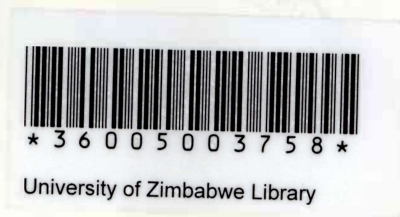


**CLINICAL PRESENTATION, AETIOLOGY, COURSE AND SHORT TERM  
OUTCOME OF ACUTE BACTERIAL MENINGITIS IN CHILDREN WITH AND  
WITHOUT CLINICAL HIV INFECTION**

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## ABSTRACT

A prospective descriptive study involving 55 patients between 1 - 60 months of age was undertaken at Harare Central Hospital to find out whether there are any differences in the clinical presentation, aetiology and short term outcome of bacterial meningitis in those with clinical HIV infection and those without. Clinical HIV infection was diagnosed in 24 (44%) of the children. There were no apparent differences in the clinical features or aetiology of meningitis. The case fatality rate (CFR) for the study population was 20% of which 45% had clinical HIV infection. The main predictor for mortality was unconsciousness on admission. Seizures occurring before and after admission were a significant risk factor for neurological abnormalities on discharge from hospital.

Eight of the 27 (30%) seen on follow up had evidence of neurologic sequelae. Hearing loss was present in 4 of the 15 patients that were tested. Clinical HIV infection was not a risk factor for neurologic sequelae.

Children who had clinical HIV infection responded well to the standard treatment given for acute bacterial meningitis and their short term outcome was not different from those without HIV infection.

## ABBREVIATIONS

|                  |                                      |
|------------------|--------------------------------------|
| AIDS             | - Acquired Immunodeficiency syndrome |
| CFR              | - Case fatality rate                 |
| CNS              | - Central nervous system             |
| CSF              | - Cerebrospinal fluid                |
| HIV              | - Human Immunodeficiency Virus       |
| H. influenza b   | - Haemophilus influenza type b       |
| H. parainfluenza | - Haemophilus parainfluenza          |
| LA               | - Latex Agglutination                |
| N. meningitis    | - Neisseria meningitidis             |
| PEM              | - Protein Energy Malnutrition        |
| S. Pneumonia     | - Streptococcus pneumoniae           |
| S. viridans      | - Streptococcus viridans             |
| USA              | - United States of America           |
| WHO              | - World Health Organisation          |

## INTRODUCTION

Acute bacterial meningitis, a pyogenic infection of the cranial and spinal leptomeninges, continues to be a major cause of morbidity and mortality throughout the world but particularly so in developing countries (1,2,3).

Case fatality rates from the industrialized countries range from 3% to 7% in infants and children (4,5,6,7,). Mortality figures are much higher in developing countries with rates of 22.2% in Addis Ababa (Ethiopia) (8), 31.3% from Durban (South Africa) (9), 18.9% from Malaysia (10) and 19% from Sudan (11). The few studies carried out in developing countries give mortality figures from hospital based studies thereby limiting the sampling to the very sick children who are referred to large or teaching hospitals (12). The higher mortality in developing countries may be a result of the delayed diagnosis, misdiagnosis or a delay in instituting effective treatment (13). Limited resources for optimum patient care may also be contributing factors. Better intensive care facilities, optimum and appropriate antibiotic therapy have improved mortality in developed countries (4,5).

Morbidity patterns also vary between developed and developing countries. Neurological sequelae occur in at least 10-20% of survivors in developed countries (4) and figures ranging between 20 and 50% are quoted for developing countries (1).

Three organisms, Streptococcus pneumoniae, Haemophilus influenza type b and Neisseria meningitidis account for the majority of reported cases of acute bacterial meningitis from all parts of the world. There are however marked geographical and sometimes racial differences in the bacterial organisms most commonly causing meningitis. In USA, H. influenza type b is currently the commonest pathogen but there are interracial differences with S. pneumoniae being more common in the black population (6,7,14,15). In England and France bacterial meningitis is most commonly caused by N. meningitidis (type B and C) (12). In Africa there is a meningitis belt where regular epidemics of N. meningitidis type A meningitis occur (12,16). Outside the meningitis belt S. pneumoniae and H. influenza type b are the most important aetiological agents (12). The type of infecting organism also influences the mortality and morbidity from meningitis. Various studies have conclusively shown that S. pneumoniae causes the highest mortality and morbidity followed by H. influenza type b and lastly N. meningitidis (7,13,14,15,16,17).

Kendall (18) reviewed cases of acute bacterial meningitis occurring in children from birth up to the age of 12 years in Harare Hospital during the years 1967 - 1969 inclusive. two hundred cases were analysed. In this series S. pneumoniae was the commonest pathogen (38%) followed by H. influenza b (25%) and lastly pyogenic meningitis (37%) where no organisms were

isolated.

Susceptibility to bacterial meningitis is affected by factors related to the host, infecting organism or to an interaction between the host and organism (7,14,15). An increased incidence and severity of bacterial meningitis has been observed in the very young (15,19). Boys are affected more frequently than girls (14,15). Patients with congenital or acquired deficiencies of the immune system are also more susceptible to bacterial meningitis (7,14,15). Deficiencies of the terminal components of the complement system (C5 through C8) increase the frequency of meningococcal infections (20,21).

#### Study site

Human Immunodeficiency Virus (HIV) infection is increasingly recognized as an important cause of mortality and morbidity in children in Africa (21). The course of this infection in children is often complicated by serious bacterial infections such as, sepsis, pneumonia and meningitis (20,21). The most frequent isolates in these patients are the encapsulated bacteria, S. pneumoniae, H. influenza type b and Salmonella species with S. pneumoniae being the commonest (20,21).

#### Study population

All children aged between 2 months and 5 years with a provisional or possible diagnosis of meningitis on clinical examination were studied.



Over recent years an increasing number of HIV infected children are being admitted to the wards of Harare Hospital with meningitis. In view of this present epidemic and the paucity of recent local data on meningitis, this study was carried out to determine whether the pattern of meningitis has changed.

## **OBJECTIVES**

To determine whether there are any differences in the:-

- (a) presenting clinical features
- (b) clinical course and short term outcome between clinically HIV infected and non HIV infected children with meningitis.

## **METHODOLOGY**

### **Study site**

The study was conducted in the paediatric wards of Harare Central Hospital which is a referral centre for municipal clinics and health centres in the surrounding provinces. The duration of the study was six months, from 1 March to the end of August 1993.

### **Type of study**

Prospective descriptive.

### **Study population**

All children aged between 2 months and 5 years with a provisional or possible diagnosis of meningitis on clinical examination were studied.

### Inclusion criteria

A diagnosis of bacterial meningitis was made and the child included in the study if one of the following criteria was met:-

- i. Clinical signs positive, CSF culture negative, blood culture positive
- ii. Clinical signs positive, CSF and blood culture negative, CSF Gram stain positive
- iii. Clinical signs positive, CSF and blood culture negative, CSF Gram stain negative with more than 5 leucocytes per microlitre on microscopy of the CSF and when >50% polymorphonuclear leucocytes were present.
- iv. CSF culture positive
- v. Latex Particle Agglutination positive

### Exclusion criteria:-

- a. congenital CNS abnormalities
- b. treatment for meningitis for more than 1 week elsewhere
- c. strong suspicion of TB meningitis.



Clinical data including age, sex, nutritional status, previous admission to hospital, previous use of antibiotics and signs and symptoms of meningitis and course in hospital were recorded by means of a standard questionnaire. (See appendix 1)

### Investigations

All CSF samples were initially examined microscopically for cells, and also with India ink for cyptococci and Gram stain, followed by standard bacteriological methods of culture. Sensitivity to penicillin, choramphenicol, gentamicin, methicillin were determined by disc sensitivity tests. An attempt was made to perform Latex Agglutination (LA) tests on all CSF specimens from which no organisms had been grown. CSF biochemistry and blood cultures were also done.

