CLINICAL MANIFESTATION OF

ACQUIRED IMMUNE DEFICIENCY SYNDROME

IN ADULTS AS SEEN

AT THE KENYATTA NATIONAL HOSPITAL

A dissertation in part fulfillment for the Degree of Master of Medicine (Medicine) in the University of Nairobi

by

DR. ERASTUS OLONDE AMAYO MB, ChB (NBI)



MEDICAL LIBRARY UNIVERSITY OF NAIROBI FACILITY OF MEDICILE KENYATTA TATICI 1. HOSPITAL D.C. NAIRODI - KENYA

DECLARATION

I certify that this thesis is my own original work and has not been presented for a Degree in any other University.



DR. AMAYO E. O. MB, Ch.B (NAIROBI)

This dissertation has been submitted for M.Med (Medicine) examination with our approval.

Signed:

BIAmelo

Prof. G.B.A. Okello, MD. FRCP M.B, B.S, D.T.M.&H (BIOL, MI BIOL (LOND). ASSOCIATE PROFESSOR AND CHAIRMAN DEPARTMENT OF MEDICINE UNIVERSITY OF NAIROBI.

Signed: MACAOULL.

Dr. D. M. IOwili, M.D., D.D.V., (Eng.) Senior Consultant Dermatologist KENYATTA NATIONAL HOSPITAL.

----/2

	TABLE OF CONTENTS		
		P	ages
• •	Summary	-	3
•	List of Abbreviations	-	4
	List of Tables	-	5
	List of Figures	-	6
•	List of Photographs	-	7
•	Introduction and Literature review	-	8
•	Objectives	-	15
•	Materials and Methods	-	16
•	Results		19
•	Discussion	-	40
•	Conclusion	-	47
	Recommendation	-	48
	Appendix	-	49
	Acknowledgements	-	56
	References	-	57

- 2

SUMMARY

50 confirmed AIDS patients admitted in the medical wards between March to December, 1987 were studied. Male to female ratio was 1:5:1. The mean age was 31 - 7 years. Females had an earlier peak at 21 - 25years as compared to the males at 26 - 30 years. The commonest risk factor was heterosexual contact with multiple partners in 80% of the cases. The patients were of low socio-economic status.

The commonest general signs and symptoms were unexplained weight loss in 92%, fever in 66% and generalized lymphnode enlargement in 24% of the cases. In the gastrointestinal system the commonest signs and symptoms were oral thrush 66%, chronic diarrhoea 60% and dysphagia in 50% of the cases. 46% of the patients had chronic cough. The most significant radiological finding in the abnormal chest x-ray was pleural effussion in 50% of the cases. The central nervous system was involved in 36% of cases, with meningitis being the commonest sign accounting for 28% of all the central nervous system signs.

10% of the cases had Kaposi's sarcoma on histology of which 60% were of the aggressive form. The commonest skin manifestation was maculo-papular pruritic skin rash. 56% of all the patients had hemoglobin less than 10g.dl.

List of Abbreviations

AIDS Acquired Immune Deficiency Syndrome

HIV Human Immunodeficiency Virus

ARC Acquired Immunodeficiency Syndrome related complex

.

CMV Cytomegalovirus

T₄(CD₄) T helper/inducer cell

T₈ (CD₈) T suppressor cells

List of Tables

Distribution of the marital status 21 Table 1. of patients. Distribution of patients by Table 2. occupation. 22 Table 3. Distribution of recognized risk factors in the patients 24 Table 4. General signs and symptoms 25 Table 5. Signs and symptoms in the Gastrointestinal system 26 Radiological signs on the chest Table 6. x-ray. 28 Table 7. Symptom in the Central Nervous 29 System. Table 8. Diagnostic features in the Central Nervous System. 29 Table 9. Skin signs 30

Pages

List of Figures

Pages

Figure 1. Age group distribution of males - 20

Figure 2. Age group distribution of females - 20

List of Photographs

				rages
Photograph	1.	Oral thrush	-	33
Photograph	2.	Genital ulcers	-	34
Photograph	3.	Fungal skin infection	-	35
Photograph	4.	Oral thrush, Right sided facial nerve weakness, and right sided hypoglossal		
		nerve weakness.	-	36
Photograph	5.	Kaposi's sarcoma involving the tongue.	-	37
Photograph	6.	Kaposi's sarcoma of the tonsils also note the		
		jaundice	-	38
Photograph	7.	Kaposi's sarcoma with lymphodenopathy	_	39

Do

INTRODUCTION AND LITERATURE REVIEW

- 8 -

The term Acquired Immune Deficiency Syndrome(AIDS) was first used in 1981 in the U.S.A. to describe the condition in a number of previously healthy young homosexual who presented with severe opportunistic infection(s) and or Kaposi's sarcoma which was indicative of a deficiency in cellular immunity (1,2,3). In 1983 clinicians in Brussels and Paris described AIDS in African patients of Central African origin (4). Obel et.al (5) and Okello (6) reported the first cases in Kenya in 1984.

Agent

The Human Immunodeficiency virus (HIV) previously known as Human lymphotropic virus (HTLV III), lymphadenopathy associated virus (LAV) or AIDS associated virus (ARV) was identified as the causative agent for AIDS by workers in U.S.A. and France (7,8,9). The virus is a human retrovirus characterized by the enzyme reverse transcriptase which converts viral RNA into a double stranded DNA (7,8,9).

Immunopathogenesis

The HIV virus preferentially infects the CD_4 (T_4) subset of the lymphocytes (10). There is evidence that CD_4 antigen expressed on the T helper/inducer lymphocyte is the receptor for HIV virus. Due to the tropism for the CD_4 (T_4 cells) and its cytopathic affect there is absolute reduction of CD_4 cells and a reversal of the CD_4 to CD_8 ratio. (11) The CD_4 lymphocyte is a central figure in the immune response intimately involved with monocytes, macrophages cytotoxic T cells, natural killer cell and B cells in modulating the immune response. (11, 12, 13, 14).

Furthermore there are cellular defects in the lymphocytes which include decreased blast transformation to mitogens and antigens (11, 13), decreased lymphokine production (11, 12, 14), diminished cytotoxic response (14) and depressed, initiator of B cell immunoglobulin production (11, 14). The B cells in AIDS patients are polyclonally activated and this is depicted as raised level of total immunoglobulin predominantly 1gG and 1g A(15). Since B cell are actively proliferating they are incapable of responding to signals that normally trigger them hence the frequent occurence of pyogenic infection (15).

Monocytes and macrophages are also infected and this leads to defective chemotaxis and extracellular killing (46). In addition to T and B cell abnormalities substances capable of suppresing the in vitro immune response have been found in serum of AIDS patients (17).

Transmission

HIV is readily transmitted in human beings. Initially homosexuality was regarded as the major route of transmission (1,2,3,). However more recently heterosexuality and bisexuality have been identified as important routes of transmission (18). In studies conducted among African AIDS patients heterosexuality was found to be the major route of transmission. Furthermore these cases tended to be more promiscious as compared to the unaffected (19). T

Transmission can also occur through transfusion of whole blood (20) or its products (21). It can further be transmitted through contaminated needles as in the intravenous drug abusers. Vertical transmission has been reported (22). Less established transmission route are thought to include scarification by traditional heaters.

