THE CLINICAL PRESENTATION AND OUTCOME OF TUBERCULOSIS IN CHILDREN ADMITTED TO A PAEDIATRIC INTENSIVE CARE UNIT IN AN AREA WITH A HIGH INCIDENCE OF PULMONARY TUBERCULOSIS

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DECLARATION

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ABSTRACT

The purpose of this study was to measure and evaluate the clinical presentation, outcome and longterm effects of tuberculosis in children admitted to the paediatric intensive care unit at Tygerberg Hospital. A retrospective, descriptive study was conducted among 57 children admitted to the paediatric intensive care unit between January 1991 to December 1994.

The sample comprised all the children with tuberculosis aged one month to twelve years who were admitted to the paediatric intensive care unit. Audit measures were taken to ensure that all the children with tuberculosis were identified. Data was collected by means of a structured working sheet and questionnaire that was sent to the clinics. Respondents completed the questionnaire in the clinics.

There was an increase in the incidence of children suffering from pulmonary or disseminated tuberculosis who required admission to the PICU, although the incidence of HIV was low. None of the index cases had MDR-TB. Fifty-one percent of children were admitted to the PICU because of primary tuberculosis or complications of the disease. Of these children 69% had respiratory failure who required ventilation. Thirty percent were admitted to the PICU for respiratory failure and were subsequently diagnosed as having tuberculosis. Tuberculosis was incidently found amongst 4 children when they were routinely examined in the PICU. Due to the difficulty in confirming the diagnosis of tuberculosis in children, a large proportion of cases go unrecognised. The chest radiographs demonstrated that hilar (40%) and paratracheal (32%) adenopathy was the most common findings. Bronchial compressions was present in 12% of cases. A significantly positive Mantoux skin test was reported in 35% of cases and 53% had a positive Tine skin test. Gastric aspirates positive for M.tuberculosis were obtained in 42% of cases and of cultures other than gastric aspirates, 44% were positive. Other special investigations to confirm the diagnosis of tuberculosis included CT scan and bronchoscopies. Bronchoscopies were performed on 13 children and found to be abnormal in 12 cases. The most common finding was nodal compression of the airways. Overall the diagnosis of confirmed tuberculosis was made in 47% and of probable tuberculosis in 53% of cases. The length of stay in the PICU was 10.2 $\pm$ 22.4 days. The PICU mortality was 23%, with a total hospital mortality of 26%. The mortality for the TBM subgroup was 75%. Although a good compliance (82%) was recorded by the clinics in the follow-up study, they experienced problems with the notifications. The follow-up study pointed out that communication was a problem between the referring hospital and the clinics. Thirty-one percent of the clinics made suggestions for improving the communication.

The findings demonstrates that in an area with a high incidence of TB, children do develop severe disease requiring admission to the PICU. This places a considerable clinical and financial burden on the already limited health system. Early diagnosis of TB should prevent severe disease and subsequent admission to the PICU. The increasing incidence of HIV and MDR-TB will undoubtedly pose a major risk to ICU staff and the prevention of infection is of primary concern for those who may be exposed in this area. Due to this, certain recommendations regarding guidelines for admission to the PICU, investigations of patients exposed of having TB in the PICU, prevention of infection and detection of disease in staff in the PICU, the need for increase beds in the PICU and recommendations post discharge from the PICU were made.

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ABBREVIATIONS

ICU:	Intensive care unit
PICU:	Paediatric Intensive care unit
HIV:	Human Immunodeficiency virus
TB:	Tuberculosis
TBM:	Tuberculous meningitis
WHO:	World Health Organisation
MDR-TB:	Multiple drug resistance tuberculosis
PTB:	Pulmonary tuberculosis
VSD:	Ventricular septal defect
CDC:	Centre for Disease Control
BCG:	Bacillus Calmette-Guerin

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CHAPTER ONE

INTRODUCTION AND LITERATURE REVIEW

Tuberculosis is a significant cause of both morbidity and mortality in children throughout the world. Although tuberculosis can have profound health consequences for the affected child and his or her family, childhood tuberculosis has a limited influence on the immediate epidemiology of the disease within the community, because children are rarely a source of infection to contacts. However, the occurrence of tuberculosis in children is a marker for ongoing transmission of infection among all age groups in a society.

Today, 40 years after the introduction of effective chemotherapy for the treatment of tuberculosis, there are more new cases in the world than ever before (8 million per year).(1) In South Africa it is expected that there will be over 90 000 new cases and about 4000 deaths in 1994. The current cure rate estimated to be 70% is too low to ensure adequate control of the increasing numbers of infectious cases. In the Western Cape the incidence of tuberculosis is rising astronomically, being nearly 100 times greater than in developing countries.

1.1 INCIDENCE OF TUBERCULOSIS

1.1.1 Global and sub-Saharan Africa

The magnitude of the global tuberculosis problem is enormous. Almost 3.8 million new cases of tuberculosis were reported in the world in 1990. There were an estimated 7.5 million cases of tuberculosis in 1990, with 2.5 million deaths worldwide.(2)

The highest prevalence of tuberculosis infection and estimated annual risk of tuberculosis infection are in sub-Saharan Africa and Southern Asia. The tuberculosis incidence in Africa is the highest in the world - 272 new cases /100 000 population per annum. There are approximately 1.4 million new cases of tuberculosis and 656 000 deaths in Africa annually. The annual risk of infection varies from 1 - 2.5% with very little decline in the risk being reported.(3)

1.1.2 South Africa

The overall tuberculosis incidence for the whole of South Africa is 366 new cases per annum/100 000 (1992).(4) The incidence rate ranges from a low of 59/100 000 in the Northern Transvaal to a high of 718/100 000 per annum in the Western Cape.(4) The peak annual tuberculosis incidence rate for South Africa was reported in 1963 (372/100 000 population). The rate decreased until 1987, with a subsequent rising trend.(4)

1.1.3 Western Cape / Cape Metropole

As indicated, the reported tuberculosis incidence rate is 718 new cases/100 000 per annum. Of the national notifications, 31% are accounted for in the Western Cape and 19% in the Cape Metropole, indicating that the Western Cape carries the greatest disease burden.(5)

1.1.4 Childhood tuberculosis in South Africa and the Western Cape

Children are infected mainly by being in contact with an adult with smear positive pulmonary tuberculosis. About 60% of children coming into contact with adults who are smear positive, will become infected. It is estimated that primary infection, if not treated in children under the age of 5 years, will progress to disease in about 10% of cases. Children under one year of age are at particular risk for disseminated forms of the disease such as tuberculous meningitis (TBM) and miliary tuberculosis.

The tuberculosis incidence rates in children under 4 years of age fell from 317/100 000 in 1971 to 133/100 000 in 1986, but, as with adult tuberculosis, it has once more been increasing since 1989.(5)

As is the case for tuberculosis in adults, the incidence of tuberculosis in children in the Western Cape is much higher than in the rest of South Africa, with a 6 times higher incidence. It is especially the under four year old children that have the highest incidence (901/100 000 in 1989), compared to the incidence in the same age group for the rest of the country (158/100 000).(6)

1.1.5 Childhood serious disease: Miliary TB and TBM

As mentioned, children less than one year of age are at particular risk for developing disseminated forms of disease such as miliary tuberculosis and tuberculous meningitis.

The incidence of miliary TB and tuberculous meningitis is considerably higher in the Western Cape, than in the rest of the country. TBM is of particular importance as it leads to severe morbidity and has a high mortality.

Miliary tuberculosis occurs significantly more frequently in children than in adults, accounting for 0.7 and 8% of all paediatric notifications and hospitalizations, respectively, whereas in adults the respective figures are 0.3 and 1.3%.(7)

In a study by Hussey et al, 52% cases of childhood miliary tuberculosis were younger than 1 year. The case fatality rate has been reported as 13.8%, with TB meningitis as the only significant risk factor for mortality.(7)

Kibel et al reported that tuberculous meningitis can occur in any age, but 80% were seen in children younger than 5 years of age. This fact is important, as it is well recognized that the outcome of TBM is less favourable in very young children.(8) In active surveillance studies in the Western Cape, the overall mortality for TBM for the period 1979 - 1981 was 24%. A study of 130 child survivors of TBM revealed that 53% had cerebral palsy: many were severely or profoundly retarded or had other neurological sequelae.(9)

1.2 FUTURE PROJECTIONS OF TUBERCULOSIS EPIDEMIC IN THE WESTERN CAPE

1.2.1 Cohort studies

It has been projected by analysis of cohort studies that the incidence of tuberculosis in the coloured population in the Western Cape is on the upward limb of an epidemic, and that the incidence will continue to rise if the present policy is followed. For example, in the age group 30 - 34 years the incidence will rise from 690/100 000 in 1991 to 1080/100 000 by the year 2001.(6)

1.2.2 Effect of HIV on tuberculosis

The pandemic of human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS) has caused marked increases in tuberculosis notifications in some countries, particularly in sub-Saharan Africa. The impact of HIV infection on tuberculosis is greatest in populations in which the prevalence of tuberculosis in young adults (who are at greatest risk of HIV infection) is relatively high.

It has been estimated that, if the annual risk of infection is 2%, the TB infection prevalence 60% and HIV prevalence 2%, the percentage increase in the smear positive TB cases will be 52%. If the same conditions hold, but the HIV infection prevalence increases to 10%, the increase will be 280% by the year 2001.(10)

In 1993 in the old Cape Province it was estimated that the HIV incidence of infection was 2.48%.(11) The incidence in the Western Cape is evidently lower and the doubling time is slower than the national mean. It can therefore be conservatively estimated that there will be an increase of up to 52% in smear positive cases in the Western Cape as a result of HIV infection by the year 2001.

