A CROSS-SECTIONAL STUDY OF HUMAN IMMUNODEFICIENCY VIRUS (HIV) Infection in a Rural Population in Rakai District. Serology and Risk factors.

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A Thesis submitted in part fulfilment for the degree of

MASTERS OF PUBLIC HEALTH (MPH)

UNIVERSITY OF NAIROBI

1987.

DECLARATION:

This thesis is my original work and has not been presented for a degree in any other University. The research work was carried out by me in LYANTONDE in RAKAI DISTRICT, SOUTH WESTERN UGANDA, UGANDA from September 1986-April 1987.

DATE 23/7/82

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DECLARATION

I, WARREN RWANYAKACWAMBA NAAMARA, do hereby declare, that this thesis is my original work, and it has not been presented in any other University. The research work was carried out by me in LYANTONDE in RAKAI DISTRICT, South Western Uganda, Uganda from September 1986 to April 1987.

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DEDICATION

This work is dedicated to my late Father YERIMIYA RWANYAKACWAMBA who was my greatest source of inspiration and made me study Medicine. The work is also dedicated to my children NISHA NUNU NYONGA (Daughter) and YERIMIYA KUDU KANYWANI (Son) like any other children, they should do better in research than their fathers.

The work is further dedicated to all victims, living and dead, of this wretched disease, AIDS.

ACKNOWLEDGEMENTS

I am most grateful to the DCM of Nairobi University without which this work as part of the M.P.H. would not have been done. The members of staff especially Dr. R. Knight, Dr. A Minawa were a great source of encouragement, save the time they were willing to put at my disposal on my consultations. Dr. Frank PLummer of the University of Manitoba, and Visiting Lecturer of the Department of Microbiology University of Nairobi provided all the laboratory support and expertise. Besides he reviewed my protocal and I am grateful for the criticisms.

This work would never have been done in Uganda if it was not the President of the Republic of Uganda H.E. YOWERI K. MUSEVENI. He provided all the logistical and financial help he could, but most inspiring was his committment to finding the truth about AIDS. He continues up to now to teach and inspire not only research about AIDS but in every field. I am most grateful. I am also grateful to the Ministry of Health of Uganda for their encouragement and the Uganda expanded programme of Immunisation (UNEPI) for the vaccines used in this study.

I extend my gratitude to P. Piot, A. Ronald and K.K. Holmes of Antwerp Belgium, Mannitoba Winnipeg, and Seattle Washington U.S.A. respectively for their great source of support in this project. They provided the laboratory supporting facilities. Above all I found their criticisms about my work a great reserviour of knowledge. To them I am greatful.

I wish to thank the International development research centre (IDRC) for their support in this project. Joyce and

retyping. To them I am grateful. Last but not least, I wish to apologise and thank my family Elizabeth my wife, Nunu and Kudu my children, for bearing with me during the period of my absence while in the field and during the written up stage. It must have been a rather uncomfortable time for them except Kudu who was a neonate!

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GLOSSARY.

1. AIDS - Acquired Immunodeficiency Syndrome.

2. ARC - AIDS Related Complex.

3. Antibody - A protein in the blood produced in response to exposure to specific foreign molecules. Antibodies neutralize toxins and interact with other components of the immune system to eliminate infectious micro-organisms from the body.

4. Antigen - A substance that sitimulates the production of antibodies.

5. B-lymphocyte (B-cell) - A type of white cell that produces antibody in response to stimulation by an antigen.

6. CD4 Lymphocyte (CD4 T-cell) - A .T. Lymphocyte that expresses the cell surface marker molecule CD4. The majority of these cells are thought to consist of helper/inducer lymphocytes; which play important regulatory roles in human immune system.

7. CD8 Lymphocyte or CD8 .T. cell - A .T. cell that expresses the cell surface marker molecule CD8. The majority of these are thought to consist of suppressor/cytotoxic lymphocytes which play

important regulatory and functional roles in the human immune sytem.

8. ELISA - An Acronym for "Enzyme Linked Immunosorbent Assay" a test used to detect antibodies against HIV in blood samples.

9. HIV - Human Immunodeficiency Virus. The name proposed for the causative agent of AIDS by a subcommittee of ICTV.

10. HTLV III - Human .T. cell Lymphotropic Virus type III.

11. Interleukin-2 - A substance produced by T-lymphocytes that stimulates activated T-lymphocytes and some activated -B-lymphocytes to proliferate. Also known as T-cell growth factor.

12. KAPOSI'S SARCOMA - A cancer or tumour of the blood or lymphatic vessel walls. There is the Endermic (KS) and the AIDS associated KS. The latter being more aggressive than the former.

13. LAV - Lymphadenopathy Associated Virus. The same virus as HIV and HTLV III but called so by the French when they isolated.

14. Opportunistic Infection (OI) - An infection caused by a micro-organism that rarely causes disease in persons with normal defense mechanisms.

15. 3'Orf - 3' Open Reading Frame. A recent gene on the HIV whose function is not known.

16. "pol" genes - genes coding in nucleic acid
Polymerase - reverse Transcriptase

17. "env" genes - This is the external portion of the HIV. This is mainly glycolipid in content.

18. "gag" genes - genes coding for core structural proteins.

19. Provirus - A copy of the genetic information of an animal virus that is integrated into the DNA of an infected cell. Copies of the provirus are passed on to each of the infected cell's daughter cells.

20. Retroviruses - A class of viruses that contain genetic material RNA and that have the capability to copy this RNA into DNA inside an infected cell. The resulting DNA is incorporated into the genetic structure of the cell in the form of a provirus.

21. RNA - Ribonucleic Acid.

22. RC III - Resistance Committee number III. A new political-administrative political structure. This is the (9) house cell system.

23. Reverse Transcriptase - An enzyme produced by retroviruses that allows them to produce a DNA copy of their RNA. This is the first step in the viruses natural cycle of replication.

24. Sensitivity - In serological testing, the percentage of people who test positive who in fact do have the condition being tested for.

25. Specificity - In serological testing, the percentage of people who test negative who in fact do not have the condition being tested for.

26. Seroconversion - The initial development of antibodies specific to a particular antigen.

27. Seropositive - In the context of HIV, the condition in which antibodies to HIV are found in blood.

28. "SOR" - Short Open Reading frame. An extra gene found in HIV whose function is not yet fully known.

29. SYNDROME - A pattern of symptoms and signs, appearing one by one or collectively, that together characterise a particular disease or disorder.

30. T-Lymphocyte (T-cell) - A cell that matures in the thymus gland found primarily in blood, lymph and lymphoid organs.

31. "tat III" Transactivator III - Another gene found on the HIV that is believed to play a leading role in cytopathicity of the T-4 cells.

32. Western-Blot Test - A test that involves the identification of antibodies against specific protein molecules. This test is believed to be more specific than the ELISA in detecting antibodies to HIV in blood samples. It is at present used as a confirmatory test on samples found to be repeatedly reactive to ELISA. It is very expensive for routine laboratory use.

SUMMARY

This study was conducted in Lyantonde, Rakai district, South Western Uganda, Uganda.

Four hundred (400) study participants were enrolled for study. One hundred and eighty five (185) were high risk population, one hundred and twenty four (124) were medium risk population while ninety one (91) were children below age 15 yrs and above 2 years.

These three study participants had a point prevalence of HIV Infection of 67% 17.7% and 1.1% respectively. Most of the study participants were symptoless.

The most consistent feature of symptomless HIV infections was painless posterior cervical Lymphademopathy, which could easily be used as a screening sign. HIV Infection was associated very strongly with diarrhea, STDS, Marital status. Marriage seemed to have a protective effect on HIV.

The number of sexual contacts and number of injections were linearly related to HIV Infection mostly in the high risk population. This will be very important in health Education. There was no association found between HIV and blood transfusion, may be because the transfusion rate was low in this area.

No association was found between HIV and HBV sero markers. The female to male ratio was averagely 1.2:1. These last two

observations indicate that the main transmission route is heterosexual.

In conclusion, health Education, Condom use, further research to understand the disease better, observation of sterility in hospitals and screening of blood before transfusion were recommended for control of HIV Infection.

C H A P T E R 1.

INTRODUCTION.

The world has yet to see a more threatening health problem than the ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS). When the first cases were seen in the USA, it looked as if it was limited to the homosexuals and drug abusers. The clergy and those who were strong believers of the notion "HOLIER THAN THOU" thought God was now unleashing his anger in confirmity with Romans Chapter 6 verse: 23 (RVS Bible) which says "FOR THE WAGES OF SIN IS DEATH".

Soon the problem got out of these so called relics of society and the "holier" were afflicted. Since that time AIDS has become an International health disaster of our times affecting every body despite their race, creed and colour.

By November 1986 cases of AIDS had been reported from 74 countries all over the world with 25,000 cases from USA, nearly 3,000 cases in other countries in America and more than 3,000 cases in Europe.

In AFRICA it has all been a question of guess work. Some estimates talked of several thousands people suspected and other thousands unrecognised.(1)

It was not until 1983 when Africans seen in Europe with illness similar to the AIDS cases seen in USA, that epidemiological studies, on a limited basis started in Central Africa.

The initial surveillance in Central Africa suggested an annual incidence of AIDS of 550 to 1,000 cases per one million adults. The male to female ratio was 1:1 with age-sex specific rates in females less than 30 years of age being greatest, and greater in males over age 40 years.(2)

The predominant clinical presentation of AIDS seems to be the same the world over. This includes chronic or recurrent diarrhoea of unexplained origin, opportunistic infections mainly respiratory tract infections and in Africa extensive loss of weight. Generalised lymphadenopathy and kaposis sarcoma (KS) are some of the persistent clinical features.

In Uganda the predorminant clinical presentation is chronic diarrhoea and extensive loss of weight. The loss of weight is so striking that it has acquired the name "Slim" in Uganda.(3)

Much of the data in the tropics about AIDS or human Immunodeficiency Virus Infection (HIV) has been based on urbanised populations or hospital based information.(4)

This type of data gives little information about prevalance of the disease and risk factors due to information biases in most of the studies. There is therefore a great need to do community based studies, considering that 80-90% of African population is rural.

For surveillance purposes AIDS, which is an infectious disease caused by the HIV virus, a definition must be given. It is that illness characterised by the presence of a reliably diagnosed disease at least moderately predictive of cellular immunodeficiency and by the absence of an underlying cause for immunodeficiency or any defined cause of reduced resistance to the disease (WHO 1986).

There is a huge percentage of the population that does not have AIDS but has been exposed to the human immunodeficiency virus (HIV). These form the biggest source of spread and are believed to carry the virus life long.(2) These are considered to have HIV infection. They are also believed to be infectious while they continue to be healthy.

The main objective of this study was to gather vital information about the magnitude of the problem in a rural population. This would be helpful in formulating a policy on the control of AIDS.

The information gathered would also assist in

formulating other studies to be carried out in Uganda. The data would also help on generating new (and more) hypothesis about the epidemiology of AIDS and HIV infection.

1.1 Study Objectives:

The objectives of the study were:

1. (a) To measure the seroprevalence of Human Immunodeficiency Virus (HIV) infection in a highly promiscuous population between 16-60 years of age living in Lyantonde Township (truck town) in Rakai district, southwestern Uganda, using the ELISA and Western Blot techniques.

(b) To measure the seroprevalence of HIV infection in a non-promiscuous population aged between 16-60 years, living around Lyantonde, using the same methods.

(c) To measure the seroprevalence of HIV infection in school children less than 15 years attending different primary schools in and around Lyantonde and living in the same area- using the same methods.

2. To determine the risk factors for HIV infection in the above population from the same area.

3. To determine the morbidity of HIV infection in the above study groups.

4. To determine the relationship between HIV infection, Hepatits -B- virus and sexually transmitted diseases.

1.2 Justification of the Study:

Much work done in Uganda has been hospital based either in Mulago National Hospital, Nsambya hospital or Rubaga hospital. This was due to the fact that the disease was apparently new in Uganda and the available laboratory and man-power resources were in the capital city.

Before February 1986, the political atmosphere was such that it would not be possible to carry out any work in a rural population. Now it is possible to do meaningful work in the rural areas.

In Africa in general terms, research seems to be the sole preserve of our former colonial masters. Since they are also willing to put in more efforts and resources, the research results or findings are deservedly theirs, leaving us at their mercy as to what they have discovered. Furthermore, AIDS with its political overtones, it is essential that rather than be told about our situation by outsiders and afterwards blame them for false propaganda,

we should be very conversant with our local situations Hence the need for such a study of a rural Ugandan Community undertaken by a Ugandan.

CHAPTER 2.

LITERATURE REVIEW.

2.1 History of Acquired Immunodeficiency Syndrom (AIDS).

The Acquired Immunodeficiency Syndrome was first described in U.S.A. in patients with overwhelming Opportunistic Infections (OI) in 1981.[5,6]

Shortly after that more cases were seen in other centers in the U.S.A. with increased frequency. Simultaneously cases were being reported in U.K. In the following year, 1982 after Centers for Diseases Control (CDC) in Atlanta Georgia had made a diagnostic definition, more cases were reported from all over Europe and North America.[7,8,9]

Clearly a "New" disease had appeared but nobody knew which epidemiological path it would take. Cases increased rather linearly with greater and greater frequency. Although cases were being reported from many areas, it was not until 1983 that cases from Africa were reported.[10,11]

More cases were subsequently reported from other African countries. In Uganda the first cases to be reported was in 1985.[3] Although no cases were being reported from other countries, when the serological assays appeared, there were overwhelming seropositive

people with little infection indicating an older disease.[4]

There was mounting evidence of an International and Intra-national spread of the epidemic The virus that caused AIDS had already been isolated by two independent workers in U.S.A. and France. Those in U.S.A. called it Human-T-Lymptropic Virus Type III (HTLV III) while those in France called it Lymphadenopathy Associated Virus (LAV).[12,13]

Subsequent studies showed that LAV and HTLV III were essentially the same virus. In 1986 an International committee on Taxonomy of viruses proposed that the AIDS retroviruses be officially designated as the Human Immunodeficiency Virus (HIV).

Although the disease being seen in Europe and America was the same clinically as that in Africa, there were strong variations about risk factors. This was reported by Clummek, N., et al., in 1983,[14] Sonnet, et al, in 1983[15] and Brunnet, et al, in 1983[16], that an AIDS-like illness among Africans was not related to any known risk factors for AIDS, although immunological assays of the T-Lymphocytes were altered like in Americans.

These observations prompted investigations in certain Central African States (former colonies of France and Belgium) where in-patients with similar illness were readily found.[17,18] The HIV was subsequently isolated

from the Africans seen in those former colonies. It was the same virus as was being seen elsewhere. Clearly the dreaded disease was now present in the African continent.

It is not clear when the first cases may have appeared in Africa because of poor record keeping. However if AIDS had existed in Africa long time ago, it would have been recognised as a clinical entity by some of the old clinicians. It is rather inconceivable that the way AIDS presents with florid oral candidiasis and massive lymphadenopathy and extensive loss of weight could be consistently missed over the continent and for a long time. This makes it rather impossible for the disease to have been in Africa for a long time (Jaggwe, personal communication).

In Uganda where the disease was reported in 1985, a disease was limited to only one district which shares a common boarder with North Western Tanzania. Furthermore there were popular centres for long distance truck drivers from Zaire to Mombasa in Kenya. The Department of Pathology in Makerere University is well known for its record keeping and that such a disease would not have been occurring with this frequency and only misinterpreted (Wamukola, W. personal communication).

Cases of AIDS or "Slim", as it is now known in Uganda because of extensive loss of weight due to diarrhoea are increasing tremendously but still rather limited to

urban and peri-urban areas.

To-date, several prevalence studies have been done mostly using the Elisa Techniques and Western Blot to confirm the positives. Although massive figures of seropositivity continue to be documented, little of the disease is being seen (Kress, J.). This may question the specificity of the tests. This may be due to recurrent parasitic infections and repeated pregnancies. (Perhaps because of antibodies to DR4 or other HLA types). In the case of Western Blot the binding profile was weak and varied from one individual to another. Therefore surveys in Africa could easily be overestimating the true seropositivity.[19]

The risk factors in Africa and Uganda are clearly different from those of Europe and North America. In Uganda and Central Africa it is mainly heterosexual promiscuity as opposed to homosexual promiscuity in Europe and America. The ratio male to female in Africa is 1:1 while in America it is 19:1. The risk factors in Africa include blood transfusion where screening techniques have not reached.

Although homosexuality is known in Africa and Uganda, people will adamantly deny because of the stigma attached. (Personal observation).

For purposes of control of AIDS in Africa in general and Uganda in particular, full epidemiological approach

to the problem is necessary. Reporting and surveillance will be necessary and health education about the disease intensified.

By March 1986 only 24 African countries mostly from Central Africa were reporting AIDS cases with increased frequency while others continued to deny and hide the facts. WHO collaborating centre on AIDS, AIDS surveillance in Europe Report 9 WHO Paris, France 1986. In the meantime AIDS has become a global public health problem if not a disaster of our time.

C H A P T E R 3.

3.1 Definition.

Acquired Immunodeficiency Syndrome (AIDS) is the more extreme expression of Human Immunodeficiency Virus (HIV) infection. At the end of the spectrum of that infection are those who have been exposed to it and infected, carry antibodies and usually also the virus itself, but who are healthy.

Between these two extremes fall a large number of cases showing a wide variety of clinical and immunological effects of HIV.

WHO has put up a case definition for AIDS, as an illness characterised by:

(a) One or more of the opportunistic infection, diagnosed by methods considered reliable, that are at least moderately indicative of underlying cellular immunodeficiency, and

(b) Absence of all known underlying causes of cellular immunodeficiency (other than HIV infection) and absence of all other causes of reduced resistance reported to be associated with at least one of those opportunistic diseases.

Despite having the above, patients are excluded as

AIDS cases if they have negative results on testing for serum antibody to HIV, do not have a positive culture for HIV and have both a normal or higher number of T-helper (OKT4 or LEU3) lymphocytes and a normal or high ratio of T-helper to T-suppressor (OKT8 or LEU2) lymphocytes. The ratio T4/T8 in healthy individuals is between 1.5 and 2. This case definition could easily be dangerous in areas where only the Elisa and Western Blot are done and no viral isolation. Some terminal cases with AIDS clinically may be both negative on Elisa and Western Blot tests indicating a 100% immuno-decompasation (Personal Observation).