CLINICAL MANIFESTATION

A patient infected by the HIV virus can present asymptomatically by seroconversion only or a infectitious mononucleosis like illness. Furthermore a patient may develop generalized persistent lymphodenopathy with or without constitutional symptoms which includes; fever, night sweats, malaise, diarrhea and weight loss of unknown actiology (ATLS related complex).

- 9 -

The classic Acquired Immunodeficiency is characterized by opportunistic infections, Kaposi's sarcoma and lymphoid malignancies (1,2,3,12). A patient may present in any of the stages mentioned above, there is a progression to the next stage although the determinant for this is still unknown. The time for development from one stage to another being very variable.

Respiratory system

Pneumocystis carinii pneumonia is the commonest respiratory presentation in Western literature (1, 2, 3). It is the index presentation in about 50% of all AIDS patients and accounts for 85% of all the pulmonary infection (1,2,3,23). Pneumocystis carinii pneumonia can be acute, but is more often characterized by a subacute and insidious onset as patients complain of mild cough or chest discomfort shortness of breath of two to ten week duration eventually leading to progressive hypoxemia (23). Despite the high in incidence of pneumocystis carinii in Western literature it was only isolated in 14% of the African patient with AIDS seen in France (4).

Other causes of pneymonitis include virus like cytomegalovirus, fungus like cryptococcus neoformans, histoplasma capsulatum coccides immitis bacteria like mycobacteruim intracellulare, legionella pneumophilia and even Kaposi's sarcoma (23, 24).

Bacterial pneumonia caused by conventional pathogens such as streptococcus pneumonia, hemophilus influenzae occur more frequently in AIDS patients (24). The incidence of tuberculosis caused by mycobaterium tuberculosis has been noted to be increasing in patients with AIDS (25). Patient with tuberculosis and HIV infection are much more likely to have extrapulmonary involvement and also to have unusual radiographic features. The breakdown of sites are pulmonary 61.9, pleural 0.1%, millary 9.5%, lymphatic 19.0% and other sites 8.6% in cases reported in Florida (25).

Gastrointestinal tract

Persistent or recurrent diarrhoea is one of the most striking presentation in African and Haitian AIDS patients (26, 27, 28, 29, 30). In Uganda (27) Rwanda (28), Zaire (29) and Haiti (30) the incidence has been found to be 55%, 59%, 89% and 84% respectively. Various pothogens have been isolated in the stools with cryptosporidium being more frequently isolated (31), others include isospora belli and coccidia.

Cytomegalovirus (CMV) colitis characterized by fever abdominal pain and bloody diarrheoa has been reported (32). Mycobacterium intracellulare may also cause diarrhoea which mimicks whipple disease (33). On the other hand cases with diarrhoea or malabsorption without any isolatable pathogen are known to occur.

Oropharygeal candiasis is commonly seen, in Uganda (27), Rwanda (28), Zaire (29), Haiti (30) with an incidence of 48%, 48%, 82% and 42% respectively. It presents as dysphagia, odomyphagia or retrosternal pain. Herpes simplex oesophagitis, may present a similar clinical picture.

Kaposi's sarcoma is ocassionally found in the gastrointestinal tract and may present with bleeding and non-specific symptoms.

In the liver biochemical and morphological changes frequently occur (34). The biochemical changes include raised serum transaminases and raised alkaline phosphatase. Morphological changes include hepatic granuloma either non specific or due to mycobacterium tuberculosis, mycobacteruim intracellulare and cytomegalovirus. Viral hepatitis particular hepatitis. B and Non A, Non B, is a frequent presentation. Other culprits include cytomegalovirus and Ebstein Barr virus (34).

Central nervous system

It is recognized that 30 - 40% of AIDS patients develop neurological complaints (35, 36). In about 10 - 20% this constitutes the presenting complaint. 35, 36).

The commonest neurological presentation is sub acute encephalitis "AIDS dementia complex" (37) which is related to primary HIV infection. This has an insidious onset leading to progressive dementia with impaired memory and concentration, psychomotor slowing, motor deficits, legs weakness and tremor, behavioural changes with apathy and withdrawal and signs of organic psychosis (37).

Another presentation related to primary HIV infection is a vacuolar myelopathy presenting with sensorimotor deficit, spinal ataxia eventually leading to paraplegia and urinary incontinence. (38). Involvement of peripheral nerves (polyradiculopathy polyneuritis and cranial nerve palsy have been, reported in 15% of AIDS patients (35, 36).

Other presentation are related to opportunistic infection of the central nervous system. Toxoplasmosis

is a common infection typically presenting with focal symptoms and signs (39). Other opportunistic infection include cytomegalorirus and herpes simplex encephalitis (35, 36). Cryptococcal meningitis is the commonest opportunistic Central nervous infection in African patients (4, 26, 28,29). Other causes of meningitis includes candida albicans, coccidiomycosis, aspergillus fumigatus and mycobacterium tuberculosis (35). Progressive multifocal leukoencephalopathy a demyelinating disease caused by JC virus presenting with mental aberration, blindness, aphasia, hemiparesis ataxia and other focal deficits has also been reported (35, 40).

Intracranial space occupying lesions due to primary central nervous system lymphoma, Kaposi's sarcoma, toxoplasmosis and systemic lymphoma has been reported in upto 29% of AIDS patient (35, 36, 41).

Cerebrovascular accident both infarction and hemorragic types have been reported (35).

Kaposi's sarcoma and other malignancies

AIDS patients have an increased indidence of malignancies with the main types being Kaposis sarcoma (1, 2) and a variety of hon-Hodgkins lymphomas (42, 43). 35% of AIDS patients in Europe and U.S.A. present with Kaposi's sarcoma. (1, 2). Unlike the classical form.AIDS related Kaposi's sarcoma can occur in any part of the body particularly the tip of the nose, behind the ears, glans, penis and mucous membranes. It also often affects the viscera

••••••/7

Workers (44) in Zaire did not find any association between the "endemic" indolent form of Kaposi's and AIDS. Anne Bayley (45) in Zambia found upto 81% seropositivity for HIV antibodies in patients with a typical Kaposi's sarcoma. The incidence of Kaposi's sarcoma in Ugandan (27) Rwandese (28) Zairein (29) has been reported as 10, 27 and 16% respectively.

SKIN SIGNS

The commonest AIDS associated skin manifestaion in Europe and U.S.A. is Kaposi's sarcoma (46). (Serborhoiec) dermatitis which may be mild or severe and thought to be due to (pityrosporum) fungi is also common (45,)). Other manifestation include acneiform folliculitis, recurrent herpes simplex, molluscum contagiosum, - cutaneous vasculitis, butterfly eruption resembling systemic lupus erythromatosis, and multidermatome herpes zoster (45). In Africa a non specific maculopapular pruritic rash has been seen in upto 60% of the patient (27, 28, 29).