1.3 HIV AND TUBERCULOSIS

1.3.1 In adults

Until recently it was believed that HIV gave rise to tuberculosis by reactivation of previously acquired infection. It is now clear from investigations that HIV infected individuals can also develop disease from recently acquired infection.(12)

Throughout the world young adults have the highest prevalence of HIV infection. The lifetime risk for developing TB in an HIV positive patient is 50%, with an annual risk of 5 - 8%.

Most cases of HIV-associated tuberculosis presenting in sub-Saharan Africa are pulmonary and a high proportion have a smear positive sputum.(12)

In a study conducted at a rural hospital in Zululand to describe the clinical features of patients who are HIV seropositive, it was shown that 45% of the adult HIV positive patients had a diagnosis of tuberculosis on presentation to the health services. Pulmonary tuberculosis was eventually diagnosed in 57% of all the cases.(13)

The mortality of tuberculosis in HIV is greater than 50%. In spite of a generally good response to anti-tuberculosis drugs, patients with HIV-associated tuberculosis still have a 5 - 14 fold greater chance of dying during treatment than HIV negative patients.(12)

1.3.2 In children

The HIV epidemic increases the risk in children of developing tuberculosis by two mechanisms:

(I) HIV infected adults with tuberculosis may transmit M.tuberculosis to children, a portion of whom will develop tuberculous disease.
(II) Children with HIV infection and immune depression are at increased risk of progressing from tuberculosis infection to disease.

A retrospective study in Florida implied that an observed increase in paediatric tuberculosis cases was linked to an increase in cases in HIV infected adults.(14)

In the study previously mentioned which was done at a rural hospital in Zululand, 38% of the children diagnosed with AIDS had TB. The diagnosis was usually made on chest x-ray or by positive histology.(13) The diagnosis of TB on chest radiograph is fraught with imprecision. Other opportunistic infections, lymphocytic interstitial pneumonitis and immune mediated lung disease are often confused with thoracic tuberculosis.

1.4 MULTIPLE DRUG RESISTANT TUBERCULOSIS

Primary resistance is defined as the presence of drug resistance to one or more anti-tuberculosis drugs in a tuberculosis patient who had not received prior treatment. Acquired resistance is defined as resistance to one or more anti-tuberculosis drugs, which occurs during the course of treatment, usually as a result of non-compliance with the recommended regimen or incorrect prescribing. Multiple drug resistance is when the patient is resistant to both INH and Rifampicin.

Both primary and acquired drug resistant tuberculosis are becoming increasingly important in industrialized countries. During 1990 - 1992 the CDC investigated outbreaks of MDR-TB in eight hospitals. Most, but not all of the cases occurred in persons with HIV infection. Among patients with MDR-TB, the mortality was approximately 70%, and the median interval from tuberculosis diagnosis to death was 4 to 16 weeks.(2)

Drug resistance is a serious problem encountered in the treatment of tuberculosis. Concern that the increasing TB epidemic in the Western Cape is partially attributable to drug resistance has been expressed by health workers. In 1992 - 1993 the incidence of primary drug resistance rates were as follows: INH 3.9%, Rifampicin 1.1%, Ethambutol 0.2% and multiple drug resistance 1.1%.(15) For patients who had been previously treated for TB the incidence was higher, namely: INH 10.8%, Rifampicin 4.2%, Ethambutol 0.35% and multiple drug resistance 4.0%.(15) The reported mortality of patients with MDR-TB is 56% and the treatment costs of MDR-TB can be as high as 30 times that of drug sensitive TB. In 1993, 347 patients were identified in the Western Cape region with MDR tuberculosis.(16) This amounts to 1,3% of the total tuberculosis case load, but does not include children under the age of 15 years.

1.5 TUBERCULOSIS DIAGNOSIS AND THE CHILD

1.5.1 Difficulties in diagnosis

A large proportion of cases in children goes unrecognized because of the poor sensitivity of currently available diagnostic methods. While an acid-fast stain of sputum will identify up to 75% of adults with pulmonary tuberculosis, fewer than 20% of children with tuberculosis have positive cultures of sputum or gastric contents.(17)

Due to the difficulty in confirming the diagnosis, reliance is usually placed on a constellation of symptoms, clinical signs, tuberculin testing, chest radiography and a history of close contact with an adult case of active pulmonary tuberculosis. This information is often all that is available in areas where TB has its highest incidence, and the World Health Organization has suggested provisional guidelines making use of these and other clinical features to classify children as having suspected, probable or confirmed pulmonary tuberculosis.

A summary of the WHO guidelines is as follows:(18,20)

Suspected Tuberculosis:

(I) An ill child with a history of contact with a confirmed case of pulmonary tuberculosis.
(II) Any child:
Not regaining health after measles or whooping cough.
With loss of weight, cough and wheeze not responding to antibiotic therapy for respiratory disease.
With painless swelling in a group of superficial nodes.

Probable Tuberculosis:

(I) Positive ($\geq$ 10mm) induration on tuberculin testing.
(II) Suggestive appearance on chest radiograph.
(III) Suggestive histologic appearance of biopsy material.
(IV) Favourable response to specific anti-tuberculosis therapy.

Confirmed Tuberculosis:

(I) Detection by microscopy or culture of tubercle bacilli from secretions or tissues or
(II) The identification of the tubercle bacilli as Mycobacterium tuberculosis by culture characteristics.
Modifications of the above criteria have been described by several groups.(19,20) The modified form of categorisation is used with success in the Western Cape and plays an important role in limiting over-notification of childhood tuberculosis.(19)

1.5.1.1 Clinical criteria

Internationally clinical criteria for the diagnosis of tuberculosis in children have lacked uniformity and are not generally accepted. In spite of the proposed WHO criteria for the diagnosis of pulmonary tuberculosis in children, studies have shown that one must be careful when interpreting the score result, particularly in a child with tuberculosis and bacterial superinfection.(21)

At Lusaka's University Teaching Hospital (UTH) criteria were accepted for the diagnosis of probable tuberculosis. Like other scoring criteria it missed a significant number of diseased children.(21) In Papua New Guinea, the scoring scheme had the same disadvantages as the other systems, but had the advantage of not needing any radiological and/or bacteriological backup services.(21)

Although scoring systems are useful to use at clinics in the diagnosis of tuberculosis, they are not specific enough to be sure that the diagnosis is accurate.

1.5.1.2 Tuberculin skin test

Malnutrition or overwhelming disease, including HIV infection, limit the use of tuberculin testing as a useful diagnostic tool in determining both tuberculosis infection and disease. On the other hand, a positive tuberculin test, particularly in a malnourished or immunosuppressed, unvaccinated child, becomes highly suggestive of probable tuberculosis. In a study done by Schaaf et al, only 41% of the children with probable and proven tuberculosis had a significantly positive tuberculin test recorded, demonstrating the limitation of this test.(18)

1.5.1.3 Chest radiograph

Radiological findings are not always helpful, particularly in small children and can at times be confusing. The picture becomes even more uncertain when there is superadded bacterial pneumonia. In HIV infected children some of the other opportunistic infections have similar radiological findings as in tuberculosis, increasing the difficulties.

Schaaf et al demonstrated that 10% of the children with tuberculosis confirmed by culture of M.tuberculosis from gastric aspirate had a normal chest radiograph.(18) Culture of M.tuberculosis from the gastric aspirate of children with a normal chest radiograph is not necessarily unexpected, as the Ghon focus is not always visible on the chest radiograph.(22,23)

Chest radiography plays a major role in the diagnosis of childhood tuberculosis, but even this process is marked by inconsistencies among different readers and between the opinions of the same reader on different occasions.(24) In diagnosing primary tuberculosis in childhood, the presence or absence of enlarged hilar glands is of crucial importance. Although lateral chest radiography may be of help in this respect, the normal pulmonary vasculature may be a source of considerable confusion.(25) Smuts et al showed that the lateral chest radiograph increases the yield by 11%.(26)

1.5.1.4 Mycobacterium tuberculosis - culture

In adults, culture of Mycobacterium tuberculosis is the gold standard for the diagnosis of tuberculosis. Many children with undoubted probable tuberculosis on radiologic and clinical grounds, will have persistently negative cultures, whereas other children with apparently normal chest radiographs may have positive cultures for Mycobacterium tuberculosis.

Culture positive paediatric specimens at Lusaka UTH have ranged from 0.9% to 57%, depending on age, number of obtained specimens, disease severity and, to a lesser extent, prevalence of tuberculosis.(21)

Furthermore, peripheral clinics lack the facilities for gastric aspirates or other cultures, making culture positive TB difficult to diagnose.

1.5.1.5 Complicated by HIV

The challenge of diagnosing paediatric tuberculosis has now been complicated by the HIV epidemic. The WHO's clinical case definition of AIDS among adults with tuberculosis was not specific enough to predict which tuberculosis cases were HIV positive.(21) The same may be true for children with dual disease.

In developing countries the diagnosis of HIV infection in children under 15 months is in itself difficult, because of lack of access to viral culture facilities and newer diagnostic techniques. This is important considering the high number of suspected tuberculosis cases in this age group.