An attempt was made to perform the human immunodeficiency virus (HIV) antibody test by the Abbott Laboratories enzyme linked immuno absorbent assay (ELISA) on all patients. A positive HIV serology test in the presence of 2 of the following: generalised lymphadenopathy, hepatosplenomegaly, pneumonia or failure to thrive was diagnosed as clinical HIV infection (23). In the absence of HIV serology test results the clinical case definition for paediatric AIDS suggested by Lepage et al (24) was used. The definition considers the presence of one or both of respiratory distress secondary to lower respiratory tract infection and generalised lymphadenopathy as having a better sensitivity,

specificity and positive predictive value than the WHO clinical case definition for paediatric AIDS (24).

### Treatment

Penicillin and chloramphenicol are the standard antibiotics used for the treatment of bacterial meningitis in children beyond one month of age at Harare Hospital. Antibiotics may be changed during the course of treatment depending on the organism cultured and its sensitivity, the patient's response to therapy and the consultant's preference.

Daily changes in temperature, seizures and head circumference were recorded. Patients were also examined neurologically on discharge. They were then reviewed 3 months after discharge to assess the neurological status and any hearing deficit. Distraction audiometry was used to assess hearing impairment. This was done by a qualified speech therapist.

### Analysis and statistical methods

All data were entered and analysed on an Olivetti M380/c computer using the EPI INFO version 5 1990 programme for Epidemiology and Disease surveillance. Initial analysis was done on all the patients with meningitis and they were then divided into 2 groups, those with clinical HIV infection and those without.

Statistical analysis was done using the chi-square test with Yates correction. Fisher's exact test was used when necessary. The level of significance chosen was a p value of less than 0.05.

### Ethical Issues

Informed verbal consent was obtained from the parents or guardian for inclusion in the study. HIV screening was done as part of the investigations. Precounselling and post-counselling were offered before and after HIV antibody testing.

### Problems and Confounding factors

A number of problems were encountered during this study which may affect the results directly or indirectly.

The number of patients studied was small. A large study population would be required to compare findings in HIV infected and non-HIV infected patients. The limited duration of the study also meant that a further selection bias was introduced.

Incidence of meningitis is known to vary with seasons (17,25,26). The follow up period was limited to 3 months and it has been shown that some neurological sequelae of bacterial meningitis resolve over a period of time (27).

The aim of this study was to compare different features of meningitis in infants and children with and without HIV infection. It is well known that there are problems in making a

conclusive diagnosis of HIV infection in patients less than 15-18 months of age because of the persistence of maternally acquired antibody (21,28) Most of the study patients were less than 18 months of age. It was also realized that some infants may not have exhibited signs of HIV infection and presented with meningitis as their first severe infection and on the other hand some of the younger HIV-seropositive children may not have been infected.

A review paper by Gray and Fedorko (29) on the laboratory diagnosis of bacterial meningitis emphasizes the importance of early transport to the laboratory and immediate processing of the CSF sample. CSF is hypotonic and neutrophils may lyse and thereby reducing counts by 32% after 1 hour and by 50% after 2 hours at room temperature. In some centres during a lumbar puncture 3 or more separate samples are collected for different tests (29). The CSF in this study was collected in one bottle for all the tests. Initially cell count and bacteriological investigations were done followed by biochemistry on the same specimen some hours later. The 3 main bacteria causing meningitis have been described as fastidious and may not survive long transit times or variations in temperature (29). There may have been delays of one to several hours between the collection of CSF and its processing in the laboratory because of shortage of staff especially at night and during weekends. It was not easy to determine the sensitivity and specificity of the



laboratory tests used because the CSF was processed routinely in the Public Health Laboratory. Experienced senior staff were, available during working hours and inexperienced junior staff were available at night when most of the patients were seen.

Latex agglutination was used in this study as an adjunct to the laboratory diagnosis of meningitis. The test identifies antigens of the infecting organism and is useful even after prior antibiotic therapy. Antigen detection can however be hampered by non-specific reactions, cross-reactions and/or low concentrations of antigen in the CSF. CSF for latex agglutination should be stored at  $< 4^{\circ}\text{C}$  if processing is delayed, because bacterial polysaccharide antigens often tend to break down faster at room temperature (29). However in this study CSF was stored at  $-20^{\circ}\text{C}$  on completion of the other microbiological investigations.

Follow up of the patients was incomplete despite adequate explanation to the mother regarding its importance. Only 27 of the 44 patients came back for review. As a result the figures for neurological sequelae and/or hearing deficit are not representative as there may have been selection bias. Hearing tests were performed on a small number (16) of patients because of limited availability of the speech therapist. The hearing tests were done by the distraction method. The test relies on the ability of the child to sit up with good back and head control and turn the head to localize a sound source in the

horizontal plane (31). It is accepted that the test is less reliable in young infants and in those with neurological deficits. Results in poor head control. Distraction hearing test is useful as a screening measure but brainstem auditory evoked potentials for young infants and pure tone audiometry for older children are more sensitive tools for hearing assessment.

a) Clinical Features (Table 1, 11 and 11)

Mean birth weights were available in all the children. Sixty-nine per cent of the children were found to have normal birth weights in accordance with the expected weight for age. Approximately 15% of the children were found to have low birth weights for age and 15% had severe malnutrition with weight for age below 50%. Thirteen percent of the children had been previously hospitalized for pneumonia and one patient had had one previous episode of pneumococcal meningitis. The commonest symptoms were fever (85%), cough or difficulty in breathing (73%), irritability (47%), anorexia or poor feeding (53%) and convulsions (44%) (Table 1). Neck rigidity was the commonest sign (56%) as well as a positive Kernig's sign (56%). Twenty four percent of the children were unconscious on admission. Most of the patients (47%) presented to hospital within 48 hours of the onset of illness.



## RESULTS

During the study period a total of 2990 children were admitted to the paediatric wards and of these, 55 aged between 2 months and 4 years were studied. The male to female ratio was 1.3:1.

Eighty-nine percent of all cases were under the age of 2 years with the peak age group being 1 to 6 months. All the children resided in the greater Harare area especially in the high density suburbs. Most of the patients were from a low socio-economic background.

### a) Clinical Features (Table 1, 11 and 111)

Admission weights were available in all the children. Sixty-nine per cent of the children were found to have normal nutrition ie >80% of the expected weight - for - age. Approximately 25% of the children weighed 60-80% of the expected weight for age and 6% had severe malnutrition with weight-for - age below 60%.

