St. John's Medical College
Journal of Medicine

HE SHALL LIVE BECAUSE OF ME
जीविष्यति मयैवासौ

August 2004

Editorial

INFORMATION FOR CONTRIBUTORS

SUBMITTING THE MANUSCRIPTS

The St. John's Medical College Journal of Medicine accepts scientific contributions from all fields of medicine from all institutions and health care professionals. The journal will be published twice a year. Articles and editorial communications should be addressed to the Editor, Alumni Office, St. John's Medical College, Bangalore 560 034.

PREPARING THE MANUSCRIPTS

All manuscripts should be submitted in 2 copies (including the glossy prints). They should be neatly typewritten on bond paper, one side of the paper only, with double spacing and margins of at least 2.5 cms. Please be sure to include an accurate address for editorial communications and for reprint requests. Measurement should be in metric system.

ILLUSTRATIONS AND TABLES

Figures and tables should be cited in order in the text. Their position should be marked in the margin of the manuscripts. All line drawings should be submitted in duplicate as clear, glossy black and white, 5"x7" photographs. Photomicrographs should also be submitted in duplicate with allowance made for the effects of reduction if necessary. Legends for illustrations should be typewritten, double-spaced, on a separate sheet and included at the end of the manuscripts. A legend must accompany each illustration. Each table should be typed on a separate sheet and appropriately numbered legends should be typed on the same sheet as the tables.

REFERENCES

Reference should be compiled at the end of the articles. They should be typewritten and double-spaced under the heading REFERENCES. Abbreviations for titles of medical periodicals should conform to those used in the latest edition of Index Medicus. Give inclusive page numbers.

EXAMPLES OF REFERENCES

Journal articles upto six authors, list all names:
Kurpad AV, Shetty PS. Dietary fibre and the colon, St. John's J Med. 1988; 1:5-12.

Journal articles more than six authors, list three authors followed by et al.

Complete Book
Gallagher JR. Medical Care of the Adolescent (ed 2). New York, Appleton, 1966:pp 208-215.

The St. Johns Medical College Journal of Medicine is a publication of the Alumni Association of St. John's.

EDITORIAL

Well, this is the final curtain for me and hopefully not for the St. John's Journal. After six years, the Editorship now passes on to the able hands of Dr. Kanishka Das. When I look back on to what we have achieved, I am happy that we have been able to bring out all the issues, even though this one has been delayed.

Getting good quality articles has always been a challenge. Our Editorial policy has been very clear that the Journal publishes good quality peer reviewed articles or none at all. We have therefore had to reject some articles based on the comments of our reviewers. In the interest of fairness to the authors, I have sometimes had to tell authors of original research that it might be better to try and get their articles published in an indexed Journal before trying our Journal. Another strategy we used to get quality articles was to directly approach some authors to write on issues which we thought would be of benefit not just to our alumni in rural areas but to our other readers as well. Funds were also a problem, but luckily the Alumni Association has been very supportive about the money needed to finance the issues. Our future strategy to get the Journal out on the internet would probably save us some money. And I hope that it will be pursued enthusiastically.

Another future strategy is to continue to get our articles peer reviewed and get the Journal out regularly so that we could aim to get our Journal into Index Medicus. That should not be an impossible goal for us at St. John's.

All the best Kanishka! I must also take this opportunity to thank Dr. Jennifer and Dr. Arvind for their support and enthusiasm over the years.

Dr. Sunita Simon Kurpad

ERECTILE DYSFUNCTION (ED): Treatment Options

A. MOHAN

Introduction

One of the commonest problems faced by married couples is the inability to initiate, or continue, marital relations due to the inability of the male partner to complete the act of intercourse to satisfaction. While this complaint is not forthcoming in the usual doctor-patient encounter, it constitutes a major obstacle to a satisfactory family life. In India, this 'diffidence' is perpetuated by prevalent cultural practices, increasing urbanization and access to information through mass media has brought this problem out into the open and more and more couples are seeking medical help for this.

Erectile dysfunction (ED) is defined as "the inability to have or sustain an erection adequate for satisfactory sexual activity".[1] According to recent estimates, as many as 30 million men in the United States may experience some form or degree of ED.[2] Generally believed by many to be an inevitable consequence of ageing, it is not necessarily confined to the ageing population. It does however correlate with advancing age. In the United States, The Massachusetts Male Ageing Study[3] found some evidence of ED in 39% of men between the ages of 40 and 50 years, in 46% of men between the ages of 50 and 60 and in almost 70% of men over the age of 70. Severity of ED is also correlated with age, moderate-to-severe ED becomes more common as men get older. As age advances, conditions like vascular diseases, degenerative neurologic disorders and hormonal changes, affect the physiology of erections, leading to ED. The prevalence in different countries differ as erectile dysfunction is linked to cultural and sexual practices – in some societies it is accepted as an inevitable occurrence with advancing age and no medical help is sought.

A. MOHAN M.S. M.Ch.
Professor & Head

Department of Urology
St. John's Medical College Hospital
Bangalore

Far from being an "inevitable consequence of age", we are dealing with a large number of patients with ED today. Changing social mores and the plethora of information available on this subject seem to have both contributed to the increasing number of men seeking medical assistance for ED in India, too. There are also many younger persons coming with ED today – in these the aetiology is somewhat different. Stress plays a very important role. While this form of ED used to be considered "psychogenic", it is obvious that the problem is mediated through the same neuro-vascular pathways as in the ageing. This has a direct bearing on the treatment strategy for younger patients too.

ED: The medical history

A detailed medical and sexual history is the first step in assessing a patient with ED, particularly in the middle-aged or elderly individual. ED may be the heralding sign of a serious underlying disorder, for example, cardiovascular disease.[2-4] Other potential risk factors for ED include diabetes, hypertension, peripheral vascular disease, prostate disease, hormonal and metabolic disorders (primary or secondary hypogonadism, hypothyroidism), chronic renal failure, hepatic failure, psychiatric disorders (mood and anxiety disorders), neurologic disorders (multiple sclerosis, nerve-disrupting pelvic injury) and inadequate lipid control. It is necessary to carefully elicit history and findings that point to one of the above before rushing to prescribe treatment. Doing so might not only lead to treatment failure but also mean that potentially life-threatening, underlying disease.

An adequate history for a patient with ED should include

- Onset, duration and frequency of ED
- Whether obtaining an erection is difficult, or maintaining an erection once sustained is the problem.
- Whether this inability prevents penetration

- Whether it is situational (partner-specific or present only under specific circumstances)
- Occurrence and quality of spontaneous morning, nocturnal or self-stimulated erections
- History of perineal or back injury, or operations on the prostate, urethra or bladder neck
- Presence of adequate desire/libido (absence could indicate endocrine or psychiatric disorders)
- Use of prescription, non-prescription or recreational drugs
- Psychiatric symptoms or disorders

Physical examination should include

- Measurement of blood pressure
- Assessment of virilisation and male secondary sex characteristics
- Checking pulsations in the femoral, popliteal, dorsalis paedis and posterior tibial arteries
- Focused neurological examination, including evaluation of penile and perineal sensation and anal sphincter tone
- Digital rectal examination of the prostate for texture, symmetry and tenderness
- Physical examination of the penis to detect any structural abnormalities – a plaque indicating Peyronie's disease, any scars, deformities and penile sensation.

Laboratory investigations, which point to serious underlying diseases, are recommended.[5] These include urinalysis, measurement of morning total testosterone level and a test for prostate-specific antigen (PSA), especially in men older than 50 years of age, lipid profile, complete blood cell count and blood sugar assessment are advisable if one or more years have elapsed since previous testing. Points elicited in history and physical examination findings will determine what other investigations are necessary.

Specific investigations

With the evolution of a goal directed approach, extensive investigations are not often necessary. This is particularly so with the availability of oral agents, such evaluation is now resorted to only if the oral agent does not yield the desired results. Dynamic duplex doppler,[6] nocturnal penile tumescence (NPT)[7] monitoring and cavernosography may reveal specific vascular abnormalities or indicate pure psychogenic causes.

Pharmacologic penile duplex ultrasonography can provide a dynamic vascular assessment.[6] A penile injection of alprostadil or papaverine to produce smooth muscle relaxation allows for evaluation of arterial and venous blood flow patterns and can aid in the diagnosis of vascular dysfunction. If vascular insufficiency is diagnosed and the patient does not respond to an adequate trial of sildenafil therapy, intracavernosal injectable agents might be considered. If however, ultrasonography reveals normal vascular integrity, the next step might be to perform a nocturnal penile tumescence and rigidity test to assess nocturnal erectile activity.[7] This test is perhaps the best way to discriminate between organic and psychogenic ED and this may aid in referral to a sex therapist, psychiatrist or psychologist.

The Treatment Options

Once underlying conditions have been looked for and treated or ruled out, the focus obviously sifts to the treatment options available. ED can often be associated with modifiable risk factors such as smoking, overindulgence in alcohol, obesity or stress. ED provides a good motivation for change and a patient with ED should be encouraged to make necessary changes in lifestyle – the reward for doing so being normal erectile function. In some cases, stopping smoking,[8] moderation of alcohol intake and other lifestyle interventions may themselves lead to considerable symptomatic improvement. Reduction in stress through meditation or similar "stress buster" techniques is of immense benefit in appropriate cases. By inducing a feeling of well being, these alterations will facilitate any other intervention that may be necessary.

The options available for treating ED today are many. These include

- Hormone therapy
- Oral pharmacotherapy
- Vacuum constriction devices (VCDs)[9]
- Intra-cavernosal pharmacotherapy
- Intra-urethral pharmacotherapy
- Oral vasoactive agents
- Implantable penile prostheses

With the advent of these multiple options, the chances of success have grown accordingly in recent years. Nearly all patients can be helped, irrespective of the underlying aetiology.

Hormones

While the testosterone level declines with age, it does not decline to a level that can cause ED by itself. Therefore, testosterone administration has no 'universal' role in treatment. In the few men who are found to have hypogonadism on investigation and resultant low hormone levels, testosterone therapy has a role. Such patients are very few in number. Therefore, testosterone replacement[10] is an effective treatment only in a small proportion of patients[11] (about 1% to 5%). Testosterone therapy may have serious side effects (worsening symptoms of BPH, the risk of activating occult prostate cancer and hepatic dysfunction). Due to these potential risks and low response rates, testosterone replacement is best reserved for men whose baseline testosterone levels are subnormal. Patients receiving testosterone therapy must be monitored with PSA tests and digital rectal examinations every 6 months for the first 1 to 2 years, then annually thereafter. There is no scientific basis for the empirical use of testosterone in all cases of ED.

Oral non-hormonal agents

All kinds of oral agents used to be prescribed for ED more in haste than in conviction. Yohimbine, trazodone and L-arginine were the more commonly prescribed drugs. Inspite of the widespread use of these agents, there is no scientific evidence about the efficacy of these agents in the treatment of ED.[12-14]

Vacuum constriction devices

These devices draw blood into the cavernosal spaces by creating a suction effect around the penile shaft. The corpora cavernosa then engorge with blood. This blood is trapped in the cavernosal spaces by the application of a constricting ring at the base of the penis, resulting in an erect penis. Intromission and intercourse is then possible as the required rigidity is maintained as long as the constriction ring is in place. Vacuum pumps[9] and constriction devices are inexpensive and may be effective for men who prefer a non-pharmacologic, non-surgical approach and have a comfortable, well-established sexual relationship. Considerable manual dexterity is necessary and there should be no underlying impairment of penile sensations (e.g., sensory neuropathy). Side effects reported by some patients (or their partners) include pain, blocked ejaculation and penile "coldness and numbness". These devices also have the advantage of being reusable. ***These devices are definitely contraindicated if the subject cannot be trusted to take all due precautions*** – particularly with the constricting ring, which should not be left in place for longer than 30 minutes.

Intra-corporeal vasoactive agents

These agents are self-injected into the corpus cavernosum. They produce relaxation of the vascular smooth muscle and the smooth muscle of the corpora. The blood flow into the corpora is enhanced and the penis becomes turgid and erect as it would in the normal course. Intracavernosal injection of vasoactive agents is highly effective with efficacy rates of 75% to 80%.[15] The most commonly used agents are alprostadil® (prostaglandin E_1), papaverine (alone and in combination with alprostadil), and phentolamine (used in combination with the other agents). Of these, only papaverine is freely available in India. It is used in a dose of 15-90 mg, with the lowest effective dose being used. The patient is taught the self-injection technique under supervision. Once the technique is mastered, the injections can be taken at home. It is recommended that not more than one injection per day is taken and not more than ten injections per month.

The invasive nature of this treatment is a disadvantage. Side effects are pain following the injection, fibrosis of the cavernosal tissue after repeated injections and priapism. Priapism could be the result of high dosage or independent of the dosage. Counseling the patient about proper administration is essential. The patient should also be instructed that he should seek immediate medical attention if the erection does not subside within 45 minutes of intercourse. Priapism is a medical emergency and will require intervention for reversal. Prolonged priapism can lead to gangrene of the penis. This form of therapy therefore should not be chosen for patients who cannot access specialist medical services immediately, *or those that cannot be trusted to!*

Another treatment option is the alprostadil urethral suppository.[16] It is a solid pellet about the size of a grain of rice that is inserted with a plunger-like device into the urethra. When the pellet dissolves, the active agent is absorbed and subsequent events are similar to that seen with vasoactive injections. Side effects include penile pain and "burning" rare cases of mild bleeding from the urethra, hypotension and syncope have also been reported. Called MUSE®, this is not available in India. It is obviously more acceptable than injections and causes less direct damage to the cavernosal smooth muscle. The danger of priapism is present with this form of treatment too.

Penile Prostheses

Penile prostheses are modified cylinders of synthetic bio-compatible material that are surgically implanted into the cavernosal tunics in order to provide the rigidity required for intromission. These prostheses are available now in the semi-rigid and inflatable forms. They come in different sizes suitable for different physical characteristics. The components and actual design vary depending on manufacturer and model, but the basic design and function is the same. The devices are designed to improve penile rigidity and not to affect urination, ejaculation, or orgasm. Patient and partner satisfaction rates are apparently high[17, 18] reportedly ranging up to 98%.

Complications include a constant "erect" state with the semi-rigid prostheses, prosthesis extrusion, mechanical failure and infection. The surgery is irreversible and that it tends to diminish the normal functioning of the corpus cavernosum. If the device is removed, spontaneous and drug-induced erections should not be expected to resume. It is therefore reserved as the last option in the treatment of ED. Prostheses is available in India and many centres including ours are conversant with the surgical procedure.

Psychotherapy

Referral to a psychiatrist, psychologist or sex therapist might be considered for selected cases in which the sexual dysfunction is suspected to have a primary psychogenic cause.[19] Most cases of ED (upto 80%) are estimated to have an organic cause. It is not unusual to have persons with purely psychogenic ED in our country. These may be brought on by "performance anxiety", venerophobia as a reaction to a noxious experience, depression or grief. Counseling and specifically directed therapy in the case of psychiatric disorders is necessary in these cases.

However, because of the emotional issues involved in ED, secondary psychogenic components are common. Often expectations are unrealistic and the patient feels that he has ED inspite of a normal sexual profile and performance. Marital incompatibility sometimes manifests with accusations of ED and is a particularly important ground for seeking dissolution of marriage. These are situations that call for a meticulous evaluation of the cause and a co-ordinated approach involving physician, psychiatrist and psychologist will yield the desired results.

Oral Agents

Sildenafil

Oral agents for the treatment of ED were prescribed empirically until the advent of sildenafil citrate, an original research molecule of Pfizer.[20] The pharmacological action of this agent is interesting.

Sexual stimulation leads to the release of nitrous oxide in the corpus cavernosum of the penis. Nitrous oxide thus released causes an increase in the cyclic GMP level in the cavernosum. Cyclic GMP (cGMP) causes the cavernosal smooth muscle to relax, facilitating the entry of blood into the cavernosal spaces where it is trapped, producing erection. Phosphodiestrase type 5 (PDE 5), present in the smooth muscle, breaks down cGMP at the termination of erection, or on cessation of the stimulation and the smooth muscle relaxation ceases, pushing blood out and heralding the end of the erection. Sildenafil inhibits PDE 5, thereby slowing the breakdown of cGMP. By thus enhancing the levels of cGMP, sildenafil sustains erections and enhances them by promoting further smooth muscle relaxation. In conjunction with sexual stimulation, therefore, sildenafil improves and prolongs erections.

Sildenafil is available in India as 25mg, 50mg and 100mg tablets. It is recommended that the dosing schedule begin with the lowest dose. It is recommended that a single tablet is taken

approximately 1 hour before initiating sexual activity. However, the drug can be taken up to 4 hours before sexual activity and may be effective in as little as 30 minutes if taken on an empty stomach. It is important to inform the patient that sexual stimulation is necessary to initiate the action of the drug and that it will not produce erections in the absence of sexual stimulation. The exact dose required will vary and it may take a few days for the dose titration. However ***not more than one tablet in a 24-hour period is recommended.***

Extensive safety data is available on sildenafil and it is generally safe except for certain documented side effects. It is reported by some to produce a feeling of light-headedness. Diarrhoea was another common side effect reported. These were not serious and no therapy was required. However, blurring of vision and transient visual changes have been reported. This is believed to be due to the inhibition of another phosphodiestrase isoenzyme, PDE 6, that is present in the retina. For this reason, the drug is contraindicated in patients *retinitis pigmentosa,* a disorder where PDE 6 is involved. Myalgia can also be a distressing accompaniment of Sildenafil therapy. It decreases over a period of time and needs no specific treatment.

All side effects are higher at higher doses and a dose higher than 100mg is not recommended. The only absolute contraindication to the use of sildenafil is concomitant use of an organic nitrate such as nitro-glycerine, isosorbide nitrate or dinitrate, pentaerythritol tetranitrate and erythrityl tetranitrate.[20] Sildenafil potentiates the hypotensive effect of nitrates – its propensity to produce smooth muscle relaxation can lead to major haemodynamic compromise, which could be refractory to treatment with vasopressors. Its use in the elderly, hypertensive patients on multiple drugs and those taking medications interfering with the cytochrome pathways like erythromycin and ketoconazole is contraindicated.[20]

Tadalafil (Eli Lily) and Vardenafil (Bayer) are two new drugs in this category. They have a quicker onset of action but act by the same mechanism. The effects last longer.

Apomorphine

A new drug, apomorphine hydrochloride[21] has received a recommendation in the U.S.F.D.A. for use in the treatment of ED. It is reported to act more quickly than sildenafil, within 16-19 minutes. It is a centrally acting drug, acting on the dopamine receptors in the brain. It is believed that this drug can also enhance the psychological factors necessary for initiating the erectile response – something that sildenafil cannot do. It is administered as a sub-lingual tablet and nausea has been the commonest side effect. Syncopal episodes have been reported with the drug.

Conclusion

With particular reference to India, erectile dysfunction is emerging as a major concern. The unique cultural mores that are prevalent here, keep patients away from doctors and rational treatment. On the other hand, there are a number of indigenous solutions that patients resort to before seeking medical help.

There is an assortment of treatment modalities now available – the particular choice in a given case depends on the patient's circumstances. The advent of oral agents has simplified the management of ED and the other modalities are available when the oral agents are unsatisfactory.