1.6 TUBERCULOSIS AND THE ICU

1.6.1 ICU and the adult

It is estimated that approximately 1.5% of the adults being treated for tuberculosis in a tertiary care hospital require ICU admission for respiratory failure.(27)

Tuberculosis causing acute respiratory failure may become an increasing intensive care problem in areas of high prevalence. It is also estimated that the increasing incidence of MDR-TB and HIV infection will have a major influence on the admissions to the ICU, as well as running costs of the ICU.

A study done by Hayhurst et al in Cape Town showed an increase in the admissions of patients with tuberculosis to the ICU during 1988 - 1991. The reported mortality in this study was 39%, with hyponatraemia, secondary bacterial infection and barotrauma being poor prognostic signs.(28) In similar studies done in America the

reported mortality was 67% (29) and 69% (30). The study done by Levy et al in the ICU in a Hillbrow hospital reported an early mortality of 33% and a total mortality of 47%.(27)

Potgieter showed an increase in the number of patients with pulmonary or disseminated tuberculosis admitted to the ICU at Groote Schuur Hospital over the past ten years. The increase was not as a result of HIV infection or multi-drug resistant tuberculosis. The mortality in this study was 29%.(31)

1.6.2 ICU and the child

An extensive search of the literature failed to reveal a single article regarding the aspect of tuberculosis and children in the intensive care unit. Although many articles address the management of miliary and especially TB meningitis, none of these articles mention the PICU care of these patients.

CHAPTER TWO

AIM OF THE STUDY

2.1 THE AIM OF THE STUDY WAS TO DESCRIBE:

2.1.1 The clinical profile and outcome of children admitted with tuberculosis to the Paediatric Intensive Care Unit (PICU).

2.1.2 The treatment, follow-up and impact on hospital service and TB clinics of children treated for tuberculosis in the PICU.

2.2 THE MORE SPECIFIC OBJECTIVES OF THE STUDY WERE TO DETERMINE:

2.2.1 The clinical picture and reasons for admission to the PICU of children with tuberculosis.

2.2.2 The clinical course, duration of stay and interventions required for children with tuberculosis in the PICU.

2.2.3 The number of children in whom tuberculosis was the primary cause for admission to the PICU and the number of children in whom tuberculosis either co-existed or complicated the ICU course.

2.2.4 The number of children co-infected with tuberculosis and HIV who were admitted to the PICU.

2.2.5 The duration of hospitalization of the children after PICU discharge.

2.2.6 The drug compliance of the children at the community TB clinics after discharge from hospital and the duration of therapy they received.

2.2.7 The long-term outcome of the children with tuberculosis and the long-term treatment requirements.

CHAPTER THREE

METHODS AND PATIENTS

3.1 STUDY DESIGN:

A retrospective, descriptive study, conducted in the Paediatric ICU, Tygerberg Hospital, attached to the University of Stellenbosch. To determine the impact on the community, the tuberculosis clinics closest to the child's home were contacted.

3.2 SETTING:

3.2.1 Tygerberg Hospital and Paediatric ICU: The Paediatric ICU at Tygerberg Hospital is a seven bed intensive care unit, which admits both medical and surgical patients from the neonatal period up to 13 years of age. It is a referral unit for the paediatricians, general practitioners, hospitals and clinics in the Cape Town metropole, as well as for the rural districts of the Western Cape, Northern Cape, South East and Eastern Cape. Tygerberg Hospital is one of the referral centres in the Western Cape Region for complicated tuberculosis.

3.2.2 Western Cape Clinics: The patients after discharge were referred to the tuberculosis clinics closest to their home address. The method of referral was by the standard tuberculosis notification form (see Appendix C)

It serves a population base of approximately 4 million people. The annual admissions number approximately 406 patients (range 345-482).

3.3 STUDY POPULATION:

The records of all children aged one month to 12 years, who required admission to the Paediatric ICU from January 1991 to December 1994 , were scrutinized to determine if they had tuberculosis.

To ensure that all children with tuberculosis who were discharged from the ICU were identified, the following audit measures were taken:

(I) The ward records of the children's wards were examined to identify those children diagnosed as having tuberculosis after discharge from the ICU.

(II) The post mortem results were examined.
(III) The hospital register of Mycobacterium tuberculosis positive cultures was examined.
(IV) The notifications of tuberculosis from the Department of Paediatrics at Tygerberg Hospital were checked.

3.4 INCLUSION CRITERIA:

The following children were included in the study:

3.4.1 Children admitted to the PICU as a result of tuberculosis or complications of the disease.

3.4.2 Children admitted to the PICU with respiratory illness and subsequently diagnosed as having tuberculosis.

3.4.3 Children admitted to the PICU for any other clinical reason and in whom tuberculosis was diagnosed after admission.

The diagnosis of tuberculosis was made on the basis of the WHO criteria and included possible, probable and confirmed tuberculosis. (Discussed in the literature review). For the purpose of this study, a positive Mantoux skin test that was equal or larger than 15 millimetres and a Tine skin test that was a grade 3 and a grade 4 was accepted as being indicative of disease. The reason is that BCG immunization cover in the area is greater than 90%.

3.5 EXCLUSION CRITERIA:

Children with possible tuberculosis (WHO criteria), or where the diagnosis was uncertain, were excluded from the study.

Children with incomplete results regarding ICU stay, hospitalization or treatment in the community were analysed separately.

3.6 DATA COLLECTED:

3.6.1 Data collected in Tygerberg Hospital:(Appendix A)

Summary of data collected:

* General patient information
* Previous tuberculosis history and treatment.
* Reason for PICU admission.
* Special investigations.
* Clinical course.
* Classification.(Probable or confirmed tuberculosis).
* Tuberculosis responsible for PICU admission?.
* Did tuberculosis prolong the PICU stay?.

3.6.2 Data collected from clinics and other hospitals: (Appendix B)

Summary of data collected:

* General patient information.
* Tuberculosis treatment.
* Information concerning health.
* Data concerning ongoing treatment.
* Data concerning completion of the notification.
* General information.
* Suggestions for improving communication between Tygerberg Hospital and clinics or other hospitals.

3.7 DATA HANDLING:

The data were gleaned from the patients' PICU records, post mortem results and tuberculosis clinic records. The data were recorded on a previously compiled data capturing form. (Appendix A)

The hospital records of the patients were examined to see to which tuberculosis clinics or hospitals the children were referred. These institutions were contacted to inquire if the notification was received and if they were familiar with the patient. A questionnaire (Appendix B) was sent to the clinics for completion. Compliance with therapy was accepted if the child received more than 80% of the prescribed doses within 6 months after the initiation of treatment.

3.8 DATA ANALYSIS:

The data were transferred from the data capturing form onto a database programme (DBase IV). The data were analysed using the database programme. The data are reported as the mean $\pm$ the range.

3.9 ETHICAL CONSIDERATIONS:

3.9.1 Ethical permission was obtained from the University of Stellenbosch and permission to do a folder search from the medical superintendent, Tygerberg Hospital.

3.9.2 Permission to use the tuberculosis clinic file data was obtained from the Western Cape Metropolitan Council, as well as the Western Cape TB Co-ordinating Committee.

CHAPTER FOUR

LIMITATIONS OF THE STUDY

4.1 STUDY POPULATION:

The study was centred in a teaching hospital and for this reason biased in the selection of the study population. Data from the PICU's of the other tertiary hospitals in the vicinity are needed to get a complete picture of the problem in the Western Cape.

4.2 AVAILABILITY OF DATA:

Another limitation in the study was the availability of the chest radiographs, as the radiographs are destroyed after 3 to 4 years by the hospital archives. The results of the chest radiographs that have been destroyed can be obtained from the reports on the microfilm of the records. In 16% of cases where the chest radiograph was not available the reports were obtained from the records.

In some cases the results of the Mantoux and Tine skin tests were not available, because the results were recorded on the cover of the folder which was not microfilmed. In eighteen percent of cases the Mantoux skin tests and in 12% the Tine skin tests were not available.

4.3 HIV TESTING:

HIV testing was done in the patients where informed consent was obtained from the parents. HIV testing was done in 37% of the patients.

4.4 CULTURE SENSITIVITY:

Positive tuberculosis cultures are not routinely tested for sensitivity and for this reason it is not possible to comment on the prevalence of MDR-TB or what the role of MDR-TB had on the admissions to the PICU.

4.5 QUESTIONNAIRE:

The questionnaire that was sent to the clinics and hospitals has as a limitation that there is no control over the sequence in which questions are answered and that the respondents fail to read and answer some questions. A further limitation was that no control group of patients was studied. This limits the deductions that can be made.

4.6 NON-RESPONDENTS:

Before the questionnaires were sent to the clinics, they were contacted to inquire if they were familiar with the patient. Of the forty-two questionnaires, only twenty-two responded initially.

The non-respondents were contacted for a second time and five more questionnaires were returned. A response rate of 64% was finally achieved.

CHAPTER FIVE

RESULTS

A. RESULTS OF DATA COLLECTED IN TYGERBERG HOSPITAL:

Fifty-seven children (36 boys and 21 girls) who complied with the inclusion criteria were identified over a four year period: 5 patients in 1991 (1% of the total admissions to the PICU in 1991), 15 in 1992 (3.6% of the total admissions), 23 in 1993 (6% of the total admissions) and 14 in 1994 (4% of the total admissions) (Figure 1). This is 3.1% of the total TB admission (n=1 862) to the hospital for the same time period that the trial was conducted.

