.32, August 1995.
17. Krishnan, R.et al (1983). **Bull WHO,** 61 (4) 689-692
18. Jacob John, T. (1976). **Brit.Med.J.** 1 : 812
19. Galazka, A.M. et al (1984) **Bull WHO,** 62 : 357
20. Jacob John, T. (1988). **Ann N.Acad. Med.Sc.** 24 (4) 241-247
21. AHRTAG (1988) **Dialogue on diarrhoea No.** 33 June P.7
22. Ministry of Health, Govt.of India (1977). **Manual on Immunization,** Dept. of Family Welfare.
23. Nightingale, E. (1977). **N.Eng.J.Med.,** 297 : 249
24. Malnick, J.L. (1978). **Bull WHO,** 56 : 21
25. WHO (1980). **Wkly Epi.Rec.,** 55 : 361-366; 369-374
26. Jacob John, T. (1976). **Brit. Med.J.,** 1 : 812
27. Reid, D et al (1969). **Lancet,** 1 : 564
28. Ghosh, S. et al (1970). **Indian Pediatrics,** 7 : 78
29. Ussova, J. et al (1971) in **Some Problems in Pediatrics in India and Soviet Union,** Kalavati Saran Children's Hospital, New Delhi
30. Govt of India, **CSSM review,** A Newsletter on Child Survival and Safe Motherhood Programme No.11 November 1993.
31. Recommendations of the Public Health Service Advisory Committee on Immunization (1978). **Ann Intrern Med.,** 88 : 218.
32. Beale, A.J. (1969). **Brit.Med.Bull,** 25 : 148
33. Schonberger, L.B. et al (1976). **Am.J.Epi.,** 104 : 202
34. Jawetz, E. (1978). **Review of Medical Microbiology,** 13th ed., Lange Medical Publ., California.
35. Sabin, A.B. (1980). **Bull WHO** 58 (1) 141
36. John T.J. (1981). **Indian Pediatrics,** 18 (8) 503
37. WHO (1975). **Wkly Epi Rec.,** 50 : 205-209
38. WHO (1976). **WHO Chronicle,** 30 : 72-75
39. Domok, I and D.I. Magrath (1979). **Guide to Poliovirus Isolation and Serological Techniques for Poliomyelitis Surveillance,** WHO Offset Pub.No.46
40. WHO (1996), **Weekly Epidemiological Record** No.22, 31 May 1996
41. Govt of India (1995), **CSSM review,** A Newsletter on Child Survival and Safe Motherhood Programme, No.31, July 1995
42. WHO (1997), **World Health Report 1997,** Conquering Suffering, Enriching humanity

VIRAL HEPATITIS

Viral hepatitis may be defined as infection of the liver caused by any of half dozen viruses : hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis D virus (the delta agent), epidemic non-A hepatitis virus and by atleast two non-A, non-B viruses i.e., hepatitis C (HCV) and hepatitis E (HEV). It is known that many other viruses may be implicated in hepatitis such as cytomegalo-virus, Epstein-Barr virus, yellow fever virus and rubella virus. Viruses of herpes simplex, varicella and adenoviruses can also cause severe hepatitis in immunocompromised individuals, but are rare.

Problem statement

It is widely prevalent in India. Hepatitis A virus (HAV) causes a relatively benign disease and does not constitute a major public health problem in India. *(1).* In contrast, hepatitis B is responsible for severe liver damage and is associated with chronic liver disease and hepatocellular carcinoma. Hepatitis virus non-A, non-B consists of atleast two distinct viruses – one that is parenterally transmitted like hepatitis B virus i.e., hepatitis C, and the other hepatitis E, transmitted through the faecal-oral route like hepatitis A virus. Information regarding the occurrence of delta virus is lacking in India.

It has been estimated that approximately 4 million people in India suffer every year from one or the other form of acute viral hepatitis. Epidemics are almost exclusively of the enterically transmitted NANB hepatitis while in sporadic cases, all forms of acute hepatitis contribute. Among adults, NANB hepatitis constitutes a little more than 50 per cent of sporadic cases and HBV hepatitis another 40 per cent. In children, on the other hand, HAV is the major form of acute hepatitis (50%), HBV comparatively less (18%) and NANB about 30 per cent. These infections pose health problems of significant magnitude in India *(2).*

HEPATITIS A

Hepatitis A (formerly known as "infectious" hepatitis or epidemic jaundice) is an acute infectious disease caused by hepatitis A virus (HAV). The disease is heralded by non-specific symptoms such as fever, chills, headache, fatigue, generalised weakness and aches and pains, followed by anorexia, nausea, vomiting, dark urine and jaundice. The disease spectrum is characterised by the occurrence of numerous subclinical or asymptomatic cases. The disease is benign with complete recovery in several weeks. The case fatality rate of icteric cases is less than 0.1 per cent, usually from acute liver failure and mainly affects older adults. Although the disease has, in general, a low mortality (0.1%), patients may be incapacitated for many weeks.

Problem statement

Being an enterovirus infection like poliomyelitis, heptaitis A is endemic in most developing countries, with frequent outbursts of minor or major outbreaks. The exact incidence of the disease is difficult to estimate because of the high proportion of asymptomatic cases. However, according to WHO about 10–50 persons per 100,000 are affected annually. Evidence from several developed countries indicate that the incidence of hepatitis A is declining. For example, in Scandinavia, the disease is no longer endemic, where only 1 per cent of population under 16 years now has antibody *(3).* However in many others like UK, adult population have antibodies to HAV, especially adults over 50 years of age.

The exact incidence of hepatitis A in India is not known. The Indian literature is replete with numerous reports of sporadic and epidemic occurrence of this disease in various cities, residential colonies and campuses *(4).* Epidemics of hepatitis A often evolve slowly, involve wide geographic areas and last many months, but, common source epidemics (e.g., faecal contamination of drinking water) may evolve explosively *(5).*

Agent factors :

(a) AGENT : The causative agent, the hepatitis A virus, is an enterovirus (type 72) of the Picornaviridae family *(6).* It multiplies only in hepatocytes. Faecal shedding of the virus is at its highest during the later part of the incubation period and early acute phase of illness. Only one serotype is known. (b) RESISTANCE : The virus is fairly resistant to heat and chemicals. It has been shown to survive more than 10 weeks in well water *(7).* It withstands heating to 60 deg C for one hour, and is not affected by chlorine in doses usually employed for chlorination. Formalin is stated to be an effective disinfectant. The virus is inactivated by ultraviolet rays and by boiling for 5 minutes or autoclaving. In short the virus survives for long periods under variable conditions and resists many procedures that eliminate or inactivate most bacterial agents. (c) RESERVOIR OF INFECTION : The human cases are the only reservoir of infection. The cases range from asymptomatic infections to severe ones. Asymptomatic (anicteric) infections are especially common in children. These cases play an important role in maintaining the chain of transmission in the community. There is no evidence of a chronic carrier state. (d) PERIOD OF INFECTIVITY : The risk of transmitting HAV is greatest from 2 weeks before to 1 week after the onset of jaundice. Infectivity falls rapidly with the onset of jaundice *(8).* (e) INFECTIVE MATERIAL : Mainly man's feaces. Blood, serum and other fluids are infective during the brief stage of viraemia. (f) VIRUS EXCRETION : HAV is excreted in the faeces for about 2 weeks before the onset of jaundice and for up to one week thereafter. The virus may also be excreted in urine *(3).*

Host factors

(a) AGE : Infection with HAV is more frequent among children than in adults. However, people from all ages may be infected if susceptible. In young children, infections tend to be mild or

subclinical; the clinical severity increases with age. In India, by the age of 10 years, 90 per cent of healthy persons have serological evidence of HAV infection *(9)*. (b) SEX : Both sexes are equally susceptible. (c) IMMUNITY : Immunity after attack probably lasts for life; second attacks have been reported in about 5 per cent of patients. Most people in endemic areas acquire immunity through sub-clinical infection. The IgM antibody appears early in the illness and persists for over 90 days. IgG appears more slowly, and persists for many years.

Environmental factors

Cases may occur throughout the year. In India the disease tends to be associated with periods of heavy rainfall *(10)*. Poor sanitation and overcrowding favour the spread of infection, giving rise to water-borne and food-borne epidemics. Paradoxically, when standards of hygiene and sanitation are improved, morbidity from infection with enteric viruses may increase. This is what happened with poliomyelitis, and is now being seen with hepatitis A *(11)*.

Modes of transmission

(a) *Faecal-oral route :* This is the major route of transmission. It may occur by direct (person-to-person) contact or indirectly by way of contaminated water, food or milk. Water-borne transmission, is not a major factor in developed countries, where food-borne outbreaks are becoming more frequent. For example, consumption of raw or inadequately cooked shellfish cultivated in sewage polluted water is associated with epidemic outbreaks of hepatitis A *(12)*. Direct transmission comprises an array of routes such as contaminated hands or objects such as eating utensils. Direct infection occurs readily under conditions of poor sanitation and overcrowding.

(b) *Parenteral route :* Hepatitis A is rarely, if ever, transmitted by the parenteral route (i.e., by blood and blood products or by skin penetration through contaminated needles). This may occur during the stage of viraemia. This mode of transmission is of minor importance *(13)*.

(c) *Sexual transmission :* As a sexually transmitted infection hepatitis A may occur mainly among homosexual men because of oral-anal contact *(14)*.

Incubation period

15 to 45 days (usually 25 to 30 days). The length of the incubation period is proportional to the dose of the virus ingested *(7)*.

Diagnosis

A specific laboratory diagnosis of hepatitis A can be obtained by *(15)* :

a. demonstration of HAV particles or specific viral antigens in the faeces

b. demonstration of a rise in anti-HAV titre

c. Detection of IgM antibody to HAV in the patient's serum; this antibody appears early in the illness, and persists for a limited time, usually for 3 to 4 months after onset; IgG antibody indicates past infection and immunity.

Prevention and containment

a. Control of reservoir :

Control of reservoir is difficult because of the following factors : (a) faecal shedding of the virus is at its height during the incubation period and early phase of illness (b) the occurrence of large number of subclinical cases (c) absence of specific treatment, and (d) low socio-economic profile of the population usually involved. Strict isolation of cases is not a useful control measure because of (a) and (b). However, attention should be paid to the usual control measures such as notification, complete bed rest and disinfection of faeces and fomites. The use of 0.5 per cent sodium hypochlorite has been strongly recommended as an effective disinfectant *(16)*.

b. Control of transmission

The best means of reducing the spread of infection is by promoting simple measures of personal and community hygiene, e.g., handwashing before eating and after toilet; the sanitary disposal of excreta which will prevent contamination of water, food and milk; and purification of community water supplies by flocculation, filtration and adequate chlorination. A question is often asked how much chlorine is needed to inactivate the virus. Studies indicated that 1 mg/L of free residual chlorine can cause destruction of the virus in 30 minutes at pH values of 8.5 or less *(17)*. The water treatment and distribution system should be improved. During epidemics, boiled water should be advocated for drinking purposes. Several countries of the world have achieved control of water-borne HAV infection. Other control measures include proper autoclaving of syringes, needles and other equipment. If all these measures are properly implemented, a substantial reduction of HAV infection can be expected.

c. Control of susceptible population :

HUMAN IMMUNOGLOBULIN : A well established procedure is the use of normal human immunoglobulin prepared from pooled plasma of healthy donors (gamma globulin) to induce passive immunity. It is recommended for (a) susceptible persons travelling to highly endemic areas. (b) close personal contacts of patients with HAV, and (c) for the control of outbreaks in institutions *(18)*. Doses of immunoglobulin recommended by WHO are given in Table 31 on page 94.

Gamma globulin given before exposure to the virus or early during the incubation period, will prevent or attenuate a clinical illness but does not always prevent infection and the excretion of the virus *(10)*. Inapparent and subclinical infection may develop. This may be followed by passive-active immunity, which could confer prolonged immunity on the individual *(10)*. The efficacy of passive immunization depends upon the presence of hepatitis A antibody in the immunoglobulin and on the dosage and time of administration relative to exposure *(19)*. When given in proper dosage within 1 to 2 weeks of exposure, it prevents illness in 80 to 90 per cent of those exposed. If given after onset of symptoms, no benefit is likely to result.

The value of immunoglobulin in controlling outbreaks of infection in places such as nursery schools has been demonstrated. However, a WHO Expert Committee *(10)* has expressed the view that the use of immunoglobulin on a very large scale is unwise for three reasons : (i) the individual with subclinical infection may still disseminate the virus in the general community (ii) the practice appears to be wasteful, and (iii) repeated injection of immunoglobulin may be undesirable in healthy children. The largescale routine use of immunoglobulin as a preventive measure for hepatitis A among school-age children, or other special populations, has not gained widespread acceptance *(10)*.

d. Vaccines :

The successful propagation of hepatitis A virus in 1979, in cell cultures and in continuous cell strains of primate origin has opened the way to the preparation of hepatitis A vaccines, and these are now under development *(20)*.

HEPATITIS B

Hepatitis B (formerly known as "serum" hepatitis) is an acute systemic infection with major pathology in the liver, caused by hepatitis B virus (HBV) and transmitted usually by the parenteral route. It is clinically characterised by a tendency to a long incubation period (6 weeks to 6 months) and a protracted illness with a variety of outcomes. Usually, it is an acute self-limiting infection, which may be either subclinical or symptomatic. In approximately 5 to 15 per cent cases, HBV infection fails to resolve and the affected individuals the

become persistent carriers of the virus. Persistent HBV infection may cause progressive liver disease including chronic active hepatitis and hepatocellular carcinoma. There is also evidence of a close association between hepatitis B and primary liver cancer *(11)*. Hepatitis B virus can form a dangerous alliance with delta virus and produce a new form of virulent hepatitis which is considered to be a widespread threat for much of the world.

Problem statement

WORLD

Hepatitis B is endemic throughout the world, especially in tropical and developing countries and also in some regions of Europe *(11)*. Its prevalence varies from country to country and depends upon a complex mix of behavioural, environmental and host factors. In general, it is lowest in countries or areas with high standards of living (e.g., Australia, North America, N. Europe); and, highest in countries or areas where socio-economic level is lower (e.g., China, SE Asia, S. America). The patterns of hepatitis B prevalence differ enormously *(21)*. In most industrialised countries, the carrier rate is less than 1 per cent, while in some areas of Africa and South East Asia, it is higher than 30 per cent.

It has been estimated that more than 2 billion people have been infected with the hepatitis B virus (HBV) globally; this figure includes some 350 million chronically infected carriers of the virus *(22)*. Three-quarters of the world's population live in areas where there are moderate to highly endemic levels of infection. In developing countries, HBV infection usually occurs during childhood; while in developed countries it usually occurs among adult members of high risk groups defined by life style or occupation. HBV infection is directly related to 1–2 million deaths per year. Although acute hepatitis B is an important disease, most of the morbidity and mortality occurs in chronic carriers, approximately one-quarter of whom will die from chronic active hepatitis, cirrhosis or primary liver cancer. Primary liver cancer is a leading cause of death in males in most of Sub-Saharan Africa and much of East and South-East Asia and the Pacific Region.

Researchers have divided the world into areas where the presence of the infection is "high", "intermediate" or "low", with carrier rate of more than 5%, between 2% and 5%, and less than 2% respectively. In the "high" catagory, where most of the population becomes infected, either as newborn or in childhood are Africa, parts of East Asia , the Pacific Basin, portions of Middle East, Asia Minor and part of the Caribbean. The "intermediate" areas include parts of the Southern and Eastern Europe, the Middle East, Western Asia through Indian Subcontinent and some parts of Central and South America. In these areas both child-to-child and adult-to-adult transmission occur. The "low" areas include North America, Western Europe, Australia and parts of South America. Here, most infections occur in adults through sexual activities, needle sharing during drug abuse, or during occupational exposure *(22)*.

By the year 2000, applying the current prevalence of carriers on to projected year 2000 population data, it is estimated that there will be 400 million HBV carriers in the world if HB vaccine is not widely used *(23)*.

INDIA

Hepatitis B is a major public health problem in India. During 1992, a total of 98,047 cases and 1268 deaths of viral hepatitis were reported *(24)*, of which approximately 30-40 per cent are likely to be hepatitis B, *(23)*. Since many episodes go unreported or unrecognized, the actual number of hepatitis B cases would be anybody's guess. Studies conducted by the National Institute of Virology at Pune showed that the rate of chronic carriers of HBsAg (Australia antigen) varied from 0.6 to 5.8 per cent *(9)*. HBV was also implicated in a major epidemic outbreak in Ahmedabad (Gujarat) in 1984. The total number of cases in the epidemic was 1783 with an incidence of 0.59 per 1000 population, and a case fatality rate of 15.6 per cent *(25)*.

Hepatitis B has no seasonal pattern. The cyclic recurrences that have been a feature of the epidemiology of hepatitis A have not been observed *(15)*.

Agent factors

(a) AGENT : Hepatitis B virus was discovered by Blumberg in 1963. Efforts to grow this virus have been so far unsuccessful *(26)*. HBV is a complex, 42-nm, double-shelled DNA virus, originally known as the **"Dane particle"**. It replicates in the liver cells. HBV occurs in three morphological forms in the serum of a patient : (a) small spherical particles with an average diameter of 22-nm. These particles are antigenic and stimulate production of surface antibodies. The purified 22-nm particles are used in the preparation of hepatitis B vaccine; (b) tubules of varying length and diameter, and (c) the Dane particle which corresponds morphologically to hepatitis B virus. A person who is serologically positive for the surface antigen is circulating all morphological forms, of which 22-nm particles constitute the bulk. Of the three morphological forms, only the Dane particle is considered infectious, the other circulating morphological forms are not infectious.

Hepatitis B virus has three distinct antigens – a surface antigen, also known as "Australia antigen" (HBsAg), a core antigen (HBcAg), and an "e" antigen (HBeAg). They stimulate the production of corresponding antibodies e.g., surface antibody (anti-HBs), core antibody (anti-HBc) and "e" antibody (anti-HBe). These antibodies and their antigens constitute very useful markers of HBV infection. Patients with HBV infection are expected to have one or more HBV markers. The course of a typical acute hepatitis is outlined in Fig.1.

The surface antigen is the first to be detected. It appears in the serum during the incubation period before biochemical evidence of liver damage or the onset of jaundice. It persists during acute illness, and is usually cleared from the blood stream during convalescence. This may take 4 to 6 months. The next to appear are the "e" antigen and DNA polymerase. All these three markers precede the onset of disease. The "e" antigen (HBeAg) is a marker of virus replication and therefore a marker of infectivity. Detected within 3 to 5 days following the appearance of the surface antigen, it persists for 2 to 6 weeks. In carriers, the "e" antigen may persist for years without sero-conversion. The presence of "e" antigen indicates that the patient is highly infectious. The sero-conversion of "e" antigen into "e" antibody is considered a good prognostic feature *(10)*.

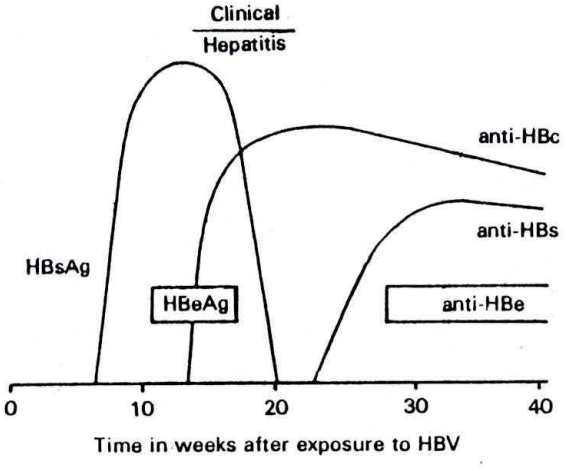

FIG.1
Markers of acute hepatitis B with time

(b) RESERVOIR OF INFECTION : Man is the only reservoir of infection which can be spread either from **carriers** or from **cases.** The continued survival of infection is due to the large number of individuals who are carriers of the virus, estimated to number over 285 million world-wide. The persistent carrier state has been defined as the presence of HBsAg for more than 9 months *(10).* Cases may range from inapparent to symptomatic cases. The risk of an adult becoming a carrier following acute infection is 5 to 15 per cent; in infants, it may exceed 50 per cent *(15).*

(c) INFECTIVE MATERIAL : Contaminated blood is the main source of infection, although the virus has been found in body secretions such as saliva, vaginal secretions and semen of infected persons.

(d) RESISTANCE : The virus is quite stable and capable of surviving for days on environmental surfaces. It can be readily destroyed by sodium hypochlorite, as is by heat sterilization in an autoclave for 30 to 60 minutes.

(e) PERIOD OF COMMUNICABILITY : The virus is present in the blood during the incubation period (for a month before jaundice) and acute phase of the disease. Period of communicability is usually several months (occasionally years in chronic carriers) or until disappearance of HBsAg and appearance of surface antibody.

Host factors

(a) AGE : In countries in which infection with HBV is relatively uncommon, the highest prevalence of the surface antigen is found in the 20-40 year age group. In countries, where infection with HBV is common, much infection occurs perinatally or during early childhood *(15).* (b) HIGH RISK GROUPS : Certain groups carry higher risks. For example, in U.S.A., the annual incidence of HBV infection in surgeons is estimated to be 50 times greater than that in the general population, and is more than twice that of other physicians. Other high risk groups comprise recipients of blood transfusions, health care and laboratory personnel, homosexuals, prostitutes, percutaneous drug abusers, infants of HBV carrier mothers and patients who are immunocompromised. Serological screening and vaccination of high-risk groups is highly recommended. (c) HUMORAL AND CELLULAR RESPONSES : Antibodies form in a week or two after onset of jaundice – the order being, first core antibody, then "e" antibody and much later surface antibody. The appearance of surface antibody signals recovery from HBV infection and the development of immunity. The occurrence of cell-mediated immunity to hepatitis B antigens has also been demonstrated *(10).*

Modes of transmission

a. Parenteral route :

Hepatitis B is essentially a blood-borne infection. It is transmitted by infected blood and blood products through transfusions, dialysis, contaminated syringes and needles, pricks of skin, handling of infected blood, accidental inoculation of minute quantities of blood such as may occur during surgical and dental procedures, immunization, traditional tattooing, ear piercing, nose piercing, ritual circumcision, acupuncture, etc. Accidental percutaneous inoculations by shared razors and tooth brushes have been implicated as occasional causes of hepatitis B *(10).*

b. Perinatal transmission :

Spread of infection from HBV carrier mothers to their babies appears to be an important factor for the high prevalence of HBV infection in some regions, particularly China and SE Asia *(27).* The risk of infection varies from country to country and may reach 40 per cent. The mechanism of perinatal infection is uncertain *(10).* Although HBV can infect the foetus in utero, this rarely happens and most infections appear to occur at birth, as a result of a leak of maternal blood into the baby's circulation, or ingestion or accidental inoculation of blood *(15).* Infection of the baby is usually anicteric and is recognized by the appearance of surface antigen between 60-120 days after birth *(10).*

c. Sexual transmission :

There is ample evidence for the spread of infection by intimate contact or by sexual route. The sexually promiscuous, particularly male homosexuals, are at very high risk of infection with hepatitis B.

d. Other routes :

Transmission from child-to-child, often called horizontal transmission, is responsible for a majority of HBV infections and carriers in parts of the world other than Asia. The researchers believe that the spread occurs through physical contact between children with skin conditions such as impetigo and scabies, or with cuts or grazes. Often transmission occurs when children play together or share the same bed *(22).*

Transmission by blood sucking arthropods (e.g., mosquitoes, bed bugs) is suspected, but there is no convincing evidence to support this suggestion *(15).*

In short, transmission occurs in a wide variety of epidemiological settings. It can spread either from carriers or from people with no apparent infection, or during the incubation period, illness or early convalescence.

Incubation period

45 to 180 days. Lower doses of the virus result often in longer incubation period. The median incubation period is said to be lower than 100 days *(28).*

Clinical picture

The symptoms and manifestations of hepatitis B are similar to those of the other types of viral hepatitis. But the picture is complicated by the carrier state and by chronic liver disease, which may follow the infection. Chronic liver disease may be severe, and may progress to primary liver cancer which, in some parts of the world, is one of the commonest human cancers, particularly in men *(29).*

PREVENTION AND CONTAINMENT

Since there is no specific treatment, prevention has been the major aim in managing viral hepatitis B. The following measures are available :

a. Hepatitis B vaccine

(i) **Plasma derived vaccine :** This is based on the surface antigen (HBsAg) which is harvested and purified from the plasma of human carriers of hepatitis B virus. The final vaccine is a formalin inactivated sub-unit viral vaccine for intramuscular injection. Each 1.0 ml dose of the vaccine contains 20 micrograms of hepatitis surface antigen formulated in an alum adjuvant. The vaccine is given in 3 doses at 0,1 and 6 months (Table 1). An effective antibody response is generally attained after 3 doses in 95 per cent of vaccinees *(2).* Immunity continues at protective levels for approximately 3–5 years. Booster doses may be given after 3–5 years.

TABLE 1

Hepatitis B vaccine : Immunization schedule

1st dose	1 ml	at elected date
2nd dose	1 ml	1 month later
3rd dose (booster)	1 ml	6 months after the first dose

Children under 10 years of age should be given half of above dosage at the same time intervals

Both pre-exposure and post-exposure administration has been recommended. Classical examples of post-exposure prophylaxis are protection of newborn infants born to carrier mothers, and individuals accidentally exposed parenterally to HBV infection through transfusion, cuts, injuries and needlesticks. It is advisable but not mandatory to give specific anti-HBs immunoglobulin with or before the first vaccine dose in post exposure cases.

Pre–exposure prophylaxis is indicated in countries with a high prevalence rate of HBV infection. In these countries, hepatitis B vaccine must be classified and used in the same category as DPT and polio *(21)*. Unfortunately, the high cost of the vaccine precluded its use in those parts of the world where it was most needed. However dramatic declines in the cost of the vaccine in the developing countries from $ 20 to between $ 0.5 to 0.2 per child dose - have allowed public health officials to consider its mass use in infant immunization programme, although it is still considered more expensive than other routine childhood vaccines. About 75 countries now use it in their national immunization programmes.

For the first time in India, Union Territory of Delhi has introduced Hepatitis B vaccine in the Universal Immunization Schedule as a pilot project. The vaccine will be administered free of cost to children with the help of WHO in the 6th, 10th and 24th week from the child's birth. his was introduced since October 1996 *(30)*.

The vaccine has no effect on the HBsAg carriers, and unnecessary in persons with surface antibody from previous infection.

(ii) **RDNA-yeast derived vaccine :** An alternate vaccine against hepatitis B has been licensed for the first time in USA in 1987, the recombinant DNA vaccine elaborated from cultures of yeast cloned with HBsAg s-gene. Several field trials have shown that this genetically engineered vaccine is as immunogenic, safe and effective as the plasma-derived vaccine *(31)* and is more cost-effective than the plasma derived vaccine. The fact that this vaccine does not depend on the scarce plasma resource is an added advantage *(32)*.

Over 90 per cent of recipients of the vaccine mount perceptive antibody to hepatitis B. The dose for adult is 10-20 µg initially (depending on the formulation) and again at 1 and 6 months; for greatest reliability of absorption, the deltoid muscle is preferred for injection. The newborn and paediatric dose is one–half the adult dose. Protection appears to be excellent even if titre wanes–at least p to 9 years – and booster reimmunization is not routinely ecommended *(33)*.

b. Hepatitis B immunoglobulin (HBIG)

For immediate protection, HBIG is used for those acutely exposed to HBsAg-positive blood, for example (a) surgeons, nurses or laboratory workers (b) newborn infants of carrier mothers, and (c) sexual contacts of acute hepatitis B patients. The HBIG should be given as soon as possible after an accidental inoculation (ideally within 6 hours and preferably not later than 48 hours). At the same time the victim's blood is drawn for HBsAg testing. If the test is negative, vaccination should be started immediately and a full course given. If the test is positive for surface antibody, no further action is needed *(34)*.

The recommended dose is 0.05 to 0.07 ml/kg of body weight *(35)*; two doses should be given 30 days apart *(35, 18)*. HBIG provides short-term passive protection which lasts approximately 3 months *(27)*. Since the median incubation period is said to be lower than 100 days *(28)*, two doses of HBIG given one month apart should suffice. The general use of HBIG for long-term prophylaxis has not been recommended because of its limited availability, its high cost and risk (although remote) of complications through repeated use over a long period of time *(21)*.

c. Passive-active immunization

The simultaneous administration of HBIG and hepatitis B vaccine is more efficacious than HBIG alone. HBIG does not interfere with the antibody response to the hepatitis B vaccine. This combined procedure is ideal both for prophylaxis of persons accidentally exposed to blood known to contain hepatitis B virus and for prevention of the carrier state in the newborn babies of carrier mothers *(27)*. HBIG (0.05-0.07 ml/kg) should be given as soon as possible and within 24 hours if possible. Hepatitis B virus vaccine 1.0 ml (20 mcg/1.0 ml) should be given intramuscularly within 7 days of exposure and second and third doses given one and six months, respectively, after the first dose.

d. Other measures

All blood donors should be screened for HBV infection, and those positive for Australia antigen should be rejected. Voluntary blood donation should be encouraged because purchased blood has shown a higher risk of post-transfusion hepatitis *(10)*. Health personnel should be alerted to the importance of adequate sterilization of all instruments and to the practice of simple hygienic measures. Carriers should be told not to share razors or tooth brushes and use barrier methods of contraception; they should not donate blood.

HEPATITIS C

Until a few years ago, the only types of viral hepatitis that could be confirmed were type A and type B. All others were described as non-A, non-B, that is neither A nor hepatitis B viral infection could be confirmed in blood tests of patients. Since the hepatitis C virus (HCV) was identified in the year 1989, it has been shown to be the major cause of parenterally transmitted non-A, non-B (PT-NANB) hepatitis *(22)*. Infection with HCV has become an issue of global significance with 170 million cases world–wide *(36)*.

The hepatitis C virus is a single-stranded RNA virus with properties similar to those of flavivirus. It bears no genomic resemblence to hepatitis B or D. The virus is mainly transmitted through transfusion of contaminated blood or blood products. Upto 50% of cases are related to intravenous drug users who share needles. The risk of sexual and maternal - neonatal transmission is small *(33)*. A low rate of secondary transmission to household contacts has been recognized. For health care workers it is an occupational hazard requiring adherence to universal precautions. Traditional practices such as circumcision, tattooing and scarification with contaminated instruments can spread HCV infection. The incubation period averages 6-7 weeks, and clinical illness is often mild, usually asymptomatic with a high rate of (more than 50%) chronic hepatitis, which may lead to cirrhosis of liver or liver cancer. It may take as long as 20 years to develop in to liver cancer, and is more likely to do so in men than in women, and in alcohol consumers.

Since it is not known whether all PT–NANB hepatitis is due to HCV infection, the diagnosis of acute NANB hepatitis must first be established in persons with signs and symptoms consistent with acute hepatitis by ruling out acute HAV and HBV infections. Currently, only immunoassays for antibodies to part of the non-structural region of HCV (anti–HCV) are available, as well as supplemental recombinant immunoblot assay (RIBA) tests used to confirm anti–HCV positive results. Patients with acute PT-NANB hepatitis who are anti-HCV negative at the onset of illness should be tested 6 months later, and if they are anti–HCV positive, the diagnosis of acute HCV can be made. Most RIBA positive persons are potentialy infectious, as confirmed in research laboratories by use of polymerase chain reaction to detect HCV RNA. Testing donated blood for HCV has helped reduce the risk of transfusion–associated hepatitis C from 10% to 1% in the industrialised countries. In India screening for HCV has been made mandatory for all blood banks from July 1, 1997 *(37)*.

Major prevention problems persist in the developing countries. Many of them cannot afford the anti–HCV blood test kits, and where the use of contaminated equipment for injection and other medical and dental procedures is widespread. Efforts are therefore necessary to persuade the manufacturers of tests to lower the costs for developing countries. Health education programmes are also needed to inform the general public and health care workers about the risk of transmitting infection with the use of unsterile equipment. Surveillance on a global scale needs to be strengthened in order to improve medical knowledge of transmission of the virus.

Interferon is the only drug that has been found effective in the treatment of HCV infection. However, treatment is very expensive thousands of dollars for the drug alone – and must be administered by injection several times a week for several months. Moreover, some patients, experience serious side–effects. Also, about half of the patients go into remission, but 50 per cent relapse when the treatment is stopped; only 25 per cent have long-term remission. Given its cost, only a minority of patients can afford it or are likely to be offered it. Studies involving less costly, orally administered drugs are continuing, but results so far have been disappointing. For a number of technical reasons, the development of a vaccine to prevent HCV infection is unlikely for many years.

HEPATITIS E

The infection caused by the hepatitis E virus (HEV) which was discovered in 1990, is essentially a waterborne disease. Formerly termed enterically transmitted hepatitis non-A, non-B (HNANB), HEV is a 29 –nm to 32 –nm RNA virus. Water or food supplies contaminated by faeces in which the virus is excreted have been implicated in major outbreaks reported in all parts of the world that have a hot climate. After an incubation period of 2-9 weeks, a self-limiting acute viral hepatitis appears, lasting for a period of several weeks, which is followed by recovery. No case of chronic disease has been reported. Mainly young adults, aged 15-40 years, have been affected by acute hepatitis E *(22)*.

In addition, HEV has a propensity to induce a fulminating form of acute disease (the mortality ranges between 0.5% to 4%), particularly in pregnant women, upto 20% of whom may develop fulminating hepatitis E, with a mortality that may reach about 80% of such cases. The importance of intrauterine infections due to hepatitis E infection during pregnancy, responsible for abortions, intrauterine death, and high perinatal morbidity and mortality, is currently under investigation *(22)*.

The first major epidemic was reported in New Delhi in the winter of 1955-56. After the flooding of Yamuna river, 30,000 cases of jaundice were described, and retrospectively attributed to hepatitis E. China reported 100,000 cases of jaundice between 1986 and 1988. Since then, additional outbreaks have been reported from Borneo, India, Indonesia, Mexico, Nepal, Pakistan etc. However, Hepatitis E outbreaks or even sporadic cases are rare in temperate climates. In Central Europe and in North America, hepatitis E has been diagnosed only in patients returning from countries with high endemicity for viral hepatitis. But screening of blood donors in these areas has shown a prevalence of anti-HEV antibodies upto 2.5%. The findings were similar for blood donors from South Africa (1.4%) and Thailand (2.8%). Seroprevalence in blood donors from Saudi Arabia and Egypt were significantly higher (9.5% and 24% respectively).

Diagnosis is made by the level of anti-HEV antibodies in the serum. No confirmatory assay is currently available. Anti-HEV Igm antibodies have been determined; however, their usefulness for the diagnosis of acute hepatitis E infection remains to be confirmed.

Hepatitis E appears to be widespread problem in developing countries where there are problems in providing safe drinking water and adequate sewage disposal. General precautions against the infection are as outlined for hepatitis A. For prevention, traveller highly endemic areas are recommended to take the usual elemen food hygiene precautions. There is no specific treatment for hepa E. Only supportive measures are required. Recovery from hepatiti is always complete. No vaccine or specific immunoglob prophylaxis is available. Preliminary studies in primates indicate protection through vaccination may be achievable in the forseea future.

DELTA HEPATITIS

A new form of hepatitis that is considered to be a widespre threat is "delta hepatitis ' or hepatitis D *(14)*. Delta hepatitis infect always occurs in association with hepatitis B (carrier state). T mode of transmission of this infection, its prevention and control identical to those for hepatitis B. Immunization against hepatitis also protects against delta infection *(28)*. Delta hepatitis has not be reported as significant in India *(1)*.

References

1. Tandon, B.N. et al (1985) **Bull WHO** 63 (5) 931-934
2. Nayak, N.C. (1988) **FAMS** 24 (4) 249-254
3. Normen, R. Grist et al (1987). **Diseases of Infection** O.U.Press
4. Indian Council of Medical Research (1980). **Viral Hepatit** Proceedings of the task force held on Jan.8, 1980.
5. Benenson, A.S.ed (1980). **Control of Communicable Diseases Man,** 13th ed.American Public Health Association.
6. WHO (1989). **Techn.Rep.Ser.** No.784 Page 25
7. Change, S.L. **Bull WHO** : 38, 401-414
8. Mc Collum Robert W. (1977) in **Viral Infections of Humans** Epidemiology and Control.
9. Pavri, K. and J. Rodriques (1982). In : **Viral Diseases in South-Ea Asia and the Western Pacific.** Proceedings of an Internatior Symposium on Viral Diseases. John. S. Mckenzie (ed). Austra Academic Press.
10. WHO (1977). **Techn.Rep.Ser.** No : 602
11. Dientardt, F. (1983). **WHO Chr** 37 (6) 203-207
12. Goh, K.T. et al (1984). **Bull WHO,** 62 (6) 893
13. Robins, W.S. (1979) In : **Principles and Practice of Infectiou diseases Mandell, G.L. et al**
14. Weller, Ian. (1984). **Brit Med.J.,** 288 : 47-49
15. Dienhardt, F et al (1982). **Bull WHO,** 60 : 661
16. Jawetz, J.L. (1980). **Review of Medical Microbiology,** 14th ed, Lang Medical Publications, California.
17. **JAMA,** 1975 : 233 : 1316
18. WHO (1983). **Tech.Rep.Ser.** No.693
19. Youmans, G.P. et al (1980). **The Biological and Clinical Basis Infectious Diseases** 2nd ed Saunders
20. Arie J. Zuckerman, (1982). **World Health** April : P.19
21. WHO (1983) **World Health Forum,** 4 (2) 135-141
22. WHO (1996), **The World Health Report 1996,** Fighting diseas Fostering development, Report of the Director-General
23. WHO, **Global Health Situation and Projections,** 1992
24. Govt of India (1994), **Annual Report 1993,** DGHS, Ministry of Healt and Family welfare, New Delhi
25. Indian Council of Medical Research (1985). **ICMR Bulletin,** 16 (5) 63
26. WHO (1983). **Techn. Rep.Ser.,** No. 691
27. WHO (1983). **WHO Chronicle,** 37 (6) 203-7
28. Krugman, S. et al (1979) **N.Eng.J.Med.,** 300 : 101 : 106
29. Zuckerman, A.J. (1987). **World Health** Dec. 1987
30. **Times of India,** dated 3rd Oct 1996
31. Scolniek, E.M. et al (1984). **JAMA** 251 : 2812
32. Ramchandran, S. (1988). **FAMSJ.** 24 (4) 231
33. Lawrence M. Tierney, Jr., Stephen J. McPhee, and Maxine A Papadakis, **Current Medical Diagnosis and Treatment,** 34th Ec (1995), a Lange medical book
34. Sherlock, S. (1984) **Post Graduate Doctor Middle East,** 7 (1) 49-56
35. WHO (1982). **Bull WHO,** 60 (1) 43-47
36. WHO (1997), **The World Health Report 1997,** Conquering Suffering Enriching humanity, Report of the Director–General
37. **Times of India,** 18 June 1997, New Delhi

Current candidate live attenuated hepatitis A vaccines require administration by injection. Preparations that may be suitable for oral administration are not available so far.

PREVENTION AND CONTROL OF HEPATITIS B

Passive immunization

Hepatitis B immunoglobulin is prepared from pooled plasma with a high titre of hepatitis B surface antibody and may confer temporary passive immunity under certain defined conditions. The major indication for the administration of hepatitis B immunoglobulin is a single acute exposure to hepatitis B virus, such as occurs when blood containing surface antigen is inoculated, ingested or splashed onto mucous membranes and the conjunctiva. The optimal dose has not been established, but doses in the range 250–500 IU have been used effectively. It should be administered as early as possible after exposure and preferably within 48 h, usually 3 ml (containing 200 IU of anti-HBs per ml) in adults. It should not be administered after 7 days following exposure. It is generally recommended that two doses of hepatitis B immunoglobulin should be given 30 days apart.

Results with the use of hepatitis B immunoglobulin for prophylaxis in babies at risk of infection with hepatitis B virus are encouraging if the immunoglobulin is given as soon as possible after birth or within 12 h of birth, and the chance of the baby developing the persistent carrier state is reduced by about 70%. More recent studies using combined passive and active immunization indicate an efficacy approaching 90%. The dose of hepatitis B immunoglobulin recommended in the newborn is 1–2 ml (200 IU of anti-HBs per ml).

Active immunization

Immunization against hepatitis B is required for groups that are at an increased risk of acquiring this infection. These groups include individuals requiring repeated transfusions of blood or blood products, prolonged in-patient treatment, patients who require frequent tissue penetration or need repeated access to the circulation, patients with natural or acquired immune deficiency and patients with malignant diseases. Viral hepatitis is an occupational hazard among health care personnel and the staff of institutions for the mentally retarded and in some semiclosed institutions. High rates of infection with hepatitis B occur in narcotic drug addicts and drug abusers, homosexuals and prostitutes. Individuals working in high endemic areas are also at an increased risk of infections. Women in areas of the world where the carrier state in that group is high are another segment of the population requiring immunization in view of the increased risk of transmission of the infections to their offspring. Young infants, children and susceptible persons living in certain tropical and subtropical areas where present socioeconomic conditions are poor and the prevalence of hepatitis B is high should also be immunized.

The failure to grow hepatitis B virus in tissue culture has directed attention to the use of other preparations for active immunization. Since immunization with hepatitis B surface antigen leads to the production of protective surface antibody, purified 22-nm spherical surface antigen particles have been developed as vaccines. These vaccines have been prepared from the plasma of symptomless carriers. Trials on protective efficacy in high-risk groups have demonstrated the value of the vaccines and their safety. There is no risk of transmission of the acquired immune deficiency syndrome (AIDS) or any other infection by vaccines derived from plasma which meet the WHO Requirements of 1981, 1983 and 1987. Local reactions reported after immunization have been minor, occurring in less than 20% of immunized individuals, and consisted of slight swelling and reddening at the site of inoculation. Temperature elevations of up to 38°C were observed in only a few individuals.

Site of injection for vaccination

Hepatitis B vaccination should be given in the upper arm or the anterolateral aspect of the thigh and not in the buttock. There are over 100 reports of unexpectedly low antibody seroconversion rates after hepatitis B vaccination using injection

into the buttock. In one centre in the USA a low antibody response was noted in 54% of healthy adult health care personnel. Many studies have since shown that the antibody response rate was significantly higher in centres using deltoid injection than centres using the buttock. On the basis of antibody tests after vaccination, the Advisory Committee on Immunization Practices of the Centers of Disease Control, USA, recommended that the arm be used as the site of hepatitis B vaccination in adults, as has the Department of Health in the UK.

A comprehensive study in the USA by Shaw et al (1989) showed that participants who received the vaccine in the deltoid had antibody titres that were up to 17 times higher than those of subjects who received the injections into the buttock. Furthermore, those who were injected in the buttock were 2–4 times more likely to fail to reach a minimum antibody level of 10 mIU/ml after vaccination. Recent reports have also implicated buttock injection as a possible factor in a failure of rabies post-exposure prophylaxis using a human diploid cell rabies vaccine (Baer & Fishbein 1987).

The injection of vaccine into deep fat in the buttocks is likely with needles shorter than 5 cm, and there is a lack of phagocytic or antigen-presenting cells in layers of fat. Another factor may involve the rapidity with which antigen becomes available to the circulation from deposition in fat, leading to delay in processing by macrophages and eventually presentation to T and B cells. An additional factor may be denaturation by enzymes of antigen that has remained in fat for hours or days. The importance of these factors is supported by the finding at the Royal Free Hospital, London, and elsewhere that thicker skin fold is associated with a lowered antibody response (Cockcroft et al 1990).

These observations have important public health implications, well illustrated by the estimate that about 20% of subjects immunized against hepatitis B via the buttock in the USA by March 1985 (about 60 000 people) failed to attain a minimum level of antibody of 10 mIU/ml and were therefore not protected.

Hepatitis B surface antibody titres should be measured in all individuals who have been immunized against hepatitis B by injection into the buttocks, and when this is not possible a complete course of three injections of vaccine should be administered into the deltoid muscle or the anterolateral aspect of the thigh, the only acceptable sites for hepatitis B immunization (Zuckerman et al 1992).

Indications for immunization against hepatitis B

The current indications for the use of hepatitis B vaccines in low prevalence areas are summarized below, although these recommendations are under revision. The recommendations for immunization against this infection in intermediate- and high-prevalance regions also include universal immunization of infants (Zuckerman 1984, Deinhardt & Zuckerman 1985). Many countries, including the USA and Italy, introduced universal immunization for infants in 1992, and it is expected that most countries will implement this policy by 1996.

Current policy

1. All health care personnel in frequent contact with blood or needles and groups at the highest risk in this category include:
   - 1.1 Personnel, including teaching and training staff, directly involved over a period of time in patient care in residential institutions for the mentally handicapped where there is a known high risk of hepatitis.
   - 1.2 Personnel directly involved in patient care over a period of time, working in units giving treatment to those known to be at high risk of hepatitis B infection.
   - 1.3 Personnel directly involved in patient care working in haemodialysis, haemophilia, and other centres regularly performing maintenance treatment of patients with blood or blood products.
   - 1.4 Laboratory workers regularly exposed to increased risk from infected material.
   - 1.5 Health care personnel on secondment to work in areas of the world where there is a high prevalance of hepatitis B infection, if

they are to be directly involved in patient care.

1.6 Dentists and ancilliary dental personnel with direct patient contact.

2. Patients:
   2.1 Patients on first entry into those residential institutions for the mentally handicapped where there is a known high incidence of hepatitis B.
   2.2 Patients treated by maintenance haemodialysis.
   2.3 Patients before major surgery who are likely to require a large number of blood transfusions and/or treatment with blood products.
3. Contacts of patients with hepatitis B:
   3.1 The spouses and other sexual contacts of patients with acute hepatitis B or carriers of hepatitis B virus, and other family members in close contact.
4. Other indications for immunization:
   4.1 Infants born to mothers who are persistent carriers of hepatitis B surface antigen (HBsAg) or are HBsAg positive as a result of recent infection, particularly if hepatitis B e antigen is detectable or HBV-positive mothers without antibody to e antigen (anti-HBe). The optimum timing for immunoglobulin to be given at a contralateral site is immediately at birth or within 12 h.
   4.2 Health care workers who are accidentally pricked with needles used for patients with hepatitis B. The vaccine may be used alone or in combination with hepatitis B immunoglobulin as an alternative to passive immunization with hepatitis B immunoglobulin only. Studies on the efficacy of these different schedules of immunization are nearing completion.
5. Immediate protection:
   5.1 Infants born to carrier mothers: Whenever immediate protection is required, as, for example, for infants born to HBsAg-positive mothers (see 4.1) or following transfer of an individual into a 'high-risk' setting or after accidental inoculation, active immunization with the vaccine should be combined with simultaneous administration of hepatitis B immunoglobulin at a different site. It has been shown that passive immunization with up to 3 ml (200 IU of anti-HBs per ml) of hepatitis B immunoglobulin does not interfere with an active immune response. A single dose of hepatitis B immunoglobulin (usually 3 ml for adults; 1–2 ml for the newborn) is sufficient for healthy individuals. If infection has already occurred at the time of the first immunization, virus multiplication is unlikely to be inhibited completely, but severe illness and, most importantly, the development of the carrier state of HBV may be prevented in many individuals, particularly in infants born to carrier mothers.
6. The immune response to the current hepatitis B vaccines is poorer in immunocompromised patients and in the elderly. For example, only about 60% of patients undergoing treatment by maintenance haemodialysis develop anti-HBs. It is suggested therefore that patients with chronic renal damage be immunized as soon as it appears likely that they will ultimately require treatment by maintenance haemodialysis or receive renal transplant. Consideration should be given to the use of blood from healthy immunized donors with high titres of anti-HBs for the routine haemodialysis of such patients who respond poorly to immunization against hepatitis B.
7. Other groups at risk of hepatitis B include the following:
   7.1 Individuals who frequently change sexual partners, particularly promiscuous male homosexuals and prostitutes.
   7.2 Intravenous drug abusers.
   7.3 Staff at reception centres for refugees and immigrants from areas of the world where hepatitis B is very common, such as South-East Asia.
   7.4 Although they are at 'lower risk', consideration should also be given to long-term prisoners and staff of custodial institutions, ambulance and rescue services and selected police personnel.
   7.5 Military personnel are included in some countries.

Developing new hepatitis B immunization strategies

There is now strong support for the introduction of universal antenatal screening to identify hepatitis B carrier mothers and the vaccination of their babies. It is important that any other strategies do not interfere with the delivery of vaccine to this group. Immunization of this group will have the greatest impact in reducing the number of new hepatitis B carriers. For children outside this group it is difficult to estimate the lifetime risk of acquiring a hepatitis infection.

There are four main approaches:

1. Continue vaccination of the 'high-risk' babies as defined above.
2. Vaccinate all infants.
3. Vaccinate all adolescents.
4. Vaccinate everybody.

Vaccination of adolescents

This approach delivers vaccination at a time close to the time when 'risk behaviour' would expose adolescents to infection. Vaccination could be delivered as part of a wider package on health education in general, to include sex education, risk of AIDS, dangers of drug abuse, smoking, benefits of a healthy diet and lifestyle.

The problems with this approach are as follows:

- Persuading parents to accept vaccination of the children against a sexually transmitted disease, a problem they may not wish to address at that time.
- Ensuring a full course of three doses is given.
- Evaluating and monitoring vaccine cover. The systems for monitoring uptake of vaccine in this age group may not operate efficiently.

Vaccination of infants

The advantages of this approach are:

- It is known that vaccination can be delivered to babies.
- Parents will accept vaccination against hepatitis B along with other childhood vaccinations without reference to sexual behaviour.

The disadvantages of this approach are:

- It is not known whether immunity will last until exposure in later life. This may become less of a problem as more people are vaccinated and thus the chance of exposure to infection is reduced.
- The introduction of another childhood vaccination may reduce the uptake of other childhood vaccinations. This problem would be avoided if hepatitis B vaccine could be delivered in a combined vaccine containing DPT (diphtheria, polio, tetanus), and this proposal may have to await the production and evaluation of a suitable vaccine.

Vaccination of infants is preferable to vaccination of adolescents, as there are sufficient mechanisms to ensure, monitor and evaluate cover. A booster dose could be given in early adolescence combined with a health education package. A rolling programme could be introduced, giving priority to urban areas.

Polypeptide vaccines

Hepatitis B polypeptide vaccines containing specific hepatitis B antigenic determinants of the major non-glycosylated peptide I of the surface antigen with a molecular weight of 22–24 000 and its glycosylated form, a polypeptide with a molecular weight in the range 22–24 000, have been prepared in micellar form (Skelly et al 1981, Young et al 1982). The individual polypeptides of the surface antigen are immunogenic, and the purified 24 000 (designated as p24) and 27 000 (gp27) molecular weight polypeptides are effective antigens. Clinical trials of the polypeptide micelle vaccine are in progress (Hollinger et al 1986).

Production of hepatitis B vaccines by rDNA techniques

Recombinant DNA techniques have been used for expressing hepatitis B surface antigen and core antigen in prokaryotic cells (*Escherichia coli* and *Bacillus subtilis*) and in eukaryotic cells, such as mutant mouse LM cells, HeLa cells, COS cells, CHO cells and yeast cells (*Saccharomyces cerevisiae*).

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HEPATITIS B SURFACE ANTIGEN SUBTYPES IN MALAYSIA[1]

S. KAMATH[2]

Kamath, S. (Kolling Institute for Medical Research, Royal North Shore Hospital of Sydney, St. Leonards, N.S.W., 2065, Australia). Hepatitis B surface antigen subtypes in Malaysia. *Am J Epidemiol* 102:191–195, 1975.—One hundred and ninety hepatitis B surface antigen positive (HB_sAg+) sera were subtyped, belonging to: blood donors, hepatitis patients, patients and staff in a hemodialysis unit, all from Kuala Lumpur; Malaysian aborigines from three jungle locations in Peninsular Malaysia; and East Malaysians from Sarawak, East Malaysia. Three subtypes *adr*, *adw* and *ayw* were present in Malaysia in the following frequencies: 44%, 29%, and 27%, respectively. In Kuala Lumpur 87% had subdeterminant *d* and 13 per cent *y*, whereas in the deep jungle aborigines of Perak and Pahang, the *y* subdeterminant was present in 87% and the *d* in 13%. A similar pattern of preponderance of *y* prevailed in Sarawak, East Malaysia. In Kuala Lumpur the two main ethnic groups, Malays and Chinese, differed in subtype distribution, in that *adr* predominated in the Malays (61%), while the *adw* predominated in the Chinese (51%). Subtype distribution was not related to age or sex of carriers of the antigen, or to whether they had hepatitis, or asymptomatic antigenemia.

aborigines; Australia antigen; hepatitis B surface antigen; Malaysia; virology

INTRODUCTION

Besides the common specificity *a*, two pairs of mutually exclusive antigenic determinants *d/y* and *w/r* have been described in the analysis of hepatitis B surface antigen positive (HB_sAg+) sera by immunodiffusion (1, 2).

Transmission experiments in human volunteers, and the presence of a single subtype in localized outbreaks of hepatitis B infection, suggest that the subtypes are determined by the virus and not the host (3). An interesting geographic distribution of HB_sAg subtypes is now evident. Thus, *adw* is common in asymptomatic carriers in North America (4, 5) and Northern Europe (6, 7). Subtype *ayw* predominates in the Mediterranean region and the Middle East (8, 9), and *adr* in the Far East and South East Asia (2).

The purpose of this study was to determine the HB_sAg subtypes prevalent in Malaysia between 1969 and 1973 and to study their pattern of distribution in the various ethnic groups in this country (figure 1).

MATERIALS AND METHODS

Source of HB_sAg+ sera. Table 1 shows the category and number of HB_sAg+ sera

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Abbreviations: HB_sAg+, hepatitis B surface antigen positive; IEOP, immunoelectroosmophoresis.

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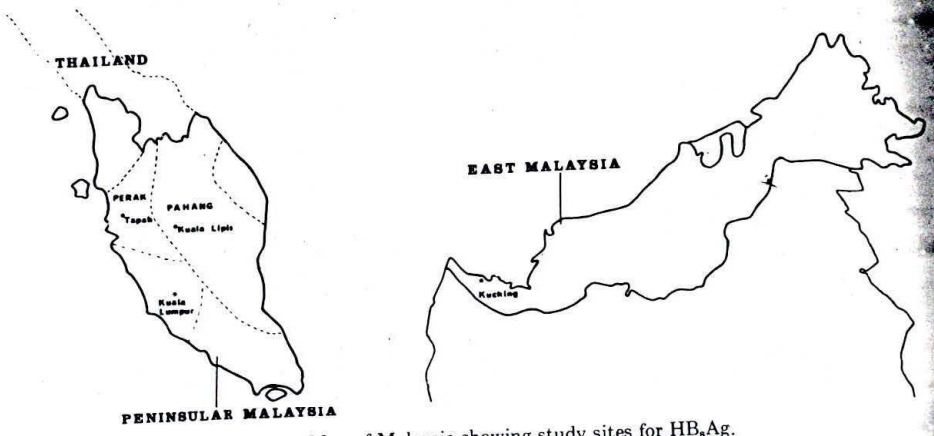

FIGURE 1. Map of Malaysia showing study sites for HB_sAg.

TABLE 1

Source of HB_s Ag+ sera subtyped

Category	Year of collection	Location	Total	No. typable (%)	No. untypable (%)
Blood donors	1971–1973	Kuala Lumpur, Selangor	130	102 (86%)	16 (14%)
Hepatitis patients	1971–1973	Kuala Lumpur, Selangor	108	43 (43%)	56 (57%)
Hemodialysis unit	1971–1973	Kuala Lumpur, Selangor	6	4	2
Deep jungle aborigines	1971	Perak and Pahang	19	15	4
Blood donors	1972–1973	Kuching, Sarawak	17	14	2
Land Dayaks	1969	Kpg. Tijirak, Sarawak	19	12	7
Total			299	190 (69%)	87 (31%)

subtyped. All sera had been previously established as HB_sAg+ by the immunoelectroosmophoresis (IEOP) method. With the exception of those from hepatitis and hemodialysis patients, sera were collected from apparently healthy persons. They belonged to the following categories:

1) Blood donors—sera from the Blood Bank, General Hospital, Kuala Lumpur.

2) Hepatitis patients—sera from patients at the General Hospital, Kuala Lumpur.

3) Hemodialysis unit. Two staff and four patients were detected as HB_sAg+, although no outbreak of hepatitis occurred in the unit.

The people in these three categories comprised mainly Malays, Chinese, and Indians.

