The group of 20 wives with pre-existing psychological symptoms throughout had much higher levels of psychological disturbance than the others (at one year half being severely distressed compared with 21% of the total group). The marriages of these wives seemed to be especially vulnerable, a third deteriorating during the year compared with 16% of the others.

Discussion

From these semi-structured interviews has emerged a more detailed knowledge of the impact of infarction than is available for any physical illness. Psychosocial disability in the wives was considerable, persistent, and comparable with that of the patients themselves. At first indeed they were more distressed than their husbands, of whom nearly a quarter denied anxiety and only 11% were rated as moderately distressed—presumably because they were in a protected environment.

The various aspects of life are affected to different extents in different women. Measures of psychosocial adjustment before the illness are good predictors of how the wives will be feeling and behaving a year after the heart attack, and they could thus identify the women who are most at risk.

Similarly, the whole quality of the family life and the marriage appear to be important determinants of psychological and social outcome for the patient. The wife (and to lesser extent other

relatives) clearly has a substantial influence on the patient's rehabilitation by her encouragement or her protectiveness and by discussing the illness and the future, making plans, and talking to doctors. She can also help her husband in his efforts to take exercise, diet, give up smoking, and so on by doing these things with him. Medical advice should therefore be given to the wife throughout convalescence so that she will have a positive influence and not be overprotective. This approach could be evaluated by our interviewing and standardised rating techniques.

The two main needs therefore to be highlighted by this study are greater practical support and advice for the wives of men with myocardial infarction while they are in hospital and advice and help for the whole family throughout the convalescence.

This work was carried out with the aid of a grant from the British Heart Foundation. We thank the physicians, staff, and patients of the Radcliffe Infirmary for their co-operation.

References

- ¹ Skelton, M, and Dominian, J, *British Medical Journal*, 1973, **2**, 101.
- ² Mayou, R A, Williamson, B, and Foster, A, *British Medical Journal*, 1976, **1**, 1577.

(Accepted 27 October 1977)

Today's Treatment

Diseases of the respiratory system

Tuberculosis

ANTHONY SEATON

British Medical Journal, 1978, **1**, 701-703

Tuberculosis is one of few diseases in which one may be dogmatic about treatment, since its management is founded on the results of extensive controlled trials. Whereas the early decreases in the death rate from tuberculosis resulted from improved social conditions, isolation of the most infectious patients in sanatoria, and to some extent surgical treatment, the more recent rapid decline of the disease as a cause of death in Britain has coincided with the introduction of effective drugs. There is now no doubt that chemotherapy alone is sufficient treatment in almost all cases of tuberculosis, no matter what organ the disease affects.

Tuberculosis should be treated when *Mycobacterium tuberculosis* is cultured from or seen in a compatible clinical lesion. Patients showing only clinical and radiographic or histological

evidence of tuberculosis also sometimes need to be treated even though the organism is not actually isolated; in such a case response to treatment may be taken as strong evidence of active disease. All forms of tuberculosis should be treated in the same manner—ideally by someone, usually a chest physician, with experience of the problems of antituberculosis chemotherapy. This is particularly true of tuberculosis presenting to surgeons—for example, bone and joint, lymph node, and abdominal disease—as arrangements for supervision and follow-up of the disease in surgical clinics are often haphazard. A chest physician should see the patient as soon as the diagnosis is suspected, as this will often prevent unnecessary surgery.

Principles of management

There are three main principles in the management of tuberculosis:

(1) Treatment should start with three drugs to which the organism is likely to be sensitive for at least eight weeks and preferably until the drug sensitivities are known, followed by two drugs thereafter. This regimen ensures rapid killing of the organisms, reduces infectivity, and prevents the development of resistant strains.

Institute of Occupational Medicine, Edinburgh EH8 9SU

ANTHONY SEATON, MD, FRCP, director (also honorary senior lecturer, Department of Respiratory Diseases, City Hospital, Edinburgh)

(2) Chemotherapy should be supervised to ensure that the drugs are being taken, and the patient should be followed up during treatment and in some circumstances for several years afterwards.

(3) Close contacts should be visited in case they also have the disease.