General signs

Severe wasting is a striking feature seen in African AIDS patients and has lead to the disease to be referred to "as slim disease". In studies in Uganda (27), Rwanda (28), Zaire (29) the incidence of wasting was reported to be 62%, 100%, 60% respectively. Many have other non specific symptoms as lethargy, malaise and intermittent or persistent fever. Many AIDS patient develop generalized lymphadenopathy and on histology of these lymph nodes most show reactive hyperplasia.

...../8

AIM AND OBJECTIVES

-

- To study the clinical manifestation of patients with confirmed acquired immunodeficiency syndrome.
- 2. To study the risk factor associated with these cases.
- 3. To form a baseline for later clinical studies.

.

MATERIALS AND METHODS

Between March and December 1987 inclusive, 50 consecutive patients admitted on the medical wards at Kenyatta National Hospital who satisfied the WHO clinical case defination for AIDS (annex 1) with a positive HIV antibody on ELISA and confirmed by Western blot were studied.

Medicolegal (Ethical considerations)

Permission was sought and granted by the Kenyatta National Hospital Research and ethical committee.

Clinical methods

Patient data was obtained by direct questioning of the patients and in cases whereby the patient was confused or was not able to communicate close relatives were interviewed.

Each patient had a medical history taken, and a physical examination carried as contained in the profoma (annex II). A list of defination of signs used is contained in annex (III).

Laboratory methods

In all cases 20ml of venous blood was obtained from a large vein in the antecubital fossa and used for the following test.

1) Hemogram

2ml of blood was put in sequestiene bottle. A full coultergram was done using the coulter counter model S.

2. Western blot

5ml of blood in a plain bottle was left to stand. Serum extracted.

The western blot test was carried out using the western blot test kit manufactured by Biotech laboratories.

T_4/T_8

T - lymphocyte sub populations were determined by flurescent microscopy. 10 ml of venous blood was withdrawn into a 10ml syringe containing EDTA dextran. Lymphocytes were seperated using "Ficoll Hypaque" density centrifugation. The cells were then washed with Hanks stock solution. The harvested cells were seperated into four and monoclonal antibodies (murine sera) of the subclasses OKT3 (anti-human T cell), OKT4 (anti-human _ inducer/helper T cells), OKT8 (anti human suppressor/cytotoxic T cell) manufactured by Ortho pharmaceutical corporation added. After 30 minutes reaction the cell suspension was washed and reacted with flurescein conjugated rabbit to mouse immunoglobin (FITC) for 30 minutes all at room temperature. The cell were then washed and counted microscopically using a fluorescent microscope and T_{1}/T_{8} ratio calculated.

Other laboratory methods

Other laboratory tests were done appropriate for the presenting symptom. All patients with meningeal signs had a lumbar puncture and CSF obtained was tested for sugar, protein, cell count, Ziel Ngelson stain, Gram stain, culture and sensitivity and indian ink preparation. Patient presenting with Central Nervous System signs and symptoms were investigated for liver function tests, blood sugar, serology for syphyllis (U.S.R.), thick blood slide for malarial parasite and urea and electrolytes.

Radiological Examination

All patients with chest symptoms had a P.A. view chest x-ray and the film reported by a radiologists.

RESULTS

Study population

50 patients were studied, comprising 30 males and 20 females giving a male to female ratio of 1.5:1. The age range was 16 - 48 years. The mean age for the total group was 31 ± 7 years while that for males alone 32.33 ± 7.63 years as compared to 28.75 ± 6.34 years in females. There was no statistical significant difference between the mean ages of males compared to the females by student T - test. In fig. 1 and 2 the age group distribution is illustrated. From these figures the female had an earlier peak 21 - 25 year group as compared to 26 - 30 year in the males. As a group there was no statistical significant difference between the male and female age distribution.

Table 1 shows the distribution of the marital status of patients with AIDS. There was a statistical significant difference between the marital status of the males and females by student T test. More females tended to be single. Most of the males were married.

Table 2 shows the distribution of patients by occupation. The highest group represented were housewives, unemployed and long distance driver. All cadres of occupation were represented. The majoir share was taken by people of low socioeconomic status apart from the accountant.

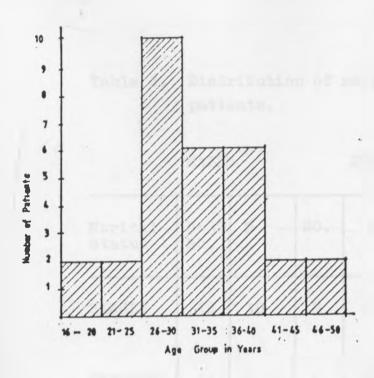


Fig 2 Age Group Distribution Of Females

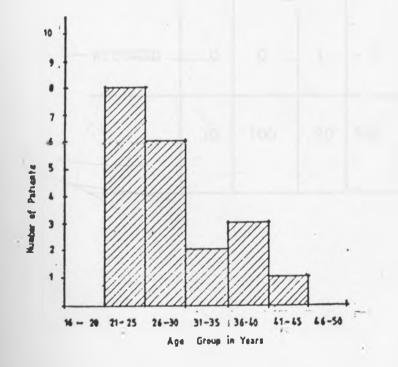


Table 1. Distribution of marital status of the patients.

MALES

FEMALES

Marital Status	N#30 NO.	76	NO.	%	NO.	%
SINGLE	12	40	9.	45	21	42
DIVORCED	1	3.33	2	10	3	6
MARRIED	17	56.67	8	40	25	50
WIDOWED	0	0	1	5	1	2
	30	100	20	100	50	100
	-					1.11

OCCUPATION	NUMBER	PERCENTAGE
HOUSEWIFE	7	14
UNEMPLOYED	7	14
DRIVERS	7	14
CASUAL LABOURERS	5	10
TECHNICIAN	5	10
PRISONERS	3	6
BARMAIDS	3.	6
BUSINESSMEN	3	6
TAILOR	3	6
WATCHIEN	2	4
SALESHAN	1	2
UNGRADED NURSE	1	2
STUDENT	1	2
HOUSEMAID	1	2
ACCOUNTANT	1	2
	50	100

Table 2. Distribution of patients by occupation.

In this study no homosexual, bisexual, intravenous drug abuser were found as depicted in Table 3. The greatest risk factor was sexual contact with multiple sexual partners where 80% of the patients admitted. There were 6% of patients who had been transfused in the last five years. Other risk factor included sexual contact with a spouse with diagnosed AIDS. 10% of the patients did not have any attribute risk. There were 12 patients (24%) who admitted history of travel to Uganda, Eastern Zaire and Rwanda and having had sexual contact with inhabitants of these areas. These were mainly the long distance truck drivers.

Table 4 shows the signs and symptoms involving the general system. The commonest symptom was weight loss in 92% of the patients. There was a statistical significant difference in lymphadenopathy with males predominanting over females.