References:

1. NIH Consensus Conference. Impotence. NIH Consensus Development Panel on Impotence. JAMA 1993;270:83-90.

2. Melman A, Gingell JC. The epidemiology and pathophysiology of erectile dysfunction. J Urol. 1999, 161:5-11.

3. Feldman HA, Goldstein I, Hatzichristou DG, et al. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Ageing Study. J Urol. 1994;151:54-104.

4. Miller TA. Diagnostic evaluation of erectile dysfunction. Am Fam Physician. 2000;1;61:95-104.

5. The process of care model for evaluation and treatment of erectile dysfunction. The Process of Care Consensus Panel. Int J Impot Res. 1999;11:59-70; discussion 70-4.

6. Wahl SI, Rubin MB, Bakal CW. Radiologic evaluation of penile arterial anatomy in arterogenic impotence. Int J Impot Res. 1997;9:93-97.

7. Levine LA, Lenting EL. Use of nocturnal penile tumescence and rigidity in the evaluation of male erectile dysfunction. Urol Clin North Am. 1995;22:775-788.

8. Jeremy JY, Mikhaildis DP. Cigarette smoking and erectile dysfunction. J R Soc Health. 1998;118:151-155.

9. Derouet H, Caspari D, Rohde V, et al. Treatment of erectile dysfunction with external vacuum devices. Andrologic. 1999;31 (Suppl 1):89-94

10. Winters SJ. Current status of testosterone replacement therapy in men. Arch Fam Med 1999;8:257-263.

11. Fahmy AK, Mitra S, Blacklock AR, Desai KM. Is the measurement of serum testosterone routinely indicated in men with erectile dysfunction? BJU Int. 1999;84:482-484.

12. Kunelius P, Hakkinen J, Lukkarinen O. Is high-dose yohimbine hydrochloride effective in the treatment of mixed-type impotence? A prospective, randomized, controlled double-blind crossover study. Urology. 1997;49:441-444.

13. Costabile RA, Spevak M. Oral tradozodone is not effective therapy for erectile dysfunction: a double blind, placebo-controlled trial. J. Urol. 1999;161:1819-1822.

14. Klotz T, Mathers MJ, Braun M et al. Effectiveness of oral L-arginine in first-line treatment of erectile dysfunction in a controlled crossover study. Urol Int. 1999;63:220-223.

15. Linet OI, Ogrinc FG. Efficacy and safety of intracavernosal alprostadil in men with erectile dysfunction. The Alprostadil Study Group. N Engl J Med. 1996;334:873-877.

16. Padma-Nathan H, Hellstrom WJ, Kaiser FE et al. Treatment of men with erectile dysfunction with transurethral alprostadil. Medicated Urethral System for Erection (MUSE) Study Group. N Engl J Med. 1997;2;336:1-7.

17. Porena M, Mearini L, Mearini E et al. Penile prosthesis implantation and couple's satisfaction. Urol Int. 2000,63:185-187.

18. Sexton WJ, Benedict JF, Jarow JP. Comparison of long-term outcomes of penile prostheses and intracavernosal injection therapy. J Urol. 1998;158:811-815.

19. Beutel M. Psychosomatic aspects in the diagnosis and treatment of erectile dysfunction Andrologia. 1999;31(Suppl 1):37-44.

20. Langtry HD, Markham A. Sildenafil: A review of its use in erectile dysfunction. Drugs. 1999;57:967-989.

21. Heaton JP, Morales A, Adams MA, et al. Recovery of erectile function by the oral administration of apomorphine. Urology 1995;45:200-206.

SURGERY IN HIV POSITIVE PATIENTS AN APPRAISAL

ANGAMUTHU NATARAJAN

Introduction

AIDS (Acquired Immuno Deficiency Syndrome), first reported in 1981, has grown at an alarmingly rapid rate to become one of the most challenging major public health issues in both developed and developing countries.[1,2] It is a modern day pandemic, which has spread across 190 countries in the world.[3] The surgeon, though not the primary care physician, plays an important role in the surgical management of the AIDS patient. Surgical management often exposes the surgical team to body fluids and to the potential risk of Human Immuno deficiency virus (HIV) transmission. This risk is the basis for major controversial issues like routine preoperative serological testing, refusal to administer surgical therapy, pursuing non-operative therapeutic modalities and the need for and economics of universal precautions and post-exposure chemoprophylaxis and treatment.

Definitions

HIV positive individual:
An individual who has tested seropositive for HIV. The individual may or may not be symptomatic. The majority of HIV positive individuals develop AIDS within 7- 9 years.[4]

AIDS: The occurrence of a complication of immunosuppression including indicator diseases like opportunistic infections with low virulence pathogens or neoplasms (B-cell lymphomas, Kaposi's sarcoma - KS) in a HIV positive individual is defined as AIDS.[4,5]

ANGAMUTHU NATARAJAN
DNB, MNAMS, FRCS
Assistant Professor

Department of Surgery
St. John's Medical College Hospital
Bangalore-560034

The other current definition of AIDS is a HIV positive individual with a CD4+ (helper T cell) count of less than 200 cells per mm.[3]

ARC- AIDS Related Complex
A HIV positive individual with persistent generalised lymphadenopathy (PGL), unexplained continuous fever, significant weight loss or oral candidiasis.

These definitions are periodically reviewed by the CDC (Center for Disease Control) and are used widely by health care professionals.

AIDS: The Global and Indian scenario

The estimated number of HIV cases globally was 100,000 in 1980, nearly 20 million by 1993 and the projected number for the year 2000 was 40 million cases![2,3] An estimated 16,000 new infections occur worldwide everyday with 90% of them being reported from developing countries.[6] The CDC estimates that for every patient with AIDS there are 8 HIV positive individuals who have not yet developed clinical AIDS.[4]

In Asia, the estimated number of HIV/AIDS cases is 6 million of whom 90% are from India, Thailand and Myanmar.[3] In adults from South and Southeast Asia, a prevalence of 0.6% has been reported.[6] An estimated 3-5 million adults in India are infected with the Human Immunodeficiency Virus.[3] 911 new cases were reported in India (676 males, 235 females) between January and April 2001 increasing the number of cumulative AIDS cases in India to 21,215 (16,204 males, 5011 females).[7] NACO (National AIDS Control Organization, India) has published data on HIV estimates in India based on HIV sentinel surveillance. Their figures are 3.31- 3.97 million HIV infections in the year 2001 and 3.82-4.58 in 2002.[8]

Surgery in HIV Positive Patients

With the ever-increasing occurrence of HIV infection and of awareness regarding its

consequences, the surgeon is frequently called for a consultation or to perform a surgical procedure.

The risk of transmission and subsequent seroconversion is a crucial factor in the surgical management of a HIV positive patient. It has a profound impact on the personal, professional, psychological and social aspects of the surgeon's life, which are delicate issues, and the subject of intense debate.

Indications [4,6,9]

The indications for surgery in HIV patients can be broadly grouped as follows:

1. *Management of a surgical disease not related to AIDS*: These are the group of diseases occurring both in HIV infected patients and in the general population (e.g. - herniae, common benign soft tissue tumours and trauma management).

2. *Management of a surgical disease related to AIDS*: These are the group of diseases occurring more frequently in HIV patients as a result of immunosuppression (e.g. - anorectal diseases, KS).

3. *Diagnosis of an AIDS associated infection or neoplasm*: This includes surgical procedures in the diagnosis of a disorder (eg – excision biopsy of a lymph node or soft tissue in the diagnosis of tuberculosis, lymphoma or sarcoma).

4. *Assist medical therapy of HIV associated conditions*: Minor surgical procedures to facilitate therapy (e.g. - venous access line for chemotherapy of Cytomegaloviral (CMV) retinitis, lymphoma).

5. *Management of surgical complications of AIDS and associated illnesses*: This is often an emergency surgical intervention for an acute illness (e.g. – bowel obstruction or perforation due to visceral lymphoma or KS).

High Risk Groups

It is important for the surgical team to be aware of the high-risk groups who have a higher seroprevalence rate than the general population and hence a higher chance of transmission of HIV to Health Care Workers (HCWs). The important high risk population groups are: [1,4,10]

- Homosexual or bisexual individuals.
- Patients with hemophilia or coagulation disorders.
- Intravenous drug abusers.
- People residing in areas of high prevalence (Central Africa).
- Sexual partners of the above groups.
- Children born to HIV positive mothers.

Spectrum of Surgical Diseases

Gastrointestinal Disease

Abdominal pain occurs with increasing frequency and the number of non-surgical causes is also on the rise.[5] Abdominal pain is reported in about 10% of all AIDS patients and only 5% of these cases need a surgical intervention.[9] Opportunistic infections of the gastrointestinal tract are a common cause of abdominal pain. This highlights the need for a proper and systematic approach in a patient with AIDS, presenting with abdominal pain.

Acute appendicitis is a common cause of acute abdomen and right iliac fossa pain in surgical practice. The total leucocyte count is normal in the majority of patients with AIDS developing acute appendicitis.[5] Appendicitis in these patients could be due to a visceral KS causing obstructive appendicitis or due to an acute CMV infection.[5,6]

Gastrointestinal obstruction or perforation could be due to lymphoma or KS [4]. The terminal ileum and colon is the commonest site of acute CMV infection leading on to perforation, which indicates advanced AIDS and an unfavourable prognosis. AIDS enteropathy, an uncommon entity resulting from primary infection of the gut by HIV is diagnosed after excluding the other common conditions.

Hepatobiliary Disease[5,9]

This system is commonly affected in AIDS patients and persistent elevation of the liver enzymes is a common occurrence. Acute acalculus cholecystitis and AIDS cholangiopathy are the important hepatobiliary disorders in patients with HIV/AIDS. AIDS associated cholangiopathy is a result of biliary infection with CMV or cryptosporidium and can lead on to cholecystitis or sclerosing cholangitis.

Ano-rectal disease[1,9,10]

Disorders of the anus and rectum are the common indications for surgical intervention in HIV positive patients.

Anal warts are reported to be more aggressive, dysplastic and difficult to treat. Excision by electrocautery or laser is reported to be more effective than podophyllin.

Ano-rectal suppuration and fistulae need surgical intervention. Large perianal incisions and division of internal sphincter in patients with recurrent perianal sepsis and in homosexuals could result in delayed healing, fistula formation and incontinence. Setons are preferable in the management of fistulae-in-ano.

Anal ulceration in HIV positive individuals could be due to herpes simplex, CMV or cryptosporidium infections. Proper diagnosis and adequate treatment of these infections followed by surgical excision in patients with failed medical therapy is reported to be beneficial.

Lymphoreticular disease[1,5,9]

Splenomegaly is a common finding in AIDS but the causes are multiple. Immunodeficiency associated thrombocytopenic purpura has a poor response to steroids and often necessitates a splenectomy.

Lymphadenopathy is a common finding in HIV/AIDS and the important causes are PGL, tuberculosis, lymphoma or metastatic deposits from a primary neoplasm or KS. Reactivation of tuberculosis is more common than re-infection in HIV infected patients and often tuberculosis occurs early in HIV infection, even prior to the diagnosis of AIDS. Fine Needle Aspiration Cytology (FNAC) should be the initial investigation prior to open biopsy in the evaluation of lymphadenopathy. Increasing awareness, familiarity and knowledge of AIDS results in a decreased need for an open lymph node biopsy. Lymph node biopsy is done either to classify a lymphoma diagnosed by FNAC or in patients with a negative FNAC of a clinically suspicious node, which is persistent or enlarging.

Vascular disease[5]

Infected pseudoaneurysms are common in HIV individuals with intravenous drug abuse. An interesting entity in AIDS is Salmonella arteritis wherein salmonella has an increased affinity to the atherosclerotic plaque. An invasive infection could lead to pseudoaneurysm and potential rupture.

Occupational risk of HIV transmission

The operating surgeon and the team should be aware of the potential risk of HIV transmission due to proven or unrecognized HIV infection in their patients. Implementing established guidelines in these patients helps in avoiding or minimizing the risk of transmission of HIV and more importantly hepatitis B and C viruses. A single ml of blood approximately contains 50 HIV particles in contrast to 10^9 hepatitis B particles.[10] Popejoy and Fry in their study of 684 operations reported that 28% of the operations were associated with a blood contact and the risk was higher in cardio-thoracic, trauma and obstetric cesarean sections.[11] Occupational risk of HIV transmission depends mainly on local seroprevalence rates, route of exposure and susceptibility of the HCW.[12] Unrecognised HIV infection is estimated to be 0.07% in low prevalence areas and upto 10% in areas of high prevalence.[13] Based on current reports in literature, the pooled net estimate of HIV transmission following a percutaneous exposure is 0.3% and following a mucus membrane exposure is 0.09% - 0.11% [3,12,14]. Needle stick injury, a common event among HCWs, is associated with a 0.2 to 0.3% risk of seroconversion.[12,15] Further on, the true incidence of percutaneous exposure is under-reported by 10-50 %.[15] The probability (cumulative risk) of a surgeon being infected by HIV during his surgical career (40 years) is estimated at 1% in low prevalence areas and upto 10% in high prevalence areas.[13]. An American or European surgeon in a high prevalence area during his 30 year career has a 1 in 800 chance of acquiring HIV infection. In contrast, in Africa, the risk is as high as 1 in 4.[10]

The important factors influencing the risk of occupational HIV transmission are:[3,14,15].

- Patient HIV status and viral load.
- Depth of injury
- Visible blood on the injury device.
- Vascular access related procedures.
- Death of the source patient due to AIDS within 2 months of the event.
- Exposure to source material and its volume – blood, body fluid or discharge.
- Contact site - intact skin, breached skin or mucus membrane.
- Type and duration of surgery - cardiothoracic, orthopaedic or general surgery.
- Nature of surgery – emergency, elective or

trauma surgery.
- Infrastructure of the center.
- Education and knowledge of HIV/AIDS among the team.
- Universal precautions - applicability and compliance.
- Exposure reporting and availability of chemoprophylaxis.

Pre-operative HIV Testing

Routine pre-operative serological testing of all patients is a controversial and hotly debated issue and the CDC *does not* recommend it [4,6]. The CDC guidelines for serological testing are:

- Prior patient consent.
- Pre-test and Post- test counseling.
- Strict confidentiality.
- Ensure that care of a seropositive patient is not compromised.
- Periodic evaluation of the efficacy of Universal Precautions in the center.

Principles of Surgery in HIV/AIDS

A simple yet difficult to implement safety measure is to maintain an effective barrier between the HCW (surgical team) and the patient at all times. In 1987, the CDC laid down *Universal Precautions*, the basic guidelines aimed at reducing the risk of HIV transmission.[4,12] The basic tenet of *"Universal Precautions"* is **to assume that all patients undergoing an invasive procedure are potentially infectious and that applying protective measures to all irrespective of their serological status avoids HIV transmission.** This simple and attractive theory in principle is difficult to practice with the debatable issues being compliance, economic and financial implications especially in low seroprevalence areas.[6] In 1994, the CDC issued the modified infection control guidelines, which incorporates the principles of Universal Precautions and Body Substance Isolation recommendations[6,12,16]. This is termed as *Standard Precautions,* which are to be applied to all patients receiving care in a hospital regardless of their diagnosis or presumed infection status. It applies to potential contact with blood, all body fluids, secretions, excretions etc. Some authors opine that applying and maintaining universal precautions at a high level is often not feasible at all times. HIV screening increases the awareness of the surgical staff and, for a seropositive patient, gives a better life expectancy.[13]

The Surgeon and HIV: Guidelines for Outpatient Care and Surgical Wards[1,4,6].
- Routine use of appropriate barrier precautions to avoid skin or mucus membrane exposure when contact with a potential source is anticipated.
- Hands should be washed immediately and thoroughly with soap and water after physical examination and contact with a potential source.
- Gloves should be used during contact with open wounds and mask and eye protection used during examination of a hollow viscus, eg: proctoscopy, sigmoidoscopy, and during vascular puncture for diagnostic or therapeutic access.
- Proper disposal of sharps (eg: needles, scalpel blades), infected dressings and body fluids.
- Careful conduct of venepuncture, avoidance of resheathing of needles.
- Samples and specimens collected for further examination to be properly labeled as infectious and adequately packed to prevent spillage in the event of damage and to be handled with care with use of gloves and masks.
- HCWs with exduative lesions and weeping dermatitis should refrain from all direct contact with patients and instruments.

The Surgeon and HIV : Operating Room (OR) guidelines in a HIV positive patient.[1,6,10]
- Surgeon and the team (assistants, anesthetist, nurse and support theatre staff) should have a basic knowledge of AIDS, universal precautions, and potential risks of HIV transmission and its implications.
- Surgery to be performed by a senior or fully trained surgeon. Trainee surgeons are more likely to have blood contact and injury.
- Pre-operative discussion of the steps of the proposed surgery and anticipation of bleeding.
- Proper scrubbing, use of impervious gowns, caps, masks, goggles, shoes and covers.
- Double gloving and the use of colour indicators to detect intra-operative glove puncture.
- Use of appropriate eye protection to avoid aerosol spray or high speed fragments (eg: blood and bone during drilling or nailing in orthopedic surgery).

- No hand to hand passage of sharps.
- Avoid panic reaction and simultaneous use of sharp instruments by surgeon and the assistant.
- Orderly and systematic performance of the surgical procedure.
- Avoid repetitive direct hand contact during dissection, retraction and suturing.
- Avoid direct hand contact during removal of shoe covers, gowns and masks.
- Proper disposal of blood, excised tissues, wet mops, gauzes and drapes.
- Avoid patient transfer to the recovery room and then to the ward. Allow patient to recover on the table and then shift to the ward with appropriate personnel for further post-operative care.
- Thorough hand wash and use of disinfectants after performing the surgery.

The Surgeon and HIV: Preventive Measures[2,3,9,12,16]

It is important to implement measures, which limit occupational exposure and hence reduce the risk of HIV transmission to the HCWs. It includes minor modifications, innovative ideas, techniques and technology that are classified as

Engineering Controls.

- Magnetic trays for passage of sharps.
- Blunt tipped suture needles.
- Glove liners and cut-resistant gloves.
- Fingertip guards.
- Impervious gowns and drapes.
- The use of devices for intravenous access which avoid venepuncture.

Work practice Controls.

- Step to step modification of the procedure to reduce contact and use of sharps.
- Avoid use of hand to guide a needle, protect a structure and pick up sharps.
- Hand ties only after removing the needle and kept to a minimum.
- Use of instrument ties, stapling device for anastomosis.
- Use of electrocautery or harmonic scalpel for dissection.
- Use of staplers or tissue adhesive for skin closure.
- Drains and open wounds to be minimized.

Administrative Controls.

- Formulation of an OR committee to enforce and evaluate standard precautions.
- Periodic rotation of HCWs to minimize the risk to a particular HCW.
- Set up a programme for post-exposure prophylaxis and follow-up.
- Ongoing education programmes for the HCWs.

