

HIV INFECTION AMONG HOSPITALIZED CHILDREN AT THE UNIVERSITY
TEACHING HOSPITAL LUSAKA:
DIAGNOSIS AND RISK OF TRANSMISSION THROUGH THERAPEUTIC
PRACTICES. 240173

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CHAPTER ONE

I N T R O D U C T I O N

Although Acquired Immunodeficiency Syndrome (AIDS) was first described in adults (1,2), it has become apparent over the past few years that human immunodeficiency virus (HIV) is a major cause of childhood mortality and morbidity (3,4). Two main modes of transmission have been well documented for almost all paediatric AIDS cases, namely vertical transmission that is from mother to child and through transfusion of unscreened blood and infected blood products (3 - 13).

The risk of vertical transmission can be reduced by preventing infection in women of child-bearing age. Health education programmes with emphasis on risks of HIV infection through sexual practices are currently being conducted throughout Zambia by the health education unit in the Ministry of Health, family planning and sexually transmitted diseases clinics, the media, non governmental organisations; for example ANTI - AIDS Clubs in Schools, Copperbelt Health Education project, religious groups and Society of Women and AIDS in Zambia. Increasing public awareness may result in behavioral sexual change which will hopefully result in people seeking for counselling and testing before planning a marriage or pregnancy in cases where they are worried about their sexual behaviour.

In order to reduce infection through blood and blood products Zambia in conjunction with World Health Organisation (WHO) and other donor agencies

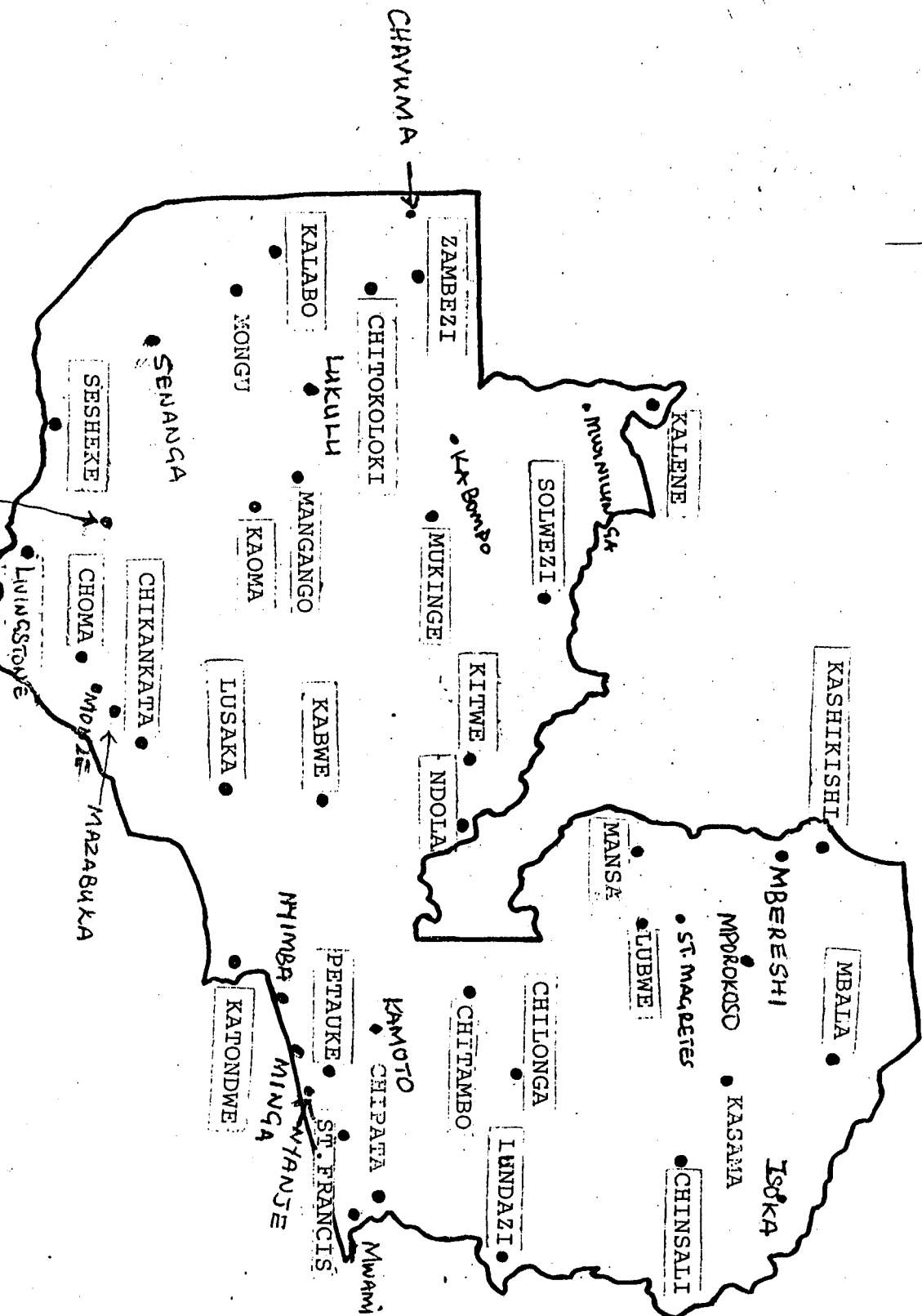
have set up 65 blood screening centres all over the the country (65 out of 100 hospitals, see map). In addition strict guidelines for indications of blood transfusion have been drawn up (30).

Seropositive children born of seronegative mothers and with no previous history of blood transfusion are occasionally seen in paediatric practice. The question then arises as to how these children acquired the HIV infection. Penetrative sexual abuse should be considered although no studies have been done in Zambia to evaluate this risk. Studies on household contacts of HIV infected persons have failed to demonstrate transmission by casual contact (14,15,16).

With increasing numbers of HIV infected persons in the community and health institutions, the use of unsterilised skin penetrating instruments should be considered as a potential hazard of HIV transmission. The risk is probably minimal but there are no documented studies done in Zambia to evaluate the importance of this risk.

An out break of HIV infection at a children's hospital in USSR was reported at the beginning of the 1989 where 75 children were infected from a single infected child through use of unsterilised needles, syringes and catheters (17,19). The infection spread to children in other hospitals through similar practices (17,19). In Romania unscreened microtransfusion together with use of unsterilised needles resulted in over 500 children being infected with HIV (18). These experiences in Romania and USSR are cause of great concern if AIDS control programmes are to be effective.

DISTRIBUTION OF SCREENING CENTRES THROUGHOUT ZAMBIA



The important question therefore is "Are children acquiring HIV through therapeutic practices?". The importance of HIV transmission through contaminated skin penetrating instruments is significant in Zambia for the following reasons :

1. There is usually strong preference for traditional therapies involving scarification marks amongst patients in Zambia.
2. Economic constraints may result in improper practices such as reuse of disposable equipment.
3. Congestion and high patient turn over because of limited health institutions may result in inadequate sterilisation or no sterilisation of tools and equipment.
4. Accidents may occur, resulting in HIV transmission from child to child in view of the high seroprevalence.
5. There is strong preference for injections among patients in Zambia

CHAPTER TWO

Literature ReviewRISK FACTORS

Human Immunodeficiency Virus (HIV) infection is spreading fast in Africa where the major mode of transmission is heterosexual (5). It is estimated that 8 - 10 million adults are currently infected with HIV through out the world, out of which 5 million are estimated to be in Africa (32). The ratio of women to men infected with HIV in Africa is 1:1 (32). Most of the infected women are of child bearing age that is between 15 and 49 years (5,31,32). 25 - 40 % of these infected women are likely to pass on the infection to their babies (5,20). Infection in children is therefore closely linked to infection in women. Infection is acquired :

- a. In utero through transplacental infection of the foetus.
- b. Through blood and vaginal secretions during labour or delivery.
- c. Postnatally through breast milk.

At present studies have shown that vertical transmission accounts for 75% of all known cases of infection in infancy and early childhood (20,33). A study on an aborted foetus from an HIV infected mother showed that infection can occur as early as 15 weeks of gestation (48). Very few studies have been able to show transmission of HIV through breast milk (21). However HIV has been cultured from breast milk of infected women (5).

Although most children acquire HIV infection vertically, a considerable number of the infected children may acquire infection through contaminated blood and blood products (5,6,7,40). Studies in UK have shown that 85% of haemophiliacs are currently infected with HIV (7) while a study in Zambia has revealed that 100% of haemophiliacs are infected with HIV (40). Screening blood for HIV before transfusion is receiving a lot of attention through out the world. However, in Africa due to limited resources, screening of blood for HIV is limited to may be only one or several major hospitals. In Zaire and Uganda, blood transfusion for anaemia resulting from malaria, in areas where routine screening is not practiced, has resulted in a significant number of children being infected with HIV (5,6).