Gastrointestinal symptoms and signs are shown in Table 5. The commonest sign being oral thrush in 66% chronic. Diarrhoea was seen in 60% of the cases. In this study there was a statistical significant difference between males and females in that more female had more oral thrush and diarrhoea than the males.

	NUMBER	₹¢
HOMOSEXUALITY	NIL	NIL
BISEXUALITY	NIL	NIL
INTRAVENOUS DRUG ABUSE	NIL	NIL
HEMOPHILLIAC	NIL	NIL
BLOOD TRANSFUSION LAST 5 YEARS	3	6
SEXUAL CONTACT WITH AIDS PATIENT	2	4
SEX WITH MULTIPLE SEXUAL PARTNER (CASUAL)	40	80
NO ATTRIBUTABLE RISK	5	10
SCARIFICATION	1	2
INFECTION	3	6

Table 4.	General	signs	and	symptoms.
----------	---------	-------	-----	-----------

.

SYMPTOM	MALE % n=30 (n) %	FEMALES % n=20 (n) %	TOTAL %	LEVEL OF SIGNIFI- CANCE \	MEAN DURATION OF OF SYMPTOM
WEIGHT LOSS FEVER WASTING LYMPHADENOPATHY JAUNDICE EDEMA	(28)93 (20)67 (28)93 (7)23.3	(18)92 (13)65 (15)92 (3)15 (1)5%	<pre>{46)92 (33)66 (46)92 (10)20 (1) 2 (1) 2 (1) 2</pre>	NS NS NS P 0.05 * *	3.8 [±] 2 month range 1 24 3 [±] 1.7 months range 1 - 24 hmonths * *

.

*Number too small to determine level of significance.

Table 5. Signs and symptom in the Gastrointestinal system MALE N=30 FEMALES n=30							
	NUMBER	PERCENTAGE	NUMBER	70		LEVEL OF SIGNIFICANT	
ORAL THRUSH	18	60%	15	75	66	P < 0.05	
DIARRHEA	15	50%	15	75	60	P<0.01	
DYSPHAGIA	14	47%	11	55	50	NS	
HEPATOMEGALY	1		2		6	*	
SPLENOMEGALY	1		1		4	*	
ASCITES	1		-				

* Too small to determine level of significance.

1

In the respiratory system the commonest symptom was cough which occurred in 46% of the patients. This had a mean duration of 2 months with a range of 1 - 24 months. There was a statistical significant difference between male and females with male predominanting. 22% of the patients had shortness of breath while 5% had hemoptysis. Table 7 shows the radiological feature in 12 patients with abnormal x-ray. In total 50% of the patients had pleural effussion.

In this study 18 patients 38% had central nervous system involvement. The commonest symptom as shown in Table 7 is headache in 67% and confusion in 50%. Table 8 shows the diagnostic signs in the study. Meningitis was the commonest symptom occurring in 27.77%, out of which 60% of the meningitis was cryptococcal, followed by acute encephalitis in 16.67%. Peripheral neuropathy was seen in three cases, two of which were sensory. The last patient had sensorimetor with wasting of the muscle on the left hand. AIDS' related dementia was seen in 2 cases. Focal neurological signs was noted in two patients. They presented with sudden onset hemiplegia which simulated cerebrovascular accident. One with 7th and 12th cranial nerve palsy is shown in photograph (4). The rest of the diagnostic features are illustrated in the table.

In table 9 the skin signs are presented, the commonest sign was maculo-papular itchy skin rash in 32% of the cases with a mean duration of 3 ± 0.9 months. Seborhoiec dermatitis was the next commonest followed by herpes zoster. The rest of the skin as per Table 9.

ł

	Number	Percentage
Pleural effusion	2	16%
Bronchopneumonia	3	25%
Perihilar haziness	2	16%
Pleural Effussion with inflitrates	4	33%
Patchy consolidation	1	8%

- 29 -

Table 7. Symptomatology in the Central Nervous System

	Number	% of total
HEADACHE	12	66.6
CONFUSION	9	50
PIN AND NEEDLE SENSATION	7	38.89
(LOSS OF SENSATION)	-	
PARALYSIS	3	16.62
VISUAL DISTURBANCE	2	11.11
CONVULSION	1	5.56

Table 8. Diagnostic features in Central Nervous System

	Number	Percentage
ACUTE ENCEPHALITIS	3,	16.67
CRYPTOCOCCAL MENINGITIS	3	16.67
PERIPHERAL NEUROPATHY	3	16.67
DEMENTIA	2	11.1
ASEPTIC MENINGITIS	2	11.1
HEMIPLEGIA	2	11.1
MYELOPATHY	- 1	5.56
NON-SPECIFIC TREMOR	1	5.56
CEREBELLAR SIGNS	1	5.56
6	18	100

Table 9. Skin signs

	NUMBER	% OF TOTAL PATIENT
MACULOPAPULAR		
PRURITIC LESION	16 '	32
SEBORRHOEIC DERMATITIS	5	10
HERPES ZOSTER	4	8
HERPES SIMPLEX	2	4
FUNGAL SKIN INFECTION (TINEA CORPORIS)	3	6
MALAR RASH	2	4
MOLLUSCUM CONTAGIOSUM	1	2

đ.,

5 (10%) of the patients had Kaposi's sarcoma on histology. The mean age was 30.8 years with a range of 22 - 40 years. All had variable manifestation. One of the five had the nodular type of Kaposi's sarcoma involving the lower limbs. The second one a female (see photograph 6) had the lymphadenopathic form with involvement of the tonsil, lymph nodes, jaundice and hepetosplenomegaly: The third had involvement of the tongue and hard palate (photograph 5). The fourth presented with orbital edema and generalized plaques all over the body. The fifth had involvement of the gum, sclera and the skin.

HAEMATOLOGICAL DATA

The mean hemoglobin level was was $9.4^{\pm}4$ gldl with a range of 3.2 - 14.6 gldl. Anaemia was common with 56% of all patients having Hb estimation below 10gldl.

Pattern of peripheral film - Normocytic normochromic - 60% - Microcytic Hypochromic - 20% - Macrocytic - 5% - Mixed picture - 15% White Blood Cell Count Mean 5.3 x 10⁹/L

Range 2.0 - 19.5 x $10^9/L$

Platelet count - Mean 220.000-80,000 range 20,000 - 400,000

There were three patients with platelet less than 50,000.

Only 15 of the patients had T_4/T_8 subset estimation

Mean ratio 0.5⁺0.12.





PHOTOGRAPH 2. GENITAL ULCER







PHOTOGRAPH 5. KAPOSI'S SARCOMA INVOLVING THE TONGUE



PHOTOGRAPH 6 KAPOSI'S SARCOMA OF THE TONSILS ALSO NOTE THE JAUDICE



PHOTOGRAPH 7. KAPOSI'S SARCOMA WITH LYMPHODENOPATHY

Between March to December 1987 fifty consecutive cases were studied. This number does not reflect the actual admission rate of AIDS cases in the medical wards during the study period. There were a few patients who were admitted and died immediately and therefore were not included in the study.