The mean age of the patients was 38.3 $\pm$ 39.6 months (range one month to 144 months). The patients were referred from various areas (Table 1), 77% being from the Boland, Kraaifontein, Kuilsriver, Bellville, Ravensmead and Belhar areas. (Figure 2)

5.1 PAST TUBERCULOSIS HISTORY:

Twenty-six (46%) of the patients had a known TB contact. In 42% of the cases the contact was the mother or father. In 17 patients (30%) no record of the contact was available. None of the index cases had multi-drug resistant tuberculosis.

Fifteen of the cases (26%) in the study had previously been treated for tuberculosis, but were not on treatment at the time of admission to the PICU. In 16 patients no record could be found of any previous treatment. Two of the fifteen cases were known to be compliant, but the compliance of the others was unknown as either the records were no longer available or the patient was not known to the clinic.

5.2 REASON FOR ADMISSION TO PICU:

Twenty-nine patients (51%) were admitted to the PICU primarily because of tuberculosis or complications of the disease. The reason for admission to the PICU is summarized in Table 2. Nine of the admissions were post surgical for primary tuberculosis.(Table 2).

Seventeen patients (30%) were admitted to the PICU with respiratory illness and respiratory failure and were subsequently diagnosed as having tuberculosis. The initial diagnosis on admission to the PICU in this group were: bronchiolitis (n=3), aspiration pneumonia (n=1), paraffin aspiration pneumonia (n=1) and bronchopneumonia or pneumonia (n=12).

FIGURE 1: ADMISSION TO PICU 1991-1994

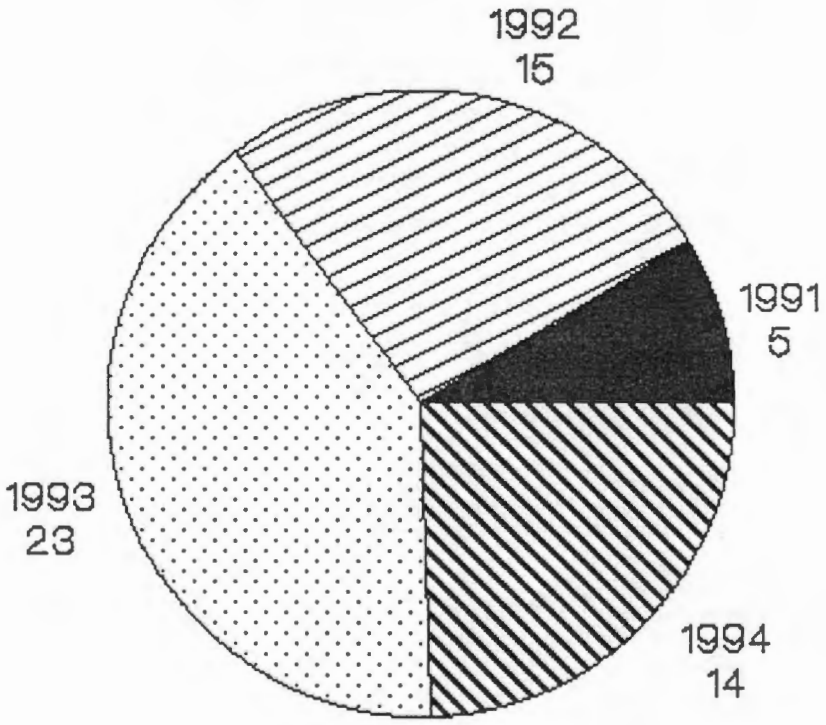
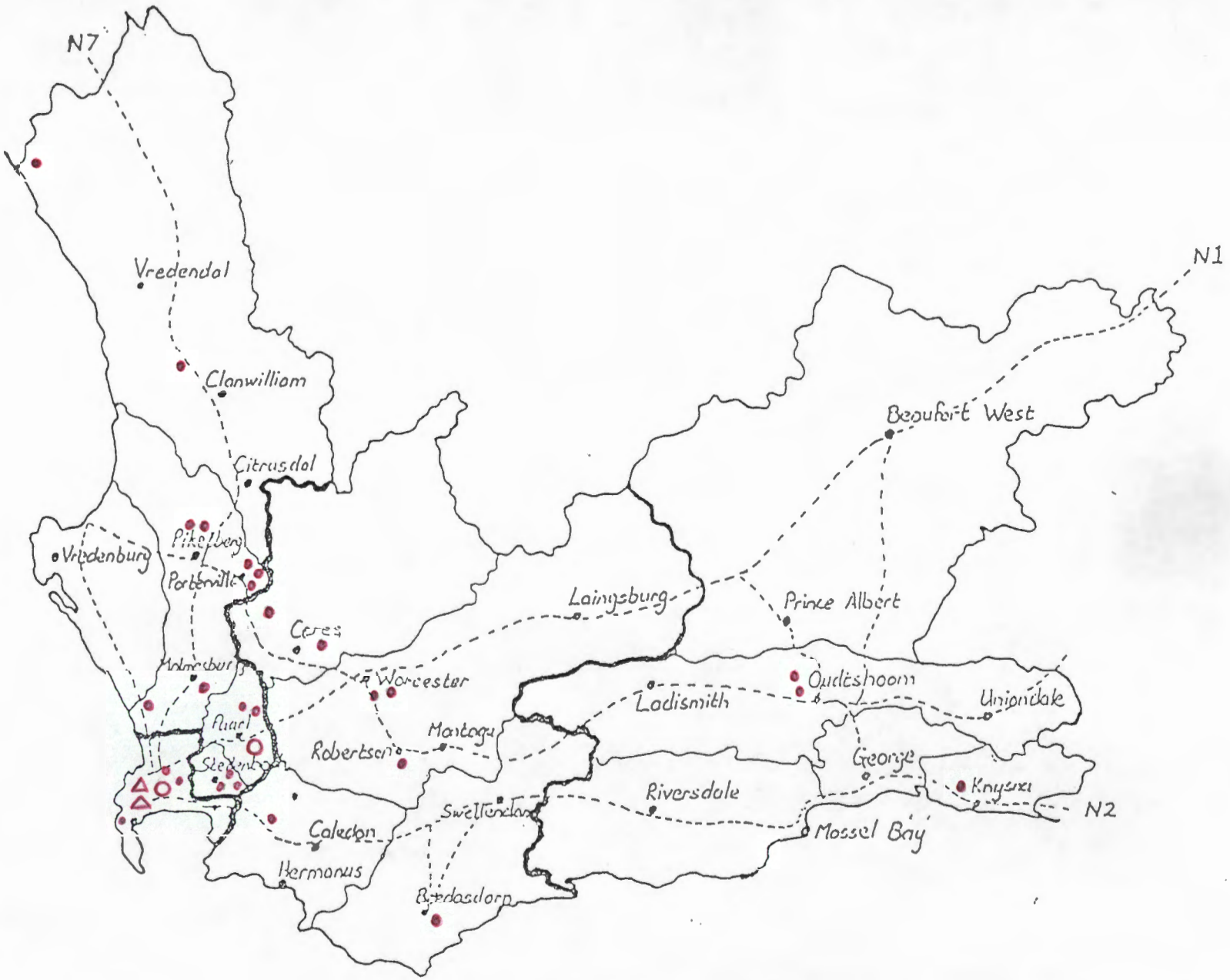


TABLE 1

DEMOGRAPHIC AREAS FROM WHERE PATIENTS RESIDED

AREA	NUMBER OF PATIENTS
Bellville/Ravensmead/Belhar	12(21%)
Elsiesriver	2(0.4%)
Kraaifontein	6(1.1%)
Kuilsriver	5(0.9%)
Langa	2(0.4%)
Stellenbosch/somerset West	3(0.5%)
Paarl/Franschhoek	5(0.9%)
Wellington/Klipheuwel	2(0.4%)
Porterville	3(0.5%)
Tulbagh	1(0.2%)
Worcester	2(0.4%)
Robertson	1(0.2%)
Oudtshoorn	2(0.4%)
Grabouw	1(0.2%)
Bredasdorp	1(0.2%)
Sedgefield	1(0.2%)
Simonstown	1(0.2%)
Riebeeck Kasteel	1(0.2%)
Port Nolloth	1(0.2%)
Piketberg	2(0.4%)
Atlantis	1(0.2%)
Prince Alfred Hamlet	1(0.2%)
Leipoldtville	1(0.2%)
Total	57



△ = 10 PATIENTS

0 = 5 PATIENTS

° = INDIVIDUAL PATIENTS

FIGURE 2 : GEOGRAPHICAL DISTRIBUTION OF PATIENTS

TABLE 2

TUBERCULOSIS OR ITS COMPLICATIONS AS INDICATION FOR PICU ADMISSION.

TB OR COMPLICATIONS		SURGERY FOR TB	
Miliary Tuberculosis	4(7%)	Thoracotomy (TB Glands)	2(3.5%)
Endobronchial TB	3(5%)	Lobectomy (Bronchiectasis)	1(2%)
Tuberculosis Lung	3(5%)	TB Granuloma (Brain)	2(3.5%)
TB Meningitis	8(14%)	Decortication (Pleura)	2(3.5%)
TB Gland Obstruction of		Volvulus (TB Glands)	1(2%)
Large Airways	2(4%)	Constrictive Pericarditis	1(2%)
Total	20(35%)	Total	9(16%)

Four children (7%) were admitted to the PICU for non respiratory disease and had tuberculosis diagnosed after admission. (Table 3).