There has been no evidence of HIV transmission by casual contact (15). Six studies done on family contacts of AIDS patients showed no transmission of HIV to older children (16). In a study by Hira et al in Lusaka, Zambia there was no evidence to show any association between seropositivity and contacts of AIDS patients. He was only able to show evidence of perinatal transmission (14).

Use of contaminated needles and syringes have been identified as potential modes of infection in Africa (9,17,18,24). In most parts of Africa economies are poor. The economic constraints have led to re-use of needles and syringes, cannulas and other skin penetrating instruments in medical practice (15). In traditional medical practices, scarification marks, have been identified as high risk of HIV transmission (16).

In the developed world however studies done in North America and Europe have demonstrated that the risk of nosocomial transmission is low (27,28,29) where as in USSR and Romania intravenous injections were shown to have been the possible source of HIV infection in the outbreaks at some hospitals (17,18,19). Although some studies done in Africa have shown a correlation between injection and HIV infection, others have shown contradictory results (22,23). The possible explanation for the differences in results may lie in difference in injections practices and safety precautions.

Skin scarification marks for beauty or treatment and other traditional skin piercing practices may transmit HIV since most of the instruments may be used from one patient to the other without adequate sterilisation due to ignorance by the traditional healer, Mann et al in a study in Zaire however found no significant increased risk related to scarification therapy between HIV positive and negative patients (9). Childhood vaccinations, surgery and acupuncture were also not associated with seropositivity in Zaire (9).

DIAGNOSIS

Clinical diagnosis of HIV infection in children is difficult. World Health Organisation (WHO) has adopted a paediatric clinical case definition with the hope of minimizing under diagnosis and under reporting (fig.1) However evaluation of this clinical case definition in Africa and Europe on African children have shown that it lacks sensitivity and specificity (38,39).

Fig 1: WHO case definition of Paediatric AIDS.

MAJOR: Weight loss or abnormally slow growth.

Chronic diarrhoea for more than a month.

Prolonged or intermittent fever for more than one month

MINOR: Generalised lymphadenopathy

oral pharyngeal candidiasis

recurrent common infection
generalised dementia.

Persistent cough for more one month.

Confirmed infection with HIV in the mother.

clinical diagnosis of AIDS using the WHO criteria is made when there is presence of two majors and two minors and in the absence of known immunosuppression (5).

The symptomatology in fig 1 is nonspecific and occur commonly in paediatric practice in Africa, making it difficult to arrive at a definite AIDS diagnosis. Colenbunders reported that when other causes of immunosuppression are removed the specificity may be as high as 85% - 95% (38).

Laboratory diagnosis of childhood HIV infection is hampered by the presence of previously acquired maternal antibodies and most commercially available tests such as Elisa and Western blot are antibody tests. Cultures are difficult to perform and are expensive. HIV specific IgM studies are nonspecific and are unreliable (43). In addition serum antigen is usually difficult to analyse when excess serum antibody is present, as

in infants with maternally acquired antibody (43). The antibody tests are useful beyond 18 months when it is expected that maternal antibodies have waned off (5). Ou et al have recently reported the use of a relatively new technique involving gene amplification called polymerase chain reaction (PCR) in the peripheral-blood monocyte cells of HIV infected persons. This technique detects HIV proviral sequence using specific restriction enzymes. This test can be performed using very small amounts of blood and is proving useful in detecting infection in infants (43). This test however is not available in Zambia.

In view of the problems in making a clinical or laboratory diagnosis of AIDS in children in Zambia, Ministry of Health has come up with its own paediatric AIDS diagnostic criteria (fig 2) based on symptomatology commonly observed. Chintu et al found 91.4% specificity, 79.3% sensitivity and a positive predictive value of 86.8% with these criteria (42). This definition has therefore been found to be more useful in Zambia.

Fig 2: Zambia's case definition of paediatric AIDS.

Major signs

- * recurrent fever > 1 month
- * recurrent oro-pharyngeal candidiasis
- * recurrent pulmonary infections

Minor signs

- * chronic diarrhoea > 1 month

- * weight loss or abnormally slow growth
- * generalised lymphadenopathy
- * persistent cough > 1 month
- * extrapulmonary tuberculosis
- * Pneumocystis carinii pneumonia
- * confirmed maternal HIV - 1 infection.

Paediatric AIDS is suspected in an infant presenting with two majors and two minors in the absence of known cause of immunodeficiency.

Malaria, malnutrition, acute respiratory tract infection and diarrhoea continue to be the major causes of childhood mortality in Zambia but no study has been done to determine the impact of seropositivity on the outcome of these illness. A recent UNICEF study has estimated the impact of AIDS on child mortality in 10 Central and East African countries:- Burundi, Central African Republic, Congo, Kenya, Malawi, Rwanda, Tanzania, Uganda, Zaire, Zambia. By the end of the century, the death toll from AIDS among under fives in these countries alone, if present HIV infection trends continue, will reach 2.7 million. The under five mortality instead of dropping to around 132 deaths per 1000 live births as earlier projected, is likely to rise to between 159 and 189 per 1000. (20).

Since studies done on paediatric HIV infection in Zambia are limited, there is need to evaluate the risk factors that may be involved in HIV transmission more especially those involving therapeutic practice so that measures can be drawn up aimed at reducing some of these risks. It is also

important to evaluate the sensitivity and specificity of the WHO clinical case definition since correct reporting of AIDS cases is necessary for planning purposes.

CHAPTER THREE

AIM AND OBJECTIVES

AIM OF STUDY.

This study proposes to identify whether medical practices in and outside hospital may be responsible for HIV transmission in children with seronegative parents.

OBJECTIVES.Main objective:

To estimate the overall prevalence of seropositive children with seronegative mothers among hospitalised children, who may have acquired infection by ~~other~~ routes other than vertically.

Specific objectives.

1. To estimate the rate of seropositivity amongst hospitalised children.
2. To evaluate the WHO clinical case definition for AIDS diagnosis in children.
3. To evaluate the role of hospitalisation, medical injections and scarification therapy in HIV transmission.

CHAPTER FOUR

MATERIALS AND METHODSStudy design.

The study is a cross sectional study evaluating HIV infection pattern among hospitalised children and an unmatched case control analysis of risk factors associated with HIV transmission.

Study subjects.

Children admitted to the Department of Paediatrics at the University Teaching Hospital (UTH) were selected for the study. Recruitment was done between 14.00 and 18.00 hours from Monday to Friday regardless of the admission diagnosis. The study period was from October 1990 to March, 1991.

An informed consent (appendix 2) was obtained from the mother before inclusion of each child in the study. Mothers who consented were interviewed by use of a standardised questionnaire (appendix 1). Blood was taken from both the mother and child for HIV testing. HIV testing allowed the designation of four groups.

GROUP 1

MOTHER HIV NEGATIVE AND CHILD HIV POSITIVE

This group of children were the "cases" in the study. Mothers and children in this group were counselled and treated after confirmatory

testing. The mother was retested at three months to exclude delayed seroconvertors.

GROUP 2

MOTHER HIV NEGATIVE AND CHILD HIV NEGATIVE

This group formed the unmatched controls in the study.

GROUP 3

MOTHER HIV POSITIVE AND CHILD HIV POSITIVE

This group was excluded from the study but was counselled and any ailments treated.

GROUP 4

MOTHER HIV POSITIVE AND CHILD HIV NEGATIVE

This group was excluded from the study but counselled and any ailments treated.

This study compared the exposure to various risk factors in the two groups - children HIV seronegative on joining the study and those seropositive and whose mothers were seronegative. The study attempted to identify possible risk factors for seroconversion. Risk factors included; blood transfusion, previous hospitalisation, previous out patient and inpatient medical injections for treatment and traditional skin piercing procedures and treatments (appendix 1).

Inclusion Criteria.

1. children aged 6 months to 59 months.

2. Presence of biological mother for HIV screening .
3. Written consent

Sample size estimate

The lowest figure of incidence of seroconversion which was anticipated to be of public health importance was 1/1000 (0.001) The minimum sample size required to estimate such a low incidence rate is 2995, with confidence level of 95% (sample size determination; a user's manual-WHO/HST/ESM/186/1[Rev.1.1]). Thus if it is found that there is no seroconversion in a cohort of 3000 children, it can be concluded with 5% chances of error that HIV transmission occurs in less than 1 per 1000 hospitalisations.

Study site and Admission Policy .

The study was conducted at the University Teaching Hospital (UTH) Paediatric wing, which admits children below 14 years. The department caters for children referred from health centres around Lusaka, private clinics and other hospitals outside Lusaka. The department admits about 1000 to 1,500 patients per month depending on the month. The busiest months being October to February.

Admission Policy

Children coming for treatment are first seen in the outpatient department where those requiring admission are referred for admission. There are two main admitting wards, A04 and A02 and patients are admitted to either of these wards on alternate days. Children may subsequently be

transferred to specialised units such as Nutrition, Isolation, Neonatal and diarrhoea. Patients for this study were recruited from the two general wards on their admission days.