4) Malaysian aborigines. This group comprised sera from 90 aborigines belonging to the Semai tribe, who lived at Pos Shean, Kuala Lipis, Pahang, and 34 from the Temiar tribe, who lived at Fort Kemar, Perak. These two villages are in isolated deep jungle locations, accessible only by helicopter. These tribal groups studied are distinct culturally and have no contact with each other and little contact with major cities. There were 13 HB_sAg+ sera among the Pos Shean group (14.4 per cent) and three among the Fort Kemar group (8.8 per cent). Three additional HB_sAg+ sera belonging to Semai aborigines at a jungle fringe settlement at Kelubi Pos near Tapah, Perak, were also subtyped.

5) Blood donors, Kuching, Sarawak. The 247 blood donors sampled comprised

TABLE 3

Distribution of HB$_s$Ag subtypes in Kuala Lumpur by ethnic group

Ethnic group	Subtype			
	ayw	*adw*	*adr*	Total
Malay	11 (14%)	20 (25%)	49 (61%)	80
Chinese	3 (7%)	23 (51%)	19 (42%)	45
Indian	1 (9%)	5 (45.5%)	5 (45.5%)	11
Others*	4 (31%)	3 (23%)	6 (46%)	13
Total	19 (13%)	51 (34%)	79 (53%)	149

* 4: *ayw* from 1 aborigine, 3 East Malaysians; 3: *adw* from 1 aborigine, 1 East Malaysian, 1 Eurasian; 6: *adr* from 5 East Malaysians, 1 Eurasian.

TABLE 4

Distribution of HB$_s$Ag subtypes in Kuala Lumpur by category of carrier

Category	Subtype			
	ayw	*adw*	*adr*	Total
Blood donors	14 (14%)	36 (35%)	52 (51%)	102
Hepatitis patients	5 (12%)	14 (32%)	24 (56%)	43
Hemodialysis unit	0	1	3	4
Total	19 (13%)	51 (34%)	79 (53%)	149

in Kuala Lumpur by category of carrier. There was no significant difference in subtype distribution between blood donors, hepatitis patients and hemodialysis unit patients and staff ($\chi^2 = 3.07$, No. = 4, $0.7 > p > 0.05$).

The subtype distribution did not vary significiantly by sex ($\chi^2 = 4.05$, No. = 2, $0.2 > p > 0.1$), or with age.

DISCUSSION

The variation of subtypes by geographic location in this study could be explained by the isolation of the aborigines in the jungle and the separation of Sarawak from the rest of Peninsular Malaysia by the sea. It could also reflect the variation of subtypes among different ethnic groups with different origins as each of the areas compared had ethnically distinct populations.

The *ayw* subtype predominated in the deep jungle aborigines of Peninsular Malaysia, the various ethnic groups of East Malaysia irrespective of whether they lived in urban Kuching or rural Kampong Tiu rak, and the group in Kuala Lumpur classified as others, composed mainly of aborigines from Peninsular Malaysia, and East Malaysians who had transferred to Kuala Lumpur in their adult life. The reason for this *ayw* preponderance in all these aboriginal groups is not clear.

In contrast, the *d* subdeterminant predominated in Malays, Chinese and Indians from Kuala Lumpur. The preponderance of the *adr* subtype in the Malays was similar to that in people in neighboring Thailand and Mainland China (2, 11). The main subtypes in the Chinese were *adw* and *adr* with the former predominating. The Malaysian Chinese studied represent mainly second or third generation migrants from either Hong Kong and Taiwan where the *adw* subtype predominates, or Mainland China where the *adr* subtype predominates (11). This would suggest that these subtypes were acquired by the Malaysian Chinese from their country of origin and subsequently maintained as their subtype by intrafamilial transmission. The observation of Feinman et al. (12) that subtypes of chronic HB$_s$Ag carriers in Canada appear to be related to country of origin of carrier rather than country of residence lends support to this explanation. Further support comes from the study of Bar-Shany et al. (9) which showed that first generation Israeli blood donors of European origin had the same frequency of subdeterminant *d* as immigrants from Europe and did not convert to the predominant subdeterminant *y* of Israel.

REFERENCES

1. Le Bouvier GL: The heterogeneity of Australia antigen. J Infect Dis 123:671–675, 1971
2. Bancroft WH, Mundin FK, Russell PK: Detection of additional antigenic determinants of hepatitis B antigen. J Immunol 109:842–848, 1972
3. Le Bouvier GL: Subspecificities of the Australia antigen complex. Am J Dis Child 123:420–424, 1972
4. Mosley JW, Edwards VM, Meihaus JE, et al: Subdeterminants *d* and *y* of hepatitis B as epidemiologic markers. Am J E 95:529–535, 1972
5. Holland PV, Purcell RH, Smith H, et al: ing of hepatitis-associated antigen (HBA plified technique using counter-electroph Immunol 109:420–425, 1972
6. Van Kooten Kok-Doorschodt HJ, van de R, Gispen R: Determination and distrib the two types of hepatitis-associated an Infect Dis 126:117–122, 1972
7. Iwarson S, Magnius L, Lindholm A, et types of hepatitis B antigen in blood dor post-transfusion hepatitis: Clinical and e ological aspects. Br Med J 1:84–87, 1973

World Health Organization, 58 (4): 621-628 (1980)

Prevalence of markers of hepatitis B virus infection in various countries: a WHO Collaborative Study*

[illegible]AVSKÝ [1]

A WHO collaborative study on viral hepatitis B in which 21 laboratories in 20 countries participated is described. The aim of the study was to define the prevalence of hepatitis B surface antigen (HBsAg), its subtypes, and its antibody (anti-HBs) by age and sex and urban or rural residence in normal populations in different parts of the world. High-risk groups in the populations and patients with various diseases were also investigated. The results of the study confirmed that HBsAg and anti-HBs prevalence rates were higher in African and Asian countries than in the Americas, Australia, and northern and central Europe. Some eastern and southern European countries, however, were also shown to have high HBsAg and anti-HBs prevalence rates, comparable with those in Africa and Asia. In countries with low HBsAg and anti-HBs prevalence, there seems to be a gradual build-up during late childhood or early adolescence, whereas in countries with high HBsAg and its antibody prevalence, they were frequently detected in preschool children. Although the trend was towards a higher frequency of HBsAg and anti-HBs in urban than in rural and in male than in female populations, the differences were in most cases not significant. On the other hand, a significantly higher prevalence of markers of hepatitis B virus infection was seen in high-risk population groups than in normal populations. This was, however, clearly defined only in areas with low HBsAg and anti-HBs prevalence in the normal population. The geographical distribution of HBsAg subtypes showed a higher prevalence of the ad *subdeterminant over* ay *in central European countries, whereas in eastern and southern Europe the* ay *subtype predominated. In West Africa,* ayw *was the only variant found, whereas in East Africa* ad *occurred more frequently than* ay. *In Australia, both* adw *and* ayw *subtypes were detected, whereas in the Far East and South-east Asia only* adw *and* adr *were seen.*

[illegible] prevalence of markers of hepatitis B [illegible] in different parts of the world has been [illegible] in a number of surveys. However, the [illegible] used in these studies often varied widely in [illegible] and specificity and consequently difficulties were encountered when attempts were made to [illegible] and evaluate the results.

[illegible], the report of a WHO consultation on viral [illegible] therefore recommended that WHO organize [illegible] collaborative study to assess the [illegible] hepatitis B surface antigen (HBsAg) and [illegible] (anti-HBs) in different parts of the world [illegible] WHO-recommended techniques, such as [illegible]assay (RIA) and reverse passive haemagglutination (RPHA).

[illegible] participating scientists and laboratories is presented in [illegible]

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MATERIALS AND METHODS

Sera for HBsAg and anti-HBs determination were collected from apparently healthy non-institutionalized individuals of both sexes and different age groups in urban and rural populations in various countries. In addition, sera were collected in several countries from populations at high risk, such as haemodialysis unit staff and patients, hospital and laboratory personnel, institutionalized persons, and from psychiatric and venereal disease patients, irrespective of sex and age.

HBsAg was determined by RIA and/or RPHA. Anti-HBs was also determined by RIA, except in Canada and Japan, where passive haemagglutination (PHA) was used. In the case of RIA, Ausria II and Ausab reagents (Abbott) were employed, whereas for RPHA the Hepatest reagent (Wellcome) was used. For comparative and quality control purposes, collections of sera were retested by RIA in the WHO Collaborating Centre for Reference and Research on Viral Hepatitis, CDC, Phoenix, Arizona, USA. On

addition, the Centre subtyped and/or confirmed the results of HBsAg subtyping from participating laboratories. Twenty-two laboratories in 20 countries took part in the study. Altogether 23 564 sera were examined.

RESULTS

Prevalence of HBsAg

Table 1 summarizes the age-specific prevalence of HBsAg in normal populations in various parts of the world. Low HBsAg prevalence rates (0.1–1.5%) detected in specimens collected in Australia, Canada, the USA, and in some countries, such as Czechoslovakia, the Democratic Republic, the Federal Republic of Germany, and the United Kingdom. In other pean countries, however, the rates were higher ing from 4.2 to 10.8% in Greece, Poland, Turkey, and the USSR. High HBsAg prevalence also detected in African and Asian countries Egypt, India, Senegal, Thailand, and Uganda. age distribution, it should be noted that in

Table 1. Age-specific HBsAg prevalence among normal urban and rural populations as determined by radioim

Laboratory location	Age group (years)															
	0–4		5–9		10–14		15–19		20–29		30–39		40–49		⩾50	
	No. tested	% positive	No. tested	% positive	No. tested	% positive	No. tested	% positive	No. tested	% positive	No. tested	% positive	No. tested	% positive	No. tested	% positive
Cairo (Egypt)	183	23.0	70	4.0	469	5.1	427	3.7	200	4.0	381	3.9	89	5.6	–	–
Dakar (Senegal)[a]	173	4.0	203	14.3	169	14.2	147	19.0	371	15.0	213	9.4	186	5.9	317	5.4
Entebbe (Uganda)	29	3.4	32	6.3	28	0	98	10.2	212	7.5	91	4.4	27	11.1	24	12.5
Rabat (Morocco)	109	1.8	71	1.4	49	3.8	53	6.1	37	8.1	14	0	–	–	–	–
Houston (USA)																
Ottawa (Canada)[b]	43	2.3	99	1.0	180	0	296	0.7	439	0.2	238	0.8	204	1.0	611	0.8
Phoenix (USA)	50	0	50	0	50	0	93	0	189	0.5	94	0	95	0	99	0
Buenos Aires (Argentina)[a]	16	0	34	0	54	0	145	1.4	204	1.6	238	0.4	158	0	177	0
Bangkok (Thailand)	19	10.5	62	3.2	97	14.4	84	9.5	184	10.9	83	7.2	53	5.7	23	4.3
Poona (India)	6	0	50	2.0	88	6.8	107	6.5	130	3.8	122	7.4	101	8.9	96	6.3
Tokyo (Japan)[a]	145	0	203	2.5	204	3.4	200	4.5	367	2.5	202	1.0	199	2.0	389	1.3
Fairfield (Australia)	67	0	92	0	96	0	83	0	173	0.6	87	1.1	92	0	168	0.6
Athens (Greece)	44	18.2	282	3.9	144	10.4	120	10.8	367	13.6	321	13.4	416	9.4	926	7.3
Berlin (GDR)[a]	94	0	100	1.0	100	1.0	100	2.0	139	2.2	99	1.0	100	1.0	188	1.6
Göttingen (FRG)	35	0	40	0	40	0	39	0	40	0	40	0	40	0	80	0
Munich (FRG)	–	–	–	–	–	–	364	0.5	633	1.6	472	1.5	330	0.9	167	0
Iasi (Romania)	58	6.9	58	17.2	102	14.7	121	11.6	108	12.0	83	6.0	94	9.6	78	7.7
Izmir (Turkey)[a]	73	8.2	84	7.1	134	6.7	194	12.4	345	12.2	193	7.8	156	5.1	142	8.4
London (UK)	–	–	–	–	–	–	–	–	228	0.4	239	0	186	0	218	0
Moscow (USSR)	25	4.0	52	5.7	54	1.8	47	6.4	118	3.4	77	5.2	41	2.4	64	1.6
Prague (Czechoslovakia)	108	0	106	0	110	0.9	104	3.8	186	0.5	110	1.8	104	2.9	164	2.4
Warsaw (Poland)[a]	51	15.7	31	12.9	75	4.0	–	–	–	–	–	–	–	–	–	–

[a] Tested by RPHA.

[b] Urban population only.

generally high HBsAg prevalence rates the was detected in children of less than 5 years of whereas in countries with generally low HBsAg rates it usually began to appear only in late childhood or early adolescence.

prevalence of HBsAg in normal populations is by sex and place of residence (urban/rural) in and 3. There was a clear tendency for HBsAg to be higher among males than among in most countries. However, the differences not significant in the majority of cases. The prevalence varied between urban and rural areas. In some countries, such as Argentina Czechoslovakia, the antigen was significantly more frequent in urban populations, whereas in the Republic of Germany, Japan, and Poland it more frequent in rural populations. In other however, the differences were small and ficant.

HBsAg prevalence by sex in normal urban and rural of all ages in various countries as determined by immunoassay

location	Male		Female	
	No. tested	% positive	No. tested	% positive
Senegal)[a]	838	12.3	940	9.4
Uganda)	381	8.1	169	6.6
Canada)[b]	1134	0.8	976	0.5
USA)	369	0	351	0.3
	546	0.9	480	0.2
Thailand)	291	12.5	343	6.7
	367	7.2	333	5.2
	943	2.3	966	2.0
Australia)	437	0.5	448	0.2
Greece)	1465	10.1	1155	8.4
	436	1.4	484	1.2
FRG)[c]	165	0	194	0
	1145	1.2	821	0.9
	356	13.2	346	7.6
	782	10.5	539	7.4
Czechoslovakia)	174	5.2	304	3.6
	472	1.2	520	1.5

RPHA.
population only
and 15 years and over only.

Table 3. HBsAg prevalence in normal urban and rural populations of both sexes and all ages in various countries as determined by radioimmunoassay

Laboratory location	Urban		Rural	
	No. tested	% positive	No. tested	% positive
Dakar (Senegal)[a]	586	11.4	1192	10.5
Entebbe (Uganda)	454	6.3	96	8.3
Buenos Aires (Argentina)[a]	765	0.7	261	0.4
Bangkok (Thailand)	415	8.0	215	11.3
Poona (India)	244	7.0	456	5.4
Tokyo (Japan)[a]	952	1.4	957	2.9
Fairfield (Australia)	442	0.5	443	0.2
Athens (Greece)	1515	9.9	1105	8.6
Berlin (GDR)[a]	445	1.1	475	1.5
Göttingen (FRG)	210	0	149	0
Munich (FRG)[b]	360	0.3	1576	1.3
Iasi (Romania)	475	11.6	227	9.2
Izmir (Turkey)[a]	677	9.9	644	8.5
Moscow (USSR)	402	4.2	76	3.9
Prague (Czechoslovakia)	582	2.4	410	0.3
Warsaw (Poland)[a, c]	201	2.5	209	5.2

[a] Tested by RPHA.
[b] Population aged 15 years and over only.
[c] Population aged 18 years and over only.

Several groups of population at high risk and some psychiatric and venereal disease patients were also investigated for HBsAg prevalence. The results are summarized in Table 4. HBsAg prevalence rates in haemodialysis unit staff and patients in four investigated countries (Australia, the German Democratic Republic, Romania, and the USSR) were significantly higher than in the general populations of those countries. In other high-risk population groups, such as hospital and laboratory personnel, institutionalized individuals, and psychiatric and venereal disease patients, the HBsAg prevalence rates were in most cases also higher than those in normal populations. This was not the case, however, in institutionalized persons and psychiatric patients in Romania, in whom antigenaemia rates were comparable with those in the normal population.

Distribution of HBsAg subtypes

The distribution of HBsAg subtypes in the investigated populations is shown in Table 5. Higher preva-

Table 4. HBsAg prevalence in different high-risk population groups and patients in various countries as determined by radioimmunoassay

Laboratory location	Haemodialysis staff / patients		Hospital and laboratory personnel		Institutionalized persons		Psychiatric patients		Venereal disease patients		Total
	No. tested	% positive	No. tested	% positive	No. tested	% positive	No. tested	% positive	No. tested	% positive	No. tested
Fairfield (Australia)	125	0.8	—	—	166	0.6	90[a]	44.4	307	5.2	688
Berlin (GDR)	96	21.9	111	3.6	142[a]	6.3	87[a]	35.6	108	13.0	544
Iasi (Romania)	23	26.1	—	—	120[a]	9.2	293	11.9	114	17.5	550
Moscow (USSR)	22	13.6	31	6.4	221	8.9	—	—	—	—	274
Prague (Czechoslovakia)	—	—	466	1.5	—	—	159[a]	5.7	—	—	625

[a] Children only.

Table 5. Distribution of HBsAg subtypes in populations of various countries

Laboratory location	Total determined	*ad*		*adw*		*adr*		*ay*		*ayw*	
		No.	%	No.	%	No.	%	No.	%	No.	%
Dakar (Senegal)	146									146	100
Entebbe (Uganda)	16	9	56.3	1	6.3			6	37.4		
Ottawa (Canada)	7	4	57.1					3	42.9		
Bangkok (Thailand)	38	21	55.3	7	18.4	10	26.3				
Poona (India)	4									4	100
Tokyo (Japan)	37			17	45.9	20	54.1				
Fairfield (Australia)	31			26	83.9					5	16
Athens (Greece)	70	1	1.4					69	98.6		
Göttingen (FRG)	253	206	81.4					47	18.6		
Munich (FRG)	279	229	81.1					50	17.9		
Iasi (Romania)	32	2	6.2	3	9.4			19	59.4	8	25
Moscow (USSR)	5									5	100
Prague (Czechoslovakia)	13	9	69.2					4	30.8		

lence of *ad* subdeterminant over *ay* was found in central European countries, whereas the *ay* subtype predominated in eastern and southern Europe. In Canada, both *ad* and *ay* were found at approximately the same rate; however, the number of subtyped specimens was very low. In West Africa (Senegal) all the 146 subtyped antigens were of the *ayw* type, whereas in East Africa (Uganda) *ad* was seen more frequently than *ay*. In Australia, subtype *adw* was significantly more common than *ayw*. The *adw* subtype was also more frequent in Thailand, but no *ayw* was found; the *adr* subtype was detected instead. In Japan, both *adw* and *adr* subtypes were common.

Prevalence of anti-HBs

The age-specific prevalence of anti-HBs in populations in different parts of the world is illustrated in Table 6. An increasing antibody prevalence rate was found with increasing age in populations in all countries studied; however, average rates were generally higher in African and Asian countries, such as Thailand (42.4%) and Uganda (49.6%), than in Australia (2.9%), Canada (3.8%), and northern and central European countries (Czechoslovakia, German Democratic Republic 16.1%, Federal Republic of Germany 5.3% and 4.6%, and United

6. Age-specific Anti-HBs prevalence among normal urban and rural populations as determined by radioimmunoassay

	Age group (years)																	
	0–4		5–9		10–14		15–19		20–29		30–39		40–49		⩾ 50		Total	
	No. tested	% positive	No. tested	% positive	No. tested	% positive	No. tested	% positive	No. tested	% positive	No. tested	% positive	No. tested	% positive	No. tested	% positive	No. tested	% positive
(Uganda)	30	36.7	26	26.9	21	33.3	81	39.5	177	48.6	79	64.6	19	89.5	21	66.7	454	49.6
(Morocco)	109	6.4	71	22.4	49	33.8	53	32.0	37	16.2	14	57.1	–	–	–	–	333	19.8
(Canada)[a, b]	79	1.3	165	0.6	208	0	303	3.0	459	4.8	245	3.3	210	6.2	638	5.2	2307	3.8
(Thailand)	46	13.0	62	9.7	96	33.3	81	27.2	176	55.1	74	64.9	51	64.7	25	76.0	611	42.4
India)	9	11.1	62	12.9	108	13.0	131	11.5	159	25.2	147	32.0	115	47.0	109	52.3	840	28.1
(Japan)[a]	145	2.1	203	3.4	204	9.3	200	14.0	367	15.5	202	23.8	199	26.1	389	25.7	1909	16.4
(Australia)	95	1.1	95	0	100	4.0	84	3.6	175	1.7	89	3.4	94	2.1	176	5.7	908	2.9
(Greece)	73	4.1	363	8.5	173	16.2	141	23.4	457	32.8	416	36.8	516	39.5	1142	49.8	3281	35.7
GDR)	60	15.0	44	9.1	53	13.2	65	23.1	119	12.6	63	11.1	64	9.4	147	24.5	615	16.1
(FRG)	40	5.0	40	0	40	2.5	39	2.6	40	2.5	40	5.0	40	7.5	80	11.3	359	5.3
(FRG)	–	–	–	–	–	–	364	0.5	633	3.5	472	4.7	330	6.4	167	13.8	1966	4.6
Romania)	56	10.7	52	17.3	98	22.5	116	43.1	108	50.9	89	58.4	98	62.2	80	56.3	697	43.0
(UK)	–	–	–	–	–	–	–	–	228	7.0	239	11.3	186	9.1	218	10.5	871	9.7
(USSR)	25	44.0	52	43.4	54	35.2	47	40.4	118	34.7	77	50.6	41	51.2	64	64.0	478	43.7
Czechoslovakia)	108	2.8	106	7.6	110	8.2	104	8.7	186	15.6	110	14.5	104	8.7	163	20.2	991	11.7

by PHA.
population only.

Nevertheless, in southern and eastern European countries, such as Greece, Romania, and the USSR, the average prevalence rates were also high and comparable with those in Africa and Asia (35.7–

prevalence of anti-HBs in different high-risk groups and in psychiatric and venereal patients is shown in Table 9. Except for and females, except in Canada and Uganda, higher rates were detected in males than in As to place of residence, the only significant prevalence rate of anti-HBs was found in Thailand; in other countries, prevalence differences between urban and rural populations were (Table 8).

prevalence of anti-HBs in different high-risk groups and in psychiatric and venereal patients is shown in Table 9. Except for where the prevalence rates in these groups comparable with those in the normal population, other investigated countries such as Australia, Czechoslovakia, the German Democratic Republic, and the USSR, were detected significantly more often in the high-risk groups and in patients.

DISCUSSION

Difficulties often arise when attempts are made to compare the results of international serological surveys in which techniques of different sensitivities and specificities are employed. Our study on the prevalence of markers of hepatitis B virus infection in various countries was devoid of such difficulties, since the same reagents and RIA or RPHA were used throughout. Owing to its specificity and simplicity, RPHA, although slightly less sensitive than RIA, was recommended by the WHO Expert Committee on Viral Hepatitis (*1*) as a technique suitable for screening large numbers of sera for HBsAg. The same applies to PHA for detection of anti-HBs.

Table 7. Anti-HBs prevalence by sex in normal urban and rural populations of all ages in various countries as determined by radioimmunoassay

Laboratory location	Male		Female	
	No. tested	% positive	No. tested	% positive
Entebbe (Uganda)	315	56.5	139	34.3
Ottawa (Canada)[a, b]	1235	4.9	1072	2.4
Bangkok (Thailand)	279	47.0	332	42.5
Poona (India)	441	30.0	399	27.3
Tokyo (Japan)[a]	943	14.3	966	18.6
Fairfield (Australia)	443	3.0	465	2.8
Athens (Greece)	1836	36.4	1442	33.6
Berlin (GDR)	289	18.0	326	14.6
Göttingen (FRG)	165	4.8	194	5.4
Munich (FRG)	1145	4.0	821	5.4
Iasi (Romania)	356	42.5	341	44.3
Moscow (USSR)	174	47.1	304	41.8
Prague (Czechoslovakia)	472	11.9	519	11.6

[a] Tested by PHA.
[b] Urban population only.

Table 8. Anti-HBs prevalence in normal urban and [illegible] populations of both sexes and all ages in various [illegible] as determined by radioimmunoassay

Laboratory location	Urban		[illegible]	
	No. tested	% positive	No. tested	[illegible]
Entebbe (Uganda)	380	47.0	74	[illegible]
Bangkok (Thailand)	407	38.3	204	[illegible]
Poona (India)	274	30.7	565	[illegible]
Tokyo (Japan)[a]	952	17.0	957	[illegible]
Fairfield (Australia)	458	2.4	450	[illegible]
Athens (Greece)	1940	37.8	1338	[illegible]
Berlin (GDR)	287	17.8	328	[illegible]
Göttingen (FRG)	210	6.1	149	[illegible]
Munich (FRG)	360	8.3	1576	[illegible]
Iasi (Romania)	469	42.4	228	[illegible]
Moscow (USSR)	402	42.8	76	[illegible]
Prague (Czechoslovakia)	581	11.5	419	[illegible]

[a] Tested by PHA.

Table 9. Anti-HBs prevalence in different high-risk population groups and patients in various countries as determined by radioimmunoassay

Laboratory location	Haemodialysis staff / patients		Hospital and laboratory personnel		Institutionalized persons		Psychiatric patients		Venereal disease patients		[illegible]	
	No. tested	% positive	No. tested	% positive	No. tested	% positive	No. tested	% positive	No. tested	% positive	No. tested	[illegible]
Fairfield (Australia)	125	16.8	—	—	166	9.0	88[a]	43.2	307	13.4	[illegible]	[illegible]
Berlin (GDR)	95	44.2	109	18.4	134[a]	37.0	75[a]	52.0	226	19.9	[illegible]	[illegible]
Iasi (Romania)	24	33.3	—	—	134[a]	43.3	295	53.6	114	49.1	[illegible]	[illegible]
Moscow (USSR)	22	86.4	31	87.1	221	40.0	—	—	—	—	[illegible]	[illegible]
Prague (Czechoslovakia)	—	—	455	35.8	—	—	159[a]	24.2	—	—	[illegible]	[illegible]

[a] Children only.

Although the study did not suffer from the pitfalls of comparing results obtained by different techniques, it faced the shortcomings related to the testing of non-homogeneous population samples. It has been shown repeatedly that the HBsAg prevalence rates in the normal population may differ considerably within a country, depending on various local ethnic, socio-economic, cultural, geographic, religious, and other factors, and it is in this sense that our [illegible] samples do not represent homogeneous [illegible] 3).[a] It should therefore be pointed out that [illegible] presented may reflect only the local situation [illegible] areas from which serum specimens were [illegible]

[a] Similar findings have been reported by [illegible] communication.

, therefore, be representative of the whole . Nevertheless, taking into consideration these factors, the study indicates a generally higher y of HBsAg chronic carriers in the investi- opulations in African and Asian countries than Americas, Australia, and some European especially those of northern and central In southern and eastern European countries, the HBsAg prevalence rates were generally and in some of them were comparable with the rates in Asian and African countries.

the data on age prevalence of HBsAg it can be that in areas with generally low rates of the antigenaemia seems to build up gradually late childhood, whereas in those with high prevalence the antigen can frequently already ed in preschool children. This would suggest act with infection, possibly as a consequence iar spread and/or vertical transmis- g-carrier mothers to their children. , it was shown that the risk of perinatal on of hepatitis B virus infection in countries carrier rates of HBsAg may reach 40–50%

the frequency of antigenaemia was higher and in urban populations in some countries, was true in others. In most cases, the were not significant. Similar variable ve also been found in other studies (*7*, *8*, *9*). gations into HBsAg prevalence in various population groups and in psychiatric and disease patients showed, as expected, higher of antigenaemia in countries with rela- HBsAg prevalence rates in the normal . Such clear differences were not seen, areas of high HBsAg prevalence in where the high-risk population categories examined (institutionalized persons and institutionalized psychiatric patients) had prevalence rates comparable with those of normal population groups matched for age and place of residence.

The results of the subtyping of HBsAg-positive specimens followed the pattern of previously reported geographical distributions of antigen subdeterminants (*10*, *11*). It should be noted that, since the number of specimens available for subtyping HBsAg varied considerably in different countries, comparison of these results is difficult. For a clearer picture of the geographical distribution of subtypes of HBsAg, additional studies are needed.

Anti-HBs prevalence in all the population categories investigated followed the trend of a steady increase with advancing age. On average, however, it appeared to be significantly greater in areas of high HBsAg prevalence than in those of low HBsAg prevalence. This is in agreement with previously reported findings (*1*). Although no significant differences in anti-HBs prevalence rates were observed relative to sex and place of residence (urban/rural), such differences were significantly more marked in high risk population groups than in the normal population. However, this was true only for areas where anti-HBs prevalence rates in the normal population were relatively low. In areas of high anti-HBs prevalence in Romania, the differences between the prevalence rates in normal and high risk populations were not significant; thus the pattern was similar to that of HBsAg prevalence rates in these two populations. This indicates clearly that high-risk population groups cannot be defined categorically, as the situation may vary from country to country. This is especially true for countries with high HBsAg or anti-HBs prevalence (*1*).

Annex

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RÉSUMÉ

FRÉQUENCE DES MARQUEURS DE L'INFECTION À VIRUS DE L'HÉPATITE B DANS DIVERS PAYS. ÉTUDE COLLECTIVE DE L'OMS

Une étude collective OMS sur l'hépatite virale B, à laquelle ont participé 21 laboratoires de 20 pays, est décrite. Cette étude visait à définir la fréquence de l'antigène de surface de l'hépatite B (HBsAg), de ses sous-types et de l'anticorps correspondant (anti-HBs) selon l'âge et le sexe et en secteur urbain ou rural, dans des populations normales de différentes parties du monde. Des groupes à haut risque dans les populations et des malades souffrant de diverses affections ont également fait l'objet d'investigations. Les résultats de l'étude ont confirmé que la fréquence de HBsAg et de l'anti-HBs était plus élevée dans les pays d'Afrique et d'Asie que dans les Amériques, en Australie et en Europe septentrionale et centrale. Néanmoins, dans certains pays de l'est et du sud de l'Europe, la fréquence de HBsAg et de l'anti-HBs était haute et comparable à celle qu'on observe en Afrique et en Asie. Là où la fréquence de HBsAg et de l'anti-HBs est faible, elle semble augmenter graduellement à la fin de l'enfance et au début de l'adolescence, alors que dans les pays où ces marqueurs sont fréquents on les décèle souvent chez des enfants d'âge préscolaire. Bien que la fréquence de HBsAg et de l'anti-HBs tende à être plus élevée [illegible] populations urbaines que rurales et masculines que [illegible] nines, dans la plupart des cas les différences n'[illegible] significatives. En revanche, la fréquence des [illegible] l'infection à virus de l'hépatite B était significativement [illegible] élevée dans les groupes à haut risque que dans les [illegible] tions normales. Toutefois, cette situation n'était [illegible] définie que dans les zones où, chez la population [illegible] fréquence de HBsAg et de l'anti-HBs était basse. En [illegible] concerne la répartition géographique des sous-types [illegible] HBsAg, on observait une plus grande fréquence [illegible] déterminant *ad* que du sous-déterminant *ay* dans [illegible] d'Europe centrale, tandis qu'en Europe orientale [illegible] nale le sous-type *ay* prédominait. En Afrique [illegible] *ayw* était le seul variant rencontré, tandis qu'en [illegible] orientale *ad* était plus fréquent que *ay*. En Australie [illegible] *ayw* étaient détectés l'un et l'autre, tandis qu'en [illegible] Orient et en Asie du Sud-Est seuls *adw* et *adr* [illegible] observés.

REFERENCES

1. WHO Technical Report Series, No. 602, 1977 (*Advances in viral hepatitis*: report of the WHO Expert Committee on Viral Hepatitis).
2. SZMUNESS, W. Recent advances in the study of the epidemiology of hepatitis. *American journal of pathology*, **81**: 629 (1975).
3. OUDART, J.-L. & ROFFI, J. Antigen HBs dans les populations rurales du Sénégal. *Medicina tropical*, **38**: 565 (1978).
4. PAPAEVANGELOU, G., HOOFNAGLE, J. H. & KREMASTINOU, J. Transplacental transmission of hepatitis B virus by symptom-free chronic carrier mothers. *Lancet*, **2**: 746 (1974).
5. STEVENS, C. A. ET AL. Vertical transmission of hepatitis B antigen in Taiwan. *New England journal of medicine*, **292**: 771 (1975).
6. OKADA, K. ET AL. Hepatitis B surface antigen in the serum of infants after delivery from asymptomatic carrier mothers. *Journal of pediatrics*, 80: 360 (1975).
7. BLUMBERG, B. S. ET AL. Australia antigen and the virus—variation in host response. *American [illegible] medicine*, **48**: 1 (1970).
8. SZMUNESS, W. ET AL. The epidemiology of [illegible] infections in Africa. Results of a pilot [illegible] Republic of Senegal. *American journal of [illegible] ology*, **98**: 104 (1973).
9. PRINCE, A. M. Prevalence of serum hepatitis [illegible] (SH) in different geographic regions. *American [illegible] of tropical medicine and hygiene*, **19**: [illegible]
10. COUROUCÉ, A.-M. ET AL., ed. HBs antigen [illegible] *Proceedings of the International Workshop on [illegible] Antigen Subtypes, Paris, April 1975*, [illegible] 1976 (Bibliotheca haematologica, No. [illegible]
11. NISHIOKA, K. ET AL. Hepatitis B [illegible] subtypes, and hepatitis B antibody in [illegible] and patients with liver disease. *Bulletin of the World Health Organization*, **52**: 293 (1975).

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EXPANDED
PROGRAMME
ON IMMUNIZATION

Hepatitis B Immunization Strategies

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WORLD
HEALTH
ORGANIZATION

7. RECOMMENDATIONS

- Chronic infection with hepatitis B virus is common in developing countries. Such infection is a cause of hepatocellular carcinoma, one of the 10 most common cancers in the world. Hepatitis B vaccine is safe and effective in preventing infection. Its use early in infancy can reduce chronic carrier rates by over 75%.

- Hepatitis B immunization programmes should be considered in all population groups who have chronic carrier rates of hepatitis B virus of over 2%; they become a major public health priority for populations with carrier rates above 10%.

- In countries with chronic carrier rates of hepatitis B of over 2%, hepatitis B immunization should be introduced as an integral part of existing childhood immunization programmes as quickly as resources permit. Efforts to use this vaccine in ways which do not strengthen existing programmes should not be encouraged.

- The specific immunization schedule adopted in national programmes needs to be adapted to national circumstances, bearing in mind the usual age of hepatitis B infection and the delivery capacities of the health system. The objective is to prevent chronic carriage of hepatitis B virus. National immunization schedules should be formulated so that the use of hepatitis B vaccine minimizes extra contacts with the health system beyond those already needed for vaccines included within national childhood immunization programmes.

- A minimum of three doses of hepatitis B vaccine is recommended, given by the intramuscular route. The first dose is recommended at birth or as soon as possible thereafter. Early immunization is a special priority for those countries in which perinatal transmission is frequent. The second dose should be given 4-12 weeks after the first, timed to coincide with other routine childhood immunizations. The third dose may be given 2 to 12 months after the second, again timed to coincide with other routine childhood immunizations. At present, additional doses of vaccine are considered a low priority.

- While the use of hepatitis B immune globulin is effective in complementing the use of hepatitis B vaccine in preventing perinatal infection, its high cost and the need to administer it within hours of birth will preclude its use in most developing countries.

APPENDIX - B.

RECOMMENDATIONS OF THE NOVEMBER 1987 HEPATITIS TECHNICAL ADVISORY GROUP

"HEPATITIS B VACCINES AND IMMUNIZATION STRATEGIES"

1. The TAG notes that over 30 million doses of plasma-derived HB vaccine have been distributed worldwide and that there are now more than 10 manufacturers of these vaccines globally. The vaccines have an impressive record of safety. In addition, several vaccines manufactured by rDNA technology are now on the market and additional manufacturers are expected to enter the market in the next two or three years. These rDNA vaccines are equivalent to plasma derived vaccines in respect to safety, immunogenicity and efficacy and neither offers any advantage over the other in these respects. Plasma-derived vaccines will continue to play an essential role in Hepatitis B control programmes worldwide for the foreseeable future.

2. There has been a dramatic decrease in the price of HBV vaccines to the level where many countries in Hepatitis B hyperendemic areas may now begin the development and implementation of large scale vaccination programmes. WHO should encourage their implementation and monitor their progress.

3. The TAG encourages the establishment of programmes and liaising with relevant groups within and without the Organization and encourages continued and increasing close collaboration between WHO and such bodies in the development and implementation of the global programme on HBV control.

4. The TAG emphatically reiterates that the most important means to control HB on a global scale and to reduce mortality due to chronic sequelae of this infection, including cirrhosis and HCC, is the large scale immunization of infants. It therefore recommends that HB vaccination be integrated into EPI as soon as possible. For incorporation into EPI, it is recommended that three doses of HBV vaccine will be given and that administration should be intramuscular into the thigh of infants. The first dose (HBV-1) should be given as soon as possible after birth. Although programmes should aim at administration of HBV-1 within the first week of life, it should be initiated at any time if it cannot be given so early. It is also desirable that HBV-1

be given simultaneously with the first EPI immunization.

The second dose (HBV-2) should be given 4 to 12 weeks after HBV-1, as it best fits into the EPI schedule of the particular Region.

A third dose (HBV-3) is currently needed to achieve high levels of antibody and prolonged protection. There is considerable latitude regarding timing of this dose. Countries can adopt schedules with 2 to 12 months following. HBV-2, at a time when it best fits into the EPI schedule of the particular Region.

HBIG may be of additional value in HB immunization programmes for infants, but cost of its inclusion into large scale immunization programmes precludes its use in most countries.

5. The TAG encourages operational research to define methods for an optimal integration of HB vaccination into EPI through the establishment of immunization projects in selected countries in hyperendemic areas of the world, and that WHO monitor the results of these projects. In particular the effectiveness of Hepatitis B vaccination in a variety of EPI settings and according to differing schedules of delivery of other EPI immunogens should be evaluated. Also thermal stability of HB vaccines should be further evaluated in order to adapt them to EPI cold chain characteristics.

Model immunization projects in Indonesia, Thailand and China are being established in collaboration with the International Task Force of Hepatitis B Immunization. These projects should be closely monitored and evaluated on an ongoing basis.

Immunization Dialogue

Hepatitis B Vaccine

Currently, universal infant hepatitis B vaccination is being promoted vigorously. The concept of hepatitis B immunization is relatively new for our country. In view of the novelty, cost, availability of different brands and the economic constraints of a developing country, several clarifications are required. In this context, Dr. T. Jacob John, Professor and Head, Department of Microbiology and Virology, Christian Medical College Hospital, Vellore, Tamil Nadu 632 004 answers important questions posed by us. Professor Jacob John, a leading International Vaccinologist, is an Adviser on Immunization to the World Health Organization and other International Agencies. He is the current Chairman of the IAP Committee on Immunization.

–Editor-in-Chief

Q1. *What are the currently known agents which can cause viral hepatitis? For how many of these are effective vaccines available?*

A1. The currently known hepatitis viruses are: Hepatitis A virus (HAV) (hepatovirus, family *Picornaviridae*); Hepatitis B virus (HBV) (family *Hepadnaviridae*); Hepatitis C virus (family *Flaviviridae*); Hepatitis D virus (HDV) (not yet placed taxonomically); and Hepatitis E virus (family *Caliciviridae*). In addition, the names Hepatitis F and G viruses have been assigned to putative agents causing hepatitis; these agents have not been characterized.

Safe and effective vaccines are available for HAV and HBV. Since HDV is a 'defective' virus, genetically dependent on the genome of HBV for replication, HBV vaccine will also protect against HDV infection.

Q2. *In the recent years, universal infant hepatitis B vaccination is being vigorously promoted by International Agencies and several Governments. How many countries have adopted universal infant hepatitis B vaccination and what are the pressing reasons for this policy decision?*

A2. The World Health Organization (WHO) has recommended the inclusion of hepatitis B vaccine in the routine schedule of Universal Immunization Programme in all countries. More than 30 countries, including many in the American continent, East Asian and South Asian regions, Europe and in Africa, have adopted this recommendation. The major reasons for this policy include the following factors: HBV causes acute hepatitis, chronic carrier state, chronic hepatitis, cirrhosis of liver and

hepatocellular carcinoma. It is transmitted person to person, the reservoir being the carriers. The chain of transmission can be broken by using the available safe and effective vaccines. Selective immunization will not reduce the reservoir; universal immunization will.

Q3. *Do epidemiological reasons support adoption of universal infant hepatitis B vaccination in India? Considering the economic constraints, what should be the current recommendations for our country? What are the high risk groups who require hepatitis B vaccine?*

A3. Epidemiological features of HBV infection in India, I must say, demand a policy of universal immunization with the HB vaccine. The HBV carrier prevalence in India ranges between 1 to 10 %, depending upon the population sample studied and the methodology of testing; 3-7% is the range quoted widely. Carrier state is mostly due to vertical transmission of HBV (from mother to her infant, perinatally) and also to lesser extent due to horizontal transmission. Only routine infant immunization will protect against both vertical and horizontal infection.

The major reason for the current inability of the nation to accept the WHO recommendation is the prohibitive cost of the vaccine. The logical solution to this problem is the indigenous manufacture of HB vaccine and some efforts are being made in this direction. I am hopeful that India will adopt the policy before the end of this decade, when locally made vaccine will be available at affordable prices. The current prices are between 100 and 500 rupees per dose.

The Immunization Committee of IAP has recommended HB vaccine for infants in all families that can afford it. I do hope that increasing demand for vaccine will encourage competition in the market with a consequent fall in prices.

In the interim, HB vaccination must be practiced in clinical situations of high risk. These include: (a) Infants born to HBV carrier mothers; (b) Subjects under preparation for kidney transplantation; (c) Any staff in hospitals, who have had needle stick injury, when the index case is HBV infected; and (d) All trainees of medicine, nursing and medical laboratory services.

Q4. *What are the various types of commercially available vaccines for hepatitis B and how are these produced?*

A4. The available HB vaccines can be broadly classified as *plasma derived* and *genetically engineered* (*recombinant*) vaccines. As the names suggest, the plasma derived vaccine is prepared from the pooled plasma of HBV carriers (who are HIV negative). The HBV surface antigen particles (HBsAg) are harvested, purified and any residual virus inactivated for the preparation of the vaccine. Only traces of human albumin may be present in the vaccine, but no other human serum protein will be present. One dose of this vaccine is usually 20 micrograms of protein, adjuvanted with an aluminum salt.

The recombinant vaccine is prepared in a vector, usually the baker's yeast (*Saccharomyces cereviseae*), into which the gene for HBsAg has been introduced. Now the yeast expresses the HBsAg protein, which is harvested and purified as the vaccine. The usual dose is 10 micrograms of protein, adjuvanted with an aluminum salt.

Different manufacturers have now altered the microgram content of the HBsAg protein per dose. The manufacturer's description must be read to know exactly how much protein is present. Currently, the amounts vary between 5 micrograms (heated, plasma derived antigen) to 20 micrograms (plasma derived or recombinant).

Q5. *What are the relative advantages and disadvantages of recombinant DNA derived hepatitis B vaccine vis-a-vis the plasma derived hepatitis B vaccine?*

A5. Both plasma derived and recombinant vaccines are, as far as we know now, completely safe from any extraneous infectious agents. Particularly, the plasma derived vaccine is made free of infectious HBV by the process of purification and inactivation, and also free of HIV by the processes of exclusion of infected subjects, purification and inactivation. There has been no record of "prions" in either vaccine. As the availability of plasma of carriers will decrease, we will have to depend more increasingly on recombinant vaccine; but this is for the future. To summarize several studies, in infants and children below 10 years, 5 microgram doses of recombinant vaccine and 10 microgram doses of plasma derived vaccines have been equally safe and effective. The cost of these vaccines, however, vary much. While the plasma derived vaccine costs about 100-200 rupees (2-5 US dollars), the recombinant vaccine costs about 400–500 rupees (10 US dollars).

Q6. *Is it true that the European Community and the USA have switched over from plasma derived to recombinant hepatitis vaccines? If yes, why?*

A6. Most developed countries use only the recombinant vaccine, partly for reasons of easy availability (many manufacturers have given up plasma collection and purification, in this era of HIV/AIDS), and partly for 'aesthetic' reasons of not using a human product, but using the fruits of biotechnology. For them the cost-difference is not a factor.

Q7. *What is the recommended age, dose, route and site for hepatitis B vaccine?*

A7. The recommended immunization schedule using either plasma derived or recombinant HB vaccine is to give 3 doses for the primary course. To obtain the best result in term of antibody levels and duration of immunity, the recommended intervals between the first and second doses is one month and between the second and third doses 6 months. Thereafter, the first booster is recommended after 5 years; the next booster 10 years later. Most probably no further boosters are needed for the rest of one's life.

The schedule could be accelerated to give 3 doses at 0, 1 and 2 months, that is to keep the intervals between the first and second as well as between the second and third doses as one month. In that case, the first booster is recommended 1 year later, second booster 5 years later and a third booster 10 years later. No further boosters are necessary.

Full doses are given for children above 10 years and for adults. Half the adult doses are given to infants and children upto 10 years. The vaccine is recommended for intramuscular route; deltoid muscle in children and adults and anterolateral thigh for infants. Gluteal injection is to be avoided since im-

mune responses are not optimal at this site.

The IAP Immunization Committee recommends the commencement of HB vaccine immunization at birth, that is, within 2-3 days of birth, preferably on the first day itself. The purpose here is to offer protection against vertical transmission in case the mother happens to be an HBV carrier. Some 3-7 % of mothers are HBV carriers; unless all mothers are screened for carrier state, all babies should be offered early protection. If mothers are screened, then babies will be classified as at risk or not at risk for vertical transmission. Those at risk must be immunized at birth, but those not at risk may be immunized at a later time, preferably during infancy itself. Indeed HB vaccine can be given at any age, for infants, children or adults.

Q8. *For how long does immunity last after immunization?*

A8. The duration of immunity after primary immunization with 3 doses at the recommended intervals ranges from 5 years to 10-15 years. Therefore, one booster is recommended after 5 years; thereafter, immunity lasts 10 years or more. With one more booster, immunity is probably life-long. In this context, immunity is taken to mean protection from hepatitis B when exposed; this is equated to antibody levels of 10 mille international units or more per ml of serum.

Q9. *What is the maximum permissible interval (if any) between the first two doses and the second and third dose?*

A9. The recommended interval between the first and the second dose is one month. Increasing this interval to 2 months or even longer, say 3 or 4 months, does not affect the overall response at the end of the 3 dose schedule. There probably is an upper limit to this interval; arbitrarily most experts would accept upto one year of interval. Thereafter, it is better to start the schedule all over again. The ideal interval between the second and third doses is 6 months. However, this interval is more flexible and probably acceptable upto 5 years.

Q10. *Can an infant receive one dose of vaccine from one manufacturer and the next dose from another manufacturer for the same type of hepatitis B vaccine? Similarly, can an infant receive one dose of vaccine of one type and the next dose of the other type?*

A10. The antigenic configuration of HBV surface antigen is nearly identical in all currently available vaccines. Some may have additional epitopes of the pre-S region. However the major epitopes are identical in all vaccines. Therefore, theoretically at least, switching of vaccines should not affect immune response. But, it is cleaner to use one particular brand of vaccine for the primary course. Booster can be given with any vaccine.

Q11. *What are the advantages and disadvantages of intradermal and subcutaneous use of hepatitis B vaccine vis-a-vis the recommended intramuscular mode?*

A11. Vaccines adjuvanted with aluminum salts, such as HB vaccine and DPT vaccine are supposed to be given intramuscularly in order to prevent nodule formation. However, even when given subcutaneously, usually there is no problem, and the immune response is satisfactory. If the vaccine is deposit-

ed within adipose tissue, then the immune response would be poor. The dose must be the same when given intramuscularly or subcutaneously. In children with bleeding disorders, the subcutaneous route is preferred over intramuscular placement.

Intradermal route is adopted when one wishes to reduce the dose of the vaccine for the purpose of reducing the cost. A full dose of vaccine is 1 ml. Intradermal dose should be no less than 0.1 ml and no more than 0.2 ml. If the dose contains 20 micrograms of protein, 0.1 ml is adequate. If the dose contains 10 or 5 micrograms, then 0.2 ml should be injected. The placement must be truly intradermal for effective immune response. I do not recommend intradermal injection, particularly for primary immunization, since the vaccine dose is very small - in the range of 1 to 2 micrograms only. The immune response to such small doses is less consistent than with the dose levels of 5 to 20 micrograms.

Q12. *What is the frequency of various reported side effects after hepatitis B vaccination? If any adverse reaction has occurred after the first dose, should subsequent doses be given?*

A12. A bit of local pain and tenderness lasting a day or two occurs in a proportion of immunized subjects. This is believed to be due to the aluminum salt. It occurs in about 10-20% of subjects. Rarely a low grade fever or mild gastrointestinal discomfort has been recorded following vaccination. Pediatricians must be aware that any injection may trigger a syncopal attack; any protein may induce anaphylaxis; any vaccine may precipitate unusual responses such as urticaria, erythema multiforme or Guillain Barre syndrome. These are extremely rare events, but any injection clinic must be alert to such events and adrenaline should always be readily available.

If any minor reactions occur after one dose, there is no reason not to give the next dose. If the reaction is a serious one, then decisions must be based on individual cases. Anaphylaxis alone is a contraindication for the next dose. However, if immunization is considered essential, then the next dose can be given with due precautions such as the prior administration of an antihistamine and the prompt administration of adrenaline following the vaccine. In such cases informed consent must be obtained from parents.

Q13. *What are the various precautions and contraindications (specifically yeast allergy, HIV infection, pregnancy and lactation) for administering hepatitis B vaccine?*

A13. There are essentially no contraindications to HB vaccination. Vaccine is not necessary in persons already immune, or in HBV carriers identified by the presence of HBsAg in serum. Theoretically, yeast allergy may be a contraindication to yeast-derived recombinant vaccine. But then, what is yeast allergy? I do not know how to diagnose yeast allergy and I have not come across any reports of yeast allergy. HIV infection is not a contraindication. Although safety to the fetus has not been specifically evaluated, pregnancy need not be a contraindication since the antigen is non-replicating. The same statement holds true for lactation also.

Fulminant Hepatitis in a Tropical Population: Clinical Course, Cause, and Early Predictors of Outcome

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The profiles of patients with fulminant hepatic failure (FHF) from developing countries have not been reported earlier. The current study was conducted prospectively, at a single tertiary care center in India, to document the demographic and clinical characteristics, natural course, and causative profile of patients with FHF as well as to define simple prognostic markers in these patients. Four hundred twenty-three consecutive patients with FHF admitted from January 1987 to June 1993 were included in the study. Each patient's serum was tested for various hepatotropic viruses. Univariate Cox's regression for 28 variables, multivariate Cox's proportional hazard regression, stepwise logistic regression, and Kaplan-Meier survival analysis were done to identify independent predictors of outcome at admission. All patients presented with encephalopathy within 4 weeks of onset of symptoms. Hepatotropic viruses were the likely cause in most of these patients. Hepatitis A (HAV), hepatitis B (HBV), hepatitis D (HDV) viruses, and antitubercular drugs could be implicated as the cause of FHF in 1.7% (n = 7), 28% (n = 117), 3.8% (n = 16), and 4.5% (n = 19) patients, respectively. In the remaining 62% (n = 264) of patients the serological evidence of HAV, HBV, or HDV infection was lacking, and none of them had ingested hepatotoxins. FHF was presumed to be caused by non-A, non-B virus(es) infection. Sera of 50 patients from the latter group were tested for hepatitis E virus (HEV) RNA and HCV RNA. In 31 (62%), HEV could be implicated as the causative agent, and isolated HCV RNA could be detected in 7 (19%). Two hundred eighty-eight (66%) patients died. Approximately 75% of those who died did so within 72 hours of hospitalisation. One quarter of the female patients with FHF were pregnant. Mortality among pregnant females, nonpregnant females, and male patients with FHF was similar ($P > .1$). Univariate analysis showed that age, size of the liver assessed by percussion, grade of coma, presence of clinical features of cerebral edema, presence of infection, serum bilirubin, and prothrombin time prolongation controls at admission were related to survival ($P <$ The rapidity of onset of encephalopathy and cau FHF did not influence the outcome. Cox's proporti hazard regression showed age ≥40 years, presen cerebral edema, serum bilirubin ≥15 mg/dL, and thrombin time prolongation of 25 seconds or more controls were independent predictors of outc Ninety-three percent of the patients with three or of the above prognostic markers died. The sensiti specificity, positive predictive value, and the neg predictive value of the presence of three or more of prognostic factors for mortality was 93%, 80%, 86%, 89.5%, respectively, with a diagnostic accuracy of 8 We conclude that most of our patients with FHF have been caused by hepatotropic viral infection, non-A, non-B virus(es) seems to be the dominant he tropic viral infection among these patients. They sented with encephalopathy within 4 weeks of the of symptoms. Pregnancy, cause, and rapidity of ons encephalopathy did not influence survival. The nostic model developed in the current study is si and can be performed at admission. (HEPATO 1996;23:1448-1455.)

Most reports on fulminant hepatic failure (F have been predominantly from the West,[1-9] and par larly from three countries: the United Kingdom, pan,[3,4] and France.[5] Based on these geographically ited observations, a new classification of this di entity into hyperacute, acute, and subacute liver ure has been suggested.[2] These authors also sugg the adoption of this classification universally for form terminology. The latter study has not been to consider the disease characteristics in the tro population, presumably because of the lack of lished data from the tropics.

The cause and rapidity of the onset of hepatic en alopathy in patients with FHF have been report important prognostic predictors.[1-3] However, the of FHF may have regional differences, and the ra of onset of encephalopathy after the occurrence of hepatitis may also vary among different popula because host factors play an important role in th verity of hepatic injury.

Various other factors, including the grade of en alopathy, serum bilirubin, prothrombin time, s alpha-fetoprotein, liver volume estimation using

Abbreviations: FHF, fulminant hepatic failure; Ig, immunoglobulin; HAV, hepatitis A virus; HDV, hepatitis D virus; HBV, hepatitis B virus; HEV, hepatitis E virus; HCV, hepatitis C virus.

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ood, blood ammonia levels, galactose elimination ca-city, and bile acid conjugation, have been suggested distinguish survivors and nonsurvivors among pa-nts with FHF.[1-3,6-8,10-15] The prognostic criteria for F developed at King's college, London,[1] and at Cli-, France,[5] when reevaluated at another center, were nd to have a lower specificity and sensitivity than orted in the original studies.[16] Orthotopic liver nsplantation has become an established treatment ion in patients with FHF[17-21] and is gradually be-ing available in developing nations. Hence, there a need for a prognostic model in patients with FHF hese countries.

The current study on FHF therefore was conducted pectively in a single tertiary care center in North a to identify the demographic characteristics, caus-e spectrum, clinical features, natural course, and dictors of outcome among patients with FHF.

PATIENTS AND METHODS

ents

onsecutive patients with FHF admitted to the gastroen-logy ward of the All India Institute of Medical Sciences, Delhi, between January 1987 and June 1993 were in-ed in the study.

Diagnosis of FHF. The diagnosis of FHF was made by the ence of encephalopathy within 8 weeks of onset of ill-.[12] Diagnosis of FHF was confirmed by presence of sub-ive or massive necrosis in the postmortem liver biopsy imen in patients who died. Consent for the postmortem r biopsy was obtained from the nearest relative of the ased after explaining the purpose of the biopsy. Liver sy in the survivors was performed whenever possible their coagulation profile was corrected and an informed ent was obtained.

Exclusion Criteria. Patients in whom the history was un-able or the diagnosis was not confirmed by a combination ypical clinical features, liver function tests, and viral kers with or without liver biopsy were excluded.

Chronic liver disease was excluded by liver biopsy. In pa-ts in whom a liver biopsy was not possible because of a nged coagulation profile, the diagnosis of chronic liver se was made on clinical, biochemical, and imaging crite-

dy Variables

uration of Prodrome. Period from onset of symptoms to nset of icterus

terus-Encephalopathy Interval. Interval between detec-n of icterus to onset of hepatic encephalopathy

-encephalopathy Period. Duration from onset of symp-s to onset of encephalopathy

uration of Coma. Time from onset of encephalopathy till plete recovery from encephalopathy or death. Complete very from encephalopathy was considered when the pa-t became conscious and was found to be oriented to time, and person.

rade of Coma. Coma was classified into four grades[22]:

rade I: Loss of sleep rhythm, presence of drowsiness, con-fusion, hepatic flap

rade II: Features of grade I encephalopathy with loss of sphincter control

rade III: Unconscious, no response to oral commands, but responds to painful external stimuli

Grade IV: Unconscious, no response to external stimuli except decerebrate posturing to painful stimuli

Cerebral Edema.[23,24] Cerebral edema was defined by the presence of spontaneous decerebrate posturing, hypertension (supine blood pressure >150/90 mm Hg), bradycardia (pulse rate <10 beats/min from the expected pulse rate for given body temperature), pupillary changes, and presence of neurogenic hyperventilation. Neurogenic hyperventilation was diagnosed by the presence of hyperventilation in the absence of any metabolic or respiratory cause for hyperventilation. Presence of decerebrate posturing alone or the presence of any two of the four features were considered as evidence of cerebral edema.

