TREATMENT OF RENAL TUBERCULOSIS*

BY

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The incidence of tuberculosis is declining rapidly in Britain, as shown by the fact that many large sanatoria have been closed down, while there is a definite redundancy problem among tuberculosis doctors, who are now called chest physicians. Genito-urinary tuberculosis, which normally shows itself 10 to 15 years after primary inoculation, is also on the decline, but in my Genito-urinary Tuberculosis Unit at Harefield we are still seeing many old and new patients, although a fair proportion of the latter are immigrants.

During the years 1951-61 334 patients have been treated in Harefield Sanatorium to a conclusion. That is to say, they have received triple-drug therapy for approximately six months as in-patients, to be followed by para-aminosalicylic acid (P.A.S.) and isoniazid for approximately 18 months as ambulatory out-patients. During the same years a further 106 patients have been treated solely as out-patients or by a short stay in a general hospital followed by out-patient treatment. This makes a total of 440 patients. The years 1962-3 are not included here, because these patients are still undergoing treatment.

Management

Our routine management is as follows:

Diagnosis.—We will not accept a diagnosis from a Ziehl-Neelsen stained slide, but insist upon positive guinea-pig inoculation or a positive urine culture, preferably from an early-morning urine specimen. We will in principle not start drug-therapy until such proof is available, and consider this to be most important, especially in young women, where the symptoms of a simple cystitis and pyelonephritis can so closely resemble a tuberculous infection, and vice versa. If drug therapy is begun purely on the evidence of an acid-alcohol-fast bacillus shown on a stained slide it may never be possible to confirm or refute the diagnosis, because there may never be another positive urine. If we subsequently decide that the condition is not tuberculous and therefore wish to stop treatment we are in real difficulties. If the drugs are stopped and the diagnosis is wrong the lesions will almost certainly relapse, but, even worse, the organisms may now be resistant to the drugs. Once started, therefore, drug treatment must be continued for two years.

We prefer, when possible, to admit the patient in the first instance to the sanatorium and to keep him there until the urine has been sterile for six months. This is, of course, not always possible, but there is no doubt that this regime has produced our best results. In principle, the tubercle bacillus will be destroyed if it comes into contact with the correct drugs in sufficient quantities for a sufficient length of time, and only in a hospital can these three vital factors be controlled when they most matter—that is to say, in the first few months of treatment. In hospital one can ensure that the patient really does take the drugs. One can ascertain whether they are too toxic for the given patient and can desensitize him to the drug if need be. We can detect early eighth-nerve damage which calls for immediate cessation of streptomycin and, most important, we can instil a sense of responsibility and discipline which

makes the subsequent 18 months' treatment at home seem a relative relief.

Drugs.—When possible our drug regime consists of streptomycin 1 g. daily, isoniazid 400 mg. daily, and P.A.S. 12-15 g. daily. These are given without intermission until the urine has been sterile for six months. Three consecutive early morning urines are cultured every month during the stay in hospital, and we have found that 60% of the urines are sterile after two months' therapy and 80% after four months. In practice, of course, we do not know these facts until the fourth and the sixth month respectively, because the cultures are left for two months in incubation. In our own unit we have not failed to produce a sterile urine, nor have we seen a drug-resistant organism develop in any acute case which we have treated in this way from the start. Our only relapses or resistant organisms have been in long-standing cases or in patients who have been previously treated. The overwhelming majority of such cases have been over 50 years of age and have had some form of poorly controlled tuberculous disease for over 10 years.

Ambulatory Treatment.—There is no doubt in our minds that patients treated for the first few months under controlled sanatorium conditions respond more rapidly to the drugs than do patients who live at home, and this is especially marked in women in their early twenties, where the counter-attractions of social life make "early nights" and conscientious drug therapy very difficult. These are the patients who "can't take the drugs" because they make them feel unwell—or who forget about them, or who actually default altogether. Our records show that we failed to sterilize the urine in some 30 of these adolescent patients until they were persuaded to come into hospital. Once admitted they all responded rapidly and have remained clear over the years.

Long-term Drug Therapy.—When the urine has been sterile for six months the patient is allowed home and is encouraged to return to work and lead a normal life. The streptomycin is discontinued, but the P.A.S. and isoniazid are given continuously for at least a further year, or longer in the many cases where there have been signs of a fibrosis and obstruction and where calcification is occurring. Calcification may be a sign of "healing," but it merely means the deposition of calcium in avascular caseous material, and avascular tissue is not accessible to blood-borne drugs. We always regard such areas with distrust. Our records show once again the value of the initial sanatorium treatment. None of these patients have subsequently developed drug resistance or toxicity or have defaulted after leaving hospital, but some of those treated only as out-patients have never developed a sense of responsibility or discipline about their therapy.