Specimen Collection and Processing.

5 mls of blood was obtained in 10 mls containers (sterilin, UK) by venipuncture from each mother and child. After labelling the blood was processed at the Immunology laboratory at UTH. The laboratory is the WHO referral centre and training centre for HIV screening. The samples were centrifuged and the serum collected in 1 ml aliquot serum containers (sastarol tubes, West Germany). One aliquot was kept in a refrigerator in case of further investigations

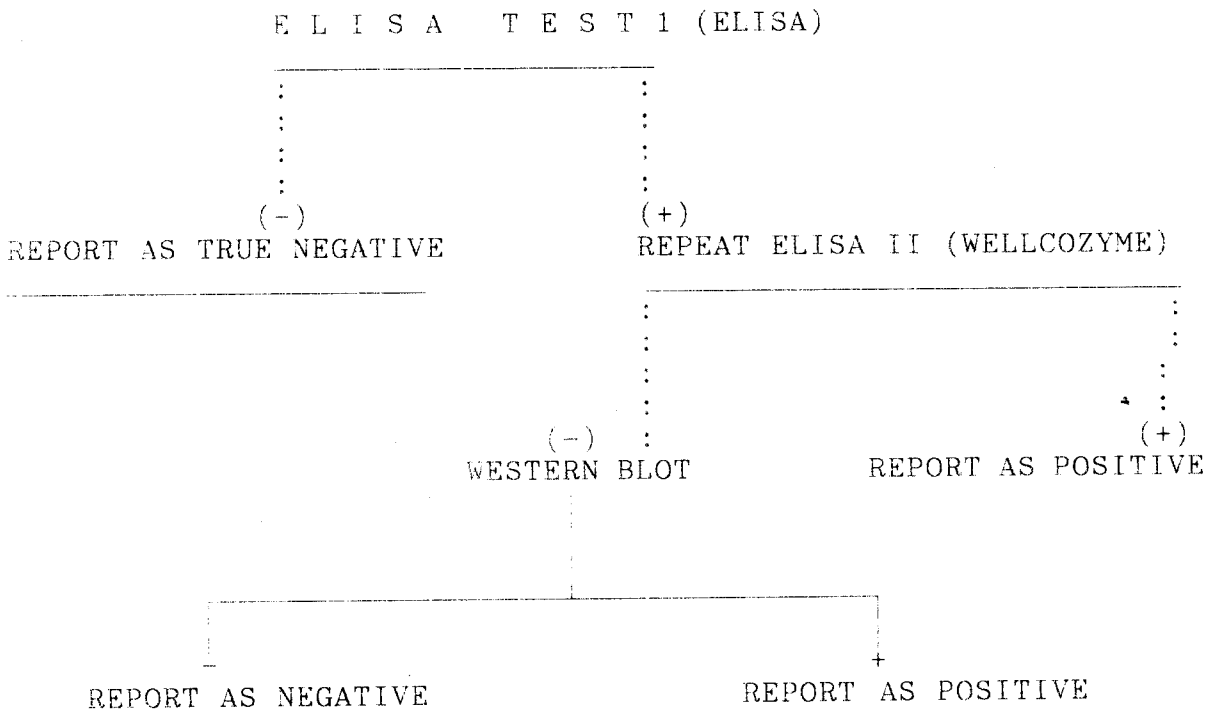
HIV Testing.

The HIV test was done using two Elisa systems employing different principles (Elavia AC - AB - AK 1, Wellcomzyme HIV Recombinant). Any sera that was indeterminant on Elisa was subjected to Western blot for confirmation of results (New LAV 1 AC - AB - AK). Western blot could not be performed on all samples because of economic constraints.

The initial test was done using Elavia which has been shown to have a sensitivity of 100% but specificity of 98% and a negative predictive value of 100% (30). All negative results on the initial test were taken as true negatives. All positive samples were subjected to a second Elisa (wellcozyme recombinant) which is a competitive Elisa, shown to have a sensitivity of 99%. Wellcozyme has a negative prediction of 98.9%

and positive prediction of 99.9% (30). Borderline or indeterminant results on any of the Elisas or both Elisas were subjected western blot for confirmation.

TESTING PROCEDURE



ELAVIA TEST(DIAGNOSTIC PASTEUR).

Elavia is an indirect enzyme immunoassay (EIA) for the detection of various HIV associated antibodies in human serum or plasma. The test is based upon the using of solid phases. The first one coated with purified and inactivated virus antigens (Ag positive), the other one coated with cellular antigen (Ag Negative) and of a peroxidase labelled affinity chromatograph purified goat anti human IGM antibody.

1. Patients and control serum samples are pippeted in Ag positive and Ag negative.

negative microplate wells. HIV antibodies, if any, bind to the immobilised virus antigen (Ag positive wells).

3. Wells are washed. Peroxidase labelled antihuman IgG antibody is added. It then becomes bound to the solid phase retained IgG.
4. Free/ bound separation takes place and immobilised enzyme colour reaction is developed in the presence of added substrate.
5. The reaction is stopped and absorbance reading is achieved through a spectrophotometer at 492 / 620 nm.

Wellcozyme HIV Recombinant.

Wellcozyme Recombinant is manufactured using HIV - 1 core and envelope antigens prepared by recombinant DNA techniques from HIV - 1 virus (weiss isolate) and captured specifically onto mouse monoclonal antibody to HIV - 1 previously immobilised in microwells.

Patients plasma and control sera are incubated in the wells with human anti HIV antibody conjugated to the enzyme horseradish peroxidase (conjugate). Competition for binding to the immobilised antigen occurs between antibodies to HIV - 1 in the sample or control serum and the conjugate: a specimen containing antibody to HIV - 1 will block the binding of the conjugate while specimen not containing antibody to HIV 1 will allow the binding of the conjugate to occur. After thorough washing of the wells to remove the sample and excess conjugate, a solution containing 3,3',5,5' - tetramethylbenzidine and hydrogen peroxide is added. After incubation the enzyme reaction is terminated with sulphuric

id to a yellow colour, which is read photometrically. The amount of conjugate, and hence colour, in the wells is inversely related to concentration of antibody to HIV in the sample.

Western Blot.

The test used is New LAV - BLOT 1 (Diagnostic Pasteur) is based on the principle of indirect Elisa on a nitro cellulose support containing all the protein which constitute the HIV - 1 virus.

Inactivated HIV - 1 viral proteins are separated according to their molecular weights by polyacrylamide gel electrophoresis in dissociating and reducing medium and subsequently transferred on to a nitrocellulose membrane sheet. The procedure comprises the following steps:

strip rehydration.

Incubation of the samples to be confirmed with the control serums.

If anti HIV - 1 antibody are present, They will bind to the virus proteins recognised, present on the strip.

After washing, the alkaline phosphatase - labelled anti human IgG anti antibodies are incubated. The conjugate binds to the anti HIV 1 antibodies captured on the solid support.

After washing and removing the excess conjugate, the colour development solution allows the enzymatic activity of the complex compounds bound to nitrocellulose to be evidenced.

The appearance of specific colour bands allows the presence of anti HIV 1 antibodies in the serum to be evidenced.

Interpretation of the results.

The presence of anti HIV 1 constitutive protein antibodies in sample examined is shown by the appearance of specific bands (blue - violet).

<u>Interpretation</u>	<u>Profile</u>
POSITIVE	2 ENU ± Gag ± Pol
NEGATIVE	Non - Classified bands
INDETERMINANT	1 ENU ± GAG ± POL
	GAG + POL
	GAG
	POL

Indeterminant results may reflect HIV 2, seroconversion or cross - reaction due to other retroviruses.

Data collection

A standard questionnaire was used (appendix 1.) after testing it in the wards. The questionnaire included questions relating to past exposure to risk factors such as :

- a. hospitalisation
- b. injections in hospital
- c. transfusion
- d. injections outside hospital
- e. scarifications for therapy.

The WHO clinical case definition for paediatric AIDS was used to make a

clinical impression of AIDS in the study population. All data collected was entered in a computer, Toshiba 1200.

Follow up.

Others of children recruited were reviewed at 6 weeks when results of the laboratory test were available. All those who were found to be positive (mother and / or child) were counselled by a trained counsellor.

Data management.

The software Epiinfo was used for data analysis. Chi square was utilised to test for significance of differences in the variables and whenever the sample number were below 10 fisher Exact test was used. When analysing the risk factors the study group were children who were HIV positive with HIV negative mothers (C + M -) and the comparative group were HIV negative children with HIV negative mothers (C - M -).

Ethical consideration.

The project was presented and cleared by the [?] Research Ethics Committee as well as the National AIDS Surveillance Committee.

CHAPTER FIVE

R E S U L T S

The results reported in this dissertation are preliminary results of an ongoing study. During the study period 250 children were recruited out of 9,563 children admitted to paediatrics.

