HISTOPATHOLOGY OF VARIOUS ORGANS IN PATIENTS WITH ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

A dissertation presented in part fulfilment for the degree of Master of Medicine (Pathology) of the University of Nairobi.

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May 1990.

DECLARATION

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

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This dissertation has been submitted for examination with my approval as a University Supervisor.

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DEDICATION

To My Daughter Ndunge

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LIST OF ABBREVIATIONS

HIV - Human immunodeficieny Virus

AIDS - Acquired Immunodeficiency Syndrome

LAV - Lymphadenopathy Associated Virus

HTLV - Human T. Lymphotropic Virus

NK Cell- Natural Killer Cell

CD8 - *Cluster Distribution Marker 8*

CNS - Central Nervous System

FSGS - Focal Segmental Glomurulosclerosis

EDTA - Ethylenediamine Tetra Acetate

Hb - Haemoglobin

HCT - Haematocrit

WBC - White Blood Cell Count

Plt - Platelets

MGG - May Grunwald Giemsa

Na^+ - Sodium

K^+ - Potassium

Cl^- - Chloride

Ca^{2+} - Calcium

BUN - Blood Urea Nitrogen

UA - Uric Acid

Creat - Creatinine

TP - Total Protein

Alb - Albumin

Bil - Bilirium

ELISA - Enzyme Linked Immunosorbent Assay

LIST OF ABBREVIATIONS (Continued)

SD - Standard Deviation

ESR - Erythrocyte Sedimentation Rate

$meql^{-1}$ - Milliequivalents per litre

$mgdl^{-1}$ - Milligrammes per decilitre

gdl^{-1} - Grammes per decilitre

$umoll^{-1}$ - micromols per litre

$mmhr^{-1}$ - millimetres per hour

g - grammes

AAFBs - Acid Alcohol Fast Bacilli

ZN - Ziehl Neelsen

GIT - Gastro Intestinal Tract

TB - Tuberculosis

PCP - Pneumocystis carinii pneumonia

KS - Kaposi's sarcoma

EEG - Electroencephalogram

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SUMMARY

The significance of histological patterns with accompanying laboratory data seen in thirty patients with acquired immunodeficiency syndrome at Kenyatta National Hospital are described in relation to symptom and sign complexes. Ten of these are postmortem and twenty antemortem.

There is a preponderance of Kaposi's sarcoma slit forming type occurring in 70% of all the cases. Forty percent of them present with skin nodules, 13% with lymphadenopathy, 13% with visceral involvement only, 3.3% with both viscreal and cutaneous lesions and 3.3% with a conjunctival lesion.

Forty percent of the lynph nodes show granulomatous lymphadenitis with necrosis, 40% Kaposi's sarcoma and 20% follicular hyperplasia. Lymphoid depletion, follicular changes and linear hyalinisation is noted in autopsy . The spleen shows paucity of follicles in all the autopsy cases.

Approximately twenty seven percent (26.7%) of the study patients are diagnosed as pulmonary tuberculosis antemortem. At autopsy 40% of the cases have non-specific areactive bronchopneumonia, 40% necrotising bronchopneumonia, 10% interstitial pneumonitis and 10% pulmonary Kaposi's sarcoma.

There is a paucity of opportunistic infections.

Neurological symptoms are not due to opportunistic infections or malignancies.

Diarrhoea occuring in 36.7% of the cases is predominantly non-infective in nature.

Myocardiolysis, focal segmental proliferative glomerulonephritis and hepatolysis are seen in all the cases. Testicular atrophy (5 cases) and paucity of primordial follicles (5 cases) are described.

Prospects for improved management of patients with AIDS at Kenyatta National Hospital and future research are suggested.

INTRODUCTION AND LITERATURE REVIEW

Less than 30 years ago, while worry was growing about thermonuclear weapons, a veritable microbilogical bomb was quietly detonated in the form of the Human Immunodeficiency Virus (HIV), which was identified by Montagnier and his group in Paris in 1983 and by Gallo and his group in Bethesda in 1984 as the aetiological agent of the Acquired Immunodeficiency Syndrome (AIDS) (1). Human Immunodeficiency Virus, sometimes designated HTLV-III, belongs to a group of almost identical retroviruses that include the lymphadenopathy associated virus (LAV), and the human immunodeficiency virus type II (HIV-2) (1, 2, 4, 5, 6, 7, 8).

Human Immunodeficiency Virus infection is spread by sexual contact (both homosexual and heterosexual), by infected blood and blood products, infected transplanted tissues and organs and perinatally from mother to infant (1, 9, 3, 5, 12, 13). It is now a world wide epidemic though its origins are obscure. North America or Central Africa which have the highest incidence of the syndrome are thought to be possible sites of origin (9, 15).

Regardless of the portal of entry, the virus has a selective predilection for the T4 lymphocytes of the immune system and certain cells of the central nervous system, resulting in

immunosuppression and neuropsychiatric abnormalities (9, 3, 10, 11, 14, 15, 16, 17, 18).

The critical basis for the pathogenesis of HIV infection is the depletion of the helper/inducer subset of T lymphocytes which express the CD4 phenotypic marker (the T4 cells), resulting in profound immunosuppression. The T4 cell is the focal and critical cell involved directly or indirectly in the induction of most normal immunological functions. Hence a functional defect of T4 cells would result in a decrease in inductive signals to multiple limbs of the immune response. This explains the apparent paradox of a selective defect in a single subset of cells causing a global immune defect. T4 cells are involved in the activation of macrophages, induction and function of cytotoxic T cells, natural killer cells (NK cell), suppressor cells (CD8), B cells, secretion of haematopoietic colony stimulating factors and secretion of growth and differentiation factors for lymphoid cells (3, 9, 19, 20, 21, 22, 23, 24).

The cell mediated immunity of an individual infected with HIV is markedly impaired. This impairment is manifestly attended by a number of serious opportunistic infections, and malignancies. The common infectious agents in patients with AIDS include viruses, fungi, protozoa, and bacteria as herebelow shown (5, 3, 26, 25, 27, 28, 29, 30, 31, 32, 33, 34).:

Viruses: Herpes viruses types I and II, Cytomegalovirus, Varicella, Adenoviruses, Epstein Barr virus.

Fungi: Candida spp., Cryptococcus (C. neoformans), Histoplasma spp.

Protozoa: Pneumocystis carinii, Toxoplasma gondii, Crytosporidium spp., Giardia lambia, Entamoeba histolytica Isospora spp.

Bacteria: Shigella Spp., Salmonella spp., Campylobacter, Neisseria gonorrhoea, Mycobacteria (typical and atypical), Treponema pallidum, Histoplasma, Legionella spp.

The malignancies associated with AIDS include Kaposi's sarcoma, non-Hodgkin's lymphomas (Burkitt - like lymphoma and B-cell lymphoblastic lymphomas) which are found mainly in the brain and bone marrow (25, 34, 35, 36, 37, 38, 40, 41, 42).

Due to the stigma and fear associated with HIV infection, few autopsies have been performed on patients dying of AIDS. However, various studies and case reports from different parts of the world tend to give a concensus on the clinico-pathological correlation of epiphenomena associated with HIV infection.

Kayembe et al (43) found that infections, especially tuberculosis, and both cutaneous and visceral Kaposi's sarcoma were frequent histopathologic findings. No cases of Pnenumocystis carinii infections were noted. Del Bianco et al (44) found Mycobacteria tuberculosis clinically in 34.2% of the cases, Pneumocystis carnii in 25.7%, Toxoplasma gondii in 11%, Herpes simplex in 8.5% and Cryptococcus neoformans in 8.5% of the cases, M. avium intracellurare in 8.5%, T. gondii in 22.8%, C. neoformans in 8.5% and Cytomegalovirus in 31.4%. Both Del and Kayembe concluded that tuberculosis is often found in patients with AIDS. This was also found to be the case by Niedt and Schinella (45) who in addition also found a very high incidence of serious non-mycobacterial infections which included pulmonary Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumoniae, Enterobacter cloacae and Legionella pneumophilla. Bacteremia due to Pseudomonas aeruginosa, Klebsiella pneumoniae, and Shigella spp. was also found Salmonella spp., Shigella spp. and Clostridium difficile were cultured from the gastrointestinal tract. Kaposi's sarcoma involving the skin, stomach and lymph nodes was found in over 50% of autopsies. Over 95% of these had disseminated disease. Less than 5% had lesions limited only to the skin, presenting with unusual histological appearances including angiosarcomatous types, anaplastic forms, sclerotic and cavernous haemangiomatous variants (45).