Sepsis. Sepsis was diagnosed in the presence of pyrexia (body temperature >101°F) or hypothermia (body temperature <98°F) and neutrophilic leucocytosis (total leucocyte count >15,000/mm^3 with 80% or more polymorphs) and one or more of the following: positive blood culture, positive urine culture, radiological evidence of pneumonitis.

Cause of Death. The immediate antecedent event occurring within 12 hours of death, in the absence of any other possible factor that could cause a fatal outcome, was considered as the cause of death.

Coagulopathy. Prolongation of prothrombin time by more than 4 seconds over controls was considered as evidence of abnormal clotting mechanism. This was determined from the distribution of the prothrombin time among normal subjects. Values were considered abnormal when they were beyond the mean ± 3 SD range at our laboratory. Thromboplastin was derived from rabbit brain (Biopool Inc., CA) with an international sensitivity index value of 1.0.

Treatment Schedule

All patients were given standard supportive treatment with energetic intensive care monitoring. H_2 receptor antagonists for stress ulcer prophylaxis, appropriate antibiotics for sepsis, parenteral mannitol (20%), and ventilatory support for cerebral edema, fresh frozen plasma as and when required, gut sterilization, and mantainance of fluid and electrolytes were the mainstay of therapy.

Methods

Each patient had clinical evaluation at admission and every 1 to 2 hours thereafter. History of consumption of hepatotoxic drugs or indigenous treatment such as herbal therapy was inquired of the relatives of each patient. Liver dullness by percussion at admission was assessed by at least two physicians (one resident and one consultant) at admission and subsequently twice daily.[25-27] Pregnancy was diagnosed by a history of amenorrhea, urinary human chorionic gonadotrophin assay, and bedside ultrasound. The trimesters of pregnancy were calculated from the history and sonographic assessment of fetal dimensions.

Blood was drawn at admission and subsequently every day for liver function tests and various hematologic and biochemical assays. Sera were separated and stored at −70°C for subsequent viral assays.

Viral Markers. Each patient's serum sample was screened for hepatitis B surface antigen, immunoglobulin (Ig) M anti-HBc, and IgM anti-hepatitis A virus (HAV) using commercial micro-enzyme-linked immunosorbent assay test kits (Organon, Teknika, Netherlands; and Abbott). Serum samples positive for hepatitis B surface antigen or IgM anti-HBc were also tested for the presence of anti-hepatitis D virus (HDV). Tests for both IgG and IgM anti-HDV antibody were performed using commercial enzyme-linked immunosorbent

TABLE 1. Demographic and Clinical Profile of Patients With FHF

	Survivors	Nonsurvivors	Total
Number	143 (34%)	280 (66%)	423
M:F	71:72 (1:1)	129:151 (1:1.2)	200:223 (1:
Age			
mean ± SE*	26.5 ± 0.9	31.4 ± 0.8	29.5 ± 0.6
range	(14-65)	(7-80)	(7-80)
Prodrome	128 (89.5%)	246 (89%)	374 (88%)
Duration of prodrome (d)			
mean ± SE	4.4 ± 0.6	5.2 ± 0.4	4.7 ± 0.5
range	(0-20)	(0-22)	(0-22)
Duration of preencephalopathy period (d)			
mean ± SE	5.8 ± 0.5	6.3 ± 0.4	5.7 ± 0.3
range	(0-28)	(0-28)	(0-28)
Preencephalopthy period (d)†			
0-7	117 (81.8%)	224 (80.0%)	341 (80.6%)
8-14	17 (11.9%)	37 (13.2%)	54 (12.8%)
15-21	6 (4.2%)	13 (4.6%)	19 (4.5%)
22-28	3 (2.1%)	6 (2.1%)	9 (2.1%)
Icterus-encephalopathy interval (d)			
mean ± SE	4.3 ± 0.5	4.9 ± 0.3	4.7 ± 0.3
range	(0-21)	(0-21)	(0-21)
Icterus-encephalopathy interval (d)‡			
0-7	104 (72.7%)	201 (71.8%)	305 (72.1%)
8-14	23 (16.1%)	48 (17.1%)	71 (16.8%)
15-21	16 (11.2%)	31 (11.1%)	47 (11.1%)
22-28	Nil	Nil	Nil

* $P < .0001$; only three patients were younger than 15 years. Other parameters were similar amongst survivors and nonsurvivors (P > .1).

† 224 of 341 (66%) patients with FHF presenting with encephalopathy within 1 week of onset of symptoms died, in comparison with of 82 (68%) similar patients who had encephalopathy after 1 week of onset of symptoms ($P > .1$). Similar observations were made wi mortality rate was compared amongst patients presenting with encephalopathy within 2 weeks and after 2 weeks of onset of symptom

‡ 201 of 305 (66%) patients who presented with encephalopathy within 1 week of onset of icterus died, in comparison with 79 of (67%) patients developing FHF after 1 week of onset of icterus ($P > .1$).

assay kits (Wellcome UK). Non-A, non-B FHF was diagnosed when the serum was negative for all of the above markers in the absence of a history of intake of hepatotoxins.

Sera from 50 consecutive patients with non-A, non-B fulminant hepatitis were also tested for hepatitis B virus (HBV) DNA to detect cryptic HBV infection, hepatitis E virus (HEV) RNA by reverse-transcription nested polymerase chain reaction using primers from nonstructural region of ORF-1, and hepatitis C virus (HCV) RNA by reverse-transcription nested polymerase chain reaction, using primers from the 5′ nontranslated region.[28-30] All samples were tested in duplicate. The amplified polymerase chain reaction products were confirmed either by Southern hybridization[29] or by liquid oligomer hybridization[31] with internal oligoprobes and label with [^{32}P]adenosine triphosphate (New England Nucle Boston, MA). The detailed steps of the procedure have already been reported elsewhere.[32]

TABLE 2. Causes of FHF

Cause	Survivors (n = 143)	Nonsurvivors (n = 280)	Total (%) (n = 423)
HAV	3 (2%)	4 (1.4%)	7 (1.7%)
HBV	39 (27%)	78 (27.8%)	117 (27.6%)
HDV	5 (3.5%)	11 (3.9%)	16 (3.8%)
Non-A, non-B	89 (62.2%)	175 (63%)	264 (62.4%)*
Antitubercular drug	7 (5%)	12 (4.3%)	19 (4.5%)

NOTE. The causative profile amongst survivors and nonsurvivors was similar ($P > .1$).

* Twenty-three (8.7%) were HBV carriers (HBsAg positive but IgM anti-HBc negative).

Statistical Analysis

Among survivors and nonsurvivors, qualitative variable were compared using the χ^2 test. Quantitative variables we compared using the Student's t test. Univariate Cox's regr sion, multivariate Cox's regression, and multiple stepw logistic regression were performed using the BMDP soft (University of California).[33-37] This was done to identify dictive variables for prognosis in patients with FHF. Kapl Meier survival analysis was performed for different strata patients.[38,39] The specificity and sensitivity for each predic identified on multivariate analysis and the combinat thereof was then assessed.

RESULTS

During the study period, 430 patients with FHF we hospitalized, which accounted for 8% of our total hos talized patients (n = 5,354) during the above perio Diagnosis was confirmed in 423 patients who were i cluded in the present study. One hundred forty-thr (34%) patients survived, and the remaining 280 (66% patients died. Most patients who died had histolog evidence of either submassive hepatic necrosis or

TABLE 3. Dichotomous Variables Influencing Outcome (Univariate Analysis)

Variables	Survivors (n = 143)	Nonsurvivors (n = 280)
...e	129	208
...40 yr	14	72
...40 yr		
...e of coma†		
	17 (11.9%)	26 (9.3%)
	44 (30.8%)	26 (9.3%)
	45 (31.5%)	87 (31.1%)
	37 (25.9%)	141 (50.4%)
...grade of coma‡	2.7 ± 0.1 (0-4)	3.2 ± 0.1 (0-4)
...size (in percussion space)*		
	56 (39.1%)	193 (68.9%)
	87 (60.9%)	87 (31.1%)
...size of liver (percussion space)†	2.8 ± 0.1 (0-6)	2.0 ± 0.1 (0-5)
...ebral edema at admission*	44 (30.8%)	201 (71.8%)
...tion at admission*	7 (4.9%)	38 (13.6%)
...n bilirubin (mg/dL)‡		
	100 (69.9%)	121 (43.3%)
	43 (30.1%)	159 (56.7%)
...mbin time prolongation ...er controls (s)*		
	115 (80.4%)	154 (55%)
	28 (19.6%)	126 (45%)

...< .0001.
...< .01.
...< .001.

...necrosis. Liver biopsy could be done in 83 patients ...survived, within 3 weeks of recovery, and showed ...presence of acute hepatitis with bridging necrosis ...all. In the remaining survivors, the diagnosis was ...ieved by clinical and biochemical features.

...ical and Demographic Profile

...The demographic profile of the patients is shown in ...le 1. Most patients (n = 334) were younger than 40 ...s of age, and the male-to-female ratio was 1:1.1. A ...rome of fever, anorexia, or vomiting was present ...4 (88%) patients. The presence or duration of pro..., preencephalopathy period, icterus-encephalop... interval, and the duration of hepatic encephalopa... among survivors and nonsurvivors were similar (*P* ... (Table 1). Encephalopathy developed within 14 ... in 395 (93.4%) patients, and none had encephalop...athy after 4 weeks of onset of symptoms of acute hepatitis (Table 1). The mean (±SE) duration between onset of symptoms and encephalopathy was 5.7 (±0.2) days.

An analysis of the icterus-encephalopathy interval showed that 376 (89%) patients in the current series developed encephalopathy within 2 weeks of onset of icterus, and all patients had encephalopathy within 3 weeks of onset of icterus. The mean (±SE) interval between detection of icterus and encephalopathy was 4.7 (±0.3) days.

There were 223 (53%) women or girls, a quarter (n = 53) of whom were pregnant. The mortality rates were similar ($P > .1$) among pregnant women (35 of 53, 66%), age-matched nonpregnant women (116 of 170, 68%), and male patients with FHF (129 of 200, 65%). The mortality rate was also similar ($P > .1$) among pregnant women during the first, second, and third trimesters.

Among the 280 patients with a fatal outcome, death occurred in 207 (74%) within 72 hours of hospitalization, and 254 (94%) died within a week of hospitalization. A Kaplan-Meier survival analysis showed that the mean (± SE) survival time was 1.03 (±0.9) days, and the median survival was 4 days. All deaths except one occurred within 1 week of onset of hepatic encephalopathy. Cerebral edema was the single most important cause of death among our patients (71.8%). The other causes of death were sepsis (23.9%), renal failure (2.9%), and gastrointestinal bleeding (1.4%).

Cause

The causes of FHF are shown in Table 2. HAV, HBV, and HDV could be incriminated in 7 (1.7%), 117 (28%), and 16 (3.8%) patients, respectively. Nineteen (4.5%) patients negative for all of these viral markers had consumed antituberculous drugs (which included rifampicin and isoniazid in optimal doses) for a mean (±SD) period of 28 (±9) days (range, 13-64 days). It was presumed that antitubercular agents caused acute hepatitis in these patients. The remaining 264 (62.4%) patients did not have any identifiable markers of acute HAV, HBV, and HDV infections in their sera. None of these patients had history of consumption of any identifiable hepatotoxins, particularly herbal drugs. Their clinical and biochemical features were suggestive of acute viral hepatitis. These patients were considered to have non-A, non-B viral infection. Sera from 50 consecutive patients with non-A, non-B FHF were ana-

TABLE 4. Variables Derived From Multiple Logistic Regression

Term Entered	*df*	Log Likelihood	Improvement in χ^2	*P*
		−250.03		
Cerebral edema at admission	1	−217.8	64.5	<.00001
Serum Bilirubin ≥15 mg/dL	1	−208.1	19.5	<.0001
Prothrombin time ≥25 s over control	1	−200.7	14.7	<.0001
Age ≥40 yr	1	−193.7	14.2	<.0001
Grade of coma III or IV	1	−191.1	5.0	.025
Infection	1	−189.8	4.7	.03

TABLE 5. Multiple Logistic Regression

Term	Coefficient	SE	Coefficient/SE	Exponential Coefficient	Lower Band	Upper Band
Age ≥40 yr	1.3	0.37	3.6	3.8	1.8	7.9
Grade of coma >2	0.7	0.31	2.4	2.1	1.1	3.7
Cerebral edema	1.3	0.29	4.5	3.6	2.1	6.3
Infection	1.0	0.49	2.1	2.8	1.0	7.3
Serum Bilirubin ≥ 15 mg/dL	1.1	0.26	3.9	2.8	1.7	4.6
Prothombin time (prolongation ≥ 25 s over controls)	1.2	0.29	4.1	3.3	1.9	5.7

lyzed for HEV and HCV RNA. Twenty (40%) of these had isolated HEV RNA, 7 (14%) had isolated HCV RNA, and 11 (22%) had both HEV and HCV RNA. The remaining 12 (24%) patients did not have any viral markers in their serum. Thus, HEV either in isolation or along with HCV was the causative agent in 31 (62%) of these patients with FHF. None of these 50 patients had cryptic HBV infection.[28]

Prognostic Markers

The clinical variables that influenced survival in our patients are shown in Table 3. Older age, higher grades of encephalopathy, smaller liver size on percussion, presence of overt cerebral edema, and sepsis at admission were detected in a significantly higher proportion of patients who died in comparison with those who survived ($P < .01$). The preencephalopathy period, icterus-encephalopathy interval, and cause among the survivors and nonsurvivors were similar (Tables 1, 2). Other hematologic and biochemical investigations were similar among survivors and nonsurvivors.

Univariate Cox's Analysis

Univariate Cox's regression was used to determine if the outcome and the duration of survival were influenced by these variables. It was observed that all of the variables found to be significantly associated with outcome on simple analysis were also significant on the univariate Cox's regression.

Dichotomization of Predictive Factors

Variables found significant on Cox's univariate regression were then dichotomized for best discrimination between survivors and nonsurvivors by the construction of receiver-operated curves. The best cutoff level for age was ≥40 years, grade of coma >2, liver size ≤2 intercostal spaces on percussion, serum bilirubin ≥15 mg/dL, and prothrombin time prolongation of ≥25 seconds over controls. For all other variables, it was the presence or absence of the event.

Multivariate Analysis

Multiple stepwise logistic regression was performed to discriminate survivors and nonsurvivors. The independent predictors of outcome were age ≥40 years, grade of coma >2, presence of infection, serum bilirubin ≥15 mg/dL, and prolongation of prothrombin time by ≥25 seconds over control (Tables 4 and 5). Cox's proportional hazard regression was then performed to identify the independent predictors of outcome as well as the duration of survival. This showed that four variables that independently predicted outcome were age ≥40 years, presence of cerebral edema at the time of hospitalization, serum bilirubin ≥15 mg/dL, and prothrombin time ≥25 seconds over controls (Table 6).

To identify the predictive value of one or more of the four variables on survival, five strata were constructed, depending on the number of adverse factors present. A Kaplan-Meier analysis of each of these five groups is shown Fig. 1. The pattern of survivors and nonsurvivors was significantly different in the five groups ($P < .01$). The sensitivity and specificity of each group depending on the number of adverse prognostic markers is shown in Table 7. It was seen that, with an increasing number of adverse prognostic factors, the mortality increased.

DISCUSSION

The cause and clinical spectrum of FHF at our center were different from those in the West.[1,5] In the current study, all patients had encephalopathy within 4 weeks of onset of symptoms of hepatitis. These observations are in contrast to reports from the United Kingdom, France,[5] and Japan,[3,4] where FHF has been documented to occur up to 8 weeks after the onset of symptoms of acute hepatitis and jaundice. Four weeks

TABLE 6. Cox's Multiple Regression Analysis

Variable	*df*	Coefficient	SE	Coefficient/SE	Global χ^2	P
1. Cerebral edema	1	0.87	0.14	5.95	58.8	<.001
2. Prothrombin time prolongation ≥ 25 s over controls	2	0.43	0.13	3.31	66.8	<.001
3. Serum bilirubin ≥ 15 mg/dL	3	0.29	0.13	2.18	73.2	<.001
4. Age ≥40 yr	4	0.29	0.14	2.02	77.2	<.001

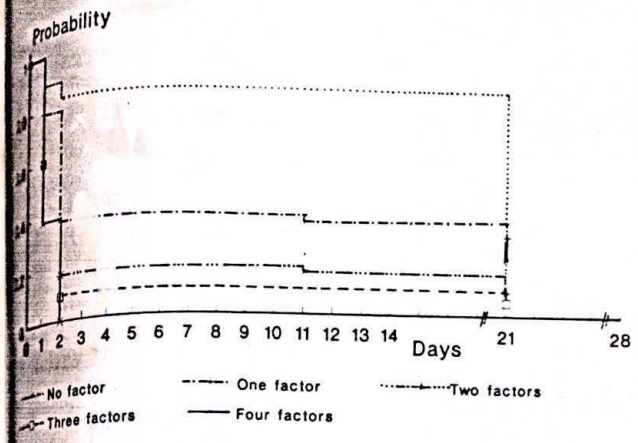

FIG. 1. Survival in patients with fulminant hepatic failure in relation to the presence of an increasing number of adverse prognostic factors. The survival in the five strata were significantly different (log rank test, $P < .0001$). Patients with three or four risk factors did not differ significantly in the duration of survival ($P = .08$).

onset of acute hepatitis, liver failure in this country has a different clinical spectrum. It is recognized as subacute hepatic failure, a distinct clinical entity in which liver failure appears as progressive ascites, and encephalopathy is rare.[40,41] Thus, the definition of FHF in the Indian subcontinent should be the onset of hepatic encephalopathy within 4 weeks of occurrence of symptoms of acute hepatitis. The difference in the timing of clinical presentation of FHF in our patients compared with those reported from the United Kingdom may be related to the differences in causative agents and the host factors.[42]

A quarter of our female patients with FHF were pregnant, which is higher than the 3% pregnancy rate among the female population in this country.[43,44] However, pregnancy per se or the duration of the gestation did not influence the mortality in the current study. During epidemics of HEV infection, pregnant women have been reported to have a high risk of developing acute hepatitis as well as FHF compared with nonpregnant females and males.[45-51] Based on these studies, it believed that pregnant women with FHF have higher mortality than nonpregnant females and males with FHF, which was not substantiated in the current study. Explanation for this difference is unclear. However, mortality rates among pregnant patients compared with nonpregnant females and males with FHF have not been prospectively evaluated in any of the previous studies.[45-50]

In the current study, one third of the patients had evidence of either acute HBV or HAV or HDV infection, and approximately 5% were diagnosed to have FHF subsequent to use of antitubercular drugs (Table 2). The remaining patients (n = 264) had clinical features suggestive of viral hepatitis, did not give history of consumption of any identifiable hepatotoxins, and their sera were negative for markers of acute HBV, HAV, and HDV infection. We diagnosed them as patients with presumptive acute non-A, non-B viral infection, although of course, alternative diagnosis, including toxic, drug-induced, or autoimmune hepatitis cannot be ruled out with certainty. Similar observations incriminating non-A, non-B virus as the major cause of FHF have been reported from this country.[52] Thus, most of our patients with FHF and conceivably as many as 95% were caused by hepatotropic viral infection.

HCV and HEV constitute the identifiable non-A, non-B viruses. Their role as causative agents of FHF in sporadic setup has remained unclear.[53-57] HEV could not be incriminated as a cause of sporodic fulminant hepatitis in the West.[53-55] The current study documented that HEV caused FHF in the sporadic setup in this country, which was evident by detection of HEV RNA either in isolation or along with HCV RNA in 31 (62%) of the 50 non-A, non-B fulminant hepatitis who were tested for HEV and HCV RNA. HEV being endemic in India, it may be an important causative agent among patients with non-A, non-B fulminant hepatitis.

The role of HCV in FHF has remained controversial. A study from Japan reported the presence of anti-HCV antibody or HCV RNA among most patients with FHF,[56] whereas studies from France,[57] the United States,[53,54] and the United Kingdom[55] have not been able to implicate HCV as an important cause of FHF. The documentation of HCV RNA in isolation (n = 7) or along with HEV RNA (n = 11) among 50 non-A, non-B FHF tested for these viruses indicate that either

TABLE 7. Assessment of Prognostic Indicators in Patients With FHF

Variable	No.	Death	Sensitivity	Specificity	Positive Prediction	Negative Prediction	Diagnostic Accuracy
40 yr	86	72	83.7	38.3	25.7	90.2	47.5
edema at admission	240	196	81.7	54.1	70	69.2	69.7
bilirubin (≥15 mg/dL)	182	141	77.5	46.8	56.6	69.9	61.3
bin time (≥25 s over control)	154	126	81.8	42.8	45	80.4	57.0
e adverse factors present							
1 factor	146	82	56.1	79.7	86.3	44.3	63.3
1 factors	115	93	80.9	79.7	87.7	69.9	80.4
1 factors	86	80	93	79.7	86.0	89.5	87.3
factors*	13	12	92.3	79.7	48	98.1	81.8

four factors were present only in 13 patients. This resulted in an apparently lower prediction of mortality in these patients. This is ...ible to the small number of patients assessed in this group.

HCV infection caused the disease or an HCV carrier state made these patients more susceptible to another hepatotropic viral infection, resulting in severe liver injury. The latter possibility seems more probable because (1) most non-A, non-B FHF with HCV RNA in their sera also had HEV RNA (11 of 18, 61%); and (2) Western reports could not incriminate HCV as an isolated cause of FHF.[53,55,57]

Thus, in contrast to Western studies, where drugs, hepatitis A, and hepatitis B viruses are the major causes of FHF, non-A, non-B presumably was the major cause of FHF in the current study.

Studies from the West have incriminated the cause of FHF and rapidity of onset of encephalopathy after occurrence of acute hepatic illness as important prognostic predictors.[1-5] In these reports, FHF due to non-A, non-B virus(es) and drugs had worse outcome than other causes of FHF,[1-3] and patients with the most rapid onset of encephalopathy had the best chance of recovery.[1,5] However in the current study, the causative distribution and rapidity of onset of encephalopathy was similar among survivors and nonsurvivors (Tables 1, 2). These differences might have been attributable to the heterogeneous cause of FHF in the West, whereas hepatotropic viruses were the predominant cause of FHF in the current study. Thus, the classification suggested by O'Grady et al.[2] may not be applicable in this country. Univariate analysis of the various other variables that were analyzed as prognostic indicators of FHF at admission (Table 3), however, showed predictors of outcome similar to those of other authors.[6,8,58] Multiple logistic regression detected two additional variables than Cox's multiple regression as independent risk factors for outcome (Tables 5 and 6). Previous studies have shown that when multivariate analysis is performed using both logistic regression and Cox's regression, the variables generated by the Cox's analysis are more reliable.[61] This is because the latter takes into account the time of the event also. Thus, the variables generated by Cox's analysis such as age $\geq$40 years, presence of cerebral edema at admission, serum bilirubin $\geq$15 mg/dL, and prolongation of prothrombin time over controls by $\geq$25 seconds were accepted finally as independent risk factors of outcome in our patients with FHF. These observations were similar to those by other authors, who found that in viral hepatitis, age, serum bilirubin, and prolongation of prothrombin time were factors that independently predicted the prognosis.[12,59,60] Earlier studies have used other measures that include factor V and α-fetoprotein.[8,10,19,58] They suffer from the disadvantage of the small number of patients studied, the complex method or expertise required for analyzing each factor, and the delay in obtaining the results.

One of the important prognostic marker in the current study was presence of overt clinical features suggestive of cerebral edema at the time of hospitalization. Cerebral edema is most often diagnosed and monitored in Western countries through the use of intracranial pressure recordings and high-resolution imaging studies. Because these were not readily available at our institution, "overt cerebral edema" was diagn based on clinical neurological findings (clinical d nostic criteria are mentioned previously in Pati and Methods).[24,62] We recognize that this probably derestimates the true incidence of cerebral edem our population with FHF. Nevertheless, given available parameter, our data suggest that "overt c bral edema," when recognizable clinically, carries it a very poor prognosis.

In conclusion, the current study is the largest ported series on hepatotropic virus–induced FHF tropical developing region. All of the patients with in this series developed hepatic encephalopathy wit 4 weeks of onset of acute hepatitis. Most of the were caused by presumptive non-A, non-B viral in tion. HEV in the sporadic setup in its endemic reg caused FHF. Mortality rate was highest within hours of hospitalization. The prognostic model de oped in this study was simple, reliable, rapid, and r vant to patients in developing countries for assessm for liver transplantation.

REFERENCES

1. O'Grady JG, Alexander GJM, Hayllar KM, Williams R. E indicators of prognosis in fulminant hepatic failure. Gastroen ology 1989;97:439-445.
2. O'Grady JG, Schalm SW, Williams R. Acute liver failure: redef ing the syndromes. Lancet 1993;342:273-275.
3. Takahashi Y, Shimizu M. Aetiology and prognosis of fulmin viral hepatitis in Japan: a multicentric study. J Gastroent Hepatol 1991;6:159-164.
4. Muto Y. Present status of fulminant hepatitis in Japan (19 1991) Gastroenterol Jpn 1993;28(suppl 4):120-127.
5. Bernuau J, Rueff B, Benhmaou JP. Fulminant and subfulmin liver failure: definitions and causes. Semin Liver Dis 1986;6 106.
6. Rakela J. Etiology and prognosis in fulminant hepatitis: a hepatic failure study group [Abstract]. Gastroenterology 19 77:A33.
7. Christensen E, Bremmelgaard A, Bahnsen M, Anderson Tygstrup N. Prediction of fatality in fulminant hepatic fail Scand J Gastroenterol 1984;19:90-96.
8. Tygstrup N, Ranek L. Assessment of prognosis in fulminant patic failure. Semin Liver Dis 1986;6:129-137.
9. Sherlock S. Acute liver failure. In: Sherlock S, ed. Diseases liver. Ed 9. Oxford, England: Blackwell Scientific Publicati 1992.
10. Karvountzis GG, Redeker AG. Relation of alpha fetoprotein acute hepatitis to severity and prognosis. Ann Intern Med 19 80:156-160.
11. Scotto J, Opolon I, Eteve J, Vergoz D, Mand T, Caroli J. Li biopsy and prognosis in acute liver failure. Gut 1973;14:927-9
12. Trey C, Davidson C. The management of fulminant hepatic f ure. In: Popper H, Schaffner F, eds. Progress in liver diseases Vol 3. New York: Grune and Stratton, 1970:282-298.
13. Gimson AES, White YS, Eddleston ALWF, Williams R. Clin and prognostic differences in fulminant hepatitis type A, B nonA nonB. Gut 1983;24:1194-1198.
14. Gazzard BG, Portmann B, Iain M, Murray L, Williams R. Cau of death in fulminant hepatic failure and relationship to quan tative histological assessment of parenchymal damage. Q J M 1975;94:615-626.
15. Kumara T, Muto Y, Moriwaki H, Yoshida T, Tomita E. Deter nation of the integrated CT number of the whole liver in patie with severe hepatitis: as an indicator of the functional reser of the liver. Gastroenterologica Japonica 1989;24:290-297.
16. Pauwels A, Kara NM, Florent C, Levy VG. Emergency liv transplantation for acute liver failure. J Hepatol 1993;17:12 127.

Bismuth H, Castaing D, Ericzon BG, Otte JB, Rolles K, Ringe B, Sloof M. Hepatic transplantation in Europe: first report of the European liver transplant registry. Lancet 1987;ii:674-676.
Peleman RR, Gavaler JS, Van Thiel D, Esquivel C, Gordon R, Iwatsuki S, Starzl TE. Orthotopic liver transplantation for acute and subacute hepatic failure in adults. HEPATOLOGY 1987;7:484-489.
Bismuth H, Samuel D, Gugenheim J, Castaing D, Bernuau J, Rueff B, Benhamon JP. Emergency liver transplantation for fulminant hepatitis. Ann Intern Med 1987;107:337-341.
Ringe B, Pichlmayr R, Lauchart W, Muller R. Indications and results of liver transplantation in acute hepatic failure. Transplant Proc 1986;18:86-88.
Vickers C, Neuberger J, Buckel J, McMaster P, Elias E. Liver transplantation for fulminant hepatic failure [Abstract]. Gut 1987;28:A1345.
Riegler JL, Lake JR. Fulminant hepatic failure. Med Clin North Am 1993;77:1057-1083.
Canalese J, Gimson AES, Davis C, Mellon PJ, Davis M, Williams R. Controlled trial of dexamethasone and mannitol for the cerebral oedema of fulminant hepatic failure. Gut 1982;23:625-629.
Ede RJ, Williams R. Hepatic encephalopathy and cerebral edema. Semin Liver Dis 1986;6:107-118.
Castell DO, O'Brien KD, Muensch H, Chalmers TC. Estimation of liver size by percussion in normal individuals. Ann Intern Med 1969;70:616-624.
Naftalis J, Leevy CM. Clinical estimation of liver size. Am J Dig Dis 1963;8:235.
Riemenschneider PA, Whalen JP. The relative accuracy of estimation for enlargement of liver and spleen by radiologic and clinical methods. Am J Roentgenol 1965;94:462-681.
Wright TL, Manish D, Combs C, Kim M, Donegan E, Ferrell L, Lake J, et al. Hepatitis 'B' virus and apparent nonA, nonB hepatitis. Lancet 1992;339:952-955.
Jameel S, Durgapal H, Habibullah CM, Khuroo MS, Panda SK. Enteric nonA, nonB hepatitis: epidemics, animal transmission and hepatitis E virus detection by the polymerase chain reaction. J Med Virol 1992;37:263-270.
Cha T, Kolberg J, Irvine B, Stempien M, Beall E, Yano M, Choo QL, et al. Use of a signature nucleotide sequence of hepatitis 'C' virus for detection of viral RNA in human serum and plasma. J Clin Microbiol 1991;29:2528-2534.
Abbott MA, Poiesz BJ, Byrne BC, Kwok S, Shinky JJ, Ehrlich GD. Enzymatic gene amplification: qualitative and quantitative methods for detecting proviral DNA amplified in vitro. J Infect Dis 1988;158:1158-1169.
Nanda SK, Yalchinkaya K, Panigrahi AK, Acharya SK, Jameel S, Panda SK. Etiological role of hepatitis 'E' virus in sporadic fulminant hepatitis. J Med Virol 1994;42:133-137.
Cox DR. Regression models and life tables (with discussion). J Roy Statist Soc 1972;34:187-220.
Dixon WJ, ed. BMDP statistical software. Los Angeles, CA: University of California Press, 1981.
Hopkins A. Regression with incomplete survival data In: Dixon WJ, ed. BMDP statistical software. Los Angeles, CA: University of California Press, 1981:587.
Snedecor GW, Cochran WG. Statistical methods. Ames, IA: The Iowa State University Press, 1967:91-134.
Colquohon H. Lectures in biostatistics. Oxford, England: Clarendon Press, 1971.
Kaplan EL, Meier P. Nonparametric estimations from incomplete observations. J Am Stat Assoc 1958;53:457-481.
Mantel N. Evaluation of survival data and two new rank order statistics arising in its consideration. Center Chemother Rep 1966;50:163-170.
Tandon BN, Joshi YK, Acharya SK. Subacute hepatic failure. Natl Med J India 1988;1:124-127.
Tandon BN, Joshi YK, Krishnamurty L, Tandon HD. Subacute hepatic failure: is it a distinct entity? J Clin Gastroenterol 1982;4:343-346.
Chouhan A, Jameel S, Dilawari JB, Chawla YK, Kaur U, Ganguly NK. Hepatitis E virus transmission to a volunteer. Lancet 1993:341:149-150.
Health Information India. Publication by central bureau of health intelligence, Director General of health services, Ministry of Health and Family Welfare. Government of India, 1989:8.
Health Information India. Publication by central bureau of health intelligence, Director General of health services, Ministry of Health and Family Welfare. Government of India, 1989:29.
Khuroo MS, Tali MR, Skidmore S, Sofi MA, Khuroo MI. Incidence and severity of viral hepatitis in pregnancy. Am J Med 1981;70:252-255.
Malkani PK, Grewal AK. Observations on infectious hepatitis in pregnancy. India J Med Res 1957;45:77-84.
Naidu SK, Viswanathan R. Infectious hepatitis in pregnancy during Delhi epidemic. Ind J Med Res 1957;45(suppl):71-76.
Borhanmanesh F, Haghighi P, Hekmat K, Rezaizadeh K, Ghavami G. Viral hepatitis during pregnancy: severity and effect on gestation. Gastroenterology 1973;64:304-312.
Christie AB, Alam AA, Aref MK, Muntasser IH, El-Nageh M. Pregnancy hepatitis in Libya. Lancet 1976;2:827-829.
Belabbes EH, Bouguer Mouth A, Benetallah A, Illout G. Epidemic nonA, nonB viral hepatitis in Algeria: strong evidence for its spreading by water. J Med Virol 1985;16:257-263.
Shrestha SM, Kane MA. Preliminary report of an out break of nonA, nonB viral hepatitis in Kathmandu valley. J Inst Med Nepal 1983;5:1-10.
Tandon BN, Gand BM, Joshi YK, Irshad M, Gupta H. Hepatitis virus nonA, nonB: the cause of a major public health problem in India. Bull WHO 1985;63:931-934.
Liong TJ, Jeffers L, Reddy RK, Silva MO, Cheinquer H, Findor A, DeMedina, et al. Fulminant or subfulminant nonA, nonB, viral hepatitis: hepatitis C and E viruses. Gastroenterology 1992;103:556-562.
Wright TL. Etiology of fulminant hepatic failure: is another virus involved? Gastroenterology 1993;104:640-643.
Sallie R, Tibbs C, Silva AE, Sheron N, Eddelston A, Williams R. Detection of hepatitis E but not C virus in sera of patients with fulminant nonA, nonB hepatitis. HEPATOLOGY 1991;14:68A.
Yanagi M, Kaneko S, Unoura M, Morakami S, Kobayashi K, Sugihara J, Chuishi H, Muto Y. Hepatitis C virus in fulminant liver failure. N Engl J Med 1991;324:1895-1896.
Feray C, Gigou M, Samuel D, Reyes G, Bernuau J, Reynes M, Bismuth H, et al. Hepatitis c virus RNA and hepatitis B virus DNA in serum and liver of patients with fulminant hepatitis. Gastroenterology 1993;104:549-555.
Bernuau J, Goudeau A, Poynard T, Dubois F, Lesamge G, Bernard Yuomnet B, Degott C, et al. Multivariate analysis of prognostic factors in fulminant hepatitis B. HEPATOLOGY 1986;6:648-651.
Brems JJ, Hiatt JR, Ramming KP, Quinones-Baldrich WJ, Busutti RW. Fulminant hepatic failure: the role of liver transplantation as primary therapy. Am J Surg 1987;154:137-141.
Trey C. The fulminant hepatic failure surveillance study: brief review of the effects of presumed etiology and age on survival. Can Med Assoc J 1972;106(suppl):525-527.
Green MS, Symons J. A comparison of the logistic risk function and the proportional hazards model in prospective epidemiological studies. J Chronic Dis 1983;36:715-724.
Stuart GG, Merry GS, Smith JA, Yelland DN. Severe head injury managed without intracranial pressure monitoring. J Neurosurg 1983;59:601-605.

Epidemiology of hepatitis B virus infection in India

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Abstract

The average estimated carrier rate of hepatitis B virus (HBV) in India is 4%, with a total pool of approximately 36 million carriers. Wide variations in social, economic, and health factors in different regions may explain variations in carrier rates from one part of the country to another. Professional blood donors constitute the major high risk group for HBV infection in India, with a hepatitis B surface antigen positivity rate of 14%. Blood transfusions represent the most important route of HBV transmission among adults. However, most of India's carrier pool is established in early childhood, predominantly by horizontal spread due to crowded living conditions and poor hygiene. Acute and subacute liver failure are common complications of viral hepatitis in India and HBV is reckoned to be the actiological agent in 42% and 45% of adult cases, respectively. HBV is reported to be responsible for 70% of cases of chronic hepatitis and 80% of cases of cirrhosis of the liver. About 60% of patients with hepatocellular carcinoma are HBV marker positive. Small numbers of patients have been reported to be infected with the pre-core mutant virus but none with the S mutant. Coinfection with hepatitis C virus or hepatitis delta virus is comparatively uncommon. In conclusion, hepatitis B is a major public health problem in India and will continue to be until appropriate nationwide vaccination programmes and other control measures are established.

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Keywords: hepatitis B virus, India, professional blood donors, acute liver failure, subacute liver failure.

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In 1995, the population of India was reported to be around 900 million.[1] The average estimated carrier rate of hepatitis B virus (HBV) is 4%, placing India in the intermediate range for hepatitis B endemicity[2] and giving an approximate total of 36 million carriers.[3] Among the estimated 400 million hepatitis B surface antigen (HBsAg) carriers worldwide, therefore, India alone contributes 9% of the total.[4] There are wide variations in social, economic, and health factors in different regions of India, which may explain the differences in HBV carrier rates reported by investigators in different parts of the country[5–8] (and S K Naik, S P Thyagarajan, Y K Chawla, personal communications). The lowest prevalence (0·97%) has been reported in Chandigarh in northern India (Y K Chawla, personal communication) and the highest (5·5%, in Madras in southern India (S P Thyagarajan, personal communication). Anti-HBs antibody positivity, indicating past infection, follows the same epidemiological pattern as that of HBsAg carriage and about 14% of healthy volunteer blood donors are estimated to be anti-HBs positive.[5] Limited studies of rural versus urban populations suggest that their HBV carrier and infection rates are similar. Overall, the HBV carrier rate in India has not changed during the last decade (Y K Chawla, personal communication) although the carrier pool has increased by nearly 5 million due to an increase in the total population of the country.

HBeAg positivity

Hepatitis B e antigen (HBeAg) positivity, which denotes viral replication and high infectivity, has been reported in 7·8% of pregnant females in north India.[9] Among HBsAg positive subjects in Madras and Chandigarh, recent reports show HBeAg positivity rates of 34·2% and 47%, respectively (S P Thyagarajan, Y K Chawla, personal communications). These rates are significantly higher than those recorded in an earlier report from Delhi,[9] and a multicentre study is needed to resolve the reasons for such differences. No large study has yet been carried out to estimate HBeAg positivity rates among Indian children, or to investigate the dynamics of natural clearance of HBeAg.

Risk groups

PROFESSIONAL BLOOD DONORS

Professional blood donors constitute nearly 40% of all blood donors in India. They represent the major high risk group for HBV infection in this country, with an HBsAg positivity rate of 15% – about five times the prevalence of HBsAg in healthy volunteer blood donors.[5 10] These professional blood donors are neither homosexual nor parenteral drug abusers, but have a low socioeconomic status and live under very poor hygienic conditions. They move from one commercial blood bank to another, and only rarely do these blood banks follow appropriate procedures for prevention of HBV transmission. It is very likely that the professional blood donors themselves are infected with HBV through this unsafe blood collection system. They then infect others through blood transfusions, which represent the most important route of HBV infection in adults in this

country.[11] A study from Delhi reported post-transfusion hepatitis in 7% of recipients, and 20% of cases were due to HBV infection.[12]

OTHER HIGH RISK GROUPS

Compared with the general population, the risk of HBV infection is higher in thallassaemic children and among renal dialysis patients and staff. However, a study at one of the major hospitals in Delhi did not show significantly higher rates of HBsAg positivity among surgeons and other health care workers with frequent occupational exposure to blood.[5]

Perinatal versus horizontal transmission

It has been observed that pre-school children have an HBV carrier rate of between 2% and 3%, which is the same as that recorded among adults in India.[9,10] This suggests that most of India's HBV carrier pool is established during early childhood. The combined factors of low HBeAg positivity rates among pregnant females, poor hygienic living conditions, and close person to person contact due to crowded living conditions have led to the conclusion that horizontal spread during early childhood accounts for about 75% of all HBV transmission in India, and less than 30% is thought to result from perinatal transmission.[9]

Sequelae of HBV infection

ACUTE AND SUBACUTE HEPATITIS

After the non-A, non-B (NANB) viruses (particularly hepatitis E virus (HEV)), HBV is the second most important cause of acute, subacute, and fulminant hepatitis in India.[12] A decade ago, HBV was reported to be the aetiological agent of these three conditions in 42%, 45%, and 33% of adult cases, respectively, and this pattern remains true to this day. In the paediatric age group, however, only 9% of acute hepatitis is due to infection with HBV.[12]

Acute and subacute liver failure are common complications of viral hepatitis in India. Each year, approximately 70 patients with these conditions are registered at Rajgarhia Liver Unit of the All India Institute of Medical Sciences.[13] Between July 1976 and December 1990, 367 cases of acute hepatic failure were reported to this unit alone.[14] In addition, 148 cases of subacute hepatic failure were reported between June 1981 and June 1987.[15] Clear differences between these two groups of patients have been reported from this unit.[12]

Definitions

Acute liver failure has been defined as development of hepatic encephalopathy within four weeks of the onset of the first symptoms of hepatitis in a patient with no previous record of liver disease.[13,16]

Subacute liver failure has been recognised as a distinct clinical entity characterised by persistent or progressive jaundice four weeks after the onset of icterus, together with appearance of moderate or severe ascites four weeks into the post-icteric period.[15,17] It has a slow, progressively deteriorating course with late development of encephalopathy, and is associated with a death rate of 75% to 80% within three to six months after the onset of illness.[15] Several authors have described this condition under alternative names such as 'protracted viral hepatitis with impaired regeneration' and a 'subfulminant hepatitis'.[14]

Aetiology

Acute liver failure – cases of acute failure in India are almost exclusively caused by infection with hepatotrophic viruses.[13] A study published about 10 years ago reported an aetiology of HBV infection in 33% of patients with acute liver failure registered at the Rajgarhia Liver Unit.[12] A more recent study in a larger series of 430 patients in the same unit reported a similar pattern, with HBV as the aetiological agent in 27·6% of patients with acute hepatic failure (personal communication).[21] Among those diagnosed as having NANB hepatitis, 62·4% were found to be positive for HEV-RNA determined by PCR analysis (S K Acharya, personal communication). Neither HBV mutant viruses nor hepatitis delta virus (HDV) have been reported as aetiological agents of acute liver failure in India (S K Panda, personal communication).

Subacute liver failure – as in acute liver failure, hepatotrophic viruses have been found to be the aetiological agents of subacute liver failure in nearly 100% of patients.[15] Again, the NANB group of viruses (including HEV in two thirds of cases) is the most important cause of subacute liver failure, followed by HBV infection (reported in 34% of patients).[15] Subacute liver failure resulting from coinfection or superinfection with HDV or hepatitis C virus (HCV) is very rare.

CHRONIC HEPATITIS

Among chronic hepatitis cases, an aetiology of HBV infection has been reported in 70%. An immunopathological study has suggested that 80% of cases of cirrhosis of the liver are due to chronic infection with HBV.[19] Furthermore, a recent communication from Madras suggests that 61·3% of patients with hepatocellular carcinoma are positive for markers of HBV infection (S P Thyagarajan, personal communication).

Mutant viruses

Infection with the pre-core mutant variant of HBV has been recorded in a small series of 13 patients with HCV negative chronic hepatitis. However, no cases of infection with the HBV S mutant have yet been detected (S K Panda, personal communication).

Coinfection with other viruses

Coinfection with HCV and superinfection with HDV are both comparatively uncommon in

India and neither has been recorded in more than 10% of patients with chronic hepatitis.[20,21]

Conclusions

Hepatitis B remains a significant public health problem in India and will continue to do so as long as commercial blood banks remain operational and until appropriate nationwide vaccination programmes and other control measures are established. Unfortunately, the shortfall between blood collected (1·5 million units per year) and blood needed (3 million units per year) in India means that commercial blood banks will remain profitable (and necessary) unless the number of volunteer donors increases dramatically. Furthermore, although programmes for the prevention and control of hepatitis B should represent a priority for the government and health services in India, the costs and difficulties associated with their initiation are a major problem at present.

1 Standing Committee on Projection confirming 1991 Consensus Data. Registrar General Office, GOI, New Delhi.

2 Suzuki H, Woodfield G. Viral hepatitis in Asia: summary of a plenary session. In: Nishioka K, Suzuki H, Mishiro S, Oda T, eds. *Viral hepatitis and liver disease*. Tokyo: Springer Verlag, 1994: 385–6.

3 Agarwal R, Naid SR. Prevention of hepatitis B infection: the appropriate strategy for India. *Natl Med J India* 1994; **7:** 216–20.

4 Andre FE. Overview of a 5 year clinical experience with a yeast derived hepatitis B vaccine. *Vaccine* 1990; **8** (suppl): S74–8.

5 Irshad M, Joshi YK, Acharya SK, Tandon BN. Prevalence of hepatitis B virus infection in healthy persons in North India. *Natl Med J India* 1994; **7:** 210–2.

6 Singhvi A, Putimood RB, John TJ, *et al*. The prevalence of markers for hepatitis B and human immunodeficiency viruses, malarial parasites, and microflora in blood donors in a large hospital in South India. *J Trop Med Hyg* 1990; **93:** 178–82.

7 Prasad SR, Rodrigues FM, Dhonie SP, Ramamoorthy CL. Prevalence and subtypes of hepatitis B surface antigen in the tribal population in Arunachal Pradesh. *Ind J Med Res (A)* 1983; **78:** 300–6.

8 Joshi SH, Gorakshakar AC, Mukerjee M, *et al*. Prevalence of HBsAg carriers among some tribes of Madhya Pradesh. *Ind J Med Res (A)* 1990; **91:** 341–3.

9 Nayak NC, Panda SK, Zuckerman AJ, Bhan MK, Guha DK. Dynamics and impact of perinatal transmission of hepatitis B virus in North India. *J Med Virol* 1987; **21:** 137–45.

10 Irshad M, Singh YN, Acharya SK. HBV-status in professional blood donors in North India. *Trop Gastroenterol* 1992; **13:** 112–4.

11 Dasarathy S, Misra SC,. Acharya SK, Irshad M, Joshi YK, Venugopal P, Tandon BN. Prospective controlled study of post transfusion hepatitis after cardiac surgery in large referral hospital in India. *Liver* 1992; **12:** 116–20.

12 Tandon BN, Gandhi BM, Joshi YK. Etiological spectrum of viral hepatitis and prevalence of markers of hepatitis A and B virus infection in North India. *Bull WHO* 1984; **62:** 67–73.

13 Acharya SK, Dasarathy S, Tandon BN. Should we redefine acute liver failure? *Lancet* 1993; **342:** 1421–2.

14 Tandon BN, Acharya SK. Fulminant hepatic failure: clinical syndrome and progress in management. In: Okita K, ed. *Frontiers in hepatology '93* Tokyo: Axel Springer Japan Publishing, 1994: 11–6.

15 Tandon BN, Joshi YK, Acharya SK. Subacute hepatic failure. *Natl Med J India* 1988; **1:** 124–7.

16 Trey C, Davidson JS. The management of fulminant hepatic failure. In: Popper H, Schaffner F, eds. *Progress in liver disease*. New York: Grune and Stratton, 1970: 282–9.

17 Tandon BN, Joshi YK, Krishnamurthy L, Tandon HD. Subacute hepatic failure: is it a distinct entity? *J Clin Gastroenterol* 1982; **4:** 362–4.

18 Acharya SK, Panda SK, Duphare H, *et al*. Chronic hepatitis in a large Indian Hospital. *Natl Med J India* 1993; **6:** 202–6.

19 Nayak NC, Dhar A, Sachdeva R, *et al*. Association of human hepatocellular carcinoma and cirrhosis with hepatitis B virus surface and core antigen in the liver. *Int J Cancer* 1977; **20:** 643.

20 Panigrahi AK, Nanda SK, Dixit RK, Acharya SK, Zuckermann AJ, Panda SK. Diagnosis of hepatitis C virus associated chronic liver disease in India. *J Med Virol* 1994; **44:** 176–9.

21 Anand AC, Gandhi BM, Acharya SK, Irshad M, Joshi YK, Tandon BN. Hepatitis delta virus infection in India. *Gastroenterol Hepatol* 1988; **3:** 425–9.

Discussion

Toukan: Why is the prevalence of hepatitis B so much higher among professional blood donors than among the general population – 12% versus about 2%?

Tandon: They are generally poor people who keep moving from one blood bank to another, and especially to those blood banks that are not properly licensed or managed. They probably acquire the infection through unsterilised needles and syringes at these poorly managed blood banks.

Toukan: Could the figures be biased by the fact that they are very poor people, and such people generally have higher hepatitis B carrier rates compared with the general population?

Tandon Some small surveys have been done to assess the prevalence of HBsAg in very poor urban slums. Although only small numbers of subjects are involved – probably not more than 800 – the HBsAg prevalence does not seem to be more than 3%. These professional blood donors are almost certainly infected through repeated exposure at badly run blood banks. They may donate as often as every two or three weeks, even though their haemoglobin concentrations fall as low as 7 or 8 g/dl, just to make a living.

Toukan: In pregnant women who die from acute hepatitis, what is the relative importance of each of the hepatitis viruses?

Tandon: Non-A, non-B hepatitis – predominantly HEV – is the most important factor for high mortality and fulminant hepatic failure in pregnant women.

Toukan: What is the mortality in pregnancy from hepatitis B or A?

Tandon: The death rate for hepatitis A is extremely low – not more than 5%. In fact, fulminant hepatitis A is very uncommon in adults. In children, however, when we find both HAV and HEV together, we often see fulminant infection. It also occurs in adults when there is superinfection of hepatitis A in carriers of hepatitis B. As far as the other hepatitis viruses are concerned, HEV is the most common cause of fulminant disease – either alone or as a superinfection in hepatitis B carriers. Hepatitis C is a very rare cause of fulminant hepatitis.

Gust: Is all blood in India screened for HBsAg?

Tandon: Legally, all blood banks in India should take only voluntary donors and blood should be screened for HBsAg, but monitoring is extremely poor, as it is in two thirds of the world today. Only about a week ago, it was recorded that the Red Cross blood supply in Bombay was contaminated with HIV and HBV, and the blood bank was closed down.

Gust: What proportion of your fulminant hepatitis B is transfusion associated?

Tandon: That is very uncommon. In our region, post-transfusion hepatitis occurs at a rate of about 7%. Roughly 70% of these cases are due to HBV but very few have fulminant disease – perhaps three or four cases out of more than 400 patients.

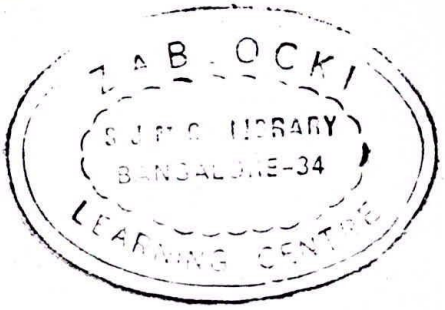
Kew: Overall, you have reported an extraordinarily high incidence of fulminant acute an

subacute liver failure. Could this be related to the age at which your population acquires the carrier state? In black Africa, the very high carrier rate is mainly established very early in life at a time when the children are immunotolerant and have asymptomatic disease. If they are infected when they are older, and past the age of immunotolerance, they are more likely to get acute clinical hepatitis but there are far fewer of these cases. Is the hepatitis B carrier state in India a childhood acquired phenomenon or is it acquired later in life?

Tandon: I will present some data on this subject tomorrow. Briefly, the carrier pool is derived from childhood infection – 80% among the preschool age group. The overall carrier rate in India is 2·5%.

Yao: In China, the incidence of acute fulminant hepatitis has been decreasing in the past decade but cases of cirrhosis of the liver due to chronic hepatitis are increasing. Is this also the case in India?

Tandon: During the past three decades, the incidence of both acute and subacute hepatitis has remained practically the same at my institution.



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...T, Kasper W, Schumacher M, Just H for the AP-...multicenter trial group. The German multicenter ...of anisoylated plasminogen streptokinase activator ...versus heparin for acute myocardial infarction. ...Cardiol 1988; 62:347–51.

...JP, Machecourt J, Cassagnes J, et al. Multicenter ...of intravenous anisoylated plasminogen streptoki-...activator complex (APSAC) in acute myocardial in-...: effects on infarct size and left ventricular func-... J Am Coll Cardiol 1989; 13:988–97.

...JL, Rothbard RL, Hackworthy RA, et al. Multi-...reperfusion trial of intravenous anisoylated plas-...streptokinase activator complex (APSAC) in ...myocardial infarction: controlled comparison with ...coronary streptokinase. J Am Coll Cardiol 1988; ...-63.

...HJRM, Visser RF, Klomps HC, Hoffmann HJML ...Dutch Invasive Reperfusion Study Group. Com-...of intravenous anisoylated plasminogen streptoki-...activator complex and intracoronary streptokinase ...myocardial infarction. Am J Cardiol 1988; ...-30.

...ML, Quilliet L, Kulbertus H, et al. Intravenous ...ylated plasminogen streptokinase activator complex ...intravenous streptokinase in evolving myocardial ...tion: preliminary data from a randomized multicen-...study. Drugs 1987; 33(Suppl 3):140–5.

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...nse No. 1097
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...in *Product Identification Section, page 430*

...IX-B® ℞

...bee]

...B Vaccine (Recombinant)

...IPTION

...B [Hepatitis B Vaccine (Recombinant)] is a nonin-...recombinant DNA hepatitis B vaccine developed ...manufactured by SmithKline Biologicals. It contains ...surface antigen of the virus obtained by culturing ...ally engineered *Saccharomyces cerevisiae* cells, which ...the surface antigen gene of the hepatitis B virus. The ...antigen expressed in *Saccharomyces cerevisiae* cells is ...by several physicochemical steps and formulated as ...sion of the antigen adsorbed on aluminum hydrox-...procedures used to manufacture *Engerix-B* result in ...t that contains no more than 5% yeast protein. ...tances of human origin are used in its manufacture.

...B is supplied as a sterile suspension for intramuscu-...ministration. The vaccine is ready for use without re-...tion; it must be shaken before administration since a ...white deposit with a clear colorless supernatant may ...storage.

...mL adult dose of vaccine consists of 20 mcg of hepati-...surface antigen adsorbed on 0.5 mg aluminum as alumi-...hydroxide. Each 0.5 mL pediatric dose of vaccine con-...of 10 mcg of hepatitis B surface antigen adsorbed on ...aluminum as aluminum hydroxide. Both formula-...contain 1:20,000 thimerosal (mercury derivative) as a ...vative, sodium chloride (9 mg/mL) and phosphate ...disodium phosphate dihydrate, 0.98 mg/mL; sodium ...gen phosphate dihydrate, 0.71 mg/mL).

...CAL PHARMACOLOGY

...hepatitis viruses are known to cause a systemic in-...resulting in major pathologic changes in the liver ...A, B, delta, non-A/non-B). The estimated lifetime risk of HBV infection in the United States varies from almost 100% for the highest-risk groups to approximately 5% for the population as a whole.[1]

Hepatitis B infection can have serious consequences including acute massive hepatic necrosis, chronic active hepatitis and cirrhosis of the liver. Sixty to 80% of neonates and 6 to 10% of adults who are infected in the United States will become hepatitis B virus carriers.[1] It has been estimated that more than 170 million people in the world today are persistently infected with hepatitis B virus.[2] The Centers for Disease Control (CDC) estimates that there are approximately 0.5 to 1.0 million chronic carriers of hepatitis B virus in the United States and that this pool of carriers grows by 2%–3% (12,000 to 20,000 individuals) annually.[1] Those patients who become chronic carriers can infect others and are at increased risk of developing primary hepatocellular carcinoma. Among other factors, infection with hepatitis B may be the single most important factor for development of this carcinoma.[1,3] Considering the serious consequences of infection, immunization should be considered for all persons at potential risk of exposure to the hepatitis B virus.

Mothers infected with hepatitis B virus can infect their infants at, or shortly after, birth if they are carriers of the HBsAg antigen or develop an active infection during the third trimester of pregnancy. Infected infants usually become chronic carriers. Therefore, screening of pregnant women for hepatitis B is recommended.[1]

There is no specific treatment for acute hepatitis B infection. However, those who develop anti-HBs antibodies after active infection are usually protected against subsequent infection. Antibody titers ≥ 10 mIU/mL against HBsAg are recognized as conferring protection against hepatitis B.[4] Seroconversion is defined as antibody titers ≥ 1 mIU/mL.