SEX DISTRIBUTION OF THE STUDY POPULATION

There was no statistical difference in the sex distribution in the population which consisted of 127 (50.8%) girls and 123 (49.2%) boys. The sex ratio therefore was approximately 1:1 (Table 1).

TABLE 1: SEX DISTRIBUTION OF STUDY POPULATION

SEX	FREQ	PERCENTAGE
F	127	50.8%
M	123	49.2%
TOTAL	250	100.0%

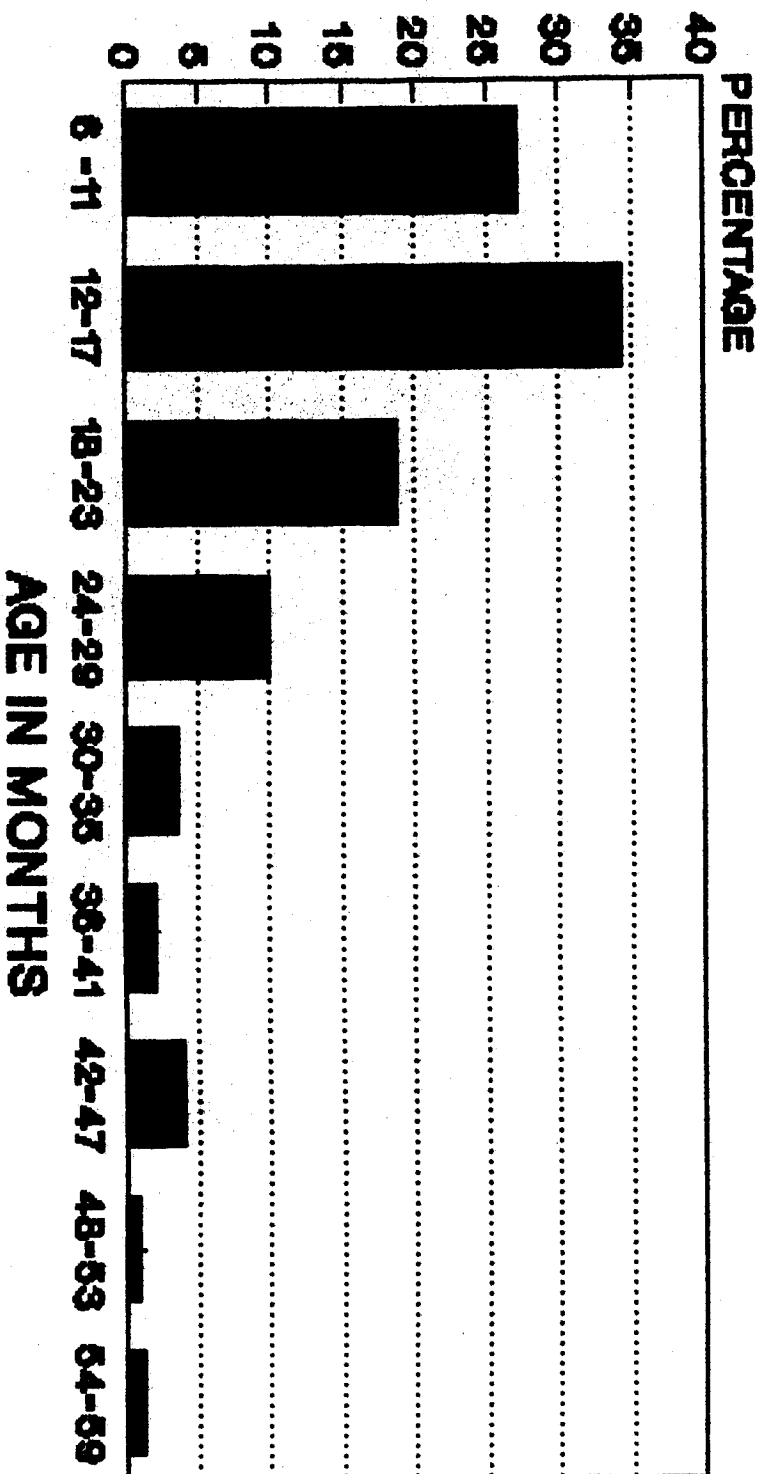
$$? P = 0.06.$$

AGE DISTRIBUTION OF THE STUDY POPULATION

The majority of the patients recruited were between 12 and 17 months of age (32.3%) followed by those between 6 and 11 months of age (26.7%) (figure 1). 59% of patients therefore were below 18 months.

FIG. 1.

AGE DISTRIBUTION OF STUDY POPULATION



■ Series 1

HIV LABORATORY RESULTS

247 children had their blood tested according to the described procedure (see methodology). 59 (23.9%) were found to be HIV antibody positive. The majority of these HIV antibody positive patients were between 12 and 17 months of age. (table 2, fig 2). Since this is the group with largest number of patients in the study population frequencies of HIV seropositivity in the different age group depending on the number of patients in that age group were calculated (fig 3). The seropositivity rate was highest between 24 and 29 months of age, as almost 50% of the patients recruited in this group were positive.

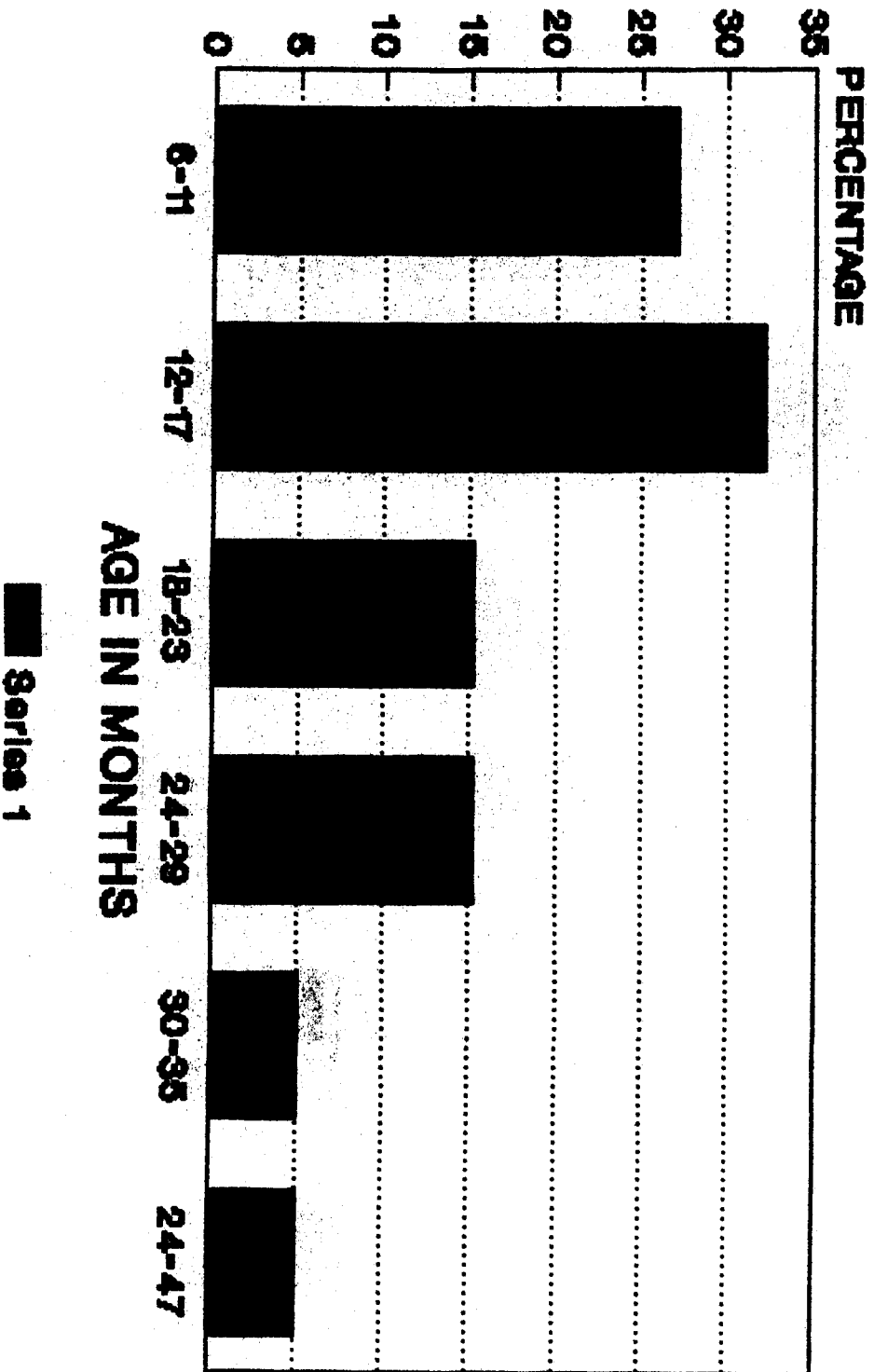
There was no significant difference in the sex distribution among the positives (P value = 0.8) (table 3).

