

TUBERCULOSIS

Tuberculosis is now the commonest infectious disease in the world. It infects one third of the world's population, and in 1995 there were about 9 million new cases with 3 million deaths.

In Papua New Guinea, the incidence of tuberculosis is about 135/100,000 population. In National Capital District, the incidence is about 750/100,000. There are currently about 8,000 newly diagnosed patients in Papua New Guinea per year, one third of whom are children. Tuberculosis is now the second or third commonest cause of hospital admission in coastal areas and ranks in the top 5 causes of death in both children and adults. Improved transport and increased mobilisation of the population has resulted in a rapidly increasing incidence of TB in areas of the country such as the highlands region where previously it was uncommon.

There is very great concern that unless urgent steps are taken, with the Tuberculosis programme of the 80s and 90s having failed, the HIV epidemic will greatly accelerate the spread of TB within the country. Multidrug resistance, currently at a relatively low level, could well become a very serious problem in the near future. The Health Department is following WHO recommendations in introducing DOTS (Directly Observed Treatment Shortcourse). It is imperative that a major effort by all concerned in the prevention and treatment of tuberculosis is supported by adequate financial and manpower resources.

The virtual eradication of TB in Europe between 1945 and 1975 was achieved by the interplay of three factors:

1. Prevention
 - a. The treatment of open cases
 - b. BCG vaccination
 - c. Improved nutrition, improved housing conditions and reduction of other diseases
 - d. The tuberculin testing of cattle and pasteurisation of milk
2. Treatment
 - a. The identification of cases
 - b. Drug treatment, with effective drugs freely available
 - c. Nonspecific treatment (good nutrition and treatment of concomitant diseases)
3. Education
 - a. That TB is an infection: it does not occur by chance, and it is not inevitable
 - b. That TB can be cured by treatment
 - c. That TB can be prevented by BCG vaccination
 - d. That prevention or treatment need not be expensive nor disruptive to a person's life.

THE NATURAL HISTORY OF UNTREATED PRIMARY TB

Initial infection is followed by a period of incubation during which the primary focus forms, the regional nodes enlarge, and organisms escape into the blood stream. At this stage, the body has not developed tuberculin sensitivity. This stage is symptomless and it is not until sensitivity develops 6-8 weeks after infection that fever, malaise and symptoms may occur. The infection in most children, however, is never clinically manifest. At this time, sensitivity phenomena are seen in a small proportion of children. Erythema nodosum is very rare in young children, but phlyctenular conjunctivitis is seen occasionally, and should always alert the clinician to the probability of tuberculosis.

After this initial phase, the clinical syndromes can be divided into those arising from the primary focus, the regional lymph glands, and dissemination. Complications from each of these three situations can occur simultaneously, especially in young children. The risk of serious dissemination is related inversely to age from birth to 10 years, with a rise again at puberty.

The tuberculin test, once positive, will usually remain so except for temporary reversion after measles, streptococcal infection or malnutrition, and permanent reversion with HIV infection.

Progressive enlargement of the primary focus leading to cavitation sometimes occurs, especially in young children (a progressive primary lesion). Pleural effusion, a manifestation of a high degree of

tuberculin sensitivity, is uncommon in children under 5 years. If it occurs, it will do so within 3 months of infection in 25% of cases and within 6 months of infection in 75% of cases.

The regional lymph nodes always enlarge in primary TB, and are bigger in young children. Symptoms and signs are related to lymph glands pressing on a bronchus and producing obstructive emphysema, or collapse with consolidation (a segmental lesion). Bronchial erosion is commoner in early childhood; it usually occurs between 3 and 9 months after infection.

Disseminated disease is more frequent in young children. The liver and spleen are often enlarged, and 20% of children under 1 year old, and 4% of children infected under 5 years old will develop tuberculous meningitis or miliary TB. In 90% of cases, this will develop within 12 months of infection. Bone and joint lesions occur mainly within 3 years of infection. Renal and skin tuberculosis are late complications, mostly occurring five or more years after infection.