WHO has also separated adults from paediatric cases using the major and minor criteria. AIDS in adults should exist of at least two (2) of major signs associated with one (1) monor sign in the absence of known causes of immunosuppresion.

Major Signs.

(a) Weight loss of greater or equal to 10% body weight.
(b) Chronic diarrhoea greater than one month.
(c) Prolonged fever greater than one month duration.

Minor Signs.

(a) Persistent cough for one month or more.
(b) Generalised pruritic dermatitis.
(c) Recurrent herpes zooster.

(d) Oral-pharyngeal candidiasis.

(e) Chronic progressive and dessiminated herpes simplex.

(f) Generalised lymphadenopathy.

The presence of Kaposi's Sarcoma alone is enough to make the diagnosis of HIV infection.

In children, it should be two major signs with at least two minor in the absence of a known cause of immuno-suppression.

Major Signs.

(a) Weight loss or abnormally slow growth.

(b) Chronic diarrhoea over one month.

(c) Prolonged fever over one month.

Minor Signs.

(a) Generalised lymphadenopathy.

(b) Oral-pharyngeal candidiasis.

(c) Repeated common childhood infections e.g. otitis media.

(d) Generalised dermatitis.

(f) Confirmed HIV infection.

WHO believes these clinical definations are a very sensitive index but need to be evaluated for their specificity and productive value.

ARC (AIDS related complex). This is a variety of chronic symptoms and physical findings that occur in some persons who are infected with HIV but do not meet the CDC definition of AIDS.

Symptoms may include chronic swollen glands, recurrent fevers, unintentional weight loss, chronic diarrhoea, lethargy, minor alterations of immune system (less severe than those that occur in AIDS), and oral thrush. According to the available information, ARC may or may not develop into AIDS. The haematological abnormalities of ARC include cytopenia such as leucopenia, thrombocytopenia and anaemia. The bone marrow usually shows dysplastic features. The pathogenesis of these abnormalities is not known, however, it has been demonstrated that there are circulating immune complexes in patients with HIV infection which coat the surface of their platelets. With such specific coating of the platelet surface by antibody - Antigen Complexes, with premature destruction by the macrophages of the spleen may result in thrombocytopenia. Antibodies to white cell Antigen have not yet been demonstrated in patients with ARC. The pathogenesis of anaemia which is normochromic normocytic is not known. It is believed that the destruction of $T4^{+}$ lymphocyte population with subsequent failure to generate growth factors for haematopoietic cells normally produced by this lymphocyte class results in the cytopenias. HIV might directly infect bone marrow stem cells leading to ineffective haematopoiesis.

Since ARC is a spectrum, each country or research institution should develop a working definition for both ARC and AIDS to assist in diagnosis and surveillance.

3.2 The Agent - HIV Virus.

The HIV belongs to the family RETROVIRIDAE.[20,21,22] This family contains RNA viruses which produce RNA - dependent DNA polymerase enzymic activity.

This enzyme is also known as reverse transcriptase. The HIV belong to the sub-family of the lentiviridea. The lentiviruses cause a number of naturally occurring progressive non-malignant disorders in animals. HIV shares a number of genetic, structural and biological similalities with members of this group although none of the previously known lentiviruses is known to directly affect the immune system of infected hosts.[23]

The genomic RNA is a 60s-70s dimer complex composed of two identical sub-units. The virus shares some genetic and structural elements with other known retroviruses but possesses distinctive features that have not been observed previously.

The replication cycles of previously known retroviruses depend on the functions of the protein products encoded by three viral genes termed as "gag", "pol" and "env".[24,25,26,27] These genes specify the structural and enzymatic functions required for viral

infection and transmission and are situated in a common left to right (5' to 3') configuration in the retroviral genome.

The "gag" gene encodes proteins that contribute the internal core of the virion particle. The "pol" gene specifies the viral enzyme known as reverse transcriptase which is responsible for synthesizing a DNA copy of the retroviral RNA genome early after infection. The "env" gene codes for the surface envelope proteins of the retrovirus, which mediate the process of virus binding to the surface membranes of host target cells. The termini of the DNA form of the retroviral genome are provided by repetitive sequences known as Long Terminal Repeats (LTRs), which contain the essential genetic regulatory elements controlling viral expression and integration. All retroviruses have the three genes and the LTSs, but HIV has in addition four other genes, two of which are required for its replication cycle. These are the "SOR" located near the "pol" gene, "tat" III and the "orf" gene. These genes produce different proteins 23KD, 14KD and 27KD respectively. They are present in some infections because antibodies against them have been detected.

The role of these genes is seen by deletion and then the ability of these mutant HIV to grow in and kill the OKT4/LEU3 lymphocytes. Viruses deleted of the "SOR" and "3' or f" is not clearly known.

HIV shows considerable genomic change. The most variable part of the genome lies within the external glycoprotein section of the "env" gene and this is rather dangerous as the epitopes normally involved in virus neutralisation reside in this region.

Mutation is confined to certain sections of the "env" gene but there are other sequences which are conserved.

The virus is 60-70% protein, 30-40% lipid and 2-4% carbohydrate and approximately 1% RNA. The cell membrane and lipid content of the virus are host cells in origin during budding. The integrity of the envelope is essential for the viral infectivity.

The virus has tropism for the helper T_4 lymphocytes possessing the cell mebrane antigen OKT4. The OKT4 antigen is the specific cellular receptor for HIV and this is why the macrophages and monocytes are attacked by HIV.[28,29]

The virus establishes "factories" in the infected host cells which continuously produce infectious progeny viruses. This factor together with evidence that the antibodies produced in response to the infections appear not to neutralise the virus, means that those who have been infected by HIV must be assumed to have persistant infection and capable of infecting others.

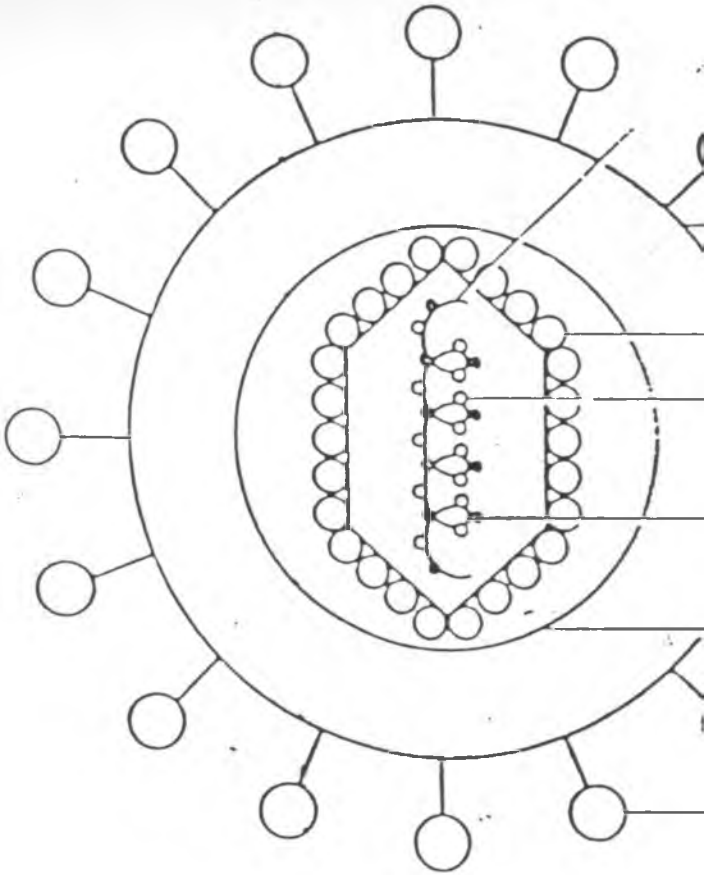
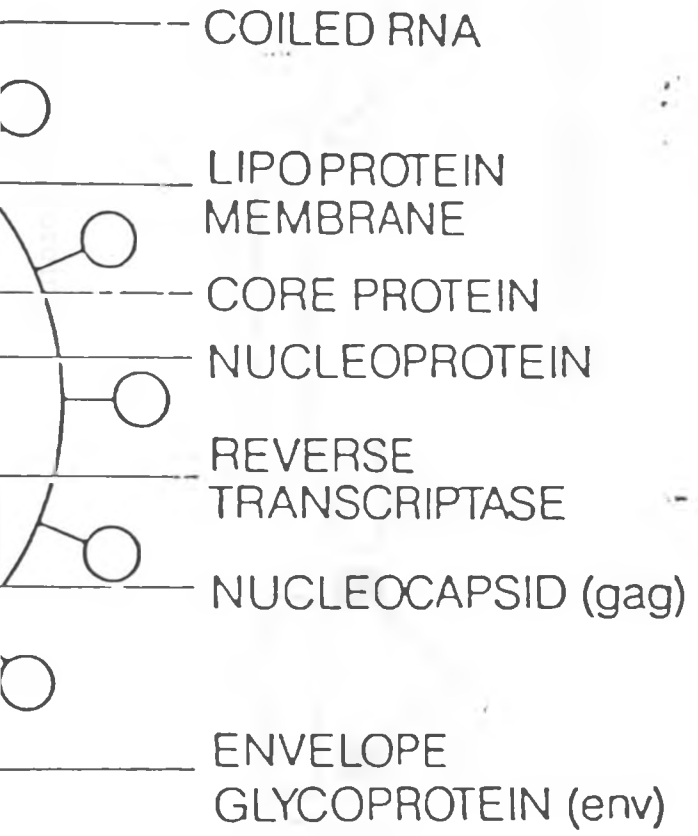
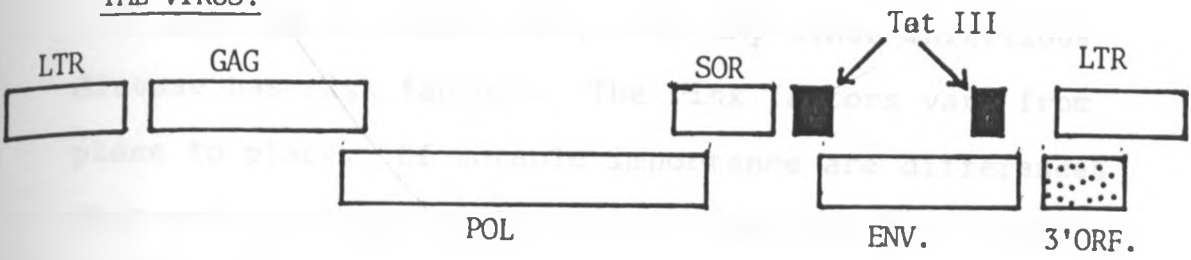


Fig. 4. Structure of HIV.


COILED RNA
LIPOPROTEIN MEMBRANE
CORE PROTEIN
NUCLEOPROTEIN
REVERSE TRANSCRIPTASE
NUCLEOCAPSID (gag)
ENVELOPE GLYCOPROTEIN (env)

GENETIC STRUCTURES OF HIV

THE VIRUS:



"GAG":- Viral core proteins.

"Pol":- REVERSE TRANSCRIPTASE

"CAT":- Viral envelope gene:

3.3 Risk Factors.

AIDS or HIV infection, like any other infectious disease has risk factors. The risk factors vary from place to place. Of notable importance are differences that exist between Africa on one hand and North America and Europe on the other.

Whatever the origin of the AIDS agent, it is now readily transmitted between human beings under certain conditions.

The conditions in America and Europe are confined largely to homosexual men and to persons exposed parentally to infected blood and blood products. Intravenous drug abusers form the second largest risk group after homosexuals.

Transmission within Africa although poorly understood must be slightly different with many variables playing a role. One notable factor is the age distribution of those who have AIDS or HIV infection. Almost all are in the sexually active age range. This tends to incriminate heterosexual route being the commonest method of spread. Heterosexual promiscuity and prostitution have been documented also where by other workers in Rwanda, Kinshasa, and Nairobi. Male to female transmission has been documented from an Australian woman who received artificial insemination and got AIDS.[30] Female to male transmission

is now known from studies of Genital Ulcer Disease (GUD) in Nairobi[31] indicating the need for a fresh site for easy transmission.

One way transmission, i.e. male to female transmission cannot possibly explain the present epidemic proportions in both sexes. Sexually transmitted diseases are common in Central Africa, and whether these could be co-factors in facilitating easy penetration of the virus remains to be answered by other studies. While homosexual accounts for the biggest source of spread in the Westernised countries, data on it in Africa is lacking. Homosexuality is however known and as old as history in Africa, but the stigma attached to it is so big that anybody will deny anywhere anytime. However even if it was present, it is on a limited scale and practised by exclusively very few individuals and therefore cannot account for the present figures of AIDS in Africa.

The other risk factors are blood transfusion in trauma or in cases of sickle cell anaemia. There is a substantial number of sicklers in Central Africa and in Uganda in particular. These will continue to be at risk where blood is not yet screened. Haemophiliacs, although relatively few now in Uganda, they may be seen with increased frequency with advanced investigative capacity and therefore at risk.

mechanism of spread, (c) a susceptible host, (d) an appropriate site of exit from the source, and (e) an appropriate site of entry into the susceptible host. Given these basic elements, infectivity will be related to such factors as the levels of the infectious agent present or the efficiency of possible mechanisms of transmission. The knowledge necessary to know the above factors is derived primarily from epidemiological studies. Human models will never be used because it is unethical and therefore HIV transmission cannot be done experimentally. Animal models may in future be a great source of knowledge.

Data available to-date indicate that transmission of HIV is limited to sexual, parenteral, and maternal infant or vertical transmission. There is growing evidence that adult infection may require direct blood exposure and may be enhanced by coincident damage to skin or mucous membranes to facilitate viral entry. There is no evidence of other routes. There is no substantial evidence against transmission through casual contact including sharing accommodation, eating utensils or even tooth brushes, that does not involve parental or sexual exposure, despite the fact that HIV has been isolated in virtually all body fluids.

3.5.1 Sexual Transmission.

Studies have identified receptive anal intercourse

(with ejaculation of semen) and having a number of sexual partners as the primary risk factors for HIV infection in homosexual men. The known risk of oral intercourse or insertive partner in anal intercourse is limited by the small sample sizes. There is definitely a risk but probably less lower than the risk from receptive anal intercourse.

In Africa where heterosexual intercourse seems to account for most of the cases, vaginal intercourse becomes a big route of transmission. This further documents male to female transmission and female to male transmission. Data is still insufficient to be able to certainly document that male to female transmission is more efficient than the reverse direction. However in both cases a history of genital ulcer disease, as is common in prostitutes and their clients, seems to facilitate entry of the agent. Workers in Central Africa showed a close relationship between the number of sexual contacts, exclusively heterosexual to be associated with higher HIV seropositivity. These studies also showed that there was no relationship between a particular sexual style and seropositivity to HIV.[4,10,11,32]

Other modes of transmission need to be evaluated in the African set-up. The role of parental transmission.

Vertical transmission rates are not known. However there is growing evidence that it occurs in the uterus as

Hospital workers, are at risk because of needle stick injuries although the risk is Low (1:1000). Unsterilised syringes and needles may be very important considering the high rate of infection abscess either due to non-qualified persons practising medicine or poor hospital sterility.

Children born of high risk mothers, like prostitutes, are of particular concern. They are a risk group because of the high chances of vertical transmission. Whether it happens in the uterus, or during birth or during breast feeding, they are at a great risk every time. With the WHO emphasis on Expanded Programme of Immunisation (EPI), disposable syringes must be readily available to avoid re-using of syringes. This is of particular interest as it is possible to transmit AIDS by unsterilised syringes and needles. Children who escape the risk of contracting AIDS from their mothers should not be exposed to another risk.

Intra-venous drug abusers, oral sex and deep kissing, however minor routes they may be, could become important when the major routes are controlled. However, such practices are still alien in Africa and Uganda in particular.

3.5 Transmission.

Transmission of an infectious agent needs five basic elements: (a) an infected source, (b) a vehicle or

early as the fifteenth week of gestation. It is extremely important to determine when and how transmission occurs so that alternative strategies for delivery can be evaluated. (Ziegler, et al, 1985 reported on possible cases of HIV transmission via breast milk bringing in oral route being a possible site. This would be dangerous because breast feeding is one absolute requisite for African children to grow.)[33]

Of greatest interest to the general public is the risk of HIV transmission from blood transfusion. This risk, however, is the easiest to stop with screening programmes. Although there is a problem of false negatives, it is likely to be lessened where the available screening machines become more sensitive and specific. One fact is clear, that the numbers of blood transfusion related AIDS would dramatically reduce.

3.6 Carriership.

In infectious diseases, the healthy carriers are always a potential danger because of the reservoir of the disease they form. The disease agent is released either continously or sporadically. In the case of AIDS it is generally agreed now that once an individual is seropositive, he or she is deemed infective to others without showing signs of the disease until proved otherwise. This is supported by the fact that they continue to secret the virus from body fluids.

The people who have already shown overt clinical signs and symptoms are usually less sexually active and there is a tendency for others to ostracise them because of the stigma attached to the disease. Therefore these people do not constitute a great danger in propagation and transmission of the disease.

The population that poses a great danger are the healthy carriers. They continue to have socially unrestricted sexual relationships. Depending on whether they are high risk groups, they form reservoir from which the virus is dynamically released to the healthy population sexually.

With the incubation period being very long, 2-7 years, it is rather worrying that one individual could release and distribute the HIV for seven years before showing any clinical signs and symptoms of AIDS. WHO has estimated that if 100 seropositive people are followed prospectively for the development of AIDS for five years to ten years only 25-50% will develop AIDS or ARC and the rest 50-75% staying free of disease.

These figures are based on prospective cohort studies on American homosexual men. In Africa and in Uganda in particular, there is an urgent need for prospective cohort studies to be able to determine whether there is a deference in the incubation period of HIV infection from the rest of the world. Such studies

would also help throw more light on our diagnostic criteria of AIDS.

3.7 Pathogenesis.

The Human Immunodeficiency Virus (HIV) gains access through the $OKT4^{+}$ receptor site of the T-helper (T4) lymphocytes. Other cells that have this receptor like monocytes are affected.[34]

After infection, the T-cell population declines gradually. The decline of these cell lines varies from individual to individual. This may account for the differences in incubation periods of different individuals.