TABLE 2:

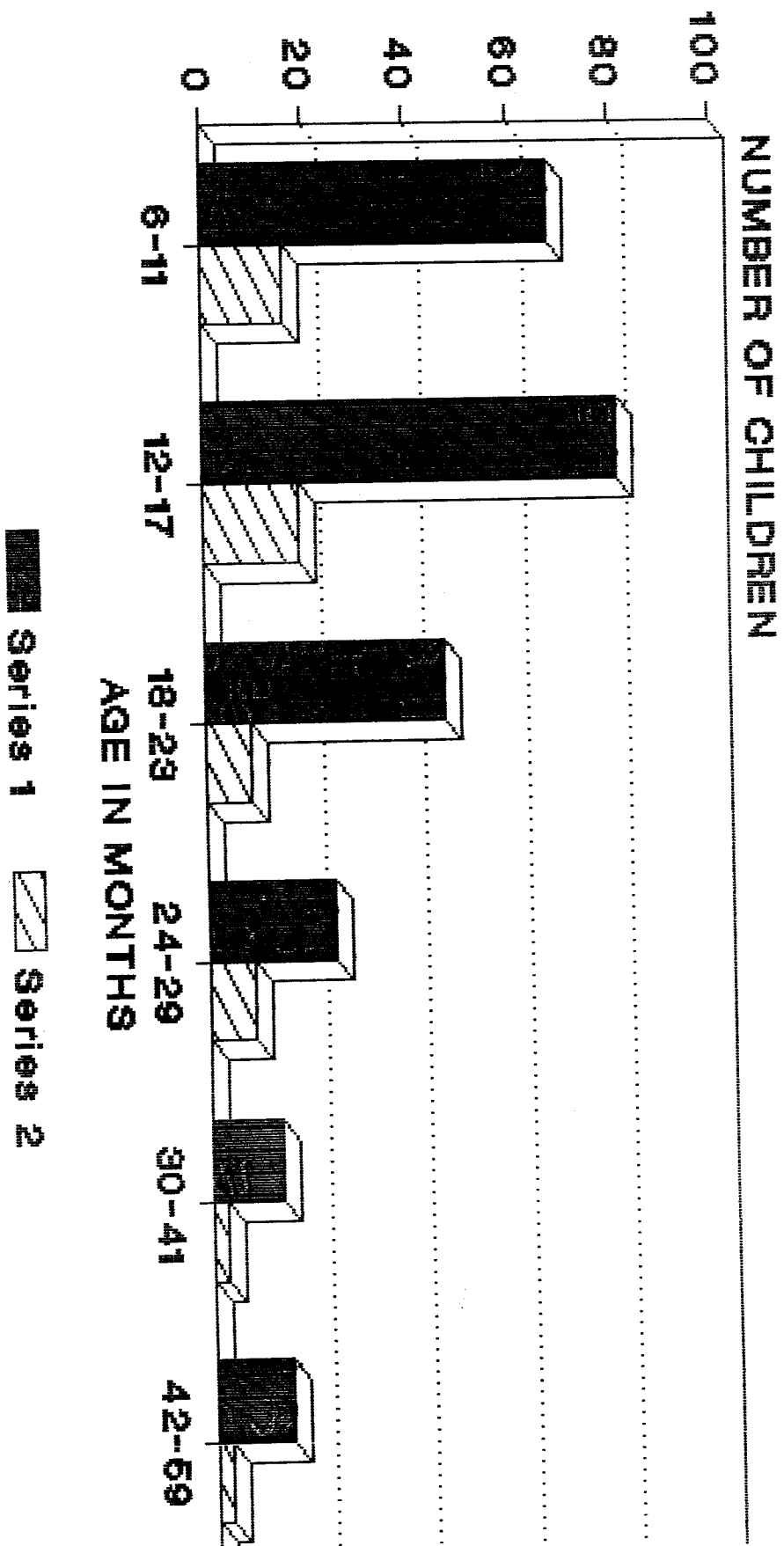
CHILDREN HIV RESULTS IN THE STUDY POPULATION

HIV RESULTS	FREQUENCE	PERCENTAGE
POSITIVE	59	23.9%
NEGATIVE	188	76.1%
TOTAL CHILDREN TESTED	247	100.0%

FIG. 2.
**AGE DISTRIBUTION OF
POSITIVE CHILDREN**



SEROPOSITIVITY ACCORDING TO AGE GROUP



SERIES 1. TOTAL NUMBER RECRUITED
SERIES 2. NUMBER HIV POSITIVE

Series 1 Series 2

TABLE 3: SEX DISTRIBUTION AMONG THE HIV POSITIVE CHILDREN

SEX	FREQUENCY	PERCENTAGE
FEMALE	31	52.5%
MALE	28	47.5%
TOTAL NUMBER POSITIVE	59	100.0%

P value = 0.8

All the mothers of the 247 children screened had blood tested for HIV antibody. 76 (30.8%) were HIV seropositive. Not all HIV positive mothers were able to transmit infection to their children: only 51 (67.1 %) children were HIV antibody positive and 25 (23%)^{32.9%} were HIV antibody negative (table 4 and 5).

TABLE 4: MOTHERS HIV RESULTS IN STUDY POPULATION

HIV RESULTS	FREQUENCY	PERCENTAGE
POSITIVE	76	30.8%
NEGATIVE	171	69.2%
TOTAL MOTHERS	247	100.0%

TABLE 5 : HIV RESULTS OF CHILDREN BORN TO HIV POSITIVE MOTHERS.

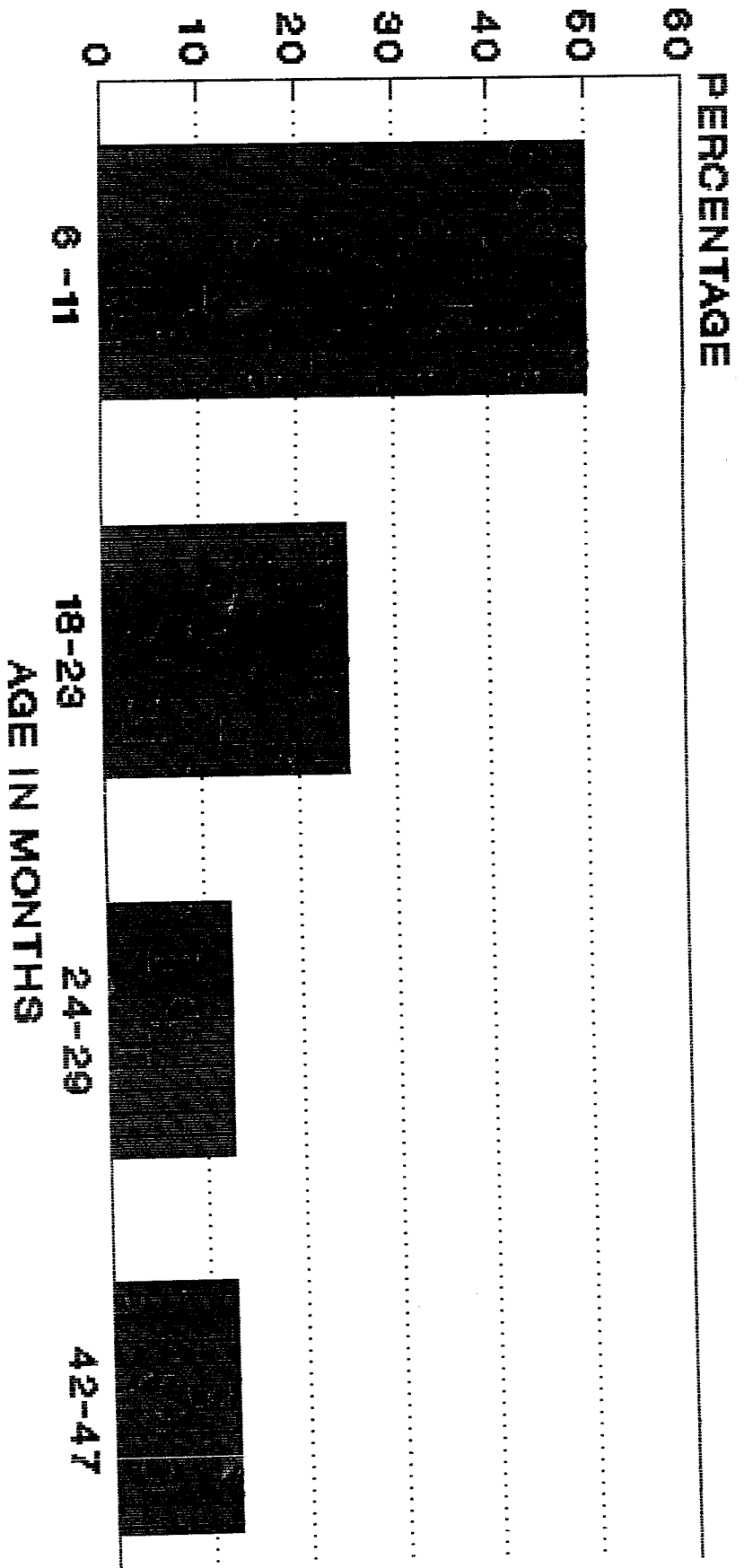
CHILDS HIV RESULTS	FREQUENCY	PERCENTAGE
POSITIVE	51	67.1%
NEGATIVE	25	32.9%
TOTAL MOTHERS	76	100.0%
POSITIVE		

Of the 171 women who were HIV negative, 8 had children whose blood tested positive (table 6). When these children were grouped according to age group 4 out of 8 (50%) were between 6 and 11 months (fig 4). The mean age was 18.13 months (SD 12.43).