Adult or secondary tuberculosis has been considered to be mainly a reactivation of a focus in the lung which originated during the state of dissemination of the primary infection and which remained dormant until the body's resistance became weakened - by malnutrition, corticosteroids, puberty, or intercurrent infection.

Tuberculosis meningitis presents either in an acute or slowly progressive form. It nearly always develops after the rupture, slow or sudden, of a pre-existing meningeal or subcortical caseous lesion occurring either alone or as part of a generalised miliary spread. Many patients have multiple caseous lesions. It sometimes presents as a space occupying lesion - an intracranial tuberculoma. In the young child, the onset of meningitis is usually insidious; there is often neck stiffness, and Kernig's sign is usually absent.

Tuberculosis of the CNS may present in 3 different ways:

1. as meningitis, with fever, headache, vomiting, and neck stiffness. CSF examination shows mainly lymphocytes, the sugar is reduced and the protein raised
2. as encephalitis, where the pathology is essentially massive caseation, with progressive changes in one or both cerebral hemispheres. Little reaction is evident in the meninges. There is fever, headache and vomiting, but no meningeal signs. The CSF contains only a few lymphocytes, but the protein is raised
3. as a space occupying lesion with headache, vomiting, papilloedema with or without localising neurological signs.

Note: The commonest cause of space occupying lesions in children in most tropical countries is tuberculoma (in up to 50% of cases). The tuberculin test is often negative, and x-rays of the chest are usually normal. A skull X-ray may show evidence of raised intracranial pressure.

The clinical picture of tuberculosis depends on the degree of tuberculin sensitivity. When the sensitivity is low, as in young infants and malnourished children, the acute inflammatory component of the pathological reaction is absent or reduced. When it is high, as in older children, the tuberculin test is strongly positive and there is often a pleural effusion or erythema nodosum (though erythema nodosum seems to be uncommon in Papua New Guinean children).

Tuberculosis should always be considered in the differential diagnosis of a pyrexia of unknown aetiology (or PUO). The diagnosis may be helped by doing a tuberculin test, a chest x-ray, fasting gastric aspirates and laryngeal swabs for AFB, and tuberculin testing and chest x-rays of household contacts. Sometimes, a therapeutic trial of antituberculous drugs is necessary.

Other conditions that may cause PUO and malaise without obvious physical signs, apart from wasting, include typhoid, malaria, urinary tract infections, bacterial endocarditis, HIV infection and malignant disease.

In children with a PUO, typhoid should always be suspected. Abdominal signs (loss of appetite, diarrhoea or constipation, and tender tumid abdomen), meningeal signs and chest signs are common. Diagnosis is made by blood culture early in the disease, and later by culture of the stools. The Widal agglutination test becomes positive after the 10th day.

CLINICAL FEATURES SUGGESTIVE OF TUBERCULOSIS IN CHILDREN

Tuberculosis is often difficult to diagnose in children. There are relatively few TB bacilli present and sputum cannot be obtained for examination. The following features suggest the diagnosis:

1. a family history of TB
2. the child comes from an area where TB is common
3. failure to gain weight
4. failure to recover after illness (eg measles or whooping cough)
5. a chronic cough
6. cough with unilateral wheeze
7. cervical lymphadenopathy (consider biopsy)
8. persistent fever (a 4 hourly temperature chart is often helpful in a child suspected of having TB)
9. absence of BCG scar
10. pneumonia that does not respond to antibiotics
11. ascites without other oedema
12. raised intracranial pressure with focal neurological signs
13. signs of meningitis, with CSF lymphocytosis and a high protein
14. signs of spinal cord compression
15. sterile pyuria while not on antibiotics, or painless haematuria
16. a positive 5u PPD Mantoux test.

Often children with features of TB have to be treated without bacteriological proof of the diagnosis. However, the decision to put a patient on potentially dangerous medication for 6 months should never be taken lightly and the clinician should always be able to justify this course of action. The use of the TB score chart (below) often helps in decision making.