Drugs

FIRST-LINE DRUGS

First-line drugs are used in combination for initial and maintenance treatment unless resistance is known or suspected. None has a known human teratogenic effect, though streptomycin may cause deafness in the fetus.

Isoniazid is a small white 50- or 100-mg tablet, rapidly absorbed by mouth, which produces bactericidal blood concentrations for over 24 hours. The normal adult dose is 300 mg daily. For children 5 mg/kg is adequate, though higher doses, up to 20 mg/kg, can be tolerated and isoniazid elixir *BPC* (50 mg/5 ml) is a useful preparation. Side effects are rare, though slow acetylators particularly may develop peripheral neuropathies or other neurological abnormalities, which can be treated with pyridoxine. Hypersensitivity reactions, usually rashes or fever but very occasionally hepatitis, are uncommon.

Rifampicin, another bactericidal drug, is marketed as red, red/brown, and red/blue capsules containing either 150 or 300 mg. There is no difference in either efficacy or cost between the two proprietary preparations. There is also a syrup, containing 100 mg/5 ml. The usual dose is 600 mg daily for adults (450 mg if the patient weighs less than 50 kg) and 12-20 mg/kg with a maximum of 600 mg for children. The drug should be taken before breakfast. Rifampicin may upset the stomach, though usually only temporarily, and turns the urine, sweat, and sputum red. Patients should be told not to worry about this. It very rarely causes fever or rashes but commonly provokes abnormalities of liver function and occasionally jaundice and hepatitis. Abnormalities of liver function short of jaundice usually settle spontaneously, and treatment does not need to be stopped. Serious side effects on blood, kidneys, and pancreas are extremely uncommon except with high doses that may be used in intermittent regimens. Enzyme induction in the liver interferes with the efficacy of anticoagulants, the contraceptive pill (necessitating an increased, perhaps double, dose or the use of alternative contraceptive methods), and steroids. If rifampicin and para-aminosalicylic acid (PAS) are combined in the regimen they should be separated by eight hours.

Ethambutol, a bacteriostatic drug, is produced as either a grey 400-mg or a small yellow 100-mg tablet. The dose for the first eight to 12 weeks of a nine-month regimen should be 25 mg/kg, but if it is used for longer the dose should then be reduced to 15 mg/kg. Occasional rashes, fever, or gastrointestinal upsets may occur, but the most important side effect is optic neuritis. This occurs only with higher than 15 mg/kg and is reversible if the drug is stopped early. It manifests itself as difficulty in reading small print or a red-green colour disturbance. Thus with high doses of ethambutol visual acuity should be tested to guard against this complication, particularly in elderly patients with cataract, who may attribute their failing sight to the cataract rather than the drug, and in young children.

Streptomycin, which is bactericidal in combination with pyrazinamide and is given by intramuscular injection, is no longer usually a part of initial regimens in Britain. Apart from the inconvenience of injection, toxic effects (eighth nerve damage, renal damage, and hypersensitivity reactions) are more common than with the other first-line drugs, making it desirable to monitor blood concentrations in elderly patients. The concentration 24 hours after a dose should not exceed 2 µg/ml. The usual dose should be 0.75 to 1 g daily (30 mg/kg in children). Despite this it remains a useful drug for difficult patients and in cases of drug resistance. An investigation is in progress of the

efficacy of streptomycin in combination with isoniazid, rifampicin, and pyrazinamide as a six-month regimen with high initial bactericidal activity.

Reserve drugs—Certain drugs are held in reserve for cases of drug resistance. These are generally more toxic than the first-line drugs and somewhat less potent. A full description is beyond the scope of this article, but the more important ones are listed in the table.

Reserve antituberculosis drugs

	Dose	Main toxic effects
Para-aminosalicylic acid	10-20 g, oral	Gastric, rashes, fever
Thiacetazone	2 mg/kg, oral	Gastric, haematological changes
Pyrazinamide	25 mg/kg, oral	Hepatitis, arthralgia, gastric
Ethionamide and prothionamide	0.75-1 g, oral	Gastric, hepatitis
Capreomycin	1 g, intramuscular	Eighth nerve, renal, rashes, fever

Regimens

For the initial treatment of tuberculosis when drug resistance is not suspected a nine-month course of rifampicin and isoniazid, supplemented by either ethambutol or streptomycin for the first eight to 12 weeks, may be used in Britain. The cost of rifampicin may prohibit this regimen in less developed countries. All these drugs should be taken before breakfast. There is not, as yet, a six-month regimen of proved efficacy. If rifampicin cannot be used, because of toxicity or cost, the regimen must last 18 months to guarantee cure and again should include an initial two- to three-month intensive phase with three drugs. The classical regimen was streptomycin, PAS, and isoniazid, but PAS has been superseded by ethambutol.