The virus enters the cell coated and once inside the cell, it is uncoated. The viral reverse transcriptase makes an initial complementally single stranded DNA copy of the viral RNA molecule. This step is followed by the generation of circular double stranded DNA called the proviral DNA some of which is integrated into the hosts chromosomal DNA.

New viral messenger RNA molecules (mRNA) are expressed by transcription of proviral DNA, the mRNA is subsequently translated into different viral capsid proteins, envelope glycoproteins and enzymes.[35]

The amount of viral protein synthesised is controlled

by feed-back mechanism. The regulatory genes being the transactivator gene III (tat III).

There are other genes which are present on the virus but whose function is not yet clear. They may help in the prossess of replication of the virus. These include the 3'-open reading frame (3'orf) and the short open reading frame (sor).

The final stage is viral replication. This in the assembly and release of fully formed mature particles of the cell membranes. The host cell membrane provides the coating of the virus.

All the above sites provide attractive avenues for therapeutic trials of different drugs.[36,37].

3.8 Pathology.

The involvement of T-4 lymphocytes and some brain cells and their death is the main feature in AIDS or HIV infection.

The mechanism by which an individual is depleted of his T-helper cells is unknown and remains a puzzle. There are however many theories. One that has attracted a lot of research and offers the best explanation is that of cytopathicity. This is the one described here below.

There seems to be premature death by cytopathic effect following infection of T-helper lymphocytes.

The mechanism is not a direct lytic effect on the cells, neither is there mechanical lytic effect by replication of the virus inside the cell.

Autoimmune reaction cannot be thought of because of selective killing of T-4 cells.(38)

The "tat III" gene may facilitate expression of cellular genes that lead to terminal deferentiation of the T-cell lines.

There may be another viral cofactor yet unknown that may induce selective killing of T-4 cells. The cells that are infected but not killed by the virus may serve as potential reservoir for infection.(39)

Whatever kills the T-helper cells, is highly selective and remains unclear. Since this is the cell line that governs antibody producing cells, the patient is left-with Impaired Immunity.

This accounts for the opportunistic infections that invade these patients and finally kill them.(36) The cancers seen e.g. Kaposis Sarcoma (KS) in HIV infection may well depend on the immune system depression to surface which may explain in a limited sense the

aetiology of these cancers.

CHAPTER 4.

STUDY AREA.

LYANTONDE township is situated along the main highway between Mombasa and Zaire and Rwanda. It is mainly an agricultural area and surrounded on the western part by ranch farming. Lyantonde township forms a single administrative structure now known as a Resistance Committee number three (RC III). (This is a new grass-root administrative structure in Uganda). It has a population of 8,000 people based on the 1980 census figures. This area is part of Rakai District in south-western Uganda.

Rakai District boarders north-western Tanzania in the south and a small part with Burundi on the south-west periphery.

There is a main trading route between this district and Tanzania. This was also the entry point by the Tanzania Peoples Defence Forces (TPDF) during the 1979 war against the Idi Amin regime.

4.1 Demographic and Economic Profile.

Lyantonde and the surrounding area are of mixed people with different customs, attitudes and practices. It is one of the most heterogenous communities in Uganda.

Most people who live in this area are aliens, some internal aliens and others international aliens from Rwanda, Burundi and Tanzania, who streamed in this area for social-economic reasons. It is not possible at this stage to gauge which group contributes what percentage.

Lyantonde being the main township has a lot of dynamic in and out migration. It is basically a truck town loved and liked by long distance truck drivers. These drivers constitute the biggest number of constant night vistors. It has also recently been designated one stop-over point for truck drivers while in transit. They constitute a big attraction for the women and girls who stay in this township.

The women and girls who work and live in Lyantonde usually come from different parts of Uganda. Very few of them actually are born and grown in Rakai district. The reason for this may be that women may wish to conceal their promscuity at least far away from where they are born.

Women in this area do not stay with their children. Most of the children stay with their grand-parents because after all they are a negative impact to promiscuity.

The women who work as bar-maids and hotel attendants do not receive a salary per month. They are given a

daily ration of foods or drinks while on duty, but otherwise they pay for their house rents and foods.

A one roomed rent per month is about thirty thousand Ugand shillings (U.shs.30,000/-) equivalent to US21 dollars. A bunch of bananas, the staple food costs between ten and fifteen thousand (10,000-15,000) equivalent to 7-10 US dollars and lasts about four days for two people. Normally these women exchange sexual favours for money. A one night encounter with a woman, pays somewhere between twenty five to fifty thousand or more shillings, equivalent to US$.17-34. One encounter during the day otherwise known as the "shot" costs about half the nights price.

Outrightly, it appears to be lucrative business and this is why the employers do not pay a salary to these girls. Those who try to pay a salary pay a rather low salary of about five thousand (5,000/-) shilling equivalent to US$.3½ per month.

Paradoxically the men who work under the same conditions are paid a higher salary per month and have more benefits compared to the women doing the same job.

4.2 Health Facilities.

The district of Rakai until recently in November 1986 did not have a hospital. The only available health

facilities were health centres and dispensaries rather widely apart from one another. There is one health centre that has been converted into a hospital and is about 40 km away from Lyantonde. Lyantonde and the surrounding area of about 15 km radius are served by one heath centre and three dispensaries. These facilities are particularly very poor with very few drugs if any and with very few trained personnel.

The nearest referral hospitals are Mbarara and Masaka each about fifty kilometres away. The referral system is also poor with no ambulances available. Patients usually relay on public transport but also rather expensive. The result of all this is that there are many private clinics. Lyantonde alone has a total of about (10) ten private clinics. None of which is run by a qualified doctor. Some are run by medical assistants and others by the registered nurses and midwives. A very small number is run by non-trained or poorly trained personnel. All these people left unsupevised by qualified doctors could be rather dangerous in spread of diseases.

Medical statistics are virtually not available since the health facilities are not available. This is rather sad considering that surveillance of diseases heavily depends on records.

CHAPTER 5.

MATERIALS AND METHODS.

5.1 Exploratory Visits.

After developing the protocol for the study at a IEA/TDR workshop held in Kisumu Kenya in 1986, the Ministry of Health Uganda, was approached with the intention of sanctioning the project. The project was reviewed by the National Chairman for the AIDS Committee. Consultations within the Committee were held and the project given a go-ahead. The President's Office was informed and gave the logistical support throughout the project period.

An initial preliminary visit was made to the study area a few weeks before commencement. The purpose of the visit was to re-equip myself with the general situation, roughly gauge the attitude of the people towards the AIDS disease.

Meetings were organised between the Local Leaders and the Resistance Committees (RCs) at different levels where the study was to be carried out.

At these meetings the general health of the area was discussed, crystallising into a dialogue about the way they view the AIDS otherwise known as "slim" disease

in this area. The Resistance Committee Chairmen agreed to mobilise the people for a talk about AIDS or "slim" disease.

At all these meetings the purpose of the study was not revealed otherwise it would have been difficult to carry out the project.

The people viewed AIDS as witchcraft from Tanzania following a bad illicit trade deal. Others believed that for someone to have AIDS must have been cursed by his fellowkins over his bad ways of life. Yet others believed that there was nothing like AIDS but people were dying of typhoid fever and tuberculosis. Very few people almost believed that there was AIDS but could only be cured by native doctors and indeed a number were on numerous herbs.

The Uganda Expanded Programme of Immunisation (UNEPI) was approached for provision of vaccines that would be used in the study. Many more materials, tally sheets, ice boxes and vaccine carriers were made available to me. This helped in keeping track of immunisation coverage.

Finally the project started in October 1986 with immunisation and treatment of all those who came to designated health facilities. The objectives of the study were concealed all through the study period.

Although a 100% sample was aimed at, perhaps about 5-10% was not reached. The group that attended like so was code named "LO". The age limit was between 16 years and above for eligibility.

(b) Normal risk were those people living in rural area other than Lyantonde Township who came for ordinary check ups after all there was a doctor. This formed a small number though. The big number was those who brought children for immunisation on designated days. This included men and women. Coverage and homogeneity was achieved by enrolling mothers who came for immunisation at other centres well outside Lyantonde Township. Three selected dispensaries were used for this purpose. They were situated deep in the rural area about 15 kilometres away from the main highway. Anybody above 16 years and living in a rural area but not Lyantonde township was eligible for recruitment. These were code named "LM".

(c) The third group were children below the age of 15 years and above 2 years. These were recruited using two methods. Children who were brought for immunisation and their parents were willing were enrolled into the study. The other children were collected from three primary schools in this same area. With the consent of headmasters, children attending primary one (P1) and primary two (P2) were enrolled as long as they were willing and of the right age. These were code named "LC".

Since there was no sample size, similar numbers were aimed at in each group for better statistical analysis.

5.3 Questionnaire Administration.

After enrolling into the study, a pretested structured questionnaire was administered by the investigator to ensure uniformity.

A detailed social, sex, economic, past medical and immunisation history was recorded on the questionnairein spaces provided. No study assistants were allowed to administer the questionnaires. The normal risk population and high risk population were admistered the same questionnaire while the children had a separate and different questionnaire.

5.3.1 Physical Examination.

After a detailed history recording in the questionnaire the study participants were subjected to a rigorous physical examination. Systems were reviewed noting any abnormality and recorded in the questionnaire.

Local examination of the skin and lymphnodes were given special emphasis and recorded as present or absent and in what region. The oral cavity was inspected and attempts to inspect the throat in all cases were done.

A vaginal examination was done on all women beyond age 16 years both inspection and digital. A speculum was used to assess the cervical lesions if any.

Genetalia of men were inspected for any discharge soft or hard chancres and any other abnormality.

In the case of children, they were weighed in accordance with Unicef requirements and the growth-monitoring charts filled in. They were also inspected for general cleanliness.

5.4 Venepuncture.

After administration of the questionnaire and general and systemic review study participants were asked to have their blood drawn for analysis. Those who accepted continued as participants while those who declined the offer were left out of the study.

The anterior cubital fossa was the commonest site used to draw blood in adults and some children. In other children, jugular and moral taps were used to obtain blood.

In all cases a verccutainer 8 mls and a multisample draw meedle were used after cleaning the site with hibscrub.

Each study participant had a new and separate verccutainer and a multi-sample draw needle. In cases where it proved difficult, syringes and gauge 23 needles were used to draw blood. In all cases no blood drawing instruments were re-used.

Rubber gloves were worn throughout the period of contact with the study participants. Multi-sample draw needles were very crucial as no blood would be spilled.

After a day's work, all used syringes, needles and swabs were collected in one container, care being taken to avoid contamination and fed into an incenerator nearby the health centre. Where there was no incenerator, pit latrines were used as the safest way of disposal after burning all for disposal under supervision.

Hands were washed with a mixture of hibscrub and potassium hypochlorite solution.

Blood in verccutainer was then transported into a nearby laboratory for serum separation under room temperature of about $25^{o}C$.

5.5 Serum Storage and Transport.

All blood samples of one day's work would be separated for serum at the end of the same day.

Serum was separated using pauster pipettes. Each blood sample had two serum samples separated into 2.5 mls serum tubes. No pipettes were re-used and rubber gloves were worn throughout all the procedures of serum handling. The serum was then labelled with corresponding codes used for the blood samples and stored at -20^{o}C using an electric fridge.

Transport of the serum from the study area to the reception centre in Kampala was achieved using cold boxes and ice packs. While in Kampala the serum was stored at -20^{o}C in an electric fridge awaiting transport to Nairobi.

Transport of the serum to Nairobi were all by air again using the cold box and frozen ice packs. A monitor thermometer was used in the cold boxes to gauge the temperature. In all cases of out-of fridge transport of the serum, the highest temperature at any time was 0^{0}C.

5.6 Serology.

The serum in the laboratory was stored at -70^{o}C and re-labelled using better material for the code numbers.

HIV serology was done using the Enzyme Linked Immunosorbent Assay (ELISA) using the DU-PONT kits and reader according to the manufacturers specifications. The ELISA is a qualitative assay for detection of antibodies to the HIV contained in human plasma or serum.

It is basically an optical density technique that is used in the reader. The test was used to screen all samples against HIV antibodies. The positive samples and negative samples were determined by calculating a cut off point in optical density, above which would be positive and below negative. This was done according to the manufacturers specifications.

The samples that were positive or boarder-line were re-screened using the same test while those that were negative, were deemed for ever negative to HIV antibodies. Those that were twice positive were taken as positive for HIV and those that were negative on second screen were regarded as equivocal HIV antibody reactive.

Rubber gloves were worn throught the handling of serum.

The equivocal results were selected for immunoblot procedure using the western-blot method by DU-PONT.

The Western Blot (WB) assay for HIV antibody is achieved by HIV specific polypeptides fractionated according to molecular weight by electrophoresis technique on a polycrylaride slab gel, in presence of Sodium Dodecyl Sulphate (SDS).

The separated HIV polypeptides are then transferred from the gel to a nitrocellulose membrane via

electrophoretic blotting.

The presence of HIV specific immunoglobulins in sample serum is indicated by in situ labelling of HIV specific proteins.

Reacted strips may be used to determine the presence of antibodies to the major HIV viral antigenes including P17, P24, gP41, P31, PS1, P55, P66, gP120 and gP160.

A positive western blot test was any strip that had all bands or P24 only or P24 with any other or gP41, P55 and any other. This was the criteria used throughout all the samples tested like so. These antigenes correspond to the those genes for the HIV virus.

"gag" coded by P55, P24, P17.

"pol" coded by P66, P51, P31.

"env" coded by gP160, gP120, gP41.

The samples that fulfilled the criteria as indicated above for positivity were confirmed positive while those that did not fulfill this criteria were regarded negative for HIV antibodies. Here the western blot assay was used as the confirmatory test.

Hepatitis -B- virus markers were also done in all cases using the JICO according to the manufacturers specifications.

5.7 Data Analysis.

Information gathered in the field was coded from the questionnaire into the COBOL CODING FORMS using predetermined variable codes.

The information was then transferred into an I.B.M. personal computer (IBM/PC) using the double density, double sided discquatte 5¼ inches. Using the SPSS/PC package for analysis, frequencies and variable distribution and chi-square wer calculated.

Estimation of the odds ratio was done from the valves obtained.

Specificity, sensitivity, negative and positive predictive values and the yield of the ELISA test were calculated using the western blot as the confirmatory test. Measures of the HIV frequency and demographic profile were also determined using the same computer.

In some parts of the test the cross product ratio is synonymous with Odds Ratio (OR) and should be taken as such.

The prevalent OR is the same as Cross Product Ratio (CPR) but bias is greater than the incident OR used in most cases control studies, however CPR still provides a fairly good estimate of Relative Risk (RR). In this

study the CPR will be biased because most study participants seen were still healthy. Neither death nor recovery applies to early HIV infection in the study participants.

5.8 Ethical Considerations.

AIDS is a highly stigmatised disease and therefore care had to be excersised throughout the whole period. No results of the blood tests were ever to be made known to anybody or to any study participant especially if they did not insist on knowing. No study assistant was allowed access to these results.

The value of disclosing the HIV positive results to the participants had to be weighed against the social background and their attitude towards the disease. Releasing the results probably would have led to increased indescriminate sex compared to with-holding the results. There were no resources for counselling of the study participants. The participants who had minor ailment were treated at the clinic and those that needed referral were given the necessary assistance.

The participants who had developed fully-blown AIDS were treated for their life threatening Opportunistic Infections (OI) and sore cases were referred. Those that were rather too sick were asked to stop working as food handlers. The mothers who were seropositive for HIV were

advised against becoming pregnant without actually releasing their serology results. All those that were seropositive were asked never to donate blood for transfusion on the pretext that they needed blood themselves. This is likely to be successful since blood donation is generally not liked in this area.

All children who were seen at the different clinics during the study period whether they were study participants or not were treated for their minor ailments where possible. They were given MCH cards and weighed. All those who needed immunisation were immunised in accordance with the Uganda Expended Programme of Immunisation (UNEPI).

Care was taken to use disposable syringes and needles during immunisation after which they were disposed in the manner indicated above. They were deemed potentially infectious. Since the work of immunisation had been started, arrangements were made to continue this at the end of the study period to make sure the children did not miss their repeat doses of immunisation.

C H A P T E R 6.

RESULTS.

A total of (400) four hundred participants were seen and the following tables give the demographic profiles.

TABLE I:

	HIGH RISK %	NORMAL RISK %	CHILDREN %	TOTAL.
FEMALES	147 (79.5%)	116 (93.5%)	46 (50.5%)	309 (77.3%)
MALES	38 (20.5%)	8 (6.5%)	45 (49.5%)	91 (22.7%)
TOTAL	185 (46.3%)	124 (31%)	91 (22.7%)	400 (100%)

There were relatively more females than males in the adult groups of High Risk and Normal Risk because of the sampling procedure.

Age Distribution by Mean.

The study participants had the the following age distribution.

TABLE II:

	MEAN AGE IN YEARS	STD DEVIATION	MINIMUM	MAXIMUM
HIGH RISK	23.5 N = 185	6.2	16	51
NORMAL RISK	25.3 N = 124	6.2	16	45
CHILDREN	7.5 N = 91	3.1	3	15

High risk means the study participants likely to acquire HIV infection because of promiscuity.

Normal risk study participants for HIV infection meaning non promiscuous.

Children below the age of 15 years in the study population.

High risk here means these study participants who lived and worked in Lyantonde Township as bar-maids, hotel workers and food handlers who because of the social economic life were likely to have many sexual contacts and some in exchange for money.

Seroprevalence of HIV Infection.

TABLE III:

	HIGH RISK	LOW RISK	CHILDREN	
ELISA	LO %	LM %	LC %	TOTAL
+	124 (67%)	22 (17.7%)	3 (3.3%)	149
-	61 (33%)	102 (82.3%)	88 (96.7%)	251
TOTAL	185(100%)	124(100%)	91(100%)	400

Of the total 400 study participants seen, the high risk population had a seropositivity to HIV antibodies of 67%, normal risk or those that were unlikely to be promiscuous had 17.7% seropositivity to HIV while the

children had 3.3%. This was on the screening test.

There was a high significant difference between these population groups with a Chi-square 135.25 P=0.0000 with two degrees of freedom (χ^2_2=135.25 P=0.0000).

It was necessary to compare which of these groups differed by what level of significance and therefore the three populations were compared two on each go.

Normal Risk Compared to High Risk population.