Cryptococcosis, the systemic infection caused by the encapsulated yeast *Cryptococcus neoformans* is an uncommon sporadic disease that occurs throughout the world in both previously healthy and immunocompromised individuals. Although cryptococci are commonly found in the respiratory tract, the most frequent clinical manifestation of cryptococcosis is meningitis. Other infections of the central nervous system (CNS) include toxoplasmosis, candidiasis, Escherichia coli meningitis, Cytomegalovirus inclusions, tuberculous abscesses and quartenary neurosyphilis (45, 56, 47, 48) consisting of a meningovascular and fulminant necrotising syphilitic encephalitis. The meningovascular component is characterised by chronic leptomeningitis, gummatous arteritis and focal well circumscribed parenchymal infarcts. The encephalitis is defined by poorly demarcated foci of necrosis with sparse inflammation, focally necrotising small vessel vasculitis and tangled masses of spirochaetes (46). Subacute encephalitis was often diagnosed in patients who had presented with neurological symptoms and signs. At post-mortem the brain was found to have diffuse atrophy with microglial nodules in both the grey and white matter, perivascular demyelination in the white matter and diffuse gliosis of both grey and white matter. This was attributed to infection with cytomegalovirus but was not proven (49). Papovavirus has been implicated in the development of

progressive multifocal leukoencephalopathy, an entity commonly found in AIDS patients. The brain is characterised by cellular changes including enlargement of the nuclei and alteration of the chromatin pattern in oligodendrocytes at the border of the lesions accompanied by extra-ordinary hypertrophy of the astrocytes with bizarre deformations of their nuclei to resemble a malignant glial neoplasm (45, 47, 48, 49, 50). Human Immunodeficiency Virus encephalitis, characterised by microglial nodules with multinucleated giant cells and rare intranuclear inclusions in both the grey and white matter has also been documented (48). Also occasional foci of perivascular lymphocyte infiltration as well as discrete foci of perivascular demyelination and necrosis in the globus pallidus, putamen, midbrain tectum, tegmentum and reticular formation have been documented. Subependymal gliosis was also present (47, 48). Vacuolar myelopathy which exhibits prominent vacuolization of the spinal white matter, closely resembling subacute combined degeneration, with the presence of characteristic multinucleated giant cells is yet another manifestation of HIV infection of the CNS (45, 47, 48, 51, 52, 53). Central nervous system malignancies associated with HIV infection are largely lymphomas. Lee et al (47) described a case in which a solitry lesion in the temporal lobe secondarily involved the meninges and on histology consisted of a diffuse large cell lymphoma with pyrinophilic cytoplasm eccentric nuclei and occasional large nucleoli.

A symmetrical extensive necrotic, friable and largely non-haemorrhagic lesion was found in the brain stem and cerebellum, the histology of which revealed a diffuse histiocytic lymphoma, B-cell type (54). There was no systemic lymphoma. Lantos et al (48) described a primary malignant immunoblastic lymphoma which had extensively invaded the cerebral hemispheres, brainstem and cerebellum (one case) and a secondary acute lymphoblastic in addition to a secondary B-cell lymphoma (two cases) both infiltrating the leptomeninges, the Virchow-Robin spaces and the adjacent brain tissue.

The respiratory system pathology associated with AIDS is largely confined to infections and disseminated Kaposi's sarcoma. In Europe and North America, Pneumocytis carinii pneumonia is the most prevalent infection followed by mycobacterial infection which has an atypical presentation. The classical upper-lobe apical disease and cavitation are rare, the lesions showing massive caseation with poorly formed granulomata (45, 55). In the tropical countries, mycobacterial infections are the most common while Pneumocystis carinii pneumonia is rare (43). Other infections include cryptococcosis, cytomegalovirus pneumonitis, aspergillosis, candidiasis and atypical mycobacterial infections (47, 55, 57). The histological findings include necrotising haemorrhagic pneumonia, consolidation, diffuse interstitial fibrosis, hyaline

membranes, organising pneumonias and lobular pneumonias. Pneumocystis carinii pneumonia is associated with a foamy exudate with organisms present in areas of histiocytic and giant-cell reaction where the pneumonia is organising and is surrounded by fibrin. Calcification may also occur (45).

Ulcerating pharyngo-oesophageal leucoplakia is a known complication of HIV infection. Histological features as documented by Kitchen et al (58) include koilocytosis, multinucleation, parakeratosis, dyskeratosis and epidermal thickening/hyperplasia. Colonic biopsies showed moderate to sever colitis characterised by preservation of normal crypt architecture and a mixed inflammatory cell infiltrate. Pancreatic lesions of opportunistic infection with Cytomegalovirus, Toxoplasma gondii, tumour infiltration by Kaposi's sarcoma lymphoma, and features of acute pancreatitis were noted by F. Brivet et al (59).

It is rare for infections to involve the spleen but in AIDS patients, cryptococcus, candiasis and mycobacterial infections have been identified (45, 55, 60, 57). Histological features have included depletion of the white pulp with fibrosis of periarterial lymphatic sheath, increased plasma cells, increased haemosiderin in macrophages and haemophagocytosis. In the mycobacterial infections, the bacilli were contained in spindle shaped macrophages confined to malphigian follicles and forming

concentric whorling patterns associated with fibrosis (45, 60). Scattered foci of extramedullary hemopoiesis and occasional areas of necrosis with foamy exudate, at the periphery of which were Gomori's methanemine silver positive organisms were documented in splenic infection with Pneumocystis carinii (60). Kaposi's sarcoma infiltrates also occur in the spleen (47).

Lymph nodes are very often involved in the pathology of AIDS. This may be by infections such as Cryptococcus neoformans, Mycobacterium tuberculosis which cause massive cesation and poorly formed granulomata and by malignant lymphomas or Kaposi's sarcoma. Other histological appearances of lymph nodes include follicular hyperplasia with follicular alterations, mixed hyperplasia and lymphocyte depletion (45, 47, 55, 61, 62, 63).

Features in keeping with aplastic anaemia, increased plasma cells, iron stores, variable cellularity and hemophagocytosis have been noted in the bone marrow of AIDS patients (47, 62), as well as mycobacterial infections. Epithelioid angiomatosis, a vascular disorder distinct from Kaposi's sarcoma, histologically composed of proliferating blood vessels and cells with epithelioid features were observed in five patients with AIDS. These may present as cutaneous lesions or affect internal organs (65).

The thymus has been found to be infected by Cryptococcus neoformans (57) and have lymphoid depletion, cystic calcified or absent Hassals corpuscles (45).

Toxoplasma and Cryptococcal myocarditis and candidiasis of the endocardium have been noted together with cytomegalovirus inclusions in the endothelial and myocardial cells. Other manifestations of HIV infection in the heart include focal lymphocytic myocarditis, lipochrome deposition, focal necrosis and mixed cell infiltrates (47, 57).

Candidiasis affecting the testes and kidneys were documented (45, 67) while renal biopsies showed focal and segmental glomerulosclerosis (FSGS), diffuse glomerulosclerosis, focal mesangial proliferation associated with the presence of fuscinophil deposits, FSGS and membranoproliferative glomerulonephritis. Alex Karlsson-Parra et al showed that glomerular cells express the CD4 antigen and suggested the existence of a specific HIV associated nephropathy (68, 73).

Specific infectious lesions of the adrenal gland include cytomegalovirus adrenalitis (45, 55) accompanied by necrosis or the presence of inclusion bodies in healthy tissue, around and inside eosinophilic necrotic areas, Cryptococcosis, tuberculosis and candidiasis (45, 69). Other lesions include inflammatory lesions with necrosis,

without necrosis or large disseminated foci usually located in the medulla, in the cortical reticularis or at the junction of the two areas, adrenal thrombosis and Kaposi's sarcoma. Adrenal insufficiency was rare clinically but from the necropsy study it is particularly affected in the evolution of AIDS and insufficiency should be looked for early (69).

Skin manifestations of AIDS range from infections including Herpes simplex, Herpes zoster, Cytomegalovirus, Cryptococcus neoformans which has been shown to mimick molluscum contagiosum (45, 55, 70) to non-infectious eosinophilic pustular folliculitis (71) and Kaposi's sarcoma. Adipose tissue serous atrophy and bone cryptococcosis have also been documented (45, 55).

Toxoplasma and cytomegalovirus retinitis are frequent ophthalmic manifestations of AIDS while lymphomas and Kaposi's sarcoma are rare (55, 72).

Literature on AIDS in Kenya has focussed on the clinical epidemiological aspects of the syndrome. This study intends to delve into pathological aspects and open up new areas of research.

AIMS AND OBJECTIVES

Aims and Objectives

The clinical features and progression of the syndrome are associated with specific histological changes. The syndrome is a spectrum of symptom and sign complex and is associated with epiphenomena including opportunistic infections and the development of certain malignancies.

This is a descriptive study that hopes to determine the clinicopathological correlation of changes in patients who are serologically positive for HIV antibody by ELISA and confirmed by Western Blot.

Specific Objectives

1. To review biopsy specimen in life and postmortem and record histological changes.

2. To review microbiological data from microscopy and culture of stool, urine, sputum, urethral swabs, vaginal swabs, CSF, pus and tissues where patients show evidence of infection.

3. To review biochemical data as relates to liver function tests, renal function tests and any other that may be relevant to the study.

4. To review haematological data specifically the haemoglobin levels, white cell count with differential counts, erythrocyte sedimentation rates and packed cell volume.

5. To determine the morbidity and mortality pattern, the mode of death and cause of death.

6. To correlate the above findings with the clinical states of the patients with a view to advising on the management of patients with AIDS at Kenyatta National Hospital.

MATERIALS AND METHODS

The study was carried out at Kenyatta National Hospital.

The clinical state of the patient was obtained using Appendix I and II. This necessitated utilisation of medical records.

Laboratory Methods

a. Peripheral Blood Examination

Venous blood collected in ethylenediamine tetra-acetate (EDTA) was processed through the Coulter Counter model S plus IV and the following haematological indices taken:

- Haemoglobin (Hb)
- Packed cell volume (Hct)
- White blood cell count (WBC)
- Platelet count (Plt)

Peripheral blood films were stained by the May Grunwald Giemsa (MGG) technique and were examined for the differential WBC count.

b. **Biochemical Indices**

Venous blood collected in a plain biochemistry container was allowed to clot and the serum processed through the SMA II processor and the following indices taken:

- Sodium
- Potassium
- Chloride
- Calcium
- Blood urea nitrogen
- Uric acid
- Creatinine
- Total protein
- Albumin
- Bilirubin

Alkaline phosphatase values were obtained mannually using kit methods.