Exposure Event and the HCW[4,6,10,14]

An exposure to a potential infectious source is a major issue of concern. The CDC issued guidelines in 1998, which include:

- Event reporting and generation of a report.
- Management of the event.
  - thorough wash with water and soap.
  - irrigation with saline or a disinfectant.
- Contact patient – HIV testing with consent.
- The HCW - base line testing for HBV, HCV, HIV.
- Counseling and risk assessment and post-exposure prophylaxis as indicated.
- Clinical and serological evaluation for HIV infection.
- Repeat HIV testing at 6 weeks, 3 & 6 months.
- HCW to report any acute febrile illness within 12 weeks of exposure.
- HCW to have protected intercourse; refrain from donation (organ, blood, semen).
- Health education.

Post exposure prophylaxis

Post exposure chemoprophylaxis is ideally instituted 1-2 hours after the exposure event. Following a percutaneous exposure, zidovudine prophylaxis is reported to reduce the chances of seroconversion by about 80%.[2,15] Post exposure prophylaxis depends on the exposure class and contact patient. The drugs used are zidovudine, lamivudine and or indinavir for a period of 4 weeks.

Surgery and its outcome

The morbidity and mortality of surgery in AIDS is influenced by a host of factors – degree of immunosuppression, hypoalbuminaemia, pre-existing malnutrition and neoplastic process (lymphoma, KS).[1] Important factors considered to determine survival are CD4+ counts, viral load and the ability to receive antiretroviral therapy.[10] However, there are reports that CD4+ counts and HIV positive status as predictors of surgical outcome are controversial but viral load assays may be useful.[8]

Conclusions

AIDS by itself is not a contraindication for surgery. Surgical treatment should be offered to a HIV positive patient when the intended procedure is believed to have a positive impact on the patient's life. The surgeon's role is not to treat HIV/AIDS but to help in the diagnosis of AIDS associated illnesses, recognize and manage complications of AIDS and its associated diseases. It is crucial for the surgeon to understand AIDS, the routes of transmission, the risk and implications of seroconversion and finally to deliver surgical care in a safe and acceptable manner based on existing guidelines.

Acknowledgements

My sincere thanks to Dr Anthony Rozario, DNB, FRCS (Glasgow), Associate Professor, Department of Surgery, for his guidance in the preparation of this article.

References

1. Miles AJG, Wastell C. AIDS and the General Surgeon. In: Taylor I, Johnson CD (eds). *Recent Advances in Surgery - 14*. Churchill Livingstone.1991: pp 85-98.

2. Al-Fallouji MAR. *Postgraduate Surgery. The Candidates' Guide*. Butterworth-Heinemann. 2nd edition.1998.pp95-99.

3. Polsky BW, Clumeck N. HIV and AIDS. In: Amstrong D, Cohen J (eds). *Infectious Diseases*. Mosby-Harcourt Publishers Ltd. 1999: Section5: 1.1-28.6.

4. Howard RJ. Surgical infections. In: Schwartz SI (ed). *Principles of Surgery*. Mc Graw Hill Publications. 7th edition.1999: pp138-142.

5. Fry DE. Surgical problems in the immunosuppressed patient. In: Townsend CM Jr (ed). *Sabiston Textbook of Surgery*. Harcourt Asia Pte Ltd- W.B Saunders Co. 16th edition. 1999:pp190-192.

6. Wastell C, Davis PA. The surgery associated with HIV infection. In: Morris PJ, Wood WC (eds). *Oxford Textbook of Surgery*. Oxford University Press Ltd. 2nd edition. 2000: pp 99-108.

7. *AIDS update: 21*. AIDS research and control center (ARCON). Mumbai. vol:6, No:2. Apr-Jun 2001.

8. http:/www.naco.nic.in/indianscene/esthiv.him (accessed April 2004)

9. Schecter WP. Surgery in HIV infected patients. In: Cohen PT, Sande MA, Volberding PA. *The AIDS Knowledge Base*. Lippincott Williams & Wilkins. Philiadelphia. 3rd edition.1999: pp 363-368.

10. Allen-Mersh TG. AIDS. In:. Russell RCG, Williams NS, Bulstrode CJK (eds). *Bailey & Love's Short Practice of Surgery*. Arnold. London. 23rd edition. 2000:pp 112-119.

11. Popejoy SL, Fry DE. Blood contact and exposure in the operating room. *Surg Gynaecol Obstet* 1991;172:480-83.

12. Rhodes RS, Bell DM. Prevention of transmission of bloodborne pathogens. *Surg Clin North Am* 1995;75:1047-1218.

13. Evrard S, Meyer P, van Haaften K, Christmann D, Marescaux J. Occupational risk to Surgeons of Unrecognised HIV infection in a low prevalence area. *World J Surg* 1993; 17:232-36.

14. Horowitz HW, Telzak EE, Sepkowitz KA, Wormser GP. HIV infection. Part-II. *Dis Mon* 1998;44:695-702.

15. Cardo DM, Culver DH, Ciesielski CA, Srivastava PU, Marcus R, Abiteboul D, *et al.* A case control study of HIV seroconversion in health care workers after percutaneous exposure. *N Eng J Med* 1997;337:1485-90.

16. De vita VT Jr, Hellman S, Rosenberg SA. *AIDS: Aetiology, diagnosis, treatment and prevention*. 4th edition. Lippincott-Raven. Philadelphia.1997: pp 645-718.

THE NEWER ANTIDEPRESSANTS

IBY NEERAKAL

The last decade has seen a sea change in the pharmacotherapy of depressive disorders with the development of a wide array of newer antidepressants. Till the late 1980's tricyclic antidepressants were the main stay of treatment of depressive disorders. They were handicapped by their troublesome anticholinergic side effects like postural hypotension, constipation, blurring of vision and dryness of mouth. The late 1980's saw the launch of a new group of antidepressants called the"selective serotonin reuptake inhibitors" (SSRIs). The first drug of this group fluoxetine was launched in the United States in 1987 and has been available in India from the early 1990's. The absence of anticholinergic, antihistaminergic, anti-alpha adrenergic, cardiotoxic effects, weight gain and potential for lethality in overdose generated wide patient and prescriber acceptance. The last few years has seen the launch of several newer antidepressants in India, which will be described in some detail below.

Newer SSRIs

Sertraline

Sertraline was the second SSRI to be made available in India. The antidepressant effect of sertraline is believed to be due to sertotonin reuptake inhibition at the presynaptic nerve terminal. It is efficacious in a wide range of psychiatric disorders like major depression, panic disorder, OCD (obsessive compulsive disorder), social phobia, dysthymia and atypical depression. Sertraline is begun at 50 mg/day with a target dosage of at least 100 mg/day in healthy adults. The dosage range is 50 to 200 mg in single or divided doses. In patients with hepatic impairment the mean half - life of sertraline increases significantly. This necessitates dosage reduction in patients with hepatic disease. The effect of renal impairment on sertraline metabolism is not clear. Elderly patients have a decreased clearance of sertraline compared to younger patients. The commonly reported side effects are nausea, diarrhea, agitation and sexual dysfunction (delayed ejaculation in males and anorgasmia in males and females). Compared to fluoxetine, certraline may have more gastrointestinal side effects and less activating effects.[1] Sertraline being highly protein bound has the possibility of interaction with other tightly protein bound drugs like warfarin and digitoxin. But significant drug interactions are much less compared to fluoxetine. Because of its intermediate half-life and favourable drug interaction profile it is a preferred drug by many prescribers.

IBY NEERAKAL M.D.
Assistant Professor

Department of Psychiatry
St. John's Medical College Hospital
Bangalore

Fluvoxamine

Fluvoxamine maleate is a selective serotonin reuptake inhibitor belonging to a new chemical series, the 2-aminoethyl oxime ethers of aralkylketones . Fluvoxamine has been mainly used in OCD but can also be used in depressive disorders. The recommended starting dose for a fluvoxamine tablets in adult patients is 50 mg, administered as a single dose at bedtime. The dose should be increased in 50 mg increments every 4 to 7 days, as tolerated until maximum therapeutic benefit is achieved, not to exceed 300 mg per day. For pediatric population (age 8-17 years) the recommended starting dose is 25 mg with 25 mg increments every 4-7 days, not to exceed 200 mg per day. In elderly patients and those with hepatic impairment, the clearance of fluvoxamine is decreased and hence will require lower initiation and increment doses.

The most common side effects are nausea, vomiting, headache and insomnia or sedation. Fluvoxamine should not be used with monoamine oxidase inhibitors (MAOI) or within 14 days of discontinuing treatment with a MAOI. Fluvoxamine increases the level of drugs like alprazolam, terfenadine, astemizole,

theophylline, warfarin, carbamazepine, beta blockers, diltiazem, sumatriptan, tricyclic antidepressants, lithium, clozapine and halperidol when used along with it. Fluvoxamine should be used with caution in patients with history of mania or seizures. Its safety in pregnancy and nursing mothers is not established.

Fluvoxamine is relatively safe in overdose. The commonly observed adverse events associated with fluvoxamine overdose included drowsiness, vomiting, diarrhea and dizziness. Other notable signs and symptoms seen with fluvoxamine overdose included coma, tachycardia, bradycardia, hypotension, ECG abnormalitites, liver function abnormalities and convulsions. The management of fluvoxamine overdose is mainly supportive with gastric lavage and activated charcoal. There are no specific antidotes. In managing overdosage, consider the possibility of multiple drug involvement.

Paroxetine

Paroxetine is the latest SSRI to be launched in India. Paroxetine is indicated for the treatment of depression, OCD and panic disorders. It is contraindicated in patients taking MAOIs. Paroxetine has to be used with caution in patients with a history of mania and seizures. There have been several reports of abnormal bleeding (mostly ecchymosis and purpura) associated with paroxetine treatment, including a report of impaired platelet aggregation. There is a risk of increased bleeding diathesis in the face of an unaltered prothrombin time when paroxetine is used along with warfarin. While cytochrome P450 inhibitors like cimetidine increase paroxetine concentration by about 50%; hepatic enzyme inducers like phenobarbital and phenytoin, reduce paroxetine levels by about 50%. Paroxetine inhibit TCA metabolism leading to higher plasma TCA concentrations. The dose of TCA may need to be reduced when co-administered with paroxetine. There are no adequate and well-controlled studies establishing its safety in pregnant and lactating women.

The commonly observed adverse events with the use of paroxetine are asthenia, sweating, nausea, decreased appetite, somnolence, dizziness, insomnia, tremor, nervousness, constipation, ejaculatory disturbance and other male genital disorders and impotence. Compared to other SSRIs, paroxetine is reported to be more sedating and cause more constipation, weight gain and sexual dysfunction. In the treatment of depression, the usual starting dose of paroxetine is 20 mg daily, increased gradually, if necessary, by increments of 10 mg to a maximum of 40 mg daily. The recommended initial dose is 10 mg/day for elderly patients, debilitated patients and patients with severe renal or hepatic impairment. Dosages may be increased if indicated but should not exceed 40 mg.

Signs and symptoms of overdose with paroxetine include nausea, vomiting, sedation, dizziness, sweating and facial flushing. There are no reports of coma and convulsions with paroxetine overdose. Treatment of over dose is mainly supportive. There are no specific antidotes for paroxetine overdose. Gastric lavage and activated charcoal are useful. In case of ECG abnormality cardiac function may have to be monitored. Due to large volume of distribution of paroxetine, forced diuresis, dialysis, hemoperfusion and exchange transfusion are unlikely to be of benefit.

SEROTONIN NOREPINEPHRINE REUPTAKE INHIBITORS (SNRI)

Venlafaxine

Venlafaxine belongs to a new group of antidepressants called serotonin norepinephrine reuptake inhibitors. Venlafaxine is a potent inhibitor of norepinephrine and serotonin reuptake and a moderate inhibitor of dopamine reuptake. At lower doses (<150 mg) the drug acts essentially like an SSRI with a short half-life. At higher doses. venlafaxine appears to recruit its noradrenergic mechanism. In this sense it is like using an SSRI with a built in combination treatment option accessed by increasing the dose if the first trial is ineffective. Venlafaxine has been indicated for the treatment of depression, generalized anxiety disorder and mixed anxiety and depression. There have been reports of venlafaxine being efficacious against resistant depression. Concomitant use of venlafaxine in patients taking monoamine oxidase inhibitors is contraindicated. The usual dosage range is 75 to 225 mg given in divided doses in a twice-daily schedule. Dosages as high as 450 mg/day have been used in seriously ill depressed inpatients. The extended release form of venlafaxine gives the convenience of

once a day dosing. Venlafaxine therapy is associated with sustained increases in blood pressure. At the higher doses, 5% to 7% of patients may develop a modest but persisting increase in blood pressure. It is recommended that patients taking venlafaxine have regular monitoring of their blood pressure. In patients who have experienced a sustained increase in blood pressure, the dose may be reduced or the drug be discontinued.

The safety and side effect profile of venlafaxine is generally similar to that of the SSRIs. Anxiety or nervousness may emerge or worsen on initiation of treatment. Other side effects include nausea, insomnia, sedation, dizziness, sweating and constipation. In patients with moderate hepatic impairment it is advisable to reduce the total daily dose by 50%. It is recommended that the total daily dose be reduced by 25% in patients with mild to moderate renal impairment and the total daily dose be reduced by 50% and the dose be withheld until the dialysis treatment is completed (4 hours) in patients undergoing hemodialysis. The safety of venlafaxine in pregnant and nursing women has not been established. During premarketing experience, seizures occurred among 0.26% of venlafaxine treated patients and mania or hypomania occurred in 0.5% of venlafaxine treated patients.[2] Venlafaxine should be used with caution in patients with a history of mania. At its usual therapeutic dose venlafaxine has no significant pharmacokinetic or pharmaco-dynamic interactions with other drugs. This is a significant advantage for venflaxine over other antidepressant drugs.

Like other newer agents venlafaxine is safer in overdose that older agents. It has a wide therapeutic index and no mortality has been reported in patients who have consumed many times the therapeutic doses. Overdosages should be managed with general supportive measures. Use of activated charcoal or gastric lavage should be considered.

Mirtazapine

Mirtazapine belongs to a new group of antridepressants called the noradrenergic and specific serotonergic antidepressants (NaSSA). Mirtazapine has a unique dual model of action. It antagonizes the presynaptic alpha-2-receptors on the adrenergic and serotonergic neurons thereby enhancing norepinephrine (NE) and 5 hydroxytryptamine (5-HT) neurotransmission. Moreover mirtazapine also blocks 5-HT2 and 5-HT3 receptors preventing many of the undesirable side effects seen with SSRIs and SNRI like insomnia, nausea and sexual dysfunction. Mirtazapine has been indicated for use in patients with major depression, painc disorder, generalized anxiety disorder and chronic post traumatic stress disorder. Mirtazapine has a faster onset of action than the SSRIs. Mirtazapine has exhibited a lower risk of hypomanic or manic switch from depression as compared to TCAs or SSRIs. Studies have found mitrazapine to be better tolerated than TCAs, SSRIs or SNRIs. Mirtazapine has some special indications like as an add-on antidepressant for patients with refractory depression. It is also useful in patients who cannot tolerate SSRIs because of sexual dysfuction. The effective dose range of mirtazapine in adults is 15-45 mg/day administered in a single dose preferably at bedtime. Dosage adjustment should not be made more often than every 1-2 weeks due to the very long half-life of mirtazapine. In elderly patients and patients with hepatic and renal impairment, lower initial dose and slower dose titration is required.

The most common side effects of mirtazapine are dose dependent drowsiness, dry mouth, increased appetite, weight gain and dizziness. These side effects tend to improve with time. In premarketing clinical trials 3 out of 2,796 patients treated with mirtazapine developed agranulocytosis. All three patients recovered completely after mirtazapine was stopped. No cases of agranulocytosis were reported during the post marketing surveillance of 9000 mirtazapine treated patients in Netherlands.[3] In controlled studies nonfasting cholesterol increases to more than 20% above the upper limit of normal were observed in 15% of patients treated with mirtazapine compared 7% for placebo and 8% for amitriptyline.[3] Mirtazapine should be used with caution in pregnant women and nursing mothers. In premarketing clinical trials with mitrazapine was assosciated with a low incidence of seizures (1 out of 2,796 mirtazapine patients).[4]

However, in the absence of controlled studies in patients with a history of seizures, it should be used with caution. In view of its sedating property, patients on mitrazapine should be cautioned about engagement in activities

requiring alertness until they have been able to assess the drug's effect on their own psychomotor performance. Since mirtazapine is a weak inhibitor of hepatic enzymes it has no clinically significant pharmacokinetic interactions with other drugs. Coadministration of mirtazapine with alcohol or diazepam results in impaired cognitive and motor performances.

Mitrazapine is considered to be relatively safe in overdose. Mortality has been reported only when taken with other drugs. Signs and symptoms reported with overdose included disorientation, drowsiness, impaired memory and tachycardia. There were no reports of ECG abnormalities, coma or convulsions following overdose with mirtazapine. There are no specific antidotes for mirtazapine. The treatment consists of general supportive and symptomatic measures with monitoring of cardiac and vital parameters. Gastric lavage, activated charcoal and maintenance of airway with adequate oxygenation may be of benefit.

Moclobemide

Monoamine oxidase inhibitors (MAOI) were introduced in 1950s, a little earlier than the tricyclic antidepressants. MAOIs were introduced as a treatment of depression in 1957. The initial MAOIs like iproniazid, phenelzine, isocaarboxazid and tranylcypromine were all irreversible and nonselective inhibitors of monoamine oxidase. The use of these drugs came down due to the report of life threatening hypertensive crisis in patients on these drugs. By 1965 the mechanism of tyramine induced hypertension was elucidated, thereafter this hypertensive crisis could be avoided by the use of dietary restrictions. They were also handicapped in view of life threatening interactions with other drugs.

Due to these complexities the use of MAOIs were significantly reduced in many parts of the world. More recently a new group of drugs RIMA – reversible inhibitors of monoamine oxidase A have been introduced. Moclobemide, a prototype of this class selectively and reversibly inhibits MAO-A and hence has a much improved tolerability profile. It eliminates the risk of hypertension occurring as a result of interaction with tyramine rich diet, hence special dietary restrictions are not required to be followed. Moclobemide is one of the first MAOIs to be introduced in India. Moclobemide has similar efficacy in both endogenous and atypical depressions. Moclobemide appears to be as effective as other antidepressants in the elderly with better tolerability and safety profile. Moclobemide is also effective in social phobia, panic disorder and post-traumatic stress disorder. The recommended initial dose of moclobemide is 300 mg daily, usually administered as two divided doses, after meals. The dosage can be increased to a maximum of 600 mg per day depending on the severity of symptoms.

In patients with severe hepatic dysfunction, the daily dose of moclobemide should be substantially reduced to one third or one half of standard dose. In patients with moderate to severe renal dysfunction no significant adjustment in dosage of moclobemide is required. Elderly patients do not require any dosage adjustments. Strict dietary adjustment are unnecessary but large amounts of tyramine-rich food such as mature cheese, yeast extracts and fermented soya bean products should be avoided.

The commonly observed adverse reactions with moclobemide were insomnia, tremors, agitation, restlessness, nausea and hypotension. Moclobemide is better tolerated than the TCAs and SSRIs. The safety of moclobemide in pregnancy and lactation is not established. Moclobemide should be used with caution in psychotic conditions. Manic episodes can be provoked by moclobemide in patients with bipolar disorders. Great caution should be exercised when moclobemide is co-administered with TCA's and SSRIs in view of risk of serotonin syndrome. Pethidine can also cause serotonin syndrome if it is administered in patients on moclobemide. Concomitant use of moclobemide and MAO-B inhibitors like selegiline should be avoided or patients receiving this combination should adhere to strict dietary tyramine restrictions.