Percentages are for Raws.

TABLE IV:

ELISA	HIGH RISK POPULATION	NORMAL RISK POPULATION	TOTAL
+	124 (67%)	22 (17.7%)	146
-	61	102	163
	185	124	309

expected

a=87

b=59

Of the total adult population that were positive for HIV infection, the high risk population were 67% while the normal risk were 17.7%. There was a high statistically significant difference between these two population. Chi square with one degree of freedom 70.38 P=0.0000. (χ^2_2=70.38 P=0.000).

The Children were Compared to the Normal Risk Population.

TABLE V:

	NORMAL RISK	CHILDREN	
ELISA			TOTAL
+	22 (17.7)	3 (3.2%)	25
-	102	88	190
TOTAL	124	91	215

There was a statistically significant difference between the two population with a Chi-square of 9.28 with one degree of freedom P value = 0.0023.

$(\chi^2_1 = 9.28$ P=0.0023).

High Risk Compared to Children.

TABLE VI:

	HIGH RISK	CHILDREN	
ELISA			TOTAL
+	124 (67%)	3 (3.2%)	127
-	61	88	149
TOTAL	185	91	276

When the children were compared to high risk population

there was a highly significant difference with an even greater value on Chi-square of 97.18 with one degree of freedom. P value 0.000 (χ^2_1=97.18 P=0.0000).

Seropositivity to HIV by Age.

Age is a factor in transmission of AIDS. The adults are likely to acquire AIDS by different routes from those of children. Besides age would throw light on how old the disease could be in this part of Uganda.

Normal Risk Population.

TABLE VII:

	AGE (YEARS)						
ELISA	16-20	21-25	26-30	31-35	36-40	41-45	.TOTAL
+	4 (11.7%)	9 (27%)	6 (15%)	3 (42%)	0	0	22
-	30	24	33	4	9	2	102
TOTAL	34	33	39	7	9	2	.124

χ^2_5 = 8.433 P=0.1339.

χ^2_3 = 3.6 when age P>0.1 groups 31-45 are combined.

High Risk Population.

TABLE VIII:

	AGE							
ELISA	16-20	21-25	26-30	31-35	36-40	41-45	45+	TO
+	53(69.7%)	39(70.9%)	20(66.7%)	7(53.8%)	3(33.3%)	1(100%)	1(100%)	12
-	23	16	10	6	6	0	0	6
TOTAL	76	55	30	13	9	1	1	18

$\chi^2_6 = 7.25821$ P=0.2976.

$\chi^2_3 = 3.7$ P>0.10 when age groups 31-45+ are combined.

Children Seropositivity by Age.

TABLE IX:

	AGE			
ELISA	0-5	6-10	11-15	TOTAL
+	0	3	0	3
-	31	43	14	88
TOTAL	31	46	14	91

$\chi^2_3 = 3.034$ P=0.3863.

In the three population groups there seems to have been no difference between the different age groups.

SEROPOSITIVITY TO HIV BY AGE

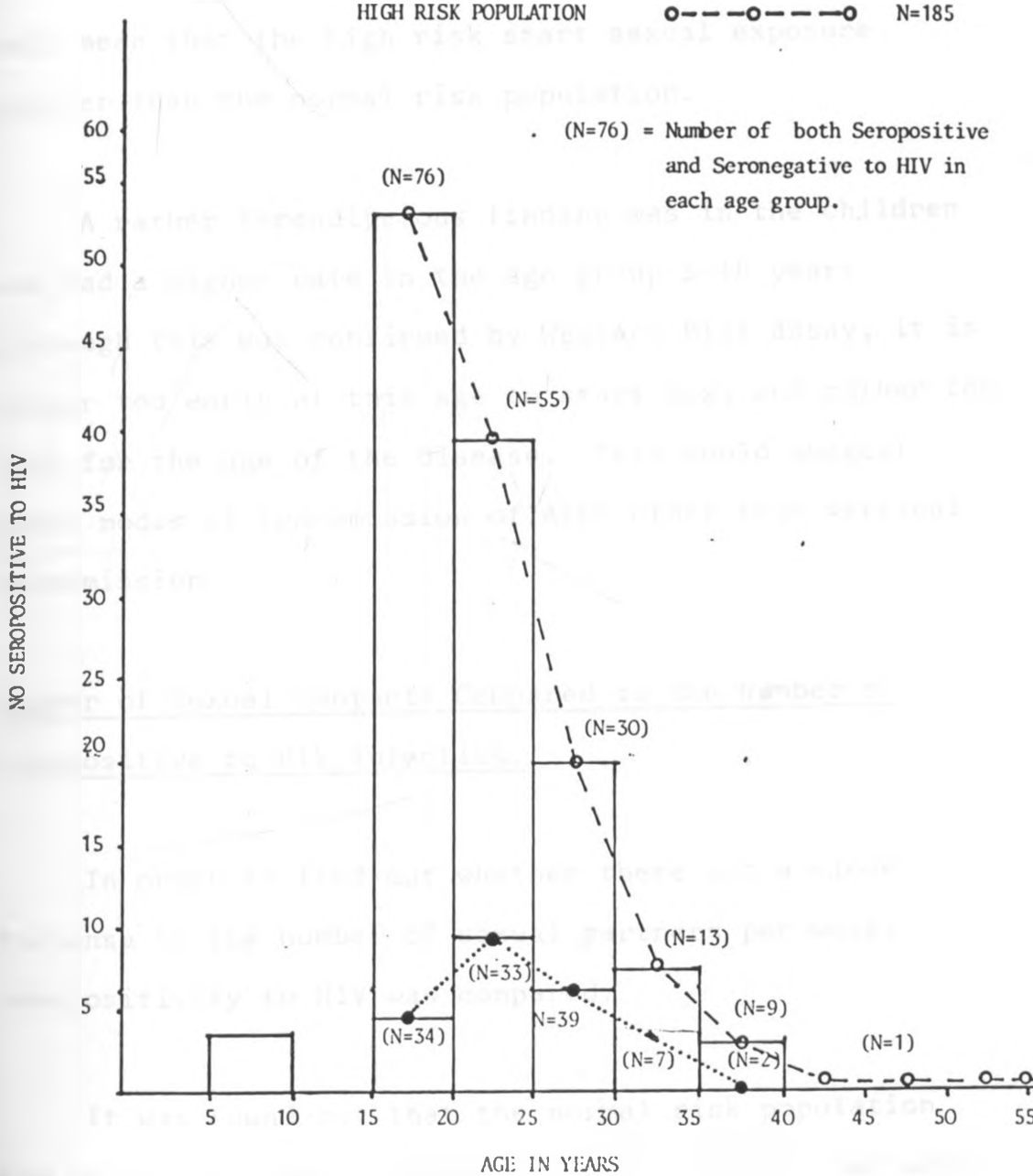
GRAPH I

CHILDREN BELOW ARE 15 YEARS ——————— N=91

NORMAL RISK POPULATION ●·····●·····● N=124

HIGH RISK POPULATION o– – –o– – –o N=185

. (N=76) = Number of both Seropositive and Seronegative to HIV in each age group.



From the age distribution compared to seropositivity, the high risk population had a higher seropositivity in the age group between 16-20 years while the normal risk reached a peak in the age group 20-25 years. It could well mean that the high risk start sexual exposure earlier than the normal risk population.

A rather serendipetous finding was in the children who had a higher rate in the age group 5-10 years. Although this was confirmed by Western Blot assay, it is rather too early at this age to start sex, and rather too late for the age of the disease. This could suggest other modes of transmission of AIDS other than vertical transmission.

Number of Sexual Contacts Compared to the Number of Seropositive to HIV Infection.

In order to find out whether there was a close response to the number of sexual partners per week, seropositivity to HIV was compared.

It was found out that the normal risk population had relatively fewer different sexual partners per week compared to the high risk population. It must be stressed that these are NOT sexual encounters but different sexual partners.

There was a statistically significant difference

in the seropositivity and number of sexual partners for the two different groups. A student's -t- test was used.

t_{α} = 11.55 p 0.001.

The mean number of sexual contacts per week was also different for the two groups.

Number of Sexual Partners per Week Compared to Seropositivity to HIV.

TABLE X:

	HIGH RISK	NORMAL RISK	
NO. OF SEXUAL CONTACTS PER WEEK	LO N = 185	LM N = 124	TOTAL
0	6 (3.2%)	8 (6.4%)	14
1	33 (17.8%)	92 (74%)	125
2	9	10	19
3	7	-	7
4	21	8	29
5	6	1	7
6	17	2	19
7	71 (38%)	2	73
8	3	-	3
9	1	-	1
10	1	2	3
11	1	-	1
14	10 (5.4%)	-	10
	185	124	309

.t = 11.55 p 0.001.

Mean number of sexual parteners per week:

High Risk = 5.29 st dev. 3.28.

Normal Risk = 1.56 st dev. 1.68.

The high risk population has 3.4 times the number of contacts of the normal population at any one time.

Seropositivity to HIV and Number of Sexual Contacts per Week.

For the two populations, the number of sexual contacts and seropositivity showed a significant difference in the case of high risk population while there was no significant difference in the case of normal population.

TABLE XI:

NUMBER OF CONTACTS PER WEEK. HIGH RISK POPULATION.

	0	1	2	3	4	5	6	7	8	9	11	14	TOTAL
	16.6%	51.5%	33.3%	42.8%	66.6%	33.3%	58.8%	83.1%	100%	100%	100%	100%	
+	1	17	3	3	14	2	10	59	3	1	1	10	124
-	5	16	6	4	7	4	17	12	0	0	0	0	61
	6	33	9	7	21	6	17	71	3	1	1	10	185

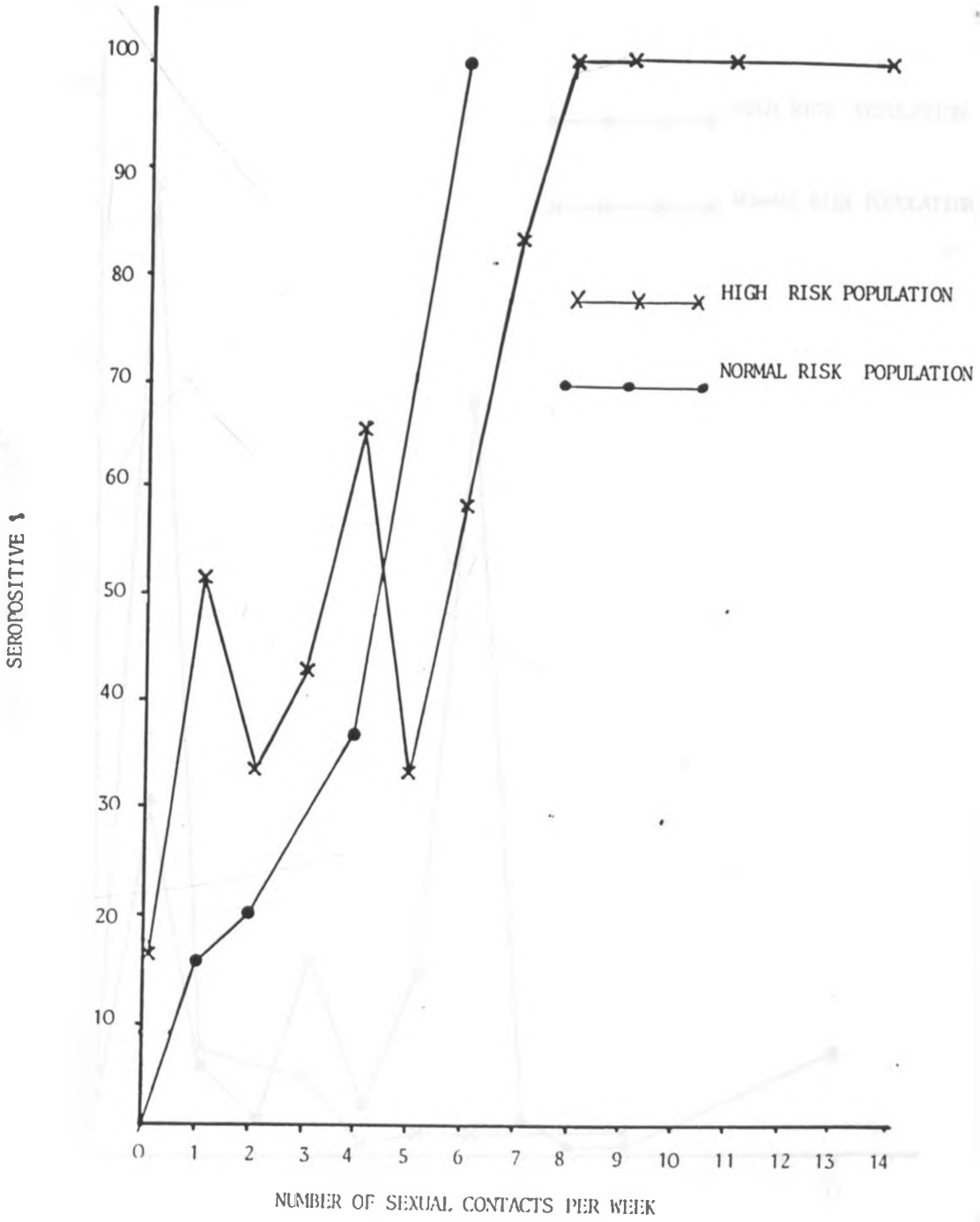
χ^2_{11}=36.22930 expected at day 7=47.

p=0.0002 when the table is aggregated to 0, 1 and 2+ contacts

χ^2_2=12.54 P<0.01.

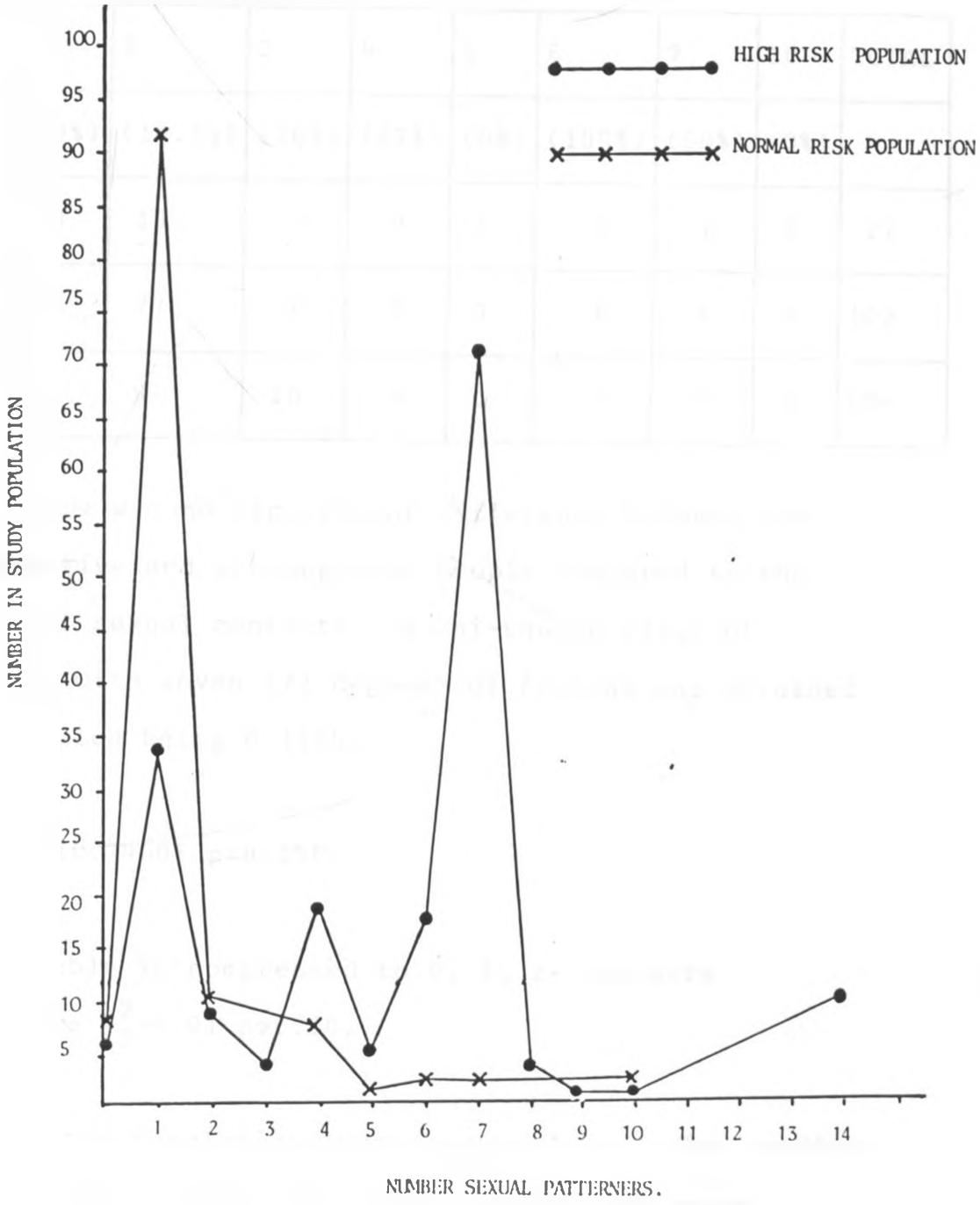
% SEROPOSITIVE TO HIV V^2 NUMBER OF SEXUAL CONTACTS

GRAPH III



NUMBER OF SEXUAL CONTACTS PER WEEK AND THE CORRESPONDING NUMBER IN STUDY POPULATION

GRAPH II



For the Normal Risk Pupulation:

TABLE XII:

Number of Sexual Contacts.

	0	1	2	4	5	6	7	10	TOTAL
	(0%)	(16.3%)	(20%)	(37%)	(0%)	(100%)	(50%)	(0%)	
+	0	15	2	3	0	1	1	0	22
-	8	77	8	5	1	0	1	2	102
TOTAL	8	92	10	8	1	1	2	2	124

There was no significant difference between the seropositive and seronegative people compared to the number of sexual contacts. A Chi-square value of 10.74008 with seven (7) degrees of freedom was obtained with p value being 0.1504.

$\chi^2_7 = 10.74008$ $p = 0.1504$.

If the table is compressed to 0, 1, 2+ contacts
Chi-square $\chi^2_2 = 4.01$ $p > 0.10$.