Microbiological Examination

This was carried out using the standard techniques for each different specimen (56).

Serology

Serum was analysed by ELISA (Organon) and Western Blot(DU Pont) for HIV antibody.

B. Postmortem

Nine postmortems were performed and one limited to the brain liver and lung, using universal precaution techniques and methods (25, 74, 75, 76).

The postmortems were carried out at the earliest possible to minimise autolytic changes. This was within seven days of death.

The tissues obtained were fixed in formalin, processed by conventional techniques and stained using routine haematoxylin oesin stain. Special staining (Grocots, muciarmine and periodic acid-schiff) were done as necessary (105).

Ethical Considerations

1. The patients' anonymity was maintained.

2. Care was taken not to cause harm or embarassment to the patient in the course of the study (Helsinki Declaration).

3. The corpses were treated with utmost respect in the course of the study, care being taken not to deform the body and observe cultural sensitivities.

4. Consent to perform the autopsy was obtained from the person/persons with custody, legal or otherwise of the body.

5. The study was carried out with the approval of the Ethical and Research Committee, Kenyatta National Hospital.

Study Population

In Life - Patients admitted with a clinical diagnosis of AIDS, screened positive for HIV by ELISA and confirmed by Western Blot, who were not less than 15 years of age.

Postmortem - Patients dying from AIDS (confirmed by Western Blot) at Kenyatta National Hospital, who were 15 years of age and above.

Data Analysis

The data collected was analysed using tables and histograms according to the parameters and variables under study. Percentages where necessary were also employed.

RESULTS

There were twenty one males and nine females. Ages ranged from sixteen to fifty one years with an average of thirty one (SD 7.9).

Table I: Age and sex distribution

Age	No. of Patients	
	Males	Females
15 - 19	1	2
20 - 24	0	0
25 - 29	4	5
30 - 34	9	1
35 - 39	2	0
40 - 44	3	1
45 - 49	1	0
50 - 54	1	0
TOTAL	21	9

Seventy percent (70%) of the patients were between 25 - 39 years.

Cases 1 - 20 were antemortem and 21 - 30 were postmortem cases.

Table II: Frequency of symptoms amongst the study patients.

SYMPTOMS	NUMBER OF PATIENTS
1. Weight loss	23
2. Skin lesions	20
3. Neurological symptoms	14
4. Abdominal pain	12
5. Diarrhoea	11
6. Fever	11
7. Cough	10
8. Chest pain	10
9. Breathlessness	8
10. Vomiting	7
11. Nightsweats	6
12. Dysphagia	4
13. Haemoptysis	3
14. Neck swelling	2
15. Abdominal swelling	1
16. Growth in the eye	1
17. Anorexia	1

Taking symptoms 1-6 as major symptoms 63% of all the symptoms expressed fell into this criteria.

Table IIA: Neurological symptoms

SYMPTOM	NUMBER OF PATIENTS
Headache	8
Weakness	3
Inability to walk	2
Drowsiness	1

Table IIB: Symptoms of skin lesions

SYMPTOM	NO. OF PATIENTS
Nodule	12
Itching	5
Ulcers	3

Figure 1: Histogram depicting frequency of symptoms.

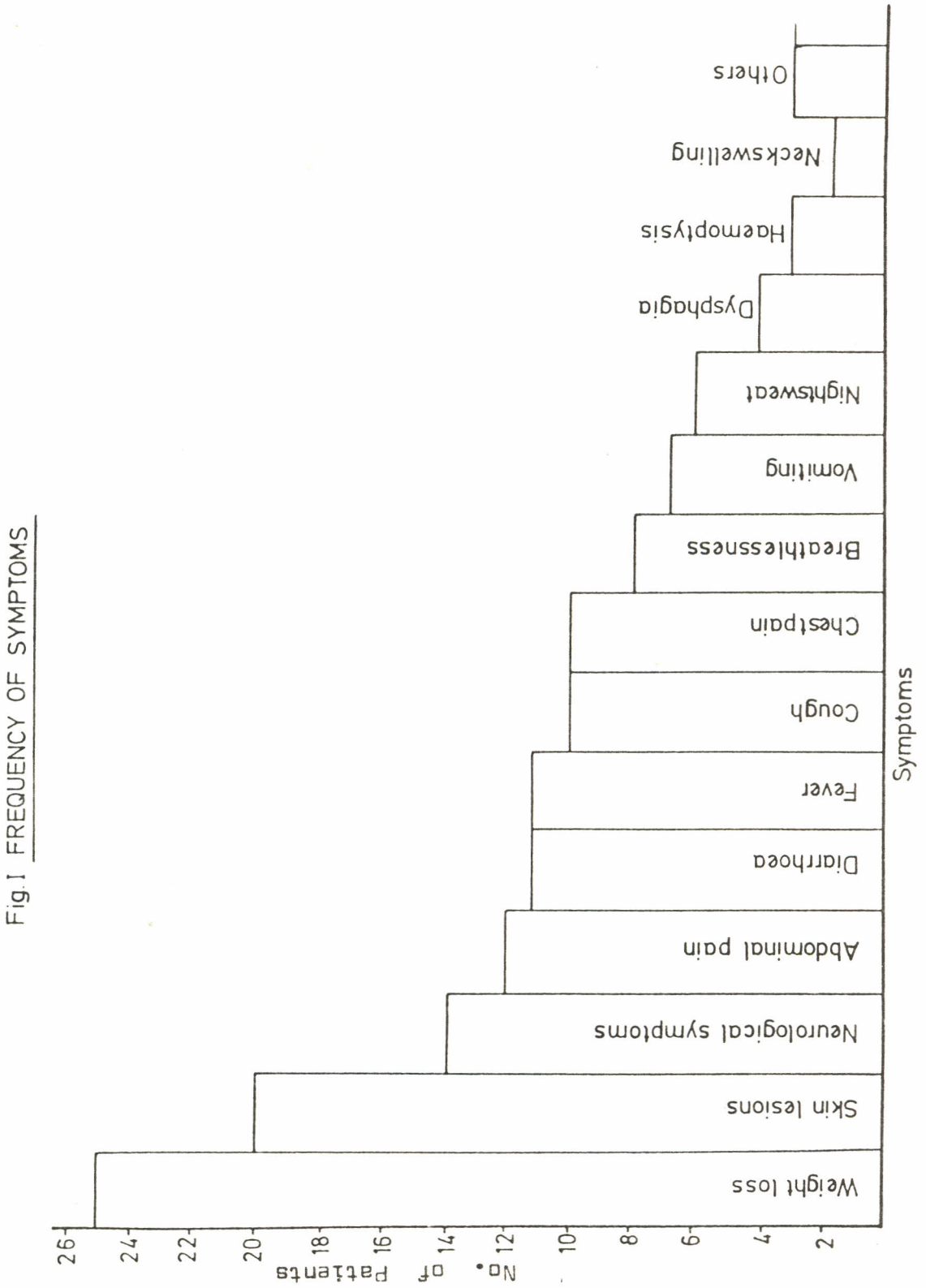


Table III: Frequency of signs amongst the study patients

CLINICAL SIGNS	FREQUENCY
1. Skin lesions	23
2. Wasting	21
3. Lymphadenopathy	12
4. Fevers	12
5. Abdominal tenderness	16
6. Lung Consolidation/cavitation	9
7. Leg edema	8
8. Oral thrush	7
9. Neurological signs	6
10. Dehydration	5
11. Generalised edema	2
12. Jaundice	1
13. Pallor	1
14. Pleural Effusion	1
15. Ascites	1
16. Splenomegaly	2
17. Hepatomegaly	2

Taking signs 1-6 as major signs 70% of all the signs elicited fell into this criteria.

Table IIIA: Neurological Signs

SIGNS	NO. OF PATIENTS
Confusion	4
Hypereflexia	1
Coma	1

Table IIIB: Skin Lesions

SKIN LESIONS	NO. OF PATIENTS
Skin nodules	15
Perineal ulceration	4
Maculopapular rash	4

Wasting is a rather subjective parameter as it was the cachetic individuals that were selected by this criteria. This introduced a large source of error since `wasting' in terms of basal weights and body weights at the time of the study were not assessed; neither was subcutaneous fat. However 96.7% of the patients were wasted.