Moclobemide is relatively safe in overdose. Mortality has been reported in mainly mixed drug overdoses. Signs and symptoms of overdosage with moclobemide include nausea, drowsiness, mild disorientation, slurred speech, amnesia and reduced reflexes. Treatment consists of general supportive measures. Gastric lavage or induction of emesis, activated charcoal and fluid control maybe of benefit.

Bupropion

Bupropion is a unicyclic antidepressant of the aminoketone class. The primary indication of bupropion is for the treatment of major depression. It is comparable in efficacy to TCAs, SSRIs and MAOIs. This drug is also beneficial in treating patients suffering from depression associated with psychomotor retardation, as it has a mild stimulant rather than sedative property. It has also been extensively used to treat bipolar depression in view of its decreased propensity to cause a manic or hypomanic switch. Bupropion is also a popular combination agent with other antidepressants like SSRIs and venlafaxine. Other indications for bupropion are attention deficit hyperactivity disorder in children and adults and smoking cessation. Patients are generally started on 100 mg twice daily with an increase to 100 mg three times daily as tolerated. An initial antidepressant effect decomes apparent within 2 to 4 weeks. It has a more favourable side effect profile than TCAs. It is not sedating, does not produce significant orthostatic hypotension or cardiac abnormalities even in patients with cardiac disease. Compared with SSRIs, bupropion has the advantage of not being associated with sexual dysfunction.

The adverse effects observed with bupropion are agitation, restlessness, insomnia, anxiety and gastrointestinal disturbances. Some patients may develop psychotic symptoms due to which it has to be used with caution in psychotic disorders. The primary side effect attributed to bupropion is the increased incidence of generalized seizures in 4/1000 patients taking a prescribed dose up to 450 mg daily.[5] There is a tenfold increase of seizures in higher doses between 450 and 600 mg. Therefore a maximum dose of 450 mg daily is recommended. Bupropion is relatively safer in overdose than TCAs. No major cardiovascular toxicity was seen in patients with bupropion overdose. Neurological toxicity included tremors, lethargy and seizures. Combined use of bupropion with MAOIs should be avoided because of the risk of hypertensive reaction. When used in combination, carbamazepine decreases bupropion blood concentration and bupropion increases valproate concentration.[5] Addition of bupropion to antiparkinsonism medication can bring down the dosage requirement of antiparkinsonism medication. But caution is required in this combination in view of reports of hallucinations, confusion and dyskinesias when bupropion was added to previous therapeutic dosages of levodopa.[5]

Conclusion

The availability of the many new antidepressants have improved the treatment options in depressed patients. Since most of them have comparable efficacy, the choice of medication will be dependent on side effect profile and prescriber's comfort level with the medication.

Note

Since the original submission of this article, two other selective serotonin reuptake inhibitors are now available in the Indian market.

Citalopram: a bicyclic pthalane derivative is usually used in the dose range of 20-40 mg per day. The side effects reported are nausea, dry mouth, drowsiness, insomnia, tremor, increased sweating, diarhoea and sexual dysfunction (ejaculatory difficulties). Caution is advised if co administered with TCAs. It has been used in depression, OCD, binge eating disorder and panic disorder.[6] Inspite of its low toxicity profile, arrythmias and seizures have been reported in overdose.[7]

Escitalopram : is the pharmacologically active S enantiomer of citalopram. It is effective in the treatment of major depression in the dose of 10-20 mg per day. It has also been used in treatment of panic disorder. Side effects reported with it are nausea, fatigue, insomnia, drowsiness, ejaculatory dysfunction and increased sweating. It is contraindicated in patients who are also taking MAOIs or with hypersensitivity to escitalopram or citalopram.[8,9]

References

1. Arana GW & Rosenbaum JF. "Antidepressant drugs", Chapter 3; Handbook of psychiatric drug therapy. Philadelphia; Lippincot Williams & Wilkins., 2000. 53 – 113.

2. Dollery. Therapeutic drugs, 1999 editiion. Venlafaxine, V16-V20.

3. Montgomery SA. Safety of mirtazapine : A review. Int Clin Psychopharmacology 1995, 10 suppl. 4,37-45.

4. Stimmel GL. Mirtazapine; An antidepressant with noradrenergic and specific serotonergic effects. Pharmacotherapy 1997, 17(1), 10-21.

5. Golden RN & Nathan LM. "Bupropin", Cchapter in Comprehensive textbook of psychiatry. Kaplan & Sadock, New York, 2000, 234-2328.

6. Tan JY, Levin GM. 1999m Citalopram in the treatment of depression and other potential uses in psychiatry. Pharmacotherapy. Jun;19(6):675-89.

7. Cuenca PJ, Holt KR, Hoefle JD. 2004. Seizure secondary to citalopram overdose. J Emerg Med.26(2):177-81.

8. Hirschfeld RM, Vornik LA (2004). Newer antidepressants: review of efficacy and safety of escitalopram and duloxetine. J Clin Psychiatry. 65 Suppl 4:46-52.

9. Stahl SM, Gergel I, Li D. (2003). Escitalopram in the treatment of panic disorder: a randomized, double-blind, placebo-controlled trial. J Clin Psychiatry. 64(11):1322-7.

THE ELDERLY INDIA – a health challenge

ARVIND KASTHURI

The term "elderly" has been defined in many dimensions. Biologically the process if ageing begins at least as early as puberty and is a continuous process through adult life Socially the characteristics of members of society perceived as being old vary with the cultural setting and from generation to generation. Economically, especially in rural areas, the elderly are simply seen as being those who are too old to work and earn. Chronologically numeric age has been traditionally used in defining the term "elderly". Even though a single "cut off" age which would define the elderly would vary between country and region considering the biologic, sociologic and economic and differences in their populations, the United Nations in 1980 defined 60 years as the age of transition of people to the elderly segment of the population.[1] Some authors classify the elderly as the *young* old (60-70 yrs), the *old* old (70-80 yrs) and the *oldest* old (80+ yrs).[2]

The global population of persons aged 60 yrs and above is estimated at 600 million in the year 2000. Two of every three of these persons are living in the developing world. The global population of elderly person is expected to reach 1.4 billion in 2030. Of this rise, more than half will be in Asia. (World Bank 1994).[3]

In India, the number of persons 60 years and over was 12 million at the turn of the century.[4] This has increased 6 fold to about 71 million (expected) in 2001.

The proportion of population aged 60 years and above is also rising. It was 5.63% in 1961, and is expected to 7.1% in 2001 and 9.87% in 2021.

ARVIND KASTHURI M.D., D.N.B.

Associate Professor
Department of Community Health
St. John's Medical College
Bangalore.

This makes India a "greying" nation, with the growth rate of the elderly segment being greater than the growth rate of the population as a whole. It is expected that by 2021 the growth rate of the elderly will be 1.5 times higher than the growth rate of the general population.

The determinants of this rise in proportion of elderly include fertility and mortality, as measured by the Total Fertility Rate (a measure of the number of children a woman will bear during her lifetime), the Crude Death Rate and the expectation of life at birth.

The Total Fertility Rate for India as a whole was around 6 in 1971, has since reduced to 4.8 in 1981 and is projected to reach 2.6 by 2021. This implies that the proportion of young persons will reduce in the years to come, as the "bulge" in the age-sex pyramid moves upward from the base, leading to a higher proportion of people in the older age groups. The median age, which is defined as the age that divides the population into two equal halves, was 20 years in 1961, and is expected to reach 28 years in 2021.

The Crude Death Rate has dropped phenomenally from 28.5 per 1000 persons in 1951-61 to 8.7 per 1000 persons in 2001. (Sample Registration Scheme 2001).

The expectation of life at birth was 49.3 years in 1971 and has risen to 62.2 years in 1996 and is expected to reach 70.2 years by 2021.[5] The expectation of life at 60 years in 1970-75 was 13.8 years. This has risen to over 16 years now. At 70 years of age, a person was expected to live for an additional 8.9 years in 1970-1975. This has also risen to 10.2 years currently.

The high and growing number of persons above the age of 60 (70 million is more than 4 times the size of the entire Australian population) poses challenges to Indian society. The problems faced by the elderly include social problems, stemming from the lack of an organized social security system as exists in many western societies. Added to this is the

changing social fabric especially in urban India, where migration and change in value systems leads to isolation and loneliness in old age. Economic insecurity can lead to a renewed poverty at the time it hurts most – old age.

Groups have been identified within the elderly segment as those likely to face particular risk with respect to their health or socio economic status. Such "high risk" elderly include[6]

1. The oldest old, more than 80 years old
2. Elderly living alone and couples living by themselves
3. Elderly women, especially single and widowed
4. An elderly couple where one member is ill
5. Elderly living in institutions as opposed to those living in families.

The health problems of the elderly are an important cause of concern in this segment of the population. It is estimated that 45% of the elderly have chronic diseases and disabilities. The 10 most common diseases in this segment of population are hypertenison, cataract, osteoarthritis, chronic obstructive pulmonary disease, coronary heart disease, diabetes mellitus, benign prostatic hypertrophy, dyspepsia, constipation and depression. The five most frequent causes of death include bronchitis and pneumonia. coronary heart disease, cerebrovascular accidents, cancer and tuberculosis.

The health care of elderly people is envisaged at the following levels:

1. Primary health care including primary medical care which includes the point of first contact and has elements of community education and community participation in addition to simple health service delivery.

Primary care is organized based on the fact that the majority of elderly people live in their own homes or that of their relatives. Old age in itself does not indicate a need for specialist geriatric care.

Such primary care may be delivered by professionals ranging from general practitioners to nurses trained in the care of the elderly. The components of such a service would include a simple clinic or health centre-based outpatient service and a domiciliary service component.

2. Specialised Geriatric Care, which should ideally be a referral service based at an institution which offers multidisciplinary services.

The specialized geriatric unit situated at a hospital will serve the function of a referral centre for a primary care unit and will look after those elderly who are acutely or critically ill. The specialized unit will ideally work along with the other disciplines in a referral hospital. Other functions which the specialized care unit could serve include training of the primary care team and rehabilitation and long term care, if the infrastructure and resources permit.

India is an example of a developing country which lacks organized services for the elderly in the health, social or economic sectors. The health services available for the elderly in India are generally contained within the health services for the general population, without any special or specific initiatives for this group.

Such services include

1. Services provided to persons retired from the Government or from employment in the organized sector – the Central Government Health Service (CGHS) and the Employees' State Insurance (ESI) would be examples.

2. Services provided to patients attending specialized Geriatric clinics / units / departments in hospitals – this exists in a miniscule proportion of existing medical colleges / teaching hospitals.

3. Services provided by private commercial organizations to the elderly at their homes / providing ambulances / other forms of commercial medical service.

4. Services provided by voluntary organisatiions, mostly on an ad hoc basis.

Departments / Units of Geriatric medicine have been established at only 2 medical colleges out of more than 150 institutions in the country. This discipline, which places emphasis on functional assessment, holistic care and a personalized approach, has yet to make a mark on the Indian health professional.

With the numbers of people above 60 years of age in India poised to double over the next 20 years and reach a staggering 135 million, the

challenge for the health sector in this country is to make a meaningful health service available in some form to this growing and needy segment of the population.

References

1. WHO Technical Report series (TRS 779 "Health of Elderly" – report of a WHO expert committee, 1987.
2. Socio economic problems (of the elderly) – Venkoba Rao, in Geriatric care in India. OP Sharma (Ed), A n B Publishers 1999 pp 627.
3. India's Elderly – burden of challenge? Irudaya Rajan, Mitra, Sankara Sarma, Sage publications 1999.
4. Health care of the elderly – A manual for trainers of physicians in Primary and Secondary Health care Facilites – WHO, Ministry of Health and FamilyWelfare and All India Institute of Medical Sciences.
5. Irudaya Rajan, S and Mohanachandran P "Infant and Child Mortality estimates "Economic and Political Weekly Vol XXXIII No 19 May 9-15, 1998.
6. WHO Technical report series 548, "Planning and organization of geriatric service" Report of a WHO expert committee 1974.

LASER THERAPY

SUJATHA RAJ HARSHAD

The term laser is an acronym for 'light amplification by stimulated emission of radiation'. Lasers were first used in the early 1960's for treatment of port wine stains, tattoos and cutaneous tumours. Although the early layers were effective in the treatment of these conditions, there were considerable side effects in the form of necrosis, scarring and hyper-pigmentation. With advances in technology, newer lazers were developed which are much safer and have lesser side effects.

Types of Lasers

A variety of lasers are available: carbon dioxide, Er:YAG, Ruby, Nd:YAG and Alexandrite etc. They are named according to the material that constitutes their active medium. (for example, in the CO_2 laser – active medium contains CO_2) They differ in the wavelength of light that is emitted and in the modes of emission of the laser beam (continuous or pulsed or Q-switched).

Principles of Lasers

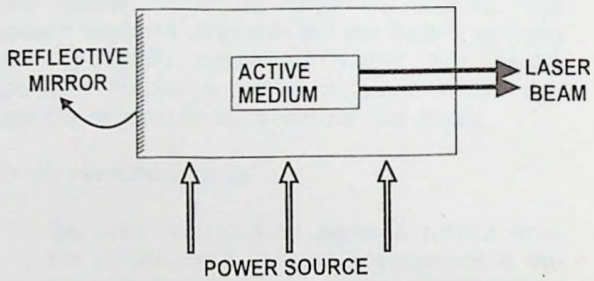
Electrical energy from a power source excites the atoms in the lasing/active medium. These excited atoms are unstable and return to their stable state releasing energy in the form of light (laser beam). The laser beam has high energy and is a concentrated beam of light. This laser beam is then applied to the target to produce the desired effects. By choosing the appropriate wavelength, pulse duration and energy a particular skin target can be selectively destroyed with minimal damage to the surrounding areas, e.g. when the target is hemoglobin the wavelengths suitable are 418nm, 524nm or 577 nm. For melanin the 600-1200nm wavelengths are suitable.[1]

SUJATHA RAJ HARSHAD
MD, DVD, DNB
Assistant Professor
Department of Dermatology
St. John's Medical College Hospital
Bangalore

Components of laser machine (Fig 1)

1. Power Source
2. Lasing medium or active medium
3. Reflecting mirrors

Figure 1 : Schematic representation of the component of laser machine



Indications

A wide variety of skin lesions can be treated with laser therapy. (Table 1)

Pigmented lesions

Freckled, lentigines and café au lait macules respond to Nd:YAG, Alexandrite and Q-switched ruby lasers. However recurrences have been reported.[2] The treatment of melanocytic nevi with lasers is controversial. Recurrences appear to be common.[3] The cosmetic results are better with laser irradiation than with standard excision. Atypical pigmented lesions should be biopsied prior to laser therapy to rule out malignant melanoma. The results with lasers in the treatment of post-inflammatory hyper-pigmentation and melasma have been unpredictable. Lasers have been shown to give better cosmetic results in the treatment of tattoos than conventional surgical methods.

Vascular lesions

Pulsed dye and Nd:YAG lasers have been used to treat superficial cutaneous hemangiomas and portwine stains.[4] Other lesions which have been reported to respond to laser therapy are

telangiectasias, angiokeratomas, angiofibromas, pyogennic granulomas, cherry angiomas and lymphnagioma circumscriptum.

Resurfacing

Carbon Dioxide and Er:YAG lasers have been used in resurfacing of skin for treatment of acne scars and photoageing. The Er:YAG causes less thermal damage, less scarring and faster wound healing and therefore ita is considered more efficient than the CO_2 laser.

Benign superficial tumours

Neurofibromas, syringoma, xanthelasma, trichoepithelioma and a number of other benign dermal tumours have been successfully removed with the help of lasers.

Inflammatory

Lasers have proven to given better access than conventional surgery in treating intertriginous areas like the axilla and groin. The conditions in which there has been reported benefit include – Hailey-Hailey disease. Darier's disease and hidradenitis suppurativa.

Hair removal

Several lasers are available for removal of hair Viz.: alexandrite, Nd:YAG, ruby and diode lasers. Temporary removal of hair does occur. Permanent hair growth reduction has been reported. Response rates are variable and multiple sessions are required for the same area.[5,6]

Miscellaneous

CO_2 lasers have been used for treatment of plantar and periungual warts resistant to conventional modes of therapy like electrodessication, cryotherapy and chemical cautery. High cure rates have been reported. The wart virus (Human Papilloma Virus) has been well documented in the laser smoke plume and the laser staff should take adequate precautions against contracting the infection.

Hair transplantation[7] and punch grafting (for vitiligo) have been aided by laser therapy.[8,9] The advantages are that there is reduced bleeding from the site and the time required for surgery is shortened. The thermal damage to the recipient site may result in poor graft survival.

Pre-operative checklist

It is important to discuss the expectations, limitations, outcome, risks and cost of the procedure with the patient.

- Obtain written informed consent for the procedure
- Check for medications being taken by the patient, history of drug allergies or infections.

Post laser care

Regular dressings and antibiotics need to be prescribed along with sunscreens.

Side effects

The laser is beneficial if used properly. However, side effects can occur. The common side effects are hyper or hypopigmentation and scarring. Post-operative erythema and infection may be other limiting factors.

Precautions to be taken

Use of face mask, gloves and eye protection is a must for persons within the operating room.

Use of the suction/smoke evacuator is necessary to minimize the risk of viral particle exposure to staff in the operating room.

Recent Advances

Lasers are also being used for diagnostic purposes such as imaging and for photodynamic therapy. Thus the different forms of laser and its use in skin disorder continue to evolve and the future seems exciting.

References

1. Lask GP, Lowe NJ. Lasers in cutaneous and cosmetic surgery. Pennsylvania, Churchill Livingstone, 2000.

2. Grossman ME, Anderson RR, Farinelli W et al. The treatment of café au lait macules with lasers. Arch Dermat 1995;131:1416-1420.

3. Grevelink JM, Van Leewuwen RL, Anderson RR et al. Clinical and histological responses

of congenital melanocytic nevi after single treatment with Q-switched lasers. Arch Dermat 1997;133(3):349-353.

4. Spicer MS, Goldberg DJ. Lasers in dermatology. JAAD 1996;34:1-25.

5. Dietrickx CC, Grossman ME, Farinelli WA. Permanent hair removal by normal mode Ruby laser. Arch Dermat 1998;134:837-842.

6. Roger CJ, Glaser DA, Siegfrid EC. Hair removal using topical suspension assisted Q-switched Nd:YAG and long pulsed Alexandrite lasers: A comparative study. Dermatol Surg 1999;844-850.

7. Chu EA, Rabinov CR, Wong BJF et al. Laser-assisted hair transplantation: Histologic comparison between CO_2 and Ho:YAG lasers. Dermat Surg 2001;27(4):335-342.

8. Knoell KA. Treatment of vitiligo with the Ultrapulse Carbon dioxide laser in patients concomitantly receiving oral psoralen plus UV-A therapy Arch Dermat 1997;133(12):1605-1606.