MANTOUX TESTING

Use 5u PPD (not 1u) by intradermal injection. The reaction to measure is the area of induration, not the area of erythema. A positive reaction is over 5 mm induration if the child has not had a BCG, and over 15 mm if the child has had a BCG.

Malnourished children often have a negative Mantoux even if they have TB. A person given his or her first BCG vaccination who does not have TB usually starts to react (erythema, swelling, ulceration) at about 5-7 days. A person given a BCG vaccination who has TB (or who has had a previous BCG) has an "accelerated reaction" starting at 2-3 days - even if he or she is malnourished. Providing a BCG has not been given before, BCG vaccination can be used instead of a Mantoux test in malnourished children who are suspected of having TB: a reaction at 2-3 days demonstrates past or present TB (or previous BCG), and a reaction at 5-7 days suggests no TB (past or present) or overwhelming TB.

In "developed" countries, there is usually a bimodal distribution of tuberculin reactions into small reactions caused by non-specific sensitivity (or sensitivity to atypical mycobacteria), and large reactions caused by infection with pathogenic human tubercule bacilli. In "developing" countries, this bimodal pattern is obscured by a high proportion of intermediate reactions. In areas where tuberculosis is prevalent, and where BCG vaccination is practiced, the finding of a positive Mantoux reaction in apparently healthy individuals makes the interpretation of the test very difficult.

THE PAEDIATRIC TB SCORE

Because it is often difficult to diagnose childhood TB with certainty (by positive bacteriology or histology), a TB score has been devised. If a child scores 7 and no other disease is more likely, TB treatment should be started.

Paediatric Tuberculosis Score Chart				
<i>Basic score chart - for each feature decide on score and write in box:</i>				
Feature	0	1	3	Score
Length of illness	Less than 2 weeks	2 to 4 weeks	More than 4 weeks	
Nutritional status	More than 80% line	Between 60-80% line	Less than 60% line	
Family history of TB	No family history	Verbal family history	Sputum +ve family history	
<i>Give score for any other features (if present) as below:</i>				
Significant Mantoux (mm)			Score 3	
Enlarged, painless rubbery neck glands			Score 3	
Night sweats or unexplained fever			Score 2	
Angle deformity of spine			Score 4	
Malnutrition not improved after 1 month treatment			Score 3	
Firm, non-fluid, non-traumatic swelling of joint			Score 3	
Unexplained abdominal swelling (ascites)			Score 3	
Coma for more than 48 hours (with or without convulsions). Send to hospital if possible.			Score 3	
			TOTAL	
If total score is 7 or more and the child has NO OTHER DISEASE MORE LIKELY TO EXPLAIN THE ILLNESS, then commence TREATMENT FOR TUBERCULOSIS according to the child's weight (see STB, p.106).				
Notes:				
1. Beware of OVER SCORING a child, as each item may be wrongly assessed if care is not taken. If you have not used the score chart before, then you must refer to the notes in the Standard Treatment Book.				
2. Always keep a record of the score chart result in the child's notes so that it can be checked later.				

TREATMENT OF TUBERCULOSIS BY SHORT COURSE CHEMOTHERAPY - RATIONALE

At the start of chemotherapy, there is a large number of actively dividing tuberculosis bacilli in the body. These bacteria are killed by the bactericidal action of rifampicin and INAH. At the end of 2 months, all these organisms should have been killed. There is also, however, another population of bacteria which multiplies slowly either inside macrophages or inside solid caseous lesions - the so-called "Persisters".

PZA during the intensive phase deals with the bacilli in the macrophages, whilst rifampicin penetrates caseous lesions. Not all of the persisters will have been destroyed by the end of 8 weeks - hence the need for continuation treatment to kill the organisms. The longer the continuation phase, the lower the relapse rate after cessation of treatment. Six months is the shortest duration which gives acceptable relapse rates.

TREATMENT OF TUBERCULOSIS IN PAPUA NEW GUINEA

There are basically two regimens in Papua New Guinea.