Immunogenicity in Healthy Adults and Adolescents: Clinical trials in healthy adult and adolescent subjects have shown that following a course of three doses of 20 mcg *Engerix-B* given according to the Immunization Practices Advisory Committee (ACIP) recommended schedule of injections at months 0, 1 and 6, the seroprotection (antibody titers ≥ 10 mIU/mL) rate for all individuals was 79% at month 6 and 96% at month 7; the geometric mean antibody titer (GMT) for seroconverters at month 7 was 2,204 mIU/mL. On an alternate schedule (injections at months 0, 1 and 2) designed for certain populations (e.g., neonates born of hepatitis B infected mothers, individuals who have or might have been recently exposed to the virus, and certain travelers to high-risk areas. See INDICATIONS AND USAGE.), 99% of all individuals were seroprotected at month 3 and remained protected through month 12. On the alternate schedule, an additional dose at 12 months produced a GMT for seroconverters at month 13 of 9,163 mIU/mL.

Immunogenicity in Neonates: Immunization with 10 mcg at 0, 1 and 2 months of age produced a seroprotection rate of 96% in infants by month 4, with a GMT among seroconverters of 210 mIU/mL (N=311); an additional dose at month 12 produced a GMT among seroconverters of 2,941 mIU/mL at month 13 (N=126).

Immunization with 10 mcg at 0, 1 and 6 months of age produced seroconversion in 100% of infants by month 7 with a GMT of 713 mIU/mL (N=52), and the seroprotection rate was 97%.

Clinical trials indicate that administration of hepatitis B immune globulin at birth does not alter the response to *Engerix-B*.

Immunogenicity in Children 6 Months to, and Including, 10 Years: In clinical trials with 242 children ages 6 months to, and including, 10 years given 10 mcg at months 0, 1 and 6, the seroprotection rate was 98% one to two months after the third dose; the GMT of seroconverters was 4,023 mIU/mL.

Immunogenicity in Older Subjects: Among older subjects given 20 mcg at months 0, 1 and 6, the seroprotection rate one month after the third dose was 88%. However, as with other hepatitis B vaccines, in adults over 40 years of age, *Engerix-B* vaccine produced anti-HBs titers that were lower than those in younger adults (GMT among seroconverters one month after the third 20 mcg dose with a 0, 1, 6-month schedule: 610 mIU/mL for individuals over 40 years of age, N=50).

Hemodialysis Patients: Hemodialysis patients given hepatitis B vaccines respond with lower titers,[5] which remain at protective levels for shorter durations than in normal subjects. In a study in which patients on chronic hemodialysis (mean time on dialysis was 24 months; N=562) received 40 mcg of the plasma-derived vaccine at months 0, 1 and 6, approximately 50% of patients achieved antibody titers ≥ 10 mIU/mL.[5]

Since a fourth dose of *Engerix-B* given to healthy adults at month 12 following the 0, 1, 2-month schedule resulted in a substantial increase in the GMT (see above), a four-dose regimen was studied in hemodialysis patients. In a clinical trial of adults who had been on hemodialysis for a mean of 56 months (N=43), 67% of patients were seroprotected two months after the last dose of 40 mcg of *Engerix-B* (two × 20 mcg) given on a 0, 1, 2, 6-month schedule; the GMT among seroconverters was 93 mIU/mL.

Protective Efficacy: Protective efficacy with *Engerix-B* has been demonstrated in a clinical trial in neonates at high risk of hepatitis B infection.[6,7] Fifty-eight neonates born of mothers who were both HBsAg and HBeAg positive were given *Engerix-B* (10 mcg at 0, 1 and 2 months) without concomitant hepatitis B immune globulin. Two infants became chronic carriers in the 12-month follow-up period after initial inoculation. Assuming an expected carrier rate of 70%,[1] the protective efficacy rate against the chronic carrier state during the first 12 months of life was 95%.

Other Clinical Studies: In one study,[8] four of 244 (1.6%) adults (homosexual men) at high risk of contracting hepatitis B virus became infected during the period prior to completion of three doses of *Engerix-B* (20 mcg at 0, 1, 6 months). No additional patients became infected during the 18-month follow-up period after completion of the immunization course.

Interchangeability with Other Hepatitis B Vaccines: Recombinant DNA vaccines are produced in yeast by expression of a hepatitis B virus gene sequence that codes for the hepatitis B surface antigen. Like plasma-derived vaccine, the yeast-derived vaccines are protein particles visible by electron microscopy and have hepatitis B surface antigen epitopes as determined by monoclonal antibody analyses.

Yeast-derived vaccines have been shown by *in vitro* analyses to induce antibodies (anti-HBs) which are immunologically comparable by epitope specificity and binding affinity to antibodies induced by plasma-derived vaccine.[9] In cross absorption studies, no differences were detected in the spectra of antibodies induced in man to plasma-derived or to yeast-derived hepatitis B vaccines.[9]

Additionally, patients immunized approximately three years previously with plasma-derived vaccine and whose antibody titers were <100 mIU/mL (GMT: 35 mIU/mL; range: 9–94) were given a 20 mcg dose of *Engerix-B*. All patients, including two who had not responded to the plasma-derived vaccine, showed a response to *Engerix-B* (GMT: 5,069 mIU/mL; range: 624–15,019).

There have been no clinical studies in which a three-dose vaccine series was initiated with a plasma-derived hepatitis B vaccine and completed with *Engerix-B*, or vice versa. However, because the *in vitro* and *in vivo* studies described above indicate the comparability of the antibody produced in response to plasma-derived vaccine and *Engerix-B*, it should be possible to interchange the use of *Engerix-B* and plasma-derived vaccines (but see CONTRAINDICATIONS).

A controlled study (N=48) demonstrated that completion of a course of immunization with one dose of *Engerix-B* (20 mcg, month 6) following two doses of Recombivax HB®* (10 mcg, months 0 and 1) produced a similar GMT (4,077 mIU/mL) to immunization with three doses of *Recombivax HB* (10 mcg, months 0, 1 and 6; 2,654 mIU/mL). Thus, *Engerix-B* can be used to complete a vaccination course initiated with *Recombivax HB*.

INDICATIONS AND USAGE

Engerix-B is indicated for immunization against infection caused by all known subtypes of hepatitis B virus. As hepatitis D (caused by the delta virus) does not occur in the absence of hepatitis B infection, it can be expected that hepatitis D will also be prevented by *Engerix-B* vaccination.

Engerix-B will not prevent hepatitis caused by other agents, such as hepatitis A virus, non-A/non-B hepatitis viruses, or other pathogens known to infect the liver.

Immunization is recommended in persons of all ages, especially those who are, or will be, at increased risk of exposure to hepatitis B virus,[1] for example:

Health Care Personnel

Dentists and oral surgeons.
Dental, medical and nursing students.
Physicians, surgeons and podiatrists.
Nurses.
Paramedical and ambulance personnel and custodial staff who may be exposed to the virus via blood or other patient specimens.
Dental hygienists and dental nurses.
Laboratory and blood-bank personnel handling blood, blood products, and other patient specimens.
Hospital cleaning staff who handle waste.

Selected Patients and Patient Contacts

Patients and staff in hemodialysis units and hematology/oncology units.
Patients requiring frequent and/or large volume blood transfusions or clotting factor concentrates (e.g., persons with hemophilia, thalassemia, sickle-cell anemia, cirrhosis).
Clients (residents) and staff of institutions for the mentally handicapped.
Classroom contacts of deinstitutionalized mentally handicapped persons who have persistent hepatitis B surface antigenemia and who show aggressive behavior.
Household and other intimate contacts of persons with persistent hepatitis B surface antigenemia.

Continued on next page

SmithKline Beecham—Cont.

Infants Born of HBsAg-Positive Mothers Whether HBeAg Positive or Negative (See DOSAGE AND ADMINISTRATION.)
Subpopulations with a Known High Incidence of the Disease, such as:
Alaskan Eskimos.
Indochinese immigrants.
Haitian immigrants.
Persons Who May Be Exposed to the Hepatitis B Virus by Travel to High-Risk Areas (See ACIP Guidelines, 1985.)
Military Personnel Identified as Being at Increased Risk
Morticians and Embalmers
Persons at Increased Risk of the Disease Due to Their Sexual Practices, such as:
Persons with more than one sexual partner in a six-month period.
Persons who have contracted a sexually transmitted disease.
Homosexually active males.
Female prostitutes.
Prisoners
Users of Illicit Injectable Drugs
Others:
Police and fire department personnel who render first aid or medical assistance, and any others who, through their work or personal life-style, may be exposed to the hepatitis B virus.
Adoptees from countries of high HBV endemicity.

CONTRAINDICATIONS

Hypersensitivity to yeast or any other component of the vaccine is a contraindication for use of the vaccine.

WARNINGS

Patients experiencing hypersensitivity after an Engerix-B [Hepatitis B Vaccine (Recombinant)] injection should not receive further injections of *Engerix-B*. (See CONTRAINDICATIONS.)
Hepatitis B has a long incubation period. Hepatitis B vaccination may not prevent hepatitis B infection in individuals who had an unrecognized hepatitis B infection at the time of vaccine administration. Additionally, it may not prevent infection in individuals who do not achieve protective antibody titers.

PRECAUTIONS

General
As with any percutaneous vaccine, epinephrine should be available for use in case of anaphylaxis or anaphylactoid reaction.
As with any vaccine, administration of *Engerix-B* should be delayed, if possible, in persons with any febrile illness or active infection.

Pregnancy
Pregnancy Category C: Animal reproduction studies have not been conducted with *Engerix-B*. It is also not known whether *Engerix-B* can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. *Engerix-B* should be given to a pregnant woman only if clearly needed.

Nursing Mothers
It is not known whether *Engerix-B* is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when *Engerix-B* is administered to a nursing woman.

Pediatric Use
Engerix-B has been shown to be well tolerated and highly immunogenic in infants and children of all ages. Newborns also respond well; maternally transferred antibodies do not interfere with the active immune response to the vaccine. (See CLINICAL PHARMACOLOGY for seroconversion rates and titers in neonates and children. See DOSAGE AND ADMINISTRATION for recommended pediatric dosage and for recommended dosage for infants born of HBsAg-positive mothers.)

ADVERSE REACTIONS

Engerix-B [Hepatitis B Vaccine (Recombinant)] is generally well tolerated. During clinical studies involving over 10,000 individuals distributed over all age groups, no serious adverse reactions attributable to vaccine administration were reported. As with any vaccine, however, it is possible that expanded commercial use of the vaccine could reveal rare adverse reactions not observed in clinical studies.
Ten double-blind studies involving 2,252 subjects showed no significant difference in the frequency or severity of adverse experiences between *Engerix-B* and plasma-derived vaccines. In 36 clinical studies a total of 13,495 doses of *Engerix-B* were administered to 5,071 healthy adults and children who were initially seronegative for hepatitis B markers, and healthy neonates. All subjects were monitored for 4 days post-administration. Frequency of adverse experiences tended to decrease with successive doses of *Engerix-B*. Using a symptom checklist,‡ the most frequently reported adverse reactions were injection site soreness (22%) and fatigue‡ (14%). Other reactions are listed below.

Incidence 1% to 10% of Injections
Local reactions at injection site: Induration; erythema; swelling.
Body as a whole: Fever (> 37.5°C).
Nervous system: Headache‡; dizziness.‡

‡ Parent or guardian completed forms for children and neonates. Neonatal checklist did not include headache, fatigue or dizziness.

Incidence < 1% of Injections
Local reactions at injection site: Pain; pruritus; ecchymosis.
Body as a whole: Sweating; malaise; chills; weakness; flushing; tingling.
Cardiovascular system: Hypotension.
Respiratory system: Influenza-like symptoms; upper respiratory tract illnesses.
Gastrointestinal system: Nausea; anorexia; abdominal pain/cramps; vomiting; constipation; diarrhea.
Lymphatic system: Lymphadenopathy.
Musculoskeletal system: Pain/stiffness in arm, shoulder or neck; arthralgia; myalgia; back pain.
Skin and appendages: Rash; urticaria; petechiae; pruritus; erythema.
Nervous system: Somnolence; insomnia; irritability; agitation.
Additional adverse experiences have been reported with the commercial use of *Engerix-B*. Those listed below are to serve as alerting information to physicians.
Hypersensitivity: Anaphylaxis; erythema multiforme including Stevens-Johnson syndrome; angioedema; arthritis.
Cardiovascular system: Tachycardia/palpitations.
Respiratory system: Bronchospasm including asthma-like symptoms.
Gastrointestinal system: Abnormal liver function tests.
Nervous system: Migraine; syncope; paresis; neuropathy including hypoesthesia, paresthesia, Guillain-Barré syndrome and Bell's palsy, transverse myelitis.
Hematologic: Thrombocytopenia.
Skin and appendages: Eczema; purpura; herpes zoster.
Special senses: Vertigo; conjunctivitis; keratitis; visual disturbances.
Potential Adverse Experiences: In addition, certain other adverse experiences not observed with *Engerix-B* have been reported with Heptavax-B®† and/or *Recombivax HB*. Those listed below are to serve as alerting information to physicians:
Nervous system: Optic neuritis.

DOSAGE AND ADMINISTRATION

Injection: *Engerix-B* should be administered by intramuscular injection. *Do not inject intravenously or intradermally.* In adults, the injection should be given in the deltoid region but it may be preferable to inject in the anterolateral thigh in neonates and infants, who have smaller deltoid muscles. *Engerix-B* should not be administered in the gluteal region; such injections may result in suboptimal response.
Engerix-B may be administered subcutaneously to persons at risk of hemorrhage (e.g., hemophiliacs). However, hepatitis B vaccines administered subcutaneously are known to result in lower GMTs. Additionally, when other aluminum-adsorbed vaccines have been administered subcutaneously, an increased incidence of local reactions including subcutaneous nodules has been observed. Therefore, subcutaneous administration should be used only in persons who are at risk of hemorrhage with intramuscular injections.
Preparation for Administration: *Shake well before withdrawal and use.* Parenteral drug products should be inspected visually for particulate matter or discoloration prior to administration. With thorough agitation, *Engerix-B* is a slightly opaque white suspension. Discard if it appears otherwise.
The vaccine should be used as supplied; no dilution or reconstitution is necessary. The full recommended dose of the vaccine should be used.
Dosing Schedules: The usual immunization regimen consists of 3 doses of vaccine given according to the following schedule:

1st dose: at elected date
2nd dose: 1 month later
3rd dose: 6 months after first dose

There is an alternate schedule with injections at 0, 1 and 2 months designed for certain populations (e.g., neonates born of hepatitis B infected mothers, others who have or might have been recently exposed to the virus, certain travelers to high-risk areas. See INDICATIONS AND USAGE.). On this alternate schedule, an additional dose at 12 months is recommended for infants born of infected mothers and for others for whom prolonged maintenance of protective titers is desired.
dosage for neonates through children up to, and including, 10 years: 10 mcg administered on either schedule.
dosage for other children and adults: 20 mcg administered on either schedule.
schedule and dosage for adult hemodialysis patients: 40 mcg (2 × 20 mcg in one injection) at 0, 1, 2 and 6 months.
For hemodialysis patients, in whom vaccine-induced protection is less complete and may persist only as long as antibody levels remain above 10 mIU/mL, the need for booster doses should be assessed by annual antibody testing. 40 mcg (two × 20 mcg) booster doses with *Engerix-B* should be given when antibody levels decline below 10 mIU/mL.[1] Data show individuals given a booster with *Engerix-B* achieve high antibody titers. (See CLINICAL PHARMACOLOGY.)
booster vaccinations: Whenever administration of a booster dose is appropriate, the dose of *Engerix-B* is 10 mcg for children 10 years of age and under; 20 mcg for other children and adults. Studies have demonstrated a substantial increase in antibody titers after *Engerix-B* booster vaccination following an initial course with both plasma- and yeast-derived vaccines. (See CLINICAL PHARMACOLOGY.)
See previous section for discussion on booster vaccination for adult hemodialysis patients.

STORAGE

Store between 2° and 8°C (35.6° to 46.6°F). *Do not freeze; discard if product has been frozen.*
Do not dilute to administer.

HOW SUPPLIED

20 mcg/mL in Single-Dose Vials in packages of 1, 10 and 25 vials.
NDC 58160-860-01 (package of 1)
NDC 58160-860-11 (package of 10)
NDC 58160-860-16 (package of 25)
10 mcg/0.5 mL in Single-Dose Vials in packages of 1 vial.
NDC 58160-859-01 (package of 1)

REFERENCES

1. *MMWR:* Recommendations for protection against viral hepatitis. 39(Suppl. 2), Feb. 9, 1990.
2. Robinson, W.S.: Hepatitis B virus and the delta virus. In Mandell, G.L., Douglas, R.G., Bennett, J.E. (eds): *Principles and practice of infectious diseases*, vol. 3, New York, John Wiley & Sons, 1990, pp. 1204–1231.
3. Beasley, R.P., et al.: Efficacy of hepatitis B immune globulin for prevention of perinatal transmission of hepatitis B virus carrier state: final report of a randomized double-blind, placebo-controlled trial. *Hepatology* 3:135–141, 1983.
4. Ambrosch, F.: Persistence of vaccine-induced antibodies to hepatitis B surface antigen—the need for booster vaccination in adult subjects. *Postgrad. Med. J.* 63(Suppl. 2):129–135, 1987.
5. Stevens, C.E., et al.: Hepatitis B vaccine in patients receiving hemodialysis. *N. Engl. J. Med.* 311:496–501, 1984.
6. Andre, F.E., and Safary, A.: Clinical experience with a yeast-derived hepatitis B vaccine. In Zuckerman, A.J. (ed): *Viral hepatitis and liver disease*, Alan R. Liss, Inc., 1988, pp. 1025–1030.
7. Poovorawan, Y., et al.: Protective efficacy of a recombinant DNA hepatitis B vaccine in neonates of HBe antigen-positive mothers. *JAMA* 261(22):3278–3281, June 9, 1989.
8. Goilav, C., et al.: Immunization of homosexual men with a recombinant DNA vaccine against hepatitis B: immunogenicity and protection. In Zuckerman, A.J. (ed): *Viral hepatitis and liver disease*, Alan R. Liss, Inc., 1988, pp. 1057–1058.
9. Hauser, P., et al.: Immunological properties of recombinant HBsAg produced in yeast. *Postgrad. Med. J.* 63 (Suppl. 2): 83–91, 1987.

* yeast-derived, Hepatitis B Vaccine, MSD.
† plasma-derived, Hepatitis B Vaccine, MSD.

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Philadelphia, PA 19101
DATE OF ISSUANCE DEC. 1990

Shown in Product Identification Section, page 430

ESKALITH®

[*ess-kah 'lith*]
(brand of lithium carbonate)
Capsules, 300 mg.
Tablets, 300 mg.

ESKALITH CR®

(brand of lithium carbonate)
Controlled Release Tablets, 450 mg.

PRODUCT OVERVIEW

KEY FACTS
'Eskalith' contains lithium carbonate, and is available in 300 mg. capsules and tablets. It is also available in 450 mg. Controlled Release tablets.

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Epidemiology & molecular biology of *Vibrio cholerae* O139 Bengal

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The emergence of *Vibrio cholerae* O139 Bengal as the second aetiologic agent of epidemic cholera in October 1992 in the south Indian coastal city of Madras has shattered the long-held notion that only *V. cholerae* belonging to serogroup O1 are capable of causing epidemic (and pandemic) cholera. Within months of its appearance in Madras, *V. cholerae* O139 engulfed the entire Indian subcontinent in a series of outbreaks of cholera. It also spread to several neighbouring countries in Asia. Several western countries also reported imported cholera cases due to this organism. In the regions of the Indian subcontinent where cholera due to *V. cholerae* O1 is endemic, children are mostly susceptible because adults would have acquired at least some immunity due to earlier exposure. However, when *V. cholerae* O139 struck people in these areas, even though all age groups were affected, the disease was more prevalent in adults, which suggested that the disease is new in this population. As with O1 cholera, water and food seemed to be the vehicles of infection. Many family contracts of index cases of O139 cholera were found to be infected with *V. cholerae* O139, and in many of them, the infection was asymptomatic which is reminiscent of O1 ElTor infection. Again as with O1 ElTor infection, individuals of blood group O were more susceptible to O139 infection than those with other blood groups. In its molecular aspects, O139 vibrio resembles O1 ElTor vibrio. The virulence genes encoding cholera toxin, zonula occludens toxin, accessory cholera enterotoxin and core-encoded pilin are present in a 4.5 kb 'virulence cassette' region of the chromosome as in ElTor vibrios and the expression of these virulence factors, toxin coregulated pilus (TCP) and several outer membrane proteins are found to be under the control of the master regulator ToxR as in ElTor vibrios. The iron-regulated genes involved in virulence are also found in the same locus as in ElTor vibrios. However, the genes involved in the somatic antigen synthesis in O1 vibrios are found to be deleted in O139 vibrios and are replaced by a new region of chromosome which encodes the new surface antigen synthesis in O139 vibrios. When *V. cholerae* O139 emerged and caused outbreaks, the prevailing O1 ElTor vibrios virtually disappeared from most of the areas. The disappearance of ElTor vibrios, the rapid spread of O139 vibrios and the resemblance of O139 vibrios to ElTor vibrios seemed to suggest that O139 vibrios might be the causative agent of the 'eighth' pandemic of cholera. However, after a year of its appearance, O139 vibrios are on the wane and O1 ElTor vibrios have re-emerged as the predominant organism, in the Indian subcontinent. Thus, the immediate threat of a new cholera pandemic posed by *V. cholerae* O139 may not be as large as it first seemed. However, whether it will follow the pattern of ElTor vibrio which took approximately 60 yr since its first isolation before emerging as the seventh pandemic strain of cholera, is not clear. The factor(s) contributing to the diminished isolation of O139 vibrios and the re-emergence of O1 ElTor vibrios are not understood. The vibrios might have undergone changes that would have affected their ability to survive and compete in the environment.

Key words 'Eighth' cholera pandemic - epidemiology - molecular biology - *Vibrio cholerae* O139

The outbreak of clinical cholera due to a non-O1 serogroup of *Vibrio cholerae* (*V. cholerae* O139 Bengal) in the south Indian coastal city of Madras in October 1992 was a novel event. It was a departure from the long-held dogma that only *V. cholerae* belonging to serogroup O1 are capable of causing epidemic (and pandemic) cholera.

EARLY ISOLATION OF *V. CHOLERAE* 0139

Even though the existence of *V. cholerae* O139 came to the attention of world with the appearance of the cholera outbreak in Madras in October 1992, reexamination of *V. cholerae* stock cultures stored at the Communicable Disease Hospital, Madras showed that *V. cholerae* O139 serogroup began to infect the local population as early as January 1992. However, it took nearly 10 months before it flared into an epidemic[1].

Outbreaks of cholera due to *V. cholerae* O139 occurred in the south Indian towns of Vellore and Madurai soon after the outbreak in Madras. However, more than a year earlier from April to July 1991 there was an unprecedented number of isolations of non-O1 *V. cholerae* from the stools of patients with clinical cholera in the microbiology laboratory of the Christian Medical College Hospital (CMCH), Vellore, indicating an outbreak. Again, from September 1992, increasing numbers of non-O1 organisms were obtained from patients with cholera which were subsequently identified as *V. cholerae* O139[2]. However, the non-O1 *V. cholerae* isolates from the 1991 outbreak were not saved for later probable identification as *V. cholerae* O139. Therefore, it is difficult to state unequivocally whether the non-O1 isolated in the 1991 outbreak in Vellore was indeed *V. cholerae* O139[3]. By hindsight, due to the failure of studying the 1991 isolates, a historical opportunity might have been missed.

In 1993, most parts of India were affected by *V. cholerae* O139 outbreaks. Non-O1 *V. cholerae* isolates suspected to be *V. cholerae* O139 from outbreaks of clinical cholera from different parts of India were sent to the National Institute of Cholera and Enteric Diseases (NICED), Calcutta, for confirmation. Based on the response to a questionnaire sent out by NICED to the participating laboratories, the probable date of appearance *V. cholerae* O139 in each area was determined. The direction of the spread of *V. cholerae* O139 based on its first appearance in each area was also deduced. These data are presented in Fig. 1[4].

Long-term surveillance for *V. cholerae* infections in India has been maintained at CMCH, Vellore; Communicable Diseases Hospital, Madras; and the Infectious Diseases Hospital, Calcutta through NICED. In Vellore, the number of isolates of *V. cholerae* serogroups O1 and non-O1 cultured at the CMCH from January 1990-November 1993 is shown in Fig. 2. Yearly epidemics of cholera occur in Vellore between May and October. However, from September 1992, non-O1 isolates and cholera cases increased, but the isolation of *V. cholerae* O1 was unusually low. From September 1992 until the end of September 1993, most of the non-O1 isolates were identified as *V. cholerae* O139. From January-July 1993, there were no isolates of *V. cholerae* O1[5]. Between December 1993 and April 1994, there were more strains of *V. cholerae* O1 than *V. cholerae* O139. However, in May and June 1994, there were more isolates of *V. cholerae* O139 than *V. cholerae* O1. Later data from Vellore for 1995 indicate that only *V. cholerae* O1 are isolated, no *V. cholerae* O139[2,3].

INDIA

Madras

The rates of isolation of *V. cholerae* O1 and *V. cholerae* non-O1 at the Communicable Diseases Hospital, Madras are shown in Fig 3[1]. A changing pattern of cholera was observed during the major epidemic which started in October 1992. There was a steady increase in the number of admissions during November, then a slow decline phase began by early December 1992. As many as 11,000 patients were admitted during this period. The rates of isolations of *V. cholerae* O1 and non-O1 vibrios were 2.7 and 31.3 per cent respectively. A representative sample of 84 strains of non-O1 vibrios isolated during this period was confirmed as *V. cholerae* O139. Between January 1993 and June 1994, a total of 17,540 patients were admitted for cholera and cholera-like illness. The prevalence of O1 and non-O1 vibrios were found to be 3.8 and 37.8 per cent respectively. All non-O1 vibrios were serologically confirmed as O139

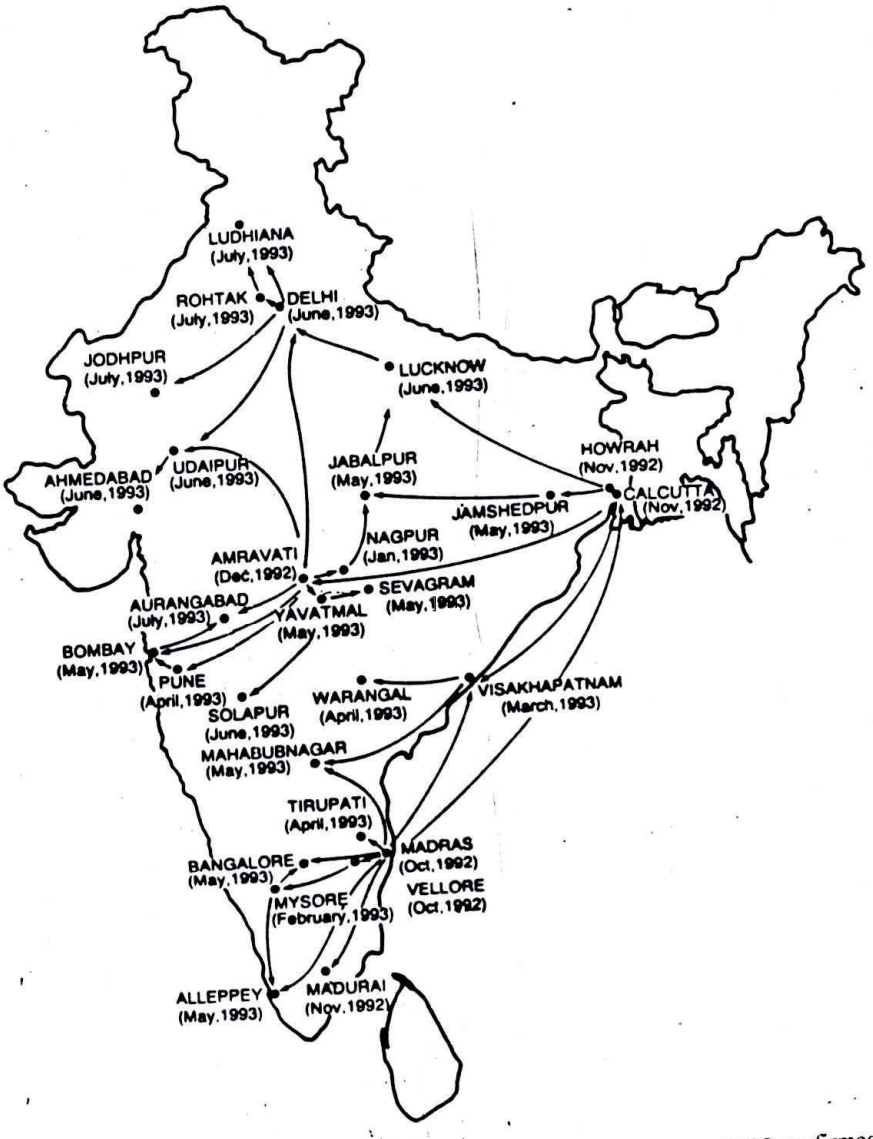

Fig. 1. Spread of *V. cholerae* O139 in India. Sites marked had *V. cholerae* O139 confirmed by National Institute of Cholera and Enteric Diseases, Calcutta, India. Arrows indicating probable direction of spread are speculative and based on first isolation of *V. cholerae* 0139 in a given area. (Ref. 4. Reprinted with permission).

serogroup. There was a significant fall in the incidence of cholera in the first half of 1994. However, the isolation of *V. cholerae* O139 was predominant.

Calcutta

The surveillance for cholera was conducted at the clinical unit of NICED, which is located at the 780 bed Infectious Diseases Hospital (IDH), Calcutta (Fig. 4)[6,7]. In 1993, there was an unusual increase in the number of admissions of patients with acute diarrhoea (44522 patients in 1993 versus 23333 patients in 1992). The cases started increasing fr January 1993 and continued until May and there w a second peak during September-October. During t peak of the epidemic, 180 to 300 patients were mitted daily at the IDH. During this time, up to per cent of acute secretory diarrhoeal cases were to *V. cholerae* O139. The first case of O139 detected in Calcutta in November 1992. From Ja ary to June 1993, no *V. cholerae* O1 serogroup isolated. From July 1993, *V. cholerae* O1 serogr started reappearing and by February 1994, it bec

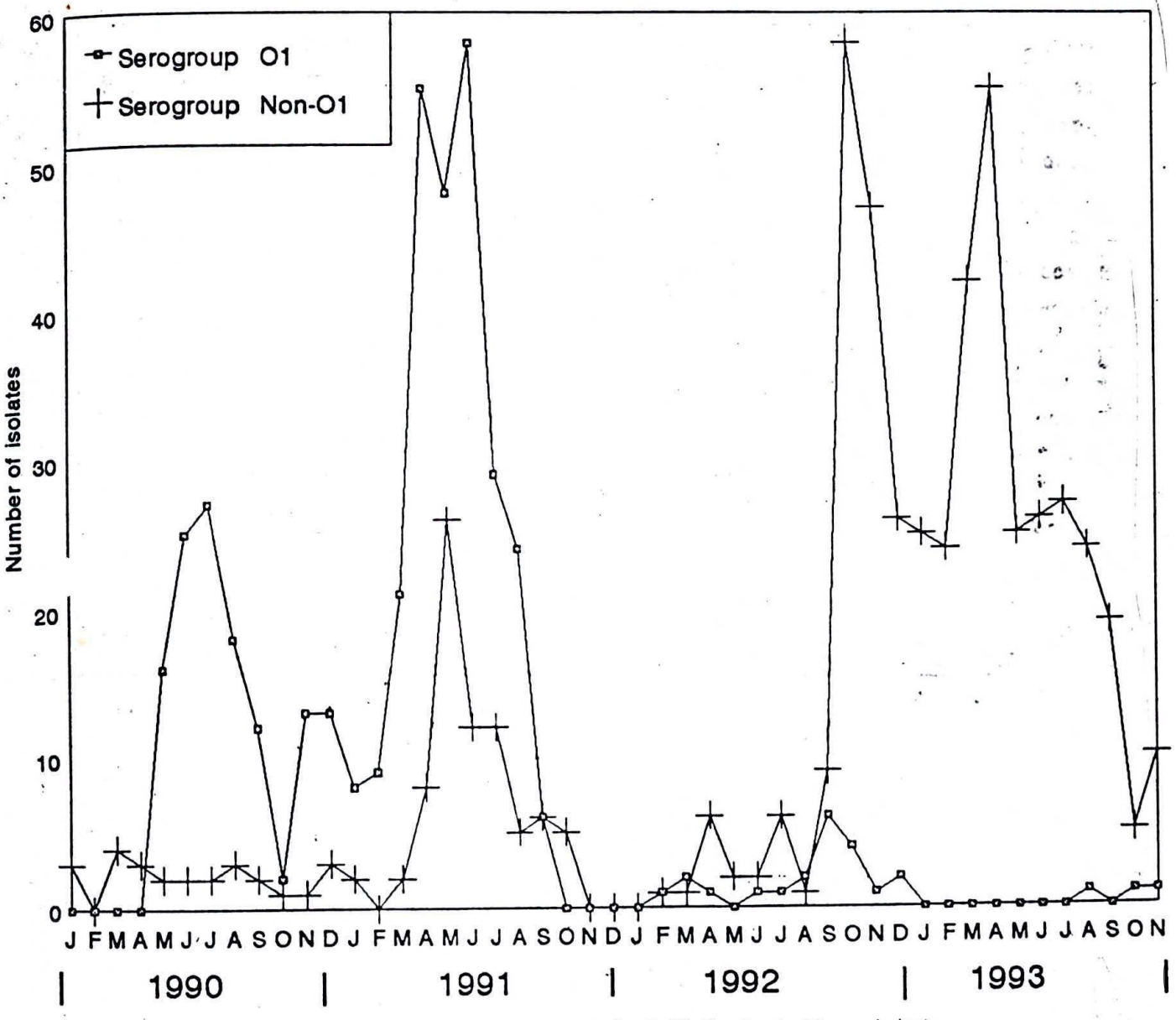

Fig. 2. *V. cholerae* isolated in Vellore, India (Ref.2. Reprinted with permission).

the predominant isolate again.

Other parts of India

Investigations conducted in other parts of India during the period of outbreaks in 1993 showed a higher isolation of *V. cholerae* O139 than *V. cholerae* O1[8-12].

Bangladesh

Field outbreaks : An epidemic of cholera due to *V. cholerae* O139 first started in some of the temporary islands off the coast of the Sundarban area in the south-western coastal districts of Bagerhat[13,14]. The epidemic was not noticed until December 1992 when it reached the mainland of Bagerhat and within a few days in the five neighbouring districts (Fig. 5)[14]. This is the usual cholera season for this part of the country. The Epidemic Control Preparedness Programme (ECPP) of the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) in collaboration with the Government of Bangladesh investigated the epidemic in the six southern districts between January and May 1993. The epidemic lasted 18 wk instead of the usual 6-8 wk for *V. cholerae* O1

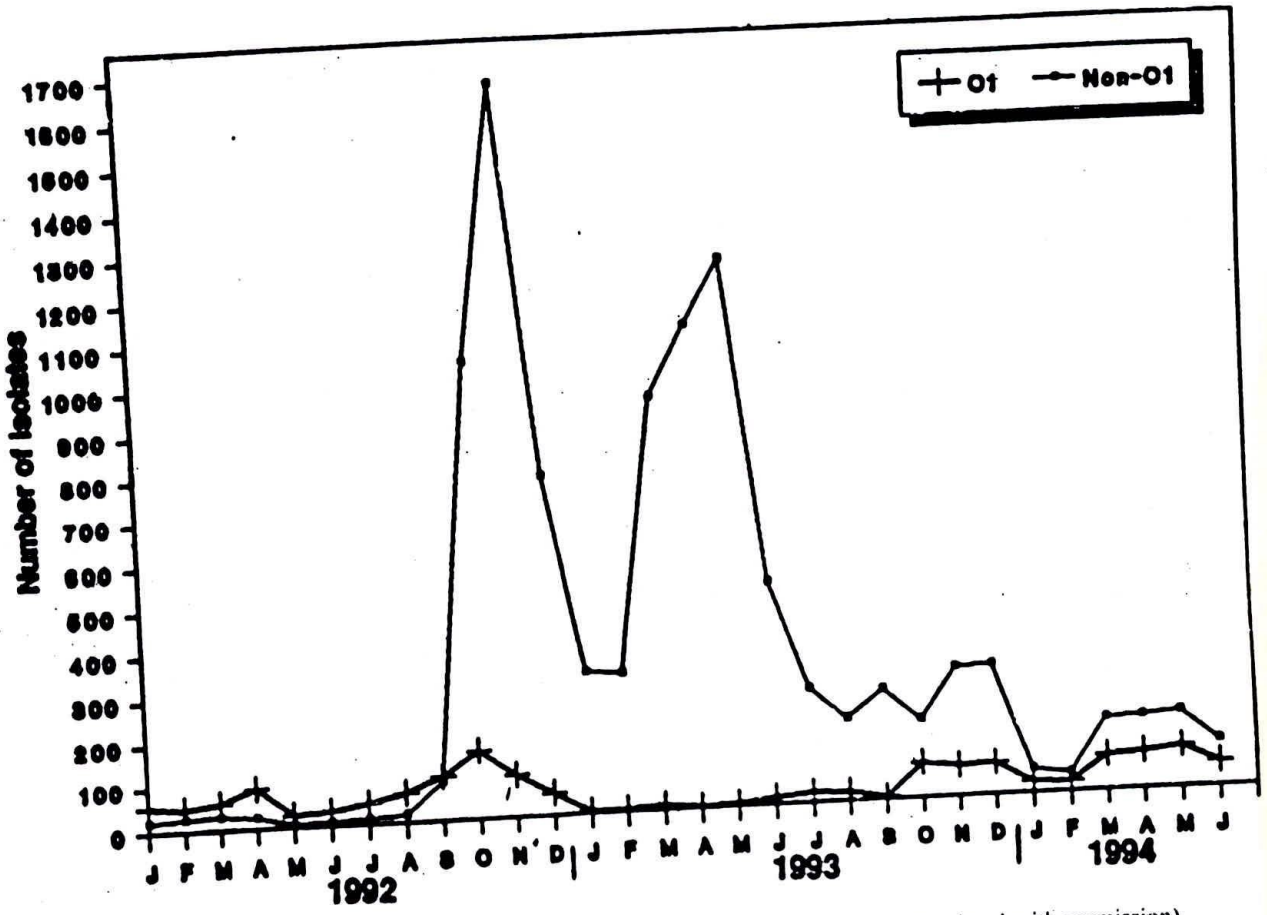

Fig. 3. Isolation pattern of *V. cholerae* O1 and non-O1 in Madras, India (Ref. 1. Reprinted with permission).

in southern Bangladesh. During this period, there were a total of 46,965 cases and 846 deaths. Of the 161 systematic sample of stool specimens cultured, 69 per cent yielded *V. cholerae* O139 with no *V. cholerae* O1 isolation. In September 1993, three months after the decline in the southern areas, the epidemic moved to the northern region. The appearance of the epidemic in a number of northern districts at the end of the monsoon period coincided with the seasonal outbreaks of the *V. cholerae* O1 epidemics in Bangladesh. Between August and September 1993, *V. cholerae* O139 only was detected in the north and north-eastern areas. When cholera broke out in north-western districts, both *V. cholerae* O1 and *V. cholerae* O139 were detected, and *V. cholerae* O1 accounted for 77 per cent of isolates. Between January and March 1994, even though *V. cholerae* O1 had re-emerged (21%), *V. cholerae* 0139 still predominated (79%) in the southern districts[15]. Epidemic investigations in the northern districts between September and November 1994 showed the total displacement of *V. cholerae* O139 by ElTor strains. The initial outbreak in the south spread very fast during the dry season (December-April), whereas the spread in the north coincided with the wet season and moved slowly[16]. Between June 1995 and April 1996, ECPP investigated several outbreaks of cholera in the northern districts. The most striking observation was the re-emergence of *V. cholerae* O139 in the north-eastern districts (A.K. Siddique, personal communication). *V. cholerae* O139 initially spread to this region in 1993 and disappeared in 1994. The reappearance of *V. cholerae* O139 in this area indicates that the organism is re-establishing in non-coastal areas.

Dhaka

The ICDDR,B has been maintaining two diarrhoeal treatment centres: one in urban Dhaka and the other in rural Matlab, a riverine delta 45 km south-east of

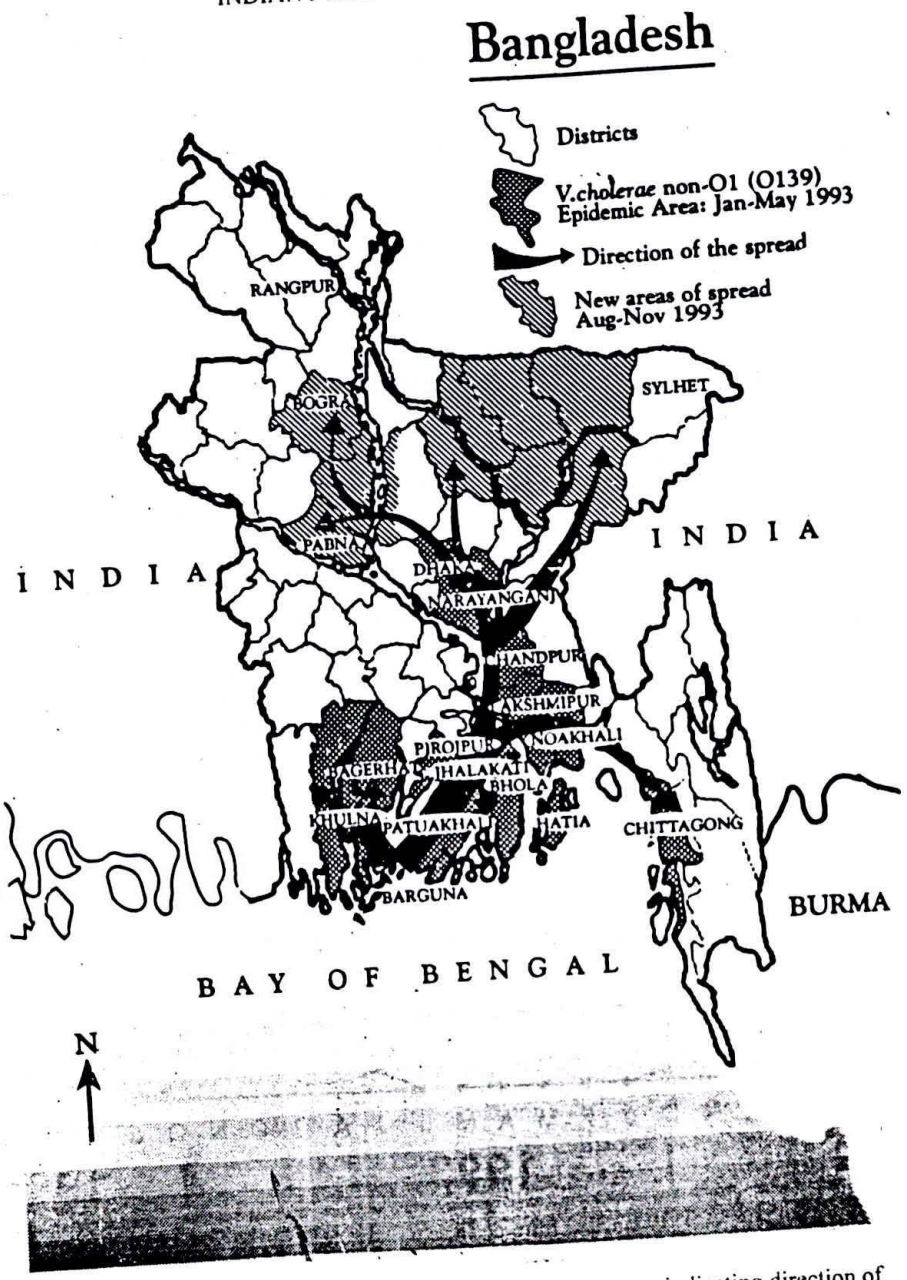

Fig. 5. Spread of *V. cholerae* O139 in Bangladesh in 1993. Arrows indicating direction of spread are based on investigation of outbreaks (Reprinted with permission from Siddique A.K, Epidemic Control Preparedness Programme, ICDDR, B, Annual Report, 1993).

(the isolates from the outbreak in southern Bangladesh had not then been characterized) these hospital isolates were not saved for later probable identification as *V. cholerae* O139. It is possible that the *V. cholerae* O139 vibrios were brought to Dhaka from southern Bangladesh or India by the pilgrims and then carried back to their homelands.

The epidemic reached its peak in Dhaka in March, when 500-600 patients (two to three times the number usually treated at this time of the year) were treated. During this period, the isolation of *V. cholerae* O1 was very low[17]. The second peak appeared on schedule, during August-November, but continued to be dominated by *V. cholerae* O139. But towards the end of the year, *V. cholerae* O1 began to appear in increasing numbers. From the beginning of 1994 till date, *V. cholerae* O1 continued to dominate in Dhaka. The isolation rates of *V. cholerae* O

and 0139 are shown in (Fig 6)[18].

At the rural diarrhoeal disease hospital of ICDDR,B in Matlab, admissions due to *V. cholerae* 0139 peaked around the same time as in Dhaka[17]. There were approximately 125 admissions per day (the usual number for this time of the year is 25-40). These patients came from a demographic surveillance population of approximately 200,000 people. The *V. cholerae* O139 isolates predominated during February-July of 1993. Subsequently, *V. cholerae* O1 ElTor became the predominant organism again as seen in Dhaka (data not shown).

Other countries

V.cholerae O139 was first isolated from patients with diarrhoea in Bangkok, Thailand in early 1993[19]. Soon after, a surveillance was instituted in three different hospitals. By 1994, all hospitals had experienced an increase in *V. cholerae* O139 infections[20]. *V. cholerae* O139 was also reported from Karachi, Pakistan in 1993. During the outbreak, *V. cholerae* O139 displaced *V. cholerae* O1[21]. There was an outbreak of *V. cholerae* O139 infection in the northwest part of China[22]. Patients with cholera due to *V. cholerae* O139 have been reported from Nepal, Myanmar, Malaysia, and Sri Lanka, but details are not available[22]. The spread of *V. cholerae* O139 in Asia is shown in Fig. 8[22]. Imported cases of *V. cholerae* O139 infections have been reported from Estonia, Germany, Hong Kong, Japan, Singapore, the United States of America and the United Kingdom[22]. There was an intriguing case of *V. cholerae* O139 diarrhoea involving a Vietnamese woman resident in Denmark for the previous 9 months[23]. She

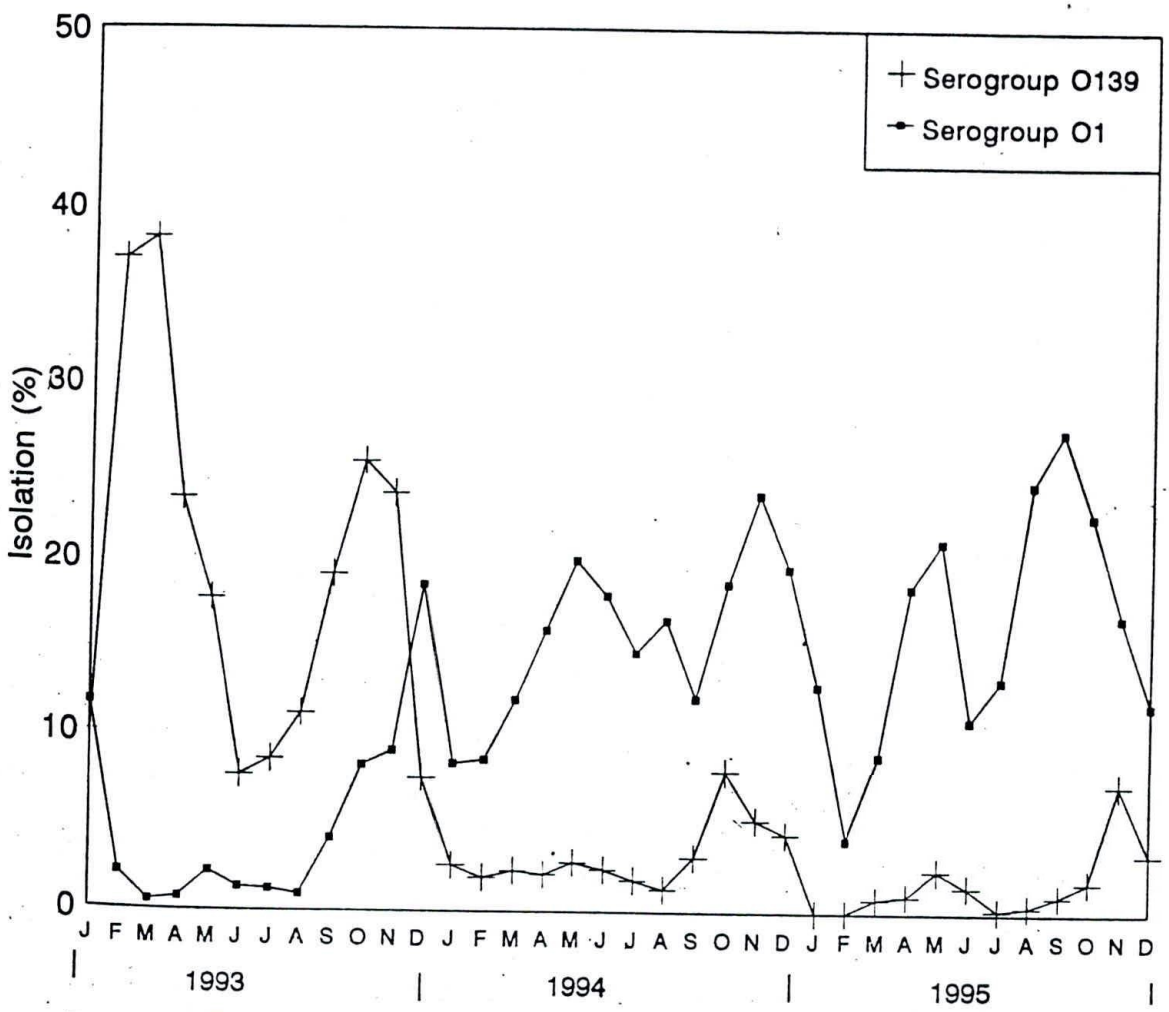

Fig. 6. Isolation rate of *V. cholerae* O1 and O139 in surveillance patients at ICDDR,B, Dhaka, Bangladesh.

had not travelled outside of Denmark during that period and had not eaten food imported from south-east Asia. The isolate was identical to the isolates from India, Bangladesh and Thailand. The origin of this isolate is a mystery. Vietnam has not reported *V. cholerae* O139 infection so far.

Age and gender distribution of cases and association with blood group O.

In areas where cholera is endemic, the predominant age group affected is children, 2-9 yr old, because adults would have acquired some immunity due to earlier exposure[24]. However, in the outbreaks of O139 cholera in India, Bangladesh, and Thailand, the majority of cases occurred in adults[4,17,20]. This pattern of age-related incidence of *V. cholerae* O139 cholera is similar to that seen in Latin America when O1 cholera appeared in the non-immune population there in 1991[25]. This suggested that O139 cholera is a new disease in the population and that in O1 cholera endemic areas, prior exposure to O1 cholera has not afforded any cross-immunity to O139 cholera. In the outbreaks in both Bangladesh and India, more males than females were affected, which probably indicated greater mobility and exposure of the male population[4,17]. For reasons that are not completely clear, those with blood type O exhibit an increased severity of disease with ElTor cholera[26]. This

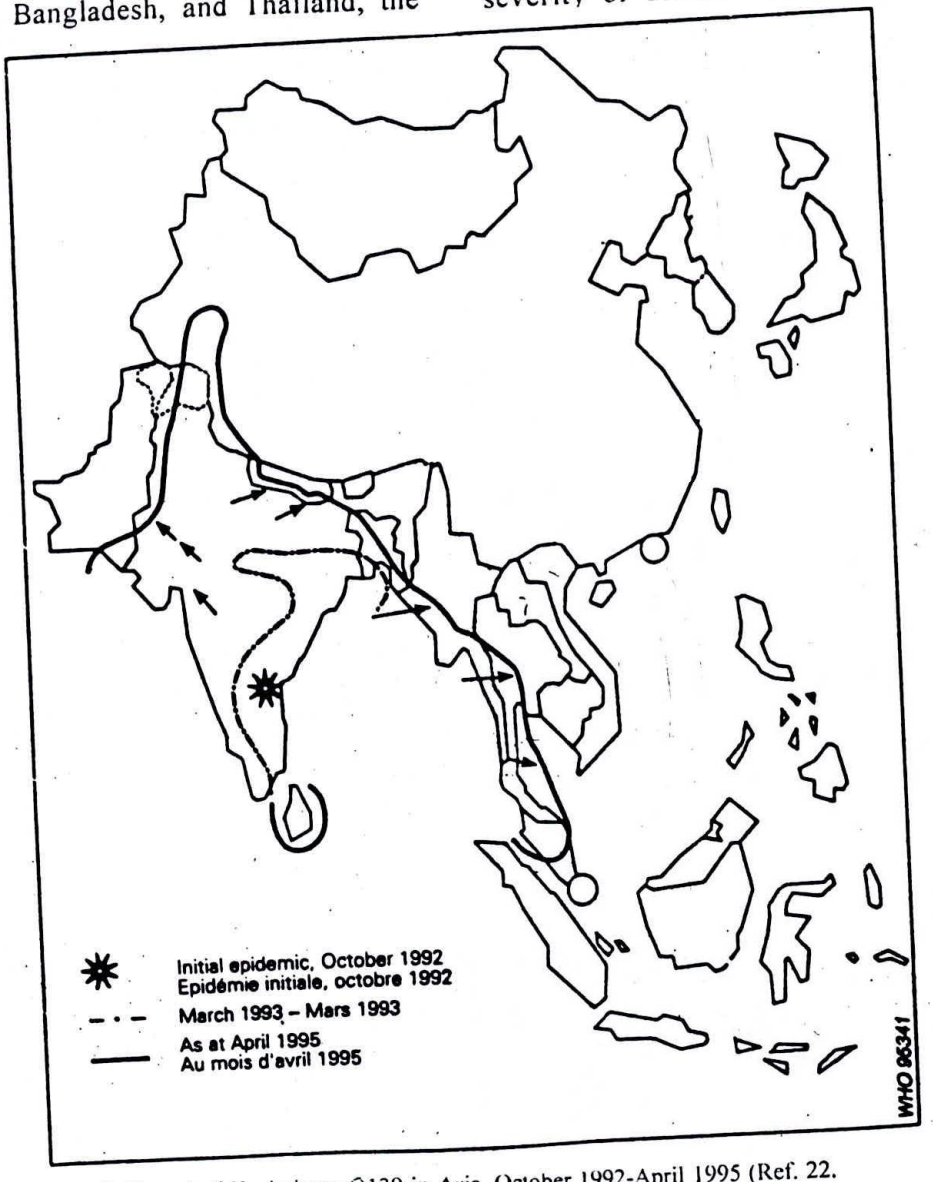

Fig. 7. Spread of *V. cholerae* O139 in Asia. October 1992-April 1995 (Ref. 22. Reprinted with permission).

enhanced susceptibility to cholera for individuals with blood type O has been observed for *V. cholerae* 0139 as well[27].

Intrafamilial infection and route of transmission

Cholera caused by *V. cholerae* O1 is a water-borne and food-borne illness. *V. cholerae* O1 is recoverable from surface waters at a rate of less than 1 per cent in areas of outbreaks[28]. *V. cholerae* O139 not only appears to show the same predisposition for water-borne spread, but in a study in Bangladesh a higher rate of isolation of 12 per cent from surface waters was noted during outbreaks, suggesting, perhaps, that *V. cholerae* O139 has a greater ability to survive in the aquatic environment than *V. cholerae* O1 isolates[28]. Also, during surveillance of a freshwater lake in Calcutta, India during 1993, the year of the *V. cholerae* O139 epidemic, of the 150 strains of *V. cholerae* recovered, 15 per cent were *V. cholerae* O139, and no O1 vibrios were isolated[29].