- 4'0 -

Because of limited diagnostic facilities we used a combination of the WHO clinical case defination and positive serology for HIV antibodies by ELISA and Western blot. We intended to include in each patient the CD_4/CD_8 ratio but due to unavoidable circumstances we only managed to do it in fifteen cases which showed a definate reduction in the ratio.

The mean age of $31^{\pm}7$ years found in this study compares with that found in Uganda of 26 years (27), Zaire 27 years (29) and Haiti of 33 years (30). Females in this study had an earlier peak as compared to the males. A similar finding was noted in Zaire (29) where it was found that females were much younger than the males. A possible explanation is probably African females become sexually active at an earlier age than the males.

The male to female ratio in the study was 1.5:1 which is comparable to that found in Uganda 1.2:(16), Rwanda 1:1 (28) Zaire 1.1:1 (29). The ratio is contrary to that found in U.S.A. and European studies where males predominate (1,2,3). The ratio would favour heterosexual mode of transmission. Homosexuality, bisexuality or intravenous drug abuse did not feature as a risk factor in the patient seen. This is unlike in western literature where these factors are most important risk factor (1, 2, 3, 12).3 (6%) of our patients had a history of blood transfusion between six months and five years prior to presentation. In fact one of these patients had been transfused six times in the year preceeding presentation. At the time they were transfused no routine screening of blood for HIV had been established there was a possibility that they were transfused with HIV contaminated blood. Furthermore they did not have other associated risk factor for seroconversion.

From this study 80% of patient admitted having had casual sexual contact with multiple sexual partners. In studies in Uganda (27) Rwanda (28) and Zaire (29) AIDS patient tended to be more promiscious than unaffected. 24% of the patient had trayelled out of Kenya to Rwanda, Eastern Zaire and Rwanda all of which are said to be endemic for AIDS. Furthermore they admitted having had sexual contact with partners from this areas therefore this seems to be a risk factor in our patients.

10% of our patients did not have any attributable risk factors. One case was a 16 year old primary school student who denied any sexual encounter, blood transfusion, parenteral injection and scarification. Another case was of ungraded nurse who was involved in only recording patient attendance for the last 10 years and denied any sexual encounter for the last eight years. One drawback was that one had to rely on the patients history and it is possible some of these patients did not tell the truth. If this 10% had given a true information then there may be other risk factors that are yet to be determined.

The patient studied were of low socio-economic status This is in contrast to studies in Europe. In African patient with AIDS which showed a higher socio-economi status (4,26). A similar predominance in higher socio-economic studies was reported in Zaire (29) and Rwanda (28). Our low representation of patient from the higher socio-economic group could be attribu table to use of available private medical facilities. In the occupational history we only had 3(6%) of our patients who admitted prostitution. This conflicts with the high rate of HIV seropositivity it would be expected that they would have a higher representations amongst the actual AIDS cases. - 43 -

Clinical manifestation

The most striking feature in this study was weight loss which was seen in 92% of our patients. This was the earliest symptoms and occured 3.8 months prior to admission. A similar picture is seen in Uganda the so called "slim disease", Zaire, Haiti where weight loss occurred in 62%, 100% and 70% respectively. Similar weight loss is reported in western literature (). In our study the patient who had no weight loss where those with Kaposi's sarcoma and one with cryptococcal meningitis.

- The next commonest symptom and sign was fever which was seen in 66% of the patients. The rate compares with that found in Uganda 62%, 84% in Zaire and 70% in Haiti. As a symptom this had the disadvantage in that one had to rely on the patients interpretation of fever.

In this study there was a comparatively low incidence of lymphadenopathy at 20% as compared to 55% in Zaire (29) and 38% in Uganda. Significantly more male in the study had lymphadenopathy compared to females. The reason for this difference is not clear.

In the gastrointestinal system the commonest sign was oral thrush which occured in 66% of the patient. Oral thrush which is caused by candida albicans infection was the commonest opportunistic infection, this compared with that seen in Uganda (28) Rwanda (28), Zaire (29) Haiti (30). The next commonest symptom was diarrhea which was either intermittent or continous. This is a common finding in african studies leading to the coinage of the word enteropathogenic AIDS. In Zaire (29) 89% had diarrhea while in Haiti (30) 84% had diarrhoea. This is a much higher proportion as compared to our findings. Unfortunately in our study we did not look at the actiologic factors for the diarrhoea and hence the difference in the incidence between the groups can not be fully explained. Dysphagia was present in 50% of the study patients which was much higher than reported in Zaire of 31% (30). Dysphagia in all cases was associated with oral thrush implicating the possibility of candida oesophagitis.

46% of the study group had chronic cough of more than a months duration a similar finding has been reported in Zaire. Although no invasive procedure were carried out we did not suspect any cases of Pneumocystis carinii in the patients. Pleural effusion was the commonest clinical and radiological finding and occurred in 50% of patients. No pleural biopsy were carried out but it was likely that the effusion was of tuberculous origin. This is a high rate of pleural effussion, for studies in San Francisco on AIDS patient with tuberculosis only found a rate of 20% (25).

Central Nervous System signs were seen in 36% of the patient. A similar figure of 30 - 40% incidence among AIDS patient is reported in studies in U.S.A. (35, 36). This study was handicapped by the lack of specialized investigation such as CT scan, nerve conduction, biopsy and so most of the diagnoses were clinical. "AIDS related dementia" subacute encephalitis was diagnosed in only 2 of our patients, this is in contrast to higher incidence of reported in U.S.A. (35, 36). Meningitis was the commonest presentation with 60% of then being cryptococcal. The incidence of cryptococcal meningitis 6% in this study is significantly lower than that reported in Rwanda (28) 11.1% and Zaire (29) 15.6%. Our patient with cryptococcal meningitis were all males and they tended to have been quite well prior to the onset of the meningitis. Two cases presented with sudden onset of focal neurological signs with hemiplegia simulating a cerebrovascular accident (CVA). These patients had neither a cardiac lesion, Kaposi's nor thrombocytopenia, unfortunately no carotid angiogram and CT scan was done in them. A 16 year old patient presented with flaccid paraplegia of sudden onset with incontinence urin and stool. Myelography was done in this case and no block noted this patient was thought to have AIDS related myelopathy. The spectrum of involvement of the central nervous is so diverse that if possible all patient with neurological symptom and signs should routinely be tested for HIV in infection.

Kaposi's sarcoma was found in 5 (10%) of the patients studied. This compares with 10% in Uganda (27) 27% in Rwanda (28) and 16% in Zaire. This is unlike the presentation of 35% in U.S.A. (1,2). Only one of the patients had the nodular or indolent type of Kaposi's sarcoma. The remaining four had what is described as a typical or epidemic Kaposi's sarcoma. Ann Bayley (45) described similar aggressive Kaposi's sarcoma in Zambia, when these patients were tested later on 81% were seropositive (45).