Seven patients (12%) admitted to the PICU for other reasons were already receiving treatment for tuberculosis. (Table 4).

5.3 SPECIAL INVESTIGATIONS:

5.3.1 Chest Radiograph:

All of the fifty-seven patients had chest radiographs. Forty-three (75%) were available for assessment and the results of the remaining patients were obtained from the patient records. The interpretation of the chest radiographs are shown in Table 5.

The major findings were hilar adenopathy (40%) and paratracheal adenopathy (32%). Of note was the high proportion of tracheal and bronchial glandular compression (14% and 18%) respectively.

5.3.2 Tuberculin skin test:

5.3.2.1 Mantoux skin test:

Of the total of 57 patients, skin tests were done on 41. Skin tests were not done on patients who were already on treatment for tuberculosis (n=7) and in post-surgical cases (n=9).

Of the reported 38 patients who had Mantoux skin tests, the results of 31 could be obtained from the folders. Forty-eight percent (n=15) had a negative Mantoux skin test. The results of the Mantoux skin test are reflected in Table 6, with only 11 (35%) having a diagnostic skin test of greater than 15 mm induration.

5.3.2.2 Tine skin test:

Tine skin tests were done in 17 patients. Of the 15 available Tine results, 6 were negative. The results are reflected in Table 6.

Nine patients had both Mantoux and Tine skin tests done. The Mantoux or Tine test was diagnostic in 16 patients, and in 3 patients both were positive.

TABLE 3

PATIENTS ADMITTED FOR NON RESPIRATORY DISEASE AND TUBERCULOSIS SUBSEQUENTLY DIAGNOSED

VSD/Cyanotic Attacks	1(1.7%)
Pericardial Effusion	1(1.7%)
VSD/Respiratory Failure	1(1.7%)
Non-accidental Injury	1(1.7%)
Total	4(7%)

TABLE 4

PATIENTS ADMITTED TO THE PICU AND ALREADY RECEIVING TREATMENT FOR TUBERCULOSIS

Pancraniosynostosis Repair/PTB	1(1.7%)
Pericardial Effusion	4(7%)
Fulminating Heart Failure/PTB	1(1.7%)
Adrenogenital Syndrome/Tuberculosis Abdomen	1(1.7%)
Total	7(12.3%)

TABLE 5

CHEST RADIOGRAPH FINDINGS.

RESULTS	NUMBER OF RADIOGRAPHS
Hilar Adenopathy	23(40%)
Paratracheal Adenopathy	18(32%)
Tracheal Compression	8(14%)
Bronchial Compression	10(18%)
* Opacification	38(67%)
Cavitation	6(11%)
Miliary Pattern	6(11%)
Pleural Effusion	9(16%)
Pericardial Effusion	6(11%)
* Site Of Opacification	
Right Upper Lobe	13(34%)
Right Middle Lobe	7(18%)
Right Lower Lobe	2(5%)
Left Upper Lobe	3(7%)
Left Lower Lobe	4(11%)
Entire Right Lung	5(13%)
Widespread (Both Lungs)	7(18%)

TABLE 6

TUBERCULIN SKIN TEST

MANTOUX SKIN TEST		TINE SKIN TEST	
Negative	15(48%)	Negative	6(40%)
≤5mm	1(3%)	Grade 1	0(0%)
≥5mm but <10mm	2(6%)	Grade 2	1(6.7%)
≥10mm but <15mm	2(6%)	Grade 3	2(13%)
≥15mm	11(35%)	Grade 4	6(40%)
Total	31	Total	15

5.3.3 Tuberculosis culture:

5.3.3.1 Gastric aspirates:

Gastric aspirates for culture of M.tuberculosis were done in 36 patients. Cultures positive for M.tuberculosis were obtained in 15 (41.6%).

5.3.3.2 Other cultures:

Cultures other than gastric aspirates for Mycobacterium tuberculosis were done in 32 patients. Positive cultures for M.tuberculosis were obtained in 14 patients (43.7%). In 5 patients the gastric aspirates were also positive. Twenty-four patients (42%) had either a positive gastric aspirate or a positive culture from another site. Positive results in culture sites other than gastric aspirates were as follows:

Bronchial aspirates	10
Transbronchial biopsy of a granuloma	2
Pericardial fluid	1
Open lung biopsy	1

5.3.4 HIV status:

HIV tests were done 21 patients; 3 (14%) had positive results. One had active disease and the other two were admitted with pneumonia and clinically suspected of having TB. In none of the 3 HIV positive cases was the culture for M.tuberculosis positive, but all were already receiving TB therapy at the time that the cultures were performed.

5.3.5 Other tests:

CT scans were done in 28 patients. Fourteen had scans of the chest, 13 of the brain and 1 of the abdomen. Of the twenty-eight scans done, twenty-seven were reported as abnormal and consistent with tuberculosis. The CT scans of the chest were done to confirm the complications of tuberculosis, namely airway compression and bronchiectasis. The CT scans of the brain confirmed the diagnosis of TBM or TB granuloma of the brain and the abdominal CT scan revealed the presence of tuberculosis lymphadenopathy.

Bronchoscopies were done in 13 patients. Twelve of the bronchoscopies were reported as abnormal and consistent with the diagnosis of PTB. Indications for bronchoscopics were large airway obstruction or radiological evidence of endobronchial tuberculosis.

Surgery was performed in 9 patients. This included 5 tracheostomies. Four of the tracheostomies were done for severe airway obstruction following extubation and one was done in a patient with a posterior fossa tumour and bulbar palsy. Three patients had drainage for pericardial effusions and 1 patient had a thoracotomy for glandular decompression of the airways.

5.4 CLINICAL COURSE:

5.4.1 Patients ventilated / Days in PICU:

Forty-three patients (75%) were mechanically ventilated for 7.3 ± 11.5 days (range 1 to 60 days).

The length of stay in the PICU was 33.1 ± 138.9 days (Table 7). The length of stay in the PICU was influenced by the patients who had tracheostomies which prolonged the PICU stay. If the PICU stay was calculated excluding the patients with tracheostomies, then the length of stay in the PICU was 10.2 ± 22.4 days (range 1 - 141 days)

Only 6 cases (11%) could be identified where tuberculosis prolonged the PICU stay.

5.4.2 Days in Hospital:

Length of stay in the hospital was 70.3 ± 148.9 days (range 1 to 999). The length of stay in the hospital was influenced by the patients with tracheostomies. The days in hospital included the patient's stay in the PICU (Table 7). The length of stay of the patients with tracheostomies was 261 ± 384.3 days. The length of stay in hospital excluding the data for patient still in hospital and for those who died was 74.1 ± 163.8 days (range 5 to 999).

5.4.3 Discharge home/hospital/clinic/mortality:

Seventeen patients were discharged to another ward and subsequently to another hospital. Twenty-five were discharged to another ward and then home, to be followed up by the local clinic. One patient was still in the ward at the time of the study.

Thirteen patients (22.8%) died in the PICU (95% CI 0.12, 0.34). Their mean age was 54.1 ± 42.5 months (range 7 to 144). Two patients died in the ward after discharge from the PICU. The hospital mortality of the study group was 26% (15 out of 57) (95% CI 0.15, 0.37). The data between the survivors and the non-survivors are compared in Table 9.

The causes of death are reflected in Table 8. Of the children that died from pneumonia, two were HIV positive. Of the 8 children with TBM, 6 died, giving a mortality of 75% for this subgroup.

A further 2 patients died at home. (See follow-up).

TABLE 7

HOSPITALIZATION, PICU STAY AND OUTCOME

Length Of Stay In Hospital (Days)	*70.3 ± 148.9
Length Of Stay In PICU (Days)	*33.1 ± 138.9
Length Of Stay In PICU (Days) (Corrected)	*10.2 ± 22.4
Hospital And PICU Mortality	15 (26%)
PICU Mortality	13 (23%)

* Mean ± standard deviation.

Length of stay in PICU (Corrected): Stay in PICU without the influence of the tracheostomy patients.

TABLE 8

CAUSES OF DEATH

Tuberculous Meningitis	5
Pseudomonas Septicaemia / Pneumonia	1
Miliary Tuberculosis	1
Tuberculosis Lung	1
Pneumonia	6
Fulminating Heart Failure/PTB	1
Total	15

TABLE 9

MORTALITY: NON-SURVIVORS VERSUS SURVIVORS (HOSPITAL)

	NON-SURVIVORS	SURVIVORS
Sex	*F = 7 *M = 8	*M = 14 *M = 28
Age	Mean age: #51.9 ± 44.3 months Range (3-144)	Mean age: #32.8 ± 36.4 months Range (1-144)
Disease:		
Miliary tuberculosis	1	3
TB Meningitis	5	3
Tuberculosis lung	2	1
Pneumonia	7	5

*F = Female

*M = Male

#Mean ± standard deviation

5.4 4 Patients on tuberculosis treatment:

Twenty-eight patients were already receiving anti-tuberculous therapy prior to their admission to the PICU. Of these 19 (68%) were admitted to the PICU primarily because of TB.

5.5 CONFIRMED TUBERCULOSIS / PROBABLE TUBERCULOSIS:

The diagnosis of tuberculosis was confirmed in 27 patients (47.4%). Confirmation was by means of a positive gastric aspirate, a positive culture from another site or at post mortem. In 3 patients, TB was confirmed by post mortem examination: tuberculous meningitis (n=2) and tuberculosis of the lung (n=1).