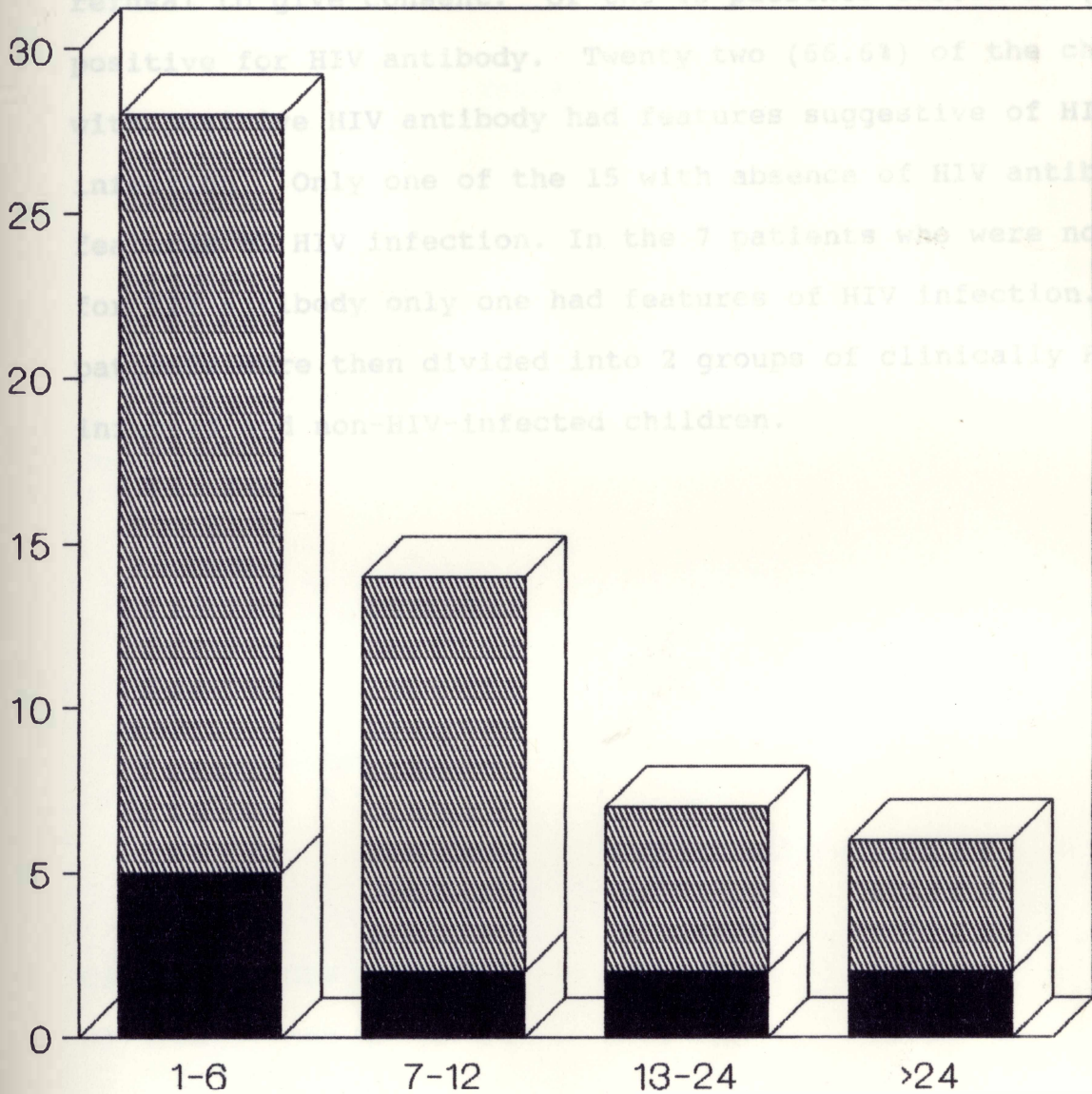
Thirteen percent of the children had been previously hospitalized for pneumonia and one patient had had one previous episode of pneumococcal meningitis. The commonest symptoms were fever (85%) cough or difficulty in breathing (73%), irritability (47%)

anorexia or poor feeding (53%) and convulsions (40%). (Table 11)

Neck rigidity was the commonest sign (56%) as well as a positive Kerning's sign (56%). Twenty four percent of the children were unconscious on admission. Most of the patients (64%) presented to hospital within 48 hours of the onset of illness.

# AGE AND MORTALITY

NUMBER OF CHILDREN

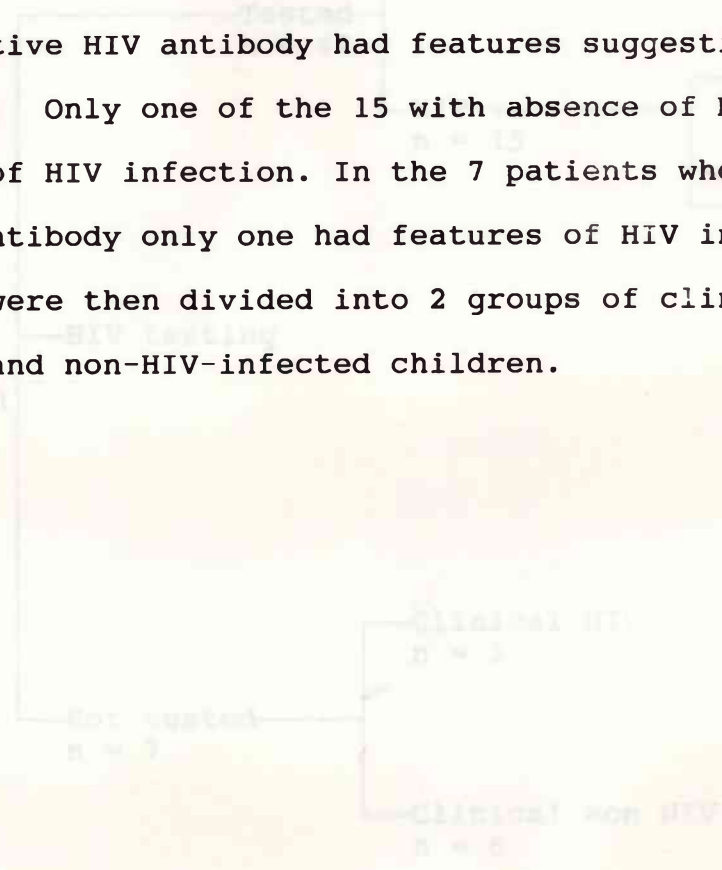


■ DIED    ▨ SURVIVED

AGE IN MONTHS

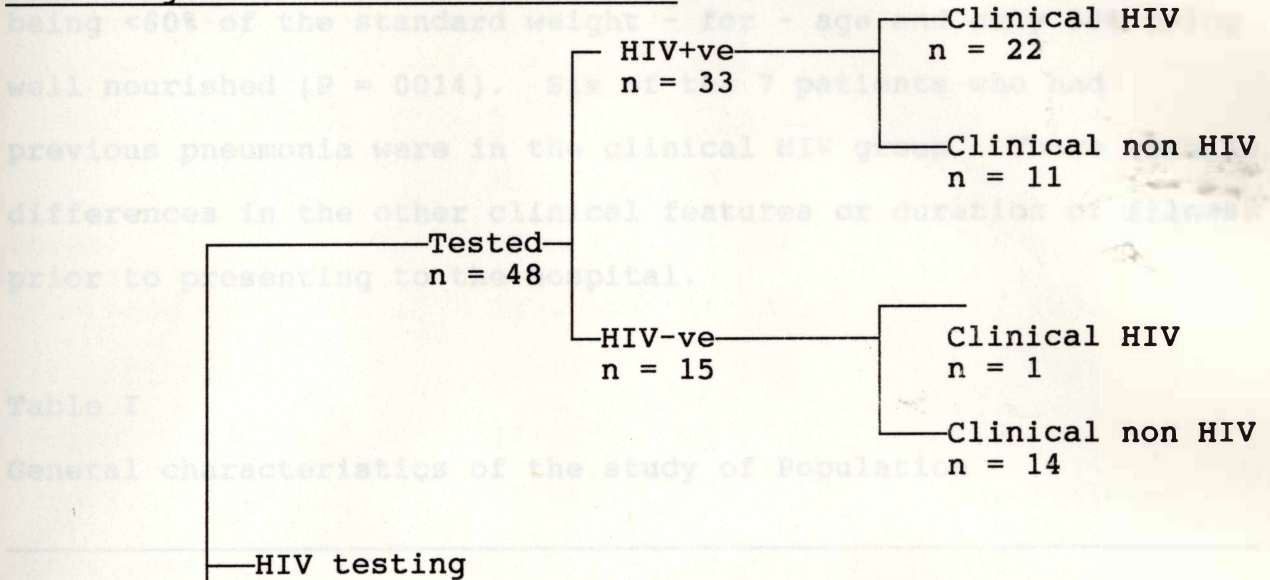
b) HIV status (Flow diagram)

Of the 55 children that were seen 48 were tested for the presence of HIV antibody. Seven were not tested due to early demise or refusal to give consent. Of the 48 patients tested 33 (69%) were positive for HIV antibody. Twenty two (66.6%) of the children with positive HIV antibody had features suggestive of HIV infection. Only one of the 15 with absence of HIV antibody had features of HIV infection. In the 7 patients who were not tested for HIV antibody only one had features of HIV infection. The patients were then divided into 2 groups of clinically HIV infected and non-HIV-infected children.