1. "Standard" treatment for pulmonary TB, glandular TB, and TB pleural effusion, consisting of:
Intensive phase 2 months daily (rifampicin, INAH, PZA). "A" Treatment
Continuation phase 4 months twice weekly (rifampicin, INAH). "B" Treatment*
ie total of 6 months: 2HRZ + 4H2R2
2. Treatment for "severe" extrapulmonary TB ie TB of CNS, bones, joints, pericardium, abdomen, kidneys:
Intensive phase 2 months daily (rifampicin, INAH, PZA). "A" Treatment
Continuation phase 7 months daily (rifampicin, INAH). "CDT" (Continuous Daily Treatment)
ie total of 9 months: 2HRZ + 7HR.

IT IS VERY IMPORTANT TO NOTE THAT THE DRUG DOSES OF INAH USED IN "B" (twice weekly) and "CDT" (continuous daily treatment) ARE DIFFERENT. BE ABSOLUTELY SURE THAT

YOU AND YOUR STAFF KNOW EXACTLY WHAT REGIMEN THE PATIENT IS FOLLOWING AND ALWAYS CHECK THEY ARE TAKING THE CORRECT DOSES OF DRUGS.

*It is possible that during the life of this book, “B” Continuation Treatment will consist of drugs given three times per week instead of twice.

The use of a fourth drug in the intensive phase of treatment of children with TB

The risk of the spontaneous development of resistance to the standard antituberculous drugs is proportional to the number of organisms present. Most children with primary and progressive primary tuberculosis have relatively few organisms - “paucibacillary”. Treatment with three drugs during the intensive phase is adequate. A few have large numbers of organisms - “multibacillary”. These are children who are sputum or gastric aspirate positive, or who have CXR changes of very severe tuberculous bronchopneumonia. These children are treated with a fourth drug. Those below the age of 7 years are treated with streptomycin, and those 7 years or older are treated with ethambutol for the duration of the intensive phase of treatment (ethambutol can cause a retrobulbar neuritis and optic atrophy. Children less than 7 years will probably not report early changes in vision - so it is not used. Older children taking ethambutol should be checked regularly for visual disturbance).

ANTITUBERCULOUS DRUG DOSES

Rifampicin

10 (8-12) mg/kg daily in “A” and “CDT” regimens, twice weekly in “B” regimen

INAH

5 (4-6) mg/kg daily in “A” and “CDT” regimens (maximum of 300 mg)

15 mg/kg twice weekly in “B” regimen (pyridoxine added if dose >300 mg)

PZA (Pyrazinamide)

25 (20-30) mg/kg daily in “A” regimen

Streptomycin, the fourth drug for children less than 7 years of age with multibacillary disease

15 (12-18) mg/kg daily in “A” regimen

Ethambutol, the fourth drug for children 7 years or older with multibacillary disease

15 mg/kg (maximum) daily in “A” regimen.

INAH PROPHYLAXIS

Untreated, 20% of children under the age of 1 year and 4% of those under 5 years who have a primary infection will develop miliary TB or TB meningitis. Ninety percent of those children who develop miliary TB or TB meningitis do so within 1 year of their initial infection. It is therefore very important to protect young children with a primary infection from these severe forms of tuberculosis. INAH is given in a dose of 5 mg/kg daily for 6 months to children under the age of five years who are household contacts of known sputum positive patients.

Anyone who is asymptomatic but has recently converted from Mantoux negative to Mantoux positive (without the conversion being the result of a recent BCG vaccination) should be given INAH prophylaxis for 6 months (in practice, this situation does not commonly present).

MANAGEMENT OF A NEWBORN BABY WHOSE MOTHER HAS TUBERCULOSIS

This depends on the likely infectivity of the mother.

1. If the mother
 - a. is newly diagnosed
 - b. has been on treatment for less than 2 months
 - c. has been on treatment for more than 2 months but is still sputum positive, or

- d. if there is another sputum positive household contact
 - i. DO NOT give the baby BCG in the newborn period
 - ii. DO give the baby prophylactic INAH for 6 months
 - iii. DO give BCG after prophylaxis is complete
 - iv. DO encourage the mother to look after her child
 - v. DO encourage the mother to breastfeed
2. If the mother
 - a. has been on treatment for more than 2 months
 - b. and is sputum negative
 - i. GIVE BCG.
 - ii. Encourage the mother to breastfeed.