The diagnosis of probable tuberculosis was made in 30 children (53%). This group included 4 children with pericardial effusions, suspected of being tuberculous on clinical and histological basis, 3 children with clinical, CSF and radiology compatible with the diagnosis of TBM, a child with the radiological picture of a TB granuloma of the brain and a child with abdominal TB. Although the clinical picture and special investigations were indicative of TB, in none of the cases was TB proven histologically or by culture.

B. RESULTS OF DATA COLLECTED FROM THE CLINICS OR OTHER HOSPITALS:

Twenty-seven questionnaires (64%) were returned. Of these only 26 could be used for analysis. Two of the patients died after discharge from Tygerberg Hospital: one in Brewelskloof Tuberculosis Hospital and one in Sonstraal Tuberculosis Hospital. One died of tuberculous meningitis and one of endobronchial tuberculosis. The questionnaire of the patient who died in Brewelskloof was incomplete and was not used in the analysis of the data. In 4 cases the clinic had not received any notification of the tuberculosis and responded only to the questions that were relevant.

5.6 NOTIFICATION RECEIVED AND COMPLETED CORRECTLY:

Of the 27 questionnaires, 17 (63%) indicated that they had received the notification and that the notification was completed correctly. Four (15%) indicated that they had not received notification at all and in 5 cases the responders were uncertain about the notification.

Where the respondents were uncertain about the notification, 2 indicated that the notification had been done prior to the present staff joining the clinic.

5.6.1 Was sufficient information given by the referring hospital?:

Seventeen clinics stated that sufficient information was given, although there were some problems.

Two clinics experienced problems with the completion of the notification. In 1 case the results of the special investigations were outstanding and in the other case the section on chemotherapy was incomplete, with the dose and total daily dosages not being specified.

5.7 TUBERCULOSIS TREATMENT:

5.7.1 Number of drugs:

Eighteen of the patients received three drugs (INH, Rifampicin, Pyrazinamide). Two patients received the combination drug (Rifater) and 2 patients received four drugs (INH, Rifampicin, Pyrazinamide and Ethionamide)

5.7.2 Compliance:

Compliance was accepted if the child received more than 80% of the prescribed doses in six months.

Eighty-two percent of patients were compliant (18 out of 22). Two patients were not compliant and in 2 cases the compliance was unknown. In the cases where the compliance was unknown, this question was not completed by the respondents.

One of the patients that who was not compliant, has defaulted and was untraceable.

5.7.3 **Treated at clinic:**

Eighteen patients were treated at the clinic and 4 patients were treated as inpatients at a hospital. Two patients were under the supervision of a voluntary worker.

5.7.4 **Problems during treatment:**

Three patients were reported to have had problems during treatment. The problems documented were diarrhoea, pneumonia and hepatitis as a side effect of anti-tuberculous therapy.

5.8 INFORMATION CONCERNING HEALTH:

General health/Respiratory/Neurological problems:

In general the health of the patients was reported as good. Two patients, one with Down's syndrome and one with adrenogenital syndrome, required ongoing treatment and follow-up. Three patients were reported to have bronchitis/pneumonia and 2 patients had residual neurological problems following TBM, namely, hemiplegia and quadriplegia.

5.9 ONGOING MEDICAL TREATMENT:

Six patients were documented who required ongoing medical treatment. Four cases required ongoing treatment at Tygerberg Hospital, one at Brewelskloof Hospital and one at 2 Military Hospital and Tygerberg Hospital.

Ten cases were followed up by the referring hospitals. In 2 cases it was uncertain whether the patients were followed up.

5.10 GENERAL:

5.10.1 **Sufficient information concerning the children referred from the tertiary hospital:**

Eighteen respondents (69%) indicated that they had received sufficient information from the referring hospital. Three indicated that they did not receive sufficient information and one was uncertain.

5.10.2 Suggestions from the clinics to improve communication:

Eight clinics/hospitals responded to this question. Their suggestions can be summarized as follows:

* The clinic should be phoned before the patient is discharged from the hospital.
* A complete summary of the patient, including the special investigations done and the results, should be sent to the clinic.
* The handwriting must be legible and the referring doctor must clearly identify his name, contact address and telephone number.
* It must be clearly stipulated when the patient has to be followed up and at which clinic, as well as a contact telephone number.
* The chest radiographs must be sent to the clinic for revision and to help in estimating if the child has improved on treatment.

CHAPTER SIX

DISCUSSION

6.1 INTRODUCTION

The increased incidence of tuberculosis world-wide together with the incidence of pulmonary tuberculosis in the Western Cape being amongst the highest in the world necessitate an assessment of impact of these on the health services. This applies specifically to the PICU, as an extensive search of the literature failed to reveal a single article regarding tuberculosis in children requiring intensive care.

It is speculated that the increasing incidence of MDR-tuberculosis and HIV infection will play a major role in increasing the number of admissions to the ICU. Of great concern is the increased demand on the already limited ICU resources and the considerable health risk that these conditions pose to the ICU staff. A further consideration is the financial burden of treating these patients in the ICU, together with the additional costs incurred in preventing the disease spreading from patients requiring mechanical ventilation to staff and other patients.

6.2 INCIDENCE

6.2.1 Increased incidence of tuberculosis:

The data from a cohort study (6) suggest that there will be a 50% increase in the incidence of tuberculosis in the Western Cape by the year 2001. If this increase continues, the number of patients admitted to the ICU may double in the next 3 - 5 years.(31)

A six-fold increase occurred in the number of children suffering from pulmonary or disseminated tuberculosis who required PICU care at the Tygerberg Hospital between 1991 and 1993. Potgieter demonstrated a similar pattern in his admissions to an adult ICU, but recorded that the increase could not be attributed to HIV infection or multi-drug resistant tuberculosis.(31)

6.2.2 Increase in HIV disease:

In the Western Cape the seropositivity rate is 1.16% (0.76%-1.5%).(32) The fact that only 3 patients (14%) tested positive is accordance with this data. Two of the 3 patients positive for HIV died. However, this data should be interpreted with care as only 21 patients were tested for HIV. The predicted increase in the prevalence of HIV infection will pose major problems for critical care medicine in the future.

6.2.3 MDR-tuberculosis:

It is speculated that the increasing incidence of MDR-TB will play a major role in the admission of patients to the ICU. In this study not one of the contacts had multi-drug resistant tuberculosis. It is however not possible to comment on the sensitivities of the positive tuberculosis cultures, since they were not routinely tested. The favourable response to treatment seemed to indicate that MDR was not a problem among our patients, and it is thought that index cases with MDR-TB are less infectious than drug sensitive index cases, making MDR-TB an unlikely problem in the PICU. This is also influenced by the fact that the incidence of MDR-TB is only 1.1% in the Western Cape.(15)

6.3 PREVIOUS TREATMENT FOR TUBERCULOSIS AND COMPLIANCE

Of the children admitted to the PICU, 26% had previously been treated for tuberculosis. According to the records only two of the 15 cases were known to have been compliant. In the other cases the compliance was unknown, as the records were no longer available or the patients were not known to the clinic. Hayhurst et al (28), in an adult ICU in the same region, showed that their patients were similarly non-compliant, with 8 out of 11 patients having had inadequate treatment as evidenced by poor follow-up arrangements or non-compliance. The impact of poor compliance on the health system could be considerable, with the effects being felt by the TB clinics, referral hospitals and the PICU.

In contrast to this the children that were admitted to the PICU were compliant post discharge (82%). This figure is similar to a study on childhood compliance done in the Western Cape where the compliance rate was 88%.(35)

6.4 REASONS FOR ADMISSION TO PICU

Although it was initially published in the literature that pulmonary tuberculosis seldom results in respiratory failure (27), several researchers have shown evidence to the contrary. Studies done by Penner et al (30), Frame et al (29), Levy et al (27) and Hayhurst et al (28) in adults, recorded that acute respiratory failure (ARF) as a complication of pulmonary tuberculosis frequently was the indication for mechanical ventilation in patients with TB admitted to the ICU.

In this study tuberculosis was the primary reason for admission to the PICU in 29 children. Of these children 69% had respiratory failure requiring ventilation. The 2 reasons for ventilatory support were large airway obstruction (40%) and type 1 respiratory failure (60%). In contrast, 30% children were admitted for respiratory failure thought to be the result of pneumonia (n=13) or bronchiolitis (n=2) and subsequently found to have TB. It was not possible to determine if TB was the primary cause of the respiratory failure or a contributory factor. TB

was incidently diagnosed in 4 children admitted to the ICU for other reasons. It appears therefore that TB may be the reason for admission for respiratory failure in certain children, contribute to the respiratory failure in others, incidently found on admission, or modify treatment in those already diagnosed as having TB.

6.5 DIFFICULTIES IN DIAGNOSIS

A large proportion of cases in children goes unrecognized because of the poor sensitivity of currently available diagnostic methods. Due to difficulty in confirming the diagnosis in children, reliance is usually placed on a constellation of symptoms, clinical signs, tuberculin testing, chest radiography and a history of close contact with an adult case of active pulmonary tuberculosis in order to make the diagnosis.