The two populations were compared in as far as the sexual contacts were concerned and those who were seronegative. For easy calculation the number of sexual partners were grouped.

TABLE XIII:

	NUMBER OF SEXUAL CONTACTS				
	0	1	2-5	6+	TOTAL
HIGH RISK POSITIVE	1(100%)	17(53%)	22(81%)	84(97.6%)	124
NORMAL RISK POSITIVE	0(0%)	15(46%)	5(18%)	2(2.3%)	22
	1	32	27	86	146

χ_1^2=36.3 P value =<than 0.001.

This shows a highly significant difference between the two seropositive population.

CONSIDER HAVING MORE THAN ONE SEXUAL CONTACT AS A RISK.

High Risk Population.

TABLE XIII(a):

	ELISA		
CONTACTS	+	-	
More than one	106(72%)	40	146
One or Less	18(46%)	21	39
	124	61	185

χ_1^2=6.42.

P<0.05.

The Cross Product Ratio (CPR) = 3.09 which is very high if we use it to estimate the Relative Risk. 95% CL the CPR lies between 1.4 - 6.39 which is significant.

Normal Risk Population.

TABLE XIII(b):

	ELISA		
CONTACTS	+	-	
More than One	7(29%)	17	24
Less or Equal to One	15(15%)	85	100
	22	102	124

$\}^2_1 = 2.6$

$P > 0.05$

The Cross Product Ratio (CPR) is high also 2.3 indicating an increased risk with more than one partner. The 95% CL the CPR lies between 0.82 - 6.4.

Marital Status Versus Seropositivity to HIV.

It was conceived that marriage was a factor in the spread of AIDS and therefore the two groups i.e. High Risk Population and Normal Risk Population were compared for seropositivity.

High Risk Population.

TABLE XIV: (a).

ELISA	MARRIED	DEVORCED	NEVER	TOTAL
+	20 (68.9%)	3 (50%)	101 (67.3%)	124
-	9	3	49	61
TOTAL	29	6	150	185

It will be noted that out of 185 study participants 81.1% had never married and 67.3% of these were seropositive. However in this population there was no significant difference between seropositivity to HIV and seronegativity to HIV in as far as marital status was concerned. The Chi-square with two degrees of freedom was low - 0.84276 with the corresponding P value of 0.6561.

χ^2_2=0.84276 P=0.6561. Estimation of odds ratio taking not being married as a risk was equal to 0.95% CL shows the OR between 0.38 - 2.1.

Risk Factor Being: NOT MARRIED.

Table XIV (b):

	ELISA		
	+	-	TOTAL
DIVORCED	7 (31.8%)	8 (7.8%)	32
MARRIED	15 (68%)	77 (75.4%)	92
TOTAL	22	102	124

Estimated Odds Ratio by Cross Product Ratio = 4.49. This shows a significant association between marital status and seropositivity and seronegativity to HIV infection. The 95% CL CPR lies between 1.42 - 14.25, showing that the divorcees are at a high risk of acquiring HIV infection.

Normal Risk Population.

TABLE XV:

ELISA	MARRIED	DEVORCED	NEVER	TOTAL
+	15 (16.3%)	7 (46.7%)	0 (o%)	22
-	77	8	17	102
TOTAL	92	15	17	124

In this group it will be noted that 74.2% out of the total 124 seen in the study were married and only 16.3% were seropositive to HIV. However of the 12.1% devorced, 46.6% were seropositive to HIV infection. A Chi-square with two degrees of freedom indicated a high significant difference between seropositivity and seronegativity to HIV with respect to marital status.

(χ^2_2=12.39600 P=0.0020). Estimation of odds ratio, taking devorced as the risk factor the OR=4.49.95% CL 1.42 - 14.25.

Relationship Between HIV Seropositivity and History of Injections.

Injections are a potential danger in transmission of infectious diseases especially viral diseases. The three population groups were looked at for a possible relationship.

High Risk Population.

TABLE XVI:

ELISA	HISTORY OF INJECTIONS		TOTAL
	YES	NO	
+	(a) 73 (82.9%)	(b) 51 (52.6%)	124
-	(c) 15	(d) 46	61
	88	97	185

Expected values:
(a) = 58
(b) = 66
(c) = 30
(d) = 31

There is a statistically significant difference between those who gave a history of injection and those who gave no history of injections in as far as seropositivity and seronegativity to HIV was concerned. Chi-square with one degree of freedom was 17.92% with P=0.000.

The observed value in the case of those who gave the history of injection was more than the expected (58) which shows a strong association between injections and seropositivity. Estimation of the cross product ratio was 4.3 which is highly significant. 95Cl CPR lies between 2.1 - 8.4.

Normal Risk "LM".

TABLE XVII:

ELISA	HISTORY OF INJECTIONS		TOTAL
	YES	NO	
+	(a) 3 (42.8%)	(b) 19(16.2%)	22
-	(c) 4	(d) 98	102
TOTAL	7	117	124

Expected values:

(a) = 2
(b) = 20
(c) = 5
(d) = 97

χ^2_1=1.64197 P=0.2001

Cross Product Ratio 3.8 95%CL 0.84 -17.

Fisher's exact test 0.5863.

There was no significant difference in those who gave a history of injection or no history of injection as regards serology of HIV. The expected values are no different from the observed values.

Children.

TABLE XVIII:

ELISA	HISTORY OF INJECTIONS		TOTAL
	YES	NO	
+	1(25%)	2(2.3%)	3
-	3	85	88
TOTAL	4	87	91

$\}_1^2$=1.11160 P=0.2917.

Fisher's exact test:

The figures show there is no significant difference. Very few children 4.3% out of 91 seen gave history of injection. The calculated expected values were close to the observed values indicating no significant difference.

In order to be able to find out whether there is a significant relationship or association between seropositivity and history of injections for both the high risk and normal risk populations, a hierachical Chi-square was done.

TABLE XIX:

	HIGH RISK POPULATION			LOW RISK POPULATION			
ELISA	HISTORY OF INJECTIONS			HISTORY OF INJECTIONS			
	YES	NO		YES	NO		
+	73(82.9%)	51(52%)	124(67%)	3(42.8%)	19(16%)	22(17.7%)	146
-	15	46	61	4	98	102	159
TOTAL	88	97	185	7	117	124	309

The overall $\chi^2_{(3)}$=108.73 P<0.001.

Between history of injections for the two groups the χ^2_2=18.74 P<0.001. History rejected.

Between the high risk and low risk the χ^2_1 the χ^2_1=89.0 P<0.001.

These values show that there is a strong association between seropositivity for HIV and history of injections.

HIV Infection and association of Lympnodes

The French Scientists in 1983 isolated the HIV from patients who had pesistent enlarged lymphnodes, and this is why it was known as Lymphodenopathy associated virus (LAV). Therefore the association of lymphnodes in different regions was sought for and compared in the three population in this study.

STUDY POPULATION: POSTERIOR CERVICAL ENLARGED LYMPHNODES

HIGH RISK TABLE XX

	ENLARGED POSTERIOR CERVICAL NODES		TOTAL
ELISA	Yes	No	
+	41(93.18%)	83(58.8%)	124
-	3	58	61
TOTAL	44	141	185

Expected values

a = 29.5

b = 94.5

c = 14.5

d = 46.5

The Chi-square with 1 degree of freedom in 16.35 P =0.0001. This shows that there is a strong association between posterior Cervical nodes enlargement and seropositivity. This is confirmed by the expected values being less in cell (a) than the observed.

If the enlarged posterior cervical nodes are used a screening sign for HIV Infection, a very a high sensitivity is found with a very high negative predictive value.

Sensitivity $= \frac{41}{44} \times 100 = 93.18\%$.

Specificity however is low $\frac{58}{141} \times 100$

$= 41.1\%$

The Positive predictive value

$= \frac{41}{124} \times 100 = 33.0\%$ rather very very low.

The Negative predictive value was however higher

$= \frac{58}{61} \times 100$

$= 95.1\%$

The yeild $= \frac{124}{185} \times 100 = 67.02\%$

It is noted that there is a very high sensitivity and a very high Negative predictive value.

NORMAL RISK POPULATION

TABLE XXI

	POSTERIOR CERVICAL NODES		
ELISA	Yes	No	TOTAL
+	6(85.7%)	16(13.6%)	22
-	1	101	102
TOTAL	7	117	124

$X_1^2 = 18.81$ P = 0.00001.

Used as a screening device in this population

Sensitivity = $\frac{6}{7} \times 100 = 85.7\%$

Specificity = $\frac{101}{117} \times 100 = 86.3\%$

The Positive predictive value

$$= \frac{6}{22} \times 100 \qquad = 27.27\%$$

The Negative predictive value

$$= \frac{101}{102} \times 100 \qquad = 99\%$$

$$\text{yeild} = \frac{22}{124} \times 100 =$$

IN CHILDREN TABLE XXII

	POSTERIOR CERVICAL NODES		
ELISA	Yes	No	TOTAL
+	1(16.6%)	2(2.3%)	3
-	5	83	88
	6	85	91

In Children there was no significant association between seropositivity to HIV and enlarged posterior cervical lymphnodes.

Chi-Square with one degree of freedom = 0.51113

P=0.4746.

The other lymphnodes that were assessed were the anterior cervical nodes.

ANTERIOR CERVICAL ENLARGED NODES:

HIGH RISK POPULATION TABLE XXIII

	ANTERIOR CERVICAL NODES ENLARGED		
ELISA	Yes	No	
+	8 (100%)	116 (65.5%)	124
-	0	61	61

There was no significant association between anterior cervical nodes enlargement and seropositivity to HIV Infection. Chi-square with 1 degree of freedom

2.702 P = 0.1002.

Normal Risk Population

TABLE XXIV

Elisa	ANTERIOR CERVICAL ENALRGED NODED		TOTAL
	Yes	No	
+	2(66.6%)	20(16.5%)	22
-	1	101	102
Total	3	121	124

There was no significant association between enlarged anterior cervical lymph nodes and seropositivity. Chi-square of 2.19 and P value 0.1387 (X^2_1 = 2.19. P = 0.1387).

In children none-was found to have enlarged anterior cervical nodes.

The Epitrochlear nodes. Association with HIV:

HIGH RISK POPULATION: TABLE XXV

ELISA	ENLARGED EPITROCHLEAR NODE		Total
	Yes	No	
+	11(91.6%)	113 (65.3%)	124
-	1	60	61
Total	12	173	185

There is no significant association between these enlarged nodes and seropositivity. Chi-square with one degree of freedom = 3.525 P = 0.0604.

This is very close to the rejection level of the null hypothesis (0.05) and therefore more studies would be appropriate.

NORMAL RISK POPULATION:

TABLE XXVI

ELISA	ENLARGED EPITROCHLEAR NODES		TOTAL
	Yes	No	
+	2(66.6%)	20(16.5%)	22
-	1	101	102
TOTAL	3	121	124

There seems to be no significant relationship between enlarged epitrochlear nodes in the normal population and seropositivity to HIV infection. Chi-square with 1 degree of freedom being 2.194 P = 0.1347.

There were no children who were noted with enlarged epitrochlear nodes.

There were other nodes in other regions other than the Inguinalarea, Epitrochlear, and the cervical nodes, these were analysed for association with HIV Infection.

HIGH RISK POPULATION: TABLE XXVII

NODES

Elisa	Yes	No	Total
+	8(88.8%)	116(72.5%)	124
-	1	60	61
Total	9	176	185

There was no significant association between these nodes and seropositivity to HIV. Chi-square with 1 degree of freedom was 2.045 P = 0.1526. It must be noted that some of these included those that had nodes enlarged elsewhere.

NORMAL RISK POPULATION: TABLE XXVIII

OTHER NODES

ELISA	Yes	No	Total
+	1(33.3%)	21(17.3%)	22
-	2	100	102
	3	121	124

There was no significant association between the other nodes and seropositivity. Chi-square with 1 degree of freedom = 0.5121 P = 0.4742.

No children were analysed for this because all those that were positive for HIV did not have nodes other than the sites already analysed for.

Morbidity of HIV Infection:

One of the signs and symptoms of HIV infection is diarrhea:. This can be consistently present or on and off. The association between HIV and diarrhea was looked in the study population.

HIGH RISK POPULATION TABLE XXi

ELISA)	HISTORY OF DIARRHOEA		TOTAL
	Yes	No	
+	(a)39.86.%	(b) 85(60.2%)	124
-	(c)5	56(d)	61
ELISA	44	141	185

There seemed to be a strong association between seropositivity and history of diarrhea. The Chi-square with 1 degree of freedom was 10.9486 P value = 0.0009. This is supported by the fact

that the expected value in cell (a) is (29) far less than the observed value of 39. This shows a strong association.

NORMAL RISK POPULATION

TABLE XXX

	HISTORY OF DIARRHEA		
ELISA	Yes	No	Total
+	4(36.3%)	18(15.9%)	22
-	7	95	102
Total	11	113	124

There is no association between history of diarrhea and seropositivity to HIV Infection. The Chi-square with one degree of freedom was 1.639 and corresponding P-value 0.2005. So that diarrhea was not as good an associate for HIV Infection in the Normal risk population as it is in the high risk population. Fishers exact test two tailed was 0.2106.

CHILDREN

The children in the study were analysed for association between diarrhea and HIV Infection.

TABLE XXXI

	HISTORY OF DIARRHEA		
ELISA	Yes	No	Total
+	3(8.3%)	0 (%)	3
-	33	55	88
Total	36	55	91

Fishers exact test two tailed = 0.1175.

This shows that there is no significant association between history of diarrhea and seropositivity to HIV Infection.

HERPES ZOOSTER

Herpes Zooster (HZ) has recently been seen in high numbers in different hospitals and medical institutions. The association between HZ and HIV was booked for. Both present and past HZ were considered.

HIGH RISK POPULATION TABLE XXXII

	HERPES ZOOSTER (HZ)		
ELISA	Yes	No	Total
+	10(100%)	114(65%)	124
-	0	61	61
	10	175	185

There was an association although weak but was present. Chi-square with one degree of freedom was 3.74285 with P value of 0.0530. However, the observed value - all (a) which is 10 is more than the expected value which is 6.7. This means that there is a strong association between herpes zooster and HIV seropositivity. Fishers exact test two tailed = 0.032.

NORMAL RISK POPULATION TABLE XXXIII

	H/Zooster		
ELISA	Yes	No	Total
+	1(20%)	21(17.6%)	22
-	4	98	102
Total	5	119	124

There was no association between history or presence of herpes zooster and seropositivity in the normal population. The Chi-

square with one degree of freedom was 0.000 P value 1.

No children reported history of herpers zooster or clinically had herpes zooster.

ASSOCIATION BETWEEN HEPATITIS-B-Virus Markers and HIV Infection:

Hepatitis-B-Virus Infection is akin to the AIDS virus Infection in many ways. Both are blood born and HBV can also be transmitted sexually. We analysed for the association.

Prevalence of HBV surface antibody in the HIGH Risk population out of 185 study participants was 72 equivalent to 38.9%.

TABLE XXXIV HEPATITIS B VIRUS

	SURFACE ANTIBODY	SURFACE ANTIGEN
HIGH RISK	(72/185) 38.9%	(11/185) 5.9%
NORMAL RISK	(28/124) 22.5%	(11/124) 8.9%
CHILDREN	(19/91) 20.9%	(12/91) 2.19%
TOTAL	(119/400) 29.75%	(24/400) (6%)

HIGH RISK POPULATION TABLE XXXV

	HBVsAb		
ELISA	+ve	-ve	Total
+	45(36.1%)	79	124
-	27(44.3.)	34	61
	72	113	185

There is no association between seropositivity and hepatitis -B- virus surface Antibody. Chi-quare with 1 degree of freedom was 0.78343 with P value of 0.3761.

NORMAL RISK POPULATION TABLE XXXVI

	HBVsAb		
ELISA	+VE	-ve	
+	7(31.8%)	15	22
-	21( )	81	
Total	28	96	124.

There was no association between HVsAb and HIV seropositivity in the normal population. The difference observed were by chance. The Chi-square with one degree of freedom was 0.74212 with a P value of 0.3890.

CHILDREN TABLE XXXVII

	HBVsAb		
ELISA	+	-	Total
+	0	3	3
-	19	69	88
Total	19	72	91

In the children, no child P was seropositive of those who were HBVsAb positive. Chi-square with one degree of freedom was 0.03332 with P value if 0.8552.

SURFACE ANTIGEN ASSOCIATION: TABLE XXXVIII

HIGH RISK POPULATION

	HBVsAg		Total
ELISA.	+	-	
+	8(65%)	116	124
-	3	58	61
Total	11	174	185

There was no association between HIV Infection and HBVsAg. Chi-square with 1 degree of freedom was 0.00706 with P value 0.9331.

NORMAL RISK TABLE XXXIX

ELISA	HBVsAS		
+	+	-ve	
+	2(9.1%)	20	22
-	9	93	102
	11	113	124

There was no association between HBSAg in the normal risk population and HIV Infection. Chi-square with 1 degree of freedom was 0.000 P value 1.0.

In Children, there were none found to have the surface Antigen to Hepatitis B virus who were also positive for HIV.

SYPHILIS ASSOCIATION WITH HIV INFECTION

Syphilis is one of the common sexually transmitted diseases. Therefore the common sufferers of syphilis may also be at risk of acquiring HIV Infection. An association was looked for with history of treatment and serology.

HIGH RISK POPULATION: TABLE XL

ELISA	Treatment of Lues		
	Yes	No	
+	57(83.8%)	67(57.3%)	124
-	11	50	61
Total	68	117	185

Although this was based on memory recall, it is very well known that once a person has been treated for Syphilis he continues to remember. There was a very strong association between history of treatment for syphilis and HIV Infection. Chi-square with 1 degree of freedom was 12.54 corresponding P value was 0.0004. This is confirmed by having a greater value observed (57) while the expected value would have been 45.5 should we accept the null hypothesis.

NORMAL RISK POPULATION TABLE XLI

	History of Lues		
ELISA	Yes	No	
+	6(31%)	16(15%)	22
-	13	89	102
Total	19	105	124

There was no significant association between the people with history of lues treatment and with HIV Infection. Chi-square with 1 degree of freedom was 1.93 with a corresponding P value of 0.1647.

The Children were not analysed for this because of the unreliability of the information.