PREVENTION

1. BCG to all newborn. This has been a controversial subject but the combined evidence from around the world and from PNG indicates some protective effect even though this is far from complete.
2. FIND AND TREAT INFECTIOUS CASES. Do sputum smears for AFB on all patients with cough of more than one month's duration.

INDICATIONS FOR STEROIDS IN PAEDIATRIC TB

There are 3 situations in which steroids are probably of benefit:

1. CNS TB (tuberulous meningitis or tuberculoma).
2. Mediastinal compression from tuberculous lymphadenopathy.
3. Pericardial effusion.

In these situations give prednisolone 1-2 mg/kg daily for 4 weeks and then taper the dose over the next 2 weeks.

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TYPHOID

INTRODUCTION

Typhoid has been endemic in Papua New Guinea for many years, but it is only during the 1980s and 1990s that it has become a major health problem. There have been a couple of major water borne epidemics in educational institutions - but by far the most common means of spread is by the faecal-oral route, the result of poor personal and food hygiene. A typhoid control programme has not been particularly effective, and there are about 7,000 new cases reported each year with a case fatality of about 3%. Typhoid ranks in the top 6 causes of hospital admission in most parts of the country.

CLINICAL PRESENTATIONS

Typhoid may present in a very similar fashion to malaria. Certainly, it should be considered in any febrile child not responding to antimalarial therapy. Common features are:

- headache
- abdominal pain
- abdominal tenderness
- abdominal distension
- constipation
- diarrhoea, with or without blood
- confusion
- talking nonsense
- dehydration
- looking/feeling very sick.

Experienced practitioners are often able to make an accurate diagnosis based on the "typhoid facies" but children with prolonged malaria and with TB also sometimes have a similar appearance. Diarrhoea is as common as constipation in children with typhoid, relative bradycardia is not so prominent a feature as it is in adults and the classic leucopaenia may be absent in children.

Indications of severity include:

1. distended tender abdomen
2. rectal bleeding
3. severe abdominal pain
4. semi/unconsciousness or confusion.

DIAGNOSIS

Do blood, stool and urine cultures and a Widal test, if possible. Positive H and O titres of $>1/160$ or rising titres are virtually diagnostic. Leucopenia is supportive evidence - but is by no means invariable in children - who may have leucocytosis.

TREATMENT

Antibiotic - chloramphenicol

Treatment with chloramphenicol should be continued for three weeks to ensure a low relapse rate. It is usually given parenterally initially and then changed to orally as soon as the child will tolerate it. The quinolone antibiotics such as ciprofloxacin are currently used in many parts of the world - but are very expensive - and no more efficient in their cure rates than chloramphenicol (though the temperature may come down more quickly).

It is important to understand that the patient may remain febrile for up to a week and sometimes longer in spite of antibiotics. Patients with typhoid only rarely make a rapid recovery.

Antimalarials

Patients should be treated as for severe malaria even if the blood slide is negative unless the evidence for typhoid is unequivocal.

Fluids

Attention to fluid balance is important.

If the child is dehydrated:

- rehydrate with ORS or with IV half strength Darrow's solution

If the child is not dehydrated but is vomiting a lot, and the abdomen is distended or tender:

- give intravenous maintenance fluids

If the child is not dehydrated, not vomiting and has a soft abdomen:

- give milk and other fluid orally.

Nutrition

Ensure that the children receive plenty of food and vitamin supplements.

Education

It is important that the parents gain understanding of the fact that typhoid is spread from faeces onto hands and food, and that they appreciate the need for hand washing and food hygiene. Studies from Goroka have indicated that in PNG, it is common for patients having completed treatment for typhoid to continue to excrete the organism for 7 months or longer.

TYPHOID VACCINE

A number of typhoid vaccines are available - but none has been shown to be more than moderately effective. The main educational message and the main preventative strategy must be hygiene.