The skin manifestation seen in our patient may not reflect the clinical picture at Kenyatta National Hospital since some patients with only skin involvement are seen in the dermatology clinic rather than on the medical wards. The commonest skin manifestation was maculopopular skin rash which is similar to that reported in African (27, 28, 29) in contrast to seborrhoeic dermatitis which is the commonest in European studies (46). From unpublished data from the dermatology clinic herpes zoster with high seropositivity for HIV infection is commonly seen. In our study only 8% had herpes zoster. The reason for the difference is not clear.

The median survival rate in the study was 5 months. 70% patient admitted died within 2 weeks of admissi The high rate of morbidity in the study may however be due to the admission criteria where it is likely that only the very ill patient are admitted. A better indicator would have been a study both inpati and outpatients.

CONCLUSION

1. The major clinical manifestation were weight loss fever, oral thrush, chronic diarhoea and dysphagia This is comparable to that reported in other African studies.

- 41 -

- 2. Majority of AIDS patient were sexual active group with age range 20-49 years.
- 3. The majority of AIDS patient were of low socioeconomic.
- 4. The highest risk factor was heterosexual relationship with multiple partners.
- 5. The median survival rate was between 4-6 months.

RECOMMENDATION

- 1. A detailed study to identify the opportunistic infection in each of the system should be undertaken.
- 2. A more detailed study of the Gentral Nervous system involvement including CT Scan, nerve conduction biopsy and EEG should be carried out.
- 3. There is a heed for the laboratory services to co-operate with other investigator.
- Studies of the clinical manifestation at outpatient
 basis where HIV infected person with early manifestation are present should be looked into.
- 5. There is a group of patient with no atributable risk factor who require a detailed study to investigate other modes of HIV transmission.

ANNEX 1

- 49 -

CLINICAL CASE - DEFINATION OF AIDS

AIDS in an adult is defined by the existence of at least 2 major signs associated with at least 1 minor sign in the absence of known causes of immunosuppression such as cancer or severe malnutrition or other recognized etiologies.

MAJOR SIGNS

- a) Weight loss equal to or greater than 10 per cent of body weight.
- b) Chronic diarrhoea for more than 1 month
- c) Prolonged fever for more than 1 month (intermitten or constant).

MINOR SIGNS

- a) Persistent cough for more than 1 month
- b) Generalized pruritic dermatitis
- c) Recurrent herpes zoster
- d) Oropharyngeal candiasis
- e) Chronic progressive and disseminated alpha herpes simplex virus infection
- f) Generalized lymphadenopathy

The presence of generalized Kaposi's sarcoma or cryptococcal meningitis is alone sufficient for a diagnosis of AIDS.

Bulletin of WHO 64 (1) 37 - 46. 1986

ANNEX II

PROFOMA

Name.

Age.

Sex.

Marital status

Occupation.

Sexual Relationship

- . Homosexual
- . Heterosexual
- . Bisexual
- . Number of different sexual partners in one year
- Episodes of venereal disease in last 5 years (men only)
- Blood transfusion in last 5 years but not later than in last 6 months
- . Travel in last 5 years outside Kenya where and when

SYMPTOMATOLOGY (general System)

•	Weight loss	Yes/No	Duration	a
•	Fever	Yes/No	Duration	
	Night sweats	Yes/No	Duration	ر بن ہے۔ سے عدم نے بر اور اور

..../4

- 51 -

GASTROINTESTINAL SYSTEM

•	Sorts in the mouth	Yes/No	Duration	
•	Dysphagia	Yes/No	Duration	
•	Diarrhoca	Yes/No	Duration	
•	Bleeding per rectum	Yes/No	Duration	

RESPIRATORY SYSTEM

Breathlessness	Yes/No	Duration
Cough	Yes/No	Duration
Hemoptysis	Yes/No	Duration
Miscellaneous		

CENTRAL NERVOUS SYSTEM

Headache	Yes/No	Duration
Confusion	Yes/No	Duration
Convulsion	Yes/No	Duration
Behavioural change	Yes/No	Duration
Paralysis	Yes/No	Duration
Disturbance in vision	Yes/No	Duration
Pin and needle sensation	Yes/No	Duration

SKIN

•	Itching	Yes/No	Duration
-	Skin rash	Yes/No	Duration
	Change in skin colour	Yes/No	Duration

GENITAL SYSTEM

Ulcers	Yes/No	Duration
Discharge	 Yes/No	Duration

...../5

E.N.T.

CARDIOVASCULAR -----

CLINICAL SIGN

- . Wasting
- . Jaundice
- Pallor
- . Edema
- . Lymph node enlargement
- . (Lymph node bigger than 1 cm extrainguinal)

1

. Oral thrush

CENTRAL NERVOUS SYSTEM

- Confusion
- . Memory loss
- Concentration (series of 7)
- Dementia
- Meningeal irritation
- . Peripheral neuropathy

(reduced sensation to pin prick, vibration and temperature)

0 thers

ABDOMINAL EXAMINATION

- . Hepatomegaly
- Splenomegaly
- . Other masses

SKIN

- . Herpes Zoster
- . Herpes simplex
- . Se barholec dermatitis
- Kaposi's sarcoma (an histopethology)
- . Fungal skin infection
- Other state

GENITAL SYSTEM

Circumcision (males only)

ulcers

Fissures

Balanitis

Candiasis

Other state

CARDIOVASCULAR SYSTEM

...../7

EAR, NOSE, THROAT

LABORATORY DATA

Hb

WBC

Platelets

Differential

Neutrophils	%
Eosinophils	%
Monocytes	%
Basophils	%
Lymphocyles	%

- 541 --

T lymphocytes

T₄/T₈ ratio

C.S.F. where indicated Organism

C.X.R. report

Other investigation

.

Annex III

- 22 -

1.	Peripheral Neuropathy		Detected by loss of pain,
	8		temperature and vibration.
2.	Kaposi's sarcoma	-	Histopathological diagnosis
3.	Lymphadenopathy	-	Extrainguinal lymph nodes greater than 1 cm.
4.	Oral thrush	-	Creamy white colouration of the tongue and oral mucosa.

5. DIAGNOSTIC FEATURES OF AIDS - RELATED DEMENTIA

- 1. Positive HIV serology (confirmed by Western blot)
- 2. History of cognitive/behavioural changes including apathy, memory loss
 - impaired concentration and attention
- 3. Neurologic findings hyparreflexia, hypertonia, release signs, myelopathy
- 4. CT/MRI Atrophy: changes in white matter
- 5. CSF elevated 1gG, protein, normal cell count, negative cryptococcal antigen and VDRL
- 6. Exclude metabolic/drug encephalopathy, cryptococcal meningitis, intracranial mass lesion, neurosyphilia

Optional

- 1. Detailed neuropsychiatric testing
- 2. C.S.F HIV isolatio
 - HIV isolation, p24 antigen, intrathecal synthesis of HIV specific antibodies
- 3. Brain biopsy/autospy multinucleated giant cells, microglal nodules, HIV isolation/ in site hybridization/immunestaining.