Secondary transmission of infection in family members of index cases hospitalized with *V. cholerae* O139 diarrhoea were carried out in urban Dhaka[30] and rural Matlab[31] in Bangladesh, and in Calcutta[32], India. In the Dhaka study[30], a secondary infection rate of approximately 16 per cent was found within 7 days of the hospitalization of index cases; a prevalence of symptomatic infection of 38 per cent was found. Of the infected contacts, approximately 63 per cent became symptomatic, and of the symptomatic people, approximately 80 per cent had severe diarrhoea. In the rural Matlab study[31], a secondary infection rate of 25 per cent was found among family members within 10 days of the infected cases, and 27 per cent of those infected had diarrhoea. Children under 5 yr of age were more frequently infected than adults. Tubewell water, which was free of vibrios at its source, frequently became contaminated with O139 vibrios on storage in the house. In the Calcutta study[32], where family contacts of index cases and neighbourhood families were studied, a secondary symptomatic infection of approximately 15 per cent was found among family contacts and none among neighbourhood contacts. The organism could be cultured from the handwashings of contacts of index cases, stored drinking water, open well water, flies and pond water used by the index case families and none from neighbourhood families. In an intercontinental outbreak of *V. cholerae* O139 infection involving passengers in a cruise ship to southeast Asia, eating yellow rice at a buffet restaurant was associated with the risk of cholera[33]. The initial cluster of cases in the Madras outbreak had a history of marine food consumption[1]. From the forgoing data, similarities between ElTor vibrio and O139 vibrio infections are found. As with ElTor vibrios, surface water and food were found to be the vehicles of infection, and stored water at home become easily contaminated which may spread the infection further. In addition, as with ElTor vibrio infection, family members of index cases become infected, with a large proportion having asymptomatic infection.

Molecular epidemiology

Several studies were conducted on the molecular epidemiology of *V. cholerae* O139 isolates obtained during the early part of the outbreaks. The isolates compared were from different parts of India and Bangladesh, Thailand, China and other parts of the world where imported cases occurred[34-38]. The techniques used for these studies included multilocus enzyme electrophoresis, ribotyping, *ctx* genotyping and pulsed-field gel electrophoresis. In all of these typing methods, *V. cholerae* O139 isolates were either indistinguishable from or similar to the seventh pandemic strain (ElTor biotype) of cholera and were distinctly different from other non-O1 vibrios. However, some polymorphism was observed among *V. cholerae* O139 isolates. This may suggest that the *V. cholerae* O139 serogroup is undergoing changes in a manner analogous to those seen among ElTor strains of the seventh cholera pandemic.

Molecular biology of *V. cholerae* O139

Most of the virulence genes in *V. cholerae* O139 are organized in the same fashion as in *V. cholerae* O1 in a 4.5 kb core region or virulence cassette of the chromosome. The genes in the core region are: *ctxAB* (that encodes cholera toxin A and B subunits), *zot* (that encodes zonula occludens toxin), *ace* (that encodes accessory cholera enterotoxin), and *cep* (that encodes core-encoded pilin). Moreover, as in O1 vibrios, the core region is flanked by one or more copies of RS1 element. The core region and RS1 element constitute the CTX element, and this element is indeed a site-specific transposon. As with *V.*

cholerae O1 strains, some strains of *V. cholerae* O139 carry multiple copies of the CTX element. In addition, *V. cholerae* O139 isolates carry the *tcpA* gene (which encodes the structural subunit of TCP, TcpA) that has structural identity with that of ElTor vibrios[39-42]. Further, the in iron regulated genes important in virulance such as *irgA* (a virulence gene of unknown function), *viuA* (the gene for the receptor for the siderophore vibriobactin), and *fur* (an iron regulating gene) previously described for O1 vibrios are present in the same chromosomal locations as in ElTor vibrios[43]. Further relatedness with ElTor vibrios was suggested by the identity of sequences for *ctxAB* and 16SRRNA genes between *V. cholerae* O139 and ElTor vibrios[36]. In addition, the expression of cholera toxin, *TcpA*, and the outer membrance protein, OmpU, in O139 vibrios is dependent on toxR (transcriptional activator) as it is in O1 vibrios[40]. Moreover, the optimal conditions required to induce production of cholera toxin are the same as those for ElTor O1 isolates and not classical O1 isolates[40]. Further similarity between O1 and O139 vibrios is also found in the induction of several iron-regulated outer membrane proteins[43].

Thirteen genes in the *rfb* region of the chromosome of *V. cholerae* O1 are responsible for the synthesis of the lipopolysaccharide (LPS) antigen. An additional gene of the *rfb* region, *rfbT* is responsible for conversion of the Inaba serotype into Ogawa serotype. All of these genes and also at least a 6kb additional contiguous DNA are found to be deleted in the chromosome of *V. cholerae* O139[44]. However, the three remaining genes of the *rfb* region, *rfb* Q, -R, and -S, are still present as a modified locus in the chromosome of *V. cholerae* O139. The region defined by *rfb* Q, -R and -S genes is related to an open reading frame called the H-repeat of RHS elements in *Escherichia coli*. RHS elements are chromosomal rearrangement hot spots[45]. This region is closely related to the transposases of a number of insertion sequence elements and has all the features of an insertion sequence element. All the evidence indicates that *V. cholerae* O139 evolved from an ElTor strain by deletion of the genes of the *rfb* complex encoding the O1 antigen, and by the acquisition of novel genes that confer O139 specificity. One likely scenario is that the insertion sequence when linked to the novel LPS antigen genes, was able to recombine into the *V. cholerae* O1 chromosome. Following the acquisition of the novel LPS genes, one might expect incompatibility with the original O1 *rfb* genes, that would select for the O139 genes[44]. In further studies of the genes involved in the synthesis of LPS antigen, it was found that the extent of the DNA region in *V. cholerae* O139 that is not present in *V. cholerae* O1 is approximately 35 kb. Also, *V. cholerae* O139 Bengal contains a deletion of 22 kb that in serogroup O1 contains the *rfb* region. These data reinforce the notion that an ElTor strain had undergone genetic rearrangements including the deletion of the O1 *rfb* region and acquisition of a 35 kb region of DNA which encodes the polysaccharide of a new specificity to become *V. cholerae* O139[46].

By transposon mutagenesis, derivatives were obtained that lost the ability to synthesize both capsular polysaccharide and LPS. This implied that there are genes common to the biosynthesis of both these macromolecules[47,48]. In one study, a DNA probe based on the transposon insertion region hybridized to all *V. cholerae* O139 isolates and some other vibrios, but not to *V. cholerae* O1 isolates. This suggested that this region in *V. cholerae* O139 was recently acquired[47]. Partial homology of the novel LPS gene sequences in *V. cholerae* O139 with the sequences in *V. cholerae* non-O1 serogroups has been demonstrated. This suggested that *V. cholerae* O139 strain arose by horizontal gene transfer between a non-O1 and an O1 strain[49].

Is *V. cholerae* O139 Bengal, the causative agent o the 'eighth' pandemic of cholera?

Within a few months of causing the first outbrea of cholera in Madras, *V. cholerae* O139 spread swiftl throughout the Indian subcontinent and invaded sev eral neighbouring countries in the Asian region. A the peak of the epidemic in the Indian subcontinen the ElTor strains virtually vanished. Moreover, th strain closely resembled ElTor vibrios in cultura physiologic, and genetic properties. All of the observations prompted the speculation that *cholerae* O139 might have initiated the 'eight pandemic of cholera[50]. However, after the peak activity in 1993, the strain has not invaded ne countries, and in the various regions of the Indi subcontinent where continuous surveillance is place, the O139 strain is on the retreat and O1 str

has become the dominant strain again. A number of host and environmental factors may be responsible for the diminished isolation of *V. cholerae* 0139. Aquatic environment is the main reservoir for vibrios[51]. One possible explanation is that after the initial period when it caused large epidemics and survived well in the surface water, *V. cholerae* O139 might have undergone changes, for example in colonization factors that determine the long-term persistence in the aquatic environment. This in turn would have made the organism less suited for survival in the environment. Alternatively, subsequent to the emergence and peak prevalence of *V. cholerae* O139, *V. cholerae* O1 might have undergone changes that would have enabled it to outcompete *V. cholerae* O139 and become the predominant strain again. However, the continued isolation of *V. cholerae* O139 from the areas it has invaded, albeit at a low level, suggests that this strain has established itself as an endemic strain. The lack of spread of the strain to new countries since 1993, and the diminished isolation from areas where it has already established, suggest that the immediate threat of a cholera pandemic posed by *V. cholerae* O139 may not be as great as it first seemed. However, the lessons from cholera history may be instructive. The causative agent of the seventh pandemic of cholera, the ElTor strain, was first isolated in Sinai, Egypt in 1906, and it caused local outbreaks in Celebes, Indonesia in the 1930s. It was not until the early 1960s that it started progressing as the seventh pandemic strain[52], and it took another 30 yr for the strain to reach the South American continent[53]. Whether a similar fate is awaiting the *V. cholerae* O139 strain is difficult to predict.

Acknowledgment

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References

Dhamodaran S, Ananthan S, Kuganantham P. A retrospective analysis of the Madras epidemic of non-01 *Vibrio cholerae* new serogroup 0139 Bengal. *Indian J Med Res* 1995; *101* : 94-7.

Jesudason MV, John TJ. The appearance and spread of *Vibrio cholerae* 0139 in India. *Indian J Med Res* 1994; *99* : 97-100.

John TJ. Emerging and re-emerging bacterial pathogens in India. *Indian J Med Res* 1996; *103* :4-18.

4. Nair GB, Ramamurthy T, Bhattacharya SK, Mukhopadhyay AK, Garg S, Bhattacharya MK, *et al*. Spread of *V. cholerae* 0139 Bengal in India. *J Infect Dis* 1994; *169* : 1029-34.
5. Jesudason MV, Samuel R, John TJ. Reappearance of *Vibrio cholerae* 01 and concurrent prevalence of 01 and 0139 in Vellore, south India. *Lancet* 1994; *344* : 335-6.
6. Bhattacharya SK, Goswami AG, Bhattacharya MK, Dutta D, Deb A, Deb M, *et al*. Epidemic of *Vibrio cholerae* 0139 in Calcutta. *Indian J Med Res* 1994; *100* :213-6.
7. Mukhopadhyay AK, Garg S, Nair GB, Kar S, Ghosh RK, Pajni S, *et al*. Biotype traits and antibiotic susceptibility of *Vibrio cholerae* serogroup 01 before, during and after the emergence of the 0139 serogroup. *Epidemiol Infect* 1995; *115* : 427-34.
8. Jalgaonkar SV, Fule RP. Cholera outbreak due to *Vibrio cholerae* serogroup 0139 in Yavatmal (Maharashtra) in March-July, 1993. *Indian J Med Res* 1994; *99* : 101-2.
9. Agarwal V, Biswas M, Chande CA, Pathak AA, Saoji AM. Changing bacteriological profile of cholera in Nagpur, 1991-93. *Indian J Med Res* 1994; *100* : 93-4.
10. Prabhakar H, Lal M, Kaur H. Outbreak of gastroenteritis due to a new strain of non O group 1 *Vibrio cholerae*, in Ludhiana in May-August 1993. *Indian J Med Res* 1994; *99* : 107-8.
11. Narang P, Mendiratta DK, Kannathe J, Ramnani VK, Wasekar V, Deotale V. Characteristics of *Vibrio cholerae* 0139 strains isolated in Sevagram (Maharashtra) during April-August 1993. *Indian J Med Res* 1994; *99* : 103-4.
12. Sabherwal S, Sikka R. Emergence of *Vibrio cholerae* serogroup 0139 in Haryana in May-June 1993. *Indian J Med Res* 1994; *99* : 105-6.
13. Albert MJ, Siddique AK, Islam MS, Faruque ASG, Ansaruzzaman M, Faruque SM, *et al*. Large outbreak of clinical cholera due to *Vibrio cholerae* non-01 in Bangladesh [letter]. *Lancet* 1993; *341* : 704.
14. Siddique AK, Zaman K, Akram K, Mutsuddy P, Eusof A, Sack RB. Emergence of a new epidemic strain of *Vibrio cholerae* in Bangladesh. *Trop Geogr Med* 1994; *46* : 147-50.
15. Siddique AK, Akram K, Zaman K, Mutsuddy P, Eusof A, Sack RB. *Vibrio cholerae* 0139: how great is the threat of a pandemic? *Trop Med Intl Health* 1996; *1* : 393-8.
16. Albert MJ. Personal reflections on the discovery of *Vibrio cholerae* 0139 synonym Bengal: A tribute to team work and international collaboration. *J Diarrhoeal Dis Res* 1993; *11* : 207-10.
17. Cholera Working Group, International Centre for Diarrhoel Diseases Research, Bangladesh. Large epidemic of cholera-like disease in Bangladesh caused by *Vibrio cholerae* 0139 synonym Bengal. *Lancet* 1993; *342* : 387-90.
18. Faruque ASG, Fuchs GJ, Albert MJ. Changing epidemiology of cholera due to *V. cholerae* 01 and 0139 Bengal in Dhaka, Bangladesh. *Epidemiol Infect*. In press.

19. Changsa-nguan M, Chaicumpa W, Moolasart P, Kandhasingha, P, Kurazono H, Shimda, T. *et al Vibrio cholerae* 0139 Bengal in Bangkok. *Lancet* 1993; *342* : 430-1.

20. Bodhidatta L, Echeverria P, Hoge CW, Pitarangsi C, Serichantalergs O, Henprasert-Tae N, *et al. Vibrio cholerae* 0139 in Thailand in 1994. *Epidemiol Infect* 1995; *114* : 71-3.

21. Fisher-Hoch SP, Khan A, Haq I, Khan MA, Mintz ED. *Vibrio cholerae* 0139 in Karachi, Pakistan [letter]. *Lancet* 1993; *342* : 1422-3.

22. World Health Organization. Cholera in 1994. *Weekly Epidemiol Rec* 1995; *70* : 201-8.

23. Dalsgaard A, Nielsen GL, Echeverria P, Larsen JL, Schonheyder HC. *Vibrio cholerae* 0139 in Denmark [letter]. *Lancet* 1995; *345* : 1637.

24. Glass RI, Becker S, Huq MI, Stoll BJ, Khan MU, Merson MH, *et al.* Endemic cholera in rural Bangladesh, 1966-1980. *Am J Epidemiol* 1982; *116* : 959-70.

25. Swerdlow DL, Mintz ED, Rodriguez M, Tejada E, Ocampo, C, Espejo E, *et al.* Waterborne transmission of epidemic cholera in Trujillo, Peru: lessons for a continent at risk. *Lancet* 1992; *340* : 28-32.

26. Clemens JD, Sack DA, Harris JR, Chakraborty J, Khan MR, Huda S, *et al.* ABO blood groups and cholera: new observations on specificity of risk and modification of vaccine efficacy. *J Infect Dis* 1989; *159* : 770-3.

27. Faruque AS, Mahalanabis D, Hoque SS, Albert MJ. The relationship between ABO blood group and susceptibility to diarrhea due to *Vibrio cholerae* 0139 *Clin Infect Dis* 1994; *18* : 827-8.

28. Islam MS, Hasan MK, Miah MA, Qadri F, Yunus M, Sack RB, *et al.* Isolation of *Vibrio cholerae* 0139 Bengal from water in Bangladesh [letter]. *Lancet* 1993; *342* : 430.

29. Ghosh AR, Koley H, De D, Garg S, Bhattacharya MK, Bhattacharya SK, *et al.* Incidence and toxigenicity of *Vibrio cholerae* in a freshwater lake during the epidemic of cholera caused by serogroup 0139 Bengal in Calcutta, India. *FEMS Microbiol Ecol* 1994; *14* : 285-91.

30. Faruque AS, Mahalanabis D, Albert MJ, Hoque SS. Studies of infection with *Vibrio cholerae* 0139 synonym Bengal in family contacts of index cases. *Trans R Soc Trop Med Hyg* 1994; *88* : 439.

31. Sack RB, Albert MJ, Siddique AK. Emergence of *V. cholerae* 0139. In: Remington JS, Swartz M, editors. *Current clinical topics in infectious diseases.* Boston: Blackwell, 1995; 172-93.

32. Sengupta PG, Sircar BK, Mondal SK, Mukhopadhyay AK, Nair GB, Gupta DN, *et al.* Epidemiology of *Vibrio cholerae* 0139 with special reference to intrafamilial transmission in Calcutta. *J Infect* 1995; *31* : 45-7.

33. Boyce TG, Mintz ED, Greene KD, Wells JG, Hockin JC, Morgan D, *et al. Vibrio cholerae* 0139 Bengal infections among tourists to southeast Asia: an intercontinental foodborne outbreak. *J Infect Dis* 1995; *172* : 1401-4.

34. Faruque SM, Alim ARMA, Roy SK, Khan F, Nair GB, Sack RB, *et al.* Molecular analysis of rRNA and cholera toxin genes carried by the new epidemic strain of toxigenic *Vibrio cholerae* 0139 synonym Bengal. *J Clin Microbiol* 1994; *32* : 1050-3.

35. Kurazono H, Okuda J, Nair GB, Albert MJ, Sack RB, Chongsa-nguan M, *et al. Vibrio cholerae* 0139 Bengal isolated from India, Bangladesh, and Thailand are clonal as determined by pulsed-field gel electrophoresis [letter]. *J Infect* 1994; *29* : 109-10.

36. Popovic T, Fields PI, Olsvik O, Wells JG, Evins GM, Cameron DN *et al.* Molecular subtyping of toxigenic *Vibrio cholerae* 0139 strains that causing epidemic cholera in India and Bangladesh 1992-1993. *J Infect Dis* 1995; *171* : 122-7.

37. Yuen K-Y, Yam W-C, Wong SS, Kam K-M, Leung T-H. *Vibrio cholerae* 0139 synonym Bengal in Hong Kong [letter]. *Clin Infect Dis* 1994; *19* : 553-4.

38. Echeverria P, Hoge CW, Bodhidatta L, Serichantalergs O, Dalsgaard A, Eampokalap B, *et al.* Molecular characterization of *Vibrio cholerae* 0139 isolates from Asia. *Am J Trop Med Hyg* 1995; *52* : 124-7.

39. Waldor MK, Mekalanos JJ. Emergence of a new cholera pandemic : molecular analysis of virulence determinants in *Vibrio cholerae* 0139 and development of a live vaccine prototype. *J Infect Dis* 1994; *170* : 278-83.

40. Waldor MK, Mekalanos JJ. ToxR regulates virulence gene expression in non-01 strains of *Vibrio cholerae* that cause epidemic cholera. *Infect Immun* 1994; *62* : 72-8.

41. Johnson JA, Salles CA, Panigrahi P, Albert MJ, Wright AC, Johnson RJ, *et al. Vibrio cholerae* 0139 synonym Bengal is closely related to *Vibrio cholerae* E1Tor but has important differences. *Infect Immun* 1994; *62* : 2108-10.

42. Hall RH, Khambaty FM, Kothary MH, Keasler SD, Tall BD. *Vibrio cholerae* non-01 serogroup associated with cholera gravis genetically and physiologically resembles 01 E1 Tor cholera strains. *Infect Immun* 1994; *62* : 3859-63.

43. Calia KE, Murtagh M, Ferraro MJ, Calderwood SB. Comparison of *Vibrio cholerae* 0139 with *V. cholerae* classical and E1 Tor biotypes. *Infect Immun* 1994; *62* : 156-6.

44. Stroeher, UH, Jedani KE, Dredge BK, Morona R, Brown MH, Karageorgos LE, *et al.* Genetic rearrangements in the rfb regions of *Vibrio cholerae* 01 and 0139. *Proc Natl Acad USA* 1995; *92* : 10374-8.

45. Xiang SH, Hobbs M, Reeves PR. Molecular analysis of the rfb gene cluster of a group D2 *Salmonella enterica* strain: evidence for its origin from an insertion sequence-mediated recombination event between group E and D1 strains. *Bacteriol* 1994; *176* : 4357-65.

46. Comstock LE, Johnson JA, Michalski JM, Morris Jr JG, Kaper JB. Cloning and sequence of a region encoding a subunit polysaccharide of *Vibrio cholerae* 0139 and characteriz

of the insertion site in the chromosome of *Vibrio cholerae* 01. *Mol Microbiol* 1996; *19* : 815-26.

47. Comstock LE, Maneval D Jr, Panigrahi P, Joseph A, Levine MM, Kaper JB, *et al*. The capsule and O antigen in *Vibrio cholerae* 0139 Bengal are associated with a genetic region not present in *Vibrio cholerae* 01. *Infect Immun* 1995; *63* : 317-23.
48. Waldor MK, Colwell R, Mekalanos JJ. The *Vibrio cholerae* 0139 serogroup antigen includes an O-antigen capsule and lipopolysaccharide virulence determinants. *Proc Natl Acad Sci USA* 1994; *91* : 11388-92.
49. Bik EM, Bunschoten AE, Gouw RD, Mooi FR. Genesis of the novel epidemic *Vibrio cholerae* 0139 strain: evidence for horizontal transfer of genes involved in polysaccharide synthesis. *EMBO-J* 1995; *14* : 209-16.
50. Albert MJ. *Vibrio cholerae* 0139 Bengal: probable causative agent of the eighth pandemic of cholera. *Hong Kong J Paediatr* 1995; *6* suppl 1 : 56-62.
51. Colwell RR, Spira WM. The ecology of *Vibrio cholerae* In: Barua D, Greenough WB III, editors. Cholera. New York: Plenum Press, 1992: 107-27.
52. Barua D. History of cholera. In: Barua D, Greenough WB III, editors. Cholera. New York: Plenum Press, 1992: 1-36.
53. Centers for Disease Control. Cholera - Peru, 1991. *MMWR* 1991; *40* : 108-9.

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Eradicating Hepatitis B

Universal immunization makes it possible

Hepatitis B virus (HBV) infection is on the increase in all those countries where immunization is not being effectively provided. In spite of a vaccine being available for more than 12 years, about 200,000 to 300,000 new cases of hepatitis B infection occurred annually in the USA alone.

In Italy, about 400,000 new cases used to occur each year. Because of this high rate of HBV infection, vaccination of hepatitis B was made compulsory in Italy in 1991. The vaccine is administered to neonates and 12 year-old adolescents. In 12 years' time, all Italians under the age of 24 will be immune to HBV.

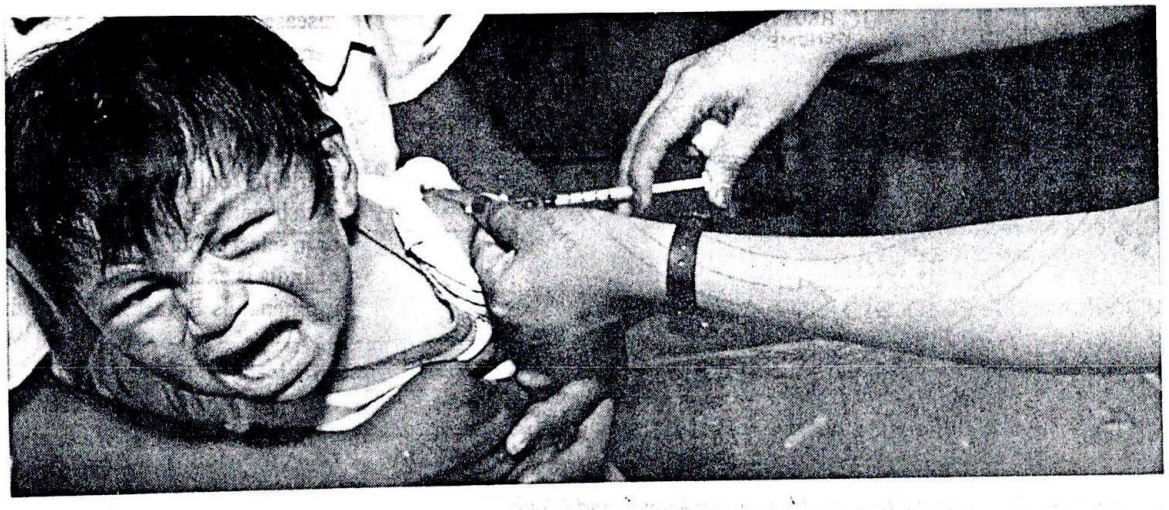
We do not have community-based figures of HBV infection showing the extent of disease or the pevalence rate in this country. A few small-scale surveys have been carried out in different parts of the country by various workers to find out the carrier rate of Hepatitis B surface antigens (HBsAg). These have shown the HBsAg carrier rate being about 10-15% in adults. In children, upto the age of 5 years, it is reported to be 5%.

If the HBV infection occurs during the perinatal period, the carrier rate is extremely high (70-90%), while the symptoms of acute viral hepatitis occur in only 5-10% of neonates. The high risk of developing chronic carrier state in neonates, makes the vaccination a high priority because of the threat of developing serious complications like cirrhosis and hepatocellular carcinoma in them after many years. Hepatitis B vaccine should, therefore, be offered to all babies at birth, if possible.

Gambia, the country with very high infection rate of HBV infection introduced Hepatitis B vaccine in 1986. By 1990, 124,577 children had been carefully identified and recruited into the 35-year longitudinal cohort study; 59,803 of them have received the vaccine. Rest of them (65,774 unvaccinated children) will serve as control. The preliminary studies have demonstrated that the rate of HBV infection has fallen to less than 5% in children who received all 4 doses of Hepatitis B vaccine.

The chronic HBV infection may lead to hepatocellular carcinoma. Vaccination against HBV may prevent not only HBV infection and the development of chronic carrier state but can also prevent the development of hepatocellular carcinoma. In the USA and some other countries, Hepatitis B vaccine was initially given to high-risk groups like health care personnel and patients who required frequent blood transfusions. After 10 years, it was seen that the infection rate did not drop significantly.

In Italy, about 400,000 new cases used to occur each year, and because of this high rate of HBV infection, vaccination of Hepatitis B was made compulsory in Italy in 1991. The vaccine is administered to neonates and 12 year-old adolescents. In 12 years' time, all Italians under the age of 24 will be immune to HBV.

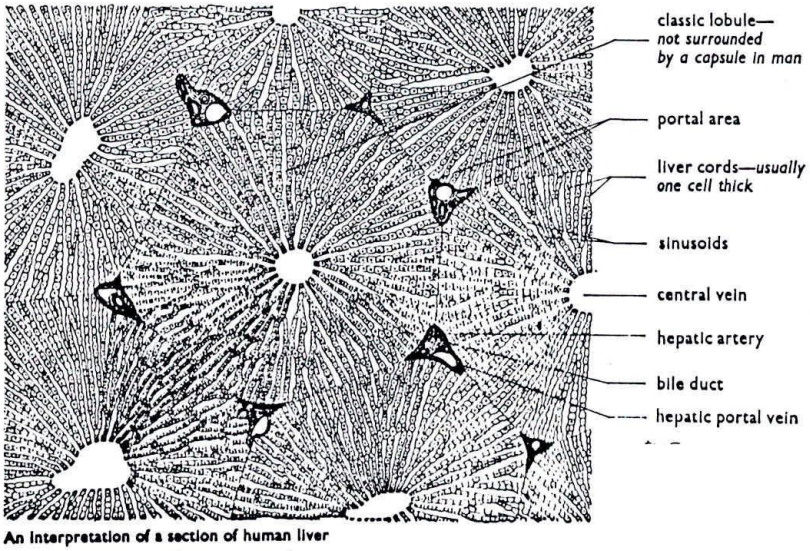


The chronic HBV infection may lead to hepatocellular carcinoma. Therefore, vaccination against HBV may prevent not only HBV infection and the development of chronic carrier state but will also prevent the development of hepatocellular carcinoma.

A number of risk factors are known for HBV infection e.g. inoculation with blood of HBV carriers, reuse of infected needles and sharp instrument without sterilization. However, no risk factor could be identified in 30-40% of cases of acute viral hepatitis with HBV. Hence, if Hepatitis B vaccine is to be given on a selective basis, then many persons will remain unprotected and may acquire HBV infection (asymptomatic or symptomatic) with possibility of some becoming carriers of HBsAg.

Many types of hepatitis B vaccine are available e.g. Engerix B by Smith Kline and Beecham and Hevac B by Meriux (France) and recently a vaccine prepared by MSD has also been marketed. Currently, the cost of these vaccines is very high. A course of three 10 mcg doses for children currently costs about Rs. 600/-. If we recommend it for universal immunization of all neonates (4.5 million babies born annually) the total cost of the vaccine alone would be Rs. 2.4 billion (240 crores). This is not feasible because of the scarcity of available financial resources. But, if the immunization is not offered to all the babies there is a real chance that the fresh infections with HBV will continue to occur and disastrous outcomes will appear with the passage of time. There are two ways by which the objective of providing universal vaccination can be achieved at a lower cost. The first one is to get vaccine at a lower cost by floating world-wide tenders for the vaccine. In Gambia, the vaccine used is of Korean origin costing less than one dollar per dose. One pharmaceutical company in Pakistan claims that the vaccine can be supplied at the rate of 25 rupees per dose provided the Government of Pakistan orders a supply of the vaccine in bulk.

This would bring down the cost of immunization to all neonates born annually to less than Rs. 400 million (40 crore) per year from the total estimated cost of Rs 240 crores, if all newborns are given the vaccine. Secondly, in Singapore, a study was published in 1992. They used four different dosages which were compared for the immunogenicity. It was shown that the reduced dosage of 2.5 micrograms and even 0.6 microgram given intramuscular was as effective as the standard dosage of 5 micrograms. This is very promising observation. If we can also prove that the small dose of 0.6 microgram is as effective as 5 microgram, we can bring down the cost of the vaccine required to immunize all our neonates to about 100 million (10 crore) rupees, which is very much whithin the resources of the government for universal immunization of our neonates.



An interpretation of a section of human liver

Before integrating Hepatitis B vaccine in our EPI health program, we need to conduct more studies to know about the prevalence rate of HBV in the community. It may help us to evolve proper strategy for prevention of the disease. We also need to look into the effectiveness of low dose intra-dermal immunization, which can, in turn, lead to significant financial savings. The possibility of having single multiple vaccines injections is another long-term strategy proposed for providing vaccination against multiple diseases.

All these aspects need further studies in our country so that we could evolve the most feasible and cost-effective method for controlling Hepatitis B by universal immunization against HBV.

(Courtesy: ACASH News April-June 1996)

Many types of hepatitis B vaccine are available e.g. Engerix B by Smith Kline and Beecham and Hevac B by Meriux (France) and recently a vaccine prepared by MSD has also been marketed. Currently, the cost of these vaccines is very high. A course of three 10 mcg doses for children currently costs about Rs. 600/-.

A, B, C, D & E OF HEPATITIS

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Viral hepatitis is one of the major health problems in India. The important causes of viral hepatitis are five well-characterised hepatotrophic viruses namely A, B, C, D and E. Main features of these viruses are summarised in the table below.

MAIN CAUSATIVE AGENTS IN ACUTE VIRAL HEPATITIS

	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis D	Hepatitis E
A_L	Hepatitis A virus, 27nm RNA virus	Hepatitis B virus, 42 nm DNA virus	Hepatitis C virus, RNA virus	Delta Agent 35 nm RNA virus	Hepatitis E virus, 34 nm RNA virus
Antigens	HAAg	HBsAg HBeAg HBcAg HBxAg	-	Delta (D) AG	-
Antibodies	Anti-HAV	Anti-HBc Anti-HBs Anti-HBe Anti-HBx	Anti-HCV	Anti-D	Anti-HEV
Transmission	Faecal-oral	Parenteral	Parenteral	Parenteral	Faecal-oral
Mortality	0.1%	1-3%	1-20%	up to 20%	20% in pregnancy
Chronicity	None	5% (neonate 90%)	6-60%	Acute 2% chronic 70-90%	None
Incubation period	15-45 days	40-180 days	15-50 days	30-50 days	30-50 days

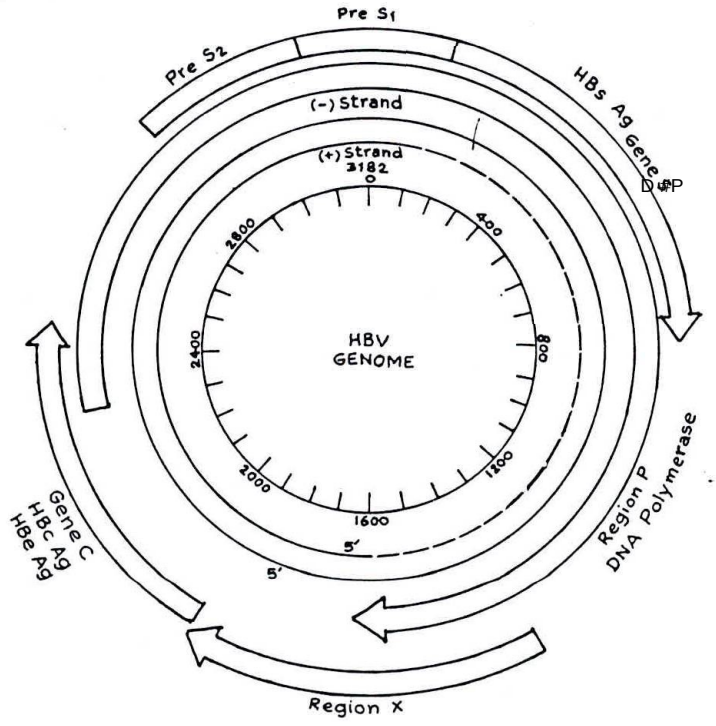
cur. Usually, there is fever (upto 39 degrees C) and chills may be present initially. Loss of appetite is very common, characterized by distaste or aversion to food and tobacco. The smell of food may induce nausea. Abdominal discomfort or pain localized to the upper right side is common. Urine becomes darker and stools might turn light or clay-coloured.

Jaundice phase: The symptoms may progress or remain unchanged, or, in some cases, may actually decrease in severity. With onset of jaundice, most of the symptoms rapidly clear. There may be mild itching all over the body in half the patients and may last only a few days. Dark urine and yellow staining of the white of the eyes become paler, the urine darker and the liver becomes easily palpable. At this time, the appetite often improves, and other symptoms gradually improve. Thereafter, jaundice gradually recedes, the stools and urine regain their normal colour, the liver regresses and in the course of 3-6 weeks the great majority of cases recover.

Table

Stage of infection	HBsAg	anti-HBs	anti-HBc IgG	anti-HBc IgM	HBeAg	anti-HBe
Late incubation	+	-	-	-	+/-	-
Acute hepatitis	+	-	+	+	+	-
Carrier	+	-	+++	+/-	-	+
Chronic Hep B	+	-	+++	+/-	+	-
Inf recent past	-	++	++	+/-	-	+
Inf distant past	-	+/-	-	-	-	-
Vaccination	-	++	-	-	-	-

As there is no effective therapy for treating chronic carrier state, control of the disease will probably depend on the prevention of transmission by immunization of the susceptible population at risk.



Schematic diagram of the hepatitis B virus

Drawings : source — Textbook of Clinical Medicine by Kumar and Clark

Course of infection

The acute infection may be followed by a persistent carrier state, the duration of which varies greatly depending upon the age, sex and immune response. Chronic carriage of HBV is associated with progression to chronic active hepatitis, cirrhosis, and finally hepatocellular carcinoma. The risk of chronic infection is believed to be highest (70-90%) for infants who acquire the infection during the perinatal period, lower (20-50%) for children younger than 5 years, and lowest (5-10%) of older children. Similarly,the risk of cirrhosis or HCC is related to the length of time that a person has chronic infection. Infants who become chronically infected have an estimated 25% life-time risk of cirrhosis or HCC. In comparison, adults who acquire the chronic HBV infection have an estimated 15% life-time risk.

Diagnosis

Provisional diagnosis is usually made on the basis of the characteristic clinical picture. Liver function tests, and serological tests for hepatitis B markers confirm the diagnosis. (The table given below summarizes the interpretation of results of serological tests for hepatitis B).

As there is no effective therapy for treating chronic carrier state, control of the disease will probably depend on the prevention of transmission by immunization of the susceptible population at risk. Availability of safe and effective vaccines has prompted several countries of the world to routinely immunize all infants with hepatitis B vaccine either nationally or in select populations. The Government of India is examining the issue of including hepatitis B vaccination in the childhood.

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ROTARY CLUB OF BANGALORE CENTRAL

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KNOW MORE ABOUT HEPATITIS

By Dr.NARESH BHAT
Consultant Gastro-enterologist
Bangalore Hospital

THE AIM OF ROTARY IS HEPATITIS – B VIRUS FREE INDIA IN FEW YEARS THROUGH INTENSIVE VACCINATION DRIVES

SEMINAR ON HEPATITIS 'B'

on Sunday 18th April 1999

Inaugurated by

Dr.H.C.Mahadevappa
Hon'ble Minister for Health and Family Welfare,
Government of Karnataka.

Rtn.Ramji Narsimhan
Governor Nominee 1999-2000 R.I.Dist – 3190
Chief Guest

Panel

Dr.Naresh Bhat (Moderator)
Consultant Gastro-enterologist
Bangalore Hospital

Dr.K.N.Shetty
Consultant Gastro-enterologist
Mainpal Hospital

Dr.Ravi Kottor
Head of Gastro-enterologist Dept.
St.Johns Hospital

Dr.Shivananda
Head of Pedeatric Dept.
Vanivilas Hospital

Dr.Dara S. Amar
Head of Dept. of Community Health and Vice Principal
St.Johns Medical College

How is the infection spread?

Hepatitis A and E viruses are excreted or shed in feces. Direct contact with an infected person's feces or indirect fecal contamination of food, the water supply, raw shellfish, hands and utensils may result in sufficient amounts of virus entering the mouth to cause infections.

Hepatitis B is spread from mother-to-child at birth or soon after birth, through sexual contact, blood transfusions or contaminated needles. Almost a quarter of sources in the general population. In families the virus can be spread from adults to children.

Transmission of viral Hepatitis

	A	B	C	D	E
Food Borne	***				$$$
Water Borne	***				***
Mollusk-Related	***				$$$
Infra-family	***	***	$$$	***	***
Infra-institutional	***	***			
Inoculation		***	***	***	
Transfusion	###	***	***	***	
Hemodialysis		***	***	$$$	
Oral	***	***	$$$	$$$	***
Sexual	$$$	***	$$$	***	
Maternal-neonatal		***	$$$	***	

Confirmed transmission	***
Rarely transmitted	###
Suspected but not proven	$$$

Hepatitis C is spread directly from one person to another via blood or needles. While sexual transmission and mother-to-child spread may occur, the transmission of this disease is not clearly understood.

Hepatitis D is spread mainly by needles and blood. Hepatitis D infects only individuals infected with hepatitis B and may be transmitted by carriers of hepatitis D and B.

What are the symptoms of viral hepatitis?

The most common symptoms are fatigue mild fever, muscle or joint aches, nausea, vomiting, loss of appetite, vague abdominal pain, and sometimes diarrhea.

Many cases go undiagnosed because the symptoms are suggestive of a flu-like illness or may be very mild or absent.

Minorities of patients notice dark urine and light colored stools, followed by jaundice in which the skin and whites of the eyes appear yellow. Itching of the skin may be present. With the onset of jaundice, other symptoms tend to subside. Some people may lose 5 to 10 pounds during the illness.

Do you always turn yellow when you have hepatitis?

No, most individuals with viral hepatitis do not develop jaundice.

Can I get hepatitis again?

Yes, because there are five or more hepatitis viruses, you can acquire different ones at different times. You will not be infected by the same virus as each produces its own immunity after the virus disappears. However, sometimes the viruses of B, C and D hepatitis remain in the body forever. They can cause flare-ups of hepatitis that look like new disease.

What is a carrier and how can I tell if I am one?

A carrier is a person who has hepatitis B, C or D in his or her blood even after all symptoms (except fatigue) have disappeared. Because the virus is present in the blood, it can be transmitted to others. Hepatitis A does not have a carrier state. The hepatitis B carrier can be recognized by a simple and specific blood test. Some of the carriers are contagious and others are not; this too can be determined by a simple blood test. A test for the hepatitis C carrier is being developed but is not yet available. Prior to transfusion, all blood is now tested for abnormality of the liver function and for the hepatitis B virus. These tests have reduced the rate of the post-transfusion hepatitis C by about 50%. Blood banks notify donors if they have found such abnormalities. Hepatitis D can be detected by a simple blood test for antibody to the virus and by a positive test for hepatitis B; both must be positive to be sure that the hepatitis D virus is present. Testing for hepatitis E is being developed but is not yet available.

If I am pregnant and develop hepatitis, is there a risk for my baby?

Hepatitis does not increase the risk of still births and malformations. Miscarriages, however, occur more frequently and conception may be more difficult in those with chronic hepatitis.

When hepatitis B occurs during pregnancy of a mother who is a carrier of the virus, the chances are very high that the baby will become infected at birth. Infection of the baby in the uterus is rare. Most of the infected babies become carriers. A few become very sick and some seem to escape infection. All pregnant women should be tested for hepatitis B so that the infants of those who test positive can be immunized at birth. Some of the countries with a high incidence of hepatitis B carriers are beginning to vaccinate all newborn babies.

Viral hepatitis tends to run its course and is no more severe than in the non-pregnant individuals as long as the pregnant woman is receiving good prenatal care. However, hepatitis E does have an unexplained high mortality rate during pregnancy. When jaundice occurs with viral hepatitis, especially in the last half of pregnancy, it may persist with itching until after delivery.

What should I do if I have been exposed to or suspect that I have hepatitis ?

Consult your physician who will examine you and order blood tests to confirm the diagnosis, identify the specific type of hepatitis and advise you about diet and activity. Your contacts should be notified about your infection and the needs for gamma (immune) globulin and vaccination.

Should I see a specialist if I have hepatitis ?

Most physicians can care for a patient with an ordinary case of viral hepatitis. However, referral to a specialist in disease of the liver (hepatologist, gastreneterologist) may be necessary if the disease appears to be unusually severe or complications are recognized.

Is hospitalization necessary ?

In most cases, no. Some patients are hospitalized if neither liquids nor food can be tolerated or if the disease is unusually severe or complications arise.

Are there medications for viral hepatitis ?

No medicine now available alters the course of acute viral hepatitis. Prevention is the only effective treatment. Several antiviral drugs are being tested and studies are underway to determine whether interferon, a natural substances in the human body but now synthetically produced, will rid the chronically infected patient of hepatitis B and C viruses. Whether interferon has any role in acute hepatitis has yet to be determined.

If I take medicine for other purposes, can I continue to do so ?

Medications taken regularly should be reviewed by a physician and a decision made regarding their continuation. Because the liver plays a key role in processing drugs and this function may be impaired in the patient with hepatitis, medications are usually withheld unless they are essential for the treatment of other problems.

Can I take birth control pills if I have hepatitis ?

Although the pill itself occasionally produces abnormalities in the liver, continuation during and after viral hepatitis appears to be harmless. However, if jaundice with itching is present, the pill should be discontinued until the symptoms disappear.

Can I exercise while I have hepatitis?

Vigorous exercise during the acute stage of the disease should be discouraged. Light or moderate exercise may be undertaken as symptoms subside .

Must I stay in bed ?

Restriction to bed is not necessary for patients with viral hepatitis. A good general rule is "if you fell well , get up , but if you do not , take it easy"

How great is the risk of hepatitis to me and my family ?

Spread within the family can occur with hepatitis A, B or E. Prompt diagnosis and appropriate precautions with gamma globulin or vaccination are important for those who are exposed.

Do I need a special diet or vitamins ?

A nutritious, well balanced diet with additional calorie-rich fluids (soft drinks, fruit juices) is normally sufficient during the illness. Since many patients describe a reduction in appetite and an increase in nausea as the day progresses, a hearty breakfast is often the best tolerated meal of the day. Multiple small snacks between meals are encouraged if large meals cause problems. Vitamin supplements have no clear value if a balanced diet can be eaten.

Must I give up alcohol ?

All alcoholic beverages should be avoided during the acute phase of the disease since metabolism of the alcohol stresses the already sick liver.
(Modest alcohol consumption later in the convalescent phase or after recovery is not harmful).

Should I avoid sexual activity ?

Sexual activity does not seem to affect the disease or recovery. However, your partner may be at risk of acquiring the infection, especially of hepatitis B.

Do dishes and clothing of the patient need special care ?

Hot water and soap or detergent is sufficient for cleaning dishes or clothing of patients with hepatitis A or E. Special care must be taken if anything has blood on it when the patient has hepatitis B or C. Dishes, utensils and clothing do not harbor the hepatitis B or C virus.

Can I prepare meals ?

If you have hepatitis A or E, you should not prepare meals or handle food to be eaten by others. However, you were especially contagious before the symptoms of hepatitis were recognized and you may have already transmitted the infection of exposed others unknowingly.

If you have hepatitis B,C or D, limitations on food handling are not necessary.

How long does the illness last ?

The onset if often abrupt and recovery occurs in a few weeks to a month or two. The contagious period lasts 2 to 3 weeks. With hepatitis B, the onset is more gradual and the course is longer. Over 80 % of patients recover within 6 months, another 10 % after 2 years, while 5 to 10 % either develop chronic hepatitis or become carriers. The onset of hepatitis C is often not recognized and the disease becomes apparent months to years after infection. More than half of the patients who are infected by blood transfusions will develop chronic hepatitis with fluctuating symptoms and laboratory test results. Hepatitis D coinfection with hepatitis B but recovery after a few months is usual. Hepatitis D concurrent infection in a hepatitis B carrier looks like a flare-up of hepatitis B and symptoms may become lifelong. The symptoms of hepatitis E are like those of hepatitis A, although the period of illness may be as long as several months.

How long should I continue to see a doctor ?

You should continue to see your doctor until blood tests indicate the illness is clearly over. Abnormalities in the blood tests that persist beyond six months must be carefully evaluated since they may indicate the development of chronic infections.

What are the complications of hepatitis ?

Fortunately, most people recover completely from hepatitis A,B,D and E. Mild flare-ups may occur over a period of several months. Each flare-up is usually less severe than the initial attack and a relapse does not necessarily indicate that complete recovery will not take place.

About 1 patient in 1000 dies of hepatitis A, 1 in 100 of acute hepatitis B and somewhere in between for hepatitis C. The mortality rate of hepatitis D and B is higher than for hepatitis B alone. Not enough is yet known of hepatitis E.

About 5% of patients with hepatitis B and more than 50 % of patients with hepatitis C develop chronic liver disease which may be mild and slowly progressive, or may be serious and rapidly lead to cirrhosis. The terms "chronic persistent" and "chronic aggressive " have been used for these two varieties, but we now know that the degree of activity varies with time and in different places in the liver at the same time. Cirrhosis is the final state of scarring which develops in chronic hepatitis. To determine how much scarring is present or how rapidly it may be progressing, a liver biopsy is usually necessary. Predicting who will develop chronic liver disease is not possible at the time of acute hepatitis. Identification or those at risk and methods to prevent these consequences are the subjects of ongoing research.

How can the spread of hepatitis be prevented ?

Adequate sanitation and good personal hygiene will reduce the spread of hepatitis A and E. Water should be boiled prior to its use if any question of safety exists. Similarly, in areas where sanitation is questionable, food should be cooked well and Fruits peeled. Washing hands, cleaning utensils, bedding and clothing with soap and Water is necessary for those involved in treating patients, especially in the first couple of weeks of illness. Those planning to travel to areas where hepatitis A is widespread are advised to take immune globulin before leaving. Its protection is widespread are advised to take immune globulin before leaving. Its protection is effective 3-4 months. To prevent spread of hepatitis B, avoid exposure to infectious blood or body fluids. Do not have intimate contact, share razors, scissors, nail files, toothbrushes or needles. If any risk is present, you should receive immune globulin and vaccine as soon as possible.
Blood banks are hard at work to insure the safety of the blood supply. Hepatitis B from transfusion has been largely prevented and hepatitis C has been reduced, with prospects of even further reduction soon. Sharing needles with anyone should be avoided. Dentists, doctors, nurses, laboratory technicians and others who may draw blood, perform surgical procedures or handle sharp instruments used on hepatitis patients or carries must be informed so that adequate precautions can be taken.

Family members and others intimate contacts must be advised to seek medical advice about immune globulin shots or vaccination.

Are there vaccines and can the disease be prevented ?

A vaccine for hepatitis A is currently under development but it will be many years before testing in humans begins. Several vaccines are being tested, but none is yet available.

Several vaccines are available to prevent hepatitis B. they are all safe and effective and they seem to prevent infection if started within a few days of exposure. The usual vaccination schedule used in the united state is two injections a month apart followed by a third injection 6 months after the first one. Hepatitis B immune globulin may also prevent infection after exposure but it must be given within 48 hours to be useful. Since both vaccination and immune globulin are expensive, rapid confirmation of the diagnosis of hepatitis B is needed. Hepatitis D is prevented by preventing hepatitis B. No vaccine or immune globulin is yet available for hepatitis C or E.

Does hepatitis cause cancer ?

A high incidence of liver cancer is found in some African and Asian countries where there are many hepatitis B carriers and appears to be related to the chronic hepatitis B carrier state. Research on this relationship is being actively pursued.

The number of causes of liver cancer in patients with chronic hepatitis C is increasing, but whether the cancer rate will ever be as with hepatitis B is unknown. About 15% of hepatitis B carrier in the orient are at risk of developing liver cancer, but the rate seems to be considerably less in the United States .

X not to be enclosed

INDICATIONS AND USAGE ✓

Engerix-B is indicated for immunization against infection caused by all known subtypes of hepatitis B virus. As hepatitis D (caused by the delta virus) does not occur in the absence of hepatitis B infection, it can be expected that hepatitis D will also be prevented by *Engerix-B* vaccination.

Engerix-B will not prevent hepatitis caused by other agents, such as hepatitis A virus, non-A/non-B hepatitis viruses, or other pathogens known to infect the liver.

Immunization is recommended in persons of all ages, especially those who are, or will be, at increased risk of exposure to hepatitis B virus,[1] for example:

Health Care Personnel

Dentists and oral surgeons.

Dental, medical and nursing students.

Physicians, surgeons and podiatrists.

Nurses.

Paramedical and ambulance personnel and custodial staff who may be exposed to the virus via blood or other patient specimens.

Dental hygienists and dental nurses.

Laboratory and blood-bank personnel handling blood, blood products, and other patient specimens.

Hospital cleaning staff who handle waste.

Selected Patients and Patient Contacts

Patients and staff in hemodialysis units and hematology/oncology units.

Patients requiring frequent and/or large volume blood transfusions or clotting factor concentrates (e.g., persons with hemophilia, thalassemia, sickle-cell anemia, cirrhosis).

Clients (residents) and staff of institutions for the mentally handicapped.

Classroom contacts of deinstitutionalized mentally handicapped persons who have persistent hepatitis B surface antigenemia and who show aggressive behavior.

Household and other intimate contacts of persons with persistent hepatitis B surface antigenemia.

Continued on next page

SmithKline Beecham—Cont.

Infants Born of HBsAg-Positive Mothers Whether HBeAg Positive or Negative (See DOSAGE AND ADMINISTRATION.)
Subpopulations with a Known High Incidence of the Disease, such as:
Alaskan Eskimos.
Indochinese immigrants.
Haitian immigrants.
Persons Who May Be Exposed to the Hepatitis B Virus by Travel to High-Risk Areas (See ACIP Guidelines, 1985.)
Military Personnel Identified as Being at Increased Risk
Morticians and Embalmers
Persons at Increased Risk of the Disease Due to Their Sexual Practices, such as:
Persons with more than one sexual partner in a six-month period.
Persons who have contracted a sexually transmitted disease.
Homosexually active males.
Female prostitutes.
Prisoners
Users of Illicit Injectable Drugs
Others:
Police and fire department personnel who render first aid or medical assistance, and any others who, through their work or personal life-style, may be exposed to the hepatitis B virus.
Adoptees from countries of high HBV endemicity.

CONTRAINDICATIONS

Hypersensitivity to yeast or any other component of the vaccine is a contraindication for use of the vaccine.

WARNINGS

Patients experiencing hypersensitivity after an Engerix-B [Hepatitis B Vaccine (Recombinant)] injection should not receive further injections of *Engerix-B*. (See CONTRAINDICATIONS.)
Hepatitis B has a long incubation period. Hepatitis B vaccination may not prevent hepatitis B infection in individuals who had an unrecognized hepatitis B infection at the time of vaccine administration. Additionally, it may not prevent infection in individuals who do not achieve protective antibody titers.

PRECAUTIONS

General
As with any percutaneous vaccine, epinephrine should be available for use in case of anaphylaxis or anaphylactoid reaction.
As with any vaccine, administration of *Engerix-B* should be delayed, if possible, in persons with any febrile illness or active infection.
Pregnancy
Pregnancy Category C: Animal reproduction studies have not been conducted with *Engerix-B*. It is also not known whether *Engerix-B* can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. *Engerix-B* should be given to a pregnant woman only if clearly needed.
Nursing Mothers
It is not known whether *Engerix-B* is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when *Engerix-B* is administered to a nursing woman.
Pediatric Use
Engerix-B has been shown to be well tolerated and highly immunogenic in infants and children of all ages. Newborns also respond well; maternally transferred antibodies do not interfere with the active immune response to the vaccine. (See CLINICAL PHARMACOLOGY for seroconversion rates and titers in neonates and children. See DOSAGE AND ADMINISTRATION for recommended pediatric dosage and for recommended dosage for infants born of HBsAg-positive mothers.)

ADVERSE REACTIONS

Engerix-B [Hepatitis B Vaccine (Recombinant)] is generally well tolerated. During clinical studies involving over 10,000 individuals distributed over all age groups, no serious adverse reactions attributable to vaccine administration were reported. As with any vaccine, however, it is possible that expanded commercial use of the vaccine could reveal rare adverse reactions not observed in clinical studies.
Ten double-blind studies involving 2,252 subjects showed no significant difference in the frequency or severity of adverse experiences between *Engerix-B* and plasma-derived vaccines. In 36 clinical studies a total of 13,495 doses of *Engerix-B* were administered to 5,071 healthy adults and children who were initially seronegative for hepatitis B

adverse reactions were injection site soreness (22%) and fatigue‡ (14%). Other reactions are listed below.

Incidence 1% to 10% of Injections

Local reactions at injection site: Induration; erythema; swelling.
Body as a whole: Fever (> 37.5°C).
Nervous system: Headache‡; dizziness.‡
‡ Parent or guardian completed forms for children and neonates. Neonatal checklist did not include headache, fatigue or dizziness.

Incidence < 1% of Injections

Local reactions at injection site: Pain; pruritus; ecchymosis.
Body as a whole: Sweating; malaise; chills; weakness; flushing; tingling.
Cardiovascular system: Hypotension.
Respiratory system: Influenza-like symptoms; upper respiratory tract illnesses.
Gastrointestinal system: Nausea; anorexia; abdominal pain/cramps; vomiting; constipation; diarrhea.
Lymphatic system: Lymphadenopathy.
Musculoskeletal system: Pain/stiffness in arm, shoulder or neck; arthralgia; myalgia; back pain.
Skin and appendages: Rash; urticaria; petechiae; pruritus; erythema.
Nervous system: Somnolence; insomnia; irritability; agitation.
Additional adverse experiences have been reported with the commercial use of *Engerix-B*. Those listed below are to serve as alerting information to physicians.
Hypersensitivity: Anaphylaxis; erythema multiforme including Stevens-Johnson syndrome; angioedema; arthritis.
Cardiovascular system: Tachycardia/palpitations.
Respiratory system: Bronchospasm including asthma-like symptoms.
Gastrointestinal system: Abnormal liver function tests.
Nervous system: Migraine; syncope; paresis; neuropathy including hypoesthesia, paresthesia, Guillain-Barré syndrome and Bell's palsy, transverse myelitis.
Hematologic: Thrombocytopenia.
Skin and appendages: Eczema; purpura; herpes zoster.
Special senses: Vertigo; conjunctivitis; keratitis; visual disturbances.
Potential Adverse Experiences: In addition, certain other adverse experiences not observed with *Engerix-B* have been reported with Heptavax-B®† and/or *Recombivax HB*. Those listed below are to serve as alerting information to physicians:
Nervous system: Optic neuritis.

DOSAGE AND ADMINISTRATION

Injection: Engerix-B should be administered by intramuscular injection. *Do not inject intravenously or intradermally.* In adults, the injection should be given in the deltoid region but it may be preferable to inject in the anterolateral thigh in neonates and infants, who have smaller deltoid muscles. *Engerix-B* should not be administered in the gluteal region; such injections may result in suboptimal response.
Engerix-B may be administered subcutaneously to persons at risk of hemorrhage (e.g., hemophiliacs). However, hepatitis B vaccines administered subcutaneously are known to result in lower GMTs. Additionally, when other aluminum-adsorbed vaccines have been administered subcutaneously, an increased incidence of local reactions including subcutaneous nodules has been observed. Therefore, subcutaneous administration should be used only in persons who are at risk of hemorrhage with intramuscular injections.
Preparation for Administration: Shake well before withdrawal and use. Parenteral drug products should be inspected visually for particulate matter or discoloration prior to administration. With thorough agitation, *Engerix-B* is a slightly opaque white suspension. Discard if it appears otherwise.
The vaccine should be used as supplied; no dilution or reconstitution is necessary. The full recommended dose of the vaccine should be used.
Dosing Schedules: The usual immunization regimen consists of 3 doses of vaccine given according to the following schedule:
1st dose: at elected date
2nd dose: 1 month later
3rd dose: 6 months after first dose
There is an alternate schedule with injections at 0, 1 and 2 months designed for certain populations (e.g., neonates born of hepatitis B infected mothers, others who have or might have been recently exposed to the virus, certain travelers to high-risk areas. See INDICATIONS AND USAGE.). On this alternate schedule, an additional dose at 12 months is recommended for infants born of infected mothers and for others for whom prolonged maintenance of protective titers is desired.
dosage for neonates through children up to, and including, 10 years: 10 mcg administered on either schedule.