TABLE 6: HIV RESULTS OF CHILDREN BORN TO HIV NEGATIVE MOTHERS

RESULTS	FREQUENCY	PERCENTAGE
POSITIVE	8	4.7%
NEGATIVE	163	95.3%
TOTAL MOTHERS HIV NEG	171	100.0%

AGE DISTRIBUTION POSITIVE CHILDREN BORN OF HIV NEGATIVE MOTHERS



Series 1

MOTHER HIV NEGATIVE

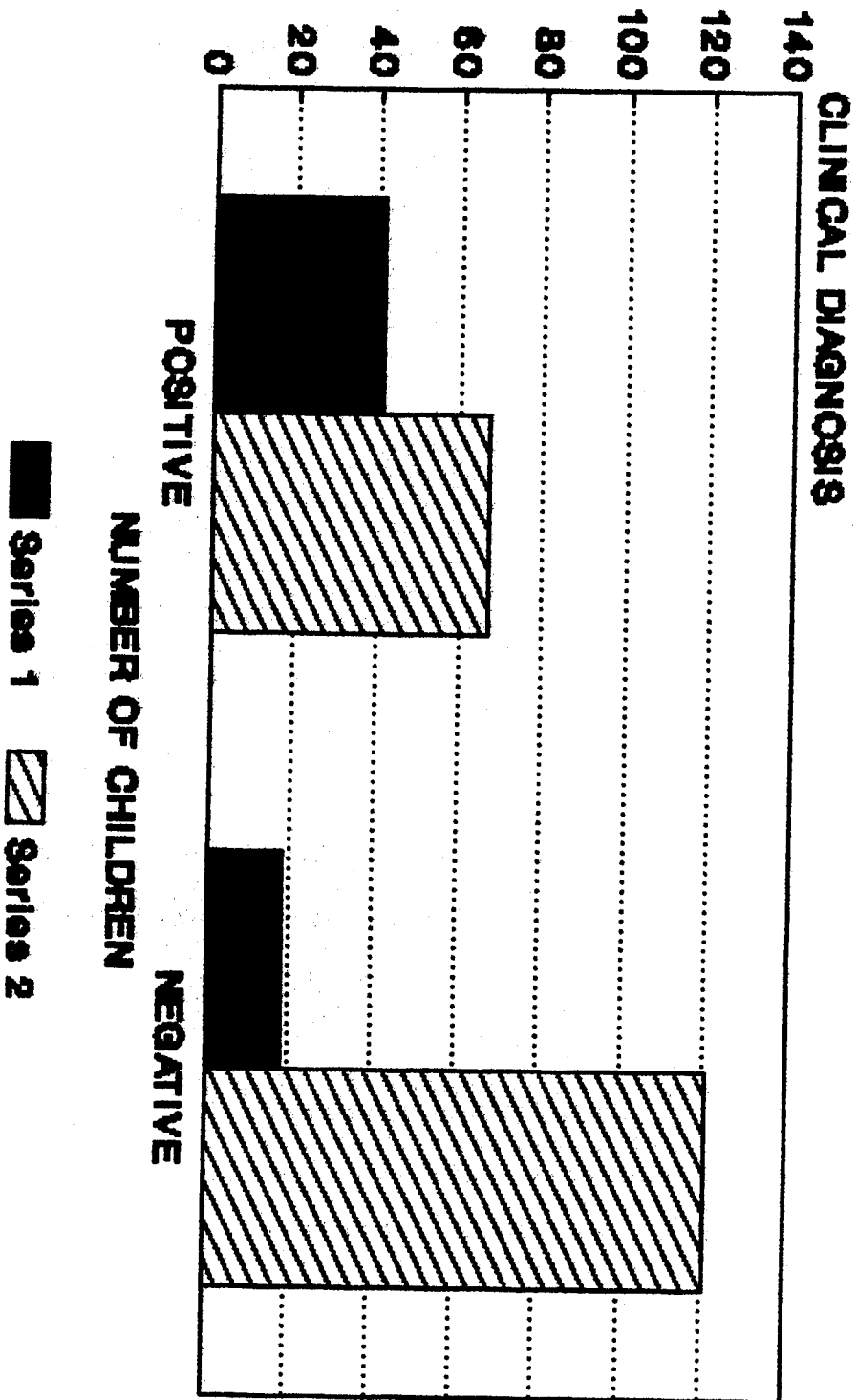
CLINICAL CASE DEFINITION.

The WHO clinical case definition was applied to all patients that were recruited and 109 (43.6%) out of 250 were found to fit the criteria for diagnosis of AIDS. This is a higher percentage than the the percentage of patients found to be HIV antibody positive on laboratory serology testing, where only 59 (23.9%) tested positive. The specificity, sensitivity and positive predictive value were determined to be 64%, 69% and 38% respectively. (Table 7 and 8, fig 5).

TABLE 7: FREQUENCY OF CLINICAL AIDS CASES IN THE STUDY POPULATION

CLINICAL DEFINITION	FREQUENCY	PERCENTAGE
POSITIVE	109	43.6%
NEGATIVE	141	56.4%
TOTAL NUMBER OF PATIENTS	250	100.0%

FIG. 5. **ASSOCIATION OF CLINICAL AIDS WITH HIV RESULTS**



SERIES 1 HIV POSITIVE
SERIES 2 HIV NEGATIVE

■ Series 1 ▨ Series 2

TABLE 8: ASSOCIATION BETWEEN CLINICAL CASE DEFINITION AND LABORATORY RESULTS

CLINICAL DEFINITION	CHILDS HIV		TOTAL
	RESULTS		
	+	-	
POSITIVE	41	67	108
NEGATIVE	18	121	139
TOTAL	59	188	247

SENSITIVITY	69%
SPECIFICITY	64%
POSITIVE PREDICTIVE VALUE	38%

TABLE 9: FREQUENCY FOR PREVIOUS HOSPITALISATION

PREVIOUS ADMISSION	FREQ	PERCENTAGE
+	81	32.4%
-	169	67.6
TOTAL	250	100.0%

TABLE 10: RELATIONSHIP BETWEEN PREVIOUS HOSPITALISATION AND HIV LABORATORY RESULT IN CHILDREN WITH NEGATIVE MOTHERS.

CHILD'S RESULTS	HIV	PREVIOUS HOSPITALISATION		TOTAL
		+	-	
+		3	5	8
-		49	114	163
TOTAL		52	119	171

Fischer Exact Test

P value = 0.5

HOSPITALISATION

1 (32.4%) patients in the study population (250) admitted to having hospitalised some time in the past (table 9). Of the study group (C + M) (37.5%) out 8 compared to 49 (30.1%) out of 163 of the comparative group (C - M-) had been hospitalised in the past. The difference between two was statistically insignificant (P value = 0.5, Fischer Exact Test) (table 10).

MEAN OF INJECTIONS AMONG HOSPITALISED PATIENTS

range of the number of IM injections was 0 to 60. The means of the number of injections were calculated and analysed statistically. There was no significant difference found between the means of the study group (C + M) and comparative group (C - M -) (table 11a). The mean of

injections received by the study group (C + M -) were then compared to the number of those received by children who were HIV positive with HIV positive mothers (C+,M+). The analysis showed that there was a statistical difference in the number of injections received by the two groups (table 11A). The children with congenitally acquired infection are exposed to a greater number of injections when admitted.

TABLE 11A

PATTERN OF IM INJECTIONS IN HOSPITAL

STUDY GROUP	MEAN	VARIANCE	STD DEV
C + M	4.0	47	6.9
C - M -	4.9	157	12.9

P = 0.85

Fischer Exact test

TABLE 11B

STUDY GROUP	MEAN	VARIANCE	STD DEV
C + M -	9.0	320	17.9
C + M +	4.0	47	6.9

P = 0.00032

Fischer Exact test

PATTERN OF BLOOD TRANSFUSION

Only 8 (3.2%) children in the study population (250) had been

nsfused and none of them were positive children with seronegative
 ners (C + M -) (Table 12 and 13). There were 6 children who had blood
 nsfusion prior to the hospitalisation in the comparative group
 - M -). The difference in exposure to blood transfusion between the two
 ups was not statistically significant (P = 0.7, Fischer Exact test)

LE 12. PREVIOUS HISTORY OF BLOOD TRANSFUSION

PREVIOUS BLOOD TRANSFUSION	FREQ	PERCENT	CUM
+	8	3.2%	3.2%
-	242	96.8%	100.0%
TOTAL	250	100.0%	

P value = 7

Fischer Exact test

LE 13: PATTERN OF PREVIOUS HISTORY OF BLOOD TRANSFUSION AMONG C + M -
 AND C - M -

CHILD LAB RESULTS	PREVIOUS BLOOD TRANSFUSION		TOTAL
	+	-	
+	0	8	8
-	6	157	163
TOTAL	6	165	171

TREATMENT OUTSIDE HOSPITAL.