If it is suspected that the patient may not take his drugs regularly a fully supervised intermittent regimen should be considered. With all these regimens, an intensive phase of daily treatment, as described above, is desirable for the first two to three months. Subsequently, the 18-month course may consist of streptomycin (1 g) or rifampicin (600 mg) plus isoniazid (15 mg/kg) twice weekly. Many other regimens have been tested and, though less satisfactory, may be used in difficult cases.

Problems in treating tuberculosis

Blame for any failure of antituberculosis chemotherapy may be divided equally between the doctors and the patients. The difficulties usually arise because patients either get confused about the regimen or are unwilling to take a prolonged course of tablets—often when they are feeling quite well. This problem is compounded by the fact that nowadays many patients with tuberculosis are vagrant or alcoholic. Asian immigrants, who also form a high proportion of tuberculous patients, may have difficulty understanding the regimen because of language problems but usually prove most compliant once they have done so. The treatment fails when the doctor does not realise that the patient is not taking the tablets regularly and therefore does not take appropriate action.

Other problems occur when the patient develops symptoms of drug toxicity or when drug resistance occurs. Toxicity may be dealt with by stopping the drug and substituting another (the regimen being continued for 18 months if isoniazid or rifampicin is stopped), though occasionally a reduction in dose or desensitisation may solve the problem. Drug resistance should always be suspected if the patient has had antituberculosis drugs before or is a contact of a patient known to harbour drug-resistant organisms. In such cases treatment should start with a regimen of three drugs excluding those to which resistance is a possibility. The use of more effective or less toxic drugs may be possible later when the sensitivities are known.

HOW TO OVERCOME THE PROBLEMS

The patient with newly diagnosed tuberculosis should have the regimen explained to him in detail. This will include showing him the tablets he must take. If he is ill or has extensive disease two to four weeks in hospital is desirable but not essential.

The drugs should be prescribed by the doctor who is supervising him and the patient should always bring his tablets to the clinic for inspection. Curiously, the wrong dose or combination is often prescribed or dispensed and the error may not be discovered if this precaution is not taken. The doctor should have samples of all the usual antituberculosis drugs in his desk for comparison with the patient's tablets.

Drugs should, if possible, be prescribed in combination tablets, no matter what is taught in pharmacology. This ensures that if one drug is taken the other is, and only one urine test is needed. It also makes things easier for the patient. Rifampicin, ethambutol, and PAS are all available in combination with isoniazid. Care with dosage is, however, necessary.

The patient should be seen at least monthly during treatment so that his tablets may be inspected and his urine tested for the drugs. If he is suspected of not taking them he should be put on to a fully supervised regimen.

If the patient is thought unlikely to comply because of alcoholism or vagrancy, or if he does not keep follow-up appointments or his urine does not contain the drugs, his treatment should be supervised. This may mean daily or twice weekly visits from the clinic or practice nurse. The nurse must watch the patient swallow the tablets. Vagrants should be kept in hospital for as long as possible, and they are often happy to remain there for prolonged periods. Alcoholics prove difficult, not least because many of the regimens are potentially hepatotoxic. Alcohol should be withdrawn in the routine manner during the initial phase of chemotherapy. As such patients often prove unable to complete a full course the initial phase should be as intensive as possible.

Other aspects of treatment

Primary tuberculosis occurs in the young and the very old and is particularly frequent in young adult Asian immigrants to Britain. It should be treated in the same way as postprimary disease.

Non-pulmonary tuberculosis should be treated in the same way as pulmonary tuberculosis. Empyemas should be aspirated and occasionally need to be resected. Abscesses should be drained. Surgery is otherwise rarely necessary.