Figure II: Histogram depicting frequency of signs

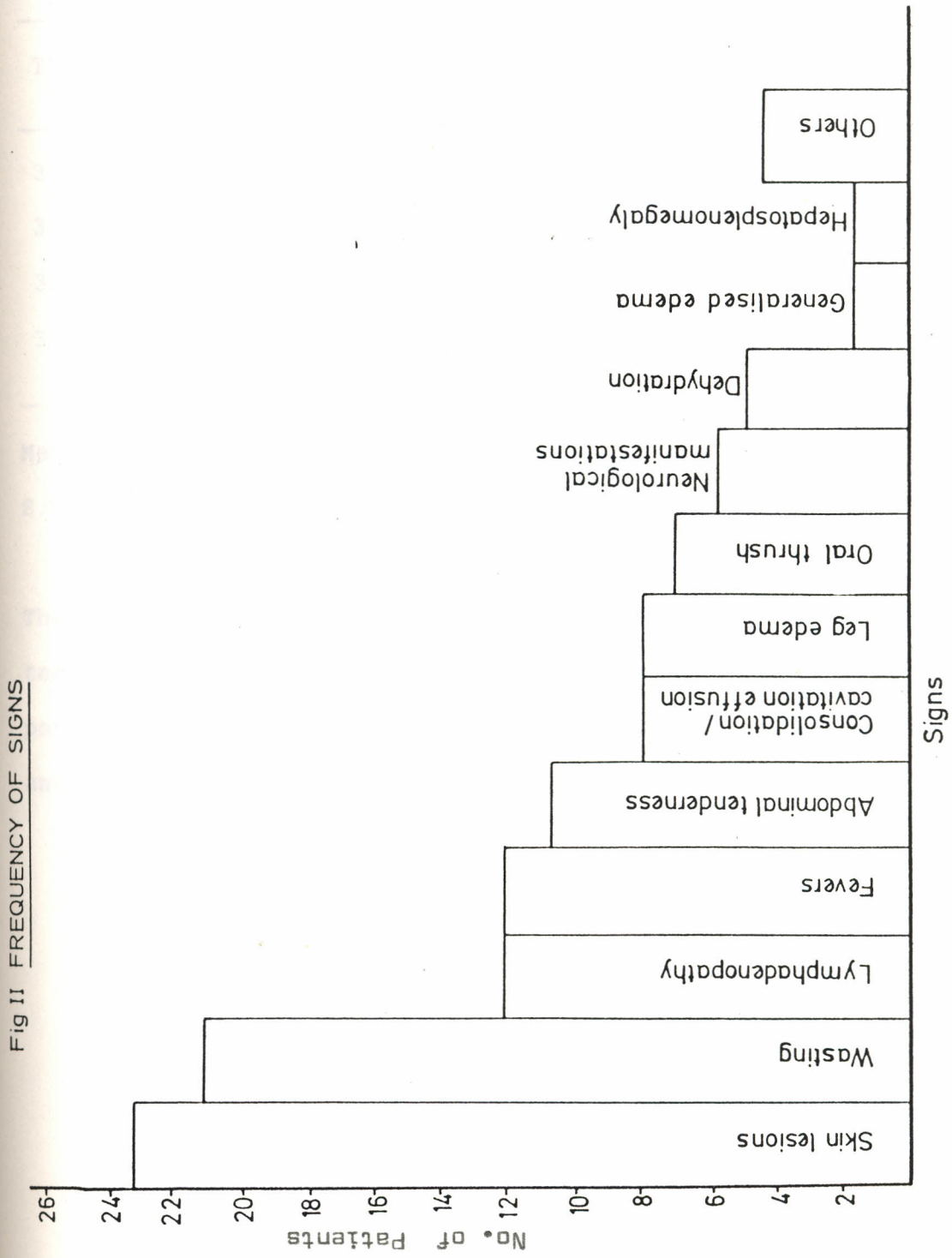


Table IV: Temperature ranges

TEMPERATURE (^{o} C)	NUMBER OF PATIENTS
37.5 - 37.9	7
38.0 - 38.4	6
38.5 - 38.9	2
39.0 - 39.5	1

Mean - 30.05^{o} C

S.D. - 0.188

The patients who were reported to have fevers had temperatures ranging from 37.5^{o} C to 39.0^{o} C. Eighty one percent (81%) of them had a low grade fever between 37.5^{o} C and 38.4^{o} C.

Laboratory Findings

Table V: Haematological Data

Case No.	Hb	WBC	Poly	Ly	Mo	Eo	Bas	Plt	Hct	ESR	*Absolute
1	5.9	20						300	17.9	-	-
2	8.8	5.6	60	34	4	2	-	293	26.7	58	1.90
3	14.3	6.4	-	-	-	-	-	118	43.5	-	-
4	7.2	10.8	54	45	-	1	-	336	25.8	71	4.86
7	5.4	6.6	78	20	2	-	-	290	15.8	26	1.32
8	9.0	5.8	-	-	-	-	-	190	26.1	-	-
9.	11.8	4.6	59	35	-	6	-	273	33.0	16	1.61
10	11.1	11.3	-	-	-	-	-	911	33.3	-	-
11	11.1	8.7	-	-	-	-	-	280	33.3	14	-
13	7.6	9.7	-	-	-	-	-	253	21.7	-	-
14	9.5	5.2	60	34	-	6	-	200	28.0	-	1.77
15	10.9	5.9	64	36	-	-	-	300	-	55	2.12
16	6.6	5.4	35	62	-	3	-	280	20.0	-	3.35
17	7.8	5.2	-	-	-	-	-	239	22.0	41	-
18	11.5	4.8	-	-	-	-	-	289	33.8	51	-
19	8.6	9.2	72	27	-	1	-	466	26.3	54	2.4

(Table V continued)

21	12.6	4.4	-	-	-	-	-	342	30.0	47	-
22	10.5	6.8	-	-	-	-	-	354	30.5	58	-
23	7.6	3.4	78	21	-	1	-	327	22.8	68	0.714
24	10.8	20.8	95	5	-	-	-	290	34.1	-	1.04
25	6.3	2.4	79	20	1	-	-	290	20.1	-	0.48
26	6.5	8.2	80	18	2	-	-	150	19.7	67	1.48
27	8.9	10.4	-	-	-	-	-	150	27.9	-	-
30	11.3	8.6	-	-	-	-	-	290	32.5	-	-

Units:

Hb - gdl^{-1}

WBC - x $10^{9}l^{-1}$

Poly - %

Ly - %

Mo - %

Eo - %

Bas - %

Plt - x $10^{3}mm^{-1}$

ESR - $mmhr^{-1}$

*Absolute - Absolute lymphocyte count (x $10^{9}l^{-1}$)

Table VI: Haemoglobin Frequency Table

Hb (gdl^{-1})	NO. OF PATIENTS
5 - 5.9	2
6 - 6.9	3
7 - 7.9	4
8 - 8.9	3
9 - 9.9	2
10 - 10.9	3
11 - 11.9	5
12 - 12.9	1
13 - 13.9	0
14 - 14.9	1

Mean - 9.23 gdl^{-1}

SD - 2.17

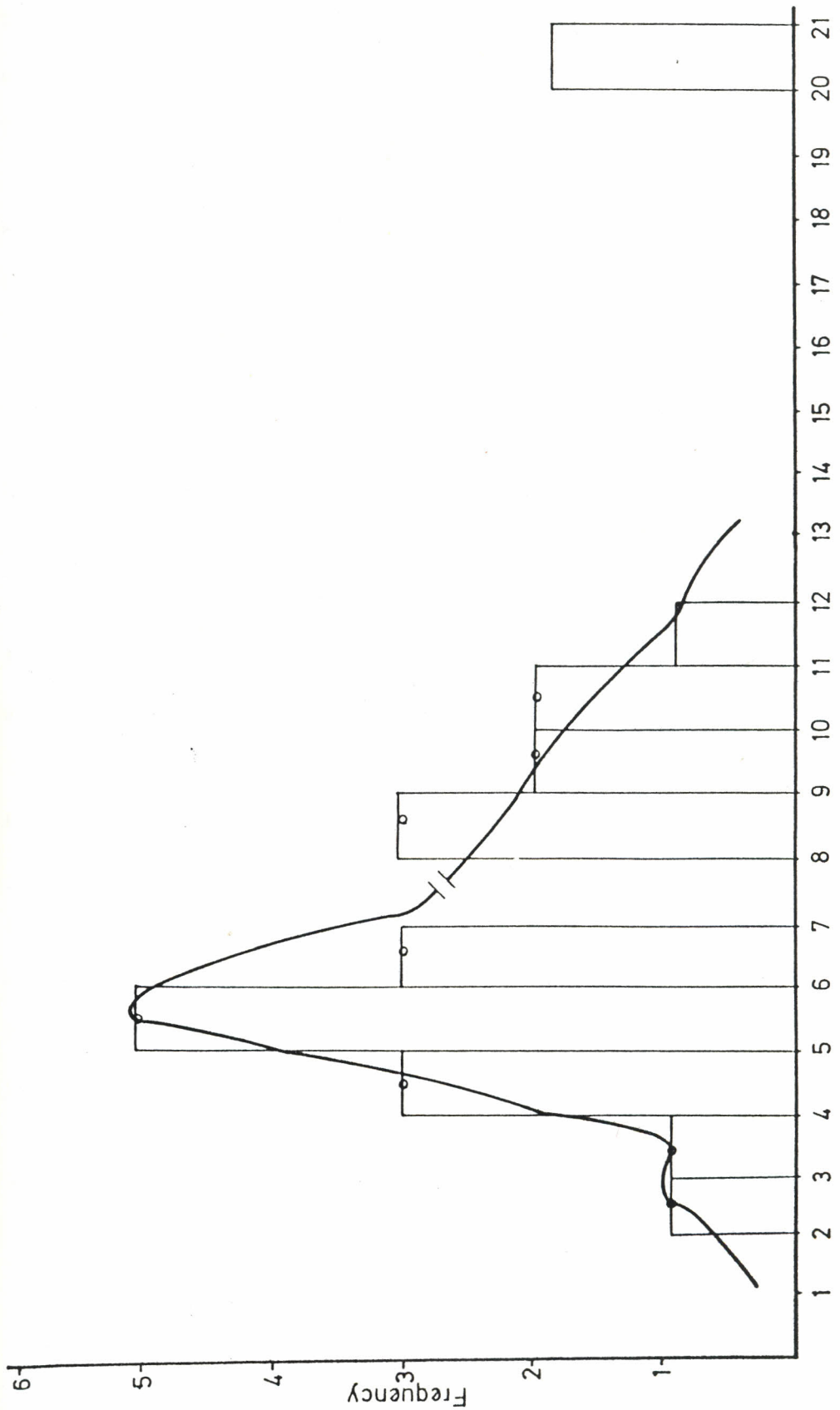
Mode - 11 - 11.9 gdl^{-1}

The reported average for Kenyan adults is 12.2 - 19.6 gdl^{-1} (77). Only 8.7% of the study patients fell within this range.