Most of the patients had had minimal previous exposure of 0 - 5 injections in both groups (C + M - and C - M -). 41 out of 163 (25.5%) children in the comparative group had had 6 - 53 injections compared to 4 out of 8 (50%) in the study group. The difference in the two groups was statistically significant. (P = 0.00002, Fischer Exact test) (Table 14)

TABLE 14 . TREATMENT OUTSIDE HOSPITAL

NUMBER OF IM INJECTIONS	CHILD'S LAB RESULT		TOTAL
	+	-	
0 TO 5	4	122	126
6 TO 11	2	29	31
12 TO 17	1	9	10
18 TO 23	0	3	3
48 TO 53	1	0	1
TOTAL	8	163	171

(Fischer Exact, P value = 0.0002)

ADDITIONAL TREATMENT

Most of the 250 (54%) patients gave a positive history of treatment with scarification marks prior to hospitalisation (Table 19). The results of the study group (C +, M -) shows that 6 out of 8 (75%) agreed to a history of scarification marks for therapy in relation to 80 out of 163 (49%) in the comparative group (C - M -). It appears that traditional scarification

therapy was commoner amongst the study group (table 16).

TABLE 15: TREATMENT WITH SCARIFICATION MARKS.

HISTORY OF SCARRIFICATION	FREQ	PERCENT	CUM
+	135	54%	54.0%
-	115	46%	100.0%
TOTAL	250	100%	

Table 16: IMPACT OF SCARIFICATION MARKS ON HIV STATUS OF CHILDREN WITH HIV NEGATIVE MOTHERS

HIV RESULTS	H/O OF SCARRIFICATION		TOTAL
	+	-	
+	6	2	8
-	80	83	163
TOTAL	86	85	171

Fischer Exact P value = 0.2

MORTALITY

Patients of out 250 (14%) died during the study period and 15 out of these were HIV positive. The difference in the number of positive children who died in relation to the negative children was however not statistically significant (P value = 0.7).

CHAPTER SIX

DISCUSSIONSEROPREVALENCE

The HIV seropositivity amongst the study population (250) was found to be 23.9% and as many males as females were positive. This figure, however, is not a true reflection of the seroprevalance among hospitalised children below 5 years of age. Identifying HIV infection in children is not as straight forward as in adults. The two ELISA's and western blot techniques used in this study are all antibody tests. In neonates, nearly all babies born to HIV positive mothers carry their mothers antibodies without necessarily carrying the virus itself (51). A positive test up to 18 months of age only confirms that the mother is infected (44,45). The mean age of loss of maternal antibodies is 9 - 10 months (53). The estimated seroprevalance of 23.9% may be an over estimate as most (59.3%) of the children who tested positive in this study were below 18 months. Another problem that has been identified when dealing with paediatric HIV disease is that some children with HIV disease may actually test negative on antibody testing due to immunodeficiency resulting from some common ailments such as malnutrition, measles and whooping cough (48,49,50). There are documented cases of ELISA and western blot assay negative infants who were infected with HIV(54).

Maternal seropositivity is a major risk factor for childhood HIV infection not only in Africa but also in Europe and United States (15,45). Seropositivity in women of childbearing age in Zambia is rapidly increasing as shown in this study and that of Hira in 1987 where seroprevalence was 30.8% and 11.6% respectively. This increase in seropositivity among women of childbearing age means more children are acquiring infection by vertical transmission. In this study out of the 76 women who were seropositive 51 (67%) had children who were also seropositive. This is a higher transmission rate than that reported in other studies but this may be because 59.3% of the study population are children below 18 month who may still possess maternal antibodies. Only 8 children among the seropositives had seronegative mothers making vertical transmission the commonest mode of transmission.

CLINICAL DIAGNOSIS

Clinical diagnosis of AIDS in children presents a major problem in paediatric practice. The most widely used instrument is the World Health Organisation (WHO) clinical criteria for the diagnosis of AIDS. This case definition has not been clinically tested in Zambia though studies in other parts of Africa, and Europe have illustrated that it lacks sensitivity, specificity and has a low positive predictive value (3,49,50). In this study 109 patients (43.6%) had clinical AIDS on the basis of the WHO criteria. Comparative analysis with laboratory findings revealed 69% sensitivity, 64% specificity and a positive predictive value

38%. The data confirms that using the WHO case definition criteria for diagnosis of AIDS, may result in a lot of false positive results in children who are ill from some other reason other than AIDS. These results confirm the findings in Uganda by Heather et al who concluded that the WHO criteria alone may be insufficient in diagnosing paediatric AIDS as they were picking up a lot of false positives (51). The prevalence of diseases like tuberculosis, malnutrition and diarrhoea makes designing a specific and sensitive clinical definition of childhood AIDS difficult in Africa. In Zambia the Ministry of Health clinical case definition has been found to be more useful. (42).

RISK FACTORS

The results show that 8 of the children who were seropositive had seronegative mothers. In Africa medical injections have been claimed by researchers in Zaire to increase the risk of HIV infection (9,24). Medical injections, however should not endanger life if given by trained personnel observing proper sterilisation or those who are aware of the risks of reusing needles and syringes that are not sterile. In a study done by Mann et al in Zaire, of children under 2 years, the risk factor analysis for none maternally acquired HIV infection showed that injections were most strongly associated with seropositivity, followed by previous transfusion and previous hospital admission (24). Seropositive children were more likely to have received a large number of

jections, as illustrated by the fact that 5 out of 6 had received 50 or more injections (compared to 5 out of 21 seronegative children). Injections were also associated with seropositivity in older children from 5 to 14 years of age as were blood transfusion and previous hospitalisation (9). Among the 2,384 hospital workers in Zaire, persons testing HIV positive somewhat reported more frequent injections in the previous years than persons testing negative (88.8% versus 80.8%) (46). Multiple seropositive patients in Kinshasa, Zaire also reported more injections prior to hospitalisation (47). Studies in Kigali Rwanda, however, failed to show any association between injections and HIV transmission. In this study the overall risk associated with hospitalisation was first analysed before looking at specific exposures. The 8 children who were seropositive with seronegative mothers (C + M -) were designated, the study group and the children who were seronegative with seronegative mothers were the comparative or "control group" (C - M -). Hospitalisation was not found to have a significant impact on HIV transmission as there was no statistical difference in the number of children that had been hospitalised before, between the cases and controls. The injection pattern was also found to be the same in the two groups. Exposure to medical injections in hospital therefore was not the cause of the seropositivity in the study group (C + M -). In the group of children where both the child and mother were seropositive (C + M +), however, the ratio of the mean number of injections when compared to the study group was almost 2 to 1 (8 versus 4.0) and this difference was

astistically significant. These observations reflect that children who acquire infection from their mothers are likely to receive more injections at the hospital because of their chronic illness and that medical injections in hospitals do not themselves increase the chance of acquiring HIV infection. One important explanation why medical injections in hospital may be safe is that it is health policy in Zambia that needles and syringes are not reused and that only disposable needles and syringes are utilised in health institutions.

Blood transfusion has been identified as an important route of transmission of HIV when unscreened blood is used (5,6,40). In order to reduce the risk associated with transfusion, all blood transfused in UTH is screened for HIV infection and despite screening blood transfusions are only given under life threatening situations. Children suffering from anaemia due to malaria for example, are treated for malaria and given ematemics and not blood. Hence, it is not surprising in this study that very few transfusions were performed amongst the study population. Only 8 out of the 250 children were transfused and none of these children were from the study group (C + M -). 6 of the children were from the comparative group (C - M -). It can be inferred from these observations that blood transfusion does not increase the risk of HIV transmission when blood is screened and indiscriminate utilisation of blood is discouraged.

There are a number of outpatient health centres and private clinics around Lusaka. Since UTH is a referral hospital most of the patients

ferred would have had some exposure to injections in these health centres or clinics before coming to UTH. This potential risk of injections outside hospital was analysed in this study. A higher ratio of children (6 out of 8, 50%) in the study group (C + M -) had been exposed to more than 6 injections with a maximum of 53 compared to the control group (41 out of 122, 25.0%). Treatment with injections outside hospital may therefore be a significant route of HIV transmission. There is a strong preference for medical injections amongst the population in Zambia and many people will go to a private practitioner just so that they can receive an injection.