ABORTIONS ASSOCIATION WITH HIV INFECTIONS:

Todate there is very little information about the effect of HIV infection on pregnant mothers.

HIGH RISK POPULATIONS TABLE XLII

NUMBER OF ABORTIONS

ELISA	0	1	2	
+	84(68.8%)	16(84.2%)	4 50%	104
-	38	3	4	45
Total	122	19	8	149

There were (36) study participants who were not analysed for abortion because they had never been pregnant before. In this study population there was no relationship between number of abortions and HIV Infection. Chi-square with two degrees of freedom was 3.41149 with corresponding P value of 0.1816.

NORMAL RISK POPULATION TABLE XLIII

NUMBER OF ABORTIONS

ELISA	0	1	2	3	4	Total	
+	13	5	2	1	0	21	8/21=38.1%
-	83	7	4	0	1	95	12/95=(12.6%)
Total	96	12	6	1	1	116	

There were(8)eight study participants who were not included because they had never been pregnant. There was a significant association between abortions and seropositivity. The Chi-square with four (4) degrees of freedom was 11.5249 with correpondence value of 0.0213.

STILL BIRTHS ASSOCIATION WITH HIV Infection

It is not yet clear whether HIV infection may be an important factor in the still births rates. A history of still births was looked at in association with HIV infection.

NUMBER OF STILL BIRTHS

HIGH RISK POPULATION: TABLE XLIV

NUMBER OF STILL BIRTHS

ELISA	0	1	2	TOTAL
+	95(67.8%)	8(100%)	1(100%)	104
-	45	0	0	45
Total	140	8	1	149

There was no significant association between still-births and HIV infection. The Chi-square with 2 degrees of freedom 4.14457 with P value of 0.1259.

NORMAL RISK POPULATION TABLE XLV

NUMBER OF STILL BIRTHS

ELISA	0	1	TOTAL
+	18(16.8%)	3(33.3%)	21
-	89	6	95
Total	107	9	116

There is significant association in this population between HIV and still births. Chi-square with 1 degree of freedom 0.6159 and Corresponding P value 0.4326.

BLOOD TRANSFUSION

Blood transfusion is one route that surely transmits the HIV infection. In this area, the prevelance of blood transfusion and association of HIV Infection was looked at as a risk factor.

HIGH RISK POPULATION TABLE XLVI

	HISTORY OF BLOOD TRANSFUSION		
ELISA	Yes	No	
+	5(62.5%)	119(67.2%)	124
-	3	58	61
	8	117	185

There was no significant associations between HIV Infection and blood transfusion in this group of people in the area. Chi-square 0.000 with P value of 1.00.

NORMAL RISK POPULATION TABLE XLVII

	HISTORY OF BLOOD TRANSFUSION		
ELISA	Yes	No	
+	0(0%)	22(18.0%)	22
-	2	100	102
Total	2	122	124

There was no significant association between blood transfusion and HIV Infection in group of people Chi-square 1 degree of freedom 0.00 P value I.

CHILDREN

No child reported history of blood transfusion although some probably may have received blood in the neonatal period which they could not remember.

PAROTID ENLARGEMENT AND ASSOCIATION WITH HIV Infection

Parotid enlargement is common in Africa due to Iron deficiency aneamia. It has also been reported from Zaire in association with HIV Infection in children.

HIGH RISK POPULATION TABLE XLVIII

	ENLARGED PAROTID		
ELISA	Yes	No	
+	11(78.5%)	113(66.1%	124
-	3	58	61
Total	14	171	185

There is no observed difference between the HIV and parotid enlargement. Chi-square with 1 degree of freedom 0.4356 P value 0.509.

NORMAL RISK POPULATION TABLE XLIX

	ENLARGED PAROTID		
ELISA	Yes	No	
+	0(%)	22(18%)	22
-	2	100	102
	2	122	124

There is no significant difference between the HIV Infection and enlarged parotid gland. Chi-square 0.00 P value 1.

CHILDREN

Although the parotid enlargement was reported in children in association with HIV Infections there.

TABLE L

	PAROTID		
	Yes	No	
+	1(0.03%)	2(0.03%)	3
-	28	60	88
Total	29	62	91

was no significant association between the two in ray study population. Chi-square 0.00 with P value 1.00.

Oral candidiasis and association with HIV Infection

Oral thrush is one the cardinal signs of an immuno-compromised state and therefore usually present in fully blown AIDS cases. In these HIV carriers an association with oral candidiasis was looked for.

HIGH RISK POPULATION TABLE LI

	ORAL THRUSH		TOTAL
ELISA	Present	Not Present	
+	6(100%)	118(65.9%	124
-	0	61	61
Total	6	179	185

There was no significant association with HIV Infection although it was close to the rejection level. The expected values however in cell (a) Are less than the observed values.

NORMAL RISK POPULATION TABLE 52 LII

	ORAL THRUSH		
ELISA	Present	Not	Total
+	0 (%)	22(18%)	22
-	2	100	102
Total	2	122	124

There was no association between Oral thrush and HIV seropositivity. The Chi-square with 1 degree of freedom was 0.00 with P value 1.00.

No Children were noted with oral thrush in the study participants.

HIV ASSOCIATION WITH STDS

It is generally believed that some sexually transmitted diseases like Chancroid and Gonorrhea offer an entry site to the HIV (Plummer personal communication-Unpublished).

TABLE 53 LIII

	CHANCROID	HERPES SIMPLEX	GONORRHEA
HIGH RISK	$13/_{185}=7\%$	$1/_{185}$	$4/_{185}$
NORMAL RISK	$10/_{124}=8\%$	$3/_{124}$	$5/_{124}$

The association of HIV seropositivity and STDs was looked and analysed with combined population.

TABLE LIV

	STDS	NONE	TOTAL
HIV +	19(52%)	127(46%)	16
-	17	146	163
Total	36	273	309

There was no significant association between STDs and HIV seropositivity $X^2_1 = 0.5$ $P > 0.05$.

The lack of association between HIV and STD may be thc small numbers observed with STDs.

ELISA and Western blot tests

The ELISA was used in this study as a screening test and Western blot (WB) was used as a conformity test. Not all the samples that were twice positive on ELISA were Western blotted. A certain number that were equivocal were Western blotted and some that were twice Elisa positive. This is because the Western blot is very expensive. The Elisa Equivocal results were excluded in the following calculations.

Combined Population

TABLE LV

	Western Blot		
ELISA	+	-	Total
+	41	19	60
-	4	23	27
TOTAL	45	42	87

Sensitivity = $\frac{41}{45} \times 100$ = 91%

Specifity = $\frac{23}{42} \times 100$ = 54.7%

PPV = $\frac{60}{87} \times 100$ = 68.3%

High Risk Population

TABLE LV1

	Western Blot		
ELISA	+	-	Total
+	28	16	44
-	1	11	12
TOTAL	29	27	56

Sensitivity = $\frac{28}{29}$ = 96.5%

Specifity = $\frac{11}{27}$ = 40.7%

PPV = $\frac{28}{44}$ = 63.6%

Normal Risk Population

TABLE LV11

	Western Blot		Total
ELISA	+	-	
+	12	1	13
-	3	5	8
TOTAL	15	6	21

$$\text{Sensitivity} = \frac{12}{15} = 80\%$$

$$\text{Specifity} = \frac{5}{6} = 83.3\%$$

$$\text{PPV} = \frac{12}{13} \times 100 = 92.3\%$$

From this study it has been shown that results of Screening using the ELISA tests may heavily depend on the population that is screened. There seemed to be more false positives in the high risk population than the normal risk population. This raises the question that the high risk population could be having cross-reacting conditions that need to be found out. The numbers tested in this study with W.B. are rather small because of expense and lack of availability of W.B. kits. It is suggested that more numbers be used in order to evaluate this point.

One interesting observation in this study was found with one study participant who had AIDS clinically and had both the ELISA and W.B. tests negative. However, he had a strong HIV-antigen reaction. So it is important to be aware that both these tests (ELISA and W.B.) could be negative while the patient has HIV infection. The explanation probably is that there is a stage in the HIV infection when the antibody production and levels may be too low to detect.

This may mark a stage of 100% Immune decomposition. This study participant had two wives who were strongly positive for HIV infection on ELISA and W.B.

Therefore was suggest that false negative results may be seen with Western blot and therefore more sensitive tests should be investigated.

Sex Distribution by Elisa.

	ELISA		
	+	-	TOTAL
MALES	22(24.1%)a	69 b	91
FEMALES	127(41.1%)c	182 c	309
TOTAL	149	251	400

a = 33.89.

b = 115.

c = 57.1.

d = 193.

Chi-square with one degree of freedom = 8.62. P value 0.001. Sex ratio female/male is 1.7:1. There seems to be a significant difference between males and females and HIV. Although the difference is not expected according to other studies in Africa, the explanation is that the population is skewed and not homogeneous. There are more females than males, and with different risks. However once the population was split into the respective groups, the significant difference disappeared as shown in the tables below.

High Risk.

Table LVIX

ELISA			
	+	-	
MALES	20	18	38
FEMALES	104	43	147
TOTAL	124	61	185

Chi-square with one degree of freedom was 3.70188 with P=0.0544 thereby accepting the Null hypothesis. The female/male ratio = 1.3:1. This ratio has been observed elsewhere in Africa.

Normal Risk Population.

Table LX

ELISA			
	+	-	
MALES	1	7	8
FEMALES	21	95	116
TOTAL	22	102	124

History was accepted at χ^2_1 of 0.00 and P value = 1. The female/male ratio = 1.4:1. This is almost the same as above.

Children.

Table LXI

	ELISA		
	+	-	
MALES	1	44	45
FEMALES	2	44	46
TOTAL	3	88	91

History was accepted at $\}^{2}_{1}$ of 0.00 and P=1. The female/male ratio being 1.9:1. This ratio is higher than the above two ratios and deserves further studies to confirm.

CHAPTER 7:

DISCUSSION

Acquired Immuno-deficiency syndrome is a world-wide epidemic. Different countries have different figures for the seroprevelance and others have very few figures for the incidence.

In this study a total of four hundred participants were seen. This was a cross section of the population of one area in Rakai district. Of the 400 study participants 185 (46.25%) were high risk population. They were considered high risk because of their social-economic lifestyle. Living and working in Lyantonde was considered a bigger risk than living in the rural area. Out of 185, 79.5% were females while 20.5% were Males. The other population was those considered normal risk. This meant that they were not at any increased risk. They were not living and working in Lyantonde township, but were living in Rakai district. These were a total of 124(31%) of the total population seen. Out of these 116 (93.5%) were females and 8(6.5%) were Males.

Children formed the third group in the study population with 91(22.75%), out of which 46 50.5% were females and 49.5% were Males.

The normal risk population had relatively fewer males because of the method of selection. Men are less likely to bring children for immunisation and because women generally are more aware of their health than men.

In the high risk population, women were more than men because they were likely to be employed as bar-maids and hotel staff than men. The benefits, for women was even higher than for men considering the money exchanged for sexual favours.

7.1. AGE DISTRIBUTION:

The mean age of the high risk population was no different from the normal risk population. The mean was 23.5 years for high risk and 25.3 for low risk. This is the age that has the highest fertility and activity both economically and sexually. The children's mean age was 7.5. This was rather high considering that HIV is about 7 years old and the average incubation period being 5 years. A much lower age group would have been appropriate to investigate the children seroprevelance. Such a study would works better if hospital based rather than community based.

7.2. SEROPREVELANCE OF HIV INFECTION

Seroprevelance of HIV Infection varies from country to country. It also varies from different population groups depending on risk factors. Risk factors include promiscuicity, blood transfusion and infections.
In the HIGH RISK POPULATION, out of 185 study participants, 124(67%) were seropositive for HIV antibodies using the Elisa Du-pont technique. This is a very high figure, perhaps one of the highest figures. Similar studies have been done else where and have shown that the high risk population, mainly those who get multiple parteners have a high seroprevelance of HIV (10,11,4). The figure

The figure of 67% seropositivity is rather worrying if it is assumed that seropositivity to HIV infection doubles every two years. Although its not known where and how long this population has been at the 67% seropositivity if we assume the doubling rate to be true, then in 1989-1990 the AIDs problem may be overwhelming. Although the incubation period is not clearly known up to this date, five years taken as the average, then the period between 1990-1992 may be a strain to hospitals admitting more and more cases of AIDs.

What is however interesting is that nearly all this group that was seropositive, none showed any fully known clinical signs of AIDs. They stay sexually active and as promiscous as they have always been, thereby continuing to spread the disease indiscriminately. This is a sad state of affairs considering that no drugs are about to come to the market and certainly no vaccines in the foreseable feature.

In the normal risk population; the seroprevelance for HIV was 17.7% by the Elisa Du-pont technique. This corresponds well to the known figures from the Uganda blood transfusion centre. Studies done elsewhere not in Uganda show a corresponding rate and sometimes higher than this (3,14,15,18).

However whatever the difference in seropositivity, this rate is unacceptably too high. It will also double in the next two years such that by 1995 the normal population in this area will be having a huge number of AIDs cases dying or sick. Either way it will be a great strain on the few existing services.

Since there are no existing control programmes, this 17.7% seropositive group will continue to have unrestricted sexual encounters thereby spreading the virus further.

7.2.1. In children, 3 out of 91 3.3% were seropositive to HIV on the Elisa Du-pont technique. However, when they were Western-blotted - only (1) one was seropositive. Therefore the actual seroprevalence in children was $1/_{91}$ which is 1.1%. This is a fairly low figure although as pointed out earlier it' falls in the age group that is rather too old for the disease. This very case is perhaps very interesting because he was a male aged 10 yrs. It is reasonable to assume that this child was too young for sexual intercourse and too old for the disease as is currently known. This suggests other routes of transmission to account for this one case. The child remains healthy without showing any signs of AIDs which may strengthen the fact that this is a recent Infection. However, in some cases there are those who are known to be seropositive without showing clinical signs for more than five years.

These three population groups were significantly different in their seropositivity indicating different risks. Chi-square with two degrees of freedom was 135.25 and corresponding P value = 0.0000 very highly significant.

It is somehow re-assuring that the under 15 years who form about 45.6[38] of the country's population has a low seroprevalence to HIV. Therefore control measures should be aimed at this age group. It is also known that the attitudes and practices in this age group can be changed more easily.

7.2.2. COMPARISON OF THE NORMAL RISK AND HIGH RISK POPS.

The normal risk population were different from high risk population for HIV infection.

This confirms the fact that these populations are actually differently at risk for HIV Infection.

For the adults, only, the High risk were 84.9% seropositive while the normal risk were 15.1% seropositive. The expected value for the populations have been indicated in the results.

7.2.3. COMPARISON OF NORMAL RISK POPULATION AND CHILDREN:

The total number seen here were 215 and out of these 22(88%) were normal risk population while the children were 3(12%). There was a significant difference between these two groups.

This difference is expected considering that the child population is not sexually active compared the adult group. This may not be the only fact to account for the seen difference. The normal risk population has other risk factors eg. blood transfusion and repeated injections for ailments.

Although the adult population, has a bigger risk than the children, (5,32,33) it is conceivable that the rate in children may increase with time due to vertical transmission. Although they may not pose a great danger in transmission, once they develop disease, they will be a great loss to nations and obviously a strain on the already few and poor medical services.

In Zaire and Rwanda already there is an over load in paediatric AIDS cases. This as usual is associated with opportunistic Infection (OI) and multiple staphylococcus infection like otitis media (OM) (P. Piot personal communication). This is definately expected with this sort of trend of AIDS. More and more cases will be seen.

SEX RATIO:

There seems to be a difference between the sex ratio between the Western countries and Africa generally. While in the USA the ratio of female/male in 1:14, in Africa it has been 1:1 thereby indicating a homosexual distribution in USA and heterosxual distribution in Africa (10,11,19,37).

In this study, it was demonstrated that a population will have different ratios if its not heterogenous. The Ho was rejected where the study population was combined while when it was split into more homogeneous groups this significance disappeared indicating that the sex doesn't influence HIV Infection thereby accepting the null hypothesis.

The Female of Male ratio for the positives was 1.3:1 in the high risk population and 1.4:1 in the Normal risk. This confirms the fact that our main route of transmission is basically heterosexual. In children however, the ratio F/M was 1.9:1 indicating more females at a greater risk than males. However, the positives were too few to make any conclusions on this peadiatric ratio. It may be better evaluated with other studies. In other studies in New York and Miani (37) the Female/Male ratios was lower 45/55. The observed defference may be due to the fact that there are more females at birth than males (40) and therefore more famles at risk of vertical transmission. What is important however is that the paediatric HIV Infection will be an important marker of continuing Heterosexual transmission. Although paediatric HIV cases in the

west are determined by drug abuse in the west, in Uganda and Africa generally it will remain a heterosexual influence.

7.3. SEROPOSITIVITY OF HIV BY AGE

In the three population groups, there were significant differences between the age distribution and HIV infection showing peaks at different ages.

However, in the high risk population the peak of HIV seropositivity appeared a little earlier between age group 16-20 years, while the normal risk peak was between 21-25 years. This could confirm that there are actually high risk because they tend to start sexual contact rather early, considering that the big risk factor in this population is sexual promiscuity Although there is a difference in age, there were 18% in the normal risk population who tended to start sexual contact early. In both cases seropositivity was highest in the age group between 16-40 years. This is consistent with finding elsewhere where the peak with highest prevalence is between 20-30 yrs (41,42).

This is dangerous because AIDS tends to attack the most productive age group such that there is likely to be a great loss in human resources in the long run. There were no seropositive individuals in the normal risk population over age 35 years suggesting that the disease may have moved into the rural areas recently while there were few seropositives beyond the age

40 years suggesting that the disease may have been present in the township a little early. This is however based on the assumption that beyond the age of 40 yrs women are likely to be less sexually active and that any seropositivity detected should be explained by previous behaviour.

All the children who were seropositive were between 6-10 years. Although only one was confirmed by Western. Blot as positive and the rest negative, it is not explainable by the known Epidemiology of AIDs.

7.4. SEXUAL CONTACTS AND HIV:

It was rather difficult in this study to make a clear line between the normal risk population and the high risk population except based on the social-economic life style. This therefore produced overlaps in these two populations as indicated by graph II on the number of sexual patterners per week.