Table VII: White blood cell count frequency table.

WBC COUNTS ($\times 10^9 l^{-1}$)	NO. OF PATIENTS
2 - 2.9	1
3 - 3.9	1
4 - 4.9	3
5 - 5.9	6
6 - 6.9	3
7 - 7.9	0
8 - 8.9	3
9 - 9.9	2
10 - 10.9	2
11 - 11.9	1
12 - 12.9	0
13 - 13.9	0
14 - 14.9	0
15 - 15.9	0
16 - 16.9	0
17 - 17.9	0
18 - 18.9	0
19 - 19.9	0
20 - 20.9	2
TOTAL	24

Figure III: Frequency polygon of WBC counts



The mean WBC count was found to be 7.93 x 10^9 l^{-1} with a standard deviation (SD) of 4.5.
The mode was 5 - 6 x $10^9 l^{-1}$.

Mukiibi et al (77) found the normal range among adult African Kenyans to be 3.0 - 10.3 x 10^9 l^{-1} with a mean of 6.2 x 10^9 l^{-1} (SD 1.6). Seventy five percent (75%) of the study patients had WBC counts within this range.

The mean platelet count was found to be 300.5 x 10^3 mm^{-3} (SD of 149.76) the range being 118 - 911 x 10^3 mm^{-3}. Mukiibi et al (77) recorded a range of 114 - 300 x 10^3 mm^{-3} for 95% of the Kenyan African population with a mean count of 211 x 10^3 mm^{-3}. Seventy five percent (75%) of the study patients had their platelet counts within this range. Twenty five percent (25%) had values higher than this.

ESR values ranged from 14 -71 $mmhr^{-1}$ in the 13 cases in which this index was evaluated. Mean ESR found was 48.15 $mmhr^{-1}$ (SD 18.92). The normal ESR range given is 0 - 7 $mmhr^{-1}$ at room temperature.

There was however no correlation between these haematological parameters.

Table VIII: Biochemical data

CASE	K^+	Na^+	Cl^-	Ca^{2+}	BUN	UA	Crea	$AlkPO_4$	TP	ALB	BILI
		($meql^{-1}$)			($mgdl^{-1}$)			KA units	gdl^{-1}		$umoll^{-1}$
1	4.7	134	107	9.0	10	4.5	0.8	9.7	-	-	-
3	-	135	-	9.7	27	11.9	0.9	-	-	-	-
4	-	137	106	10	50	4.1	0.17	-	-	-	-
7	4	129	103	7.2	53	-	2.0	9.3	65	35	35
8	4.5	144	109	8.0	9	6.1	0.2	15.5	65	28.2	15
13	4.8	135	108	7.2	15	-	1.3	-	-	-	-
14	4	131	105	9.7	10	9.1	0.8	7.4	61	34	10
16	4.6	135	101	8.2	27	-	1.8	-	-	-	-
20	4.1	121	95	7.2	33	6.7	1.7	27.1	67	21	7
21	3.7	142	104	9.7	40	9.0	-	-	60	27	4
24	4.6	148	-	5.4	85	12.0	3.9	-	59	30	3
26	1.9	137	104	7.6	11	3.2	3.2	-	-	-	-
30	4.4	131	*80	*1.84	8.0	3.03	*9.4	-	78	24	12
MEAN	4.12	135.3	102	8.24	29.08	6.96	1.52		65	28.5	12.3
SD	0.81	6.9	4.6	1.4	23.1	3.39	1.18				

*Results not utilised in the calculations of standard deviation.

The results for case No. 30 were not utilised in some of the calculations as these did not conform to any pattern that depicted a clinical disorder.

Table IX: Normal Biochemical Parameters for Kenyatta National Hospital (KNH). (Source: Clinical Chemistry Laboratory, KNH)

Na^+	135 - 145	$meql^{-1}$
K^+	3.5 - 50	"
Cl^-	95 - 105	"
Ca^+	8.5 - 10.5	$mgdl^{-1}$
BUN	10 - 26	$mgdl^{-1}$
Uric Acid	2.2 - 9.0	"
Creatinine	0.7 - 1.4	"
Total Protein	60 - 85	gdl^{-1}
Albumin	26 - 52	"
Bilirubin	3 - 21	$umoll^{-1}$
Alkaline phosphate	2 - 12	K. A. units

Except for BUN levels all the other parameters examined were within the acceptable ranges given. Only 30% of the patients had values within the normal range. The mean value was 29.08 $mgdl^{-1}$ with a standard deviation of 23.1. This was attributed to very high BUN levels observed in some of the cases.

MICROBIOLOGICAL RESULTS

Eight stool cultures were reviewed. Of these two grew Salmonella typhimurium, and two Entamoeba coli.

Ten sputum specimen culture results for acid alcohol fast bacilli were reviewed and three were positive.

Ten lung tissue culture results for acid alcohol fast bacilli were reviewed and two were positive.

Three skin wounds grew mixed growths of Citrobacter spp., Proteus spp., B haemolytic streptococci and Pseudomonas aeruginosa.

HISTOPATHOLOGICAL FINDINGS

Respiratory System (Photomicrographs 3, 12, 13, 14)

Ten postmortem lung cases were examined. They all showed gross features compatible with bronchopneumonia. Two had subpleural abscesses (cases 26, 28) and two others showed the presence of cavities (cases 28, 30). One had a pebbly cut surface suggestive of milliary tuberculosis (case 29). The weights of the lungs were as follows:

Table X: Lung Weights

MALES		FEMALES	
RIGHT	LEFT	RIGHT	LEFT
	(weight in g)		
350	335	425	405
930	435	540	400
450	300	675	535
950	875	500	525
1075	1095	550	525
3755	3040	2690	2390
Mean: 751	608	538	478

The normal range of weights for lung is right: 360-570 g with an average of 450 g, and 325 - 480 g with an average of 375 g for the left.

On histology the striking feature was areactive bronchopneumonia. Three of these cases showed necrotising bronchopneumonia (28, 29, 30) two of which had granulomata with Langhans type giant cells. The ZN stains were negative for all except one. No fungi, or viral inclusion bodies were seen. Kaposi's sarcoma slit forming type (83) was noted in one case (case 24).

One case had a focus of neovascularisation attended by the presence of red blood cells in slits in the trachea (case 25). There was linear streaming of spindle cells that were seen to extend to the tracheal glands. This was diagnosed as Kaposi's sarcoma slit forming type.

Seven of the sections showed mucinous concretions in the tracheal glands.

Cardiovascular (Photomicrograph 5)

Ten hearts were examined and eight appeared normal grossly while one was flabby (case 26) and the other showed left ventricular hypertrophy (case 28). The weights were as tabulated below:

Table XI: Heart Weights

CASE	MALES (weight in g)	FEMALES
21	160	-
22	-	210
23	-	220
24	225	-
25	-	170
26	-	175
27	350	-
28	450	-
29	-	175
30	325	-
MEAN	302	190

Normal range for males is 270-360 g with a mean of 300 g and a female range of 200-280 g with a mean of 250 g. From the study only one male was below this range and one above. The study mean is within normal limits. Three of the females had below average heart weights as is the average weights of the hearts. Histologically five cases examined showed focal myocardiolysis with lymphocytic infiltration (cases 25, 26, 28, 29, 30). The other five showed focal myocardiolysis only. The vessels were normal.

Aorta

All sections of the aorta were grossly and histologically normal.

Gastrointestinal System:

Tongue

Nine were analysed and two of these appeared grossly normal (cases 24, 29) while the remaining seven showed raised whitish plaques on the surface of the tongue. These showed mucosal and submucosal intense inflammation characterised by lymphocytes and plasma cells. There was submucosal hyalinisation and numerous telangiectatic vessels. All the sections showed muscle atrophy. The glands showed the presence of mucinous concretions. Special stains for fungi were negative.

Oesophagus

Postmortem sections were analysed from nine cases. Sections were obtained from upper, middle and lower segments. Eight were normal grossly while one showed the presence of longitudinal raised haemorrhagic lesions (case 23). At histology this proved to be a focus of slit forming Kaposi's sarcoma. This same specimen showed muscle lysis

and replacement by hyaline material. There was focal inflammation in the submucosa characterised by lymphocytes and plasma cells containing Russel bodies. There were also prominent ganglia with degenerate ganglion cells. The other eight were normal on histology.

Stomach (Photomicrograph 6)

Seven of the nine cases were grossly normal while two (cases 23, 24) had haemorrhagic firm raised lesions at the fundus. One of these showed the presence of Kaposi's sarcoma while the other showed marked cellular dissociation with prominent linear bands consisting of elongated cells with eosinophilic cytoplasm streaming from the muscularis mucosa to the surface, focal mucosal hyalinisation, neovascularisation, early thrombus formation and focal inflammation characterised by lymphocytes and plasma cells. This was taken to be a focus of early Kaposi's sarcoma. Four cases were autolysed (cases 21, 22, 27, 29) and unsuitable for histological assessment while three others were normal (cases 25, 26, 28).

Small Intestine

Six cases were grossly normal (cases 22, 24, 26, 27, 28, 29), two showed focal ileitis (cases 21, 25), and one had serosal haemorrhagic lesions (case 23). At histology five

(cases 21, 25, 27, 28, 29) of these were autolysed and unsuitable for assessment, three appeared normal (cases 23, 24, 26). Two which though grossly normal, on histology showed dilated vascular channels with organised thrombi, complete denudation of epithelium (which may be postmortem) focal loss of glandular pattern, superficial mucosal inflammation and erosion with nuclear dusting. These were few capillaries overlying the muscularis mucosa from which arose streaming spindle cells.