ACKNOWLEDGEMENTS

- My supervisors Prof.G. B. A. OKELLO, DR. OWILI for their guidance and support during the study.
- 2) DR. J. B. O. WERE Director CRC for valuable support during the initial part of the study.
- 3) SUSAN 00G0 of the Virus research center for the western blot studies.
- 4) CHRISTINE OWALA for her secretarial services.
- 5) ANDERSON MWAKUZI of the Clinical Research centre KEMRI for the initial lymphocyte studies.
- 6) DR. ALEX CHEMTAI of the Department of Immunology for encouragement and a lot of literature on AIDS.
- 7) DR. KAYIMA for having read through the initial manuscript.

REFERENCE

- GOTTLIEB, M.S., SCHROFF, R., SCHANKER, H., WISEMAN, J.D., FAN, P.T., WOLF, R.A. & SAXON, A. Pneumocystis carinii pneumonia and mucocal candiasis in previously healthy homosexual men evidence of a new acquired immunodeficiency. N.Engl.J.Med: 305:1425-1431, 1981.
- 2. FRIEDMAN, A.F., LAUBENSTEIN, L.J.P., RUBINSTEIN, P., KIEIN, E.P., MARMOR, M., STAHL, R.B., SPIGLAND, I., KWANG SOO & PANZER, S.Z. Disseminated kaposis sarcoma in homosexual men. Ann. Intern. Med. 96:693-700, 1982.
- CENTERS FOR DISEASE CONTROL. Kaposis sarcoma and pneumocystis carinii pneumonia among homosexual men in New York city and California. MMWR:30 305-308, 1981.
- 4. CLUMERCK, N., MASCART-LEMONE, F., MAUBEUGE, J., BRENEZ. L. MARCELS, L. Acquired immune deficiency in Black Africans. Lancet. : 642-657, 1983.
- 5. OBEL. A.O.K., SHARRIF, S.C., MC'LIGEYO, S.O., GITONGA, E., SHAH, M.V. & GITAU, W. Acquired immune deficiency in an African. East Afr. Med. J., 61:724-726, 1984.

- 7. BARRE-SINOUSSI, F., CHERMANN, J.C., & REY, F. Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immunodeficiency syndrome (AIDS). Science 220:868-870, 1983.
- LEVY, J.A., HOFFMAN, A.D., KRAMER, S.M., LANDIS, J.A., SHIMABURO, J.M. & OSHIRO, L.S. Isolation of lymphocytopathic retroviruses from San Franscisco patient with AIDS. Science 225:840-2, 1984.
- 9. GALLO, R.C., SALAHUDDIN, POPOVIC. Frequent detection and isolation of cytopathic retroviruses (HTLV III) from patient with AIDS and at risk at AIDS. Science 224:500-503, 1984.
- 10. KLATZMANN, D., BARRE SINOUSSI, & NUGEYRE, M.T. Selective tropism of lymphodenopathy associated virus (LAV) for helper-inducer T lymphocytes Science 312:763-767, 1984.
- 11. BOWEN, W., LANE, H., & FAUCI, A.S. Immunopathogenesis of the acquired immune deficiency syndrome. Ann. Intern. Med. 103:704-709, 1985.

- 58 -

- 12. FAUCI, A.S., MACHER, A., LONGO, D.L., LANE, C., ROOK, A.L., MASUR, H. & GELMANN, E. Acquired immunodeficiency syndrome epidemiologic, clinical, immunologic and therapeutic consideration. Ann. Intern. Med. 100:92-106, 1984.
- 13. CIOBANU, N., WELIC, K., & KRUGER, G. Defective T cell response to phytohemaglutin (PHA) and mitogenic antibodies in male homosexuals with the acquired immunodeficiency syndrome and its in vitro correction by interleukin 2. J. Clin.Immunol. 3:332-340, 1983.
- 14. HOFFMAN, B., DUM, N., PLATZ, P., RYDER, L.P., SVEJGAARD, A. & NIELSEN, J.O. Immunological studies in AIDS Scand..J.Immunol. 21:235-243, 1985.
- 15. LANE, H.C., EDGAR, H., WHALEN, G., ROOK, A.H., & FAUCI, A.S. Abnormalities of B-cell activation and immunoregulation in patients with AIDS. N.Engl. J. Med. 309:453-458, 1983.
- 16. SMITH, P.O., OHURA, K., MASUR, H., LANE, H.C., FAUCI, A.S. & WAHL, S.M. Monocyte function in the acquired immune deficiency syndrome, defective chemotaxis . J. Clin. Invest. 73:2121-2128, 1984.

- 17. RUNDLES, C., MICHELIS, M.A. & MASUR, H. Serum suppression of lymphocyte activation in vitro in acquired immunodeficiency syndrome. J. Clin. Invest. 72:398-403, 1983.
- 18. HARRIS, C., SMALL, C.B., KLFIN, R.S., FRIENDLAND, G., MOLL, B., EMESON, F.E., SPIGLAND, I., & STEIGBIGEL, N. AIDS in female sexual partners at men with the acquired immunodeficiency syndrome (AIDS). N. Engl. J. Med. 308:1181-1184, 1988.
- 19. CLUMFCK, N., VAN OF PERRE, NZARAMBA, CARAEL, M. Heterosexual promiscuity among Africans patients with AIDS. N. Engl. J. Med. 313:182-193, 1985.
- 20. AMMAN, A.J., COWAN, M.J., WARA, O.W. & DRITZ. AIDS in an infant, possible transmission by means of blood products. Lancet (i) : 965-958, 1983.
- 21. DAVIS K.C., HORSBURAN, C., HASIBA, V., SCHOCKET, A.L. & KIRKPATRICK, C. AIDS in patient with hemophilia Ann. Intern. Med. 3:284-286, 1983.
- 22. RUBINSTEIN, A., SICKLICK, M., GUPTA, A., BERNSTEIN, L., KLEIN. N., RUBINSTEIN, E., SPIGLAND, I., FRUCHTER, L., LITMANN, LEE, H. & HOLLANDER, M. AIDS with reversed T₄/T₈ ratio in infants born to promiscous and drug addicted mathers. JAMA 313:182-186, -1985.

- 23. MURRAY, J.F., FELTON, C.P., GARAY, S.M., GOTTLIEB, M.S., HOPEWELL, P.C., STOVERD, E. & TEIRSTEIN, A.S. Pulmonary complication of the acquired immunodeficiency syndrome. Special report. N. Engl. J. Med. 310:1682-1688.
- 24. OGNIBENE, STEIS, R.G., MACHER, A.M. Kaposis sarcoma causing pulmonary inflitrates and respiratory failure in acquired immunodefiency syndrome. Ann. Intern. Med. 102:471-475, 1985.
- 25. CENTERS FOR DISEASE CONTROL Tuberculosis and AIDS in Florida. MMWR, 35:587-90, 1986.
- 26. CLUMECK, J., SONNET, H., MASCART LEMONE, F., BRUYORE, M.D., VAN, DE PERRE, P. J., MARCELIS, L. LAMY, M., JONES, C., EYCKMANNS, L., NOEL, H., MICHEL, BUTZLER, J.P. Acquired immunodeficiency in African patients N. Engl. J.Med. 310:492-497, 1984.
- 27. SERWADDA, D., MUGERWA, R.D., SEWANKOMBO, M.R. LWEGATA, A., CARSWELL, J.W., KIRYA, G.B., BAYLEY, A.C., DOWNINIG, R.G., TADDER, R.A., CLAYDEN, S.D., WEISS,R.A., DAGLEISH, A.G. Slims disease. A new disease in Uganda and its association with HTLV III infection. Lancet (ii): 840-852, 1985.