It however demonstrates that the high risk-population tended to have Multiple partners per week (mean 5.29/week, 275 patterners per year) while the normal risk population tended to have less patterners (Mean 1.56/week, 81 per year). The high population out of 185 study participants seen 79% had more than one pattener per week; while in the normal risk study participants 19.6% out of 124 had more than one patterner per week. This shows that the high risk population were having about four times the number of sexual patterners compared

Table XI gives the distribution of seropositivity and number of sexual patterners per week. It is clear that the Null hypothesis that there is no difference between serology of HIV and number of sexual patterners per week except by chance is rejected. This shows that there is a strong association between the number of partners and the risk of of acquiring HIV Infection.

Table XII shows that there is no association between number of sexual partners and HIV Infection. This confirms that the high risk and normal populations are basically different in their sexual habits. If having more than one sexual partner is taken as a Risk, then table XIIIa shows the cross product ratio is 3.09. The 95% confidence limit is 1.4 below and above up to 6.39 which is significant. Compared to table XIIIb the Cross product ratio is 2.3 with the 95% confidence limits below up to 0.82 and above up to 6.4. This is not significant in this normal risk population. This confirms one fact that having more than one sexual patterner increases the risk of HIV Infection. This finding is supported by other findings elsewhere (41,42,43). Therefore in public health education the question of multiple sexual contacts should always come out strongly as a factor in HIV propagation.

However, the above results need further analytical studies especially prospective cohort studies to be able to compute the relative risk accurately. This study can only roughly estimate and generate hypotheses about the relative risks of multiple sexual contacts.

7.5. MARRIAGE

In Uganda the average year at marriage is about 18.1 years (40)

This is rather too early because it has a direct bearing on the number of children per woman and therefore a direct impact on the economy. From the study, marital status was not associated with seropositivity to HIV in the High risk population chi-square with 2 degrees was 0.84276 with P value of 0.6561, while there was a significant association between Marital status and HIV seropositivity in the normal risk population. This is what is expected, considering that Marital status in high risk population is meaningless wether one is considered married or unmarried, they will continue to be promiscous.

If we assume that NOT BEING MARRIED is the risk factor in HIV Infection, the cross product ratio (CPR) in the high population is 0.9 indicating that this may not be a risk. While if the same assumption is made in the case of normal risk population, the Cross product Ratio (CPR) is much greater 1.4, 95% confidence limits 1.42 below and 14.25 above. This incriminates not being married as a risk factor for HIV.

From the results, therefore, it is indicated that marriage is to a certain degree protective for HIV Infection (Table XVI).

Table XV shows the seropositivity by Marital status. Out of 124 seen 92(74.2%) were married while 15(12.1) and 17(13.7) were not married. Of the married only 15(16.3%) were seropositive for HIV compared to 46.7% seropositive in the Unmarried group. The null hypothesis that there is no relationship except by chance between marital status and HIV serology is rejected at P=0.0020 Chi-square with two degrees of freedom 12.39600.

The observed results in this population are likely to be explained by assuming that the normal population is less likely to be promiscous and therefore less likely to transmit the virus. This may be an important factor during health education.

7.6. INJECTIONS:

Injections have been talked about in all forums of AIDs as a possible route of transmission. It is also a well known factor that viral disease are easily transmitted by dirty syringes that have been re-used. In Uganda injection abscess have been reported very frequently as being caused by poor sterility of syringes (44). In the Western-countries or developed countries injections mainly from illicit drug use are a sure way of transmitting AIDs. This is why drug addicts tend to have high prevalence rates of HIV infection.

In Uganda and generally in Africa illicit drug abuse is virtually unknown and very unlikely to account for any disease. However, indiscriminate re-using of disposable syinges, coupled with a high number of injections given at any one time in different clinics, could be crucial in transmission of AIDs.

Table XVI shows the prevalence of injections in the high risk population. Out of 185 study participants 88 (47.6%) had a history of injections out of which 73(82.8%) were seropositive for AIDs. Compared to the normal population, table XVII shows that only 5.6% out of 124 study participants gave a history of injections and out of this 3(42.8%) were seropositive for HIV. Table XVI shows that these was a strong association between history of injections and seropositivity to HIV. Chi-square with 1 degree of freedom was 17.92 P = 0.000. There was however no strong association in the case of Normal risk population table XVIII Chi-square with 1 degree of freedom being 1.64 and P value 0.2011 thus rejecting the null hypothesis. This applied to the children seen in the study (table XVIII) where there was also no significant association between HIV serology and history of injections. Chi-square with 1 degree of freedom was 1.11160 P=0.2917.

The findings observed in table XVI for the high risk population are supported by the fact that the expected values for the 1st cell were less (58) than the observed value of 73.

If the history of injections is taken as a risk factor, then there a big Cross product ratio of 4.3. Taken as an estimation of Relative risk, the normal population has a less risk of 3.8 as the cross product ratio.

Although no study has come out to singularly pin-point injections as a route, it is clear from this study that there is a strong association.

However, it is not possible to know which one is the first. The injections first and one gets the HIV infections, or the HIV infections and therefore one is more sickly and visits the doctors more frequently and therefore gets more infections?

Whatever, the explanations, it is important to bear this in mind as a big dangerous possibility and therefore care should always be taken to clean and sterilise the reusable syringes. Those syringes that are disposable should never be reused (45, 46).

Another factor that should be high-lighted is the present WHO expanded programme of Immunisations (EPI). Unless care is exercised during the immunisation campaigns, the injections may be a great source of HIV spread.

A hierachical Chi-square was done to demonstrate that there is a strong association between injections and seropositivity to HIV. This was highly significant, Chi-square with three degrees of freedom 108.73 $P = 0.000$.

The association between high and low risk population controlling for seropositivity was equally high X_1^2 89.0 $P < 0.001$ and the association between the history of infections for the two groups was highly significant X_2^2 18.74 $P < 0.001$. These values show that there is a strong association between HIV and history of injections.

7.7. LYMPHNODES:

Workers in France isolated the virus from the patients who had persistent lymphnodes and this is why it is known in France as the Lymphadmopathy associated Virus (LAV). Since then enlarged lymphnodes have always been associated with AIDs. In this study lymph nodes were looked as an important sign for early disease. These were any extra-inguinal chains of unexplained origin. The inguinal chains were not emphasised because they are always present in Africans due to multiple skin infections. According to the CDC criteria of lymphademopathy (37), lymph nodes were evaluated in each study participant. Table XX shows the relationship between HIV seropositivity and posterior cervical enalrged nodes. This shows a very strong relationship thus rejecting it: Null hypothesis at Chi-square with 1 degree of freedom 16.35 P value =0.0001. Although posterior cervical lymphadenopathy tends to persist after infection of scalp it was found a very good screening test for AIDS with 93.18% sensitivity.

Although the other values, PPV and specificity were low 33.0% and 41.4% respectively, the NPV and the yield were high 95.1%, 67.02% respectively thereby making POSTERIOR CERVICAL ENLARGED NODES an important sign in symptomless HIV infection.

This significant association was also seen in the normal risk population shown in table XXI. With 1 degree of freedom Chi-square was 18.81 and P-value 0.0001. As a screening sign it's even more specific although less sensitive. A 86.3% and 85.7% nevertheless making it a very useful clinical sign in medical practice for HIV infection.

However in children, Ho that there is no association between lymphadenopathy and HIV, was accepted. This should be expected considering that children in rural areas are very likely to have repeated scalp infection and other staphylococcus skin infection, thereby accounting for persistence of cervical nodes.

Although this relationship has not been sighted in the literature about AIDS we feel that it may offer a good suspicion Index for symptomless HIV infection where there is no facility to screen for HIV infection. However, more studies are needed to be able qualify this observation.

7.7.1 Anterior Cervical Nodes were analysed for association with HIV wether they co-existed with other nodes elsewhere. Table XXIII and XXIV for High risk and Normal risk population respectively, showed no significant relationships thus accepting the Null hypothesis in all cases. This needs further evaluation with big numbers to be able to indicate there is no relationship.

Epitrochlear nodes were analysed for this HIV relationship and in Normal risk and High risk population (tables XXV and XXVI, the Null hypothesis was accepted at the indicated P values. Although, the epitrochlear nodes are very often enlarged in syphilis, this was not reflected in the high risk population. This may be artifactual because of small numbers seen. More studies will be necessary to clearly demonstrate presence or lack of relationship with HIV infection.

No other lymphnodes were independently associated with HIV infection from this study.

We therefore propose that posteriorcervical enlarged lymphnodes should always be examined for where there is a high prevalence of symptomless HIV infection. It may offer a clue to the diagnosis of HIV in the early stages.

7.8. DIARRHEA:

Virtually all cases of AIDs are associated with diarrhea on and off in this study area and in Uganda at large (8,45). However it has not been fully studied in HIV symptomless cases.

This study demonstrates a very strong association between symptomless HIV infection and diarrhea. Table XXIX and table XXX and table XXXI for the high risk, normal risk and children population respectively show that diarrhea was more associated with the high risk group X_1^2 = 10.9486 P = 0.0009 thereby rejecting the Null hypothesis. The rest of the study population Ho was accepted.

The strong association between HIV and diarrhea suggests that anybody with a history of persistent diarrhea especially from a high risk group should be investigated for HIV infection.

Although there was no relationship in the normal risk group and children, these should also be investigated for HIV on history of persistent diarrhea. This is supported by studies done elsewhere in Africa (42, 46, 47).

Diarrhea and vomiting is basically common in most third world countries and causes alot of deaths of the under fives. With HIV infection becoming common, the countries should expect more deaths in this group of the population. It may not be quite obvious but its a question of time in my view.

7.9. HERPES ZOOSTER: (HZ)

HZ is usually a secondary infection. An individual rarely gets HZ as a primary infection. Usually they have had chicken pox virus which lies domant in the posterior roots and flares up once there is depression in the immune system. There is increasing frequency of HZ in most medical institutions more than before (N. Sewankambo personal communication) WHO classifies HZ and herpes simplex virus (HSV) as indicative of HIV infection but rather lower on the Ladder (48).

Table XXXII in this study shows that is a strong association between symptomless HIV infection and HZ Fisher's exact test =0.032. This is a very important marker of immuno-depression because HIZ rarely is a primary infection but a secondary infection.
It is also interesting to note that all 10 study participants who gave a history of HZ were all HIV seropositive (100%). This is however distributed in the high risk population while it not reflected in the normal risk population. The explanation here is that the normal population has less prevalence of HIV infection; than the high risk population.

No children reported or was suffering from HZ at at the time of examination. It is concluded from this study that herpes Zooster is significantly associated with

HIV symptoless infection and therefore any patient presenting w ith HZ or giving a h/$_o$ of HZ should be investigated for HIV infection.

7.10. HEPATIS-B-VIRUS ASSOCIATION

Hepatitis -B- virus is one common infection, that shares some epidemiological factors with HIV. It is blood borne and also sexually transmitted especially in Homo-sexuals (40,47,48). There have been strong associations between HIV infection and HBV makers in the western world where Homosexual practise and drug abuse is very common. However the biggest worry was the association of the HBV vaccine as a risk factor for AIDs. This was however dispelled, with more work (37).

Tables XXIV, shows the carrier status of the HBVSag and those who have at one stage had HBV infection. The high risk population seem to have been more exposed to HBV with (38.9%) than the other populations in the study.

HBV has been isolated from all body fluids just like the HIV. It is also believed that bed bugs and other blood sucking arthropods can transmit the HBV mechanically. In tables XXXIV to XXXVIII we found no association between HIV infection with either HBVSAb or HBVSAg. This confirms the fact that our mode of HIV transmission is predominantly heterosexual rather than homosexual

One other factor to be considered is the role of anthropods like mosquitoes or bed-bugs mechanically transmitting HIV. If this was happening, the old ages and children would also be equally affected since there is no mosquitoe preferential bitting. Essentially the study area is basically a holoendemic area as far as Malaria is concerned (Personal observation) so that there would'nt be a big prevalence difference between the population structures. However more studies in this field especially the blood sucking insects in the role of transmitting HIV should be done.

In this study we conclude that HBV is not associated with HIV because the main route of transmission is predominantly heterosexual.

7.11. ABORTIONS AND STILL BIRTHS:

There are many definitions of abortions depending on the institutions and centres. For the purpose of this study in the rural areas, abortion was defined as miscarriage of pregnancy before and up to 24 weeks of gestation.

Still birth were defined for the purpose of this study as outcome of pregnancy between 25 weeks up to 40 weeks being a dead featus.

In the periods defined above there are other diseases that could cause abortions or still-birth

but they were not looked at independently. Table XLII shows the relationship between number of abortions and HIV in the high risk population. Of 104 who were HIV positive 80% had never had abortions while15.4% had had 1 abortion and 3.8% had had two abortions.

The Null hypothesis that there is no relationship between abortions and HIV was accepted. Chi-square 2 degrees of freedom 3.41149 P = value 0.1816. The high risk population compared to Normal risk population showed a difference. Table XLIII shows that those mothers who were seropositive tended to have more abortions than the seronegative as shown by $8/_{21}$ = 38.1% (for HIV + ve) and 12/95 = 12.6% (for HIV - ve).

There was a significant association between HIV infection and abortions in this population.

There was no association between HIV and abortions in the high risk population because they tended to have a low fertility rate and high secondary infertility rate due to sexually transmitted diseases. This is true in all high risk populations due to PID and Chylamadial infection acquired during Promescuity (Plummer Frank, Pumwani prostitute study unpublished). From this study, it is observed that there is a strong association between abortions and symptomless HIV infection in the normal risk population. More analytical epidemiological studies need to be done to investigate more of this observation. However, in ordinary medical practice HIV infection should be investigated in a mother who gets

repeated abortions in the absence of no explainable cause.

Tables XLIV and XLV show that there is no relationship between HIV infection and still births, in both the high and normal risk populations. If abortions are associated with HIV infections then inn-evitably the still births will be fewer in the normal population. The fact that the high risk population has a high secondary infertility rate, the still births are bound to be few. This may account for lack of relationship in the two populations with HIV infection

7.12 Blood transfusion AND HIV INFECTION:

Blood transfusion has been labelled, in all aspects as a sure way of transmitting HIV infection. It is almost certain that if one receives blood that is infected with HIV, then he or she will surely get infected.

In this study it was shown that the rate of blood transfusion is basically very low due to absence of the appropriate medical centres to transfuse patients. Out of 400 study participants only 10(2.5%) has received blood transfusion since 1976.

In the high risk although of the total number who received blood transfusion (8), (5/8 62.5%: were

were seropositive, Ho-that there is significant association between HIV and blood transfusion was accepted at P = 1. The same applied to the normal population. The observation can be explained by the fact that generally blood transfusion is rare in this area and or that these people may have received, however, little blood, basically non-infected blood. The former offers a better explanation in the face of the AIDS Literature and blood transfusion.

Whatever the observation in this study, blood should be screened for HIV before transfusion. Considering that the observed prevalence of HIV infection is very high, blood transfusion without screening for HIV is extremely dangerous.

We are inclined to suggest that the above observation may not be true because some of the blood receipients may not have necessarily received blood from this area, and it may have been long time ago before the AIDS virus was present. This tends to augur well with the fact that the HIV is an entirely new virus never seen before in this area.

In other countries where blood screening before transfusion is routine, the risk of contracting AIDs by this route is virtually zero, while where there is no screening the risk is very high.

7.13. PAROTID ENLARGEMENT WITH HIV

Parotid enlargement is a common clinical sign for Iron difficiency anaemia(49) in the tropics. It has however been reported in other areas as being enlarged in HIV infection. However, in this study no association was seen in all the three population groups seen. Tables XLVIII, XLIX and L show there is no relationship. Although there was no association in the high risk group. Suffice it note that out of 14 study participants 11 were HIV seropositive and had enlarged parotid gland.

These observations need further studies and evaluation to understand them better. A prospective cohort study would be most appropriate for this.

C H A P T E R 8.

8.1 CONCLUSION AND RECOMMENDATIONS.

8.1 A very high prevalence of HIV without clinical signs and symptoms was observed in this study.

The High Risk population or the promiscuous population were 67.7% seropositive to HIV which is a very high rate and needs urgent intervention to stop any further spread.

The Normal Risk population were 17.7% seropositive to HIV which is equally alarming.

The children population between 2-15 years were 1.1% seropositive to HIV infection. This figure although seemingly low, is in fact very high considering that the below 2 years children were not studied. It was also observed that the main routes of transmission were predominantly heterosexual with infections being incriminated. However now analytical studies should be done to evaluate this observation. It was further observed that the number of sexual partners were linearly related to the risk of acquiring HIV infection and that abortions and STDs were strongly related or associated to HIV infection.

Therefore, these theories and hypotheses need

further evaluation with different studies and more broad based. Intervention is highly recommended before the HIV infection is totally out of control

8.2 RECOMMENDATIONS.

It is clear from this study that HIV infections or AIDS has reached alarming proportions in this area of Uganda with the more promiscuous population forming the reservoir of infection. Urgent measures are needed to stop further spread.