The 2 groups were compared for clinical features, CSF bacteriology and outcome. There were no differences in age group distribution. The male to female ratio in the clinical-HIV group was 1:1 and 1.1:0 in the non HIV group.

Flow diagram of clinical HIV status



|                           | Total         | Clinical HIV   | Non HIV (A)    | P value   |
|---------------------------|---------------|----------------|----------------|-----------|
|                           | No. (%)       | No. (%)        | No. (%)        |           |
| Study Population          | 55            |                |                |           |
| HIV testing               | 48            | 23 (48)        | 25 (52)        |           |
| Not tested                | 7             | 1 (14)         | 6 (86)         |           |
| <b>Clinically HIV</b>     | <b>n = 24</b> | <b>24 (50)</b> | <b>1 (4)</b>   | <b>NS</b> |
| <b>Clinically non HIV</b> | <b>n = 31</b> | <b>12 (30)</b> | <b>19 (61)</b> | <b>NS</b> |

The 2 groups were compared for clinical features, CSF bacteriology and outcome. There were no differences in age group distribution. The male to female ratio in the clinical-HIV group was 1:1 and 1:1,6 in the non HIV group.



Malnutrition was more common in the clinical HIV group with 13% being <60% of the standard weight - for - age and only 50% being well nourished (P = 0014). Six of the 7 patients who had previous pneumonia were in the clinical HIV group. There were no differences in the other clinical features or duration of illness prior to presenting to the hospital.

Table I

General characteristics of the study of Population

|  | <u>Total</u> | <u>Clinical</u><br><u>HIV</u> | <u>Non HIV (%)</u> | <u>P</u><br><u>Value</u> |
|--|--------------|-------------------------------|--------------------|--------------------------|
|  | No (%)       | No (%)                        | No (%)             |                          |
| <u>Sex</u>                             |              |                               |                    |                          |
| Male                                   | 31 (56)      | 12 (50)                       | 19 (61)            | NS                       |
| Female                                 | 24 (44)      | 12 (50)                       | 12 (39)            |                          |
| <u>Age (months)</u>                    |              |                               |                    |                          |
| <12                                    | 42 (76)      | 17 (71)                       | 25 (81)            | NS                       |
| >12                                    | 13 (24)      | 7 (29)                        | 6 (19)             |                          |
| <u>Nutrition:</u><br><u>wt for age</u> |              |                               |                    |                          |
| <60%                                   | 3 (6)        | 3 (12)                        | 0 (0)              |                          |
| 60 - 80%                               | 14 (25)      | 9 (38)                        | 5 (16)             |                          |
| >80%                                   | 38 (69)      | 12 (50)                       | 26 (84)            | p=0.0014                 |

NS - not significant

Table II

Clinical features

|                                    | <u>Total</u> | <u>Clinical HIV</u> | <u>Non HIV</u> | <u>P Value</u> |
|------------------------------------|--------------|---------------------|----------------|----------------|
|                                    | No (%)       | No (%)              | No (%)         |                |
| Fever                              | 47 (85)      | 23 (96)             | 24 (77)        | NS             |
| Breathing difficulty               | 32 (73)      | 14 (58)             | 18 (58)        | NS             |
| Irritability                       | 26 (47)      | 10 (42)             | 16 (52)        | NS             |
| Anorexia/poor feeding              | 29 (53)      | 11 (46)             | 18 (58)        | NS             |
| Convulsions                        | 22 (40)      | 9 (37)              | 13 (42)        | NS             |
| Drowsiness                         | 14 (25)      | 4 (17)              | 10 (32)        | NS             |
| Previous pneumonia                 | 7 (13)       | 6 (25)              | 1 (3)          | 0.03           |
| Neck stiffness                     | 31 (56)      | 17 (71)             | 14 (45)        | NS             |
| Positive Kernig's sign             | 31 (56)      | 17 (71)             | 14 (45)        | NS             |
| Bulging fontanelle                 | 20 (36)      | 9 (37)              | 11 (35)        | NS             |
| Loss of consciousness on admission | 13 (24)      | 6 (25)              | 7 (23)         | NS             |

NS - not significant

Table III

Duration of illness prior to admission

|         | <u>Total</u> | <u>Clinical HIV</u> | <u>Non HIV</u> | <u>P Value</u> |
|---------|--------------|---------------------|----------------|----------------|
| Hours   | No (%)       | No (%)              | No (%)         |                |
| <24     | 20 (36)      | 10 (42)             | 10 (32)        | NS             |
| 24 - 48 | 15 (27)      | 6 (25)              | 9 (29)         | NS             |
| >48     | 20 (36)      | 8 (33)              | 12 (34)        | NS             |

NS - not significant



Aetiology of Meningitis (Table IV)

An organism was grown from 29 of the 55 CSF samples (53% isolation rate) and blood culture was positive in 2 children with a negative CSF culture. Four children had positive antigen identification from the CSF by latex agglutination. Two children had positive CSF Gram stain and negative blood and CSF culture. In 18 patients cultures and Gram stain were negative, but clinical findings and CSF cell count made the diagnosis of bacterial meningitis very likely. Six of them had had prior antibiotic therapy. Twenty-four patients had S pneumoniae isolated and 13 of them from the clinical HIV group. Two patients (25%) from the clinical HIV group had H. influenza b meningitis out of a total of 8 patients. One patient with clinical HIV infection had Salmonella group D meningitis. Streptococcus viridans and Hemophilus parainfluenza were isolated in patients without evidence of HIV infection.

The CSF biochemistry and white cell counts of the patients who had no organisms isolated are shown in Table V.

TABLE IV

Bacterial Isolates (CSF and blood culture positive, LA positive)

|                     | <u>Total</u> | <u>Clinical</u> | <u>Non HIV</u> | <u>P</u>     |
|---------------------|--------------|-----------------|----------------|--------------|
|                     |              | <u>HIV</u>      |                | <u>Value</u> |
|                     | No (%)       | No (%)          | No (%)         |              |
| S. pneumonia        | 24 (44)      | 13              | 11             | NS           |
| H. influenza type b | 8 (14)       | 2               | 6              | NS           |
| S. viridans         | 1 (2)        | 0               | 1              | NS           |
| Salmonella group D  | 1 (2)        | 1               | 0              | NS           |
| H. parainfluenza    | 1 (2)        | 0               | 1              | NS           |
| Total               | 35 (64)      |                 |                |              |
| No organisms        | 20 (36)      | 8               | 12             | NS           |

Table V

Features of CSF from which organisms were not isolated

|                       |        | <u>WBC</u> | <u>Protein</u> | <u>Glucose</u> |
|-----------------------|--------|------------|----------------|----------------|
| <u>Clinically HIV</u> | Median | 120        | 0.82           | 2.5            |
| <u>Positive</u>       | Range  | 15 - 1200  | 0.4 - 3.47     | 0.2 - 3.9      |
| <u>Clinically HIV</u> | Median | 65         | 1.1            | 2.2            |
| <u>Negative</u>       | Range  | 4 - > 2000 | 0.13 - 1.8     | 0.2 - 4.3      |

Protein g/l

Glucose mmol/l

WBC / mm<sup>3</sup>

## Mortality

The overall mortality was 20%. Fifty five percent of the deaths occurred during the first 24 hours after admission. Of the overall mortality 45% had clinical HIV infection and 55% did not. This was not statistically significant. Alteration of the state of consciousness on admission was associated with a higher rate of mortality compared with normal conscious level. Table VI shows the relationship between state of consciousness on admission and mortality in the study population.