9. Thissen M, Westerhof W. Laser therapy for further depigmentation in vitiligo. Int J Dermat 1997;365(5):386-388.

Table 1

Types of lasers and their common clinical uses

Laser	Wavelength (nm)	Target	Common Uses	Advantages /Disadvantage
Pulsed dye Laser	510,577	Hb	Superficial vascular lesions, hypertrophic scars	Transient purpura, scarring, dyspigmentation
Ruby	694	melanin	Pigmentation – epidermal and dermal, tattoos, hair	Transient hyper or hypopigmentation, epidermal atrophy
Alexandrite	755	melanin	Pigmentation – epidermal and dermal, tattoos, hair	Hypopigmentation
Nd:YAG	1064	No specific target	Pigmentation – epidermal and dermal, tattoos, hair, vascular	Deep tissue penetration
Erbium YAG	2940	water	Resurfacing	Quicker wound healing, less scare, less erythema, poor hemostasis
Carbon Dioxide	10,600	water	Resurfacing, excision	Delayed wound healing, hemostasis good

MANAGEMENT OF EPILEPSY

SARMA G.R.K.

Management of Epilepsy

The management of epilepsy is a complex process and requires a basic understanding of the pathogenesis, clinical features and natural history of various epilepsy syndromes as well as a logical and individualized approach to each patient. Certain special patient groups like pregnant women and the elderly require additional care and skill in the management. Decision- making is called for at every stage of management including the decision to initiate therapy, the choice of the most appropriate drug, the duration of drug treatment, the decision to withdraw anti-epileptic drugs and the decision to consider surgical management in difficult cases. These issues are discussed in detail in the subsequent sections.

1. NEWLY DIAGNOSED PATIENTS

The decision to initiate therapy in newly diagnosed patients is critical. In addition to its biological effects, therapy confers illness status, confirms the state of being epileptic and can effect the self-esteem, social relationships, education and employment. Chronic subtle side effects are not easily detected and weigh heavily on decision to treat. For example, the potential adverse effects of anti-epileptic drugs (AED) on learning in children are an important consideration in treatment of childhood epilepsies. However, the benefits of therapy include, lower risk of recurrence of seizures, potential injury and death, psychological and social benefits of more security. One hypothesis is that early therapy will prevent establishment of chronic epilepsy and improve the long-term outcome.

G.R.K. SARMA MD, DM.
Associate Professor

Department of Neurology
St. John's Medical College Hospital
Bangalore

However, there is no substantial evidence to support this hypothesis. The decision to treat depends on a balance of benefits versus drawbacks of therapy and should be individualized. Though there are no strict rules, general guidelines for starting anti epileptic therapy are:

1. Diagnosis of epilepsy must be firm. Syncope and non-epileptic attacks (pseudo-seizures) are frequently mistaken for epileptic attacks. There is no place at all for a trial of treatment to clarify the diagnosis, because it seldom clarifies. A good first hand account is essential as diagnostic tests are often non confirmatory.

2. Risk of recurrence of seizures must be sufficient. Most would accept that 50-80% of all patients with a first non-febrile seizure would have further attacks, the greatest risk being in the first 6 months after the first seizure.[1,2] The risk of recurrence is influenced by

- *Etiology*: greater risk in structural cerebral disease and least in acute symptomatic epilepsy. In patients with learning disability or cerebral damage, the risk approaches 100%.
- *EEG*: There is consensus that, the risk of recurrence is high if the first EEG shows spike and wave discharges. However, the predictive value of a normal EEG or EEG with mild abnormalities is less clear.
- *Age*: the risk of recurrence is higher in those under 16 or over 60 years.
- *Seizure type*: partial seizures are more likely (94%) to recur than generalized seizures.

3. Seizures must be sufficiently troublesome.

- *Type of seizures*: some benign epilepsy syndromes have excellent prognosis without therapy (e.g. benign rolandic epilepsy) and do not require long-term therapy. Some types of seizures have minimal impact on quality of life (e.g. partial, absence or sleep attacks). So the benefits of treating such seizures even if happening frequently can

sometimes be outweighed by its disadvantages.

- *Frequency and timing of seizures*: if the baseline frequency is low, the disadvantages of treatment can be high. It would be unwarranted to treat a person having less than one seizure a year, especially if this was confined to sleep and a minor or a partial seizure,
- *Precipitation of seizures*: occasionally, seizures occur only in specific circumstances or with certain precipitants (photosensitivity, fatigue, alcohol). Avoiding these circumstances may avoid the need for drug treatment. For example, photosensitive seizures can be prevented by using a small screen, using remote control, using 100Hz television screen with liquid crystal display, using polarizing glasses, keeping screen contrast and brightness low, avoiding exposure when sleep deprived and avoiding looking at flickering pattern.[3]

4. Good compliance must be likely.

5. Patient must be fully counseled and patient's wishes must be fully accounted for. The role of physician is to explain the relative advantages and disadvantages of therapy and the final decision must be left to the patient.

Protocol for treatment of newly diagnosed epilepsy patients

1. Establish diagnosis
2. Identify precipitating factors
3. Decide upon the need for antiepileptic drug therapy
4. Counsel the patient regarding therapy
5. Start monotherapy with the chosen first line drug, initially at low dosage and titrate up to a low maintenance dose. Loading dose is needed only in cases presenting with status epilepticus.
6. If the seizures continue, titrate to higher doses
7. If maximal doses fail, alternate monotherapy has to be started and once the recommended doses have been reached, the previous drug has to be gradually tapered.
8. If seizures continue, reassess the diagnosis and patient compliance.
9. If seizures continue, a combination therapy of two or even three drugs will be needed.

Starting AED

The goal of therapy is to achieve complete control without adverse effects. In most cases, this is achieved with initial first line therapy. In others, it may take time to find the right medication and in others, seizure control may be possible only at the expense of side effects and in still others, the goal may not be realized.

Monotherapy versus combination therapy

Single drug therapy will provide optimal seizure control in about 80% of patients.[4] Its advantages are better tolerability, simpler regimen, no interactions and less risk of teratogenicity. Combination therapy is needed in 20% patients, but carries the disadvantages of increased side effects, increased risk of pharmacokinetic interactions and teratogenicity.

Classify seizure type

This is very important in choosing the best drug. The first and second line drugs in different seizure types[5] are shown in the Table 1.

Serum Antiepileptic Drug Concentration Monitoring

This is very useful in monitoring phenytoin therapy and moderately useful in monitoring of carbamazepine and phenobarbitone therapy and is of very little use in valproate and vigabatrin therapy. Its usefulness in monitoring gabapentine and lamotrigine therapy is not established.[6]

The major indications for serum AED concentration monitoring are to check on compliance with prescribed therapy, to determine whether symptoms or signs are likely to be dose related adverse effects of the prescribed therapy, to monitor pharmacokinetic interactions to guide dosing of AED, to monitor patients who are acutely ill, pregnant and those with renal or hepatic disease.[7]

Table 1. Choice of anti-epileptic drugs in various seizure types

Seizure Type	First line drugs	Second line drugs
Simple & complex partial seizures primary & secondarily generalized tonic clonic seizures	Carbamazepine phenytoin valproate	Phenobarbitone topirmate lamotrigine clobazam clonazepam gabapentin
Absence seizures	Valproate ethosuximide	Clobazam clonazepam phenobarbitone lamotrigine
Atypical absence, tonic seizures, clonic seizures	Valproate	Ethosuximide clonazepam clobazam carbamazepine lamotrigine phenobarbitone
Myclonic seizures	Valproate	Clonazepam clobazam lamotrigine phenobarbitone

PATIENTS WITH EPILEPSY IN REMISSION

Epilepsy is said to be in remission when seizures have not recurred for long periods of time, which is arbitrarily defined as 2-5 years in different centers. In such patients, routine hematological and biochemical monitoring is not required.

Discontinuation of therapy: It must be understood that withdrawal of therapy is never risk-free. The decision to withdraw therapy then depends on the level of risk the individual patient is prepared to accept.

Assessing the risk of seizure recurrence after drug withdrawal: the factors with increased risk of recurrence of seizures are shown in Table 2.

Table 2. Factors which increase the risk of recurrence of seizures

- Age over 16 years
- Need for 2 or more drugs to control seizures
- Seizures after starting treatment
- Secondarily generalized seizures
- Myclonic seizures
- EEG with spike and wave discharges
- Short period of freedom from seizures
- Type and severity of epilepsy
- Mental retardation
- Neurological deficit
- Family history of epilepsy

The above risk factors are additive and when two or more adverse factors are present, the risk of recurrence is over 70%. Most recurrences after drug withdrawal occur within the first six months and this should be clearly explained to the patient. The risk of recurrence of seizures after stopping AED varies.[8,9] Certain childhood epilepsy syndromes like childhood absence epilepsy, benign rolandic epilepsy and uncomplicated febrile conclusions have particularly good outcome after withdrawal of AED. In a recent prospective study in children, there was a 36% recurrence rate following withdrawal of drug after a mean seizure free period of 2.9 years.[10] In general withdrawal of drugs may be attempted after a 2 year seizure free period. After a single attack, 6 months of therapy may suffice. The risks of recurrence should be explained to the patient. Only one drug at a time must be withdrawn.

Process of drug withdrawal: This needs care. Sudden reduction in dose or withdrawal of antiepileptic drugs can result in a severe worsening of seizures or status epilepticus. The fastest recommended rates of reduction of doses of standard drugs are shown in Table 3.[11]

Table 3. Recommended rates of withdrawal of anti-epileptic drugs

Drug	Dose decrement per month (mg)
Carbamazepine	200
Phenytoin	50
Phenobarbitone	30
Valproate	200
Clobazam	10
Clonazepam	1
Gabapentin	400
Lamotrigine	100
Topiramate	100

EPILEPSY IN THE ELDERLY

The incidence of epilepsy is surprisingly high in the elderly. About 30% of new cases of epilepsy occur in the people over 65 years. The prevalence of epilepsy in those over 70 years is double that in children. Epilepsy is the third most common neurological condition in the elderly after dementia and stroke. The chief cause of epilepsy in the elderly is cerebro-vascular disease.[12] They have a serious impact on the patients. The risk of fractures, head injury and

sudden death are increased. Self-esteem and independence are further compromised.

The differential diagnosis of epilepsy in the elderly is wide and includes syncope, hypoglycemic episode, transient ischemic episode, transient global amnesia, vertigo and nonspecific dizziness.

Use of antiepileptic drugs in the elderly

In the elderly, protein binding is reduced due to lower serum albumin levels and drug clearance is decreased due to renal or hepatic disease.[13] As they are on multiple co-medications, risks of drug interactions are increased. It should be noted that most drugs have not been subjected to trials in the elderly. Drug compliance is also low due to failing memory and confusion. Adverse effects of drugs may manifest in unfamiliar forms in the elderly. They may include confusion, general ill health, motor or behavioural disturbances. The side effects may be noted even with the drug levels being in the therapeutic range.

Phenytoin has complex pharmacokinetics and has to be given in low initial maintenance doses (200 mg/day) and increments should be of 50 mg each time. Drug level monitoring may be necessary in difficult cases. Similarly, carbamazepine has to be started at low doses (100mg/day) and increased by 100 mg every fortnightly as its clearance is reduced by 40% in the elderly. There are no such guidelines for the use of phenobarbitone and it is rational to follow the same principles of starting with low doses and continuing with small increments. Valproate clearance is reduced by 65% in the elderly. Encephalopathic side effects are more common in the elderly with valproate. It may be started at 200 mg/day and increased to 600 mg/day gradually. Gabapentin is a safe drug in the elderly because it is not metabolized, there is minimal protein binding and there are no significant interactions. The only limiting factor is its relatively low efficacy in controlling severe epilepsy. Lamotrigine is extensively metabolized and is protein bound. It should be used with caution in the elderly.

MANAGEMENT OF EPILEPSY IN WOMEN

Certain special issues need to be addressed while treating women with epilepsy.[14,15]

1. *Fertility*

Fertility rates have been found to be nearly 20% lower in women with epilepsy than in the general population in various studies. There are undoubtedly social effects namely, lower rates of marriage, late marriages, social isolation and stigmatization. Some avoid having children because of the risk of epilepsy in the offspring and some to avoid the teratogenic effects of antiepileptic drugs. Other patients have impaired cognition and personality disorders. In addition, biological factors include drug effects and genetic factors. Thus women with epilepsy are at disadvantage due to lowered fertility. If there are any potentially treatable causes for the infertility, these should be sought.

2. *Oral contraception*

Enzyme inducing drugs like phenytoin, phenobarbitone, carbamazepine reduce the efficacy of oral contraceptives, especially the low estrogen (< 50μg) preparations. Non-enzyme-inducing drugs like valproate, gabapentin, vigabatrin and benzodiazepines do not carry this risk. In one study, the failure rate of OCP containing at least 50μg estradiol are needed and sometimes 60, 80 or 100 μg will be needed. Since estrogen metabolism is increased in these patients, risk of adverse effects of high dose estrogen is unlikely to be increased.

3. *Injectable contraceptives*

The blood levels of depo-provera are not affected by hepatic enzyme induction because its rate-limiting step is hepatic blood flow. Thus injectable contraceptives are unaffected by concomitant use of AED.

4. *Menstruation and catamenial epilepsy*

Estrogen is mildly epileptogenic and the high estrogen levels during the follicular phase are responsible for the propensity for seizures during this phase. Premenstrual tension and water retention are other possible contributory factors. It is believed that up to 10% of women with epilepsy have exacerbations of their seizures in relation to menstrual cycle. If this tendency is strong, it is called catamenial epilepsy.[16] Special therapeutic regimens have been tried in these women. Intermittent clobazam taken for 5-7 days in the high-risk period is the most effective regimen with a responder rate of nearly 80%. However, in routine clinical practice, this is not completely effective because of the irregularity of the menstrual cycle and also to the tolerance to

clobazam. Thus, most neurologists treat this group with long-term antiepileptic administration.

Teratogenicity of antiepileptic drugs

There is now conclusive evidence that antiepileptic drugs increase the risk of congenital malformations. The most common of these are cleft lip, cleft palate, cardiac malformations, neural tube defects and skeletal abnormalities. As many of the patients are on multiple drugs, individual risks of AED are not known with certainty. However, in general the risk is maximal with these drugs in descending order, valproate, carbamazepine, phenytoin and phenobarbitone. The background population risk for spina bifida is 0.2-0.5%. With use of valproate, it is 1-2% and with carbamazepine, it is 0.5-1.0%. Learning disability is 2-7 times more common in off springs of epileptic mothers. All these risks are greatest in those taking high doses of multiple drugs. Folate administration decreases the risk of neural tube defects by 72% and must be given to all pregnant women and to women planning pregnancy along with antiepileptic drugs in doses of 5 mg/day.[17] No statement regarding newer drugs can be made, as experience with them is short and limited. Vigabatrin has caused cleft palate and fusion defects in rabbits and reports of children with spina bifida, cleft palate, absent diaphragm and Siamese twins exists in humans. Topiramate in animal models caused right sided limb and vertebral and rib anomalies. Gabapentin caused hydro-ureter and hydronephrosis in rabbits. Currently, the recommendation is to avoid the use of any of these newer drugs in pregnancy until more definite advice can be given.

Pregnancy

The usual complications of pregnancy are increased up to 3 times in epileptic women (Table 4). The peri-natal mortality is increased two fold. The likely causes are seizures during the delivery and the adverse effects of antiepileptic drugs.

Pregnancy has random effects on epilepsy. About one third of patients experience increased frequency of seizures due to hormonal changes, noncompliance and inappropriate dose reductions, changing drug metabolism and distribution, vomiting and sleep deprivation. A small number of women notice decreased frequency of seizures. The effect of seizures on the fetus is uncertain. In the latter stages of pregnancy, a convulsion carries a risk of trauma to the placenta and the fetus. Seizures can result in maternal and fetal hypoxia. First trimester seizures can increase the risk of fetal malformations. Status epilepticus can result in significant maternal and fetal morbidity and mortality.

Table 4.

Complications of pregnancy in epileptic patients

- Bleeding
- Premature separation of placenta
- Toxemia of pregnancy
- Miscarriage
- IUGR, low birth weight
- Still birth
- Premature labour
- Breech and abnormal presentations
- Forceps delivery, precipitant labour
- Psychiatric disorders
- Seizures and status epilepticus

Guidelines for management of epilepsy in pregnancy

1. Establish whether antiepileptic therapy is indeed required.
2. Rational uses of the drugs with the goals of using the minimum effective doses and minimize multi-drug regimens.
3. Dose adjustments must be made based on serum levels.
4. Dose increments may be needed especially in the last trimester due to fall in drug levels.
5. Folic acid supplements must be given in all women who are or have recently been taking antiepileptic drugs.
6. Screening for fetal malformations by serial ultrasound examinations at 10, 18 and 24 weeks, measurement of serum alpha fetoprotein and amniocentesis.
7. The neonate should receive 1 mg of vitamin K i.m. at birth, as they are deficient in this vitamin if the mother has been on enzyme inducing drugs.

8. The treatment of new onset epilepsy in pregnancy follows the same principles as in the non-pregnant patients.
9. A history of status epilepticus is an indication for caesarean section.
10. If seizures occur during labour, parental drugs like phenytoin have to be given.
11. During puerperium, antiepileptic drug dosage has to be reduced if this was increased during pregnancy based on serum levels.
12. Most drugs can be continued during breast-feeding except phenobarbitone and benzodiazepines, which can reach very high levels in the infant's blood. Neonatal lethargy, irritability and feeding difficulties are the signs to be watched for.

MANAGEMENT OF CHILDHOOD EPILEPSY SYNDROMES

Neonatal Seizures

While there is no doubt that most neonatal seizures are epileptic, some subtle and some tonic seizures are not associated with EEG changes and may be sub-cortical in origin, resulting from abnormal brainstem release mechanisms.[18] The most common causes are hypoxic ischemic encephalopathy, intra-cranial hemorrhage, neonatal infections and metabolic disorders (for example – hypocalcaemia, hypomagnesaemia and hypoglycaemia). The development of neonatal seizures is an ominous sign, not only because they often indicate cerebral disease, but also because the seizures themselves damage the developing brain.

If the seizures are considered non-epileptic, drug treatment may not be indicated. Indeed drug treatment may worsen the phenomenon by decreasing the level of cortical inhibition over sub-cortical structures. Opinions vary about the need to treat infants with EEG evidence of seizure activity without overt clinical signs. There is disagreement about the duration of therapy. Many neonatal seizures are self-limiting and prolonged therapy carries its own risk. For all other seizures treatment is urgent. EEG monitoring is desirable and artificial ventilation often required. The underlying cause has to be corrected. Hypoglycaemia requires correction with 2-4 ml/kg of 25% dextrose intravenously. Hypocalcaemia needs slow intravenous injection of 2-5% calcium gluconate with ECG monitoring.

Hypomagnesaemia requires 2-8 ml of 2-3% magnesium sulfate intravenously or 0.2 ml/kg of 50% solution intramuscular. Pyridoxine deficiency, although rare, responds to 50-200 mg of pyridoxine. Emergency antiepileptic drugs are indicated in all except isolated seizures. A loading dose of 20 mg/kg phenobarbitone is given to achieve blood level of 20 mg/ml, followed by maintenance dose of 3-4 mg/kg/day i.v. or i.m. Phenytoin is a second line drug and is given in loading dose of 15-20 mg/kg i.v. at a rate not exceeding 1-2 mg/kg/min and a maintenance dose of 3-4 mg/kg/day to obtain a plasma level between 15-20mg/ml. It is mandatory to monitor blood levels because of abrupt changes in half-life in the first 2-3 weeks of life.