In this study the results of the chest radiography, tuberculin skin tests and positive M.tuberculosis cultures were no different from those reported in the literature. The chest radiographs of the children in the present study demonstrated that the most common findings were hilar (40%) and paratracheal (32%) adenopathy. This is similar to the findings in previously published studies.(18,33) Bronchial compression which leads to large airway obstruction was present in 12% of cases, which also does not differ from the study of Schaaf et al.(18) The degree of obstruction was not determined, but it is possible that in this study there was a greater degree of airway obstruction as indicated by the need for ICU admission.

The limitations of the tuberculin tests were also in evidence in the children admitted to the PICU, but were not different from the 41% previously reported for a similar population.(18)

The number of culture positive paediatric specimens at Lusaka University Teaching Hospital have ranged from 0.9% to 57% depending on age, number of obtained specimens, disease severity and to a lesser extent prevalence of tuberculosis.(21) In this study at Tygerberg Hospital gastric aspirates positive for M.tuberculosis were obtained in 42% and, of cultures other than gastric aspirates, 44% were positive. Possible explanations for the high positivity rate could be methods used to obtain cultures (bronchoscopy and endotracheal tube aspirates), the emphasis placed on obtaining cultures in academic hospitals and the PICU, together with the availability of specialist culture methods in the laboratories. We were unable to analyse the number of positive gastric aspirates performed prior to admission with those performed after admission as this data was not collected. It might be speculated that the positive yield is higher in the PICU.

6.6 OTHER SPECIAL INVESTIGATIONS

6.6.1 CT scans:

The availability of a CT scanner may contribute to the diagnosis of tuberculosis or its complications. Twenty- seven out of the 28 scans done in the study were reported as

abnormal. The CT scan was particularly helpful in evaluating children suffering from TBM or airway obstruction and, although it is an expensive special investigation tool, its use can be justified in critically ill children.

6.6.2 Bronchoscopy:

Bronchoscopies were performed on 13 of the patients and found to be abnormal in 12. The most common finding was nodal compression of the airways, which was present in all 12 patients. Bronchoscopy may aid in the rapid diagnosis of TB in children with large airway obstruction or lobar collapse. This study is limited in assessing the contribution of bronchoscopy, as the sensitivity or specificity of this investigation in children presenting with airway obstruction or lobar collapse was not addressed.

6.7 PROBABLE AND CONFIRMED TUBERCULOSIS

Diagnosis of TB in the study was made according to internationally accepted standards.(18) The usage of accepted standards makes inter-regional and epidemiological comparison possible. The diagnosis of confirmed tuberculosis was made in 47% of children. The diagnosis of probable tuberculosis was made in 53% of the children, based on reliable criteria. The last group included 9 children who had a clinical and radiological picture highly suggestive of TB although tuberculosis could not be proven. It consisted of 4 children with pericardial effusions, 3 children with TBM, 1 child with TB granuloma of the brain and 1 child with tuberculosis of the abdomen. If these children are included in the confirmed group the percentage of the confirmed TB will increase to 63%.

6.8 OUTCOME

The average stay in the PICU was 33 days. The stay in the PICU was skewed by patients with tracheostomies. If the patients with tracheostomies are excluded, then the average stay in the PICU was 10 days. This is considerably longer than the average stay of children with other conditions (average 2.8 days). In a study done in adults the average stay was 14.5 days.(28) The patients in this study were mechanically ventilated for 7 days, compared to 15 days (30) and 17.2 days (27) in adult studies. To make a valid comparison between the adults and children admitted to the ICU the average adult data for those patients without TB need to be known. This data was however not published. The mortality rate in the PICU was 23%. Two patients died in the wards after discharge from the PICU, accounting for a hospital mortality of 26%. In the adult studies, Levy et al reported a mortality of 33% in the ICU and a three month post-ICU mortality of 47%.(27) Hayhurst et al reported a mortality of 39%.(28) Another two children died according to the follow-up study, accounting for a total mortality of 29.8%. Of the 8 children with TBM, 6 died, giving a mortality of 75% for this subgroup. It can be speculated whether children with TBM should be admitted to the PICU, considering the high

mortality in this group. This contention is further supported by the fact that the 2 children with TBM who survived had severe neurological damage post discharge.

6.9 FOLLOW-UP STUDY

Although a good compliance (82%) was recorded at the clinics in the follow-up study, they clinics experienced problems with the notifications. In four cases the clinics had not received any notification of the tuberculosis and in another two cases the notification form was incomplete, lacking information regarding special investigations and chemotherapy.

The follow-up study also revealed that communication between the referring hospital and the clinics was a problem. Thirty-one percent of the clinics made suggestions to improve communication. A summary of the suggestions made is given in chapter 5.

In general the health of the patients in the follow-up study was reported as good. Two patients, one with Down's syndrome and one with adrenogenital syndrome, required ongoing treatment and follow-up, but this was unrelated to their TB. Three patients were reported to have bronchitis/pneumonia after discharge and, the only two patients who survived TBM had severe neurological sequelae.

The above information suggest that the outcome of children admitted to the PICU with TB is good if they survive to hospital discharge and do not have TBM. It would appear to be poor therapy to invest so much time and money in a group of children and then not ensure adequate notification and follow-up in the community.

CHAPTER SEVEN

RECOMMENDATIONS

7.1 GENERAL RECOMMENDATIONS

This study demonstrates that, in an area with a high incidence of TB, children develop severe disease requiring admission to a paediatric ICU. This places a considerable clinical and financial load on the already limited health resources. To reduce the burden of disease in children, priority must be given to limiting TB amongst adults in the community. This can be achieved by ensuring that the WHO goals of curing 85% of smear positive adults and detecting 70% of smear positive cases in the community are met. This has to be the priority and should not be deflected by paying more attention to children suspected of being infected.

This approach should be complemented by:

(i) Increasing compliance by, among others, treating with intermittent therapy rather than a daily drug regimen. Intermittent therapy is cheaper and much more convenient for the patient and parents. Directly observed therapy should be implemented for the full duration of treatment. This is not a new approach, but it can be reinforced and expanded to include schools and school health.

(ii) Ensuring that all health workers are adequately trained and supported.

(iii) Promoting community awareness and active participation in the control of TB.

(iv) Increasing media attention to the increasing incidence of tuberculosis and the necessity of early diagnosis and treatment.

(v) Developing a mass media campaign to educate the community about TB and encourage symptomatic patients to present themselves for evaluation and treatment.

(vi) Securing a regular supply of drugs and diagnostic materials.

(vii) Searching for novel drugs and vaccines and a better knowledge regarding the pathogenesis of tuberculosis.

7.2 EARLY DIAGNOSIS OF TB IN CHILDREN

It has been shown that opportunities to diagnose TB are missed in 52% of children (34) and that the longest delay in making the diagnosis was caused by health care workers (5.1 weeks).(35) Early diagnosis of TB in childhood should prevent severe disease and therefore subsequent admission to the PICU. This can be achieved by:

(i) Retraining clinic health care workers.

(ii) Integration of primary health care clinics to ensure that opportunities for diagnosis are not missed due to fragmentation.

(iii) Well structured guidelines regarding referral of critically ill children to secondary and tertiary care institutions.

7.3 BCG VACCINATION

The efficacy of BCG vaccination in South Africa has been questioned.(36) As BCG vaccination has a 98% coverage, correct application there of might ensure greater efficacy. This area requires greater attention and urgent research. If BCG in South Africa were effective, it might be the most cost effective method of reducing serious TB.

7.4 PAEDIATRIC ICU

7.4.1 Recommendations regarding guidelines for admission to PICU:

It can be speculated that children with TBM who require admission to PICU, should not be admitted to the PICU, due to the high mortality (75%) and morbidity (100%), found in this study. At present it is recommended that these children with TBM do not receive priority for admission to the PICU. The risk factors for this specific group need to be further investigated. This probably does not apply to children who require VP shunting and are admitted electively to the ICU after the procedure.

7.4.2 Recommendations regarding investigation of patients suspected of having TB in the PICU:

Because of the poor sensitivity of the currently available diagnostic methods for TB in children, a series of special investigations is needed to confirm the diagnosis of tuberculosis. The high positivity rate of M.tuberculosis cultures in this study serves to support the use of bronchoscopic and endotracheal tube aspirates for culture. In addition, bronchoscopy and CT scan aid in the diagnosis of airway obstruction due to tuberculosis. As wide a spectrum of special investigations relevant to the diagnosis of tuberculosis should be used in critically ill children.

7.4.3 Recommendations regarding prevention of infection and detection of disease in staff in PICU:

With the increased incidence of HIV and MDR-TB, intubated and ventilated patients in PICU undoubtedly pose a major risk to ICU staff, and the prevention of infection is of primary concern to those who may be exposed to TB. Recommendations to be included in a protocol for the PICU include:

(i) All staff should wear masks that are of surgical standard when performing procedures that involve exposure to secretions of patients.

(ii) All respiratory secretions and contaminated equipment should be specially sterilised.

(iii) All staff should be regularly screened for disease (6 monthly).

7.4.4 Recommendations regarding the need for increased beds in the PICU:

The mortality of patients with TB in this study was 23%, except for the subgroup of TBM patients where the mortality was 75%. The fact that the outcome of TB in children who require the PICU is favourable, supports the decision to admit them to the PICU.

If one takes into account the high incidence of TB in the Western Cape together with the increase in admissions of children with pulmonary tuberculosis to the intensive care unit, it is evident that more beds will be needed. Whether this is feasible still needs further investigation and the cost involved need to be calculated and compared to other health costs.