+ -5

- ----
- 28. P.V. PERRO, P.N., ROUVROY, D., LEPAGE, P., BOGARTS, J.R., KESTELYN, P., KAYIHIGI, J., ANTON, C., BOTZHER, J.P. & CLUMECK, N. Acquired immunodeficiency in Rwanda Lancet ii : 62-65, 1984.
- 29. PIOT, P., QUINN, J.C., TAELMAN, H., FEINSOD, F.M., KAPITA, B.M., WOBIN, O., MBENDI, N., P. MAZEBO, P., NDANGI, K., STEVENS, W.,KALAMBAYI, K.S., MITCHELL, S., BRIDTS, C., & McCORMICK, J.B. Acquired immunodeficiency syndrome in a Heterosexual population in Zaire. Lancet ii: 65-69, 1984.
- 30. PAPE, J.N., LIAUTAUD, B., THOMAS, F., MATHURIN, J.R. MARIE, MYRTHA, ST. AMAND, BONCY, M., PEAN, V., PAMPHILE, M., LAROCHE, C., DEHOVITZ, J., JAHNSON, W.D. The acquired immunodeficiency syndrome (AIDS) in Haiti. Ann. Intern. Med. 103:674-678, 1985.
- 31. CURRENT, W.L., REESE, N.C., ERNEST, J.V., BAILEY, W.S., DVM, HFYMAN, M.B., WEINSTEIN, W.U. human cryptosporidiosis in immunocompetent and immunodeficiency persons. N. Engl. J.Med. 306: 1252-1257, 1983.
- 32. KNAPP, A., HORST, K., EUOPOULOS Widespread cytomegalovirus gastroentorocolitis in a patient with acquired immunodeficiency syndrome. Gastroenterol: 85:1399-1403, 1983.

- 33. GREENE, J.B., SIDHU, G.S., LEWIN, S., LEVINE, J.F., MASUR, H., SIMBERKOFF, M.S., NICHOLAS, P., GOOD, R.C., ZOLLA PAZNER, S.B., POLLOCK, A.A., TAPPER, M.L. & HOLZMAN, R.S. Mycobacterium avium-intracellulare: A course of disseminated life threatening infection in homosexuals and drug abusers. Ann. Intern. Med. 97:539-546, 1982.
- 34. DORWIKIN, B., STAUL, R., GIARDINO, M., WORMBE, C.P. WEISS, L., JANKOWSKI, R., ROSENTHAL, W.S. The liver in acquired immune deficiency syndrome emphasis on patient with intravenous drug abuse. Amer. J. Gastroenterol. 82: 231-236, 1987.
- 35. LEVY, R., BREDFSEN, R.E., ROSENBLUM, M.L. Neurological manifestation of the acquired immundeficiency syndrome (AIDS): Experience at UCSF and review of literature. J. Neurosurg. 62:475-495, 1985.
- 36. FISCHER, P.A., ENZENSBERGER, W. Neurological complication in AIDS. J. Neurol 234: 269-279, 1987.
- 37. NAVIA, B.A., JORDAN, B.O., PRICE. The AIDS dementia complex. Clinical feature. Ann. Neurol. 19:517-524, 1986.
- GOLDSTICK, L. MANDYBUR, T.I., & BODE.
 Spinal cord degeneration in AIDS.
 Neurology: 35:103-106, 1985.

- 39. WONG, B., GOLD, J.W.M., BROWN, A.E., LANGE, M., FRIED, RR., GRIECO, M., MILDVAN, D., GIRON, J., TAPPER, M.L., LERVER, C.W. & AMSTRONG, D. Central nervous toxoplasmosis in homosexual and parenteral drug abuser. Ann. Intern. Med. 10:36-42, 1984.
- 40. BLUM, L.M., CHAMBRES, R.A., SCHWARTZMAN, R.J., TRELFTZ. Progressive multifocal leukoencephalopathy in AIDS. Arch. Neurol. 42:137-139, 1985.
- 41. GILL, P.S., LEVINE, A.M., MEYER, P.R., BOSWELL, W.D., BURKES, R.L., PARKER, J.W., HOFMAN. F.M., DWORSKY, R.L. LUKES, R.J. Primary central nervous system lymphoma in homosexual men, clinical, immunologic and pathologic features. Am. J. Med. 78:742-748, 1985.
- 42. ZIEGLER, J., MINER, R.C., MINTZ, L., ROSENBAUM, E., DREW, W.L., LENNETE, E., GREENSPAN, J., SHILLITOE, E., BECKSTEAD, J., CASARANT, C., YAMAMOTO. Outbreak at Burkits like lymphoma in homosexual men. Lancet ii 631-633, 1982.
- ZIEFLER, J., BACKSTEAD, R., VOLBEROING, P., ABRAHAMS, P., LAVINE, A., LUKES, R., GILL, P., BURKES, R., MEYER, D., METROKA, C., MOURADIAN, J., MOORE, A., RIGGS, S., BUTLER, J., CAHANILLAS, F., HERSHS, F., NEWELL, G., LAUBENSTEIN, L., KNOWLES, D., ODAJUYK, C., RAPHAEL, B., KAZINER, B., URMACHER, C. & CLARKSON, B.
 Non-Hodgkin lymphoma in 90 homosexual men.
 N. Engl. J.Med. 311:565-581, 1984.

44. BIGGA, R.J., MELBYE, M. & KESTEIN, L. Kaposis Sarcoma in Zaire is not associated with HTLV III infection. N. Engl. J. Med. 16, 1051, 1984.

- 45. BAYLEY, A.C. Aggressive Kaposis Sarcoma in Zambia, 1983. Lancet ii: 1318-1320, 1984.
- 46. SINDRUP, J.H., LISBY, G., WEISBY, G., WEISMANN, K. & WANTZIN, G.L. Skin manifestation in AIDS - HIV infection and AIDS related complex. Int. J. Dermatol, 26:267-272, 1986.
- 47. KREISS, J.K, KOECH D, PLUMMER F.A,

HOLMES K.K, LIGHTFOOTE M, PIOT P, RONALD A.R, NDINYA-ACHOLA J.O., D'COSTA, L.J., ROBERTS, P., NGUGI, E.N., QUINN, T.C.,

Aids virus infection in Nairobi prostitutes Spread of the Epidemic to East Africa. N. Engl. J. Med. 7, 414 - 418, 1986.