Large Intestine

Three cases showed focal colitis grossly (cases 22, 25, 27), one membraneous colitis (case 21) with ulceration and five appeared normal. Histologically marked autolysis was noted in five of these cases, one was normal and the other three showed focal loss of glandular pattern (not attributed to postmortem change) with superficial mucosal inflammation and erosion with nuclear dusting (cases 21, 24, 28).

Pancreas

All cases appeared grossly normal. One was not assessed histologically, seven were autolysed and one showed the presence of mucinous concretions in the ducts and acini attended by atrophy of cells. There was dissolution of the matrix of islet cells whose cellularity was within normal

limits. There was focal disturbance of architecture by linear streaming of spindle cells.

Liver (Photomicrographs 7, 8, 11)

Weights ranged from 945 -2100 g with a mean weight of 1417.7 g. Normal weights are 1500-1800 g with an average of 1650 g. Grossly five cases were normal, two were pale (cases 26, 29) and one showed features of passive venous congestion (case 21). Histologically certain features were common to all cases. These were varied degrees of fatty change, portal triad fibrous extension, varied reduction in the number of Kupffer cells, sinusoidal dilation, and focal hepatolysis. The hepatolysis in some cases was so marked as to form small lakes. One case showed ductular proliferation (case 29). The hepatolysis was not attended by inflammation or apoptosis. There was no histological evidence of bile retention. Focal lymphocytic infiltration featured in four cases (cases 21, 26, 29, 30) two of which showed poorly formed granulomata with necrosis and abscess formation (cases 21, 29). One case had diffuse malaria pigment (27).

Spleen (photomicrographs 22, 23)

The spleens weighed between 75 - 540 g with an average of 202 g, the normal being 155 g for 20 - 65 year old individuals. The study cases were aged between 16 and 51 years. Paucity of lymphoid follicles and widening of the sinusoids were common features in all the specimen examined. Case 28 showed hemosiderin deposition with Gamma-Gandy bodies and a focus of Kaposi's sarcoma while case 27 had malaria pigment.

Lymph nodes (Photomicrographs 18, 19, 20, 21)

Several mesenteric and hilar lymph nodes were analysed. The significant features common to all were a paucity of lymphoid follicles, sinus histiocytosis and linear hyalinisation. The follicles were occasionally so atrophic as to be virtually absent. Where follicles were present there were prominent thin walled vessels that appeared to grow into the germinal centres. In the cases where there was an inflammatory process, the lymphoid reaction was not concomitant with the degree of inflammation present in the surrounding tissue. In some of these there was marked necrosis with occasional epithelioid cells, plasma cells and giant cells.

Kidneys (Photomicrographs 15, 16, 17)

The weights of the kidneys were as follows (Combined weights):

Table XII: Kidney Weights

MALES (weight in g)	FEMALES (weight in g)
235	235
300	160
285	250
315	450
TOTAL 1135	1295
Mean: 283.75	259
Normal 230-440	240-350
Mean 313	288

The weights of the kidneys were within normal limits. Grossly seven of them were normal. One showed cortical scarring (case 25) and was small and another (case 24) had a pale variagated appearance with subcapsular petechial haemorrhages. On histology they all showed variable degrees of focal segmental proliferative glomerulonephritis. In

addition one case showed interstitial inflammation characterised by lymphocytes and plasma cells with tubular hyaline casts (case 21) while another had acute tubulitis with atrophy, giant cell formation, microabscesses, necrotising papilitis, interstitial edema and fibrosis (case 24). Coagulative necrosis attended by giant cells and lymphocytes was also noted (case 29). There were no hypertensive changes.

Bladder

Grossly, punctate cystitis was noted in all of the cases which on histology proved to be non-specific focal cytitis.

Endocrine Glands

The adrenal glands uniformly appeared normal grossly but on histology showed lipid depletion and one case of focal lymphocytic adrenalitis attended by giant cells (29).

Thyroid glands had follicles containing eosinophilic colloid and lined by low cuboidal epithelium.

Musculoskeletal System (Photomicrograph 4)

Skeletal muscle from the deltoid, anterior abdominal wall and in the GIT showed focal destructive muscle atrophy and

lysis with replacement by hyaline material attended by lymphocytic infiltration.

Skin (Photomicrographs 1, 2)

Four of these postmortem study cases had extensive perineal ulceration (cases 23, 25, 26, 28). On histology the ulcers had hyalinised bases and exhibited poor inflammatory reaction. Two cases showed the presence of Kaposi's sarcoma with thickened vessel walls showing myxoid degeneration (cases 26, 28). The other three were normal.

Female Reproductive Organs (Photomicrograph 24)

Half of the postmortem study patients were females. The ovaries showed a paucity of primordial follicles and one case showed a granulomatous perioophritis attended by Langhan's type of giant cells, lymphocytes and plasma cells (case 29). The myometria and endometria were atrophic with scarce atrophic glands. One case showed a necrotising endometritis (case 29).

Male Reproductive Organs

While four of the prostate glands examined were normal, one showed benign prostatic hyperplasia (case 27). This case presented with what appeared grossly as penile warts but on

histology was found to be an infiltrationg squamous cell carcinoma.

Testes (Photomicrograph 10)

All the testes examined showed maturation failure with paucity of Leydig cells and tubular cellular dissociation. One of them showed interstitial fibrosis and hyalinisation of the tubules (case 28).

Central Nervous System (Photomicrograph 9)

The weights of the brains were as follows:

Table XIII: Brain Weights

	MALES (weight in g)	FEMALES
	1100	980
	1250	925
	1435	1325
	1320	1030
	1250	1190
TOTAL	6355	5450
MEAN	1271	1090
NORMAL	1100-1700 g,	1050-1550 g,
AVERAGE	1400 g	1275 g.

All the brains from the male cases were within the normal range. However, three of the female cases had brain weights below the expected range.

Nine of the brains examined were normal grossly. One appeared congested with thickened basal leptomeninges (case 30). Two cases showed histological abnormalities. This was an intense lymphocytic and plasma cell infiltration with foci of coagulative necrosis attended by large histiocytes in one case (case 29). Parenchymatous oedema with focal thickening of the meninges infiltrated by sparsely scattered lymphocytes was seen in yet another case (case 30). The rest were normal histologically.

	Clinical Diagnosis	Postmortem Diagnosis	Cause of Death	Major Histopathological Findings
21	HIV Infection	Chronic HIV infection A1. Chronic Diarrhoea with dehydration A2. Membraneous focal colitis and ileitis A3. Fungal glossitis and punctate oesophagitis B1. Haemorrhagic Bronchopneumonia B2. Haemorrhagic tracheitis C. Cachexia D. Punctate cystis	1. Haemorrhagic bilateral bronchopneumonia 2. Dehydration	Necrotising Bronchopeumonia AAFBs positive on ZN stain
22.	HIV Infection	Chronic HIV Infection A1. Chronic diarrhoea A2. Focal Colitis B. Bilateral broncho-pneumonia C. Cachexia D. Punctate cystis	1. Bilateral bronchopneumonia 2. Dehydration	a. Non-specific areactive bronchopneumonia b. Visceral Kaposi's sarcoma

TABLE XIV (continued)

23.	AIDS	Chronic HIV Infection A1. Chronic diarrhoea with dehydration. A2. Haemorrhagic oesophagitis, gastritis and enterocolitis A3. Fungal glossitis B1. Bilateral bronchopneumonia B2. Haemorrhagic tracheitis C. Cachexia D. Punctate cystis	1. Bilateral bronchopneumonia 2. Dehydration	a. Non-specific areative bronchopneumonia b. Visceral Kaposi's sarcoma
24.	AIDS	Chronic HIV infection A1. Chronic diarrhoea with dehydration A2. Membraneous colitis with ulceration A3. Fungal glossitis B. Bilateral bronchopneumonia C. Pyelonephritis D. Punctate cystis	1. Bilateral bronchopneumonia 2. Pyelonephritis 3. Dehydration	a. Non-specific areactive bronchopneumonia b. Pyelonephritis c. Visceral Kaposi's sarcoma

25.	AIDS Infection	Chronic HIV Infection A. Bilateral bronchopneumonia B. Focal enterocolitis C. Haemorrhagic cystitis D. Punctate cystis	1. Bilateral bronchopneumonia	a. Non-specific areactive bronchopneumonia b. Visceral Kaposi's sarcom c. Cutaneous Kaposi's sarcom
26.	HIV Infection Adult malnutrition Genital Ulceration	Chronic HIV Infection A1. Bilateral bronchopneumonia A2. Subpleural Lung abscess B. Hepatomegaly C1. Extensive perineal ulceration C2. Right lateral maleolar ulceration C3. Generalised exfoliative dermatitis D. Cachexia	1. Bilateral Dehydration bronchopneumonia	a. Non-specific bronchopneumonia b. Menigitis c. Parenchymatous brain edema
27.	Labour Pneumonia Tuberculosis Gastroenteritis	Chronic HIV Infection A. Disseminated Tuberculosis B. Penile Warts	1. Disseminated tuberculosis	a. Interstitial pneumonitis b. Roaring confluent bronchopneumonia c. Penile infiltrating squamous carcinoma

			tuberculosis	attended by multiple giant cells b. Lung abscess c. Visceral Kaposi's sarcoma
	HIV Infection	A. Disseminated tuberculosis		
29.	Meningitis	Chronic HIV Infection A. Miliary tuberculosis B. Meningitis C. Bilateral Ovarian abscesses D. Colitis	1. Meningitis 2. Pulmonary milliary tuberculosis	a. Necrotising meningitis b. Necrotising bronchopneumonia c. Disseminated chronic necrotising granulomatous inflammation
30.	HIV Lymphoma Tuberculosis	Chronic HIV Infection A. Disseminated Tuberculosis B. Lymphadenopathy C. Dehydration D. Cachexia	1. Disseminated tuberculosis	Necrotising bronchopneumonia

Thirty percent (30%) of cases had a clinical diagnosis of TB. All the patients had pulmonary pathology; 40% necrotising bronchopneumonia, 10% interstitial pneumonitis, and 50% a non-specific areactive bronchopneumonia. In addition pulmonary Kaposi's sarcoma in one case. Visceral Kaposi's sarcoma occurred in 50% of the cases; only one of which had cutaneous manifestation.

