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Tubercle and Lung Disease

Editorial

Drugs are not enough

Failure of short-course chemotherapy in a district in India

The world owes a debt of gratitude to India for its research in the field of tuberculosis. It is India that taught us about the supreme importance of bacteriology in the diagnosis and control of tuberculosis; it is the research conducted in India that has shown that hospitalization is not essential; it has provided us with principles of chemotherapy, including the increasingly important knowledge that intermittent treatment is as good as daily treatment.

During the Jubilee celebrations of the National Tuberculosis Institute (NTI) in Bangalore, Halfdan Mahler, the then Director General of the WHO and a former researcher of the NTI, was quoted as saying: 'All countries benefit from the fruits of Indian research – all countries except India'. The study reported by Dr Manjula Datta and her colleagues in this issue constitutes both a powerful and a rather sad confirmation of Dr Mahler's assessment.

In this study a fully intermittent 6 month regimen with twice weekly rifampicin, isoniazid and pyrazinamide was offered to almost 4000 smear-positive patients with pulmonary tuberculosis in North Arcot district; those who could not attend twice weekly (about one third of the patients) were offered a 'standard' regimen of isoniazid and thiacetazone.

The way this study was conducted and the results it obtained constitute an unmitigated disaster – there were apparently 416 registrations with 2 or more treatment cards (we are not told if such patients received double or triple dosage). Only a little more than 40% of patients completed 80% or more of treatment while a slightly larger group took less than 50% of chemotherapy. The fatality rate was extremely high, with over one quarter of the patients dying, while another quarter remained bacteriologically positive when examined 6–36 months after starting treatment. Resistance to antimicrobial agents was common among such cases, with 60–80% of them showing resistance to INH and 12% to rifampicin.

These results are no better than would have been the case if no treatment whatsoever had been given.[1] The causes of this disaster are multiple, but most likely relate to non-compliance of the health staff with regulations governing treatment, and non-compliance of patients with taking their medication.

There have been numerous attempts to improve patients' compliance, among the more successful being those undertaken in Beijing, China, where twice-weekly, completely supervised treatment resulted in the cure of many new patients[2] and later of many chronic patients.[3] In the IUATLD supported programmes in Africa and Central America,[4–8] Styblo introduced hospitalization during the initial phase of chemotherapy for patients unable to attend treatment centres daily, with gratifying results.

It is to be hoped that India will not only solve the problems presented in Datta's report, but that it will again assume scientific leadership in this area. Perhaps the way to proceed is not to try to add minor improvements to the existing programme, but to start from 'the other end', as it were, by organizing perfect, completely supervised treatment (this is possible due to the excellence of the epidemiological teams working in the Tuberculosis Research Centre in Madras) and then start removing individual, more costly components of such an experimental programme, while retaining excellent results. Even a wealthy country would be too poor to allow treatment programmes of the kind described by Dr Manjula Datta to continue; possibly even expensive hospitalization would prove more cost effective in terms of epidemiological impact.

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relevance to the pathology. It was recommended that Salazopyrin be taken life-long, but the runner withdrew this after 6 months and has had no further episodes. It is obvious that since that time there has been an increased awareness of lower gastrointestinal problems in runners. I would suggest that the runner described by myself had a milder version of inflammatory bowel disease to that described in your Journal.

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Gut fermentation

Eaton's paper on gut fermentation (November *JRSM* 1991, p 669) drew my memory back many years. I think it was believed[1] that the condition - intestinal carbohydrate dyspepsia - was due to colonization of the small gut by coliforms following a bout of gastroenteritis. A high starch diet maintained the abnormal bacterial population leading to abdominal distension, the production of excess flatus and, as months passed, increasing introspection, frustration and polysymptomatology in the patient.

When I was serving in the RCAF in the mid-fifties a fighter pilot saw me with symptoms of intestinal carbohydrate dyspepsia to such an extent that he could not tolerate high altitude flying. He gave a typical history. I took him off bread and other cereal based food, potatoes, and pulses for 3 days - he was then to fly again; he did so and was very much better.

I kept him on the same regimen for 2 weeks and then added firstly bread, then other cereals and finally potatoes over a further fortnight. He did not consult me again.

I have seen many patients with similar symptoms since then and they all did well. Patients were always told the reasons for the low starch regimen.

I see fewer patients now, being partially retired and working in a different field, but if I saw a patient tomorrow with a bubbly distended gut following, even remotely, an attack of diarrhoea, I would ask for a stool culture and microscopy and if these were normal I would advise the low starch regimen. Only if symptoms continued would I ask for further investigation.

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What is the best dosage schedule for patients?

Peter Keen (November 1991 *JRSM*, p 640) states 'non-compliance by patients is not a new discovery . . .' quoting a perceptive and witty Stephen Leacock reference. However, Hippocrates wrote that 'the physician should keep aware of the fact that the patients often lie when they state they have taken certain medicines'. In 1710, during a plague outbreak, a judicial edict was read from pulpits in a district of east Prussia that 'all those would be regarded as suicides and their corpses would be publicly hanged who refused to take the prescribed medicines even if these proved to be of no avail'.[1] Keen states 'It was only about 20 years ago that compliance was formally identified as an important factor in therapeutic evaluation . . .' referring to a valuable 1979 publication[2].

Tuberculosis physicians were well aware, in the mid-1950s, of non-compliance of patients taking bulky, unpleasant PAS. In 1958 and 1962 I documented the *general problem* of self-administration of drugs, quoting examples from other diseases and chemoprophylaxis and summarized our findings from the Tuberculosis Research Unit, Madras, that the problem applied not only to PAS but to isoniazid, a drug given in small dosage, and even a placebo[3,4]. Compliance led the two MRC tuberculosis units to develop intermittent regimens, making fully supervised chemotherapy possible, then to shortening the duration of chemotherapy and then to short duration fully intermittent regimens. We have moved far beyond once daily dosage, discussed by Keen, to intermittency as infrequent as once weekly in the continuation phase of treatment and MRC colleagues[5] have studied in depth the mechanisms of action of pulses of anti-tuberculosis drugs. Physician compliance[6] remains another essential issue.

Our MRC view is problems of patient compliance are best solved by the development of intermittent and depot regimens.

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Crohn's disease of the vulva

The letter from Hossain and Bazaz (November 1991 *JRSM*, p 693) suggests that if medical therapy fails for Crohn's disease of the vulva, vulvectomy or debridement therapy may be required. I suggest before resorting to surgery try local injection of triamcinolone as a suspension into the vulval areas both intradermally and below any ulcerated areas.

I discussed this in 1985 at my Presidential Address to the Section of Coloproctology and I use this technique for perianal, peristomal Crohn's disease and pyodermal gangrenosum. I have only seen one mild Crohn's disease involvement of the vulva which did not require this therapy but I would very strongly recommend that it be tried before radical surgery. It does require general anaesthetic and up to 40 mg can be given at one time.

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