Twenty-four patients had loss of consciousness on admission and this was associated with a 54% mortality. There was no difference in mortality between children with or without clinical HIV infection who had loss of consciousness on admission. However severity of illness measured by state of consciousness on admission alone appears to be a significant factor relating to mortality ( $p=0.001$ ). The case fatality for pneumococcal meningitis was 4 out of 24 (17%), 3 out of 8 (37%) for Haemophilus meningitis and 4 out of 20 (20%) for the CSF from which there was no growth. Of the 17 mainourished (<80% standard weight for age) patients 5 died (29%) compared with 6 (16%) of the 38 well nourished (>80% standard weight for age) patients. ( $P=0,42$ ) Concurrent illness (mainly pneumonia) was not associated with increased risk of death.

Table VI

Mortality and neurological complications before and after admission

|                          | <u>Alive</u> | <u>Dead</u> | <u>Total</u> | <u>CFR%</u> | <u>P value</u> |
|--------------------------|--------------|-------------|--------------|-------------|----------------|
| Seizures                 | 20           | 6           | 26           | 23          | 0.83           |
| No seizures              | 24           | 5           | 29           | 17          | 0.83           |
| Conscious on admission   | 38           | 4           | 42           | 9           |                |
| Unconscious on admission | 6            | 7           | 13           | 52          | 0.001          |

Table VII

Mortality in relation to Organism

| <u>Organism</u> | <u>Clinical HIV</u> |             | <u>Non HIV</u> |             | <u>Total</u> | <u>Total Died</u> |
|-----------------|---------------------|-------------|----------------|-------------|--------------|-------------------|
|                 | <u>Total</u>        | <u>Died</u> | <u>Total</u>   | <u>Died</u> |              |                   |
| S pneumonia     | 13                  | 2           | 11             | 2           | 24           | 4                 |
| H influenza     | 2                   | 2           | 6              | 1           | 8            | 3                 |
| No organism     | 8                   | 2           | 12             | 2           | 20           | 4                 |

### Course in hospital

The average duration of stay in hospital for all the patients was 10 days. Thirteen patients were discharged before the 10th day to complete oral chloramphenicol treatment at home. All children were initially treated with a combination of benzylpenicillin and chloramphenicol intravenously. In 5 children penicillin and chloramphenicol were replaced with ceftriaxone between 2-4 days after observing a poor clinical response. Fluid restriction and mannitol therapy were used in 4 patients who had clinical signs of cerebral oedema which consisted of prolonged or frequent seizures and depressed level of consciousness.

Seizures were managed with phenobarbitone alone in most patients and phenytoin was added when seizure control was poor. Only 10 patients received dexamethasone. Five of them received it with the first dose of antibiotic and the rest 24-96 hours after the first antibiotic dose. Distribution of seizures before and after admission was not related to HIV status. (Table VIII)

The mean duration of fever ( $T > 37.5^{\circ}\text{C}$ ) in all the patients was 66 hours (standard deviation 47hr). The clinical HIV group had a mean duration of fever of 62 hours (standard deviation 50hr) compared with 69 hours (standard deviation 45 hours) for the non HIV group.

Table VIII

Pattern of seizures in relation to admission and clinical HIV infection

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|                            | <u>Total</u> | <u>Clinical</u> | <u>Non HIV</u> | <u>P</u>     |
|----------------------------|--------------|-----------------|----------------|--------------|
|                            |              | <u>HIV</u>      |                | <u>Value</u> |
| Before admission           | 22           | 9               | 13             | NS           |
| Before and after admission | 16           | 7               | 9              | NS           |
| After admission only       | 10           | 5               | 5              | NS           |

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NS - not significant



### Sequelae at discharge

Forty-four patients were examined and (head circumference recorded) on discharge. Abnormalities were noted in 7 patients (2 had clinical HIV infection) whose details are given in Table IX.

### Follow up examination (Table X)

Only 27 of the 44 patients that were discharged came back for review. Twenty-six percent of the patients seen had neurological sequelae manifested by developmental delay or spastic cerebral palsy. Of the 27, 15 had hearing tests performed. Twenty seven percent of those who had hearing tests had evidence of hearing loss.

Table IX

## Neurological sequelae at Discharge

| <u>Age</u><br>(months) | <u>Clinical</u><br><u>HIV</u> | <u>Non</u><br><u>HIV</u> | <u>Organism</u> | <u>Abnormality</u><br><u>or Sequelae</u>                         |
|------------------------|-------------------------------|--------------------------|-----------------|--|
| 5                      | -                             | yes                      | H influenza     | hypertonia   |
| 3                      | -                             | yes                      | none            | hypertonia<br>hyperreflexia                                      |
| 5                      | yes                           |                          | S pneumonia     | hypotonia<br>prolonged<br>seizures                               |
| 4                      | -                             | yes                      | none            | s p a s t i c<br>quadriparesis                                   |
| 33                     | -                             | yes                      | none            | hypertonia<br>hyperreflexia                                      |
| 2                      | -                             | yes                      | S pneumoniae    | decerebrate<br>posturing      no<br>head control                 |
| 8                      | yes                           | -                        | S pneumoniae    | s p a s t i c<br>quadriparesis<br>left      VIIth<br>nerve palsy |

Table X

Late sequelae of meningitis

| <u>Age (months)</u> | <u>Duration after meningitis (months)</u> | <u>Organism</u> | <u>Late sequelae</u>   |
|---------------------|---|-----------------|--|
| 15                  | 3   | S pneumoniae    | Developmental delay; R profound hearing loss, L mild high frequency hearing loss |
| 10                  | 6   | none            | Developmental delay  |
| 12                  | 4   | S pneumonia     | Poor head control Spastic cerebral palsy   |
| 10                  | 5   | H influenzae    | spastic cerebral palsy   |
| 8                   | 4   | S pneumonia     | L severe profound hearing loss   |
| 6                   | 2   | S pneumonia     | Developmental delay floppy. Profound bilateral hearing loss.                     |
| 11                  | 7   | none            | Developmental delay; R profound hearing loss, L severe hearing loss              |
| 7                   | 3   | none            | spastic cerebral palsy   |

## DISCUSSION

Infections of the CNS account for the majority of cases of neurological disease admitted to paediatric wards in developing countries (1). Bacterial meningitis is the most common CNS infection and it can progress rapidly resulting in death or permanent neurological abnormality.

There were 55 patients with acute bacterial meningitis admitted to the paediatric wards during the 6 month period. The male to female ratio of 1,3:1 is similar to what has been shown in other studies (7,15,32,33). Seventy six percent of the patients were aged between 2-12 months and the rest were over 12 months. Studies have shown that there is an increased incidence and severity of bacterial meningitis in the very young (14) and the risk is greatest among infants between 1 and 12 months of age (7,8,26). The increased risk of meningitis in children between 1 month and 12 months of age may reflect qualitative or quantitative differences between the inflammatory and immunologic responses seen in older children as compared with infants (15).

### a) Nutritional Status

Approximately 31% of the children with meningitis had moderate to severe malnutrition with a weight for age <80% of the standard. In a retrospective study performed by Mulla et al in South Africa (9) the prevalence of malnutrition was 30% and a similar finding was reported from Ethiopia by Hailemeskel et al (8).

Two studies from South Africa which looked at nutritional status of children with pyogenic meningitis found that malnourished children are not any more prone to develop pyogenic meningitis than well nourished children (9,34). Mortality was however found to be higher in malnourished children (8,9). Hailemeskel also found a higher frequency of neurological sequelae in children with protein energy malnutrition (8).