Table XV: Antemortem Histological Results

Specimens	No.	Results	No.
A. Lympnodes	10	a. Granulomatous lyphadenitis with coagulative necrosis	4
		b. Follicular hyperplasia	2
		c. Kaposi's sarcoma	4
B. Skin	12	a. Kaposi's sarcoma slit forming type (83)	12
C. Omentum	1	Chronic granulomatous inflammatory lesion	1
D. Conjunctiva	1.	Kaposi's sarcoma slit forming type	1

Of the sections that showed granulomatous inflammation one was positive for AAFBs while the rest were negative. However, all of them had an antemortem diagnosis of tuberculosis.

DISCUSSION

This study was based and undertaken on the hypothesis that in Kenya, like reports emanating from other parts of the world, the clinical features and progression of the syndrome present a spectrum of symptom and sign complexes with associated epiphenomena including opportunistic infections, specific histological changes and the development of certain malignancies. Hitherto little work had been done in Kenya on the clinicopathological aspects of the syndrome. The clinical states of the patients and specimen obtained both premortem and postmortem were analysed to test the validity of the hypotheses and to lay down basic working data with a view to determining prospects for improved management of AIDS patients, and future research.

Weight loss, skin lesions, neurological symptoms, abdominal pain, diarrhoea and fever were the major symptoms that the patients presented with. The major signs elicited were those pertaining to skin lesions, wasting, dehydration, lymphadenopathy, fevers, abdominal tenderness and respiratory abnormalities. Amayo (93) found weight loss, fever, lymphadenopathy, oral thrush, diarrhoea, dysphagia, respiratory symptoms and signs and neurological abnormalities contributed significantly to the morbidity in patients with AIDS at KNH. Unlike Amayo, skin lesion,

abdominal pain and tenderness featured prominently while oral thrush and neurological signs were not as common.

Skin lesions showed features of Kaposi's sarcoma (KS) slit forming type as described by Kungu and Gatei (83). This contrasts with what Heyer et al (82) described whereby HIV associated Kaposi's sarcoma presents an angiosarcomatous appearance. Kaposi's sarcoma is the presenting feature in 14% of patients with AIDS in the USA and 21% in the UK (97). Amayo found it to be 10% at KNH. In Uganda it was 10% (94), 27% in Rwanda (95) and 16% in Zaire (96). Forty three percent (43%) of the study patients had cutaneous manifestation of KS. Kaposi's sarcoma in AIDS may be disseminated without skin involvement in approximately 5% of cases (45). Amongst the postmortem cases 20% had cutaneous manifestations as well as visceral involvement, while 80% had visceral lesions without cutaneous involvement. Acquired Immunodeficiency Syndrome KS differs from the classical type occurring in non-immunocompromised host because it is seen in the younger age group and is often described as aggressive with involvement of lymph nodes and other viscera especially the GIT (97). The viscera involved in this study were the lungs, the trachea, oesophagus, stomach, and spleen. The patients were between 16 - 51 years of age with a mean of 32.1 years (SD 9.3), 38% of whom were in the 26 - 30 age bracket and 83% under 41 years of age. The male to female ratio was 2.6:1. This contrasts

with what was found by Kungu and Gatei (83) where most of the cases were in the fifth decade with a male to female 8.5:1 ratio, which compares with what has been described elsewhere (45, 97).

Unusual histological patterns of Kaposi's sarcoma in AIDS have been described including the angiosarcomatous types as well as blood vessel involvement. All the KS described were of the slit forming type.

The only other malignancy found was an infiltrating squamous cell carcinoma of the penis. This was in an uncircumsised adult male and was thus considered an incidental finding though squamous carcinoma of the anorectal region have been described as end stage phenomena in AIDS (97). No lymphomas were seen.

The focal muscle atrophy with hyaline replacement and lymphocytic infiltration in some cases and individual muscle fibre variation seen, depicts a destructive myopathy thought to be a direct consequence of HIV muscle infection. This muscle destruction was also noted in the myocardium, though there was no clinical indication of cardiac disease. This is in accordance with Niedt et al (45) who found that although cardiac disease in most cases was clinically silent, pathological changes were seen in as many as 55%. The commonest feature was a lymphocytic myocarditis

sometimes associated with toxoplasmosis. Welch et al (85) described focal interstitial fibrosis and acute myocardial necrosis which were not clearly defined.

Salmonella typhinurium was cultured in stool specimen from 6.7% of the patients and Entamoeba histolytica in yet another 6.7% who presented with diarrhoea. Salmonella typhinurium, Entamoeba histolytica, Giardia lamblia, Isospora belli, Strongyloides stercoralis, Shigella flexueri, Yersinia enterocolitica and mycobacteria species have been isolated from the GIT of many patients with AIDS (85, 89). They have not been proven to be the cause for the diarrhoea in AIDS patients (89). The bowel of the postmortem cases showed varied degrees of mucosal cellular dissociation. The cellular changes thought to be due to postmortem antolysis were histologically determined in only a few cases. The mucosal absorptive capacity may be reduced resulting from this dissociation or from inteference with the intercellular matrix and cell cytoplasmic membranes resulting in the diarrhoea. Two of the cases showed spindle cells streaming through the mucosa and a diagnosis of early Kaposi's sarcoma was entertained. The GIT is the most common site of visceral KS involvement and the small intestine the commonest site of intestinal involvement. Gastrointestinal KS is usually multifocal and asymptomatic but may be associated with haemorrhages, diarrhoea, obstruction, perforation and rarely with protein losing

enteropathy. The patients under study presented with diarrhoea, but their serum total protein and albumin levels were within normal limits.

Epithelial dissociation was most marked in the liver in the form of lakelets without attendant inflammation or features of apoptosis. Fatty change and granulomata as was seen has been associated with malnutrition, infections and with end stage AIDS phenomena (79, 80, 97). Sinusoidal dilatation with adjacent atrophy of liver cells, fatty change, widening of portal areas with fibrosis, chronic inflammatory cellular infiltrate and bile duct proliferation were also described by Welch et al (83). In addition Welch noted the presence of Kaposi's sarcoma.

Testicular atrophy as described also by Niedt et al (45), Welch et al (83) and Lucas (98) has been seen even in patients of less than two months duration indicating that the atrophy is not related to chronic disease and will always be present regardless of the duration of the symptoms (45, 85). Some workers have suggested that sperm may be immunogenic and that anti-sperm antibodies may be related to AIDS by cross reacting and acting as anti-T-cell antibodies (100). This does not hold true for Africa where heterosexuality is thought to be the main mode of transmission in adults (93, 95, 96, 98) and another

etiology, possibly HIV infection itself, should be investigated.

The paucity of ovarian primordial follicles requires further investigation.

Despite the prevalence of neurological symptoms in the study, it was only in 20% of postmortem cases that histological changes were noted. Progressive multiple leukoencephalopathy commonly described in AIDS patients, primary cerebral lymphoma and cryptococcal meningitis (45, 47, 48, 49) were not seen. The majority of the symptoms may thus be as a result of the neurotropism and subsequent CNS infection by the virus. However, considering the small number of brains examined a cohort study of HIV patients with neurological symptoms is recommended in order to delienate the types of CNS abnormalities in AIDS patients at KNH. Weakness and inability to walk is thought to be as a result of combined muscular and neural pathologies. The presence of prominent ganglia with degenerate ganglion cells seen in the oesophagus may be an indication of dissolution of neurons akin to that seen in the hepatocytes, the seminiferous tubules and the GIT and may be ascribed to neurogenic muscle atrophy. In addition to the factors afore-mentioned, this too may contribute to the etiology of the diarrhoea as seen and described in patients with diabetes mellitus. In view of the muscle abnormalities

seen, abdominal pain and tenderness were attributed to intestinal causes rather than to the anterior abdominal wall. This requires further investigation.

AIDS patients have a high incidence of serious bacterial infections. Fifty three point three percent (53.3%) of the patients presented with a fever. Ten percent (10%) had infected skin wounds and 30% had tuberculosis. Of the autopsy cases there was pulmonary pathology in all correlating with the preponderance of respiratory symptoms as has also been noted by other investigators (45, 85, 87, 93). Forty percent (40%) had a diagnosis of tuberculosis 10% of which were undiagnosed antemortem. The pulmonary lesions histologically were non-reactive with much necrosis as seen by other workers (91, 85, 89).

Three hundred and sixty seven out of 68,598 admissions at KNH in 1987 were diagnosed to have tuberculosis representing 0.53%; 445 out of 70,111 in 1988 which is 0.6% and 534 out 76,334 in 1989 which is 0.69%. This shows a rising trend though the `p' value was not significant. In an unpublished study at the Infectious Diseases Hospital which is part of KNH, 50% of patients admitted with TB between February and April 1990 were found to be HIV positive. HIV seroprevalence among TB patients in several African countries are consistently higher than those in the general population (91). With reference to the study under discussion, the proportion of AIDS patients with TB may be

much higher and this requires further investigation due to the public health implications especially as regards their infectivity and response to therapy. In other centres, antituberculous therapy is empirically given to AIDS patients (91).