Consult 1992 Supplements for revisions

For hemodialysis patients, in whom vaccine-induced protection is less complete and may persist only as long as antibody levels remain above 10 mIU/mL, the need for booster doses should be assessed by annual antibody testing. 40 mcg (two × 20 mcg) booster doses with *Engerix-B* should be given when antibody levels decline below 10 mIU/mL.[1] Data show individuals given a booster with *Engerix-B* achieve high antibody titers. (See CLINICAL PHARMACOLOGY.)

booster vaccinations: Whenever administration of a booster dose is appropriate, the dose of *Engerix-B* is 10 mcg for children 10 years of age and under; 20 mcg for other children and adults. Studies have demonstrated a substantial increase in antibody titers after *Engerix-B* booster vaccination following an initial course with both plasma- and yeast-derived vaccines. (See CLINICAL PHARMACOLOGY.)

See previous section for discussion on booster vaccination for adult hemodialysis patients.

STORAGE

Store between 2° and 8°C (35.6° to 46.6°F). *Do not freeze;* discard if product has been frozen.

Do not dilute to administer.

HOW SUPPLIED

20 mcg/mL in Single-Dose Vials in packages of 1, 10 and 25 vials.

NDC 58160-860-01 (package of 1)
NDC 58160-860-11 (package of 10)
NDC 58160-860-16 (package of 25)

10 mcg/0.5 mL in Single-Dose Vials in packages of 1 vial

NDC 58160-859-01 (package of 1)

HEPATITIS B VAC('E

HB IMMUNISATION, PRIMARY AND BOOSTER

- **Primary Immunisation**
  either 3 doses : Birth, 6 weeks and 6-12 months
  or 4 doses : Birth, 6, 10 weeks and 12 months
  or 4 doses : 6,10,14 weeks and 12 months
- **Booster Immunisation**
  1 dose : 10 years

In India, some 3-7% of persons, from school age upwards, are found to be chronic carriers of Hepatitis B virus (HBV). In their blood, Hepatitis B surface antigen (HBsAg) test is positive. Infection with HBV may occur perinatally (vertical transmission), during early childhood (usually intrafamilial spread), through sexual contact, or nosocomially. The younger the age of infection, the higher the chance of becoming chronically infected as a carrier. Children usually do not get acute icteric hepatitis with HBV infection. Therefore, paediatricians do not see the consequences of the prevalence of HBV infection. HBV is the major cause of chronic hepatitis, cirrhosis of liver and hepatocellular carcinoma. These are all preventable by early childhood immunisation.

The World Health Organisation recommends either the plasma-derived or the genetically engineered HB vaccine. The plasma-derived HB vaccine is safe and free from all known blood-borne viruses. However, in spite of purification procedures, some human serum proteins are intimately attached to the HBsAg particles. The yeast derived HBsAg particles do not contain any such additional proteins and is a purer product.

As an adjuvanted vaccine, it should not be frozen. If frozen accidentally, the vaccine should be discarded. It should be injected intramuscularly, avoiding the gluteal region since it has been shown to be sometimes less immunogenic at this site. It is believed that the microgram dose of HBsAg might be deposited within the fat tissue, thereby reducing its bioavailability to antigen-presenting cells.

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We have inadequate data regarding the n of booster doses. Many believe that the primary 3 dose or 4 dose schedule is sufficient for protection against Hepatitis B disease, as well as against the development of HBsAg carrier state if infected with HBV, for the entire childhood and adolescence period. However, such vaccinees may become susceptible to silent HBV infections which can be detected by the development of antibodies to HBV core antigen (Anti HBc).

The IAP has recommended one booster dose of HB vaccine at 10 years of age in order to boost the antibody levels and hence the degree of protection during adult age, especially the sexually active age. Earlier, a booster had been suggested even at 5 years of age: this is considered to be unnecessary.

RUBELLA AND MUMPS VACCINES

- **Live attenuated Rubella vaccine, developed by Weller, 1962**
- **Live attenuated Mumps vaccine, developed by Hilleman, 1966**
- **Supplied as Rubella(R), Mumps-Rubella (MR) or Measles-Mumps-Rubella (MMR) vaccines**
- **IAP recommends Rubella and Mumps immunisation**

PREVENTION OF CONGENITAL RUBELLA

- **Selective Rubella immunisation of adolescent girls**
- **Selective Rubella immunisation of pre-school and adolescent girls**
- **Universal immunisation of pre-school boys and girls**
- **Combination of the above.**

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- **Inject IM; give at o**
- **Dose 0.5ml SC**

HB Vac - Product Monograph - Cadila

Hepatitis B (your Questions Answered - Smithkline Beecham

Hepatitis B - An Overview

Hepatitis B - The Taiwan Experience - Dr. S D Lee, Dr. S K Mellal

Advance in Herpesviruses.

Engerix - B

Qual India Novimm - Shanvac - B.

A Board of Experience in Hepatitis B. Protection

Facts you need to know about Hepatitis B

Interim Result - Clinical study of Shanvac B in Neonates

Solution to a silent killer.

Immunogenicity of Shanvac - B (Recombinant DNA Hepatitis B Vaccine) in infants

Clinical Spectrum of Hepatitis B. (13 pages)

Hepatitis B in India problems & Precautions

Hepatitis vaccines in India. *Wh*

Dr HARSHAD DEVARBHAVI

JAUNDICE is a yellowish discoloration of skin and mucus membranes. It is not a disease but a symptom or sign of several liver diseases. The commonest cause of jaundice in all age groups except new-borns (where it is normal) is viral hepatitis. The common viruses causing hepatitis (or inflammation of the liver) leading to jaundice are hepatitis A, B, C, D, E and G. Hepatitis A & E are transmitted through contaminated food and water; while B & C are transmitted through contact with infected blood or body fluids. Hepatitis D occurs in persons who already are infected with hepatitis B (HB). A clear role for Hepatitis G is yet to be determined.

Hepatitis A & E viruses cause diseases which are self-limiting and need no specific treatment. Most cases of hepatitis B recover without treatment and the long term problem only depends upon the age of the person contracting the virus. A new born who contracts the B virus from the mother has a 60-90 % chance of developing chronic hepatitis whereas older children and adults have only a 5 % chance of developing chronic hepatitis. In India, approximately 5 % of the population carry this virus in their body and yet most remain without symptoms, not even jaundice. A fourth of these carriers of B virus develop end stage liver disease like cirrhosis and liver cancer after 10-20 years.

Hepatitis B is transmitted through contact with infected blood or blood products, saliva, semen and vaginal fluids. Hence it can be transmitted through sexual activity, both heterosexual and homosexual. It can also be transmitted through tatooing, ear piercing, through shared razors and toothbrushes. The blood of a person with hepatitis B is 1000 times more infectious than a person with HIV/AIDS. However, unlike AIDS, hepatitis B can be prevented by vaccination. And it is this vaccine that is currently the subject of much debate.

There are two types of vaccines available - a) plasma derived and b) genetically engineered recombinant DNA vaccine. Both the vaccines have shown to be equally efficacious and safe. The aim of vaccination is to create protective HBS antibodies rapidly which perhaps last a life time. Three injections at 0, 1 & 6 months are sufficient in most people. While a protective efficacy of 95% is being claimed by most vaccines, in reality recent studies in India show the efficacy is less. The causes for this reduced efficacy vary from genetic factors, faulty vaccine storage, decreased efficacy in older age, gender, obesity and smoking, to wrong site of injection (buttock instead of deltoid).

There is no doubt that universal vaccination against HBV infection is essential to break the long-standing cycle of mother-to-infant transmission. The World Health Organization (WHO) recommended in 1992 that all countries should introduce universal hepatitis B vaccination into their immunization schedules by December 1997. Over 80 countries have complied with the recommendation. Based on this, the Indian Academy of Paediatrics (IAP) has recommended hepatitis B vaccine to newborns. However a number of political and economic factors will influence the rate at which this new vaccination will be incorporated into the vaccine schedule by the Government.

In some countries, HB vaccine is offered to select risk populations only. This approach did not decrease the incidence of B in the population. In fact in the US, the incidence went up. Against this back drop, HB vaccination is given to all new borns in the USA.

However, there are no guidelines regarding vaccinating adults randomly as is happening in the mushrooming camps. A proper quantity of vaccine, at the proper place (arm) and at proper regular intervals need to be stressed upon. While the vaccine efficacy in producing effective antibodies is around 95 per cent in the population, the reality in India is different.

In two studies last year in young medical personnel, only 84-85 % of them developed adequate antibodies. A vaccine failure rate of 15 % is high. Hence all brands of HB vaccine should undergo frequent assessment of the potency of the vaccine when exposed to "field conditions."

Unless this is done there will be a large number of "silent" vaccine failures and the limitations of such programmes will only come to light in the next century. To optimize immunogenecity, vaccine manufacturers should be aware of variation in temperature, humidity, air velocity and atmospheric pressure, which are likely to be encountered during field usage of HB vaccine.

Since the potency of HBV vaccine can only be tested after innoculation in human subjects, all vaccinees after one month from the 3rd dose should get their blood tested for estimation of adequate antibody. This way, one can have an objective assessment of the potency of the vaccine. Undoubtedly our aim is the worldwide eradication of hepatitis B virus. But it should be done in a proper way.

The author is with St John's Medical College.

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How serious is Hepatitis

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A vaccine programme for Hepatitis B

Hepatitis B is a global health problem that affects adults and children alike. As the vaccines are costly, the government should come forward to introduce mass immunisation programmes that work out cheaper.

HEPATITIS B virus (HBV) infection is a major global public health problem. Though this virus is commonly recognised as one of the many causes of jaundice, medically called as "hepatitis", most of us are not aware that it also causes more sinister and delayed health problems. A short lasting attack of hepatitis may frighten a patient but is usually only a minor illness which does not leave behind any scar on the liver or the human body.

Thus, contrary to popular belief that jaundice due to hepatitis B virus is a dangerous illness, a large majority i.e. 95 per cent of such adult patients recover completely in a matter of a few weeks and in fact are rendered immune for life to this infection. We wish to focus our attention in this article at making people aware of the long-term effects of this infection.

The virus may attack either adults or children. Adults develop hepatitis and follow the course outlined above. On the other hand, when it infects children, 90 per cent of them (as opposed to only about five per cent of adults) develop a low grade and unapparent infection which persists for many years, at times throughout life; such persons may be apparently healthy. But they are at a high risk of developing liver cirrhosis and liver cancer, both very serious illnesses. Further, these diseases occur in the prime of youth and cost the society heavily in the form of loss of manpower and expenditure on medical care. It has been estimated that nearly 30 per cent of hepatitis B carriers ultimately die entirely due to complications of this infection.

Why should we in India worry about a disease that occurs world-wide? This is because of the nearly 350 million hepatitis B carriers all over the globe, nearly 40 million are in India. It can be estimated that nearly 200,000 persons in India die every year of HBV infection.

The figures should make every Indian sit up and think how exactly does this infection spread and how it can be prevented. Most educated people are fully aware that transfusion of blood or blood products may cause this infection. Doctors, nurses and other hospital staff may get infected with this virus through close contact with secretions of patients infected with this virus and pricks from used needles.

Similarly, use of needles that are not sterilised can transmit infection from one patient to another. What however, is not common knowledge

HEALTHWATCH

even among medical persons is that numerically far more persons get infected in early childhood through contact either with infected mother, siblings or playmates, as also from an injection. In fact, the carrier pool is maintained more by infection at a young age than that during adulthood since as previously mentioned, the later infections hardly ever lead to carrier state.

If hepatitis B is such a serious infection and we know how it is caused, a common question is why can not we prevent it. It was not possible to answer this question a decade ago. The answer today is an emphatic "yes" because of development of hepatitis B vaccines in the early 1980s.

These vaccines are by far the safest and the most effective. To make the maximum impact, these vaccines should be administered in early infancy along with other childhood vaccines like those against tuberculosis, diphtheria, whooping cough, tetanus, polio and measles. Introduction of hepatitis B vaccine programme has been shown to convincingly reduce the number of HBV carriers in many countries where this infection was extremely common. In fact, like most infective diseases for hepatitis B too, immunisation of children is the most effective preventive strategy. It has been estimated that a rupee spent on vaccination against childhood infections will save Rs. 10 in cost of medical care; for a disease like hepatitis B which causes delayed and prolonged illness in adulthood, the relative advantage would be much larger.

Impressed with the cost-effectiveness of hepatitis B vaccine, over 80 countries have already introduced HBV immunisation programmes covering their entire population and several others have either initiated or are planning programmes covering a part of their population. The World Health Organisation in fact foresees that all its member countries will introduce this vaccine to cover their entire population by 1997.

Admittedly, India has lagged behind in this important public health area. Barring some activity on the part of some hospitals to immunise their staff members, there has been little realisation that the real target is the newborn child.

First, as mentioned, hepatitis B vaccine can be easily administered to infants along with other vaccines that are being used in our country's vaccination programme as a routine. As compared to other vaccines, hepatitis B vaccine is stabler and does not get destroyed easily at room temperature, making it easier to transport. The main issue indeed is the cost. In Indian market, the vaccine currently costs between Rs. 250 and Rs. 400 a dose; each person needs three such doses for developing immunity. Therefore most of our doctors find it difficult to recommend this vaccine to all the children. Cost is also the major reason that has made our government hesitant to support the vaccination programme.

A responsible government will have to find ways to introduce this vaccine. In fact, the financial implications would change substantially if our government takes up the issue in due earnest. Price of vaccine is known to have fallen drastically in every country that has decided to introduce universal immunisation. India has a special advantage in this respect because of its large population.

Competition for bagging this large order of approximately 75 million doses every year will stimulate competition among manufacturers and definitely bring down the unit cost of vaccine drastically. The World Health Organisation has already offered to assist in purchase of vaccine at a price of US $0.55 per dose; this translates to under Rs. 60 for three doses needed for each newborn.

To this may be added some infrastructural costs which should not amount to more than Rs. 30 for vaccinating each newborn. In the very near future, a single vaccine which is effective against many infections including hepatitis B, diphtheria, whooping cough and tetanus will become available. This vaccine is likely to cost the same as the hepatitis B vaccine and will diminish the expenditure on syringes.

The estimated number of total live births a year in India is 2.5 crores. As the expenditure of immunisation of each child is estimated at Rs. 90, the total expenditure on HBV immunisation will be approximately Rs. 225 crore a year. This is surely not too formidable a sum considering that we could expect to save at least Rs. 2,250 crores directly on medical costs or indirectly by reducing man days lost. It is however regrettable that in spite of such vaccines having been available for more than a decade, we have not introduced mass vaccination against hepatitis B in our country. Surely, it does not make economic sense to spend resources on costly facilities, for instance liver transplantation, when the need for these could be easily nipped in the bud by spending a much smaller amount on its prevention.

Our population has generally been apathetic to public health issues except during large epidemics. For instance we are aware of recent furores over plague and dengue. However, long-standing public health problems, which kill many do not seem to attract any attention, with the media showing interest only when things become a disaster.

In advanced countries, on the other hand, every public health issue attracts attention and support of the public and the media. Unless public health becomes a mass movement, we will not emerge out of our morass of poor health and backwardness.

RAKESH AGGARWAL,
SITA NAIK,
SR NAIK.

The authors work at the Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow and have been campaigning for introduction of Hepatitis B vaccine in the national immunisation programme.

D1S16a.2.

HEP B VACCINE VICTIMS IN FRANCE SUE;

FRANCE SUSPENDS HEP B VACCINE MANDATE

In October 1998, the Minister of Health in France suspended the hepatitis B vaccine requirement for school children after repeated reports of the development of autoimmune and neurological disorders after hepatitis B vaccination. **The action came following reports in the medical literature as well as lawsuits against vaccine manufacturers and the French government.**

According to a July 31, 1998 issue of *Science*, an American scientific journal, **French attorneys representing 15,000 French citizens have filed a lawsuit against the French government "accusing it of understating the vaccine's risks and exaggerating the benefits for the average person."** One French physician has reportedly collected data on more than 600 people suffering from serious immune and neurological dysfunction following hepatitis B vaccination, many with symptoms resembling multiple sclerosis.

Litigation by hepatitis B vaccine victims and citizens seeking informed consent to vaccination is being reinforced by data from France released at the 62nd Annual Meeting of the American College of Rheumatology, held November 8-12, 1998 in San Diego, California linking hepatitis B vaccine to the development of autoimmune rheumatoid disease such as lupus and rheumatoid arthritis. The French data confirms a 1998 Canadian study published in *The Journal of Rheumatology* (1998: 25:1687-93) by Pope et al discussing evidence that recombinant hepatitis B vaccine may trigger the development of rheumatoid arthritis in genetically susceptible individuals.

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Once considered the most potent weapon against disease, vaccination's method of fighting fire with fire has today divided medical opinion the world over

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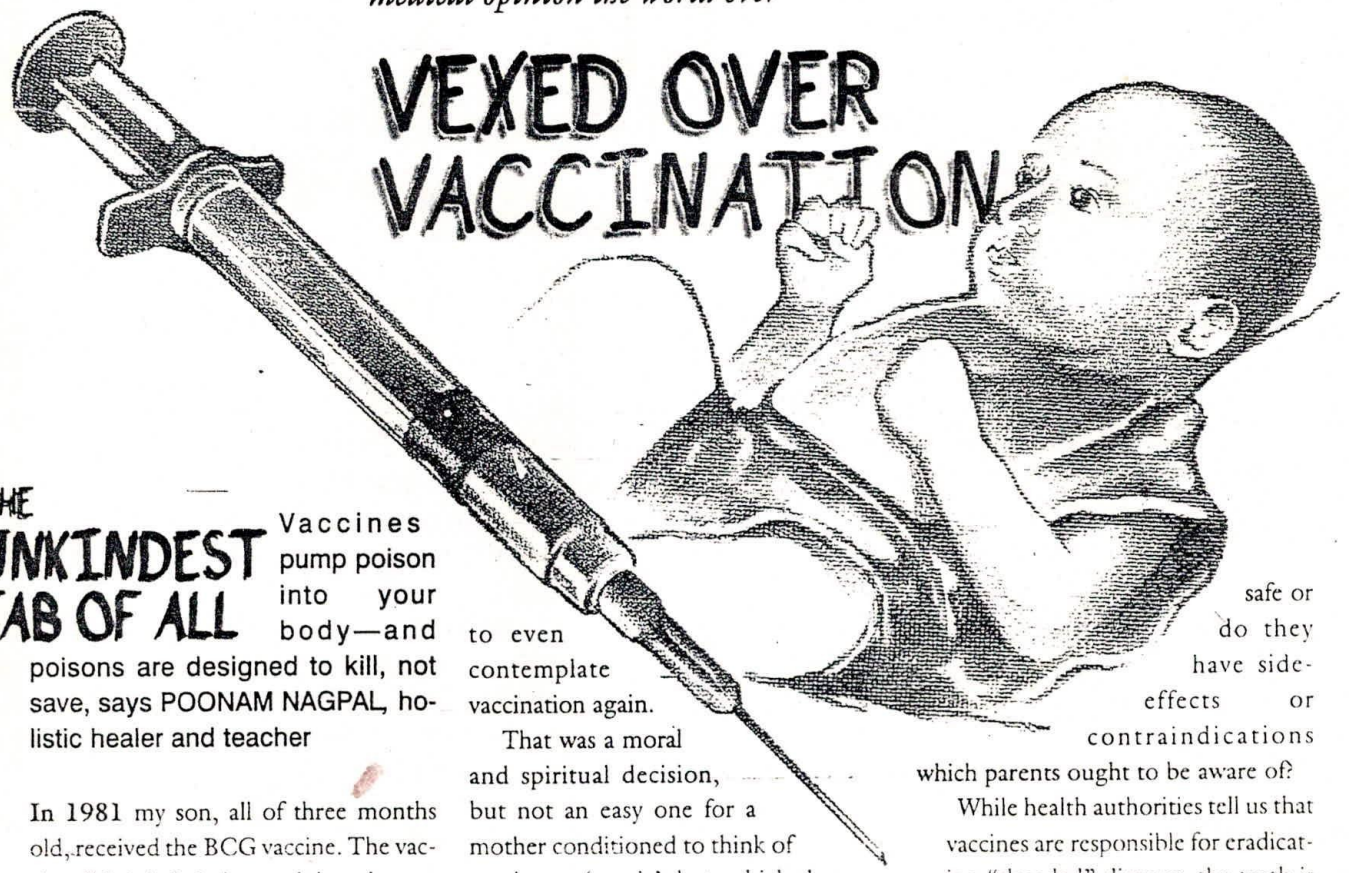


THE UNKINDEST JAB OF ALL

Vaccines pump poison into your body—and poisons are designed to kill, not save, says POONAM NAGPAL, holistic healer and teacher

In 1981 my son, all of three months old, received the BCG vaccine. The vaccine didn't 'take'. A month later he was re-vaccinated. The vaccine didn't 'take' again. On being tested, he was found not to have developed antibodies to tuberculosis. The doctors wanted to give the shot yet again.

I approached a family friend, a doctor with over 35 years of experience. Her advice to me was brief: "Forget it—he will develop natural immunity as he grows up."

In a casual conversation, another friend explained how vaccines were made—'grown' on animals, causing them immeasurable pain. "I have not vaccinated any of my children," she said. "Karmically, how can I expect something that has destroyed another's baby to provide protection to mine?"

I was stunned. I was not a 'believer' at that time but I was a mother, and I could feel the pain of the cow, the mare, the lamb, the monkey. I decided never to even contemplate vaccination again.

That was a moral and spiritual decision, but not an easy one for a mother conditioned to think of vaccines as 'magic' shots which absolutely 'must' be had. At that time, I was studying the various complementary systems of medicine, during the course of which I became convinced of the toxic long-term effects of vaccinations. It was much later that I realised that vaccinations, far from providing protection, could actually be responsible for considerable damage, including epilepsy, paralysis, cerebral palsy, autism, juvenile diabetes, jaundice—paradoxically, the very diseases that the vaccines were supposed to protect against.

Your family doctor is likely to disagree. You may be told that as a tool, vaccination is modern medicine's most effective invention, preventing more suffering and saving more lives than any other medical procedure. But if you do decide to investigate, you will be confronted by these questions: Do vaccinations prevent diseases? Are vaccinations safe or do they have side-effects or contraindications which parents ought to be aware of?

While health authorities tell us that vaccines are responsible for eradicating "dreaded" diseases, the truth is that childhood diseases decreased by 90 per cent between the year 1850 and 1940 largely because of improved hygiene, nutrition and living conditions, long before vaccinations were mass-introduced. Whooping cough (pertussis) deaths—credited to blanket vaccinations—decreased by more than 75 per cent before the vaccine was introduced; and records show that following that, people who were fully vaccinated against measles, mumps, smallpox, polio, diphtheria and whooping cough continued to get the disease.

In 1950, Dr B.P. McCloskey published evidence demonstrating that polio was caused by the DPT vaccine itself. Every known case of polio in the USA since 1979 has originated from the Oral Polio Vaccine (OPV). Today, America has chosen to move away from the OPV and revert to the tried and

tested IPV (injected polio vaccine).

Dr Robert Mendelsohn, one of America's best known paediatricians, says that "there is an ongoing debate among the immunologists regarding the relative risks of killed virus (IPV) vs live virus (OPV). Supporters of the killed virus vaccine maintain that it is the presence of live virus organisms in the other product that is responsible for the polio cases that occasionally appear. Supporters of the live virus type argue that the killed virus vaccine offers inadequate protection and actually increases the susceptibility of those vaccinated for the disease. I believe that both factions are right and that the use of either of the vaccines will increase, not diminish, the possibility that your child will contract the disease. In short, it appears that the most effective way to protect your child from polio is to make sure that he doesn't get the vaccine!"

In 1995, the *New England Journal of Medicine* revealed that many Romanian children were contracting polio from the polio vaccine. Even more startling was the finding that a single antibiotic injection given within a month of vaccination escalated the risk of polio by eight times; two to nine injections raised the risk 27 fold; and 10 or more injections raised the risk 182 times (*The Washington Post*, February 22, 1995).

Dr Viera Schiebner, author of the book *Vaccinations—100 years of Orthodox Medical Research Shows that Vaccines Represent a Medical Assault on the Immune System*, points out that 90 per cent of polio cases were erased from the monster list of statistics by the world's health authorities' redefinition of the disease variant which occurred when the vaccine was mass introduced. Today, thousands of cases of polio are diagnosed each year all over the world as viral and aseptic meningitis. Before the vaccine, they were called 'polio'. Schiebner also makes the chilling disclosure that every country employing the intensive or mandatory vaccination of infants shows a whopping 400 per cent increase in cerebral palsy not diagnosed at birth.

Says Kathi Williams, director of the National Vaccine Information Centre, USA: "There is gross under-reporting of adverse events associated with the administration of drugs and vaccines. In addition, past studies as well as reports to our centre by parents of vaccine-injured children have revealed misdiagnoses of neurological events which, in fact, turn out to be polio-vaccine-induced."

Recently, in an Indian daily newspaper, there was an article with a headline: "Polio Vaccine Totally Safe, Can Never Pose Risk to a Child". However, the article, quoting a Unicef official, makes some interesting revelations: the worst scenario is that the polio vaccine can cause a 'polio-like' illness; that this happens in children with a weak defence mechanism; that in India 10,000 children die daily of malnutrition; and that it is medically proven that a child cannot die of a polio vaccine.

Several questions go abegging: what difference does it make to a stricken child if the disease is called 'polio' or 'polio-like'? Wouldn't malnourished children constitute children with "a weak defence mechanism"? Shouldn't such vulnerable children be screened out of the programme?

What kind of 'protection' is there in a vaccine which requires the body to defend itself against the vaccine itself? In the same article, the Unicef official said that India had only 886 cases of polio in 1996. Eighty-five million children vaccinated in a country having only 886 cases of polio in a total population of 1 billion?

Says Dr Mendelsohn, author of *How to Raise a Healthy Child... In Spite of Your Doctor*: "The greatest threat of childhood diseases lies in the dangerous and ineffectual efforts made to prevent them through mass immunisation. I not only have grave misgivings about them; if I were to follow my deep convictions, I would urge you to reject all inoculations for your child."

Adds Dr Schiebner: "The body has proper, natural mechanisms to create immunity to diseases. It has been demonstrated time and again that infectious diseases of childhood are very beneficial for children to catch. Orthodox medicine's futile efforts to stop children from getting childhood diseases is a sign of ignorance and a naive approach."

Dr Schiebner had chanced upon the vaccine issue when she started a research programme to find possible causes of SIDS (Sudden Infant Death Syndrome, or 'cot death'), one of the medical world's more enduring mysteries and now the catchall phrase for babies who die "without apparent cause". What she found was chilling—the DPT vaccine was found to be SIDS' chief cause. When

> *...I am, and have been for years, a confirmed anti-vaccinationist. Anti-vaccination has no backing from the orthodox medical opinion. A medical man who expresses himself against vaccination loses caste. Tremendous pecuniary interests too have grown round vaccination.*
>
> Mahatma Gandhi in *Young India* (Vol XI-29, July 18, 1929)

Japan raised its vaccination age from 2-4 months to 2 years, SIDS almost completely vanished.

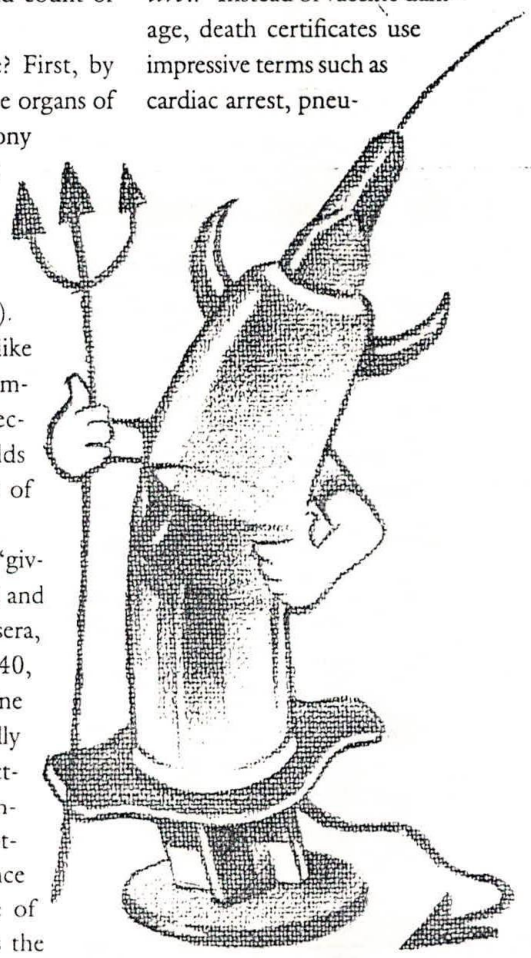
This started Schiebner off on the arduous task of precision-researching vaccination data. Her book showcases statistics that have been skewed either deliberately or through unforgivable ignorance, to convey the falsehood that vaccinations actually made diseases back off. She found that studies were conducted using control groups—one group was given the vaccination and the other group was given "not a placebo but a deadly combination of noxious substances". Says Dr Schiebner: "There is now an enormous pile of 'coincidental' adverse reactions or onset of illness within 14 or more days of vaccinations all over the world amounting to tens of thousands of cases." In some cases, children who died of the experimental vaccine were excluded from the final head count of 'necessary fatalities'.

How are vaccines made? First, by passing the virus through the organs of live animals in terminal agony and sometimes through dead human foetuses (the polio vaccine is actually the ground and mashed diseased kidneys of monkeys). The vaccines contain toxins like aluminium, mercury and formaldehyde. A considerable section of scientific opinion holds that there is no 'safe' dose of formaldehyde.

Second, in the process of 'giving' the disease to an animal and then 'extracting' the needed sera, many animal viruses like SV-40, SIV, monkey coryza and bovine retrovirus make that potentially deadly crossover to unsuspecting humans. SV-40 is a confirmed cancer tumour-promoting virus found in abundance (1,000 viruses per millilitre of vaccine) in the OPV. SIV is the simian equivalent of HIV, the virus linked to AIDS. Says Dr Schiebner: "The truth about polio and smallpox vaccines is that they are heavily contaminated with animal viruses. This gave us AIDS which started in Central East Africa, in those states where the WHO conducted the eradication campaign against smallpox and polio. It is beyond coincidence that the present raging epidemic of AIDS is affecting mostly those states where the polio/smallpox eradication was conducted."

Dr Mendelsohn is equally damning: "Immunisations may be responsible for the dramatic increase in auto-immune disorders. These are fearful diseases... Have we traded measles and mumps for cancer and leukaemia?"

Neil Miller, a journalist, says in his comprehensively documented book *Vaccines—Are They Safe and Effective?*: "Instead of vaccine damage, death certificates use impressive terms such as cardiac arrest, pneumonia, septicaemia due to septic tonsillitis, lymphatic leukaemia, streptococcal cellulitis, tubercular meningitis, infantile paralysis and SIDS, to name a few."



Defensively, the medical profession dismisses anti-vaccine protests with utter contempt, often with accusations of unpatriotism.

But the truth is that vaccinations are an imported technique discredited and rendered non-mandatory in most of the European Union and Australia. America is lagging way behind but the chorus of disenchanted parents, doctors and scientists is getting louder. Yet, the world's richest government has had to fork out more than $550 million (approximately Rs 2,000 crore) in the past four years as compensation to parents of dead and brain-damaged children.

More and more of the world has begun to comprehend the value of ancient Indian holistic health traditions—traditions where measles and the poxes were a visitation by the mother goddess as milestones in the progressive maturation of the endocrine system and the reproductive system, and where mumps was seen as a sure sign of future fertility.

Needles of Suspicion

- Whooping cough deaths decreased by more than 75 per cent before its vaccine was introduced
- Every known case of polio in the USA since 1979 has originated from the Oral Polio Vaccine (OPV)
- Every country doing mandatory vaccination of infants shows a 400 per cent increase in cerebral palsy
- The DPT vaccine was found to be the main cause of 'cot deaths'
- Vaccines contain toxins like aluminium, mercury and formaldehyde, for which there is no 'safe' dose
- In the process of 'giving' the disease to an animal and then 'extracting' the needed sera, many potentially lethal animal viruses cross over to humans

Teaching a child not to step on a caterpillar is as valuable to the child as it is to the caterpillar"-

— Bradley Miller

"How can I go back on the principles I have held so dear all my life, when I find that it is these very principles that are being put to the test ? I have not in the least doubt in my mind that vaccination is a filthy process, that it is harmful in the end and that it is little short of taking beef."

— Gandhiji

(On being asked to vaccinate the ashram inmates during the small pox epidemic).

"Whenever people say 'we mustn't be sentimental', you can take it they are about to do something cruel. And if they add, 'we must be realistic', they mean they are going to make money out of it."

—Brigid Brophy

"The time will come when men such as I will look on the murder of animals as they now look on the murder of men."

—Leonardo Da Vinci

THE HEART OF INDIA BEATS IN THE LITTLE ONES !

I would humbly ask you to do what you can to influence students' opinion, youth opinion, in regard to animal welfare.

Legislation, you say, - yes. But what is legislation ? What is the State ?

And if your children are going to grow, in the years of their manhood, to be patriots of the true type, **you must ask them to look with friendly eyes upon the bird and the beast.**

The State has two sides. One, I call the 'form-side," that whch we call 'organisation." The other, I call the 'Function-side." Organisation is necessary : but it is not so important, I submit, as the functioning of the State. **And the State must function through the heart and through wisdom.** So you must teach your students, **you must teach young men to think of birds and beasts as their brothers and sisters.** Build your work in the minds and hearts of students and youths of this generation.

I believe, the heart of humanity is *beginning to awake ; and humanity lives in our schools.

The heart of India beats in the little ones. Train them in the spirit of sympathy and love.

Blend information with inspiration. Blend knowledge with love.

Remember, the coming world, - the world to be, the world of tomorrow, - will be a world of sympathy radiant with the light of love !

— Sadhu T.L. Vaswani

with love and gratitude

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NATIONAL VACCINE INFORMATION CENTER

LIVE POLIO VACCINE VOTED OUT

LIVE POLIO VACCINE VOTED OUT - At a June 20 meeting of the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control, members of the federal vaccine policymaking panel voted to move away from use of the live oral polio vaccine (OPV) and toward increased use of the injectable inactivated polio vaccine (IPV) in order to cut down on the number of cases of polio disease caused by OPV in the U.S. each year. Although this action may reduce the number of vaccine associated polio cases in children and adults who swallow live OPV, it will have little effect on the cases of vaccine associated polio that occur in children and adults who get polio by coming into contact with the body fluids of a person who has recently swallowed live OPV On September 18, 1996, Dr. David Satcher, Director of the CDC accepted the recommendation.

Historic Policy Change - ACIP's vote marked an historic change in America's 32-year old policy of vaccinating all babies with four to five doses of live OPV, the vaccine which has been credited by health officials with eliminating wild polio disease from the western hemisphere but, today, is the only cause of polio in America. Because IPV is not "live" and is reputed to be incapable of giving vaccine recipients or close contacts polio, ACIP maintains that two doses of IPV will provide babies with polio antibodies without the risk of getting the disease and that babies will also be protected from getting polio from future doses of live OPV. However, ACIP also stated that an all-OPV or all-IPV schedule is also acceptable.

Moms Can Still Get Polio - Many parents of OPV damaged children, OPV damaged adults, as well as survivors of wild polio epidemics in the 1940's and 50's are not satisfied with ACIP's new recommendations. Like Lenita Shaefer, who got "contact" polio from her OPV vaccinated daughter in 1988, they want the live polio vaccine taken off the market and only IPV used in America. They maintain that ACIP's policy change will not prevent parents, babysitters or other children without antibodies to polio from getting polio after coming into close contact with a recently OPV-vaccinated child whose body fluids and waste products can "shed" the live polio virus for weeks following vaccination. Lenita told scientists at a 1995 Institute of Medicine Vaccine Safety Workshop that "No one had the right to immunize me without my consent. Now I am paralyzed for life for something I never agreed to receive. Immunization without consent invades my right of privacy as protected by the constitution. This insult is worsened by the fact that the only polio in this country since 1979 has been caused by the oral vaccine and most of the cases are contact polio like the one I have."

Parents Make Pleas - John Salamone, whose six year old son, David, got polio when he was just a few months old from an OPV vaccination, has spearheaded a public campaign to replace OPV with IPV to prevent vaccine associated polio. John told the panel that "It has been more than 15 years since a case of naturally occurring polio has been found in the U.S.; yet we can fill this room with Americans who have contracted polio from the oral vaccine since then.... In 1996, can we honestly look into the faces of parents whose children will contract vaccine-related polio this year and say we did our best?" Standing by her four year old OPV damaged son, Gordon, who sat paralyzed in a wheelchair on a respirator, Susan Pierson told the panel "Little did we know how our actions for our son would have the exact opposite effect. We thought we were doing what was in Gordon's best interest."

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NEW DELHI ◆ THE HINDUS

Counterpoint

HEALTH

Vaccination: A shot in

With every infant a potential recipient of multiple doses of vaccine system and government a potential buyer, every medical student eas information taught, it is little wonder that huge money has been sp vaccine industry. ALAN PHILLIPS puts forward reasons why pa vaccinate their children but make an informed responsib

WHEN my son began his routine vaccination series at the age of two months, I did not know there were any risks associated with immunisations. But the clinic's literature contained a contradiction: the chances of an adverse reaction to the DPT vaccine were one in 1,750, while his chances of dying from pertussis each year were one in several million. When I pointed this out to the physician, he angrily disagreed, and stormed out of the room mumbling, "I guess I should read that sometime..." Soon I learned of a child who had been permanently disabled by a vaccine, so I decided to investigate for myself. My findings have so alarmed me that I feel compelled to share them, hence, this report.

Health authorities credit vaccines for disease declines, and assure us of their safety and effectiveness. Yet these seemingly rock-solid assumptions are directly contradicted by health statistics, medical studies, Food and Drug Administration (FDA) and Centres for Disease Control (CDC) reports, and reputable research scientists from around the world. In fact, infectious diseases steadily declined for decades prior to vaccinations, US doctors report thousands of vaccine reactions each year including hundreds of deaths and permanent disabilities, many fully vaccinated populations have experienced epidemics, and researchers attribute dozens of chronic immunological and neurological conditions to mass immunisation programmes. My point is not to tell anyone whether or not to vaccinate, but rather, to point out some good reasons why everyone should investigate the issue before submitting to the procedure.

Some vaccination myths:

• **"Vaccines are completely safe..."**

The Vaccine Adverse Effects Reporting System receives about 11,000 reports of adverse vaccine reactions annually, some one per cent of which are deaths from vaccine reactions. The majority of these reports are made by doctors, and the majority of deaths are attributed to pertussis (whopping cough) vaccine, the "P" in DPT. The FDA estimates that only about 10 per cent of adverse reactions are reported. "In New York, only one out of 40 doctor's offices (2.5 per cent) confirmed that they report a death or injury following vaccination," — 97.5 per cent of vaccine related deaths and disabilities go unreported there. These findings suggest that vaccine deaths actually occurring each year may be well over 1,000.

Unfortunately, the vaccine-related-deaths story doesn't end here. Both national and international studies have shown vaccination to be a cause of SIDS ("Sudden Infant Death Syndrome," a "catch-all" diagnosis for cases when the specific cause of death is supposedly unknown; estimates range from 5-10,000 cases each year in the US). One study found the peak incidence of SIDS occurred at the ages of two and four months in the US, precisely when the first two routine immunisations are given.

Vaccinations cost us much more than just the lives and health of our children. The US Federal Government's National Vaccine Injury Compensation Programme (NVICP) has paid out over $650.6 million to parents of vaccine injured and killed children, a rate close to $90 million per year in taxpayer dollars. The NVICP has received over 5,000 petitions since 1988, including over 700 for vaccine-related deaths, and there are still some two thousand total death and injury cases pending that may take years to resolve.

• **"Vaccines are very effective..."**

The medical literature has a surprising number of studies documenting vaccine failure. Measles, mumps, small pox, polio and Hib outbreaks have all occurred in vaccinated populations. In 1989 the CDC reported: "Among school-aged children, (measles) outbreaks have occurred in schools with vaccination levels of greater than 98 per cent. (They) have occurred in all parts of the country, including areas that had not reported measles for years." The CDC even reported a measles outbreak in a documented 100 per cent vaccinated population. A study examining this phenomenon concluded, "The apparent paradox is that as measles immunisation rates rise to high levels in a population, measles becomes a disease of immunised persons."

Japan experienced yearly increases in small pox following the introduction of compulsory vaccines in 1872. By 1892, there were 29,979 deaths, and all had been vaccinated.

• **"Vaccination is based on sound immunisation theory and practice..."**

The clinical evidence for vaccinations is their ability to stimulate antibody production in the recipient, a fact which is not disputed. What is not clear, however, is whether or not such antibody production constitutes immunity. Agamma globulin-anemic children are incapable of producing antibodies, yet they recover from infectious diseases almost as quickly as other children. Furthermore, a study published by the British Medical Council in 1950 during a diphtheria epidemic concluded that there was no relationship between antibody count and disease incidence; researchers

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found resistant people with extremely low antibody counts and sick people with high counts. Natural immunisation is a complex phenomenon involving many organs and systems; it cannot be fully replicated by the artificial stimulation of antibody production.

Research also indicates that vaccination commits immune cells to the specific antigens involved in the vaccine, rendering them incapable of reacting to other infections.

Another component of immunisation theory is "herd immunity", which states that when enough people in a community are immunised, all are protected. There are many documented instances showing just the opposite — fully vaccinated populations have contracted diseases.

Carefully selected epidemiological studies are yet another justification for vaccination programmes. However, many of these may not be legitimate sources from which to draw conclusions about vaccine effectiveness. If 100 people are vaccinated and five contract the disease, the vaccine is declared to be 95 per cent effective. But if only 10 of the 100 were actually exposed to the disease, then the vaccine was really only 50 per cent effective. Since no one is willing to directly expose an entire population to disease — even a fully vaccinated one-vaccine effectiveness rates cannot be taken at face value.

Finally, vaccination practice assumes that all recipients, regardless of race, culture, diet, or any other circumstances, will respond the same. This was perhaps never more dramatically disproved than an instance a few years ago in Australia's northern territoty, where stepped-up immunisation campaigns resulted in an incredible 50 per cent infant mortality rate in the native aborigines.

Almost as troubling was a very recent study in the New England Journal of Medicine which revealed that a substantial number of Romanian children were contracting polio from the vaccine, a less common phenomena in most developed countries. Correlations with injections of antibiotics were found; a single injection within one month of vaccination raised the risk of polio eight times, two to nine injections raised the risk 27-fold, and 10 or more injections raised the risk 182 times (Washington Post, February 22, 1995).

● Polio was one of the clearly great vaccination success stories.

Six New England states reported increases in polio one year after the Salk vaccine was introduced, ranging from more than doubling in Vermont to Masachusetts' astounding increase of 642 per cent. In 1959, 77.5 per cent of Massachusetts' paralytic cases had received 3 doses of IPV (injected polio vaccine). During 1962 US Congressional hearings, Dr Bernark Greenberg, head of the Dept. of Biostatistics for the University of North Carolina School of Public Health, testified that not only did the cases of polio increase substantially after mandatory vaccinations (50 per cent increase from 1957 to 1958, 80 per cent increase from 1958 to 1959), but that the statistics were manipulated by the Public Health Service to give the opposite impression. According to researcher-author Dr Viera Scheibner, 90 per cent of polio cases were eliminated from statistics by health authorities' redefinition of the disease which occurred when the vaccine was introduced, while in fact the Salk vaccine was continuing to cause paralytic polio in several countries at a time when there were no epidemics caused by the wild virus (thousands of cases of viral and aseptic meningitis are diagnosed each year in the US, prior to the polio vaccine, these were diagnosed as polio). In 1985, the CDC reported that 87 per cent of the cases of polio in the US between 1973 and 1983 were caused by the vaccine, and later declared that all but few imported cases since were caused by the vaccine (and most of the imported cases occurred in fully immunised individuals). Jonas Salk, inventor of the IPV, testified before a Senate subcommittee that nearly all polio outbreaks since 1961 were caused by the oral polio vaccine.

● "Vaccines are the only disease prevention option available..."

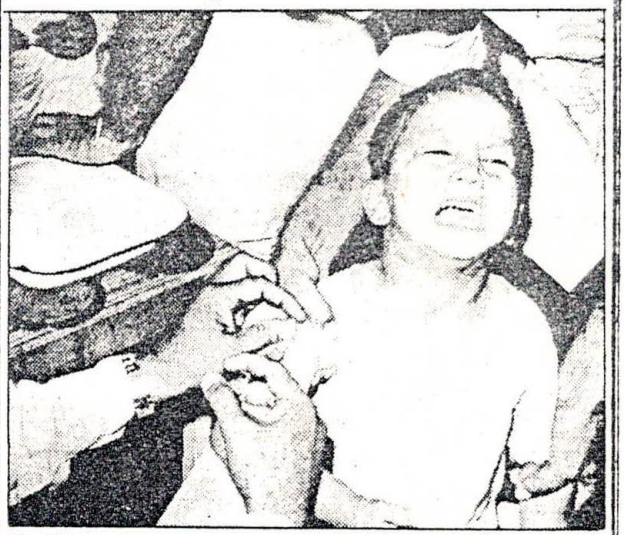
Most parents feel compelled to take some disease-preventing action for their children. While there is no 100 per cent guarantee anywhere, there are viable alternatives. Historically, homoeopathy has been more effective than "allopathic mainstream" medicine in treating and preventing disease. In a US cholera outbreak in 1849, allopathic medicine saw a 48-60 per cent death rate, while homoeopathic hospitals had a documented death rate of three per cent.

Alan Phillips is an independent investigator and writer on vaccine risks and alternatives. This report appeared in the April 1996 edition of "Wildlife Magazine".

□ **Point**

India has been in full cry with the Polio Plus programme. SUDARSHAN VAID on the relevance of vaccines which are imperative for the health of the child.

A doctor speaks for vaccination



MEDIA has a crucial role in disseminating scientific knowledge for the general good. By and large Indian media has fulfilled this responsibility quite carefully. However, some overzealous eager-to-earn-quick-money free-lance journalists, by filling controversial and unsubstantiated articles have done more damage than good to the people's psyche, particularly, on the health front.

As it is, most Indians are not literate. And those who are literate are quite superstitious and obscurantist. Even the educated among us don't have a scientific bent of mind and easily fall prey to both misinformation and disinformation through the Press. Except for a minuscule minority, we as a nation still believe in all sorts of myths and are inclined to oppose anything 'Western' or modern.

A lot is being written against vaccination, much to the deterriment of the health of the nation. I wish some of these writers were around in the pre and post Independence era to realise the damage done by a host of diseases, like Small Pox. I clearly remember how around 1974 with the help of WHO funds thousands of medical students and Interns went to every nook and corner of the country including Bihar to vaccinate each and every individual against Small Pox with the result that the scourge was banished forever from the world except for some 'virus samples' safely and securely kept in the laboratory, which too has either been or shall be destroyed soon. Just over 20 years ago this killer disease used to kill or blind millions of hapless men, women and children.

There are scores of diseases against which no treatment is hundred per cent successful. Take Rabies or Tetanus for that matter. Hardly any patient would survive their attack if not vaccinated. Thanks to schemes like Maternal and Child Health and vaccinations the maternal and infant mortality figures have been dropping over the years. But for Polio drops many a child would have been crippled for life.

Those who are opposing vaccinations are not only ill-informed but by spreading disinformation are causing irredeemable damage to future generations. As for reactions during vaccinations like Polio, Tetanus or DPT, their incidence in India is not more than the International figures. Most often, the deaths due to vaccination are not because of the vaccine per se but because of the "Toxic Shock Syndrome" due to contamination of the vaccines by *Staphylococcus aureus bacterium*.

Since India accounts for 50 per cent of all the polio cases in the world any one opposing vaccinations as such must think once more before speaking against them.

NIIN: Hepatitis B Vaccine

VACCINATION UPDATE

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Hepatitis B Vaccine- Experimenting on our Children

According to the Mortality and MorbidJty Weekly Report, there were 358 reported cases of Hepatitis B in New York City and 438 cases in Upstate New York for all of 1992. Despite CDC claims that there would be 200,000 cases nationwide in 1992, there were, in fact, only 13,857 reported cases. The vast majority of these cases were contracted through high-risk sex, drug abuse and medical contact. Hepatitis B disease peaked in the mid 1980's and has been declining ever since. Despite these facts, our legislators in Albany are trying to mandate this vaccine for all newborn babies in New York State. The vaccine has been added to the list of mandated vaccines for entry to school.

This genetically engineered vaccine, developed in 1987, is so new that little is known about it. It is not known whether immunity will last until the babies receiving it reach an age when they might engage in high-risk sex or drug abuse. They will find this out after experimenting on our-babies.

The risks, however, are very real. For the 20-month period between November 1, 1990 and July 31,1992, there were 4,227 reports of side effects from the Hepatitis B vaccine made through the Vaccine Adverse Effects Reporting System. Of this number, 383 were characterized as serious, 57 as life-threatening, 241 cases resulted in hospitalization, 108 individuals were disabled, and 17 died. These figures represent only the tip of the iceberg, as the FDA estimates that only 10% of doctors report vaccine injuries and deaths. The number of injuries and deaths will probably soar when this vaccine is mandated for use in all newborn babies. Nothing is known about the long-term effects of this vaccine, as no long-term, large-scale, controlled studies have been conducted.

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VIR Foundation

Vaccination Information & Research

Dear brothers and sisters: June 1997

Re: Vaccination Risks - Are we educated and aware?

In 1981 my son received the BCG vaccine at age 3 months. The vaccine didn't "take". A month later he was re-vaccinated. The vaccine didn't "take" again. On testing he was found not to have developed antibodies to tuberculosis. The doctors wanted to vaccinate yet again.

I approached a family friend who was a doctor with over 35 years experience. Her quiet advice to me was brief - "forget it - he will develop natural immunity as he grows up". I was very grateful for this advice because it somehow did not seem right to go on injecting the same vaccine into a child again and again.

I had another dear friend - Mrs. Patel was her name. A modern outgoing person, she was also full of the Ancient Wisdom . I casually mentioned the matter to her. She took a deep breath and in her quiet and gentle voice explained to me her views (which were also Gandhiji's views) on vaccinations. Her father was a staunch Gandhian - she herself as a young school girl had spent some time in Gandhiji's company. She gently and patiently explained to me how vaccines were made - "grown" on animals, causing immeasurable torture to them. **"I have not vaccinated any of my children" she said - "karmically, how can I expect something that has destroyed another's baby to provide protection for my baby."**

I was stunned - I was not a "believer" then - but I was a mother and I could feel the pain of the cow, the horse, the lamb, the monkey. I decided never to vaccinate again.

That was a moral and spiritual decision. It was not an easy decision for a mother who has been conditioned to think of vaccines as "magic" shots - which absolutely "must" be had, and without which her child will probably get some terrible disease.

At that time I was studying the various alternate therapies - Acupressure, Ayurveda, Homoeopathy, Naturopathy (and its various offshoots) and as I studied I began to be convinced about the long term toxic effects of vaccinations (skin disorders, asthma, mental diseases etc.). Later, much later, I realised that vaccinations, far from "providing protection" could in fact be responsible for considerable damage including epilepsy, paralysis, cerebral palsy, autism, juvenile diabetes, blood clotting disorders, jaundice, death and - paradoxically - the very diseases that the vaccines were supposed to provide protection against.

Naturopaths and Homoeopaths have long known the disastrous effects of vaccinations especially the role they play in the development of chronic diseases. However, as in other issues, in vaccinations too

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the view that has prevailed in the media and in government policies is the one that has money on its side. There is no money to be made in saying "don't vaccinate" or "watch out - educate yourself before you decide to vaccinate". And vaccinations are a multi-billion dollar business world wide.

Up until now the recommendations of the government, WHO, UNICEF and other welfare organisations supporting vaccinations have been based on studies conducted/funded, directly and indirectly, by pharmaceutical companies, who of course stand to benefit enormously from vaccinations.

However, in the western countries from where this "technology" has been imported, in the last 15 years or so, a steadily increasing movement has been building up - of parents, of medical professionals, scientists and socially conscious people - who have dedicated themselves to resolving this issue through ***independent and impartial scientific research***. This information is now becoming widely and easily available as books, research papers, audio and video tapes and on the Internet. A brief list of selected references is given at the end of this letter.

One of the most comprehensive documents on the subject "Dispelling Vaccination Myths" by Alan Phillips has already been sent to many of you within India. Those overseas can access the information on the Internet on Alan Phillips web site at : *http://www.unc.edu/~aphillip/www/vaccine/informed.htm*. Publishing of this article by two leading Indian dailies and a few Journals during the last few months was a watershed in the mass awareness of vaccination risks.

An abridged version of this article as it appeared in one of the newspapers, is enclosed.

In India, those who have so far not received and are interested, can write to us for a free copy of Alan's *unabridged* study in English. An abridged translation in Hindi is also available.

There is an urgent need for parents to take the initiative to study this matter independently and ***take responsibility for making informed choices for their children*** without allowing themselves to be brow-beaten by irrational fear of childhood diseases propagated by various agencies. In the USA , the UK, Europe and Australia, parents of children who have either died or are brain damaged from the vaccinations, have set up organisations to educate and inform other parents about the dangers.

The issue of vaccinations has not been addressed with any degree of seriousness in India and many developing countries. Only very recently has the print media taken a bold and admirable initiative to spread the knowledge of the risks associated with vaccinations, to the masses.

Vaccination is a serious medical process with serious side effects both acute and degenerative.

Did you know :

- that the oral polio vaccine is the ***live*** virus (grown on the kidneys of monkeys who are tortured to death in the process) and that the baby, and anyone coming in contact with the baby, can actually contract polio from the vaccine itself? That the saliva, phlegm and the faeces of the vaccinated child are full of the live virus ***for two and a half months*** and anyone coming in contact with them is being exposed to polio? (The main targets of the vaccine campaign are slum children who use footpaths as toilets).

- that every bit of antibiotics that the child may be given for any other problem for two and a half months following the vaccination increases the risk of the child getting polio manifold?
- that the child must not be vaccinated if he or she is having so much as a cold? That the resistance must be high as the child has to ***protect itself against the vaccine?***
- that ***every case of polio in the USA since 1979 was caused by the polio vaccine?***
- that the Oral Polio Vaccine has been ***voted out*** of the USA on September 18, 1996?
- that in the last 4 years the US Food and Drug Administration (FDA) ***received over 34,000 reports of adverse vaccine reactions including more than 700 deaths. That the FDA itself estimates that this figure represents just 10% of the true damage being done?***
- that over US$650 million (over Rupees 2275 crore) has been paid as compensation to parents of these children?
- that in the United States deaths from whooping cough (pertussis) in the peak year (1993) were 8 whereas adverse reactions from the DPT vaccine were 100 times this figure and this includes epilepsy, permanent brain damage, autism and death ?
- that a vast majority of medical personnel in the USA, thought to be at maximum risk from Hepatitis B have refused the vaccine because of fears of serious side effects and doubts of it being contaminated with a micro-organism responsible for the AIDS epidemic?
- that deaths from Small Pox tumbled only ***after people refused the shots?***
- that measles, polio, mumps, rubella, whooping cough - all occur in fully vaccinated populations too ? (in many instances the vaccinated cases outnumber the unvaccinated victims!)
- that it is becoming increasingly clear that AIDS in Africa came most likely from the Polio and Small Pox Vaccine? That SIV and BIV - two viruses very similar to HIV (found in monkeys and cows respectively) ***crossed over*** to the human species through the medium of contaminated vaccines?
- that SV 40 is another monkey virus present in the vaccine and that this causes cancerous tumours?
- that most Indians have a high natural immunity to polio and really do not need the vaccine?