Meningitis—Treatment should start with streptomycin, pyrazinamide, isoniazid, and rifampicin to ensure adequate drug concentrations in the cerebrospinal fluid. Intrathecal treatment is not usually necessary, but corticosteroids are advisable (see below).

Surgery is rarely necessary, owing to the efficacy of proper chemotherapy. Nevertheless, it may occasionally be necessary to remove cervical lymph nodes, which do not always respond satisfactorily to chemotherapy alone, to resect empyemas, or to remove areas of lung containing organisms with multiple drug resistance. The most frequent indication for surgery now is the actual or suspected presence of bronchial carcinoma in addition to tuberculosis.

Corticosteroids make a toxic or moribund patient feel better quite quickly and are often used. But there is no evidence that they produce more rapid sputum conversion, and they should not be used routinely in pulmonary tuberculosis. They are also useful for suppressing the hypersensitivity reaction that is associated with rupture of lymph nodes into the bronchi in primary tuberculosis and for reducing the size of these nodes if they are compressing large airways. Corticosteroids probably prevent fibrous tissue formation and in the absence of evidence to the contrary should be used in tuberculous meningitis and in renal tuberculosis if there is evidence

of ureteric obstruction. Finally, they may be used to control drug reactions in desensitisation and as replacement treatment in Addison's disease.

Other opportunist mycobacteria

The two most frequently pathogenic organisms are *M. kansasii* and *M. avium/intracellulare*. These occur especially in patients with other lung disease, are not usually transmissible from man to man, and generally cause slowly progressive disease. The former usually responds to a combination of rifampicin, ethambutol, and ethionamide but the latter is usually resistant to all drugs in vitro. Management is often difficult and surgery may be necessary.

Follow-up and contact tracing

Patients who seem very likely to have been assiduous in taking their treatment for the full period do not need to be followed up for more than a year after finishing. If they have been unreliable a longer follow-up may be desirable but in such patients this is rarely possible. Generally, if relapse occurs in a patient who is no longer being followed up he will recognise it quickly, and medical attention will not be long delayed. Follow-up is, of course, necessary in trials of new short regimens or in patients treated, because of resistant organisms, with less satisfactory regimens.

Close contacts of a new patient (those living in the same house or working daily in the same room) should be investigated as soon as possible after diagnosis. Adults should have chest radiography and children a Heaf test. If the result of either is positive it should be followed up by a chest radiograph and if negative by BCG vaccination. If the radiograph shows primary infection this should be treated routinely; but if it is normal in the presence of a positive Heaf test, indicating that preclinical infection has occurred, a 12-month course of isoniazid alone may be given—such chemoprophylaxis is the only case in which treatment with one drug has been shown to be effective.

Further reading

- Ross, J D, and Horne, N W, *Modern Drug Treatment in Tuberculosis*, 5th edn. London, Chest and Heart Association, 1976.
Lancet, 1975, **1**, 117.
 Macdonald, J B, *Thorax*, 1977, **32**, 1.

What is the best method of delaying or postponing a period in a girl of 15 due to take important examinations at the time of her next period. She normally has painful periods with considerable premenstrual tension.

If this problem had been foreseen some time ago it would probably have been best to take over the cycles with a combined contraceptive pill. This could have been expected to control the premenstrual tension and the dysmenorrhoea. It now seems too late for this, so one should try to maintain a degree of raised concentrations of both oestrogen and progesterone, or progesterone only for a few days. Dalton¹ is enthusiastic about progesterone in treating the premenstrual syndrome, given either rectally or vaginally in doses of 200 to 400 mg daily from day 14 of the cycle. The dose should be divided. With luck this should prevent the tension and the dysmenorrhoea. Alternatively progesterone may be given by intramuscular injection, and in high enough dosage should postpone the period. Is this the right thing to do? Is such treatment only an addition to the stress? Could the treatment introduce an unknown factor and make matters worse than they might otherwise have been? If it is thought possibly unwise to try a therapeutic experiment at this stage, the parents or the teachers may approach the examiners and tell them of factors in a candidate that may affect performance adversely, and teachers can make representations to them if examination results are not in accord with class work.

¹ Dalton, K, *Journal of Maternal and Child Health*, 1977, **2**, 69.