The absence of an obvious association between meningitis and malnutrition is at marked variance with the known high incidence of other infections in malnourished children. In a study by Nathoo et al in Harare on acute lower respiratory tract infection the incidence of malnutrition was 30% (35). Malnutrition is associated with depressed cell mediated immunity (36). Parts of the immune system concerned with defence against S. pneumoniae, H influenza and N. meningitidis are the humoral system, polymorphonuclear function and complement activity. Of these the complement activity and concentrations of complement proteins except C4 are reduced in children with severe malnutrition (36). B lymphocyte distribution is normal and serum immunoglobulin concentration is usually normal or elevated. Controversy about polymorphonuclear function still exists but it is generally accepted that phagocytosis in malnourished children is reasonably effective (36).

The absence of an association between bacterial meningitis and malnutrition suggests that malnourished HIV infected children will not be at greater risk for meningitis because of their nutritional status.

#### (b) Clinical Features

The presenting symptoms and clinical findings of the patients did not differ from those reported in the literature (13,17,18,33). Respiratory symptoms, which were more common in the younger infants, were not a confounding factor in making a diagnosis of meningitis. Poor feeding irritability and restlessness increases the suspicion of meningitis in infants. Ten of the 55 (18%) patients also had bronchopneumonia. Bacterial meningitis most commonly is the result of haematogenous dissemination of microorganisms from a distant site of infection (15).

Six patients who had HIV infection been previously treated for pneumonia. Recurrent bacterial infections are a feature of HIV infection in children(21). Only one 3 year old HIV infected patient had had pneumococcal meningitis 8 months previously. No patients had recurrence of meningitis during the study period.



Seizures were a common symptom in this study group. Feigin (15) gives a figure of 20% which is the same as that from Tefuarani's study in Papua New Guinea (3). Seizures which occur prior to or during the first few days of hospitalization are of no particular prognostic significance as far as development of a permanent seizure disorder is concerned (15). However, seizures that are focal or are difficult to control or persist beyond the 4th day in hospital as well as seizures that occur for the first time late in the patient's hospital course are of a greater significance and have been associated with permanent neurological sequelae of meningitis (15,27). The level of consciousness of a child with meningitis at the time of hospital admission has prognostic significance (14). An adverse outcome is associated with coma as opposed to lethargy or drowsiness. The relationship of the state of consciousness and outcome are discussed under mortality.

### (c) Aetiology of Bacterial Meningitis

The isolation rate of organisms from CSF by culture of 53% is comparable to figures from Malawi, India and Papua New Guinea (7,18). Higher isolation rates have been reported in other studies (35,21). Causes of the low isolation rate include prior antibiotic therapy (33%) or delay in the processing of CSF. Latex agglutination is a useful adjunct to the laboratory diagnosis of meningitis in cases where conventional procedures fail to identify an organism.

Streptococcus pneumonia and H. influenza were the main causative agents of meningitis. Streptococcus pneumoniae has also been found to be the commonest causative organism of bacterial meningitis in other African countries outside the meningitis belt (17,26). Streptococcus pneumoniae is associated with higher mortality and morbidity than H influenza and N meningitis (7,16,25,26). High mortality has been described as a characteristic feature of pneumococcal meningitis in tropical Africa (16). Late diagnosis and poor medical care may play a role but Baird in his study on mortality from pneumococcal meningitis showed that mortality is highest among those with a short history (37). Some genetic predisposition to pneumococcal disease independent of possession of the sickle cell gene has been suggested as a possible explanation for this high mortality (16). All S.pneumoniae cultured from CSF and blood were sensitive to penicillin and chloramphenicol by the disc diffusion test.

Haemophilus influenzae type b isolates were also uniformly sensitive to chloramphenicol and ampicillin. Pneumococcal resistance to penicillin has now been described world wide. The disc diffusion sensitivity test in use in our laboratory cannot distinguish between intermediate and high-level resistance of pneumococci. Mean inhibitory concentration of penicillin against the pneumococci is used to assess degree of resistance.

Other organisms isolated were Salmonella group D, S. viridans and H parainfluenza is a human commensal but can infrequently become pathogenic. Meningitis and endocarditis are the most frequently reported infections caused by H parainfluenza (37a). Hemophilus parainfluenza was isolated from both CSF and blood of a 5 month old infant who did not have clinical HIV infection. The organism was sensitive to chloramphenicol, ampicillin and gentamicin. Although usually regarded as a human commensal parainfluenza can be pathogenic causing meningitis or endocarditis in normal patients (37a).

Streptococcus viridans was isolated in the CSF of a 4 month old baby boy who did not have clinical HIV infection. His blood culture yielded no growth. He did not have evidence of congenital heart disease. Streptococcus viridans is an alpha-haemolytic streptococcus which commonly causes bacterial endocarditis. No previous association with meningitis was found in the literature.

(d) Mortality

The overall case fatality rate of 20% from bacterial meningitis was lower than the 43% reported by Kendall in 1971 (18). Bushan and Chintu reported a mortality rate of 21% for infants and children under 12 years of age but the age group 4 weeks to 4 years had a much higher figure of 30% (17). A study done in Papua New Guinea had a case fatality rate of 16.7% for children between 2 weeks and 10 years of age (3). Mortality from bacterial meningitis is highest in the first year of life. In this study mortality was higher in children older than 12 months of age, (31%) compared with 17% in those under 12 months of age but this was not statistically significant. Poor prognostic factors in the older age group were, unconsciousness on admission which was present in 2 patients, recurrence of meningitis in 1 patient and focal neurological signs. Three out of the 4 patients were also HIV antibody positive with clinical signs of HIV infection. Some studies have shown that a short history and impaired consciousness on admission are associated with poor outcome (3,8,14). Fifty four percent of the deaths in this study occurred in patients who were unconsciousness on admission to hospital.

There was an apparent association between malnutrition and mortality in this study. Case fatality rate of the malnourished children was 29% compared with 16% in the well nourished children. Conclusions regarding mortality in relation to the infecting organisms could not be drawn because of the small sample size.

(e) Sequelae at discharge Table VII

Abnormalities were detectable on neurological examination at the time of discharge in 7 out of the 44 (16%) survivors. Shaitout et al found a 28% frequency of sequelae after pneumococcal meningitis compared with 7% after Haemophilus (38). Neurological sequelae are reported to be more common after pneumococcal meningitis than after Haemophilus (14,27,38).

A significant association was found between seizures and sequelae at discharge ( $P=0.03$ ). Seizures which are associated with neurologic sequelae tend to be focal and occur late during the course of treatment. The observed sequelae in patients in this study included quadriparesis, muscular hypertonia and hypotonia and seventh nerve palsy. (14,27,39). Ataxia can also occur as a sequela of bacterial meningitis (39)

(f) Follow up Table X

Children were followed up at varying periods ranging from 2-6 months after discharge. Neurologic abnormalities detected included spastic cerebral palsy, development delay and hearing



deficits. It was not possible to compare neurologic examination on discharge from hospital with a follow up examination because only 27 out of the 44 survivors came back.

No abnormalities had been detected on discharge in the children who had subsequently isolated developmental delay. However patients who developed cerebral palsy had exhibited signs of neurological deficit at the time of discharge in the form of hypertonia or hypotonia of muscles. A large prospective study of bacterial meningitis in children revealed that 32.8% of children had abnormalities detectable on neurologic examination at the time of discharge but 5 years later specific deficits were noted in only 11.1% (14, unpublished data). Studies have shown that neurologic abnormalities detected soon after the acute illness do not always persist (14,27).

Hearing deficit was present in 4 of the 15 patients tested. The frequency of hearing loss of 27% is not representative as it was done on approximately 33% of the survivors whose selection may have been biased. Sensorineural hearing loss occurs more frequently than other neurological deficits after meningitis. In Fortnum's review of hearing impairment after meningitis incidence rates as low as 3.5% or as high as 37.2% were quoted (40). The wide range reflects large sampling errors associated with small samples and also bias due to case selection and methodology (40).