Febrile Seizures

3-5% of children will have at least one attack of febrile seizures. The important risk factors appear to be an acute temperature rise and attainment of high fever. In majority of the cases, viral infection is the underlying cause of fever. 8% are caused by viral or pyogenic meningitis. Hence all the children with first episode of febrile seizure must be subjected to lumbar puncture. 30-50% of susceptible children will have second attack and 10% have three or more. Prolonged febrile seizure can result in cerebral damage with consequential focal neurological deficit, intellectual deficits and HHE syndrome (hemiplegia, hemi atrophy and epilepsy syndrome). Therefore febrile seizures require emergency therapy if they continue for 15 minutes or more. Between 6-18% of children may show subsequent learning difficulties, probably reflecting an underlying cerebral dysfunction. Years later, between 6-12 years of age, epilepsy may develop in less than 10%.

Emergency treatment includes administration of diazepam 0.5 mg/kg per rectally, given if the seizure has continued for 15 min or more or if there is a past history of prior prolonged seizures. Child should be cooled by external measures including cooling blankets and other means. Emergency prophylactic treatment can be given by rectal diazepam or oral diazepam as soon as fever develops. Suitable doses include 0.3-0.5mg/kg twice a day rectally or 5mg orally for children less than 3 years and 7.5 mg orally

for those over 3 years. Measures to lower temperature should also be taken, including tepid sponging, removing clothing and administering paracetamol. Unfortunately, seizure occurs before the fever is apparent in one third of cases and prophylaxis is not feasible in these patients.

The need for long-term prophylaxis is debated. It is now restricted for those at a particularly high risk of frequent or complex febrile seizures in view of long term adverse effects and risk to learning and development. Either phenobarbitone 15 mg/kg/d or valproate 20-40 mg/kg/day in two divided doses are most commonly used drugs.

West Syndrome

It is a severe epileptic encephalopathy characterized by regression of acquired milestones, infantile spasms and hypoarrhythmia pattern in the EEG.[19] The prognosis depends on the etiology, which includes hypoxic injury, metabolic disorders, neuronal migration disorders, neuro-cutaneous syndromes, degenerative diseases and idiopathic cases. Urgent treatment of the underlying disorder must be initiated wherever possible. Hormonal therapy with ACTH is probably more effective than conventional anti-epileptic drugs, though there are no case controlled studies. Low dose regimen with 1 U of ACTH/kg/day should be tried and if this fails, high dose regimen with 60-80 U/kg/day should be given. Pyridoxine has been reported to be very effective in some cases and may be tried in refractory cases. Vigabatrin is found to be very effective in cases of West Syndrome due to tuberous sclerosis, where it is more effective than ACTH. In a few cases where focal abnormalities can be demonstrated, surgery is very effective in abolition of seizures, but it is not certain if this improves cognitive function. 70-96% of the children have learning difficulty and in 30-50% cases chronic epilepsy develops.

Lennox-Gastaut Syndrome.

Its etiology is same as that of the West Syndrome. The prognosis for control of seizures and intellectual development is poor.[20] Currently, the usual drugs preferred are sodium valproate and benzodiazepines. Valproate is particularly effective against atypical absences, myoclonic or atonic seizures. Clinical trials of lamotrigine and topiramate have shown significant reductions in multiple seizure types, though very few became completely seizure free. Awareness and responsiveness also improved with use of these newer drugs. Ketogenic diet has a dramatic effect on the seizure frequency but is very complicated and needs utmost understanding and motivation of the parents. Surgical therapy includes corpus callosotomy and hemi-cortical resection to control the generalized seizures.

EPILEPSY IN PATIENTS WITH ADDITIONAL HANDICAPS.

Epilepsy in patients with learning difficulty is often severe and resistant to drug therapy. Its treatment demands the knowledge of some additional principles. Vigilance for side effects is particularly important. In the presence of cerebral damage, drug induced side effects occur more frequently and at lower levels. These include confusion, behavioral effects, mental deterioration, encephalopathy, weight gain and hyperactivity. Cluster attacks and status epilepticus can be precipitated by seemingly trivial insults such as inter-current infections and environmental changes. Overmedication in the face of intractable epilepsy has to be avoided so as to prevent cognitive side effects. Surgical option can be considered in refractory cases and the presence of handicap by itself is not a contraindication for surgery.

STATUS EPILEPTICUS

Status epilepticus is defined as a condition in which seizures occur with such a frequency that the patient fails to recover consciousness in-between the attacks. It is also defined as a seizure, which lasts longer than 30 minutes. It may be classified based on the seizure type as tonic clonic, simple partial, complex partial and absence status epilepticus. It occurs in 1-4% of patients with epilepsy and is commonest in patients with partial epilepsy.

Tonic clonic status epilepticus is the commonest and its management will be discussed in detail. The guidelines are provided by the Working Group on status epilepticus of the Epilepsy Foundation of America in 1993.[21] General measures include maintenance of airway, oxygenation, blood pressure, fluid electrolyte status, blood glucose estimation, correction of hypo or hyperglycemia, control of hyperthermia

and identification and correction of the precipitating factors.

Pharmacological measures:

Diazepam and lorazepam are the most common initial drugs in status epilepticus. Diazepam is distributed rapidly in the adipose tissue and has a short duration of action (less than one hour) though it acts very rapidly (within 5-10 minutes). It is given in doses of 0.15-0.25 mg/kg in adults and 0.1-1.0 mg/kg in children. Lorazepam has a longer duration of action (12-24 hours) and is given in doses of 0.1 mg/kg in adults and 0.05-0.5 mg/kg in children.

Phenytoin and phenobarbitone are the drugs available for perenteral administration in status epilepticus. Their loading doses are 15-20 mg/kg and maintenance doses are 3-5mg/kg/day. Fosphenytoin is a prodrug of phenytoin, which has advantages including less local toxicity, less hypotension and solubility in any aqueous solution. If the seizures are refractory to these drugs, pentobarbital (15-20 mg/kg loading dose and 1-2 mg/kg/hr of maintenance dose) or thiopentine (5-10 mg/kg loading dose and 2 mg/min maintenance dose) have to be administered to induce a burst suppression pattern in the EEG.

The management of simple and complex partial status epilepticus is similar but can be less aggressive since vital functions like respiration are not compromised in these seizures.

MEDICALLY INTRACTABLE EPILEPSY

Drug therapy fails in 10-20% cases which are called refractory. There are over ten widely used anti-epileptic drugs and far more combinations. All combinations cannot be therefore tried. The chances of a new drug controlling seizures after two drugs have been tried are less than 5%. Therefore, the practical definition of intractable epilepsy is one which is uncontrolled with two mono-therapy regimens and at least one poly-therapy regimen. The initial steps in the management of refractory epilepsy are:

1. *Review diagnosis:* In any uncontrolled epilepsy patient, it is important to ascertain if the diagnosis of epilepsy is correct. It is not uncommon to treat non-epileptic phenomenon like syncope or pseudo-seizures for prolonged period of time with multiple anti-epileptic medication with disastrous results. A review of the history from an eyewitness, review of EEGs and other investigations are essential.

2. *Establish the etiology:* It is essential to ascertain the possible cause of epilepsy and to exclude a progressive pathology.

3. *Review compliance:* This is one of the most important and often missed reasons for treatment failure.

If the above factors are taken care of, then appropriate patients have to be selected for referral for epilepsy sugery.[22] The indications and contraindications for epilepsy surgery are tabulated below. (Table 5)

Table 5
Indications and contraindications for epilepsy surgery

Indications
1. Intractable seizures 2. Seizures must significantly reduce the quality of life 3. A localized seizure focus by EEG and MRI.
Contra-indications include
1. Benign self-limited epilepsy syndromes 2. Severe mental retardation or psychosis 3. Neuro-degenerative and neuro-metabolic disorders 4. Severe family dysfunction

SURGICAL PROCEDURES

1. *Temporal lobe seizures*

Temporal lobe resection is an effective procedure in patients with uncontrolled complex partial seizures of temporal lobe origin. The amount of tissue removed is determined by intra-operative corticography and stimulation studies. The remission rates with this procedure vary from 70-80% (either complete seizure control or significant improvement). The potential risks of the procedure include quadrantanopic field defect, cerebrovascular accident, 3rd nerve palsy and memory and language deficits.

2. *Non-temporal lobe seizures*
The most common procedure is extra-temporal resection usually involving the frontal lobe. The outcome is less satisfactory than temporal resection and the chances of achieving seizure free state or significant reduction in seizure frequency is only 50%.

3. *Hemispherectomy*
This drastic procedure is used in patients with severe unilateral motor seizures who already have hemiparesis and non-functional hand. Examples include Rasmussen encephalitis and Sturge-Weber syndrome, cerebral infarctions, hemi-megalencephaly and trauma. 75% of patients have gratifying reduction in seizure frequency. The main risks of this procedure are superficial hemosiderosis, bleeding into hemispherectomy cavity or fatal brain-stem shift.

4. *Corpus callosotomy*
In this procedure, spread of seizures is restricted. This is particularly useful in patients with very frequent seizures, particularly drop attacks due to rapid generalization.

NONPHARMACOLOGIC MODALITIES

These include vagus nerve stimulation, ketogenic diet, behavioral therapy, biofeed back are all useful modalities and are currently under evaluation.

References

1. Hart YM, Sander JWAS, Johnson AL, Shorovon SD. The National General Practice Study of Epilepsy: Recurrence after a first seizure. Lancet 1990; 1271-1274.

2. Sander JWAS, Hart YM, Johnson AL, Shorovon SD. The National General Practice Study of Epilepsy: Newly diagnosed epileptic seizures in a general population. Lancet 1990a; 336:1276-1277.

3. Fish DR, Quirk JE, Smith SJM, Sander JWAS, Shorvon SD. Vidoegames and epilepsy. Final Report 1994, HMSO, London.

4. Reynolds EH, Shorvon SD. Monotherapy or polytherapy for epilepsy? Epilepsia 1981; 22:1-10.

5. Mattson RH. Selection of antiepileptic drug therapy. In: Levy RH, Mattson RH, Meldrum BS, eds. Antiepileptic drugs, 4th ed. New York: Raven Press 1995.

6. Patsalos PN, Sander JWAS, Oxley JR, Lascelles PT. Immediate anticonvulsant drug monitoring in management of epilepsy. Lancet 1987, 2:39.

7. Mattson RH. Antiepileptic drug monitoring: a reappraisal. Epilepsia 1995; 36 (Suppl 5): S22-S29.

8. MRC antiepileptic drug withdrawal study group. Randomized study of antiepileptic drug withdrawal in patients in remission. Lancet 1991;337: 1175-1180.

9. MRC antiepileptic drug withdrawal study group 1993. Prognostic index for recurrence of seizures after remission of epilepsy. Br Med J 1993;306: 1374-1378.

10. Shinnar S, Berg AT, Moshe SL et al. Discontinuing antiepileptic drugs in children with epilepsy: A prospective study. Ann Neurol 1994; 35:534-545.

11. Duncan JS, Shorvon SD, Trimble MR. Discontinuation of phenytoin, carbamazepine and sodium-valporate in patients with active epilepsy. Epilepsia 1990a; 31: 584-591.

12. Shorvon SD, Gilliat RW, Cox TCS Yu YL. Evidence of vascular disease from CT scanning in late onset epilepsy. J Neurol Neurosurg Psychiatry 1984; 47: 225-230.

13. Schener ML. Drug treatment in the elderly. In: Engel J, Pedley TA, eds. Epilepsy a comprehensive textbook. Philadelphia: Lippincot-Raven, 1997.

14. Delgado-Escueta AV and Janz D. Consensus guidelines: preconception counseling, management and care of pregnant women with epilepsy. Neurology 1992; 42(Suppl 5) 149-160.

15. Yerby MS. Treatment of epilepsy during pregnancy. In Wyllie E, ed. The treatment of epilepsy: principles and practice, 2nd ed. Baltimore: Williams and Wilkins, 1997.

16. Rosciszewska D. Epilepsy and menstruation. Epilepsia 1987; 12:373-378.

17. Medical Research Council Vitamin Study Ressearch Group. Prevention of neural tube defects: results of Medical Research Council vitamin study. Lancet 1991; 338:131-137.

18. Volpe JJ. Neonatal seizures: current concepts and classification. Paediatrics 1989; 84: 422-428.

19. Holmes GL, Vigerano F. Infantile spasms. In: Engel J, Pedley TA, eds. Epilepsy: A comparenhensive textbook. Philadelphia: Lippincot-Raven, 1997.

20. Pravet C, Genton P. Lennox-Gastaut Syndrome and other childhood epileptic encephalopathies. In: Engel J, Pedley TA, eds. Epilepsy: A comprehensive textbook. Philadelphia: Lippincot-Raven, 1997.

21. Treatment of convulsive status epilepticus. recommendations of the Epilepsy Foundation of America's working group on status epilepticus. JAMA 1993; 270: 854-859.

22. Engel J. Surgery for seizures. N Engl J Med 1996; 334:647-652.

THE IMCI – AN IMPORTANT INITIATIVE FOR THE SICK CHILD

REYNOLD G. WASHINGTON

What is IMCI?

IMCI is a strategy, which expanded reads: Integrated Management of Childhood Illness.

Whose initiative is the IMCI?

The IMCI is a collaborative initiative of the WHO and UNICEF. The WHO division of Child Health and Development (CHD) has collaborated with UNICEF, the World Bank and other agencies for the development of the IMCI.

What is the rationale behind the IMCI?

Every year 11.6 million deaths occur among children in developing countries before they reach their fifth birthday. Seventy percent of these deaths are due to five main causes. Death may result from any of these causes independently or in combination in a given child. These causes include Acute Respiratory Infections (ARI mainly pneumonia), diarrhoea, measles, malaria and malnutrition.(Fig 1) Three out of four children seeking care at a health facility also present with one or more of these conditions.

IMCI is an integrated strategy which focuses on the child as a whole who may present with more than one apparent disease condition. IMCI strategy is appropriate in any country where the infant mortality rate is more than 40 per thousand live births and where transmission of falciparum malaria is common. The Infant Mortality Rate in India is currently 71 per 1000 live births (UNICEF 2000) and falciparum malaria is endemic in many parts of the country. By these criteria, India is a country which qualifies for the adoption of the IMCI.

REYNOLD G. WASHINGTON MD, DNB
Associate Professor

Department of Community Health
St. John's Medical College
Bangalore.

What is the aim of the IMCI?

The IMCI strategy is targeted towards improving health and thus growth and development among children under the age of five years. In terms of measurable outcomes the IMCI aims at:

1. Reducing deaths in children under the age of five years.
2. Reducing the frequency and severity of illness and disability in this age group.
3. Improving practices both at the health facilities and at home.

Potentially fatal illnesses in children are often brought to the attention of health workers at first level primary health care facilities. The initial focus of the Integrated Management of Childhood Illness (IMCI) therefore is on:

1. Improving the performance of primary health care workers through training and support. To consolidate gains made earlier and to progress towards greater and better infant and child health, staff in primary health care facilities who are already managing and treating some of these conditions need to now be trained to deal with individual children who may present with more than one condition.
2. Improvement in the health system required for management of childhood illness, not merely administration of immunization or distribution of ORS or Cotrimoxazole.
3. Improvement in family and community practices through education and counseling focused mainly on the primary care givers of children under five at home.

Have we not had programs for the under five before? So, what is different about IMCI?

In the past WHO and UNICEF have focused on disease specific programs. Prominent among these are:

1. The Expanded Program of Immunization (1978), expanding the number of antigens included in the program, the coverage of immunization and the definition of the target group.

2. The Universal Immunization Program (1985) focusing on universal immunization of all infants and pregnant women against the 'six killer diseases' of childhood.

3. Diarrheal disease control program (modified 1992) which took into consideration other conditions such as malnutrition, dysentery, persistent diarrhoea and fever (malaria), as part of standard case management.

4. Acute Respiratory Infections (ARI) standard case management (modified 1995) which added management protocols on ear discharge and sore throat to the already existing protocols aimed at classifying and treating children based on age and on whether they had severe disease, severe pneumonia, pneumonia or no pneumonia.

The disease-specific standard case management protocols have been useful in contributing to reduction in the mortality associated with these diseases in children under five years of age. The limitations of these disease specific approaches was that they failed to take into account the following facts:

1. Diseases occur in combination: a child may present simultaneously with both ARI and diarrhoea. Managing this child using two different disease specific protocols could be confusing to a health worker.

2. Symptoms in the under five especially are not system or disease specific. Both pneumonia and malaria may present with fever, cough and chest wall indrawing. Depressed conciousness may be due to diarrhoea with severe dehydration, meningitis, severe malaria, severe hypoglycaemia, severe hypoxia or other conditions.

3. Immunization programs targeted at universal coverage aimed only at prevention of the six killer diseases. Not much in terms of guidelines were issued with regard to management of disease in the event of vaccine failure, or failure to administer the vaccine. Further, a fatal outcome of the six killer diseases is often not due to the disease per se but due to complications arising out of the disease (e.g., pneumonia following measles).

The development of IMCI guidelines will perhaps counter these limitations of disease specific programs.

What are the components of the IMCI?

Components of the IMCI include both curative and preventive interventions.

These include:

Case Management Interventions	Preventive Interventions
❖ Pneumonia ❖ Diarrhoea Dehydration Persistent diarrhoea Dysentery ❖ Meningitis, sepsis ❖ Malaria ❖ Measles ❖ Malnutrition ❖ Anaemia ❖ Ear infection	❖ Immunization during sick child visits to reduce missed opportunities ❖ Nutrition counseling ❖ Breast feeding support including assessment and correction of breast feeding technique

What is new in the IMCI strategy?

The new inclusions in the IMCI strategy include:

1. Improved case management by integration of disease specific guidelines.

2. The use of more specific clinical signs, such as use of palmar pallor for detecting anemia in children.

3. The inclusion of periodic doses of mebendezole to counter anemia as a result of worm infestation.

4. Specific guidelines to make a clinical diagnosis of measles and administration of a dose of Vitamin A to all children diagnosed

to have measles. In addition, case management of complications that can lead to death or disability following measles are paid attention to.

5. Simplification of the clinical signs for the classification of dehydration due to diarrhoea. Dry mouth and tongue and absence of tears have now been excluded.

6. Inclusion of the current WHO case management strategies for pneumonia and ear infection, diarrhoea with dehydration, dysentery, persistent diarrhoea and malnutrition.

7. Simplification of the classification of nutrition status to detect malnutrition even in early stages before it becomes overt.

8. Emphasis on the nutritional therapy of persistent diarrhoea, stressing the importance of feeding and micronutrient supplementation.

9. Counselling of the mother or primary care giver at home to ensure proper care at home.

For whom is the IMCI?

IMCI guidelines have been developed primarily for outpatient health facilities. Personnel included in its implementation therefore include doctors, nurses, auxiliary nurse midwives and literate health workers. In addition to health personnel, the logistic and laboratory support that is available in a given facility will also determine the ability to implement IMCI guidelines. A doctor can do little more than a trained literate health worker in health facilities which lack logistic support or laboratory facilities to manage children with severe illness.