In "Young India" Vol XI-29 of July 18,1929, **Gandhiji said**

> *"I have no anger in me for the indifference of the public or Press over the incident (Secretary, Anti-Vaccination League, was imprisoned for not vaccinating his child). I am and have been for years a confirmed anti-vaccinationist. Anti-vaccination has no backing from the orthodox medical opinion. A medical man who expresses himself against vaccination loses caste. Tremendous pecuniary interests too have grown round vaccination."*

We have come a long way since then - the media is the keeper of the nation's conscience and it has been heartening to see the media take on its role in the field of vaccination too. There is a new awakening - most definitely a paradigm shift is taking place - more and more orthodox doctors are turning to holistic healing. More and more of the world has begun to realise the value of ancient Indian traditions in the upkeep of health of body, mind and spirit - traditions where measles and the poxes were not diseases to be shunned, but welcomed as a visitation by Mother Goddess.

We earnestly urge you to ***read, digest and share*** the enclosed information with patients, with new/prospective parents or grandparents, homoeopaths, ayurveds, naturopaths, allopaths and their Associations in your town or city. Share it with journalists and translate it if necessary in the language of your region. Child welfare organisations too need to be made aware so that their good intentions do not get misguided into harming the children.

Share it in a spirit of loving care and harmony.

May the Lord bless mankind with the wisdom to make the right choice on this vital issue.

With Love and Light,
Mrs Poonam Nagpal

Enclosures:

1 Vaccinations - A Shot in the Dark (abridged version of Alan Phillips study)
2 Hepatitis B Vaccine - Experimenting on Our Children (from the NIIN site on the Internet) - printed on reverse of above article.
3 Live Polio Vaccine Voted Out (from the NVIC site on the Internet)
4 Vexed Over Vaccination - an article from Life Positive.

Recommended reading

1. Dispelling Vaccination Myths - by Alan Phillips (a documented study) available free from SSF.
2. Vaccinations - Are They Really Safe and Effective? - by Neil Miller ISBN 1-881217-10-8
3. How to Raise a Healthy Child In Spite of Your Doctor - Dr. Robert Mendelsohn MD ISBN 0-345-34276-3
4. Immunisations - What Your Doctor Won't Tell You About Them - Dr. Robert Mendelsohn MD
5. Immunization - Theory vs. Reality by Neil Miller ISBN 1-881217-12-4

Also visit the Internet at :

http://www.unc.edu/~aphillip/www/vaccine/informed.htm
http://www.909shot.com/ (or search NVIC)
http://www.i-wayco.com/niin/index.html (or search NIIN)
http://www.new-atlantean.com/global/immun.html (or search New Atlantean) - this site gives details of books available.

Gandhiji's opinion on the small pox vaccine

On being asked to vaccinate the ashram inmates during the small pox epidemic, Gandhiji said.

" How can I go back on the principles I have held so dear all my life, when I find that it is these very principles that are being put to the test ? I have not in the least doubt in my mind that vaccination is a filthy process, that it is harmful in the end and that it is little short of taking beef."

ॐ

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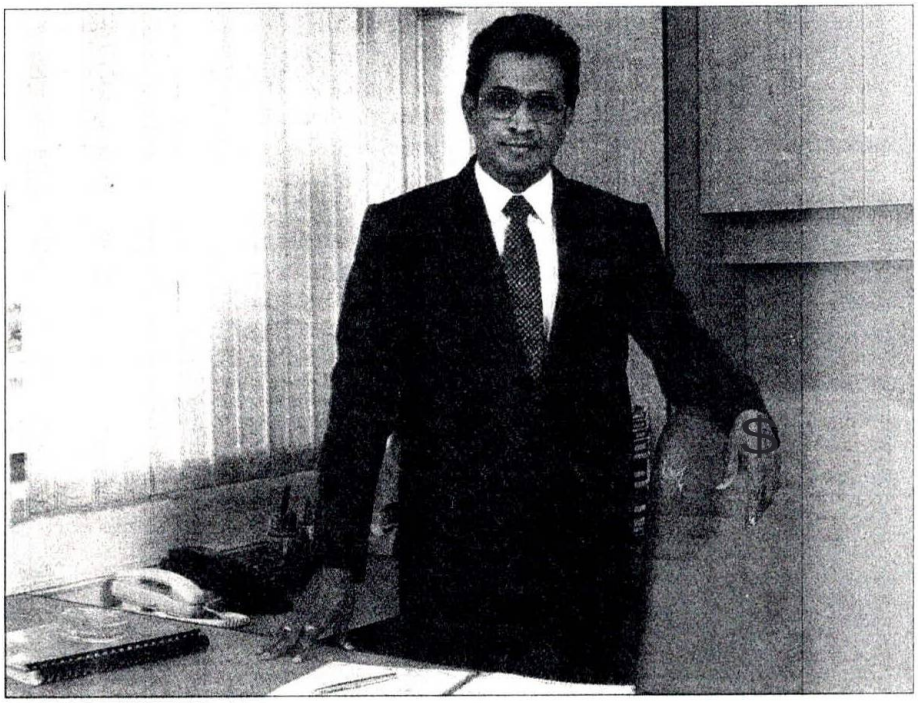
War of the doses

An "Indian" genetic vaccine for Hepatitis B enlivens the race to bag the world's single largest order



"I knew it could be done," says Varaprasad Reddy

Forty-two million Indians suffer from Hepatitis B. The disease claims 10 million adult Indians every year and accounts for between 50 and 70 per cent of chronic liver disease, 80 per cent of liver cancers and a large chunk of liver cirrhosis cases.

The WHO recommends that all countries with a Hepatitis B prevalence of 8 per cent or more should introduce the vaccine into their immunisation programmes by 1997. Though 85 countries worldwide have done so, India is yet to allocate a budget for the purpose. This is despite the recommendations of Indian medical experts and intensive lobbying by SmithKline Beecham, which already sells its Hepatitis B vaccine in the open market.

India needs 75 million doses annually (3 doses each for 25 million children) if it is to introduce the vaccine into the Extended Programme of Immunisation (EPI). This represents the single largest order for the vaccine in the world (China has bought the technologies and is manufacturing the vaccines in domestic plants).

With the patent for the vaccine expiring in 1998, companies are suddenly racing to get the EPI's orders for the Hepatitis B vaccine placed as soon as possible. Prices could crash after that as anybody could then manufacture the vaccine. For SmithKline Beecham, the Indian order could well be the final kill: in ten years of selling its vaccine the company has sold 330 million doses worldwide. Over a five-year period, India's EPI alone could use 375 million doses.

"Take $15 million and leave the country," Varaprasad Reddy was threatened on the phone. There have been other such anonymous calls, he says. Why? Millions of dollars are at stake, along with a large government tender. Most important, the man orchestrated a major *coup d-etat*: an almost all-too-easy 'Indian' development of a new vaccine that calls for extremely sophisticated biotechnology.

Reddy's company, Shanta Biotechnics startled the medical fraternity a fortnight ago when it announced that it had developed a vaccine for Hepatitis B. Health minister, Renuka Choudhary, also from Hyderabad, made the announcement amidst much euphoria over the fact that finally, here was India's first genetically engineered vaccine. The clincher: the vaccine was priced at a fraction of similar products in the market.

What on earth was Shanta Biotechnics? Where did it come from? Who were the scientists that developed the vaccine? How did they manage to do what so many multinational pharma companies could not? Why did they reinvent the wheel when the technology already existed? And how was the feat accomplished with less than Rs15 crore when the technology for the recombinant vaccine costs around $28 million worldwide? The assumptions: the product must be of inferior quality; if it isn't, the technology must have been bought, or stolen. Was there truth in these notions or was the establishment simply resisting what it could not explain?

Reddy, an engineer and an MBA, says he tied up with an Omani partner to start Shanta Biotechnics in 1992 with the express purpose of developing biotechnology products, "I knew it could be done, you look at all the major centres in the US where biotechnology research is the best, the field is full of Indians and Chinese." A study of the market clearly indicated that there was a need for affordable Interferon (for the treatment of cancer) and the Hepatitis B vaccine, which was not marketed in India at the time, in the US it was being sold at $74 per dose. Could it be done? Three of his cousins who are in the biotechnology field in the United States advised him that it could. Five years later, the conviction of these men stands vindicated.

Dr Philip Abraham, a gastroenterologist at KEM hospital in Mumbai has worked closely on the clinical trials of Shanta B's vaccine. "The vaccine is excellent," he says. Abraham admits that his department was taken aback when this unknown company approached the hospital for clinical trials.

The medical fraternity, particularly those in the field of gastroenterology and hepatology had never heard of the company. Trials on 100 patients proved a 100 per cent conversion rate (number of patients who develop the necessary antibodies). Moreover, the patients showed very high levels of the antibodies, which meant that the immunity they developed would last a long time. "We were surprised, all the more since the product came from a source we had no knowledge of," says Abraham.

Unfortunate associations

The first suspicion was that Reddy had bought the technology. But costs were clearly prohibitive. Did he simply manage to lift the technology or a critical part of it from somewhere? Varaprasad's antecedents went against him here. Before he started Shanta Biotechnics, he worked with A.J. Prasad in Hyderabad Batteries. He says he quit because he fell out with Prasad. In 1995, Prasad was arrested along with an NRI, Subramaniam Kota, by the FBI in the US for allegedly trying to steal defence technology: a formula for paint that helped aircraft evade radar scrutiny. It was Kota's second arrest, the first was in 1994 when he was caught trying to pass on biotechnology secrets to an FBI official posing as a KGB agent. The cell line in question was given to him by another NRI, Vemura Reddy who had stolen it from his previous employer, Integrated Genetics in Masachussetts.

So Varaprasad had the 'right' connections too. Moreover, Kota himself was also an initial investor in Shanta Biotechnics. But Gita Sharma, the scientist who worked closely with the Shanta Biotechnics project from day one, is categorical, "The associations are just coincidental and unfortunate." In fact, she says that Kota was removed from the board as soon as he was accused of espionage. Also, Vemura Reddy has no connection at all with Varaprasad.

Sharma, who is now vice-president, biotechnology, at Cadila Laboratories in Ahmedabad, spells out clearly how Varaprasad approached her with the idea of developing a biotechnology project. "I was just back from working on a number of biotechnology projects in the US and was determined to do something on those lines in India." Sharma approached a number of institutions for finance but only Osmania University was prepared to let her work on projects of her choosing in their labs. In Varaprasad, Sharma found her sponsor. Sharma details how she bought the necessary genome (cluster of chromosomes) library from the ATCC, an American pool of genomes that anybody can buy (for as little as $300!). Under the guidance of Dr Guntaka Ramareddy, Missouri, USA, the appropriate gene was isolated and cloned. "They (Shanta Biotechnics) believed in me and I did not let them down," says Sharma.

Shanta Biotechnics undoubtedly went through the grind. Dr Ramareddy, a cousin of Varaprasad, confirms this. This scientist has illustrious work in the field of molecular biology to his credit (he was part of the Harold Varmus-Michael Bishop team that first cloned the prototype virus to study cancer, it won the latter duo the Nobel prize for Medicine in 1989).

Sharma worked at Ramareddy's lab in Missouri during 1993, and, from 1994 continued the work at the government's Centre for Cellular and Molecular Biology (CCMB) in Hyderabad until Shanta Biotechnics' own high-tech laboratory got ready in October 1995. But how did Shanta Biotechnics manage to do all this for as little as they did?

Dr P. Balasubramaniam, director CCMB says that it was possible. Dr Ramareddy explains the arithmetic: most companies developed their technologies upto 12 years ago when it was far more expensive to do so. Ten years ago, one gram of certain tools (oligonucleotides) that are used a lot in such work cost $200,000, today a gram would cost $200! The host vector Sharma used to clone the gene was not even available till recently. Existing vaccine makers cannot simply switch processes, it would call for new FDA approvals.

The reason why Shanta Biotechnics succeeded where a lot of international companies did not, despite cheaper technology, according to Ramareddy, is because of the high cost of clinical trials abroad. Also, scientists of similar calibre working on such projects would earn $100,000 for every Rs100,000 earned in India, he says.

All things being equal, as far as quotes to the government are concerned, what will tip the scales? Shanta Biotechnics is using the indigenous argument, but given that much of the early critical work was done in the US, how much water should this hold? Ramareddy admits that he was 'intimately' involved with the project and guided Sharma in the finer points of isolation and cloning. Meanwhile, a Cuban company is expected to launch its Hepatitis B vaccine, Cadila and Wockhardt are also in the process of clinical trials. The government has made no provision for the vaccine in the EPI as yet, but the war is getting hotter and grubbier.

◆ MERLE ALMEIDA with MEERA SHENOY

What will tip the scales?

Company	Market prices Rs/dose	Minimum indicated rate for EPI Rs/dose	Clinical Trial
SmithKline Beecham	Adult: 485 Child : 310 Multivial: 3000	Child: 37	16,000 (10 years)
Shanta Biotechnics	Adult: 190 Child: 140 Multivial 1800	Child: 37	100 (1 year)

A vaccine programme for Hepatitis B

Hepatitis B is a global health problem that affects adults and children alike. As the vaccines are costly, the government should come forward to introduce mass immunisation programmes that work out cheaper.

HEPATITIS B virus (HBV) infection is a major global public health problem. Though this virus is commonly recognised as one of the many causes of jaundice, medically called as "hepatitis", most of us are not aware that it also causes more sinister and delayed health problems. A short lasting attack of hepatitis may frighten a patient but is usually only a minor illness which does not leave behind any scar on the liver or the human body.

Thus, contrary to popular belief that jaundice due to hepatitis B virus is a dangerous illness, a large majority i.e. 95 per cent of such adult patients recover completely in a matter of a few weeks and in fact are rendered immune for life to this infection. We wish to focus our attention in this article at making people aware of the long-term effects of this infection.

The virus may attack either adults or children. Adults develop hepatitis and follow the course outlined above. On the other hand, when it infects children, 90 per cent of them (as opposed to only about five per cent of adults) develop a low grade and unapparent infection which persists for many years, at times throughout life; such persons may be apparently healthy. But they are at a high risk of developing liver cirrhosis and liver cancer, both very serious illnesses. Further, these diseases occur in the prime of youth and cost the society heavily in the form of loss of manpower and expenditure on medical care. It has been estimated that nearly 30 per cent of hepatitis B carriers ultimately die entirely due to complications of this infection.

Why should we in India worry about a disease that occurs world-wide? This is because of the nearly 350 million hepatitis B carriers all over the globe, nearly 40 million are in India. It can be estimated that nearly 200,000 persons in India die every year of HBV infection.

The figures should make every Indian sit up and think how exactly does this infection spread and how it can be prevented. Most educated people are fully aware that transfusion of blood or blood products may cause this infection. Doctors, nurses and other hospital staff may get infected with this virus through close contact with secretions of patients infected with this virus and pricks from used needles.

Similarly, use of needles that are not sterilised can transmit infection from one patient to another. What however, is not common knowledge even among medical persons is that numerically far more persons get infected in early childhood through contact either with infected mother, siblings or playmates, as also from an injection. In fact, the carrier pool is maintained more by infection at a young age than that during adulthood since as previously mentioned, the later infections hardly ever lead to carrier state.

If hepatitis B is such a serious infection and we know how it is caused, a common question is why can not we prevent it. It was not possible to answer this question a decade ago. The answer today is an emphatic "yes" because of development of hepatitis B vaccines in the early 1980s.

These vaccines are by far the safest and the most effective. To make the maximum impact, these vaccines should be administered in early infancy along with other childhood vaccines like those against tuberculosis, diphtheria, whooping cough, tetanus, polio and measles. Introduction of hepatitis B vaccine programme has been shown to convincingly reduce the number of HBV carriers in many countries where this infection was extremely common. In fact, like most infective diseases for hepatitis B too, immunisation of children is the most effective preventive strategy. It has been estimated that a rupee spent on vaccination against childhood infections will save Rs. 10 in cost of medical care; for a disease like hepatitis B which causes delayed and prolonged illness in adulthood, the relative advantage would be much larger.

Impressed with the cost-effectiveness of hepatitis B vaccine, over 80 countries have already introduced HBV immunisation programmes covering their entire population and several others have either initiated or are planning programmes covering a part of their population. The World Health Organisation in fact foresees that all its member countries will introduce this vaccine to cover their entire population by 1997.

Admittedly, India has lagged behind in this important public health area. Barring some activity on the part of some hospitals to immunise their staff members, there has been little realisation that the real target is the newborn child.

First, as mentioned, hepatitis B vaccine can be easily administered to infants along with other vaccines that are being used in our country's vaccination programme as a routine. As compared to other vaccines, hepatitis B vaccine is stabler and does not get destroyed easily at room temperature, making it easier to transport. The main issue indeed is the cost. In Indian market, the vaccine currently costs between Rs. 250 and Rs. 400 a dose; each person needs three such doses for developing immunity. Therefore most of our doctors find it difficult to recommend this vaccine to all the children. Cost is also the major reason that has made our government hesitant to support the vaccination programme.

A responsible government will have to find ways to introduce this vaccine. In fact, the financial implications would change substantially if our government takes up the issue in due earnest. Price of vaccine is known to have fallen drastically in every country that has decided to introduce universal immunisation. India has a special advantage in this respect because of its large population.

Competition for bagging this large order of approximately 75 million doses every year will stimulate competition among manufacturers and definitely bring down the unit cost of vaccine drastically. The World Health Organisation has already offered to assist in purchase of vaccine at a price of US $0.55 per dose; this translates to under Rs. 60 for three doses needed for each newborn.

To this may be added some infrastructural costs which should not amount to more than Rs. 30 for vaccinating each newborn. In the very near future, a single vaccine which is effective against many in fections including hepatitis B, diphtheria, whooping cough and tetanus will become available. This vaccine is likely to cost the same as the hepatitis B vaccine and will diminish the expenditure on syringes.

The estimated number of total live births a year in India is 2.5 crores. As the expenditure of immunisation of each child is estimated at Rs. 90, the total expenditure on HBV immunisation will be approximately Rs. 225 crore a year. This is surely not too formidable a sum considering that we could expect to save at least Rs. 2,250 crores directly on medical costs or indirectly by reducing man days lost. It is however regrettable that in spite of such vaccines having been available for more than a decade, we have not introduced mass vaccination against hepatitis B in our country. Surely, it does not make economic sense to spend resources on costly facilities, for instance liver transplantation, when the need for these could be easily nipped in the bud by spending a much smaller amount on its prevention.

Our population has generally been apathetic to public health issues except during large epidemics. For instance we are aware of recent

"Hepatitis B" The Jaundice less known to people

Dr K Narsimhan
Dr Ilka M Varma

Realising the magnitude of the problem of Hepatitis B — which has assumed alarming proportions among the infectious diseases. the Catholic Medical Guild (M.G.) Hyderabad held a Seminar conducted by Dr D Nageshwar Reddy D.M. on 18th August, 1990 to highlight this oblem.

"Hepatitis B" infection has assumed dangerous levels as the carrier rate in A.P. is 10% — This stems from the fact that the modes of transmission of this virus ranges from skin contact to sexual contact and is also transmitted from mother to child — mainly by early close contact.

Added to this, is the fact that individuals harbouring this virus without any apparent ill effects (Carriers) greatly outnumber the frank cases of this disease.

Another feature which compounds the problem is the fact that the risk of developing subsequent complications is inversely related to the severity of the initial ailment and those are the ones nich are likely to go for the complications which range from chronic active hepatitis to Hepatoma (Cancer). To complete the grim story, the virus, like the AIDS virus, is not eradicated by ordinary means of disinfection and sterilization.

The Virus:

Is a D.N.A. virus with an inner core (Core antigen) and an external coat (Surface antigen — Australia antigen). The Surface antigen circulates in the blood unlike the Core Antigen which remains fixed in the Hepatic cell.

Another antigen "Hbe" is believed to be a component of the Core antigen and does circulate in the blood.

Source of Infection

(1) Patients'

(2) Carriers — The risk of an adult becoming a carrier following an attack is 5-15% and in infants it may exceed 50%.

Carrier rates are higher in patients with Leprosy, Leukemias, Hemophiliacs, Steroid drug users, etc.

Carriers are of two types:

(a) Super carrier: Highly infectious in the early stages, have Hbe antigen. A very minute amount of infected material can transmit the infection.

(b) Simple Carrier: One who has an anti Hbe antibody and low levels of HbsAg — transmit infection only when large amounts of blood or serum are transferred.

Mode of Infection:

The virus is present in blood and most of the body fluids — most important being Semen and Saliva.

The modes of transmission are:

(a) Percutaneous (through skin): Blood transfusion and other diagnostic and therapeutic procedures.

(b) Intimate Contact: Sexual/Kissing etc.

(c) Transplacental: Most infections occur at birth sequel to leakage of maternal blood into the baby's circulation or by ingestion or accidental inoculation of blood.

Whether it is spread through food or water intake is not clear.

Incubation Period

6 Weeks to 6 months

Clinical Features: Occurs in any age group. The features include:

Constitutional symptoms Gastro-intestinal symptoms — vomitting and abdominal pain. The onset is usually insiduous and a frequent clinical feature preceeding the main illness is the presence of joint pains, fever, maculopapular rash — all resembling a serum sickness-like syndrome.

The signs include deep jaundice, enlarged and tender liver, Ascites, Spider nevi may be present rarely. An enlarged spleen and palpable lymph nodes in the neck may occur in 10-20% cases.

Lab Investigations

The blood picture may show a depression of the white blood cell count. The Liver Function Tests show marked rise of Serum Bilurubin, mild increase in Serum Alkaline phosphatase, 10-100 times increase in SGOT and SGPT.

The Prothrombin time may be prolonged and serves as a good prognostic indicator.

The first serologic marker is the appearence of HbsAg — precedes the rise of Serum enzymes.

It usually disappears in 2 months in 90% cases and is followed by Anti-HbsAg antibodies which are protective.

Course of the Disease:

Complications: The HbsAg disappears in 2 months in 90%. 5% take 6 months for clearance.

The rest become chronic carriers. This carrier state may be quiescent or may progress to

— Chronic active Hepatitis
— Cirrhosis
— Hepatoma (cancer liver)

During the active phase the patient may go into Fulminant hepatitis

This is the way Hepatitis B vaccine is being promoted in schools & neighbourhoods. Pharmaceutical co's are behind the promotion.

HEPATITIS B

Hepatitis B kills more people in 1 day than AIDS does in 1 year.
Hepatitis B is the 2nd biggest cause of cancer after tobacco

Ignorance of this viral liver disease may be fatal. There is no cure. Prevention is the only way to stop the disease. Please consult your doctor.

Hepatitis B is a serious disease caused by a virus that attacks the liver – leading to lifelong infection, cirrhosis, liver cancer, liver failure and death.

India has the 2nd largest pool of carriers in the world. ANYONE – can contact the virus from the blood or body fluids of infected persons or carriers. ANYTIME. ANYWHERE.

* ***At school/playground***: on body contact with carriers having open wounds/cuts, contact sports – soccer, hockey, wrestling, karate...
* ***At the beauty saloon, barber shop***: common usage or sharing of infected razors, scissors, piercing instruments, etc.,
* ***At home***: living in the same house with someone who has life-long Hepatitis B infection, new born of infected mother, contacts with chronic liver disease patients, bed sharing, physical contact with infected members such as domestic help, sharing of toothbrushes, razors, etc.,
* ***At other places :*** on body contact with infected persons, sex with infected person, usage of contaminated needles, instruments, etc., inadvertent contact during play with open wounds, cuts, blood of carriers

For Koramangala residents a camp will be held in association with
ACTS HEALTH CENTRE & HOSPITAL, *Bangalore 68 by*

ROTARY CLUBS OF KORAMANGALA & INDIRANAGAR
on Saturday 24 & Sunday 25October 1998 from 9.00 A to 4.30 P
at the Asian Institute of Theology Hall, 93, 17th Main, KHB Colony
5th Block Koramangala, Bangalore95. Camp Tel: 553 8060 or 553 1025

For registration/details, contact : ACTS at 852 1538, 852 1539 or 553 1154
Rtn Ravi Kumar on Tel : 530 0894 or Rtn Col Madappa on Tel: 553 2126

Vaccination charges per dose: Adults/children above 10 years: Rs260 Children below 10 years: Rs130. Three doses need to be taken to complete a course.
First dose: Day 1, Second dose: Day 30 and Third: Day 180

ಗುಣಪಡಿಸುವ ವಿಧಾನ :

ಪೂರ್ಣ ಗುಣಪಡಿಸುವ ವಿಧಾನ ಯಾವುದು ಇಲ್ಲವಾದರು ಈ ರೋಗ ಬರದಂತೆ ತಡೆಗಟ್ಟಬಹುದು.

ಹೆಪಟೈಟಿಸ್ - ಬಿ ವಾಕ್ಸಿನೇಶನ್ :

ಮಕ್ಕಳು ಮತ್ತು ಯುವಕರಲ್ಲಿ ಈ ರೋಗ ಬರದಂತೆ ಹಿ ಬಿಟಿಸ್ - ಬಿ ಚುಚ್ಚುಮದ್ದು ಹಾಕಿಸಿ ಕೊಳ್ಳವುದು ಮುಖ್ಯ. 6 ಲೆಂಗೆಗಳು ಅಂತರದಲ್ಲಿ 3 ಇಂಜೆಶ್ಶನ್‌ಗಳನ್ನು ಕೊಡಬೇಕು. ಚುಚ್ಚುಮದ್ದು ಹಾಕಿಸಿದ ನಂತರ ದೇಹವು ರೋಗನಿರೋಧಕ ಶಕ್ತಿಯನ್ನು ಪಡೆದು ರೋಗಬರದೇ ನೋಡಿಕೊಳ್ಳುತ್ತದೆ.

95% ಪ್ರತಿಶತ ಹಬ್ಬುವಿಕೆಯನ್ನು ತಡೆಯುತ್ತದೆ.

ಹೆಪಟೈಟಿಸ್ - ಬಿ ಮತ್ತು ನಿಮ್ಮ ಮಗು :

ತಾಯಿಗೆ HBV ಕಂಡುಬಂದಲ್ಲಿ ಜನನಕಾಲದಲ್ಲಿ ಮಗುವಿಗೆ ಮೊದಲನೆಯ ಡೋಜು ಕೊಡಬೇಕು. 1 ತಿಂಗಳ ನಂತರ 2 ನೇ ಡೋಜು ಮತ್ತು 2 ತಿಂಗಳ ನಂತರ 3ನೇ ಡೋಜು ಕೊಡಬೇಕು.

12ನೆ ತಿಂಗಳಲ್ಲಿ ಒಂದು ಬಲವರ್ಧಕ ಡೋಜನ್ನು ಕೊಡಬೇಕು.

ಉಳಿದೆಲ್ಲ ವಯಸ್ಸಿನ ಮಕ್ಕಳಿಗೆ 0-1-6 ರೀತಿಯಲ್ಲಿ ಹಾಕಿಸಬೇಕು.

ಭಾರತೀಯ ಮಕ್ಕಳರೋಗದ ಅಕಾಡಿಮಿಯ ಸಲಹೆ :

ತಾಯಿ ರೋಗಗ್ರಸ್ತ ವಿರಲಿ ಇಲ್ಲದಿರಲಿ ಮಗುವಿಗೆ ಜನನ ಕಾಲದಲ್ಲಿ ಈ ಚುಚ್ಚು ಮದ್ದು ಹಾಕಿಸಲು WHO ಕ್ಕೆ IPA ಯು ಸಲಹೆ ಕೊಟ್ಟಿದೆ.

ಜನನ ಕಾಲದಲ್ಲಿ ಹಾಕಿಸದಿದ್ದರೆ ವೈದ್ಯರ ಸಲಹೆಯ ಮೇರೆಗೆ ಯಾವಾಗಲೂ ಈ ಚುಚ್ಚುಮದ್ದು ಹಾಕಿಸಬಹುದು.

ಪೇಟೆಯಲ್ಲಿ ಈ ಚುಚ್ಚುಮದ್ದು ಎರಡು ರೀತಿಯಲ್ಲಿ ಲಭ್ಯವಿದೆ.

ಮೊದಲನೆಯ ತಲೆಮಾರು :

ಪ್ಲಾಸ್ಮಾದಿಂದ ತಯಾರಿಸಿ ಅಭಿವೃದ್ಧಿ ಹೊಂದಿದ ರಾಷ್ಟ್ರಗಳಲ್ಲಿ ಬಳಸುವಂತಹುದು.

ಎರಡನೆಯ ತಲೆಮಾರು :

r-DNA ತಂತ್ರಜ್ಞಾನದಿಂದ ತಯಾರಿಸಿದ್ದು. ಈ ದೀಗ ಭಾರತದಲ್ಲಿ ಮೊಟ್ಟಮೊದಲಿಗೆ ಶಾಂತಾ ಬಯೋಟಿಕ್‌ನಿಕ್ಸ್‌ರವರು r-DNA ಹಿಪಾಟಿಟಿಸ್-ಬಿ ಚುಚ್ಚುಮದ್ದುನ್ನು ತಯಾರಿಸಿದ್ದಾರೆ. ಇದರಲ್ಲಿ ರಕ್ತ ಮತ್ತು ಅದಕ್ಕೆ ಸಂಬಂಧಿಸೆ ಯಾವುದೆ ಪದಾರ್ಥಗಳನ್ನು ಉಪಯೋಗಿಸಿಲ್ಲ.

ಹೆಪಟೈಟಿಸ್ - ಬಿ ಮತ್ತು ಶಾಂತಾ ಬಯೋಟಿಕ್‌ನಿಕ್ಸ್ :

ಹೊರದೇಶಗಳಿಂದ ಈ ಚುಚ್ಚುಮದ್ದು ತರಿಸಿಕೊಳ್ಳುವ ಬೆಲೆ ಜಾಸ್ತಿಯಾಗುವುದರಿಂದ ಇದನ್ನು ರಾಷ್ಟ್ರಯ ರೋಗ ನಿರೋಧಕ ಯೇಜನೆಯಲ್ಲಿ ಸೇರಿಸಿಲ್ಲ. ಆದರೆ ಶಾಂತಾ ಬಯೋಟಿಕ್‌ನಿಕ್ಸ್‌ದವರು ತಯಾರಿಸಿದ್ದಾರೆ. ಸಾಮಾನ್ಯ ಮನುಷ್ಯನಿಗೂ ತಲುಪುವಂತಿರುವ ಜಗತ್ತಿನಲ್ಲೆ ಶ್ರೇಷ್ಠ ಚುಚ್ಚು ಮದ್ದು ಇದಾಗಿದೆ.

ಹೆಪಟೈಟಿಸ್ - ಬಿ ಯ ಚುಚ್ಚು ಮದ್ದಿನಬಗ್ಗೆ ಸಂಬಂಧಿಸಿದಂತೆ ನಿಮ್ಮ ಸನ್ನಿಹೆದ ವೈದ್ಯರನ್ನು ಹೆಚ್ಚಿನ ಸಲಹೆಗಾಗಿ ಭೇಟಿಯಾಗಿರಿ.

ಸಾರ್ವಜನಿಕ ಹಿತಾಸಕ್ತಿಗಾಗಿ ಹೊರಡಿಸಿದ್ದು :

SHANTHA BIOTECHNICS PVT. LTD.
Plot No. 1355 C, Road No. 45,
Jubilee Hills,Hyderabad - 500 033.
Ph: 213010, 238843 Fax : +91-40-248476

ಹೆಪ

ನಿಮ

ಯು

Man Publications, Ph : 3315547

ಹೆಪಟೈಟಿಸ್ - ಬಿ: ಒಂದು ರೋಗ -

''ಹೆಪಟೈಟಿಸ್ -ಬಿ'' ವೈರಸ್ (HBV) ನಿಂದ ಸಾಂಕ್ರಾಮಿಕವಾಗಿ ಹರಡುವ ರೋಗ - ಹೆಪಟೈಟಿಸ್ - ಬಿ. ಒಬ್ಬರಿಗೆ ಅಸ್ಮಿಕವಾಗಿ ಬಂದರೆ ಇನ್ನೊಬ್ಬರಿಗೂ ಹರಡುವಂತಹುದು. ಇದು ಯಕೃತ್ತನಲ್ಲಿರುವ ಜೀವಕೋಶಗಳ ನಾಶಮಾಡುವುದರ ಮೂಲಕ ಯಕೃತ್ತಿನ ಸಿರೋಸಿಸ್ ಇಲ್ಲವೆ ಯಕೃತ್ತಿನ ಕಾನ್ಸರ್ ಆಗಿ ಪರಿಣಮಿಸುವುದು.

ಹೆಪಟೈಟಿಸ್ - ಬಿ ಮತ್ತು ಎಡ್ಸ್ :

- ಹೆಪಟೈಟಿಸ್ - ಬಿ ಎಡ್ಸ್ (AIDS) ಗಿಂತ 350 ಪಟ್ಟು ಹೆಚ್ಚು ಸಾಂಕ್ರಾಮಿಕವಾದುದು.
- ★ ಪ್ರತಿವರ್ಷ ಎಡ್ಸ್ ಗಿಂತ ಹೆಚ್ಚಾಗಿ ಹೆಪಟೈಟಿಸ್ - ಬಿ ಯಿಂದ ಹೆಚ್ಚು ಜನ ಸಾಯುತ್ತಾರೆ.

ಭಾರತದಲ್ಲಿ ಹೆಪಟೈಟಿಸ್ - ಬಿ

- ★ 20 ಭಾರತೀಯರಲ್ಲಿ ಒಬ್ಬ ಹಿಪಟೈಟಿಸ್ - ಬಿ ಯಿಂದ ನೆರಳುತ್ತಿದ್ದಾನೆ.
- ★ ತರುಣರಲ್ಲಿ 1% ಜನ ಹೆಪಟೈಟಿಸ್ - ಬಿ ಯಿಂದ ಸಾಯುತ್ತಿದ್ದಾರೆ.
- ★ 60% ಯಕೃತ್ತಿನ ರೋಗಗಳು 80% ಯಕೃತ್ತಿನ ಕಾನ್ಸರ್ ಗಳು ''ಹೆಪಟೈಟಿಸ್-ಬಿ ಯ ಕೊರತೆಯಿಂದ'' ಕಾಣಿಸಿಕೊಳ್ಳುತ್ತವೆ.

ಹೆಪಟೈಟಿಸ್ - ಬಿ ರೋಗ ಹೇಗೆ ಹಬ್ಬುತ್ತದೆ ?

'ಎಚ್ ಬಿವಿ' ವೆರಸ್ ಗಳ ಜಲಾಶಯಗಳಿಂದೆ ಮನುಷ್ಯರು ಹೆಸರಾಗಿದ್ದಾರೆ. ಮತ್ತು ಇತರ ದೇಹ ದ್ರವಗಳಾದ ವೀರ್ಯ, ಯೋನಿದ್ರವಗಳು, ಗಾಮಗಳು ಇತ್ಯಾದಿಗಳು ಮೂಲಕ ಇದು ಹಬ್ಬುತ್ತದೆ.

ಒಬ್ಬರಿಂದ ಇನ್ನೊಬ್ಬರಿಗೆ ಸೇರಿಕೊಳ್ಳುವ ಈ ರೋಗ ನಾಲ್ಕುದಾರಿ ಗಳೆಂದರೆ -

ಅ) ಒಬ್ಬರಿಂದ ಇನ್ನೊಬರಿಗೆ ರಕ್ತಕೊಡುವಾಗ - ರೋಗಗ್ರಸ್ತ ರಕ್ತ ಮತ್ತು ಇತರ ಪದಾರ್ಥಗಳ ಜತೆಗೆ.

- ಇಬ್ಬರು ಅಥವಾ ಹೆಚ್ಚು ಜನ ಒಂದೇ ಸಿರಿಂಜು ಮತ್ತು ಸೂಜಿ ಗಳನ್ನು ಉಪಯೋಗಿಸುವುದರಿಂದ
- ಹಚ್ಚೆ ಮತ್ತು ಸೂಜಿ ಚಿಕಿತ್ಸೆ ಮಾಡಿಸಿಕೊಳ್ಳುವು ದರಿಂದ.

ಬ) ಒಬ್ಬರಿಂದ ಇನ್ನೊಬ್ಬರ ಸಂಪರ್ಕದಿಂದ

ಕ) ರೋಗಗ್ರಸ್ತ ತಾಯಿಯಿಂದ ಮಗುವಿಗೆ ಜನನ ಕಾಲದಲ್ಲಿ

ಡ) ಲೈಂಗಿಕ ಸಂಪರ್ಕದಿಂದ (HIV ಗಿಂತಲೂ ಹೆಚ್ಚು ಸುಲಭವಾಗಿ ಈ ವೈರಸ್ ಹಬ್ಬಬಹುದು).

ಈ ರೋಗ ಕಾಣಿಸಿ ಕೊಳ್ಳುವ ಜನರು :

ಅ) ಆರೋಗ್ಯ ಕೇಂದ್ರದ ಉದ್ಯೋಗಿಗಳು

ಬ) ಮೇಲಿಂದ ಮೇಲೆ ರಕ್ತವನ್ನು ಪಡೆಯುವ ಅಥವಾ ಡಯಾಲಿಸಿಸ್ ನ ಪ್ರಯೋಗಕ್ಕೆ ಒಳಗಾದ ರೋಗಿಗಳು

ಕ) HBV ಹೊಂದಿದ ಜನಿಸಿದ ಮಗುಗಳು.

ಡ) HBV ಹೊಂದಿರುವ ಕುಟುಂಬದ ಸದಸ್ಯರು ವೇಶ್ಯೆಯರು.

ಇ) ವೇಶ್ಯಯರು

ಈ) ಸ್ವಲಿಂಗರತಿ ಮತ್ತು ಅನೇಕರ ಜತೆ ಲೈಂಗಿಕ ಸಂಬಂಧ ಹೊಂದಿ ದವರು.

ಗ) ಮತ್ತು ಬಳಿಸುವ ಇಂಜೆಕ್ಸನ್ ತೆಗೆದುಕೊಳ್ಳುವವರು.

ಚ) ಸರಣಿ ಆಟಗಳನ್ನು ಆಡುವವರು.

ಛ) ಹಚ್ಚೆ ಮತ್ತು ಸೂಜಿಚಿಕಿತ್ಸೆ ಹಾಕಿ ಹಿಸಿಕೊಳ್ಳುವವ.

ಜ) ಹಾಸ್ಟೆಲ್ ಗಳಲ್ಲಿ ಇರುವವರು.

ಝ) ಮೇಲಿಂದ ಮೇಲೆ ಪ್ರವಾಸಮಾಡುವವರು.

ಮಕ್ಕಳಲ್ಲಿ ಈ ರೋಗ ಕಾಣಿಸಿ ಕೊಳ್ಳುವ ಬಗೆ :

HBV ವೈರಸ್ ಮಕ್ಕಳಲ್ಲಿ ಕಾಣಿಸಿಕೊಳ್ಳುವ ಅಥವಾ ಹರಡುವ ರೀತಿ ಎರಡು ತರವಾಗಿದೆ. ರೋಗಗ್ರಸ್ತ ರಕ್ತ ಮತ್ತು ದೇಹದ್ರವಗಳಿಂದ.

ಅ) ತಾಯಿಯಿಂದ ಮಗುವಿಗೆ ಜನನಕಾಲದಲ್ಲಿ ನೇರವಾಗಿ ಬರುವ ಸಂಭವವಿದೆ.

ಬ) ಮಗುವಿ
ಮೂಲ

15 ವರ್ಷಗಳ
ಕೊಳ್ಳುವುದು ಹ
ತುಂಬಾ ಅಪಾ

HBV ಮಕ್ಕಳ

ಬಹಳಷ್ಟು ಮಕ್
ದಿಲ್ಲ. ಬಾಹ್ಯ ಲ
ಬ್ಬರಿಗೆ ಈ ರೋ
ಸಿರೋಸಿಸ್ ಅ
ನಾಲ್ಕು ಜನರ

ಹೆಪಟೈಟಿಸ್ -

ಬಾಹ್ಯ ಲಕ್ಷಣಗ
ಎಂದು ಕರೆಯ
ಬಹುದು.

ಆರಂಭಿಕ

ಹಸಿವೆಯಿಲ್ಲದಿ
ದಣಿವು ಆಗುವ
ಚಳಿ ಮತ್ತು ಜ್ವ
ದೇಹದ ನೋ

ಬಹಳಷ್ಟು ರೋ
ವರು; ಆದರೆ
ರೋಗವಾಗಿ
ಜೀವ ಸಾಗಿಸ

ಹೆಪಾಟೈಟಿಸ್

ಹೆಪಾಟೈಟಿಸ್
ತಿಳಿಯುವುದು

DIS 16a.27

REGISTERED

No. 1/C-2N/98-DC.

From :

The Drugs Controller (India)
Directorate General of Health Services

To :

M/s Cadila healthcare Limited
244, 1Ghedasar, mganinagar, Ahmedabad-38008

New Delhi, dated the

6 MAY 1998

Sub. :—Import Licence under the Drugs Act, 1940 and Drugs Rules thereunder.

Dear Sir/Sirs.

With reference to your application for import licence forwarded to this office with your letter No.....nil..... .....datec..29.4.98.....I enclose licence(s) No. 1009 ..... dated ..... 6 MAY 1998 This/these licence(s) has/have been granted under the Drugs Act: 1940 and the Rules thereunder.

2. I am to point out that the provisions of the Drugs Act 1940 are in addition to and not derogration of any other law for the time being in force and as such the licences issued under Drugs Act will be in addition to and distinct from any licences which may be necessary under the Import Trade Control Regulations made of the Government of India, Ministry of Commerce

3. The Import Licence(s) mentioned in para 1 above will not accordingly to itself themselves be sufficient authority for import of the drugs covered by that those licences if under the Import Trade Control Regulations of the Commerce Ministry separate licences are required for Import of such drug(s).

4. I am therefore to advise you to obtain, where necessary licences for import of drugs in question under the Import Trade Control Regulations.

5. Any literature or packing accompanying the drug or any matter stated on the label should not contravene the provisions of the Drugs and Magic Remedies (Objectionable Advertisement) Act.

6. The Assistant Drugs Controller (India), and Technical Officer of the Central Drugs Control Organisation at the ports will be officers authorised to Inspect the premises of importers establishments for the purpose of Rule 26 of the Drugs Rules.

7. Please acknowledge receipt of this letter and its enclosures.

Yours faithfully,

R. Narasimha

for Drugs Controller (India)

REGISTERED

No. 1/S-2N/98-DC.

Dated the

Copy together with a copy of Licence No. 1009 ..... dated .....

1. Asst. Drugs Controller (India), New Customs House Fort Bombay.
2. Asst. Drugs Controller (India), Customs House Calcutta.
3. Asst. Drugs Controller (India), Customs House, Madras.
4. The Asstt. Drugs Controller (India), Customs House, Indira Gandhi International Airport, New Delhi.
5. Technical Officer, C.D.S.C.O., Customs House, Cochin.

THE DRUGS AND COSMETICS RULES, 1945

(See Rule 27) FORM-10

LICENCE TO IMPORT BIOLOGICAL AND OTHER SPECIAL PRODUCTS SPECIFIED IN SCHEDULES C AND C (I) TO THE DRUGS AND COSMETICS RULES, 1945

Number of Licence 1009

(1) M/s Cadila Health Care Limited of Ahmedabad is/are hereby licenced to import into India during the period for which this licence is in force, the drugs specified below, manufactured by M/s Korea Green Cross Corp. 1465-4 Seocho-dong, Secocho-ky, Seoul, Korea. of Korea. and any other drugs manufactured by M/s Korea Green Cross Corp. as may from time to time be endorsed on this licence.

(2) This is subject to the conditions prescribed in the Drugs and Cosmetics Rules, 1945 and shall be in force from 6 MAY 1998 to 31 DEC 1999 unless it is sooner suspended or cancelled under the said Rules.

(3) The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

NAMES OF DRUGS AND CLASSES OF DRUGS TO WHICH THE LICENCE APPLIES

SCHEDULE 'C'

RECOMBINAT DNA HEPATITIS B VACCINE.

Item(one=)only.

XX Shelf life of vaccine = 26 months from the date of manufacture.

Storage - 2° to 8°C

You should comply all the conditions as given in New Drug Permission letter No.12-30/86-DC dated 28.4.98.

R. Narayana Swamy

LICENSING AUTHORITY

for Drugs Controller (India)

Directorate General of Health Services

NEW DELHI

Date 6 MAY 1998

8. RESULTS - SAFETY

32 volunteers were included for safety analysis

Adverse events

Clinical Variables

The adverse events have been listed in Table 6 . Two vaccinees have experienced flu like symptoms and pain at injection site.

Table 6 : ADVERSE REACTIONS

Serial Number	Adverse Reaction	Drugs used
1	Mild pain at injection site on Day 0	
20	Mild pain at injection site on Day 0	Crocin
23	Mild pain at injection site on Day 30 lasting for 6 hrs	
25	Fever - Flu like symptoms lasting for 10 hrs	Crocin
42	Itching at injection site Flu like symptoms on all three vaccinations	Combiflam

Laboratory Investigations

All the laboratory values have been converted to SI units before assessment .

Laboratory abnormalities are assessed based on the predefined changes as mentioned in "Method of Investigations" . None of the laboratory values have shown clinically significant noteworthy changes (Table 7) based on the predefined change criteria

Table 7 : Laboratory Variables

Parameter	Pre Vaccination	Post vaccination
	Mean ± S.E	Mean ± S.E
Hematology		
Hemoglobin (mmol/l	8.24 ± 0.13	8.06 ± 0.08
Leucocytes (G/L)	7.18 ± 0.22	7.24 ± 0.11
Biochemistry		
Serum Creatinine (µmol/L)	74.98 ± 3.25	65.93 ± 2.55
Serum bilurubin total (µmol/L)	12.73 ± 0.21	14.61 ± 0.68
Alkaline Phosphatase (IU/L)	60.37 ± 2.81	58.75 ± 2.78
SGOT (IU/L)	28.93 ± 2.64	24.12 ± 2.09
SGPT (IU/L)	26.33 ± 2.33	19.92 ± 2.05

10. SUMMARY AND CONCLUSIONS

A number of studies have been undertaken with KGCC's Hepavax-Gene in different countries like Korea, Vietnam, Turkey etc and registration of the product has been proceeded in various other countries like Indonesia, Malaysia , Thailand , Phillipines , Vietnam , Cambodia , Iran , Bangladesh , Brazil , Chile etc.

The seroprotective rate of the vaccine seems to be extremely satisfactory with very few adverse events reported and that too non serious like pain at injection site and flu like symtoms lasting for few hours.

Nguigen trong hieu et al in a study in vietnam has assessed the safety and immunogenicity of the vaccine in infants with a dosing schedule of 0 , 1, 2 months. They reported an immune protection in 97 % of the vaccinees with a geometric mean of 446.5 mIU/ml and a median of 418 mIU/ml which is very much similar to our study results in adults.

Lee kye Hein in a korean study used a vaccination schedule of 0, 1 , and 6 months and reported similar seroprotective rate of about 95.7 %

In both the studies i.e adults (0,1, 6 mths) and infants (0,1,2mths) schedules the immunoprotective rate is similar which is greater than 95 %.

Apart from KGCC's vaccine Smithkline beecham markets yeast derived (Saccharomyces Cervisae) recombinant hepatitis vaccineThe effectiveness of this vaccine was demonstrated by many researchers. Dientag et al reported 94 % Jilg et al 93% and Davidson et al 98% in different study populations.

In both the type of vaccines adverse events are very minor and no vaccinee had to discontinue vaccination because of adverse drug events.

KGCC has developed yeast derived hepatitis vaccine using Hansenula Polymorpha system which has an improved productivity and plasmid stability and no hyperglycosylation problem.

The present study also confirms the vaccine's efficacy giving a seroprotective rate of 100 % and geometric mean of 503.50 mIU/ml

A comparative analysis of the current study and an International study done in UK is presented in table 5

The results show that the range of seroconversion in our study being 46.2 to 3204.3 mIU/ml with a median value 587.4 mIU/L .The mean values are not statistically significant from UK study of 450.82 mIU/L.($p=0.44$)

The adverse events documented in both the studies are minor such as pain or itching at injection site for a day

In conclusion it can be stated that KGCC's vaccine is not only effective but safe as well with very few nonserious adverse events and without causing any laboratory abnormalities and is a good suppliment to the existing vaccines in order to the increased demand.

This study was conducted and reported in compliance with:

1) Declaration of Helsinki (1964).
2) Good clinical practice for Trials on medicinal products in European Community.
3) ICH guidelines.

The undersigned confirm that this report appropriately reflects the findings and conclusions of this clinical study.

(Clinical project manager, *study coordinator*)

(Biometrician)

10.12.97

(Principal Investigator)

FACSIMILE

WORLD HEALTH ORGANIZATION
CH - 1211 GENEVA 27 - SWITZERLAND
Telegr.: UNISANTE GENEVA
Tel.: 41 (22) 791 2111 Telex: 415416
FACSIMILE: 41 (22) 791 0746

GLOBAL PROGRAMME FOR VACCINES AND IMMUNIZATION
Tel: 41 (22) 791 4798/4804
FACSIMILE: 41 (22) 791 4889/4192
GPV Internet address: GPV@who.ch
Internet address: leejw@who.ch

Message No. ..... Page 1 of 1 pages Date 6 November 1997

From: Director, Global Programme for Vaccines and Immunization

To: Mrs Veronica Li-Frankenstein
Director, Supply Division
UNICEF (Denmark)
Copenhagen

Fax No.: 45 35 27 35 04

Our ref.: VSQ/Ndfax19/kol

Subject:

TEXT

Dear Dr Li-Frankenstein,

We are pleased to inform you that, following review of documentation, testing of samples, audit of the manufacturing facilities, and receipt of further documentation to proof safety of the vaccine and adequate implementation of recommendations for compliance with GMP, Hepatitis B recombinant vaccine manufactured by Korea Green Cross Corporation (trade name: Hepavax-Gene) has been found acceptable in principle for purchase by UN agencies.

With best regards.

Signed: Dr J. W. Lee
Director, GPV

Copies to:

Ms Nelly Escobar-King, Chief Technical Services Centre, Supply Division, UNICEF	Fax: 45 35 26 94 21
Mr John Gilmartin, Supply Division, UNICEF	Fax: 45 35 26 94 21
Mr Hyuk Soo Kwon, Supply Division, UNICEF	Fax: 45 35 26 94 21
Dr Ciro de Quadros, AMRO	Fax: 1 001 202 974 32 47
Dr Gabor Szalay, WHO Supply Division	Fax: 4196
Mr Jee Han, Director of International Affairs, KGCC	Fax: 82 2 584 9802
Regional Director, WPRO	Fax: 632 521 10 36
Mr Chris Maher, Technical Officer, EPI, WPRO	Fax: 632 521 10 36
Dr I. K. Kim, Senior Pharmacist, Division of Pharmaceutical Affairs	Fax: 822 521 13 01

SAFE GUARD YOUR FAMILY FROM JAUNDICE (HEPATITIS-B) " THE SILENT KILLER "

Facts about Hepatitis-B

- Caused by HEPATITIS-B virus
- It is a disease that causes inflammation of liver leading to liver cancer
- Two million people die due to this disease every year.
- 60% of liver diseases and 80% of liver cancer are due to this disease
- The infection does not show up till it reaches the advanced stage.
- Cost of treatment is around Rs. 1,00,000 - and the success rate is only 30%.
- Prevention is the only way out and prevention is through vaccination.
- ADULTS ALSO MUST BE VACCINATED

In India

- In India, the problem of HEPATITIS-B is much more serious than AIDS
- More number of people die in a day due to HEPATITIS-B than AIDS
- One in every 20 Indian is a carrier of HEPATITIS-B VIRUS
- 45 Million people in India are carriers of this Virus.

Symptoms

Early stage

- Chills
- Poor appetite
- Tiredness
- Mild fever
- Body ache

Late stage

- Joint Pains
- Jaundice
- Yellow coloration of skin and eyes
- Pale faces
- Dark urine

SPREAD BY :

- BLOOD-Sharing razors, Dentists, Transfusion, etc. (Minute volume as small as 0.00004 ml)
- BODY FLUIDS - Saliva, sweat, secretions of wounds.
- INFECTED NEEDLES - Tattooing, acupunture
- From an infected Mother to Child.
- Through sexual contact
- Even accidental contacts with a carrier like helping out a person with a cut or wound.

THE VACCINE

- Produced by Genetically engineered vaccine using recombinant DNA technology which is developed, sophisticated and safe.
- After many tests and clinical trials it is licensed for commercial marketing 18th August 1997.
- No side effects after vaccination

Janapriya Printers, Phone 3350363

This arrived at our doorstep yesterday morning!
13/11/97

EXPERT RECOMMENDATION

World Health organisation (WHO) and Indian Academy of Pediatrics (IAP), Nizam Institute of medical sciences, Central research laboratory, Kasauli (Regulatory requirement of MInistry of Health, Govt. of INDIA) has recommended this vaccine against HEPATITIS-B.

VACCINE SCHEDULE

By vaccination body immune system will provide protection against infection.

3 doses of injection to be taken over a period of six months i.e., (0-1-6) First dose at elected date, second dose a month later, and third dose six months after first dose.

OUR ACTIVITIES :

1st Sunday : Hep.-B-Vacc. at Sanjaynagar, by LCB Industrial town.
2nd Sunday : Hep.-B-Vacc. at Indiranagar by LCB Industrial town and Indiranagar.
3rd Sunday : Hep.-B-Vacc. at Koramangala by LCB Industrial town
4th Sunday : Hep.-B-Vacc. at Sundarnagar, Gokula by RECREATORS®
Now : LIONS CLUB INDUSTRIAL TOWN Conducts mass vaccination camp for children and adults on the THIRD SUNDAY of EVERY MONTH.

Venue : SRI RAGHAVENDRA SWAMY SCHOOL
4th Cross, 5th Block,
KHB Colony,
Koramangala
Bangalore-560 095.

Time : 9 a.m. to 5.30 p.m.

Dates	
1998	1999
NOV 15th	JAN 17th
DEC 20th	FEB 21st
	MAR 21st
	APR 18th
	MAY 16th
	JUN 20th

DO NOT COME ON EMPTY STOMACH

SUBSIDISED RATES

CHILD : Rs. 90 per dose (Below 10 years)
ADULT : Rs. 180 per dose
Only Disposable syringes will be used (FREE)

CAUTION : ALL ADULTS OF EVERY AGE MUST BE VACCINATED.

PEOPLE OF ALL AGES CAN BE INFECTED BY HEPATITIS-B IF THEY ARE NOT VACCINATED. VACCINATION IS THE ONLY WAY OUT.

LIONS CLUB aim at a HEPATITIS-B VIRUS FREE India in few years through intensive vaccination drives.

GET VACCINATED AND SAVE YOURSELF AND YOUR FAMILY'S LIFE.

FOR MORE DETAILS CONTACT : 3414423, 3354946

DIS 16a.19.

SAFE GUARD YOUR FAMILY FROM HEPATITIS-B JAUNDICE

Hepatitis-B Jaundice : Disease of the Liver caused by infectious virus Hepatitis-B. The Hepatitis-B virus damages the Liver tissue leading in some cases to cirrhosis of the liver (Liver Failure) and /or liver cancer. **Hepatitis-B is 350 times more infectious than AIDS. One in every 20 Indians is a carrierof the deadly Hepatitis-B virus**

Mode of Spread : Infected blood and Body fluids like Saliva, Sweat, Secretions of wounds.

High Risk : School Children, Residents of hostels, Frequent travellers, Health Care Professionals, Patients on dialysis, IV drug abusers.

Children at Risk : Infected mother to the infant at the time of birth, children are more exposed to disease due to Scratches & cuts occurring at play, Children below 5 years are worst affected by hepatitis-B Virus Infection.

People at Risk : Sharing Razors, Scissors, Tooth brushes with Carriers, people involved in contact sports.

Treatment: No Full treatment is available for infection. Vaccination alone can prevent the infection in both Adults and Children.

Hepatitis-B Jaundice Vaccination : Three injections to be taken over a period of six months.(0-1-6) first dose, after one month second dose and after Six months 3rd dose.

Experts Recommendation: World Health Organisation (WHO) & Indian Academy of Paediatric Doctors (IAP) has recommended vaccination for Children and adults against Hepatitis-B Jaundice.

LIONS CLUB OF BANGALORE INDUSTRIAL TOWN HAS ORGANISED VACCINATION CAMP FOR CHILDREN AND ADULTS ON FIRST SUNDAY OF EVERY MONTH.

Venue : Rotary Community Hall
No: 4, 31st Cross, 11th Main,
Near Jayanagar 4th Block Complex,
Behind Vijaya Junior College,
Jayanagar, Bangalore -11.

Time : 10 Am to 5 Pm

Dates :

Jan 3rd (99)	June 6th (99)
Feb 7th (99)	July 4th (99)
Mar 7th (99)	Aug 1st (99)
April 4th (99)	Sept 5th (99)
May 2nd (99)	Oct 3rd (99)

Vaccine Type : r-DNA Genetically Engineered Vaccine. No Blood products are used in manufacturing this vaccine. Hence better & Safe vaccine. **Subsidised rates: Child** : Rs. 90 per dose (below 10 yrs) + disposable syringe **Adult** : Rs. 80 per dose + disposable syringe.