## HIV Infection

Over the last decade, HIV infection in children has emerged as a new public health problem. Countries in sub-Saharan Africa, the Caribbean and South America where heterosexual transmission is the major route of HIV transmission are particularly affected (41). In a survey done in 1991, HIV seroprevalence was 18% among pregnant women booked for antenatal care at Harare Hospital and two of its peripheral municipal clinics (42). The rate of mother-to-child transmission of HIV has been estimated to vary from 33 to 49% in Africa (41). Likewise infant mortality rate may increase by as much as 30% in high HIV prevalence areas of Africa (43).

HIV infection is often manifested as recurrent serious bacterial infections (eg pneumonia, sepsis, meningitis), failure to thrive, generalised lymphadenopathy, Pneumocystis carinii pneumonia, hepatosplenomegaly or lymphocytic interstitial pneumonitis (21,23). Death commonly results from sepsis or pneumonia. Children born to HIV positive mothers in Africa have a higher mortality and morbidity than those in Europe (41). Some of the reasons given for this disparity include (a) the higher mother-to-child transmission rates (b) exposure to pathogens in the environment resulting in salmonella and pneumococcal bacteraemias being diagnosed more frequently in immunocompetent febrile children in Africa than in the USA and (c) malnutrition an endemic problem in Third World countries may aggravate the cause

of HIV disease. The most common CNS manifestations of HIV infection are due to the virus itself (41,21,45). Primary and persistent HIV infection in the CNS is responsible for the HIV associated progressive encephalopathy of childhood (44). The incidence of this condition following vertical HIV transmission is unknown but a "trimodal" pattern of clinical features has been suggested (44). Early onset disease occurs between 5-12 months of age and presents as a severe encephalopathy associated with a high mortality (41,44). The late or childhood onset is a more benign disease and the third category occurs in late childhood and preadolescence (44). Common neurological findings of HIV encephalopathy include developmental delays, corticospinal tract signs, acquired microcephaly, cognitive impairment and movement disorders (44,45). The CNS can also be affected by opportunistic infections but these are rare in children as opposed to adults probably because most of them are caused by reactivation of latent infection and the young child has had a relatively short period of exposure to these pathogens (21,44,45).

While most attention has been focused on the effect of HIV on the CNS in HIV infected children, it is important to remember that these patients may also acquire infection with those organisms commonly causing CNS infections in the general population (45,46).

There have been few reports of bacterial meningitis HIV infected children in the literature (46). HIV infected children presenting with clinical features suggestive of meningitis should be investigated and CSF examined for both common and opportunistic pathogens.

In the present study it was found that the common pathogens S.pneumoniae and H.influenzae infected children with clinical HIV infection. This is expected because HIV infected children are prone to infection by encapsulated organisms especially S. pneumoniae. The susceptibility to infection with polysaccharide-encapsulated bacteria in the face of hypergammaglobulinaemia has been explained by evaluation of immunoglobulin subclass level in patients with disease due to HIV (46). Decreased levels of IgG2 have been found in adults with AIDS. IgG2 subclass levels in patients with HIV disease and pyogenic infection were significantly lower than HIV negative controls, consistent with the hypothesis that protective antibody against polysaccharide pathogens is primarily found in this subclass.

One HIV infected patient had Salmonella group D meningitis. In a review of all cases of meningitis in Brazil (1973-1982), salmonella species caused 28% of the gram negative enteric infections in those under 2 years of age (47). The main age group affected was 2 - 6 months. No mention is made of these

children's nutritional or immune status.

Salmonella species are a common cause of bacterial illness in HIV infected children (21,46). Salmonella species are also a cause of diarrhoeal diseases in HIV infected children and there is often an association with invasive disease (46) which may lead to bacterial meningitis. No case of cryptococcal meningitis was found by microscopy using the India ink stain.

One of the features of HIV infection in children is failure to thrive. There was a significant relationship between nutritional status and HIV status ( $p = 0.01$ ). As has already been discussed malnutrition has not been found to be a risk factor for meningitis. A higher incidence of pneumonia and bacteraemia in malnourished patients may however predispose them to meningitis.

Clinical course in hospital did not differ between clinically HIV infected patients and those without. Mortality was even lower in the clinical HIV group but not significantly so. Incidence of neurological sequelae was related to the presence of seizures during the course of meningitis and not to HIV infection. The number of patients available for follow up was not sufficient to draw up conclusions but because of the neurotropic nature of the HIV and the HIV associated progressive encephalopathy of childhood it may be difficult to attribute neurological abnormalities to bacterial meningitis per se. HIV infected children commonly have chronic suppurative otitis media, a known



cause of deafness.

Again it may be difficult to attribute hearing deficit to meningitis alone with this confounder.

Bacterial meningitis appears to behave in the same manner in children with or without HIV infection as regards the clinical features on presentation, bacterial aetiology and short term outcome. It is therefore imperative that patients be investigated thoroughly on clinical suspicion and be treated adequately with the appropriate antibiotics. Corticosteroids may be used in conjunction with antibiotics for therapy of H.influenza type b and pneumococcal meningitis because of the beneficial effect in preventing hearing loss (45).

Theories of how hearing impairment occurs after meningitis include:

- (a) suppurative labyrinthitis. From direct spread of infection from the subarachnoid space, leading to destruction of sensory structures with no recovery of hearing.
- (b) serous labyrinthitis resulting in partial and reversible hearing loss and
- (c) direct nerve fibre damage and secondary ischemic damage (27).

It is now generally accepted that any damage to hearing occurs early in the infection according to studies quoted by Fortnum (40). Early diagnosis and treatment of meningitis do not prevent deafness in many children in whom loss of hearing develops as a consequence of bacterial meningitis (14). Ways of reducing the risk of deafness include prevention of meningitis by immunization and the use of dexamethasone prior to or with the first dose of antibiotic (7,14). In the present study dexamethasone was used in only 10 patients and in only 5 of them was it used appropriately.



## CONCLUSION

No differences were apparent in the clinical presentation and aetiology of bacterial meningitis between the clinical HIV and non HIV group. Case fatality rates were comparable in the 2 groups. There was no significant difference in mortality between children aged less than 12 months those older than 12 months. A risk factor for mortality was unconsciousness on admission. Seizures before and after admission were a significant risk factor for development of neurological sequelae and not for mortality.

Neurologic sequelae on follow up could not be compared owing to the high drop out rate but confounding factors were the possibility of HIV progressive encephalopathy of childhood causing symptoms and also the possibility of chronic suppurative otitis media contributing to the hearing deficit. The difference between HIV infected and non-HIV infected children may have been small and was missed because of the small sample size.

## RECOMMENDATIONS

1. Meningitis in children who have HIV infection has a good short term prognosis and should be treated aggressively.
2. HIV infected children with meningitis respond well to standard treatment given for bacterial meningitis and therefore management should not differ from that given to children without HIV infection.
3. Laboratory diagnosis of bacterial meningitis should be improved by the immediate transport to the laboratory of the CSF and processing. Adjunctive tests such as latex agglutination would be useful in improving identification of organisms.