IMCI guidelines have been adapted even for inpatient care. Instructions for counseling mothers to deliver proper care at home prior to discharge are particularly relevant.

It is essential that doctors including general practitioners and specialist in the field of Paediatrics and Community Medicine are reoriented to the IMCI approach. This will in addition facilitate training of the nurses, ANMs and literate health workers in the appropriate use of IMCI. It is only appropriate if trainers practice what they teach.

Doctors, nurses and ANMs and literate health workers need both technical and higher care facility supports. An appropriate referral system for prompt referral of children and for provision of continuing education is an essential prerequisite for better effectiveness of the IMCI approach. Mutual trust and appreciation of all partners in the implementation process and the referral system is essential to the successful implementation of the IMCI.

What are the steps in the use of IMCI guidelines?

The case management process as laid out in the charts involves the following steps:

1. The health worker must first assess the child. This is done by identifying if the child has any of the danger signs and asking about the four main symptoms in all children (cough or difficult breathing, diarrhoea, fever and ear problem). The health worker then carries out further assessment if a main symptom is reported. She/he will also review the nutritional and immunization status in all children.

2. The health worker must then **classify** the child's illness. The classification of illness is based on a colour-coded triage system. Health workers are already familiar with this through use of the WHO case management guidelines for diarrhoea and acute respiratory infections (ARI). *The disease classification tables from the chart on the assessment and classification of the sick child aged 2 months to 5 years are shown in (Fig. 2); the left and middle columns show how the signs are used to classify the child's illness, while the right column indicates the treatments.*

   Each illness if classified according to whether it requires:

   - urgent referral
   - specific medical treatment and advice; or
   - simple advice on home management

   Action oriented classifications are used rather than exact diagnoses

3. After classification, the health worker identifies the **specific treatments** that need to be administered. If the child has to be referred to a hospital, the health worker gives only essential treatment before departure. An integrated treatment plan is developed since most children have more than one illness classification.

4. The health worker then carries out practical **treatment instructions.** This includes instructions to the mother on the administration of oral drugs, on the need to increase fluid intake during diarrhoea and on the treatment of small ailments at home. The mother is advised on the signs which indicate that the child should immediately be brought back to the clinic. She is also instructed on when she must return for routine follow-up.

5. The health worker assesses feeding and **counsels** the mothers on feeding problems as necessary.

6. **Follow up** instructions for various conditions are given when the child returns to the clinic.

Conclusion

IMCI must go hand in hand with measures to:

1. Increase and sustain immunization coverage levels by raising immunization activities and avoiding missed opportunities.

2. Increase the coverage of Vitamin A supplementation by using sick child encounters to give supplements in areas with Vitamin A deficiency.

3. Improve infant and child feeding and growth by nutritional counseling.

IMCI requires action at the level of the health facility, home and community. It requires you to act and to act now.

References

1. 1992: WHO, Program for Control of Diarrhoeal diseases: "Management of the child with diarrhoea".

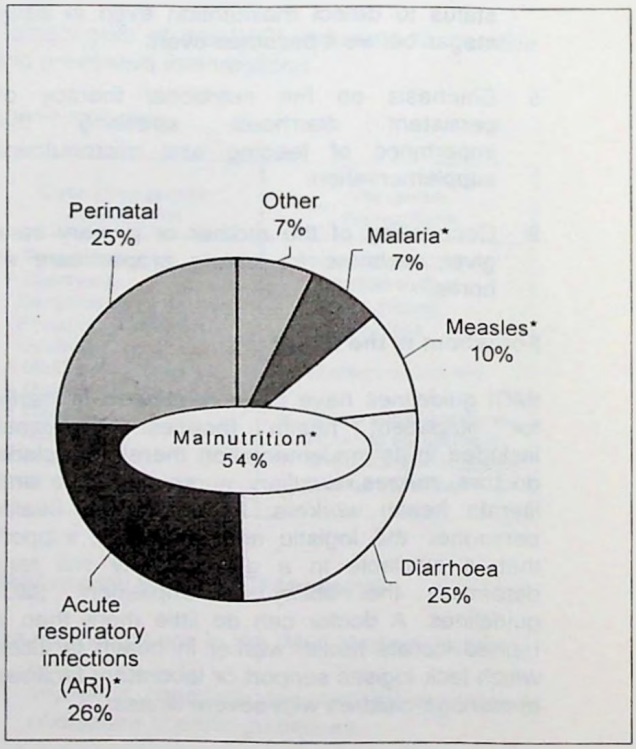
2. 1995: WHO' Program for Control of Acute Respiratory Infections: "Management of the child with ARI".

3. 1997: WHO, "Integrated Management of Childhood Illness": a WHO/UNICEF initiative – Supplement No. 1 to Volume 75 of the Bulletin of the WHO.

4. 1999: WHO, "IMCI Information".

5. 2000: UNICEF. "The State of the World's Children 2000".

Fig 1 Causes of death among children under 5 years of age in developing countries, 1995.



* Approximately 70% of all childhood deaths are associated with one or more of these 5 conditions.

Reprinted with permission in Integrated Management of Childhood Illness: A WHO/UNICEF Initiative - Bulletin of the WHO. Suppl. 1 (75) 1997.

Fig. 2. **Classification tables for integrated management of childhood illness, based on four main symptoms and nutritional status.**

Classify COUGH or DIFFICULT BREATHING

SIGNS	CLASSIFY AS	TREATMENT (Urgent pre-referral treatments are in bold print.)
• Any general danger sign or • Chest indrawing or • Stridor in calm child	**SEVERE PNEUMONIA or VERY SEVERE DISEASE**	► **Give first dose of an appropriate antibiotic.** ► **Refer URGENTLY to hospital.**
• Fast breathing	**PNEUMONIA**	► **Give an appropriate antibiotic for 5 days.** ► Soothe the throat and relieve the cough with a safe remedy. ► Advise mother when to return immediately. ► Follow-up in 2 days.
No signs of pneumonia or very severe disease	**NO PNEUMONIA: COUGH OR COLD**	► If coughing more than 30 days, refer for assessment. ► Soothe the throat and relieve the cough with a safe remedy. ► Advise mother when to return immediately. ► Follow-up in 5 days if not improving.

If the child is:	*Fast breathing is:*
• 2 months up to 12 months	• 50 breaths per minute
• 12 months to 5 years	• 40 breaths per minute

Classify DIARRHOEA

with DEHYDRATION

SIGNS	CLASSIFY AS	TREATMENT
Two of the following signs: • Lethargic or unconscious • Sunken eyes • Not able to drink or drinking poorly • Skin pinch goes back very slowly	**SEVERE DEHYDRATION**	► If child has no other severe classification: — Give fluid for severe dehydration (Plan C, see Fig. 4). **OR** **If child also has another severe classification:** **— Refer URGENTLY to hospital with mother giving frequent sips of ORS on the way.** **Advise the mother to continue breastfeeding.** ► **If child is 2 years or older and there is cholera in your area, give antibiotic for cholera.**
Two of the following signs: • Restless, irritable • Sunken eyes • Drinks eagerly, thirsty • Skin pinch goes back slowly.	**SOME DEHYDRATION**	► Give fluid and food for some dehydration (Plan B, see Fig. 4). ► **If child also has a severe classification:** **— Refer URGENTLY to hospital with mother giving frequent sips of ORS on the way.** **Advise mother to continue breastfeeding.** ► Advise mother when to return immediately. ► Follow-up in 5 days if not improving.
Not enough signs to classify as some or severe dehydration.	**NO DEHYDRATION**	► Give fluid and food to treat diarrhoea at home (Plan A, see Fig. 4). ► Advise mother when to return immediately. ► Follow-up in 5 days if not improving.

and if 14 days or more of diarrhoea

• Dehydration present.	**SEVERE PERSISTENT DIARRHOEA**	► Treat dehydration before referral unless the child has another severe classification. ► Refer to hospital.
• No dehydration.	**PERSISTENT DIARRHOEA**	► Advise the mother on feeding a child who has PERSISTENT DIARRHOEA. ► Follow-up in 5 days.

and if blood in stool

• Blood in the stool.	**DYSENTERY**	► **Treat for 5 days with an oral antibiotic recommended for Shigella in your area.** ► Follow-up in 2 days.

Fig. 2. **Continued**

***Classify* FEVER**

	SIGNS	CLASSIFY AS	TREATMENT
High malaria-risk area	• Any general danger sign or • Stiff neck.	VERY SEVERE FEBRILE DISEASE	► Give quinine for severe malaria (first dose). ► Give first dose of an appropriate antibiotic. ► Treat the child to prevent low blood sugar. ► Give one dose of paracetamol in clinic for high fever (38.5 °C or above). ► Refer URGENTLY to hospital.
	• Fever (by history or feels hot or temperature ≥ 37.5°C).	MALARIA	► If NO cough with fast breathing, treat with oral antimalarial. OR If cough with fast breathing, treat with cotrimoxazole for 5 days. ► Give one dose of paracetamol in clinic for high fever (38.5 °C or above). ► Advise mother when to return immediately. ► Follow-up in 2 days if fever persists. ► If fever is present every day for more than 7 days, refer for assessment.
Low malaria-risk area	• Any general danger sign or • Stiff neck.	VERY SEVERE FEBRILE DISEASE	► Give quinine for severe malaria (first dose) unless no malaria risk. ► Give first dose of an appropriate antibiotic. ► Treat the child to prevent low blood sugar. ► Give one dose of paracetamol in clinic for high fever (38.5 °C or above). ► Refer URGENTLY to hospital.
	• NO runny nose and NO measles and NO other cause of fever	MALARIA	► If NO cough with fast breathing, treat with oral antimalarial. OR If cough with fast breathing, treat with cotrimoxazole for 5 days. ► Give one dose of paracetamol in clinic for high fever (38.5 °C or above). ► Advice mother when to return immediately. ► Follow-up in 2 days if fever persists. ► If fever is present every day for more than 7 days, refer for assessment.
	• Runny nose PRESENT or • Measles PRESENT or • Other cause of fever PRESENT.	FEVER— MALARIA UNLIKELY	► Give one dose of paracetamol in clinic for high fever (38.5 °C or above). ► Advice mother when to return immediately. ► Follow-up in 2 days if fever persists. ► If fever is present every day for more than 7 days, refer for assessment.
If MEASLES now or within last 3 months	• Any general danger sign or • Clouding of cornea or • Deep or extensive mouth ulcers.	SEVERE COMPLICATED MEASLES	► Give Vitamin A. ► Give first dose of an appropriate antibiotic. ► If clouding of the cornea or pus draining from the eye, apply tetracycline eye ointment. ► Refer URGENTLY to hospital.
	• Pus draining from the eye or • Mouth ulcers	MEASLES WITH EYE OR MOUTH COMPLICATIONS	► Give Vitamin A. ► If pus draining from the eye, treat eye infection with tetracycline eye ointment. ► If mouth ulcers, treat with gentian violet. ► Follow-up in 2 days.
	• Measles now or within the last 3 months	MEASLES	► Give Vitamin A.

Fig. 2. **Continued**

Classify EAR PROBLEM

SIGNS	CLASSIFY AS	TREATMENT
• Tender swelling behind the ear.	MASTOIDITIS	► Give first does of an appropriate antibiotic. ► Give first dose of paracetamol for pain. ► Refer URGENTLY to hospital.
• Pus is seen draining from the ear and discharge is reported for less than 14 days, or • Ear pain.	ACUTE EAR INFECTION	► Give an antibiotic for 5 days. ► Give paracetamol for pain. ► Dry the ear by wicking. ► Follow-up in 5 days.
• Pus is seen draining from the ear and discharge is reported for 14 days or more.	CHRONIC EAR INFECTION	► Dry the ear by wicking. ► Follow-up in 5 days.
• No ear pain and No pus seen draining from the ear.	NO EAR INFECTION	No additional treatment.

Classify NUTRITIONAL STATUS

SIGNS	CLASSIFY AS	TREATMENT
• Visible severe wasting or • Severe palmar pallor or • Oedema of both feet	SEVERE MALNUTRITION or SEVERE ANAEMIA	► Give Vitamin A. ► Refer URGENTLY to hospital.
• Some palmar pallor or • Very low weight for age.	ANAEMIA or VERY LOW WEIGHT	► Assess the child's feeding and counsel the mother on feeding according to the FOOD box on the COUNSEL THE MOTHER chart. — If feeding problem, follow-up in 5 days. ► If pallor — Give iron. — Give oral antimalarial if high malaria risk. — Give mebendazole if child is 2 years or older and has not had a dose in the previous 6 months. ► Advice mother when to return immediately. ► If pallor, follow-up in 14 days. If very low weight-for-age, follow-up in 30 days.
• Not very low weight-for-age and no other signs of malnutrition.	NO ANAEMIA and NOT VERY LOW WEIGHT	► If child is less than 2 years old, assess the child's feeding and counsel the mother on feeding according to the Food box on the Counsel the Mother chart. — If feeding problem, follow-up in 5 days. ► Advise mother when to return immediately.

NEONATAL RESUSCITATION

FULTON D'SOUZA

Introduction

3-5% of the 26 million infants born in this country experience asphyxia at birth. Birth Asphyxia is the leading cause of neonatal death in India.

Asphyxia is characterized by

- Progressive hypoxia
- Hypercapnia
- Metabolic acidosis (due to hypoperfusion)

Physiology of Asphyxia

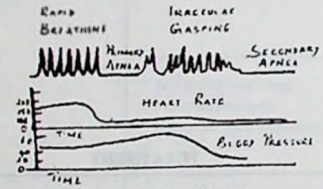


FIGURE 1A : PRIMARY APNOEA

Infants who become asphyxiated undergo a sequence of events. There is an initial period of rapid breathing, then respiration ceases and heart rate begins to fall and **primary apnea** follows.

Fulton D'Souza MD
Assistant Professor

Department of Paediatrics
St John's Medical College Hospital
Bangalore

Secondary Apnea

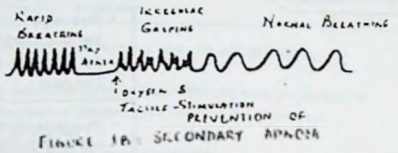


FIGURE 1B : SECONDARY APNOEA

When hypoxia continues the gasping respiration is weaker and weaker until the infant takes a last gasp and enters secondary apnea. The heart rate and arterial pressure falls and death occurs unless effective resuscitation is initiated promptly.

Assume secondary apnea

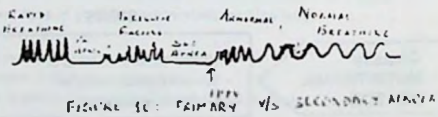


FIGURE 1C : PRIMARY V/S SECONDARY APNOEA

It may be difficult to distinguish primary from secondary apnea. Therefore apnea at birth should be treated as secondary apnea and resuscitation should be initiated promptly as apnea may begin in utero and continue after delivery.

Clearing of lung fluid

Fetal lung fluid must be cleared if air is to fill the lungs. To clear fetal lung fluid and expand the lungs may require two to three times the pressure of a normal breath.[2]

Problems in clearing the lung fluid occur in

- Infants apneic at birth
- Infants with weak initial respiratory effort
- Premature infants
- Infants depressed by asphyxia, maternal drugs and anaesthesia.

Pulmonary circulation

At birth pulmonary blood flow must increase for proper oxygenation. This is accompanied by arterioles in the lungs opening up and getting filled with blood previously diverted away from the lungs through the ductus arteriosus.

Decreased Pulmonary Perfusion

In the asphyxiated newborn, hypoxemia and acidosis maintain a fetal pattern of circulation with diminished pulmonary blood flow.[2]

Decreased Cardiac Function: Early in asphyxia, blood is shunted to the brain and the heart. With increasing hypoxemia and acidosis, myocardial function fails, cardiac output decreases and blood flow even to these vital organs is diminished.

Being prepared for resuscitation

Two major factors for prompt effective resuscitation are

- Anticipation of need for resuscitation
- Adequate preparation of equipment and personnel.

Anticipation

Delivery room staff should be prepared to handle problems and consider every delivery as a high risk one.

Preparation

To allow for the unexpected case, minimum preparation for every delivery should include:

- A radiant warmer heated and ready for use is preferred. However a room heater or 60-100 watt bulb can be used for the same purpose.
- All resuscitation equipment immediately available and in working order
- At least one skilled person is required to perform a complete resuscitation including endotracheal intubation and administration of medicines.[3,4]

Signs to evaluate

The following five questions differentiate the baby in need of assistance from the baby who can receive routine care.[3]

1. Is the amniotic fluid clear of meconium?
2. Is the baby breathing or crying?
3. Is there good muscle tone?
4. Is the baby's colour pink?
5. Is the baby term?

Apgar score

The Apgar score is generally allotted at 1 minute and again at 5 minutes of age. However, assessment of the infant should begin immediately at birth. So it is helpful only for assessing the infant's condition and the effectiveness of the resuscitative efforts.

The ABC's of resuscitation

The steps in resuscitating newborn infants follow the well-known TABC of resuscitation
T– temperature regulation
A – establish an open airway
B – initiate breathing
C – maintain circulation

Initial steps in resuscitation

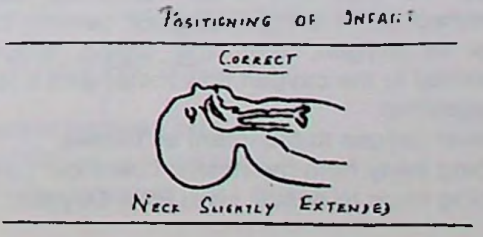
1. *Preventing heat loss* : (Fig 2)

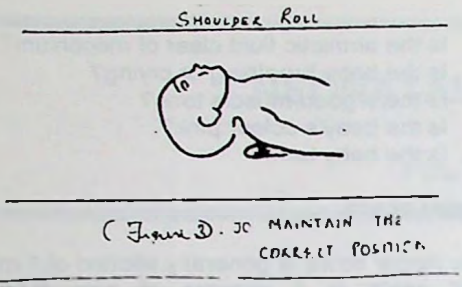
FIGURE 2: PREVENTION OF HEAT LOSS

Heat loss is prevented by[2,6]

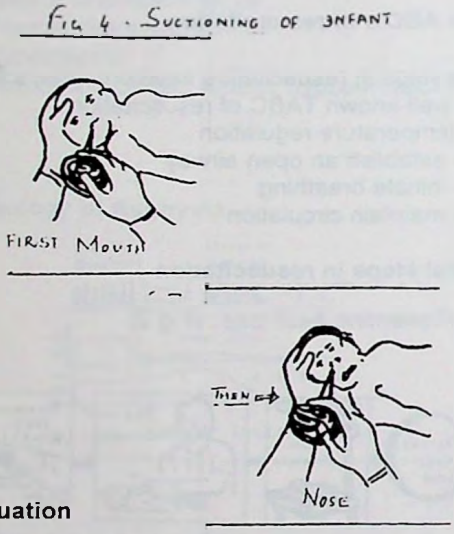
a. Placing the infant under a heated radiant warmer.
b. Quickly drying the infant and removing the wet linen.

2. *Open airways*
   a. Positioning – The neonate is placed on his / her back with neck slightly extended (Fig3)





b. Suctioning – Suction the mouth first and then the nose. (Fig 4).