7.4.5 Recommendations regarding children discharged from the PICU:

As mentioned in Chapter 6, the follow-up study showed that communication was a problem between the referring hospital and the clinics. Suggestions were made to improve the communication. Summary of recommended suggestions:

(i) The clinic should be telephoned before the patient is discharged from the hospital.

(ii) A complete summary of patient, including the special investigations done and the results there of, should be sent to the clinic.

(iii) The handwriting must be legible and the referring doctor must clearly identify his name, contact address and telephone number.

(iv) It must be clearly stipulated when patients has to be followed up and at which clinic, as well as a contact telephone number.

(v) The chest radiographs must be sent to clinic for revision and assessment of the child's response to treatment.

It is recommended that the patients discharged from the PICU be followed-up by the PICU medical staff to ensure continuity of management.

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APPENDIX A

TUBERCULOSIS: ICU STUDY

TBH FILE NUMBER:

Name: .....

Initials: ..... Date of Birth: ..... Sex: M / F

Address: .....

.....

.....

PREVIOUS TB HISTORY:

Contact:	Contact:	Y / N	Relationship:	.....
	On Treatment:	Y / N	Resistant:	Y / N
	Compliant:	Y / N		
Child:	Previous TB Rx:	Y / N	TB prophylaxis:	Y / N
	Clinic treated:	Y / N	Compliant:	Y / N

REASON ICU ADMISSION :

.....

.....

HISTORY :

Summary attached: Y / N

History: .....

.....

.....

EXAMINATION :

.....

.....

.....

SPECIAL INVESTIGATIONS:

1. **Chest radiograph**

Done:	Y / N	Available:	Y / N
Report:			
Hilar glands:	Y / N	Paratracheal glands:	Y / N
Tracheal compression:	Y / N	Bronchial compression:	Y / N
Opacification:	Y / N	Size Opacification:	<RUL
			> RUL
			<1 Lung
			>1 Lung
Cavity:	Y / N	Miliary:	Y /N
Pleural Effusion:	Y / N	Pericardial Effusion:	Y / N

2. **Mantoux/Tine skin test:**

Mantoux done:	Y / N	Read:	Y / N
Result:	.....	induration	
Tine:	Y / N	Read:	Y / N
Result:	Grade.....		

3. **Tuberculosis culture:**

Gastric Aspirate: Y / N Number: 1 / 2 / 3

Culture positive: Y / N

Other cultures: Y / N Specify .....

Culture positive: Y / N

4. **HIV Status :**

HIV done: Y / N HIV positive: Y / N

5. **Other test:**

Abnormal CSF: Y / N

CT Scan Chest: Y / N Result .....

CT Scan other: Y / N Specify ..... Result .....

Biopsy performed: Y / N Result .....

Bronchoscopy: Y / N

Glands visible on Bronchoscopy: Y / N

OTHER DIAGNOSES :

1. .....

2. .....

3. .....

4. .....

CLINICAL COURSE:

Date Admitted: ..... Date Discharge: .....

Days in ICU: .....

Discharge to ward: .....

Ventilated:

Ventilated: Y / N Days ventilated:.....

Reason ventilated: .....

Hospitalization:

Date admitted: ..... Date discharge: .....

Days in Hospital: .....

Discharge to: .....

CLASSIFICATION:

1. Confirmed TB: Y / N

   Probable TB: Y / N

2. TB responsible for ICU admission: Y / N

3. TB prolonged ICU stay: Y / N

APPENDIX B

TUBERCULOSIS: ICU STUDY (CLINIC)

NAME OF PATIENT: .....

ADDRESS OF PATIENT: .....

TELEPHONE NUMBER: .....

NAME OF CLINIC: .....

NOTIFICATION RECEIVED: Y / N DATE RECEIVED: .....

TUBERCULOSIS TREATMENT: .....

Number of drugs: ..... Specify: .....

Compliant: Y / N

Number of dosages: ...../.....

Treated at clinic: Y / N

Alive after treatment: Y / N

Any problems during the treatment?: Y / N

Specify: .....

.....

.....

IS THE CHILD AND HIS FAMILY KNOWN TO YOUR CLINIC?: Y / N

DOES THE CHILD ATTEND THE CLINIC REGULARLY?: Y / N

INFORMATION CONCERNING HEALTH:

Growth: Weight: .....

Height: .....

General Health: .....

.....

.....

.....

Respiratory Problems: .....

.....

.....

.....

Neurological Problems: .....

.....

.....

.....

DOES THE CHILD REQUIRE ONGOING MEDICAL TREATMENT?: Y / N

If YES : What treatment? .....

.....

.....

Where is the child receiving the treatment?

.....

.....

Was the child follow-up by the refering hospital? Y / N

WAS THE NOTIFICATION COMPLETED :

Correctly? Y / N

Was sufficient information given? Y / N

Any other comments: .....

.....

.....

GENERAL:

Did you receive sufficient information concerning the children refered from the tertiary care hospital?: Y / N

Any suggestions for improving communication:

.....

.....

.....

.....

CAPE PROVINCIAL ADMINISTRATION
HOSPITAL AND HEALTH SERVICES BRANCH ◆ *KAAPSE PROVINSIALE ADMINISTRASIE*
TAK HOSPITAAL-EN-GESONDHEIDSDIENSTE

Cat. no. 1904361

REFERRAL OF PATIENT TO TB HOSPITAL/CLINIC AT
VERWYSING VAN PATIËNT NA TB HOSPITAAL/KLINIEK TE

Complete in **TRIPLICATE.** One copy to Local Authority Head Office, one copy to accompany patient, one copy to patient's file.
*Voltooi in **TRIPLIKAAT.** Een afskrif na die Plaaslike Bestuur-hoofkantoor, een afskrif om pasiënt te vergesel, een afskrif bly in pt. lêer.*

PLEASE PRINT
DRUKSKRIF ASB.

PATIENT'S NAME
NAAM VAN PATIËNT .....

HOSPITAL/CLINIC No. .....
HOSPITAAL/KLINIEK Nr.

AGE .....
OUDERDOM

SEX *GESLAG* [M/M] [F/V]

POPULATION GROUP *BEVOLKINGSGROEP* [W/W] [C/K] [A/A] [B/S]

REFERRING HOSP/CLINIC
VERWYSENDE HOSP/KLINIEK

DEPT

WARD
SAAL

REFERRING DOCTOR/NURSE
VERWYS. DR/VERPLEEGKUNDE

DATE OF REFERRAL
VERWYSINGDATUM ☎

TB DIAGNOSIS(ES)
TB DIAGNOSE(S) .....

PATIENT'S ADDRESS
ADRES VAN PASIËNT .....

NOTIFIED?/*AANGEMELD?* [NO/*NEE*] [YES/*JA*] ON/*OP*

☎

OTHER DIAGNOSIS(ES)
ANDER DIAGNOSE(S)

RELEVANT HISTORY & CLINICAL FINDINGS
RELEVANTE GESKIEDENIS & KLINIESE BEVINDIGINGS

Date of admission
Toelatingsdatum

Family history of TB *Familie geskiedenis van TB* [NO/*NEE*] [YES/*JA*]

Contact with TB *Kontak met TB* [NO/*NEE*] [YES/*JA*]

.....

.....

.....

.....

.....

Weight on hospital admission *Gewig by hospitaal-toelating*

Weight on commencing TB Rx *Gewig by aanvang van TB Rx*

Weight on discharge from hospital *Gewig met ontslag uit hospitaal*

NB Reason for referral to hospital instead of clinic, or vice versa
Rede vir verwysing na hospitaal i.p.v. kliniek, of omgekeerd

PERTINENT SPECIAL INVESTIGATIONS DONE (mark block & enter number under "code" with date and result below)
***RELEVANTE SPESIALE ONDERSOEKE GEDOEN** (merk blokkie & teken die nommer onder "kode" met datum en uitslag)*

SPUTUM [1] direct smear *direkte smeer* [2] culture *kweking* | [3] TUBERCULIN TEST *TUBERKULIEN TOETS* | GASTRIC LAVAGE *GAST. SPOELING* [4] smear *smeer* [5] culture *kweking* | [6] OTHER (specify) *ANDER (spesifiseer)*

code *kode*	date sent *datum versend*	result *uitslag* ↓	code *kode*	date sent *datum versend*	result *uitslag* ↓

date *datum*	X RAY REPORTS : specify chest, spine etc *X STRAAL VERSLAE : dui aan borskas, werwelkolom ens* ↓	NB X-rays to be sent with patient *X-strale moet pasiënt vergesel*

CHEMOTHERAPY *CHEMOTERAPIE*	Rifater/HZR	Rifampicin	INH	PZA	Etham.	Other (specify) *ander(spesifiseer)* ▷
dose *dosering*						
date started *aanvangsdatum*						
total daily doses given *totale daaglikse dosisse gegee*						

NB For patients being referred to hospital : how difficult is it for the patient to receive supervised ambulatory treatment? (Please describe).
Vir pasiënte wat hospitaal toe verwys word : hoe moeilik sal dit wees om behandeling tuis onder toesig te ontvang? (Beskryf asb.)

Clinic from which patient will be followed on discharge
Kliniek waarvan pasiënt opgevolg sal word na ontslag ☎

Social circumstances (esp. in children)
Sosiale omstandighede (veral kinderes)

Additional information / pevious history
Bykomende inligting / vorige geskiedenis

NAME of Doctor/Nurse
NAAM van Geneesheer/Verpleegkundige

☎