### QUESTIONS

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APPENDIX I

Questionnaire - Dr.Bwakura

Study no.\_\_\_\_ Hospital no\_\_\_\_  
Ward\_\_\_\_ D.of Adm.(dd/mm/yy)\_\_\_\_  
Name\_\_\_\_ D.of B.(dd/mm/yy)\_\_\_\_  
Age(m)\_\_\_\_ Sex(M/F)\_\_\_\_  
Address\_\_\_\_  
Bwt(g)\_\_\_\_ Wt on Adm (g)\_\_\_\_ 50th Centile \_\_\_\_

Presentation

| Symptom                     | Duration(d)  |
|-----------------------------|--------------|
| Vomiting(Y/N)_              | Vom(days)_   |
| Grunting(Y/N)_              | Grun(days)_  |
| Fever(Y/N)_                 | Fev(days)_   |
| Convulsions(Y/N)_           | Conv(days)_  |
| Headache(Y/N)_              | Head(days)_  |
| Irritability(Y/N)_          | Irrit(days)_ |
| Bulging Fontanelle(Y/N)_    | Font(days)_  |
| Anorexia/Poor Feeding(Y/N)_ | Feed(days)_  |
| Drowsiness(Y/N)_            | Drows(days)_ |
| Others                      |              |

---

|                       |                             |
|-----------------------|-----------------------------|
| Loss of Weight (Y/N)_ | Diarrhoea Chronic(Y/N)_     |
| Cough Chronic(Y/N)_   | Previous Infant Death(Y/N)_ |
|                       | Detail_____                 |

Past Medical History

Vaccinations Appropriate for:

|  |                           |
|--|---------------------------|
| Age(Y/N)_                                  | Hot body(Y/N)_            |
| Diarrhoea(Y/N)_                            | Previous meningitis(Y/N)_ |
| Vomiting(Y/N)_                             |                           |
| Previous ARI (Admission to hospital)(Y/N)_ |                           |
| HIV1(Pos,Neg,Unknown)(P,N,U)_              |                           |

Examination

|   |                            |
|---|----------------------------|
| Temp on adm ____                              | Kernig's sign (Pos/Neg)_   |
| Bulging fontanelle(Y/N)_                      | Neck Stiffness(Y/N)_       |
| Adm. Level of consciousness(Grade 1,2,3,4,5)_ |                            |
| Tone(Increase,Normal,Decrease)(I,N,D)_        |                            |
| Focal neurological signs_____                 |                            |
| Generalised lymphadenopathy(Y/N)_             |                            |
| Hepatomegaly(Y/N)_                            | Splenomegaly(Y/N)_         |
| Oral thrush(Y/N)_                             | Otitis media(Y/N)_         |
|   | if Yes Acute/Chronic(A,C)_ |
| Head circumference(mm)____                    | Others_____                |
| Skin rash(Y/N)_                               |                            |
| Development                                   |                            |
| Smiling(Y/N)_                                 | Crawling(Y/N)_             |
| Sitting(Y/N)_                                 | Walking(Y/N)_              |
| Speaking(Y/N)_                                |                            |

Treatment prior to presentation

|                  |                |                |
|------------------|----------------|----------------|
| Drug             | Duration(days) | Doses(no)      |
| antipyretic_____ | apyr(d)____    | apyr(dose)____ |

anticonvulsant \_\_\_\_\_  
antibiotic \_\_\_\_\_  
others(eg muti) \_\_\_\_\_

aconv(d) \_\_\_\_\_  
abiot(d) \_\_\_\_\_  
othr(d) \_\_\_\_\_

aconv(dose) \_\_\_\_\_  
abiot(dose) \_\_\_\_\_  
othr(dose) \_\_\_\_\_

### Investigations

#### CSF

Appearance(Normal,Turbid,Blood)(N,T,B) \_\_\_\_\_  
Glucose \_\_\_\_\_  
Protein \_\_\_\_\_  
Globulin(-,+,++,+++,++++)(0,1,2,3,4) \_\_\_\_\_  
WBC \_\_\_\_\_  
PMN \_\_\_\_\_  
India Ink (Y/N) \_\_\_\_\_  
Gram \_\_\_\_\_  
Culture Growth (Y/N) \_\_\_\_\_  
if Yes organism \_\_\_\_\_  
and Sensitive to \_\_\_\_\_  
Latex agglutination(Y/N) \_\_\_\_\_  
if Yes specify \_\_\_\_\_

#### Blood

Glucose \_\_\_\_\_ WBC \_\_\_\_\_  
Culture Growth (Y/N) \_\_\_\_\_  
if Yes organism \_\_\_\_\_  
and Sensitive to \_\_\_\_\_  
HIV2(Pos,Neg,Not Done)(P,N,ND) \_\_\_\_\_

#### Treatment

| Drug        | Doseage     | Date Start<br>(dd/mm/yy) | Stop<br>(dd/mm/yy) | Duration<br>(days) |
|-------------|-------------|--------------------------|--------------------|--------------------|
| Drug1 _____ | Dose1 _____ | Start1 _____             | Stop1 _____        | Dur1 _____         |
| Drug2 _____ | Dose2 _____ | Start2 _____             | Stop2 _____        | Dur2 _____         |
| Drug3 _____ | Dose3 _____ | Start3 _____             | Stop3 _____        | Dur3 _____         |
| Drug4 _____ | Dose4 _____ | Start4 _____             | Stop4 _____        | Dur4 _____         |
| Drug5 _____ | Dose5 _____ | Start5 _____             | Stop5 _____        | Dur5 _____         |

#### Course

Temp subsided(hours) \_\_\_\_\_

#### Complications

Cranial nerve palsy(Y/N) \_\_\_\_\_  
Seizures(Y/N) \_\_\_\_\_  
focal(Y/N) \_\_\_\_\_  
if focal date start(dd/mm/yy) \_\_\_\_\_  
focal duration (days) \_\_\_\_\_  
generalised(Y/N) \_\_\_\_\_  
if general date start(dd/mm/yy) \_\_\_\_\_  
general duration(days) \_\_\_\_\_  
both(Y/N) \_\_\_\_\_  
if both date start(dd/mm/yy) \_\_\_\_\_

both duration(days)\_\_\_\_  
coma(Y/N)\_  
Serial OFC daily (mm) \_\_\_\_\_

Outcome

Alive or Died (A,D) \_  
if Died less than or greater than 24hrs (L,G) \_  
Sequelae at discharge(Y/N)\_  
(Disch)OFC(mm)\_\_\_\_\_ Disch)Tone(Increase,Normal,Decrease)(I,N,D)\_  
Cranial nerves \_\_\_\_\_  
Disch. Level of consciousness(Grade 1,2,3,4,5)\_  
Reflexes(Increase,Normal,Decrease)(I,N,D)\_  
Hemiparesis(Y/N)\_  
Deafness(Y/N)\_

Follow Up

Three month

Name \_\_\_\_\_

|                          |   |  |  |
|--------------------------|---|--|--|
| F.U.no _____             | Motor level<br>(ML)appr for age(Y/N)_<br>(ML)mild delay(Y/N)_ | Psychosocial<br>(Ps)appr for age(Y/N)_<br>(Ps)mild delay(Y/N)_ | Neuro Ass.<br>Normal OFC% _____<br>Abnormal-details<br>_____ |
| Age _____                | (ML)Sign.delay(Y/N)_  | (Ps)Sign.delay(Y/N)_   |  |
| Time since illness _____ | (ML)Level of Function<br>(ML)LofF _____                       | (Ps)Level of Function<br>(Ps)LofF _____                        |  |

Six month

|                          |   |  |  |
|--------------------------|---|--|--|
| F.U.no _____             | Motor level<br>(ML)appr for age(Y/N)_<br>(ML)mild delay(Y/N)_ | Psychosocial<br>(Ps)appr for age(Y/N)_<br>(Ps)mild delay(Y/N)_ | Neuro Ass.<br>Normal OFC% _____<br>Abnormal-details<br>_____ |
| Age _____                | (ML)Sign.delay(Y/N)_  | (Ps)Sign.delay(Y/N)_   |  |
| Time since illness _____ | (ML)Level of Function<br>(ML)LofF _____                       | (Ps)Level of Function<br>(Ps)LofF _____                        |  |

Final Summary

Evidence of neurological deficit (Y/N)\_  
Physical Residual handicap(Y/N)\_  
if Res Yes Detail \_\_\_\_\_  
Visual handicap(Y/N)\_  
if Vis Yes Detail \_\_\_\_\_  
Hearing deficit(Y/N)\_  
if Hear Yes Detail \_\_\_\_\_  
Mental Residual handicap(Y/N)\_  
if Mental Yes Mild,Moderate,Severe(Mild,Mod,Sev)\_\_\_\_\_