Evaluation

Now monitor for three vital signs[2]
- Respiratory rate
- Heart rate
- Colour

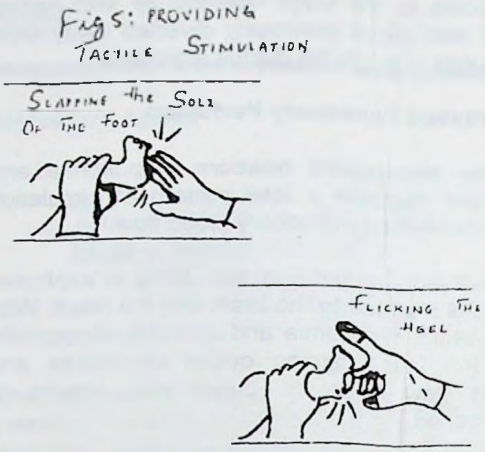
Respiration : Evaluate infant's respiration. If normal, go to next sign. If not, positive pressure ventilation.

Heart rate : If >100, then go to the next step.

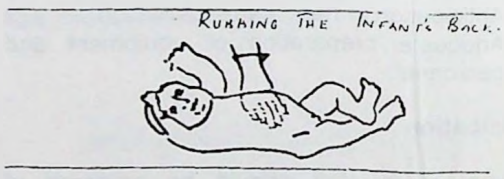
Colour : If central cyanosis present provide free flow oxygen by blowing oxygen over the infants nose so that the infant breathes oxygen-enriched air. If using tubing for delivery of free flow of oxygen, then the tubing should be attached to the oxygen flow meter with 5 litres of oxygen/min.
Deliver oxygen to the infant as follows:
Tubing away from the nostril: Low Flow Oxygen
Tubing close to nostril: High Flow Oxygen

Tactile stimulation

If an infant does not breathe, tactile stimulation may be used briefly in an attempt to initiate breathing. These are only by (Fig 5)



Slapping or flicking the soles of feet

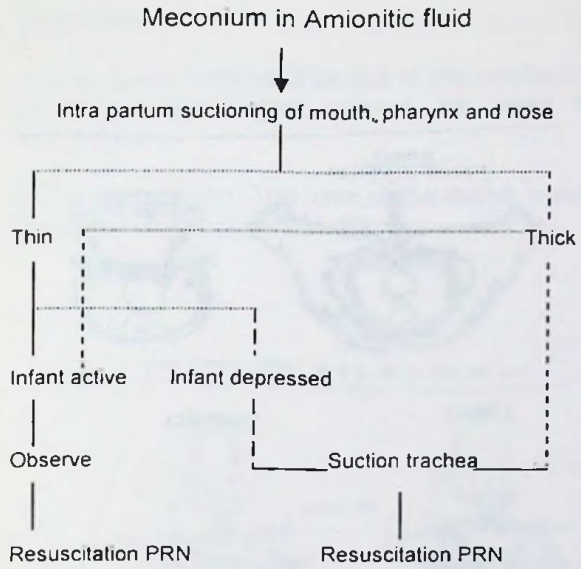


Rubbing the back[2]

Meconium

If thick and particulate or thin meconium stained amniotic fluid is present one should suction the mouth and pharynx as soon as the baby's head is delivered and before the delivery of the shoulders.

After delivery, the hypopharynx should be suctioned to remove residual meconium. Then, in case of thick meconium, trachea should be intubated if baby is depressed, to remove any residual meconium using the meconium aspirator. The tracheal suctioning is done by applying the suction directly to an endotrachael tube. If the meconium is thin and watery and the infant is active after a thorough suctioning, no endotrachael suctioning (ET) is required. If the baby is active and vigorous ET suction need not be done even in thick meconium stained amniotic fluid.[4,5]



Bag and mask ventilation : Equipment

1. Resuscitation bags
   a. Anaesthesia bag
   b. Self inflating bag

2. Pressure gauge
3. Oxygen reservoir
4. Mask – circular and anatomical
5. Oxygen source
6. Flow meter
7. Oxygen tubing

Indication: Bag and mask ventilation is indicated whenever (Fig 6)

Fig 6: POSITIONS WITH UNOBSTRUCTED VIEW OF CHEST.

a. Infant is apneic or gasping
b. Heart rate <100
c. Infant has central cyanosis and apneic after the initial resuscitation.

First select the appropriate equipment.
Obtain a resuscitation bag and connect it to an oxygen source.
Select a mask of proper size – covering nose and mouth and not eyes.
Position: Infants neck should be slightly extended to ensure an open airway.
The pressure needed to inflate the lungs will vary depending on the infant's size, the condition of the lungs and whether the infant has previously taken a breath.[5]

First breath – The initial lung inflation following delivery may require a pressure of 30-40 cm H_2O.
Succeeding breaths - pressure of 15-20 H_2O
Pulmonary disease - pressure of 20-40 cm H_2O

After placing the mask in position and checking seal and ventilation observe for appropriate rise of chest.

If chest does not rise

Action	Condition corrected
1. Reapply mask	inadequate seal
2. Reposition infants head	blocked airway
3 Check for secretions, suction if present	blocked airway
4. Ventilate with mouth slightly open	blocked airway
5. Increase pressure slightly	inadequate pressure

Normal rate 40 –60 breaths / min.

When to stop

When the heart rate is above 100.
Check heart rate: after infant received 100% oxygen for 15-30 seconds, check heart rate for 6 seconds.

Heart rate	Action
>100	observe respiratory rate and colour
< 60	continue to ventilate, begin chest compression
<100 but >60	continue ventilation alone

Signs of improvement

- Increasing heart rate
- Spontaneous respiration
- Improving colour

Orogastric tube is passed in infants receiving bag and mask resuscitation to prevent distention of abdomen and aspiration. (Fig 7).

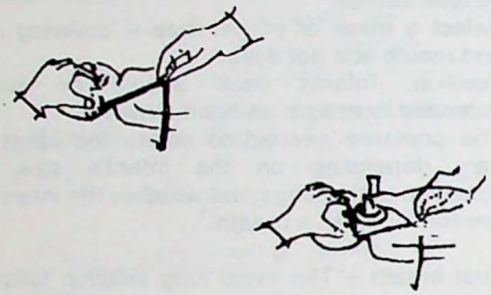


Fig 7: TECHNIQUE OF INSERTING OROGASTRIC CATHETER.

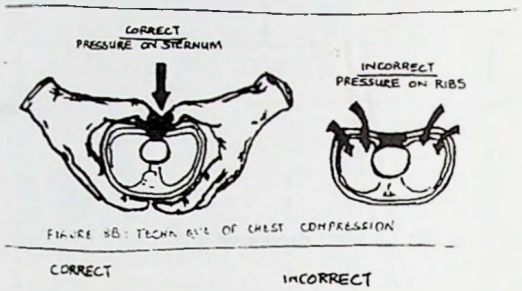


FIGURE 8B: TECHNIQUE OF CHEST COMPRESSION

(Figure B)

FIGURE 8B TECHNIQUE OF CHEST COMPRESSION (CONTINUED)

Chest compressions

Indications: It is based on neonate's heart rate. It is necessary when despite 15 to 30 seconds of ventilation with 100% oxygen, the heart rate is below 60 beats per minute.[2,3,4]
Infants position : neck slightly extended. Firm support for the back so that heart can be compressed between sternum and the spine.

Position of compression: While one person continues ventilation, quickly locate the lower third of the sternum. (1 cm below the line joining the two nipples) or area just above xiphoid.[2]
(Fig 8)

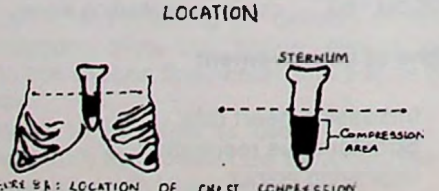


FIGURE 8A: LOCATION OF CHEST COMPRESSION

Technique[2]

1, *Two finger method*: The tips of the middle and index or ring fingers should be used for compression

2. *Thumb method*: The balls of the thumb should be used for compression. (Fig 9).

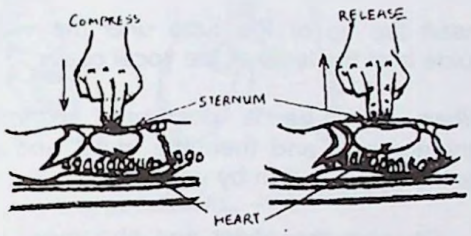


FIGURE 9A: TWO FINGER METHOD OF CHEST COMPRESSION.

FIGURE 9B: THUMB METHOD OF CHEST COMPRESSION

Rate: Sternum should be compressed to a depth of 1/3 of anterior posterior diameter of chest with three compressions and one ventilation occurring in a 2 second cycle.[5]
This provides 90 compressions and 30 ventilations per minute.

Check: After 30 seconds of compression and ventilation, check the heart rate for 6 seconds.

<60 →continue compressions and ventilation
>60 → stop chest compression but continue ventilation. Even if heart rate is found to be 0 compression and ventilation should continue until a medical decision is reached to discontinue resuscitation.

Endotracheal intubation

Preparing for endotracheal intubation

1. ET tube: Size 2.5, 3.0, 3.5, 4.0 mm[2]

Tube Size (mm)	Weight (gm)	Gestational Age (Wks)
2.5	<1000	below 28
3.0	1000-2000	28-34
3.5	2000-3000	34-38
3.5-4.0	ABOVE 3000	ABOVE 38

2. Insert stylet to appropriate distance if required. (However try to avoid stylet unless there is difficulty in intubation)

Laryngoscope:

Attach blade No. 0 for preterm
No. 1 for term infant
Check light

Additional features:
- Cut strip of tape
- Prepare suction equipment
- Prepare oxygen tube with 100% O_2
- Prepare resuscitation bag and mask

Position infant flat on the back with neck slightly extended. Insert laryngoscope. Stand at the head end of the infant. Be sure that laryngoscope blade is locked in operating position and the light is bright. Hold the laryngoscope in left hand. Introduce the blade into the mouth and advance it to just beyond the base of the tongue. This should position the blade with vallecula

Visualize Glottis: Lift the blade and observe for landmarks. As you lift the blade epiglottis and glottis should come into view.

Fig. 10

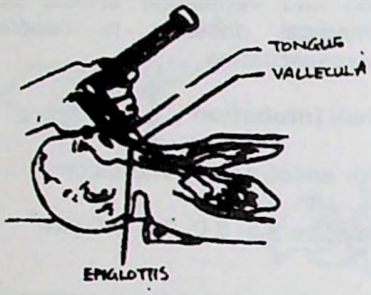


FIGURE 10 A: VISUALIZING GLOTTIS

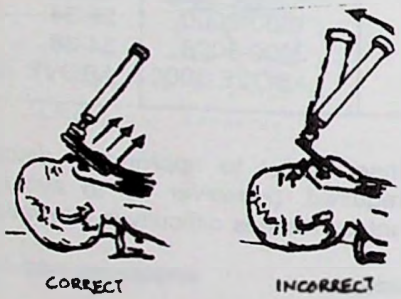


FIGURE 10B: TECHNIQUE OF USING LARYNGOSCOPE

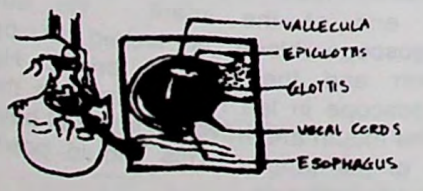


FIG. 10C: CORRECT POSITION OF LARYNGOSCOPE

When you visualize glottis

a. What landmarks do you see? If the blade is in too far, not far enough or off to one side take corrective action.
b. If view of glottis obscured by secretions, suction secretions
c. Apply tracheal pressure if you are not able to visualize glottis.

Inserting ET tube: When the glottis can be seen introduce the ET tube into right side of mouth and into glottic opening.

Insert the tip of the tube until the vocal cord guide is at the level of the vocal cords.

When the tube is positioned withdraw the laryngoscope and then the stylet and observe for the tube position by ventilation.

1. Observe the chest and abdomen. Look for good chest expansion
2. Bilateral breath sounds are of equal intensity. If unilateral withdraw tube appropriately. If no air entry withdraw and resuscitate, then re-intubate.

After initial confirmation by above methods fix the tube to the infants face. The above can also be obtained by inserting tube to following distance from angle of mouth.

Weight (kg)	Depth of insertion (cms from angle of mouth)
1	7
2	8
3	9
4	10

Now obtain a chest x-ray.

Medications

Mechanism of action

- Stimulates the heart
- Increases tissue perfusion
- Restores acid base balances

Routes of administration

a. Umbilical vein through a catheter which is inserted into the vein until there is a free flow of blood.
b. Peripheral vein

c. Endotracheal instillation (Fig 11)
Directly or using 5F catheter.

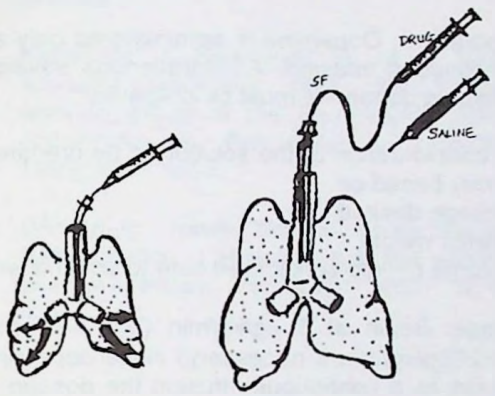


Fig 11 : ENDOTRACHEAL INSTILLATION OF DRUGS

Indications

1. The neonates heart rate remains below 60 beats/minute despite adequate ventilation (with 100% oxygen) and chest compressions for a minimum period of 30 seconds[2,3,4]
2. Heart rate is zero

Medications used

1. Epinephrine

Preparation
- Recommended concentrations 1:10,000
- Concentration available 1:1000

Preparing syringes – Prepare 1ml in a syringe

Dosage and route: Intravenous and endotracheal 1:10,000; 0.1-0.3 ml/kg

Rate : Given rapidly

Mechanism of action

a. Increases strength and rate of cardiac contractions
b. Causes peripheral vasocontraction

Expected signs: Heart rate should rise to 100 beats/min or above within 30 seconds after infusion.

Follow up: If heart rate remains below 100 beats/min consider epinephrine (re-administration) – may be repeated every 3 to 5 minutes if required.

2. Volume Expanders

Indications for use : Evidence or suspicion of acute blood loss with signs of hypovolemia.

Types of volume expanders:

Four volume expanders may be administered.
- Whole blood (O-ve blood cross-matched with the mothers blood)
- 5% albumin – saline solution
- Normal saline
- Ringers lactate

Administration :

Dosage: 10 ml/kg
Route: Intravenous
Rate: give over 5-10 mins. by syringe or intravenous drip.

Effects :

a. Increase vascular volume
b. Decrease metabolic acidosis by increasing tissue perfusion

Expected signs : Blood pressure should increase, pulse becomes stronger and pallor should improve.

Follow-up : May be repeated if signs of hypovolemia persist.

3. Sodium Bicarbonate

Indications for use:

1. Prolonged arrest that does not respond to other therapy
2. Documented metabolic acidosis

Note: Sodium bicarbonate should be used only after ventilation is established.

Preparations : Recommended concentration 0.5mEq/ml = 4.2% solution.

Administration: Prepare two 10 ml prefilled syringes.

Dosage : 2 mEq/kg.
Route: intravenous
Rate: Give slowly, over at least 2 minutes (1mEq/kg/mt) to minimize the risk of intraventricular hemorrhage.

Effects:
a. Corrects metabolic acidosis by raising the pH of the blood in the presence of adequate ventilation
b. Provides some volume expansion resulting from the hypertonic solution of sodium.

Expected signs : Heart rate should rise to 100 beats/mt or above within 30 seconds after infusion is completed.

Follow up : Heart rate below 100 – consider readministration of epinephrine and continue with volume expanders, ventilation and chest compression. If persistent hypotension is present, consider administration of dopamine.

4. Naloxone Hydrochloride

Indications for use :
a. Severe respiratory depression in the newborn AND
b. A history if maternal narcotic administration within the past 4 hours.

Preparation : Concentration available 0.4mg/ml or 1 mg/ml solution. Prepare 1 ml in a syringe.

Administration:

Dosage : 0.1mg/kg (100μg/kg)
Routes: Endotracheal, intravenous preferred.. Intramuscular, subcutaneous : Acceptable but delayed onset of action.
Rate : Inject rapidly.

Effects: Narcotic antagonist.
Signs: Spontaneous respiration.
Follow-up : Monitor respiration and heart rate closely. Re-administer naloxone if respiratory depression recurs.

Note: The duration of action of naloxone is 1 to 4 hours. The duration of the narcotic often exceeds that of naloxone, necessitating repeated doses of naloxone.

5. Dopamine Hydrochloride

Indications : After prolonged resuscitation if the infant has poor peripheral perfusion and thready pulse and continues to show evidence of shock.

Preparation : Dopamine is administered only as a continuous infusion. An intravenous solution containing dopamine must be prepared.

The concentration of the solution to be prepared will vary based on
- Dosage desired
- Infants weight
- Volume of fluid considered safe to administer.

Dosage: Begin at 5 μg/kg/min (May increase upto 20μg/kg/min if necessary) since dopamine is given as a continuous infusion the dosage is always expressed as the amount of dopamine to be infused per kilogram per minute.

Preparing solution : Commonly used formula –

$$\frac{\text{6x infants wtt in kg x desired dose/μg/kg/mt}}{\text{amount of fluid in ml/h}} = \text{Mg of desired dopamine per 100ml sol}$$

Multiplying 6 times infants's weight in kilograms with desired dose of dopamine in μg/kg/min and dividing by desired amount of fluid to infuse in ml/hr will provide you, the amount of dopamine in mg to add to each 100 ml of solution prepared.

Effects:
- Strengthens cardiac contractions
- Increases cardiac output
- Raises blood pressure

Expected signs :
- Blood pressure should rise
- Heart rate should stabilize

Infusion rates are usually increased in increments of 3-5 μg/kg/min if the blood pressure and perfusion do not improve.

Follow-up:
After 15 minutes: check heart rate and blood pressure at least every 3-5 minutes until the blood pressure is stabilized.

Caution: If an infant has an insufficient response to 20μg/kg/min of dopamine it is highly unlikely that raising the dose further will make a difference.

References

1. Operationalisation of essential Newborn care at District level: Resource Book – National Neonatology Forum & Government of India.

2. Kattwinkel J, Niermeyer S., et al. ILCOR advisory statement from the Pediatric working group of the International Liaison committee on Resuscitation. Circulation 1999; 1927-1938.

3. Deorari A. Newer Guidelines for Neonatal Resuscitation – How my practice needs to change? Indian Pediatrics 2001; 38:496-499.

4. Gupta P. Guidelines 2000 for Neonatal Resuscitation- Indian Paediatrics 2000; 37:1229-1233.

5. Kattwinkel J. Text Bool of Neonatal Resuscitation, 4th Edition Elk Grove Village, Illinois, American Academy of Paediatrics and American Heart Association, 2000.

6. International Guidelines for Neonatal Resuscitation: An expert from the guideline 2000 for Cardiopulmonary Resuscitation and Emergency Cardiovascular care: International consensus on Science 2000;106:e29.