Contact : 3383355, 3354946

Dr. Sunil
Shankar B.
Vijaya Innapar
337 8016
Prakash B.

Health of H
Business & People
not business people
People have to
interview

G614855

Enviro Supply Co

38 Reservoir Rd

Next to Rajan's? Basavangudi

B-4

INDIAN MEDICAL ASSOCIATION

BANGALORE BRANCH

HEPATITIS-B IMMUNIZATION PROGRAMME

Hepatitis-B awareness and immunization programme is organised at IMA House, AV Road (Alur Venkata Rao Road) Opp. Minto Eye Hospital, Chamrajpet, Bangalore - 560 018 on Sunday the 11th April 99 between 9 a.m. to 5 p.m.

At Affordable Rates Child : Rs.90/- per dose (below 10 years), Adult : Rs.180/- per dose. Contact : 338 3355, 670 2927

The Programme is organised on 2nd Sunday of Every Month at IMA House

To RRP / Dr. ~~Dr~~ for Hep BV file.

JN 12/4/99

DPJ 12/4/99

INVITATION TO JOIN THE MOVEMENT

History has taught us that whenever the human race was suppressed, a silent movement had begun resulting in the victory of mankind.

In the year 1942, a quiet movement started in India under the able leadership of a 73 year old man, people with respect called him Mahatma. The revolution was non-violent and was aptly called "Quit India Movement" asking the British to leave the country.

Result : 15th August, 1947. The historic day for India. **British surrendered to the Quit India Movement.**

1997, 50 years of India's Independence. India celebrates its achievements in the fields of Science and Technology, Software etc. The Indian Scientist has indigenously developed India's first genetically engineered r-DNA Hepatitis-B vaccine **Shanvac - B.** A new revolution has begun. **Shanvac-B** is being made available at an affordable cost all over India. We all know that Hepatitis-B is a dreadful disease; prevention through vaccination being its only solution. We begin yet another "Quit India Movement", this time against the dreadful Hepatitis-B virus. Let us all join hands in eradicating this dreadful disease from India. We would request you to spread the word of **Shanvac-B,** the cost effective vaccine to one and all who come to you for consultation, consolation, counselling, etc.

Taiwan, a small country was able to eradicate this dreaded virus from their country through mass immunisation. Let us also set an example and say **"Quit India to Hepatitis-B Virus".**

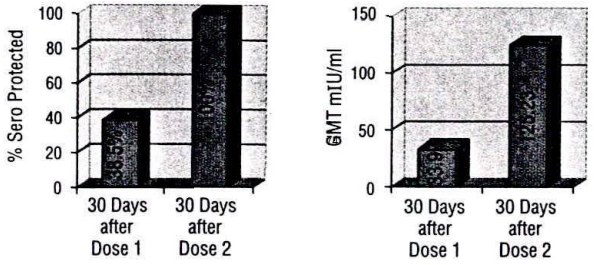
K. I. VARAPRASAD REDDY
Managing Director

Shanvac-B
r-DNA Hepatitis-B Vaccine

SAFE & EFFECTIVE IN NEONATES & CHILDREN

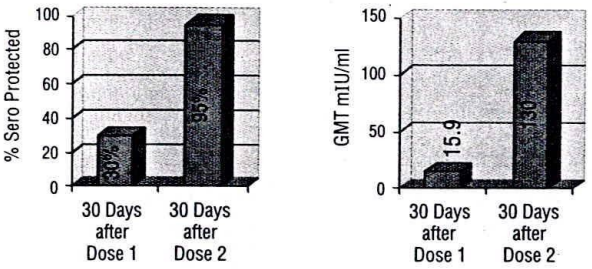
CLINICAL STUDY IN NEONATES.
(0-1-2 MONTHS SCHEDULE)

STUDY CENTRE : Deccan Medical College & Research Centre, Hyderabad.
STUDY PERIOD : Dec '97 - Feb '98



CLINICAL STUDY IN CHILDREN OF AGE 2-10 YEARS
(0-1-6 MONTHS SCHEDULE)

STUDY CENTRE : Nizam's Institute of Medical Sciences, Hyderabad.



SWADESHI **Shanvac-B**
THE SOLUTION TO A SILENT KILLER

DIS 16a.24.

DR. M. NAGARAJ RAO
MD.,DCH.,FIAP.,FCGP
CONSULTANT PAEDIATRICIAN & NEONATOLOGIST & H.O.D. NEONATOLOGY - O.H.R.C.
PROF. OF PEDIATRICS - D.C.M.S., HYDERABAD.
MEMBER : CO ORDINATION COMMITTE ON IMMUNIZATION PROGRAMME
(INDIAN ACADEMY OF PAEDIATRICS)
PRESIDENT : NATIONAL NEONATOLOGY FORUM - A.P. STATE
RESOURCE PERSON FOR : UNICEF (SOUTH EAST INDIA)
CARE (A.P. PROJECTS)
WORLD BANK - ICDS PROJECT, FAMILY PLANNING ASSOCIATION; SCHOOL HEALTH SERVICES - A.P.
FORMERLY : PROFESSOR OF PAEDIATRICS & NEONATOLOGY
OSMANIA MEDICAL COLLEGE & NILOUFER HOSPITAL
FOR CHILDREN & WOMEN, HYDERABAD.
GANDHI MEDICAL COLLEGE, HYDERABAD.
KAKATIYA MEDICAL COLLEGE, WARANGAL.
PRINCES DARU SHEHVAR HOSPITAL, HYD.

INTERIM RESULT

CLINICAL STUDY OF SHANVAC-B IN NEONATES

21 Subjects in the neonatal age group (less than 1 year) were administered Shanvac-B (5mcg in 0.25 ml) intramuscularly in the antero-lateral thigh region.

Results of seroconversion after dose I (i.e. 30 days after vaccination) were 90%. Protective seroconversion (i.e. > 10mIU/ml) was 38% with Geometric mean titre at 43.3 mIU/ml.

Subjects have been administered the II dose and blood samples will be collected before administering III dose.

There were no adverse reactions observed or reported in the subjects who received Shanvac-B.

Dr. M. Nagaraj Rao
M.D., D.C.H., F.I.A.P., F.C.G.P.
H.O.D. PEDIATRICS & NEONATOLOGY
OWAISI MEDICAL & RESEARCH CENTRE
KANCHAN BAGH, HYDERABAD A.P.

ADDRESS FOR COMMUNICATION : "SRIVATSA" A/24, SANTOSHNAGAR, D.M.R.L., ROAD,
HYDERABAD - 500 059. A.P. INDIA.
TEL : RES : 4530194/4531962, HOSP : 4443129 EXT. 270 & 223

Hepatitis B scare exploitation of gullible people, say experts

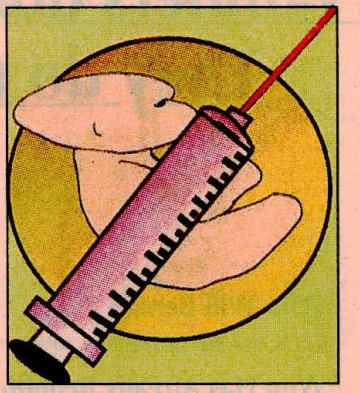
By Laiqh A Khan
DH News Service

BANGALORE, March 2

Even as the Hepatitis B scare stalks the City, a section of medical experts along with the Bangalore branch of the Indian Medical Association (IMA) and the Drug Action Forum (DAF) have taken a strong stand against the projection of the anti-Hepatitits vaccination as a necessity for every individual. They have termed it "commercial exploitation of gullible people".

Though some doctors here underscore the enormity of threat posed by the Hepatitis B virus and recommend the vaccination, which is being carried on in a big way by medical and voluntary organisations, others favour restriction of compulsory vaccination to 'high risk' categories and infants.

Hepatitis B, a virus, which causes inflammation of the liver, is described by medical experts as "more infectious than Aids". India has an estimated 45 million people infected with Hepatitis B virus, which is about 5 per cent of the



Hepatitis B can spread through blood transfusion

population. Approximately 5 to 10 per cent of the infected people become carriers and suffer chronic liver disease, cirrhosis and possibly liver cancer, says the American Liver Foundation.

The virus is transmitted through blood and other body fluids (such as semen, vaginal secretions, breast milk, tears, saliva and open sores).

Doctors who are against the vaccination campaign argue that the general public do not fall under the high-risk category, which mainly comprises persons exposed to blood and body fluids.

"Besides, 90 per cent of the infected adults successfully fight off the virus without the aid of a vaccination," said Professor of Gastro-enterology at M S Ramaiah Medical College, Dr Satyaprakash. "In the case of children, the ratio is reversed. Only 10 per cent of the children have the immunity to clear the virus on their own without a vaccination."

However, he stressed the need to compulsorily vaccinate all newborn babies and children who have not received a dose soon after birth.

The Bangalore branch of the IMA, the DAF and a section of doctors recommend vaccination only

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Subject: Packet from Dr. Thelma for Deena and TJ
Date: Thu, 14 Jan 1999 14:52:08 +0530
From: "Other Media" <admin@del3.vsnl.net.in>
To: <sochara@blr.vsnl.net.in>

Dear Dr. Thelma,

Deendayalan, Tarnjit have just received the packet you sent.

Regards,

Sunita

file
JN
19/1

19/1/99

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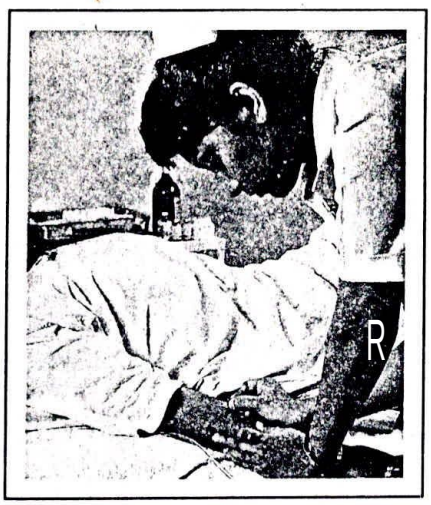
18/1/99



Hepatitis B virus transmitted through infected blood and body fluids is responsible for one out of two cases of chronic hepatitis and eight out of ten cases of primary liver cancer in our country.[1]

With over 4 crore 'carriers' of the virus in our country,[2] your next patient may be a 'carrier'.

Once infected, no effective cure exists.

Do not take chances.

Protect Yourself

Engerix®-B

[Recombinant Hepatitis B Vaccine]

Your Insurance Against Hepatitis B

SUMMARY OF PRESCRIBING INFORMATION

Description: Each 1 ml adult dose contains 20 mcg of hepatitis B surface antigen protein and each 0.5 ml paediatric dose contains 10 mcg of hepatitis B surface antigen protein. **Indication:** Active immunization against hepatitis B virus infection. **Dosage and Administration:** For intramuscular use only. To be shaken well before use. A dose of 20 mcg of antigen protein recommended for adults and children 10 years of age and older. A dose of 10 mcg antigen protein in 0.5 ml suspension is recommended for neonates, infants and children below 10 years of age. Three doses of the vaccine should be given. 1st dose at elected date, 2nd dose - 1 month later and 3 rd dose - 6 months from the date of the first dose. For more rapid immunization the 3rd dose can be given two months after initial dose with a booster at 12 months. It must not be given intravenously. **Contraindications:** Hypersensitive to any components of the vaccine and severe febrile infections. **Precautions:** Vaccination is not recommended for pregnant women. Adrenaline 1 : 1000 should be available for rare anaphylactic reaction. **Adverse Reaction:** Mild transient soreness, erythema and induration at injection site. Occasionally low grade fever, malaise, fatigue, myalgia, arthritis, headache, nausea and dizziness. **Recommended storage and shipment conditions:** The vaccine should be shipped under refrigeration and stored at +2°C to +8°C. DO NOT FREEZE. **Expiry Date:** The shelf life of 'Engerix'-B is three years from the date of manufacture when stored at +2°C to +8°C. The expiry date is shown on the labelling. **Presentation:** Packs of one mono adult dose vial, one mono paediatric dose vial and one multidose vial for vaccinating 10 adults and children above 10 years of age or 20 infants and children below 10 years of age.

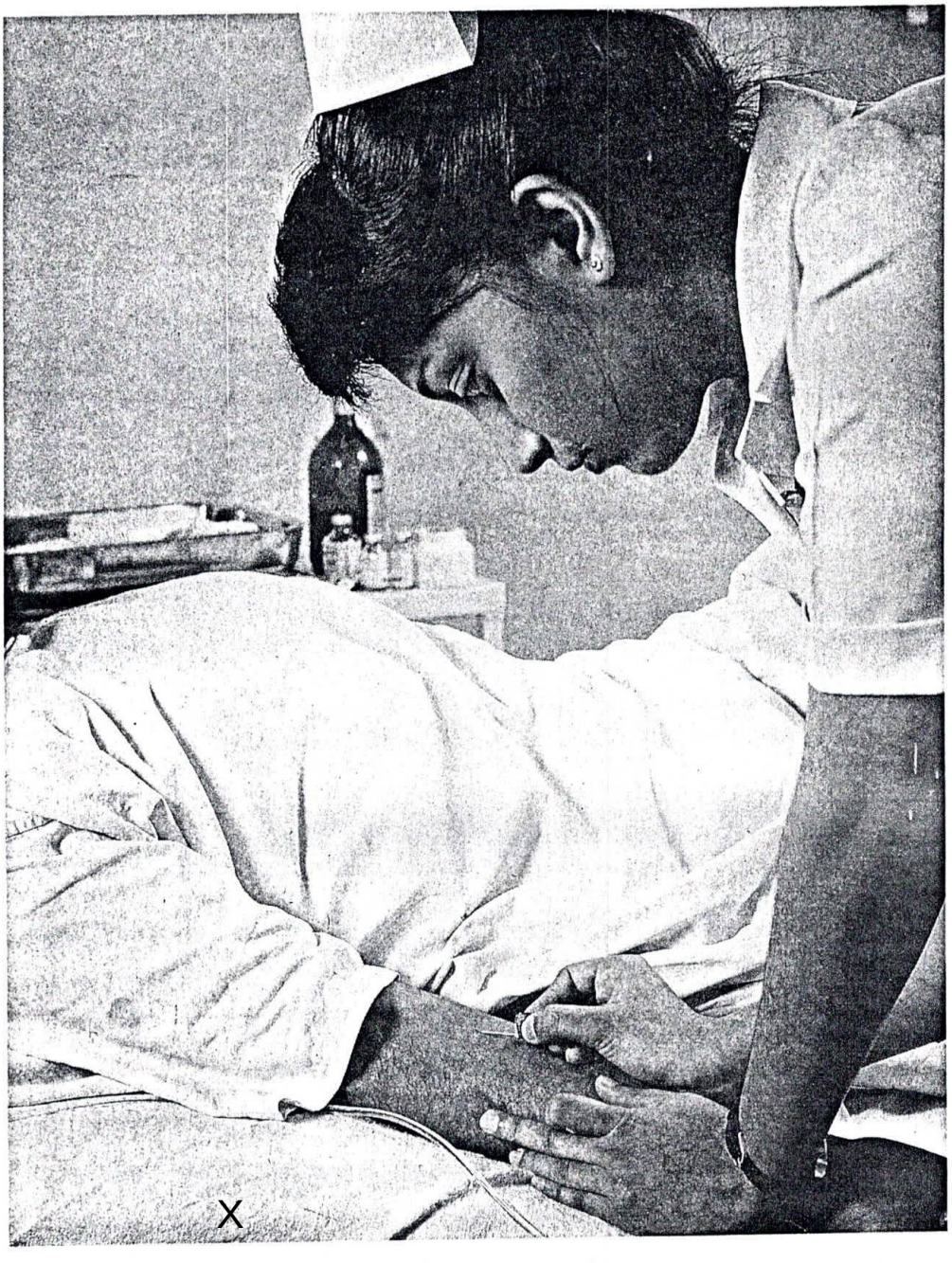
For more information about Hepatitis B and its prevention, please write to Hepatitis B Awareness Centre, P. B. No. 2, Bangalore 560 049

Reference:
1. Aggarwal R, Naik S R. Prevention of hepatitis B infection: The appropriate strategy for India. Natl Med J India 1994; 7(5): 216-20.
2. Tandon BN. Dimensions and Issues of HBV control in India. In Sarin S K, Singal A K, (Eds.) Hepatitis B in India - Problems and Prevention. New Delhi : CBS Publishers & Distributors, 1-4.

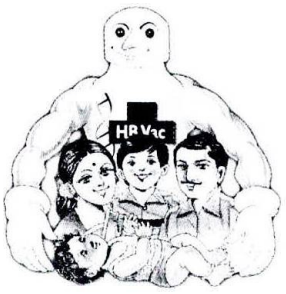
SB SmithKline Beecham Pharmaceuticals

Printed by Modern Process Printers, Bangalore

EXB : H2 : 96A (Nurse)

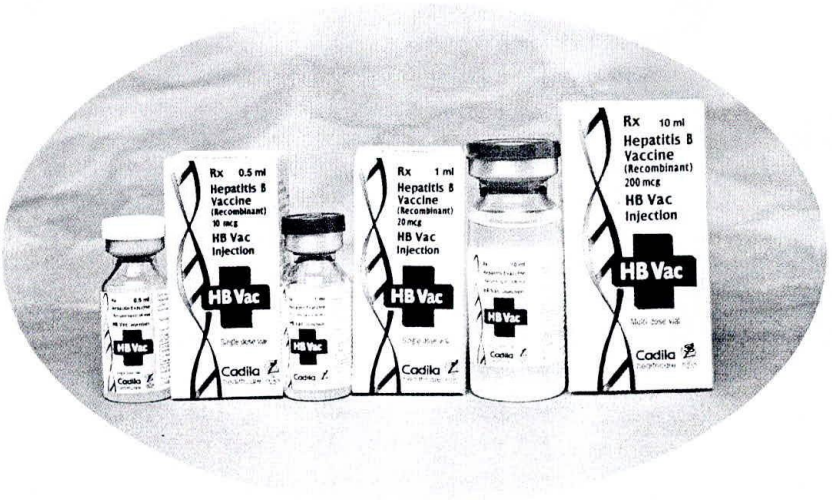


THE HIDDEN ENEMY



"Hepatitis B protection
that you can trust"

HB Vac



녹십자
GREEN CROSS

KOREA GREEN CROSS CORPORATION
1465-4, Seocho-3-dong, Seocho-ku, Seoul, Korea.

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THE ZYDUS GROUP

CADILA HEALTHCARE LIMITED
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agents such as hepatitis A, hepatitis C and hepatitis E and other pathogens known to infect the liver.

The immune response to hepatitis B vaccines is related to a number of factors, including old age, male gender, obesity, smoking habits and route of administration. In subjects who may respond less well to the administration of the hepatitis B vaccine additional doses may be considered.

INTERACTIONS WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTION

'ENGERIX'-B can be given concomitantly with BCG, DTP, DT and/or polio vaccines, if this fits conveniently in an immunization scheme recommended by the country Health Authority.

'ENGERIX'-B can also be administered together with measles-mumps-rubella vaccines, *Haemophilus influenzae* b vaccine and hepatitis A vaccine.

Different injectable vaccines should always be administered at different injection sites.

PREGNANCY AND LACTATION

Pregnancy

The effect of the HbsAg on foetal development has not been assessed. As with all inactivated viral vaccines, the risks to the foetus are considered to be negligible. However, 'ENGERIX'-B should be used during pregnancy only when absolutely indicated.

Lactation

The effect on breast-fed infants after the administration of 'ENGERIX'-B to their mothers has not been evaluated in clinical studies. No contra-indication has been established.

UNDESIRABLE EFFECTS

'ENGERIX'-B is generally well tolerated.

As with other hepatitis B vaccines, in many instances the causal relationship to the vaccine has not been established. Mild transient soreness, erythema and induration at site of injection may occur. Occasionally low grade fever, malaise, fatigue, myalgia, arthritis, headache, nausea and dizziness are reported following vaccination.

SHELF LIFE

The vaccine has a shelf life of 3 years from the date of manufacture. The expiry date of the vaccine is indicated on the label and packing.

SPECIAL PRECAUTIONS FOR STORAGE

The vaccine should be stored at +2°C to +8°C.

DO NOT FREEZE. Discard if the vaccine has been frozen.

INSTRUCTIONS FOR USE/HANDLING

The vaccine should be inspected visually for any foreign particulate matter and/or colouration prior to administration. Before use of 'Engerix'-B, the vaccine should be shaken well to obtain a slightly opaque, white suspension. Discard if the content appears otherwise.

When using a multidose vial, each dose should be taken with a sterile needle and syringe to avoid contamination of the vaccine. The vial can be used till the date of expiry marked on the label / packaging when stored at the recommended storage temperature after each withdrawal.

PRODUCT NAME

'Engerix'- B

PRODUCT DESCRIPTION

'ENGERIX'-B, hepatitis B vaccine is a sterile suspension containing the purified surface antigen of the virus manufactured by recombinant DNA technology, adsorbed onto aluminium hydroxide.

The antigen is produced by culture of genetically-engineered yeast cells (*Saccharomyces cerevisiae*) which carry the gene which codes for the surface antigen of the hepatitis B virus (HBV). This hepatitis B surface antigen (HBsAg) expressed in yeast cells is purified by several physico-chemical steps.

The vaccine is highly purified, and meets the WHO requirements for recombinant hepatitis B vaccines. **No substances of human origin are used in its manufacture.**

COMPOSITION

Adult Dose	20 mcg of hepatitis B surface antigen in 1.0 ml suspension.
Paediatric Dose	10 mcg of hepatitis B surface antigen in 0.5 ml suspension.

INDICATIONS

'ENGERIX'-B is indicated for active immunization against hepatitis B virus (HBV) infection caused by all known subtypes in subjects of all ages considered at risk of exposure to HBV. Immunization against hepatitis B is expected, in the long term, to reduce not only the incidence of this disease, but also its chronic complications, such as chronic active hepatitis B and hepatitis B associated liver cirrhosis and primary hepatocellular carcinoma.

WHO SHOULD BE VACCINATED?

The Indian National Association for the study of Liver (INASL) recommends routine hepatitis B vaccination for all individuals at risk of acquiring hepatitis B infection.

Group identified by the INSAL for routine hepatitis B vaccination:

- All medical / para-medical personnel
- Medical / Dental / Nursing college students / Laboratory technicians
- Family contacts of chronic liver disease patients.
- Patients frequently receiving blood products.
- Thalassemic / Haemophilic patients.
- Patients undergoing haemodialysis.
- Infants born to mothers who are HBV carriers.
- Alcoholic liver disease patients.
- Chronic renal failure and renal transplant patients.

Since close to 90% of hepatitis B infections in early childhood results in chronic liver disease and hepatocellular carcinoma later in life, the INASL and Indian Academy of Paediatrics recommends routine hepatitis B vaccination of all new-borns alongwith the other childhood vaccines.

DOSAGE

20 mcg dose vaccine is indicated for use in adults and children older than 10 years of age.

10 mcg dose vaccine is indicated for use in children upto 10 years of age, including neonates.

Immunization schedule

A series of three intramuscular injections is required to be administered at definite intervals to achieve optimal protection.

The first dose of the vaccine is to be administered at an elected date, second dose - 1 month after dose one and third dose - 6 months after dose one.

Alternatively, three doses of the vaccine can be administered at 0, 1 and 2 months, to confer rapid protection. A booster should be administered at 12 months from the date of the first dose.This vaccination schedule is recommended for individuals at high risk of acquiring hepatitis B infection.

Booster Dose: It would seem advisable to recommend a booster dose when the anti-HBs antibody titre falls below 10 IU/L (minimum protective antibody titres).

From available data, general recommendations for a booster dose are as follows.

After the 0, 1, 6 month primary immunization schedule a booster dose will probably not be required earlier than 5 years following the completion of the primary vaccination course.

In case of the 0, 1, 2 month immunization schedule followed by a booster dose at month 12, the next booster dose will probably not be required for at least 8 years following completion of the primary vaccination course.

Special dosage recommendations

Dosage recommendation for neonates born to mothers who are HBV carriers.

The immunization with 'ENGERIX'-B (10 mcg) of these neonates should start with the first dose of the vaccine administered at birth followed by dose 2 at one month from dose 1, dose 3 at six months from dose 1.

If available, hepatitiis B immune globulins (HBIg) should be given simultaneously with 'ENGERIX' -B at a separate injection site.

Dosage recommendation for known or presumed exposure to HBV

In circumstances where exposure to HBV has recently occurred (e.g. needlestick exposure to contaminated needle) the first dose of 'ENGERIX'-B can be administered simultaneously with HBIg which, however must be given at a separate injection site. The rapid immunization schedule of months 0, 1, 2 and booster at month 12 should be advised.

Dosage recommendation for chronic haemodialysis patients.

The primary immunization schedule for chronic haemodialysis patients is four doses of 40 mcg (2 x 20 mcg/ vaccine dose) to be administered at interval

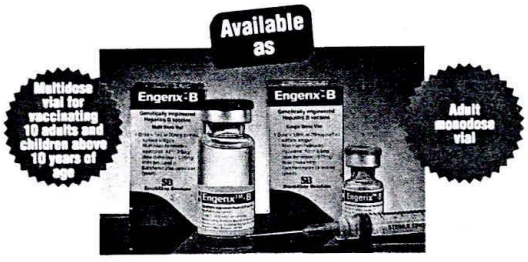
- 'Engerix'-B Multidose vial - 10 doses for vaccinating individuals above 10 years and 20 doses for vaccinating infants and children below 10 years of age.

Q **How is 'Engerix'-B vaccine to be stored ?**

A Like other vaccines, 'Engerix'-B also needs to be stored between +2°C to +8°C in the refrigerator. The vaccine should **not be frozen.** Once frozen, the vaccine should be discarded. The vaccine vial should be shaken well before use.

Engerix™ B
recombinant hepatitis B vaccine

Your Insurance Against Hepatitis B



For Routine Hepatitis B Vaccination of Adults

Engerix™ B
recombinant hepatitis B vaccine
Paediatric Dose

The 7th Childhood Vaccin Against Hepatitis B.

For Routine Hepatitis B Vaccination of Infants/Child

Engerix™ B
recombinant hepatitis B vaccine

Your Insurance Against Hepatitis B

Reference:

1. Aggarwal R, Naik S R. Prevention of hepatitis B infection: The appropriate strategy for India. Natl Med J India 1994; 7(5): 216-20.

SmithKline Beecham
Pharmaceuticals
Devanahalli Road, Off Old Madras Road,
Bangalore 560 049

Printed by : Repromen Offset Printers Pvt. Ltd.

EXB/Q&A:H2:97

SUMMARY OF PRESCRIBING INFORMATION

Description: Each 1 ml adult dose contains 20 mcg of hepatitis B surface antigen protein. **Indication:** Active immunization against hepatitis B virus infection. **Dosage and Administration:** For intramuscular use only. To be shaken well before use. A dose of 20 mcg of antigen protein recommended for adults and children 10 years of age and older. Three doses should be given. 1st dose at elected date, 2nd dose - 1 month later and 3 rd dose - 6 months from the date of the first dose. For more rapid immunization the 3rd dose can be given two months after initial dose with a booster at 12 months. It must not be given intravenously. **Contraindications:** Hypersensitive to any components of the vaccine and severe febrile infections. **Precautions:** Vaccination is not recommended for pregnant women. Adrenaline 1 : 1000 should be available for rare anaphylactic reaction. **Adverse Reaction:** Mild transient soreness, erythema and induration at injection site. Occasionally low grade fever, malaise, fatigue, myalgia, arthritis, headache, nausea and dizziness. **Recommended storage and shipment conditions:** The vaccine should be shipped under refrigeration and stored at +2°C to +8°C. DO NOT FREEZE. **Expiry Date:** The shelf life of 'Engerix'-B is three years from the date of manufacture when stored at +2°C to +8°C. The expiry date is shown on the labelling. **Presentation:** Packs of one mono adult dose vial, one mono paediatric dose vial and one multidose vial for vaccinating 10 adults and children above 10 years of age.

SUMMARY OF PRESCRIBING INFORMATION

Description: Each 0.5 ml dose contains 10 mcg of hepatitis B surface protein. **Indications:** Active immunization against hepatitis B virus infection. To be shaken well before use. A dose of 10 mcg of antigen protein of suspension is recommended for neonates, infants and children below 10 age. For routine immunization, 3 doses of the vaccine should be given; preferably at birth, 2nd dose at 6 weeks and 3rd dose at 6-9 months from the the first dose. Alternatively, 3 doses of 'Engerix'-B can be co-administered w vaccines at 6, 10 weeks and 6 to 9 months of age in case, the 1st dose vaccine could not be administered at birth. For infants born to HBsAg or mothers alongwith the first dose of vaccine at birth, HBIg can be simultaneously at a separate injection site. **Method of Administration:** 'En should be injected intramuscularly in the deltoid region in older children o anterolateral thigh in neonates, infants and young children. It must not b intravenously. **Contraindications:** Hypersensitivity to any components vaccine, severe febrile infections. **Interaction with other medicaments an forms of interaction:** 'Engerix'-B has been administered at the same vaccines of the Expanded Programme on Immunization (DPT, BCG, Meas OPV). DPT, BCG and Measles should always be administered at a different site. **Precautions:** Adrenaline 1 : 1000 should be available for rare anap reaction. **Adverse Reaction:** Mild transient soreness, erythema and indu injection site. Occasionally low grade fever, malaise, fatigue, myalgia, headache, nausea and dizziness. **Recommended storage and sh conditions:** The vaccine should be shipped under refrigeration and stored at +8°C. DO NOT FREEZE. **Expiry Date:** The shelf life of 'Engerix'-B is thre from the date of manufacture when stored at +2°C to +8°C. The expiry date i on the labelling. **Presentation:** Packs of one mono paediatric dose and m vial, for vaccinating 20 infants and children below 10 years of age.

Further information is available on request :
P. B. No. 2, Bangalore 560 049

Q What is Hepatitis B ?

A Hepatitis B is a disease of the liver caused by a virus infection. The virus causes destruction of the liver tissue and may lead to liver cancer later in life. In our country eight in every ten cases of liver cancer is due to Hepatitis B virus infection.[1]

Q How does one get infected with Hepatitis B virus ?

A There are a large number of 'carriers' of the Hepatitis B virus, who appear to be normal and healthy but can transmit the virus to others. Various instruments contaminated with the infected blood or body fluids of such 'carriers' can transmit the virus to a healthy person.

Thus the use of unsterilised needles for injections, ear piercing and tattooing, unsterilised instruments during operation or wound suturing and infected blood used during transfusion can put an individual at high risk of acquiring the Hepatitis B virus.

Q Is Hepatitis B infection a serious problem in India ?

A In India it is found that one in twenty persons[1] in our population is a Hepatitis B virus 'carrier'. Accidental contacts with such 'carriers', who are unaware about the virus they are harbouring, can transmit the virus to others. Hence a constant risk of acquiring this infection, exists in our country.

But there is a definite group of individuals who are at high-risk. They are:

At high-risk due to daily practice

- All Medical Personnel.
- All Para-medical personnel such as Nurses, Staff members of pathology labs, Blood banks, Dialysis units and Cancer units.

At high-risk due to sexual and social habits

- Heterosexuals with multiple sex partners, homosexuals and prostitutes.
- Intravenous drug users.
- People who have themselves tattooed.
- People who play contact sports.

At high-risk due to illness

- Patients like Thalassemics and Hemophiliacs who receive blood or blood related products.
- Patients on dialysis.

Others

- Infants born to Hepatitis B infected mothers.
- Family members of Hepatitis B virus 'carriers'.

Q What are the signs and symptoms of Hepatitis B infection ?

A Majority of infants and children infected with Hepatitis B do not show any signs and symptoms of Hepatitis B infection.

In the case of adults, a small number of individuals may not show any signs and symptoms. The others initially develop flu like symptoms such as:

Loss of appetite
Tiredness
Chills and mild fever
Body ache

And Later

Jaundice - yellowness of skin and eyes
Pale faeces
Dark urine

Q What test needs to be conducted to dete Hepatitis B status ?

A A simple blood test called the Australia a test will help determine whether o infected with the Hepatitis B virus.

Q Is any treatment available for this infec

A Unfortunately no. Only vaccination a the Hepatitis B virus can prevent this infe Recently, interferons have been tried in c selected patients of Hepatitis B and fou have variable results.

Q What is Hepatitis B vaccination ?

A The Hepatitis B vaccination course com of 3 injections to be given at definite int over a period of 6 months. After vaccin the body will be able to produce subst called antibodies which will protect a Hepatitis B infection.

Q What are the different Hepatitis B va available in our country ?

A There are two types of Hepatitis B vac available:

Plasma derived - manufactured using and blood-products and *genetically engi* - where no blood and blood-product used in the manufacture ('Engerix'-B).

Q Is 'Engerix'-B safe ?

A 'Engerix'-B, a genetically engin Hepatitis B vaccine is extensively used v wide and is found to be safe.

Q How effective is 'Engerix'-B ?

A Extensive clinical studies conducted v wide have shown 'Engerix'-B to be effect protecting healthy individuals of all ages borns to elderly) and also imm compromised subjects.

ಡಿ.ಪಿ.ಟಿ, ಅಥವಾ ಟ್ರಿಪಲ್ ಆಂಟಿಜನ್ ಕೊಡಿಸುವ ಸಮಯದಲ್ಲಿ
ಹೆಪಟೈಟಿಸ್-ಬಿ ವ್ಯಾಕ್ಸಿನ್‌ನ್ನು ಕೊಡಿಸಬಹುದು.

ಹೆಪಟೈಟಿಸ್-ಬಿ ಲಸಿಕೆಯನ್ನು ಇಂದೇ ನಿಮ್ಮ

ಮಗುವಿಗೆ ಹಾಕಿಸಿ.

ಇಂದೇ ನಿಮ್ಮ ಡಾಕ್ಟರನ್ನು ತಪ್ಪದೇ ಸಂಪರ್ಕಿಸಿ.

ಮಗುವಿನ ಆರೋಗ್ಯ ದೃಷ್ಟಿಯಿಂದ ಇದನ್ನು ವಿತರಿಸಲಾಗಿದೆ :

SB
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Pharmaceuticals

ಸ್ಮಿತ್‌ಕ್ಲೈನ್ ಬೀಚಮ್ ಫಾರ್ಮಾಸ್ಯುಟಿಕಲ್ಸ್
ಸ್ಮಿತ್‌ಕ್ಲೈನ್ ಬೀಚಮ್ ಫಾರ್ಮಾಸ್ಯುಟಿಕಲ್ಸ್ (ಇಂಡಿಯಾ)
ಲಿಮಿಟೆಡ್
ದೇವನಹಳ್ಳಿ ರಸ್ತೆ, ಆಫ್ ಓಲ್ಡ್ ಮದ್ರಾಸ್ ರೋಡ್
ಪೋಸ್ಟ್ ಬಾಕ್ಸ್ ನಂ. 2, ಬೆಂಗಳೂರು - 560 049.

EXB:PEL2:97 KANNADA Printed by : Rapsonan Offset Printers Pvt. Ltd.

DIS-16.

Hepatitis B.

ನಿಮ್ಮ ಮಗುವನ್ನು ಹೆಪಟೈಟಿಸ್-ಬಿ ನಿಂದ ಸಂರಕ್ಷಿಸಿ

ಕಾಮಾಲೆ ರೋಗ (ಜಾಂಡೀಸ್) ಸಂಭವಿಸುವುದರ ಬಗ್ಗೆ ಜನರಿಗೆ ನೂರಾರು ವರ್ಷಗಳಿಂದ ತಿಳಿದಿದೆ. ಆದರೆ ಕಾಮಾಲೆ ರೋಗ ಯಾವ ಯಾವ ಕಾರಣಗಳಿಂದ ಬರುತ್ತದೆ ಎಂಬುದು ವಿವರವಾಗಿ ತಿಳಿದುಬಂದಿದ್ದು ಈ ಶತಮಾನದಲ್ಲಿ ಮಾತ್ರ. ಇದೆಲ್ಲಾ ಸಾಧ್ಯವಾದದ್ದು ವೈದ್ಯಕೀಯ ವಿಜ್ಞಾನದಲ್ಲಿ ಆದ ಪ್ರಗತಿಯಿಂದ.

ಕಾಮಾಲೆರೋಗ(ಜಾಂಡೀಸ್) ಬರಲು ಬಹು ಮುಖ್ಯವಾದ ಕಾರಣವೆಂದರೆ ಹೆಪಟೈಟಿಸ್ ವೈರಸ್. ಇದಕ್ಕೆ ಎರಡು ಮುಖಗಳಿವೆ. ಒಂದು ಈ ಖಾಯಿಲೆಗೆ ಕಾರಣ ವೈರಸ್ ಎಂಬುದು, ಮತ್ತೊಂದು ಇದರ ಪರಿಣಾಮವಾಗಿ ಲಿವರ್ ತೊಂದರೆಗೊಳಗಾಗಿ ಬೆಂಕಿಯಂತೆ ಉರಿಯುತ್ತದೆ ಎಂಬುದು.

ಆದರೆ ಜನರಲ್ಲಿ ಬೇರೂರಿರುವ ನಂಬಿಕೆಯೇನೆಂದರೆ ಲಿವರ್‌ಗೆ ಸಂಬಂಧಪಟ್ಟ ಖಾಯಿಲೆಗಳೆಲ್ಲ ಆಲ್ಕೋಹಾಲ್ ಅತಿಯಾಗಿ ಉಪಯೋಗಿಸುವುದರಿಂದ ಬರುತ್ತದೆ ಎಂದು. ಸತ್ಯ ಸಂಗತಿಯೇನೆಂದರೆ 80%ರಷ್ಟು ಲಿವರ್‌ಗೆ ಸಂಬಂಧಪಟ್ಟ ಖಾಯಿಲೆಗಳೆಲ್ಲ ವೈರಸ್‌ನಿಂದಾಗಿಯೇ ಬರುತ್ತವೆ. ಹೆಪಟೈಟಿಸ್ ಖಾಯಿಲೆಯು ಯಾವುದೇ ಸೂಚನೆ ತೋರಿಸದೆ ನೀರವವಾಗಿರುತ್ತದೆ. ಯಾವುದೇ ಔಷಧೋಪಚಾರ ತೆಗೆದುಕೊಳ್ಳದಿದ್ದ ಪಕ್ಷದಲ್ಲಿ, ರೋಗಿಯು ಮೂರ್ಚೆಬಿದ್ದು ಲಿವರ್ ವಿಫಲವಾಗಿ ಸಾವಿಗೊಳಗಾಗುವ ಸಾಧ್ಯತೆಗಳಿವೆ.

ಹೆಪಟೈಟಿಸ್ ಖಾಯಿಲೆಯು ಎ, ಬಿ, ಸಿ, ಡಿ, ಇ ಮತ್ತು ಜಿ ಎಂಬ ಆರು ವಿಧವಾದ ವೈರಸ್‌ಗಳಿಂದ ಬರಬಹುದು. ಒಂದೊಂದು ವೈರಸ್‌ನ ಗುಣಗಳು ಬೇರೆ ಬೇರೆಯಾಗಿದ್ದು, ಲಿವರ್‌ನ ಖಾಯಿಲೆಯೂ ವರ್ಷಾನುಗಟ್ಟಲೆ ಇದ್ದು, ಪರಿಣಾಮವೂ ಬೇರೆ ಬೇರೆಯಾಗಿರುತ್ತದೆ.

ಹೆಪಟೈಟಿಸ್ - ಬಿ

ಹೆಪಟೈಟಿಸ್ - ಬಿ ಯು ಲಿವರ್‌ಗೆ ಸಂಬಂಧಪಟ್ಟ ಖಾಯಿಲೆಯಾಗಿದ್ದು, ಪ್ರಪಂಚದಲ್ಲೇ ಅತಿ ಹೆಚ್ಚು ಸಾವಿಗೆ ಕಾರಣವಾಗಿರುವ ಸೋಂಕು ರೋಗವೆಂದು ಪರಿಗಣಿಸಲಾಗಿದೆ. ಹೆಪಟೈಟಿಸ್ - ಬಿ ವೈರಸ್ ಈ ರೋಗ ತಗುಲಿಸಿ, ಮುಖ್ಯವಾಗಿ ಲಿವರ್‌ನ ಮೇಲೆ ದಾಳಿ ಮಾಡಿ, ಲಿವರ್ ಅಣುಕೋಶದ ಸಾವಿಗೆ ಪ್ಲಾಸ್ಮಾ(ರಕ್ತ) ದಿಂದ ತಯಾರಿಸಲ್ಪಟ್ಟ ವ್ಯಾಕ್ಸಿನ್‌ಗಳು ಕಣ್ಮರೆಯಾಗಿವೆ.

ಮಕ್ಕಳಿಗೆ ವ್ಯಾಕ್ಸಿನೇಷನ್

ಜಾಗೃತಿಕ ಆರೋಗ್ಯ ಸಂಸ್ಥೆಯು ಎಲ್ಲಾ ನವಜಾತ ಶಿಶುಗಳಿಗೆ ಈ ವ್ಯಾಕ್ಸಿನ್ ತಪ್ಪದೇ ಕೊಡಲು ಸೂಚಿಸಿದೆ. ಎಂಭತ್ತಕ್ಕೂ ಹೆಚ್ಚು ರಾಷ್ಟ್ರಗಳು ಈ ಕಾರ್ಯಕ್ರಮವನ್ನು ಈಗಾಗಲೇ ಹಮ್ಮಿಕೊಂಡಿವೆ.

ಇಂಡಿಯನ್ ಅಕಾಡೆಮಿ ಆಫ್ ಪೀಡಿಯಾಟ್ರಿಕ್ಸ್ ಮತ್ತು ಇಂಡಿಯನ್ ಅಸೋಸಿಯೇಷನ್ ಫಾರ್ ಸ್ಟಡಿ ಆಫ್ ಲಿವರ್ ಈ ಎರಡೂ ಸಂಸ್ಥೆಗಳು ನವಜಾತ ಶಿಶುಗಳಿಗೆ ತಪ್ಪದೇ ಹೆಪಟೈಟಿಸ್ - ಬಿ ವ್ಯಾಕ್ಸಿನ್ ಕೊಡಿಸಬೇಕೆಂದು ಶಿಫಾರಸ್ಸು ಮಾಡಿವೆ.

ಮಗು ಹುಟ್ಟಿದ ಸಂದರ್ಭದಲ್ಲಿ ಈ ವ್ಯಾಕ್ಸಿನ್ ಕೊಡಿಸದೇ ಇದ್ದ ಪಕ್ಷದಲ್ಲಿ ಸಾಧ್ಯವಾದಷ್ಟು ಬೇಗನೇ ಈ ವ್ಯಾಕ್ಸಿನ್‌ನ್ನು ಕೊಡಿಸುವುದು ಒಳಿತು. ಈ ವ್ಯಾಕ್ಸಿನ್‌ನ್ನು ಯಾವುದೇ ವಯಸ್ಸಿನಲ್ಲಾದರೂ ಕೊಡಿಸಬಹುದು.

ವ್ಯಾಕ್ಸಿನೇಶನ್ ಶಡ್ಯೂಲ್

ಹೆಪಟೈಟಿಸ್-ಬಿ ಲಸಿಕೆ ಹಾಕುವ ಕ್ರಮವು ಮೂರು ಇಂಜೆಕ್ಷನ್‌ಗಳನ್ನು ಒಳಗೊಂಡಿದ್ದು 0, 1 ಮತ್ತು 6ನೇ ತಿಂಗಳಲ್ಲಿ ಹಾಕಬೇಕು. ತಾಯಿಯು ಹೆಪಟೈಟಿಸ್-ಬಿ ವೈರಸ್ ಸೋಂಕಿಸಿಕೊಂಡು ಅದನ್ನು ಒಯ್ಯುವವಳಾಗಿದ್ದರೆ (ಗರ್ಭಿಣಿ ರಕ್ತ ಪರೀಕ್ಷೆ ಮಾಡಿಸಿದಾಗ ಗೊತ್ತಾಗುತ್ತದೆ) ಮಗು ಜನಿಸಿದ ಸ್ವಲ್ಪ ಸಮಯದಲ್ಲೇ ಮೊದಲನೇ ಲಸಿಕೆ, ಒಂದು ತಿಂಗಳ ನಂತರ ಎರಡನೇ ಲಸಿಕೆ, ಮತ್ತು ಮೂರನೇ ಲಸಿಕೆಯನ್ನು ಆರನೇ ತಿಂಗಳ ನಂತರ ಹಾಕಿಸಬೇಕು.

ಹೆಪಟೈಟಿಸ್ - ಬಿ ಇಮ್ಯುನೋ ಗ್ಲೋಬಿಲಿನ್‌ನ್ನು ಸಹ ಮಗು ಹುಟ್ಟಿದ ಹನ್ನೆರಡು ಗಂಟೆಗಳೊಳಗೆ ಹಾಕಿಸಬೇಕು. ಇಮ್ಯುನೋ ಗ್ಲೋಬುಲಿನ್ ಸಿಗದೇ ಇದ್ದ ಪಕ್ಷದಲ್ಲಿ, ಈ ವ್ಯಾಕ್ಸಿನ್ ಒಂದೇ ಕೂಡ ಶೇಕಡ 95ರಷ್ಟು ಮಕ್ಕಳನ್ನು ಹೆಪಟೈಟಿಸ್-ಬಿ ಬರದಂತೆ ತಡೆಗಟ್ಟಬಹುದು.

ಹೆಪಟೈಟಿಸ್-ಬಿ ವೈರಸ್ ಸೋಂಕಿಸಿಕೊಳ್ಳದೇ ಆರೋಗ್ಯವಾಗಿರುವ ತಾಯಿಯ ಮಗುವಿಗೆ ಪೋಲಿಯೋ,

ಉಳಿದ ಇತರ ಆರೋಗ್ಯವಂತ ಮಕ್ಕಳಿಗೂ ಖಾಯಿಲೆ ಸೋಂಕಿಸುವ ಅಪಾಯವಿದೆ.

ಹೆಪಟೈಟಿಸ್-ಬಿ ತಡೆಗಟ್ಟುವುದು ಹೇಗೆ?

ದುರದೃಷ್ಟವಶಾತ್ ಹೆಪಟೈಟಿಸ್-ಬಿಯನ್ನು ಗುಣಪಡಿಸುವ ಯಾವುದೇ ಔಷಧಿಗಳು ಇದುವರೆಗೂ ಲಭ್ಯವಿಲ್ಲ. ಇತ್ತೀಚೆಗೆ 'ಇಂಟರ್‌ಫೆರಾನ್ಸ್' ಎಂಬ ಔಷಧಿಗಳನ್ನು ಉಪಯೋಗಿಸಿ ನೋಡಿದ್ದರೂ ಅವುಗಳು ಅಷ್ಟೊಂದು ಉಪಯೋಗಕಾರಿ ಎಂಬುದು ಸ್ಪಷ್ಟವಾಗಿಲ್ಲ. ಆದ್ದರಿಂದ ಇರುವ ಒಂದೇ ವಿಧಾನವೆಂದರೆ ಮಕ್ಕಳಿಗೆ ಹೆಪಟೈಟಿಸ್-ಬಿ ನ ಲಸಿಕೆಯನ್ನು ಅಥವಾ ವ್ಯಾಕ್ಸಿನ್‌ನನ್ನು ಕೊಡಿಸುವುದರ ಮೂಲಕ ಈ ರೋಗ ಬರುವುದನ್ನು ತಡೆಗಟ್ಟಬಹುದು.

ಹೆಪಟೈಟಿಸ್-ಬಿ ವ್ಯಾಕ್ಸಿನ್ ಕೊಡಿಸುವುದು ಹೇಗೆ ?

ಈ ಗಂಡಾಂತರಕಾರಿ ಖಾಯಿಲೆ ತಡೆಗಟ್ಟಲು ಎರಡು ವಿಧವಾದ ವ್ಯಾಕ್ಸಿನ್‌ಗಳು ಲಭ್ಯವಿದೆ, ಮೊದಲನೆಯದು ಪ್ಲಾಸ್ಮಾ (ರಕ್ತ) ದಿಂದ ತಯಾರಿಸಿದ ವ್ಯಾಕ್ಸಿನ್ ಹಾಗೂ, ಎರಡನೆ ಪೀಳಿಗೆಯ ಜೆನೆಟಿಕ್ ಇಂಜಿನಿಯರಿಂಗ್ ವಿಧಾನದಿಂದ ತಯಾರಿಸಿದ ವ್ಯಾಕ್ಸಿನ್.

ಪ್ಲಾಸ್ಮಾ(ರಕ್ತ)ದಿಂದ ತಯಾರಿಸಿದ ವ್ಯಾಕ್ಸಿನ್ ಪರಿಣಾಮಕಾರಿ ಹಾಗೂ ಸುರಕ್ಷಿತ, ಆದರೂ ಈ ವ್ಯಾಕ್ಸಿನ್‌ನ್ನು ಹೆಪಟೈಟಿಸ್-ಬಿ ಖಾಯಿಲೆಯಿಂದ ನರಳುತ್ತಿರುವ ವ್ಯಕಿಯ ರಕ್ತದಿಂದ ತಯಾರು ಮಾಡಿರುವುದರಿಂದ, ವೈರಸ್‌ಗಳು ಸೋಂಕಾಗಬಹುದೆಂಬ ಆಧಾರವಿಲ್ಲದ ಭಯ ಜನರಲ್ಲಿ ಮನೆಮಾಡಿದೆ.

ಜೆನೆಟಿಕ್ ಇಂಜಿನಿಯರಿಂಗ್ ಅಥವಾ ರಿಕಾಂಬಿನೆಂಟ್ ಎಂಬ ಅತಿನೂತನ ವಿಧಾನದಿಂದ ತಯಾರಿಸಲ್ಪಟ್ಟ ವ್ಯಾಕ್ಸಿನ್, ಶುದ್ಧೀಕರಿಸಿದ ಆಂಟಿಜೆನ್‌ನಿಂದ ಮಾಡಲ್ಪಟ್ಟಿದ್ದು, ಸಾಕಷ್ಟು ಪರೀಕ್ಷೆಗೊಳಪಟ್ಟು ಪ್ರಭಾವಕಾರಿಯೆಂದು ಸಿದ್ಧಪಟ್ಟಿದೆ. ಈ ಜೆನಿಟಿಕ್ ಇಂಜಿನಿಯರಿಂಗ್ ಉಪಯೋಗಗಳೇನೆಂದರೆ ತಡೆರಹಿತ ವಿತರಣೆ, ತಯಾರಿಸುವ ವಿಧಾನದಲ್ಲಿ ಪ್ಲಾಸ್ಮಾ ಅಥವಾ ರಕ್ತ ಉಪಯೋಗಿಸದೇ ಇರುವುದು ಮತ್ತು ಬಹುಬೇಗ ತಯಾರಿಸಲು ಸಾಧ್ಯವಾಗುವುದು.

ಈ ರಿಕಾಂಬಿನೆಂಟ್ ವ್ಯಾಕ್ಸಿನ್‌ಗಳು ಅಮೇರಿಕಾ ಮತ್ತು ಯೂರೋಪ್ ದೇಶಗಳಲ್ಲಿ ಉಪಯೋಗಿಸಲ್ಪಡುತ್ತಿದ್ದು

ಕಾರಣವಾಗುತ್ತದೆ. ಮನುಷ್ಯ ಮಾತ್ರ ಈ ವೈರಸ್‌ನ್ನು ''ಶೇಖರಿಸಿಕೊಳ್ಳುವ ಕಣಜ'' ಎಂದು ಇದುವರೆಗೆ ತಿಳಿದಿದೆ.

ಏಯ್ಡ್ಸ್ ಖಾಯಿಲೆಗೆ ಮೂಲ ಕಾರಣವಾದ ಹೆಚ್. ಐ. ವಿ. ವೈರಸ್ ಮಾನವ ಜನಾಂಗಕ್ಕೆ ಒಡ್ಡಿರುವ ಬೆದರಿಕೆಯನ್ನು ಹೋಲಿಸಿದಾಗ, ಹೆಪಟೈಟಿಸ್-ಬಿ ವೈರಸ್ ಒಡ್ಡಿರುವ ಬೆದರಿಕೆಯು ಅತಿ ಹೆಚ್ಚು ಎಂದು ತಿಳಿದುಬಂದಿದೆ. ನಿಜ ಸಂಗತಿಯೇನೆಂದರೆ ಹೆಪಟೈಟಿಸ್-ಬಿ ವೈರಸ್‌ನ ಸೋಂಕು ಗುಣ ಏಯ್ಡ್ಸ್ ವೈರಸ್‌ನ ಸೋಂಕು ಗುಣಕ್ಕಿಂತ ನೂರು ಬಾರಿ ಹೆಚ್ಚು ಮತ್ತು ಒಂದು ದಿನದಲ್ಲಿ ಹೆಪಟೈಟಿಸ್-ಬಿ ನಿಂದಾಗಿ ಸಾಯುವವರ ಸಂಖ್ಯೆ, ಇಡೀ ಒಂದು ವರ್ಷದಲ್ಲಿ ಏಯ್ಡ್ಸ್‌ನಿಂದ ಸಾಯುವವರ ಸಂಖ್ಯೆಗೆ ಸಮ. ಜೀವನದ ಕ್ರಿಯಾಶೀಲ ವರ್ಷಗಳಲ್ಲಿ ತಂಬಾಕು ಬಿಟ್ಟರೆ ಸಾವಿಗೆ ಕಾರಣವಾಗುವ ನಾಲ್ಕು ಅಥವಾ ಐದನೇ ಬಹುಮುಖ್ಯ ಕಾರಣಗಳಲ್ಲಿ ಒಂದು ಹೆಪಟೈಟಿಸ್-ಬಿ ವೈರಸ್ ಎಂದು ಪರಿಗಣಿಸಲಾಗಿದೆ.

ಭಾರತದಲ್ಲಿನ ಹೆಪಟೈಟಿಸ್-ಬಿ ಸಮಸ್ಯೆ

ಪ್ರಪಂಚದಲ್ಲಿ ಹೆಪಟೈಟಿಸ್-ಬಿ ವೈರಸ್ ಹರಡುವವರು (ವಾಹಕ) ಸಂಖ್ಯೆ ನಾನ್ನೂರು ಮಿಲಿಯನ್. ಭಾರತದಲ್ಲಿ ಮಾತ್ರವೇ ಐವತ್ತು ಮಿಲಿಯನ್‌ಗಿಂತ ಹೆಚ್ಚು ಜನ ಹೆಪಟೈಟಿಸ್-ಬಿ ವೈರಸ್ ಹರಡುತ್ತಿದ್ದಾರೆ. ಇಪ್ಪತ್ತು ಜನರಲ್ಲಿ ಒಬ್ಬರು ಹೆಪಟೈಟಿಸ್-ಬಿ ವೈರಸ್ ಹರಡುವವರ ದೇಶವೆಂದು ನಮ್ಮ ದೇಶಕ್ಕೆ ಹೆಸರು ಬಂದಿದೆ. ಪ್ರಪಂಚದಲ್ಲಿ ಎರಡನೇ ಅತಿ ಹೆಚ್ಚು ವೈರಸ್ ಹರಡುವವರ ದೇಶವೆಂದು ವಿಶೇಷವಾದ ಸಂದೇಹವಿದೆ. ಶೇಕಡ 30ರಷ್ಟು ಹೆಪಟೈಟಿಸ್-ಬಿ ವೈರಸ್ ಹರಡುವವರು ಅಂತಿಮವಾಗಿ ಸಾವನ್ನಪ್ಪುತ್ತಾರೆ ಎಂದು ವರದಿಯಾಗಿದೆ.

ಈ ಶತಮಾನದ ಅಂತ್ಯದ ವೇಳೆಗೆ ಭಾರತ ದೇಶವು ಪ್ರಪಂಚದಲ್ಲಿ ಅತಿ ಹೆಚ್ಚು ಹೆಪಟೈಟಿಸ್-ಬಿ ವೈರಸ್ ಒಯ್ಯುವವರ ದೇಶವಾಗಲಿದೆಯೆಂದು ಅನುಮಾನವಿದೆ.

ವಿವಿಧ ಅಂದಾಜುಗಳ ಪ್ರಕಾರ 1,50,000 ದಿಂದ 4,50,000 ನವಜಾತ ಶಿಶುಗಳು ಈ ವೈರಸ್‌ನ್ನು ಸೋಂಕಿಸಿಕೊಂಡು ಮುಂದೆ ವಾಹಕರಾಗುತ್ತಾರೆ.