Another significant practice amongst the patients in Zambia is that of scarification marks for therapy. The people in Zambia believe in additional treatment strongly. Analysis of this potential risk in this study revealed that 54% of the patients had been treated with scarification marks in the past. The percentage of those exposed was higher in the study group (6 out of 8, 75%) when compared to the controls (80 out of 163, 49%). This observation suggests that there is an association between HIV infection and exposure to scarification therapy. In a similar study in Kinshasa, Zaire although more scarifications were reported amongst the seropositives there was also no significant difference in exposure between seropositives and seronegatives (9). This study shows that HIV infection did not have significant impact on mortality. This finding was contrary to what was expected maybe due to the fact that some of the patients could not be followed up because the addresses

ere not traceable and it could well be that more positive patients died
home after hospitalisation. The other explanation is that the study
period was short and the cohort needs to be followed up for a longer
period.

CHAPTER SEVEN

CONCLUSION

Where as the bulk of the children in this study acquired HIV infection vertical transmission from their HIV positive mothers, a few children 8 of 247 (3.7%) who had seronegative mother may have acquired the infection by another route. The observation in this study that more children who were seropositive with seronegative mothers were exposed to intramuscular injections outside hospital may reflect that the private clinics and out patient health centres may be responsible for some this infection. Medical injections and blood transfusions given to patients in hospital do not increase the risk of acquiring HIV infection. This is probably because all blood is routinely screened and needles and syringes are not reused. It is also concluded that despite screening all transfusion blood, very few transfusions are administered to patients in hospital. It is possible that safety precautions and awareness of risk associated with medical injections in the out patients clinics are lacking and hence the increased risk of HIV infection through injections in these institutions.

Scarification marks for therapy also seem to increase the risk of HIV infection may be because blades there usually reused without adequate sterilisation due to ignorance on the part of the traditional healer about the risk HIV transmission as a result of such practices.

Clinical diagnosis of HIV remains a major problem. The WHO clinical case definition is insufficient for accurate diagnosis in Zambia. This criteria lacks specificity and sensitivity. The positive predictive values are also low.

It is important to note that the number of children who were HIV positive with HIV negative mothers was very small to arrive at any significant conclusions but the observations are interesting. The data analysed in this study is preliminary data of an ongoing study. It is hoped that 3000 children will be recruited and hence more confirmatory conclusions are expected after completion of the study.

CHAPTER EIGHT

RECOMMENDATIONS.

To optimize public awareness about AIDS and its consequences the effectiveness of health education efforts must be evaluated if current HIV trends are to go down.

Screening all transfusion blood should be mandatory in all hospitals.

Indiscriminate use of blood and contaminated tools should be discouraged.

Medical injections and therapeutic procedures should be performed with absolute sterility and current sterilisation efforts must be reinforced.

There is need for sensitization of herbalists on the risks associated with reusing tools and exposure to blood.

Since the WHO clinical case definition lacks specificity and sensitivity, AIDS diagnosis in Zambia should be based on the Zambia criteria which should be supported by a positive laboratory test.

CHAPTER NINE

APPENDIX 1

STUDY INSTRUMENT NUMBER ONEFOR CHILDREN INTERVIEWED

N.B THESE QUESTIONNAIRES MUST BE KEPT CONFIDENTIAL AND LOCKED ALL TIMES.

NAME OF INTERVIEW: _____

DATE INTERVIEWED: ___/___/___
(DD /MM /YY)

STUDY NUMBER: _____

NAME OF CHILD: _____

FIRST NAME: _____

SEX: _____
(MALE =M)
(FEMALE =F)

DOB: ___/___/___
DD /MM /YY

AGE: _____ (MONTHS ONLY)
(N.B: MUST BE 6 TO 59)

ARE YOU THE TRUE MOTHER OF THIS CHILD: _____ (Y = YES; NO = NO)

FATHERS LAST NAME: _____

MOTHERS FIRST NAME: _____

FATHERS ADDRESS: _____

WARD / CELL / RC: _____

FATHERS WORKPLACE: _____

MOTHERS WORKPLACE: _____

Reasons for research work:

WERE MOTHER AND CHILD EXCLUDED FROM STUDY: _____
(Y = YES; N =NO)

REASONS FOR CHILD EXCLUSION: _____ (1 = MOTHER REFUSED)
(2 = REAL MOTHER UNAVAILABLE)
(3 = FAMILY LIVE TOO FAR AWAY)

ADMISSION DIAGNOSIS: (SPECIFY): _____

DOES THE CHILD FIT CLINICAL CASE DEFINITION: _____
STUDY INSTRUMENT ONE (PAGE 2)

tes for research work (continued)

DATE OF ADMISSION: ___/___/___
DD / MM YY

DATE BLED FOR THIS STUDY:

CHILD: ___/___/___
DD / MM YY

MOTHER: ___/___/___
DD / MM /YY

HISTORY:
The following information is to assess lifetime exposure to various risk factors. Try to get best possible answers.

WHERE WAS CHILD BORN ? _____
(1=HOSPITAL; 2=CLINIC; 3=DISPENSARY; 4=HOME)

WERE ANY TREATMENT GIVEN IMMEDIATELY AFTER BIRTH ? _____
(Y=YES; N=NO)

HAS CHILD BEEN ADMITTED TO HOSPITAL SINCE THEN ? _____
(Y=YES; N=NO)

IF YES HOW MANY TIMES ? _____

HAS CHILD BEEN ADMITTED IN THE LAST THREE MONTHS: _____
(Y=YES; N=NO)

LAST HOSPITAL ADMISSION: ___/___/___
(DD/MM/YY)

TAL OF PROCEDURES DURING ALL PREVIOUS HOSPITALISATIONS

NUMBER OF IM INJECTIONS IN THE LAST YEAR: _____

NUMBER OF IM INJECTIONS SINCE BIRTH: _____

NUMBER IV INFUSION SINCE BIRTH : _____

EVER TRANSFUSED ? _____ (Y=YES; N=NO)

DATE FIRST TRANSFUSION: ___/___/___ NUMBER OF UNITS: _____

DATE SECOND TRANSFUSION: ___/___/___ NUMBER OF UNITS: _____

DATE THIRD TRANSFUSION: ___/___/___ NUMBER OF UNITS: _____
(DD/MM/YY)

COMMENTS: _____

STUDY INSTRUMENT ONE (Page 3)

HAD SURGERY ? _____ (Y=YES N=NO)

FOR INVESTIGATION: _____ (Y=YES; N=NO)
SPECIFY: _____

NUMBER INVESTIGATIONS: _____

FOR THERAPY: _____ (Y=YES; N=NO)
SPECIFY: _____

NUMBER THERAPIES: _____

DENTAL RX: _____ (Y=YES; N=NO)
SPECIFY: _____

NUMBER DENTAL: _____

AL NUMBER OF TREATMENTS BY TRAINED PERSONNEL OUTSIDE HOSPITALISATION
(All treatments since birth)

INJECTIONS:

NUMBER IN LAST YEAR: _____ NUMBER SINCE BIRTH: _____

INFUSIONS NUMBER SINCE BIRTH: _____

TAL INJECTIONS FOR IMMUNISATION: _____

ER HAD SURGICAL PROCEDURES ? _____ NUMBER: _____
(Y=YES; N=NO)

SPECIFY: _____

ER HAD DENTAL PROCEDURE ? _____ NUMBER TIMES: _____
ncluding extraction) (Y=YES; N=NO)

L OF TRADITIONAL PRACTICES SINCE BIRTH:

	Y/N	
OR TREATMENT/SCARRIFICATION MARKS:	_____	NUMBER OF TIMES _____
IRCUMCISED:	_____	DATE: ___/___/___
ATTOO:	_____	
NJECTIONS BY TRADITIONAL HEALER:	_____	NUMBER OF TIMES: _____
NFUSION BY TRADITIONAL HEALER:	_____	
UMBER OF TIMES: _____	_____	
ENTAL EXTRACTION:	_____	
ONGUE TIE:	_____	
VULETOMY:	_____	
AR PIERCING:	_____	
OTHER (SPECIFYING): _____	_____	NUMBER OF TIMES _____

se make sure bloods taken and research section completed.

DISCHARGE DATE: __/__/__
(DD/MM/YY)

FOLLOW UP AT 6 WEEKS: __/__/__
(DD/MM/YY)

LOSSES TO FOLLOW UP: __/__/__
(Y=YES; N=NO)

REASON FOR LOSS: _____
(1=DIED; 2=SELF-DISCHARGE; 3=LATE REFUSER).

APPENDIX TWO

CONSENT FORM

The department of paediatrics is launching a major study on child health. This study is mainly concerned with childhood diseases that are passed on from mother to child including those that are caused by the virus that causes AIDS. You can if you wish participate in this study. This means that you will have a blood sample taken and another blood sample will be taken from your child for screening and your child will be followed up for three months after the discharge.

CHAPTER 10

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