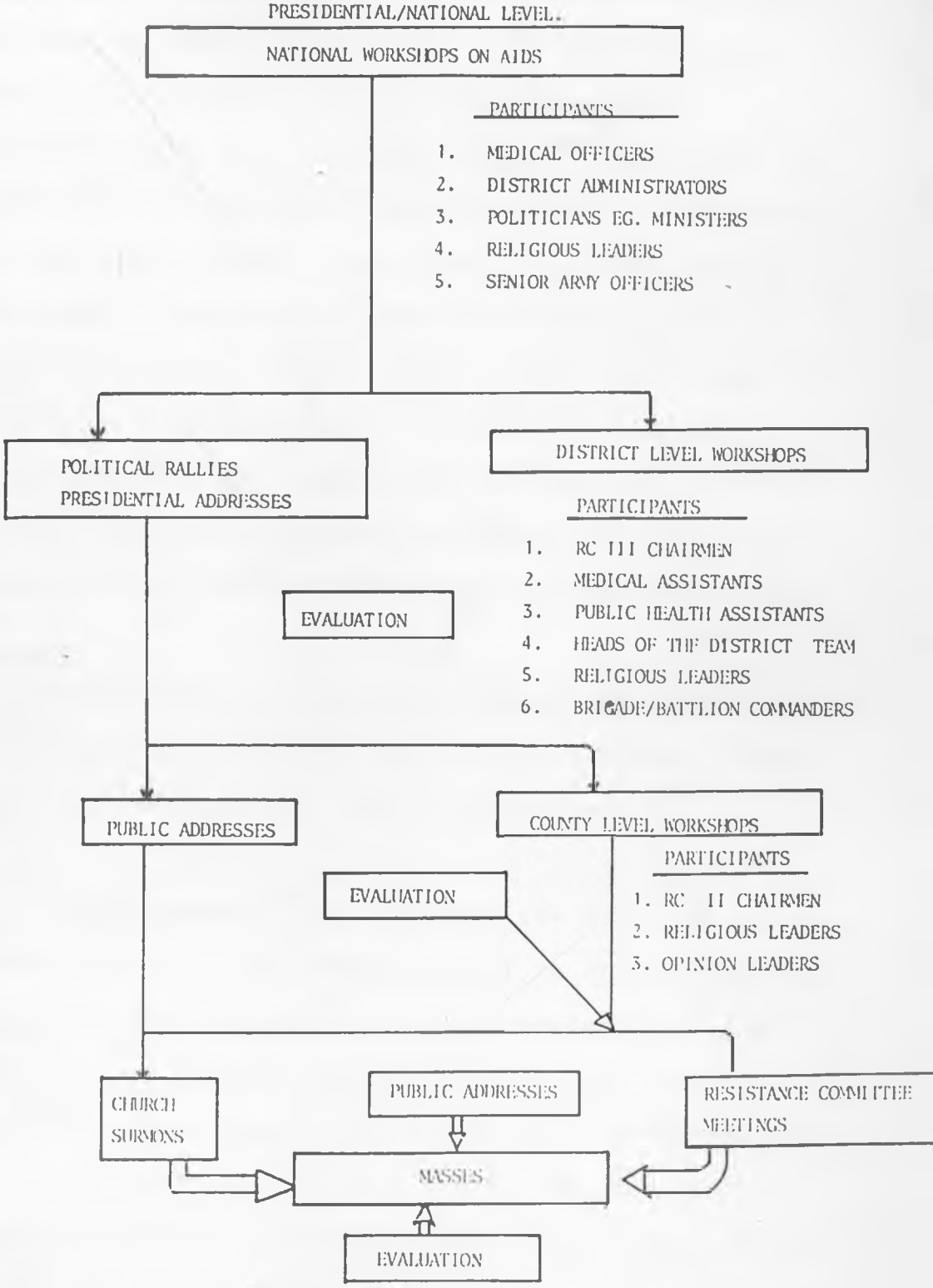
We are well aware that curative drugs will not become available in the foreseable future. Neither is a vaccine possible before the late 1990s. Therefore, the only measure that can be instituted is public education.

8.2.1 PUBLIC EDUCATION.

It is recommended that public health education should be intensified in every way possible. The objective of the education should be to CREATE AWARENESS that there is AIDS and that there is no cure except altering one's sexual behaviour.

The present level of AIDS or HIV related education is woefully inadequate both in the medical field and for the ordinary population. It must be vastly expanded and

SUGGESTED PEDIGRAM FOR HEALTH EDUCATION ON AIDS



diversified, targetted not only at the general public but also at specific subgroups. The specific groups should be those who are High Risk and capable of transmitting to more contacts, those in a position to influence public opinions and those who interact with infected individuals. Presidents, Ministers and all Government functionaries should be targetted for increasing their understanding of AIDS with a hope to passing on this awareness. As usual Government dignitaries assemble more people at any one sitting to explain a Governemnt policy and among the many issues they talk about, AIDS should always be one of the them.

In Uganda there is a very appropriate administrative structure of grass-root resistance committees. These should be targetted for health education.

Workshops should be organised for District Administrators at the central level to create awareness about AIDS and possible methods of prevention. Once these District Administrators go back into their districts, they should organise District Workshops with the help of Medical Officers for all the Resistance Committee Chairmen Level III. The objectives should be clearly defined for each level, taking into account the level of comprehension.

Then each Resistance Committee III Chairman should in-turn organise seminars for the different Resistance

Committee II Chairmen until it crystalises into the nine houses cell seminar about AIDS. This flow of knowledge is absolutely desirable if it can be achieved.

Whatever the method and language used the objective should be to create awareness about AIDS and that individuals will stop the spread by altering behaviour.

Educators must be prepared, in the face of the current threat, to specify that certain sexual practices put one at a bigger risk. Clear terminology must be used avoiding euphemistic expressions like "intimate contact", "close expression of love", and "love carefully' which at best confuse and covey the most vague and dangerous message. Clear exppressions like DON'T HAVE SEXUAL INTERCOURSE WITH MORE THAN ONE PARTNER OR DON'T HAVE SEXUAL INTERCOURSE WITH PROSTITUTES convey hard hitting but clear and sincere messages.

It is perhaps inconceivable to avoid sex altogether and therefore people should be educated about protected sex. The best available in the present circumstances is the condom. If and when used properly it should be protective. However care must be exercised and accurate information given as to the usage of the condom. It must be stressed that one condom can only serve for one sexual episode and it must be thrown away and another one worn for another sexual episode. This as can be expected will depend entirely on the supply and demand of the condom.

We suggest in order for the condom to be effective it should be abundantly available literally in every kiosk or shop, hospitals, clinics and in hotels and lodges. They should also be at an exceedingly low cost - almost free of charge. The condom, finally, should be advocated for with a degree of caution. Only studies of the integrity pressures of the condom have been done, and not usage pressures. So nobody knows at what level does the condom filter the virus or not. High pressure functional studies are needed before one can commit the whole world to "condom". If the condom is only 90% effective in family planning, one wonders what success rate there is with HIV infection spread. However considering that nobody is likely to stop sex and that there is no cure, the condom is the only available alternative.

Condoms availability may raise big concern about encouranging sexual activity among the young, and the Catholic Church may look at it as one form of family planning, however the consequences of HIV infection completely overwhelms such thinking.

Another goal of the education campaign should be to get the records clear and reduce the hysteria that surrounds casual transmission. There is unnecessary hysteria and ostracisation about somebody who has HIV infection. This is unfounded and is totally wrong. Up to now no transmission of HIV by casual contact has been

established.

The mass media especially newspapers should adopt a more responsible approach of reporting rather than sensationalising for purposes of making money. They are partly responsible for the hysteria and misinformation.

The newspapers should carry cover stories aimed at educating the public about facts as given by researchers and not as seen by the editors of these papers. They should also maintain advertisements indicating the risks and preventions rather than advertisements and cartoons that redicule AIDS victims. The newspapers should understand that AIDS is a disease like T.B. and not a curse. One sad story about papers is when they highlight falsified information or poorly conceived messages about cures for AIDS. This tends to send people on the rampage with false confidence of the cure. This in the final analysis is responsible for some peaks in the prevalence and incidence of HIV infection.

From this study the under 15 years comprise about 45.6% of the total population. These should be targetted with specific emphasis on sex education as early as possible. Fortunately, they still have a low prevalence and the incidence is not expected to increase sharply. The message they should be given clearly is that there is AIDS and it is transmitted by sexual intercourse.

The Ministry of Education should accept to have a chapter in the school curricula and syllabi about AIDS right from primary 5 (five) to higher school certificate level. This should not only be about AIDS but generally about Sexually Transmitted Diseases (STD) in general. Although the Catholic Church may feel offended about sex education, it is cost beneficial to teach about sex and AIDS than to engage on religious rhetoric.

Finally, although there is already a National AIDS Committee in Uganda, it should be better coordinated in the field of Health Education. It should organise workshops and seminars for the medical officers to increase clinical awareness of AIDS. It should be expanded and looked at as a full-time job rather than part-time. Basically there should be a department of communicable disease control under the Ministry of Health where AIDS should fall under. The President's Office should have a direct communication about the AIDS situation periodically.

The National AIDS Department should have a separate vote approved by Cabinet rather than get submerged into the already strained Ministry of Health. However, there should be close cooperation with the Ministry of Health.

8.2.2 SCREENING OF BLOOD FOR TRANSFUSION.

The next available strategy to fight and reduce the spread of HIV infection is screening of blood for transfusion. The rate of blood transfusion in the area of

study was basically very low and this accounted for lack of any demonstrable association, however it is now a non-disputable fact that transfusion is associated with HIV. It is therefore of great cost benefit to screen all blood before transfusion. This is a very expensive exercise but MUST be done.

The objective should be to establish regional blood banks or better still to have district level central blood banks where all the screening should be done, so that these central points can feed the satellite hospitals with screened blood. This is very important when man-power is not yet available and when the screening equipments are not yet available. The ultimate goal should be to have a screening machine in every health institution that will do blood transfusion.

VOLUNTARY SCREENING:

The aim of health education would be to finally convince people that voluntary screening is often desirable. This will be very difficult but should be aimed at. These people should be assured of confidentiality. Once one is screened and found positive, he or she should be counselled and educated about his disease. It is unethical not to tell the screenees and may be counter-productive. In this study it was not done because of logistical problems but where one has time and space he should counsel his seropositives and caution them against further spread of disease.

It is not necessary to have very expensive tests like the Western Blot (WB) but the ELISA should be very accurate in experienced hands.

For screening of people and blood banking, qualified and experienced personnel should be employed to try and develop the man-power. It is clear that the laboratory technique is woefully rare and therefore man-power development to handle the crisis should be given priority.

All screening tests have inevitably a number of false positives. This should be taken into account when counselling individuals, although all equivocal results should be confirmed and donors informed. With the high seroprevalence seen in this study, surveillance of the disease must be implemented without further delay.

This should be done by both passive reporting and active seeking of information, to measure prevalence and incidence of AIDS or HIV infection in the population. However massive national serosurvey for HIV are rather useless because of a very low cost effective ratio. By the time one finishes the national survey, the prevalence has actually changed. Finally the results got from the national survey cannot be utilised for planning purposes or even projecting the disease situation. For these national serosurveys to be useful they must be repeated after some time which becomes rather expensive and time consuming. However, pilot studies to gauge point

prevalences and analytic studies to identify more risk factors may be more useful in disease surveillance.

An attempt should be made to define AIDS as we see it clinically in Uganda and have a clear working definition. This will help in reporting. There should be monthly reports from each district about the number of AIDS cases diagnosed clinically and by blood screening.

This reporting should be made mandatory every month, care being taken not to duplicate numbers otherwise giving a falsely high figure. A system of labelling the cases should be used in order to keep tracing them and their contacts. It must be stressed that contact tracing in AIDS would be extremely difficult and if mishandled could be counter-productive. However, with an aggressive national AIDS health education programme the turn over may increase more than expected.

In this study the High Risk population had the highest number of sexual contacts and had the highest seroprevalence. Legally one cannot talk about prostitutes because they are not legalised. However, everybody knows prostitutes exist and form a huge reservoir of the infection. It would be worthwhile if prostitution was legalised so that this High Risk population can be concentrated in designated places for easy contact tracing and disease surveillance. Public Health Education would inevitably be delivered a lot

easier to them.

MANDATORY SCREENING:

Mandatory screening will never be a solution to the spreading of AIDS and in fact it may flare up the problem by persons who should be screened going underground. However some groups, may benefit from mandatory screening. These groups should include the armed forces, plice and prisons staff and inmates. This serves two purposes. One is to be able to plan for the man-power in the forces; two, the fact that they have an occupational hazard that may require blood transfusion, those who are seropositive would stop blood donation. One silent fact is that the forces tend to be more promiscous than the civilian population and therefore counselling after seropositivity may yield some results.

Finally the operational readiness of the army needs soldiers who are almost permanently fit. The soldiers are also in most cases stationed away from their families and therefore even if not promiscous may have sexual relationship with the population in the new area thereby spreading AIDS.

Therefore, the above arguments support mandatory screening of the forces but not of the civilian population. Therefore the decision to be tested for HIV should remain a matter for individual discretion but the Government should encourage the programme, and use mandatory screening where necessary.

Testing programmes should be coupled with strong guarantees of confidentiality. Punitive measures should be taken for any careless disclosure of the screenees results.

In this study we demonstrated that there is a low prevalence in children of 1.1% whether it is high or low there is no rationale from stopping these positive children from having unrestricted association with other children. They should also continue to enjoy unrestricte use of school facilities. However they may be poor performers in school because of repeated illness. This should be brought to the attention of the teachers so that at no time should they be unfairly punished.

The paediatric AIDS or HIV infection should fall in a separate category for surveillance. This is because the children somewhat differ from adults in as far as risk factors are concerned. The clinical features in paediatric AIDS also differ from the adult AIDS. Paediatric AIDS will also be a very important marker for monitoring heterosexual spread in the populations at different risks for HIV infection.

Paediatric AIDS may at one stage be used as an evaluation marker for the intervention programmes. Such that if a decrease is observed in the cases then it can be concluded that there is basically an alteration in the rate of transmission. In Uganda and Africa in general,

the mode of HIV transmission in children will for along time remain vertical, with drug abuse and bisexual practices which are rare, being very low risk factors.

We have also shown that one child about 10 years was confirmed positive by both antibody and antigen. This could well mean that this child has been positive for a long time and therefore capable of transmitting this virus in the future especially if we assume that this child had vertical transmission of HIV. Therefore as we get more seropositive children, health education and counselling must go along with screening.

8.2.3 RESEARCH NEEDS.

While the HIV infection continues to spread and kill unabated, the academic researchers must inevitably continue to find ways and means of fighting back. There must be International cooperation on this and an unbiased sharing of all available knowledge - however limited it may be.

Most African countries except Uganda have been reluctant to speak about AIDS as this might jeopardise the tourist industry. However this is sheer obscurantism considering that the tourists come from high prevalence areas like America and Europe. The truth of the matter is that tourists bring some HIV with them and take some away. Therefore countries must be prepared to speak the

truth about the HIV prevalence.

The only way we can report the real figures is to be able to carry out both descriptive and analytical epidemiological studies in our populations. Importation of man-power to do these studies for us is just absurd to say the least. The indigenous researchers must feel that it is their responsibility to do this research rather than think they are doing a favour to the Ugandan people. We suggest that, from this descriptive study, a number of theories and hypotheses have been raised, they should be investigated further by appropriate studies.

For quite a bit of time we will have to rely on foreign expertise in some fields like molecular biology and high powered virological research. This is because we cannot afford the equipements and in any case such polished research may lead to a white elephant situation.

The research that we need to do should be at the same level or just slightly above the social and economic service level. We should therefore try and isolate the virus that causes disease in our environment and the clear determinants of the disease in our own situation.

All attempts should be made to define our own criteria of HIV infection or AIDS for purposes of surveillance. It can be done by conducting analytical studies for over a period of time. This will reduce

heavy dependency on the big brothers for definition of AIDS. The AIDS research in Uganda needs to be broadened so that more investigators are allowed free access to the few available laboratories.

The success of the AIDS research will depend heavily on dissemination of information freely without fearing academic critisms.

Finally the Institutions, like Makerere University and Mulago Hospital and the Uganda Virus Research Institute need fully fledged Departments dealing with AIDS. All attempts should be made to keep in close liaison with other laboratories that do a lot of research for free distribution of various viruses, DNA clones, cell lines and other reagents as they are created. This will help the Institutions keep update with the AIDS information which changes very quickly.

The Government of Uganda must be prepared to provide unrestricted grants for research and man-power development. Unless this is done, Uganda will lag behind in the knowledge about AIDS and therefore measures to prevent the disease will always lag behind.

Research will continue to be necessary as long a different strains of HIV continue to imerge on the scene. Therefore in Uganda attempts should be made to isolate

and type the virus that causes disease in Uganda. This will be necessary in order to be sure that in Uganda, the virus being seen is the same or not the same as the others being seen elsewhere. Secondly, it will be useful in determining whether there are any new HIV or related viruses emerging in Uganda. Effectively one would be keeping a close look on our HIV. High technology research is not yet feasible and perhaps should receive less emphasis. Since International cooperation has already been highlighted, high technology institutes in the West would be useful in this respect.

The Institutions, Uganda Governments and researchers in AIDS must devise and develop programmes of intervention based on our own research rather than the imported knowledge about AIDS. Whatever we import be it knowledge or expertise in any field it should be modified and improved to suit our situation whenever possible.

From this study, the association between HIV infection and injections was found to be very significant. Although the interpretation of this fact needs careful reasoning, suffice it to say that the injections may be a risk factor in HIV transmission. With the current emphasis on EPI, greatest care must be taken to ensure that no syringes are re-used and sterility of the equipments used in the EPI programme of paramount importance. During the study period, a lot of

immunisation infection abscesses were seen in this area indicating that sterility of syringes and needles were poor. There was also no doubt the syringes were being re-used. This may be a great source of HIV transmission. It is therefore suggested that at the time of evaluation of the EPI programme, the rate of abscesses from immunisation infections should be found out. It is also suggested from this study that cohort studies should be done on a number of children who received immunisation since this decade started to be able to ascertain whether immunisation injections may have transmitted HIV.

8.3 CONSTRAINTS.

In any research project, the investigator inevitably gets problems that may have a lot of counter productive effects.

In this study a number of problems were encountered. First all this project was being done far away from where laboratory analysis was being done. This tended to produce delays in the serology results. Communication was poor and some of the serum collected got lost on the way. Materials for research were rather difficult to get in time because they were also being collected from Nairobi. This resulted in loss of effective time on collection of data and serum for analysis.

To be able to perform accurate tests for HIV on any

serum, it must be stored and kept at -20^{o}C or below, however during the long journey transporting this serum it was exposed to temperatures up to o^{0}C. We do not know the effect of this.

During the project, electricity was one disturbing problem because it would go on and off very frequently. So inevitably the stored serum at one time or another was exposed to very high temperatures. This effect of this exposure cannot be gauged in this study. Most of the vaccines that were being used, several times got spoiled resulting in heavy losses and reduced immunisation coverage during the project.

This project was investigating a very highly stigmatised disease and therefore the problems associated with such stigmatised disease were encountered. Some people just refused to be examined and to be recruited as study participants. Others simply refused to participate because they were aware that there was no cure of AIDS. The study involved bleeding the study participants who included children. This was one of the most difficult part. The study participants disliked the whole idea of bleeding and more so of the children. This was due to primitive conservatism associated with ignorance about the disease.

Another major constraint was time loss during the necessary journeys to the DCH in Nairobi. This resulted

in time lag in this study.

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