The treatment of genito-urinary tuberculosis is therefore essentially conservative, and if surgery becomes necessary this is an admission of failure. However, failure does occur all too often, and is due to a breakdown in the fundamental principles already referred to—namely, that the tubercle bacillus must be in contact with suitable drugs in sufficient dosage for a sufficient length of time. It is our responsibility to ensure that the patient really does take suitable

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drugs in sufficient dosage for long enough, but, even then, if the healing fibrosis leads to avascularity and caseation the drugs cannot reach the bacilli, and this explains why closed-off caseous areas may still contain living tubercle bacilli even after prolonged treatment. In the same way the healing fibrosis may produce urinary obstruction, and these two factors—avascularity and urinary obstruction, both due to the healing fibrosis—are the two major indications for surgery.

Conservative Surgery

Surgery is necessary to remove avascular tissue or to relieve urinary obstruction. The three danger areas are the neck of a calix, the pelvi-ureteric junction, and the lower end of the ureter.

The main surgical procedures are therefore: (a) cavernotomy, if the neck of the calix becomes completely closed off; (b) some form of plastic procedure at the pelvi-ureteric junction; (c) reimplantation of the lower ureter for stricture; and (d) enlargement of the systolic bladder by a colocystoplasty or diversion of the urine if all else fails.

Cavernotomy.—This is an excellent operation with a low morbidity. The removal of avascular caseous material greatly diminishes the risk of a subsequent breakdown or rupture of an abscess cavity, and the operation conforms to the best principles of surgery—the maximum amount of good with the minimum amount of damage.

Partial Nephrectomy.—This is now rarely performed for renal tuberculosis. We have not recently seen a distorted calix which did not heal with drugs alone, so that the indication for partial nephrectomy has not arisen for more than five years.

Obstruction at the Pelvi-ureteric Junction.—This is the chief indication for nephrectomy. If the kidney does not drain a pyonephrosis results and drug therapy cannot be expected to help. Minor degrees of obstruction noted when the patient first comes under treatment are a source of constant anxiety. Drainage may improve with treatment, but, on the other hand, the healing fibrosis may progress in a completely silent manner, so that constant radiological control is necessary. In such cases plastic surgery at the pelvi-ureteric junction may be possible, and we have been able to do this with success on five occasions so far.

Obstruction of the Uretero-vesical Orifice.—Excision of a stricture and reimplantation of the ureter into the bladder has been one of the more commonly performed conservative operations in our unit. Again, timing is most important and constant care is necessary to ensure that the obstruction is relieved before serious renal damage occurs.

Relapse Rate

We have not yet seen a recurrence of tuberculous activity in any single patient who was treated in our sanatorium unit from the moment of diagnosis by triple-drug therapy with or without surgery followed by a period of ambulatory treatment for approximately a further 18 months.

Seven patients with bilateral and widespread disease, five of whom were over 60 years of age, failed to respond to drug therapy, which was therefore abandoned. Only four of the total 440 patients who completed a full course

of treatment have reverted to a positive urine over the years and all of these are over 45 years of age, have a very long history of active disease in other organs, and are chronic cases in the true sense of the word.

Mortality

Among these 440 patients there have been 15 deaths. Two of these patients were over 70 and had suffered from active renal disease for at least 20 years before drug therapy was started. One patient died from a pulmonary embolus after a nephrectomy; one died from polycystic disease with only a minimal tuberculous lesion; and one patient committed suicide. This leaves 10 (2.5%) patients who died from severe bilateral renal tuberculosis which had been present for more than six years before their admission to hospital. Five had already undergone a nephrectomy and two were paraplegic owing to Pott's disease. The youngest patient, aged 14, died from malignant hypertension due to bilateral renal ischaemia. No deaths have occurred in patients who were treated initially by us from the time a diagnosis was made, while half of the patients dying were over 45 years of age.

Conclusions

Certain definite conclusions can be drawn from these cases. Moderately early cases of renal tuberculosis can be "cured" by prolonged, intensive triple-drug therapy without any surgery. Patients over 45 years of age and/or patients who have had active disease for more than five years before treatment is begun respond less well to drug therapy. It cannot be repeated too often that, although drugs may kill the tubercle bacilli, they cannot replace destroyed tissue, so that the earlier the diagnosis is made the better the prognosis.

The indications for surgery are to overcome urinary obstruction and to remove or drain avascular areas of caseation.

Summary

The tubercle bacillus will be destroyed if the correct drugs come into contact with it in sufficient concentration for a sufficient length of time. If, therefore, drug therapy fails to sterilize the urine, one or more of these basic conditions has not been fulfilled. This can occur if the wrong drugs (drugs to which the particular bacillus is resistant) are used, if the patient does not take the drugs, or if the healing fibrosis creates avascular caseous areas which are inaccessible to the drugs.

A Ziehl-Neelsen-stained slide is not acceptable for the diagnosis of urinary tuberculosis, and drug therapy should not be started until the organism has been cultured or confirmed by guinea-pig inoculation.

Over 440 patients with genito-urinary tuberculosis have been treated to a conclusion during the years 1951–61. The ideal regime is triple-drug therapy in a sanatorium or special unit for six months, during which time any necessary conservative surgery is performed. The patient can then return home and resume normal work, but must continue with ambulatory treatment with P.A.S. and isoniazid for a further 18 months.