Pneumocystis carinii, Cytomegalovirus, Histoplasma spp. and Cryptococcus neoformans were not identified. Other investigators from other parts of Africa (43, 98, 96, 97) also found few cases or none of Pneumocystis carinii infections. This is in contrast with literature from the western part of the world (45, 85, 87, 89, 90, 92).

Mucous concretions found in salivary and tracheal glands and in pancreatic ducts have not been described in literature reviewed. This abnormality may be as a result of dehydration.

The BUN was significantly raised and all the renal sections examined showed features of focal segmental proliferative glomerulonephritis. An HIV related nephropathy (focal segmental glomerulosclerosis) has been suggested (68, 73) but this has largely been associated with heroin abuse (82, 64, 85). Amayo (93) did not find intravenous drug abuse a risk factor in AIDS patients at KNH. There was no clinical indication of renal disease in any of the cases. On the basis of the renal findings it is recommended that renal

disease be investigated for in all patients diagnosed to have HIV infection and managed accordingly.

A wide variety of descriptions for lymphoreticular organs have been documented from patients with AIDS. Depletion of lymphoid elements, hyalinisation, follicular changes ranging from lysis to involution and sinus histiocytosis were seen. These have also been documented by other investigators (92, 45, 85) and are seen in late and end stage disease (92). Forty percent (40%) of the lymph nodes had Kaposi's sarcoma, 10% had tuberculosis, 30% had features in keeping with tuberculosis and 20% showed reactive follicular hyperplasia. Tuberculosis, Kaposi's sarcoma and lymphoma often underly the lymphadenopathy of AIDS patients (92). Lymphoma was not described.

In the adrenal gland variation occurs in the distribution of lipids in various conditions being poor or in fact deficient in infections. The adrenal cortex reacts to stress in both adults and children by lipid depletion. Diffuse lipid depletion as was seen in the postmortem cases occurs in older children but relatively uncommon in adults occurring in less than 5% of adult adrenals examined postmortem (99). Ten percent (10%) of the postmortem cases showed a cortical granulomatous adrenalitis which is thought to be rare. Infections of the adrenal gland in AIDS patients have commonly been found to be due to cytomegalovirus. F.

Bricaire et al (69) also noted cryptococcal, toxoplasmal and tuberculous lesions concluding that the adrenal gland is particularly affected in the evolution of AIDS, which may be clinically silent. None of the patients presented with symptoms or signs of hypoadrenalism and none of the above lesions were seen.

Though a low cuboidal epithelium was found in all the thyroid specimen, none of the patients presented with signs or symptoms that could have been attributed to hypothyroidism.

CONCLUSIONS

1. The major clinical symptoms and signs in the study patients are comparable to those seen in other parts of the world though with variable frequencies.

2.1. The study patients had histological features comparable with those described in other parts of the world though histological features such as the hepatolytic changes, paucity of primordial follicles and dissolution of ganglia had not been described in literature reviewed.

2.2 There is an absence of biochemical, haematological and bacteriological indicators of AIDS in the study patients.

3.1 Tuberculosis and Kaposi's sarcoma are the major histological findings. This is comparable with other in studies Africa.

3.2 The Kaposi's sarcoma is slit forming type.

4. Focal segmental proliferative glomerulonephritis is common in AIDS patients.

5. The wasting in AIDS patients may be significantly contributed to by muscle atrophy

6. Myocardiolysis is a histological entity amongst AIDS patients.

7. AIDS associated diarrhoea is predominantly non-infective and is most likely due to interference with the absorptive capacity of the intestinal mucosa.

8. Testicular atrophy is universal in patients with AIDS.

9. Pathogens such as Pneumocystis carinii, fungi and viruses are not responsible for the morbidity seen.

RECOMMENDATIONS

1. Because of the important clinical, educational and public health implications, the local frequency of significant infections such as tuberculosis and malignancies such as Kaposi's sarcoma requires establishment in order to evolve a more efficient means of managing AIDS patients.

2. The common feature of segmental proliferative glomerulonephritis calls for routine assessment of renal function in patients with AIDS in order to avoid the development of chronic renal failure.

3. In view of the symptoms and signs and histological features seen in the GIT and the trachea, endoscopy together with proctoscopy and bronchoscopy respectively should be performed as part of the patient management provided necessary precautions are observed.

4. The relationship and interactions of common infectious diseases such as tuberculosis and HIV need to be studied.

5. Endocrine functions in AIDS patients require investigation.

6. Patients with neurological symptoms and signs should have more detailed examinations including CT scan, nerve conduction studies and EEG as part of their management.

6.1 The brains of patients dying from AIDS require further investigation in order to delineate the types of CNS abnormalities.

7. The hepatolytic features in the liver of patients with AIDS requires further investigations as this may prove to be pathognomonic of AIDS.

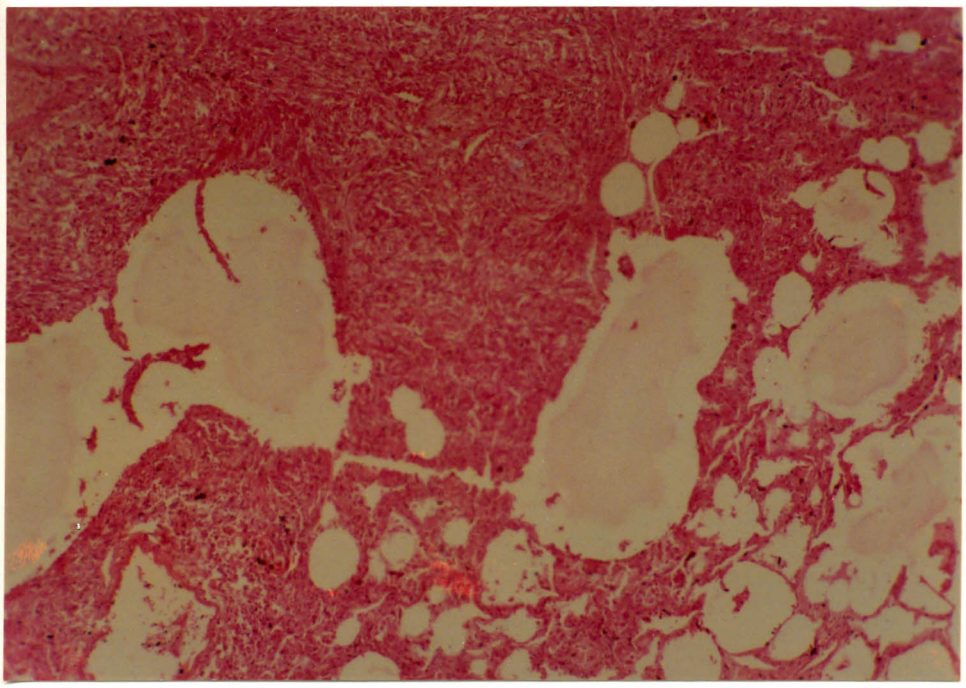
8. Electron microscopy studies for the various tissues especially those related to symptom and sign complexes should be undertaken.

9. Due to the presence of GIT muscle lysis and myometrial atrophy, GIT motility and menstrual patterns in AIDS patients requires further investigation.

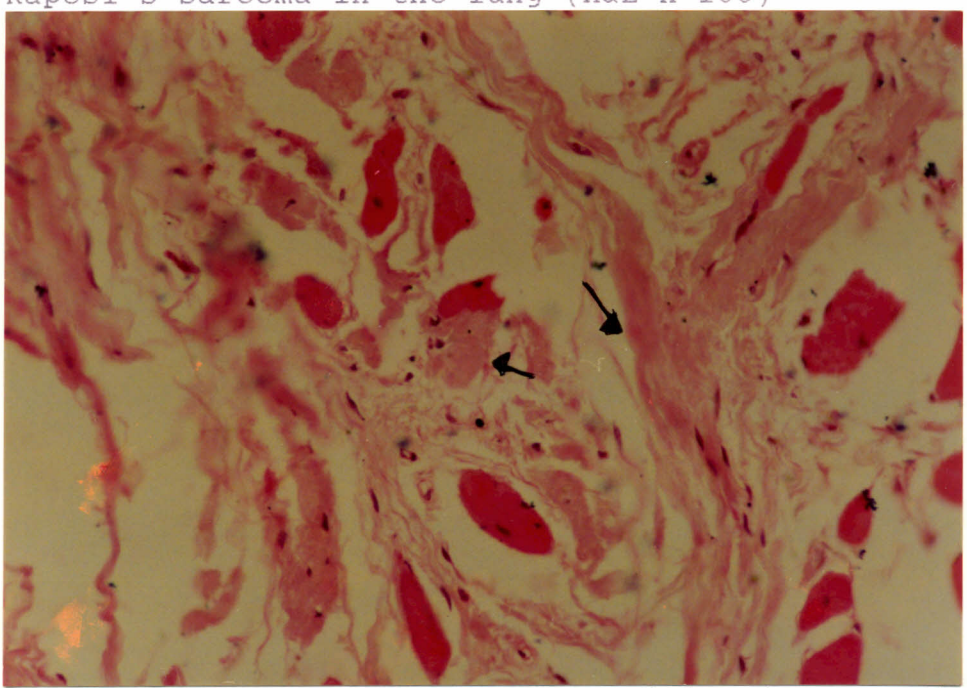
CONSTRAINTS

The major constraints were as follows:

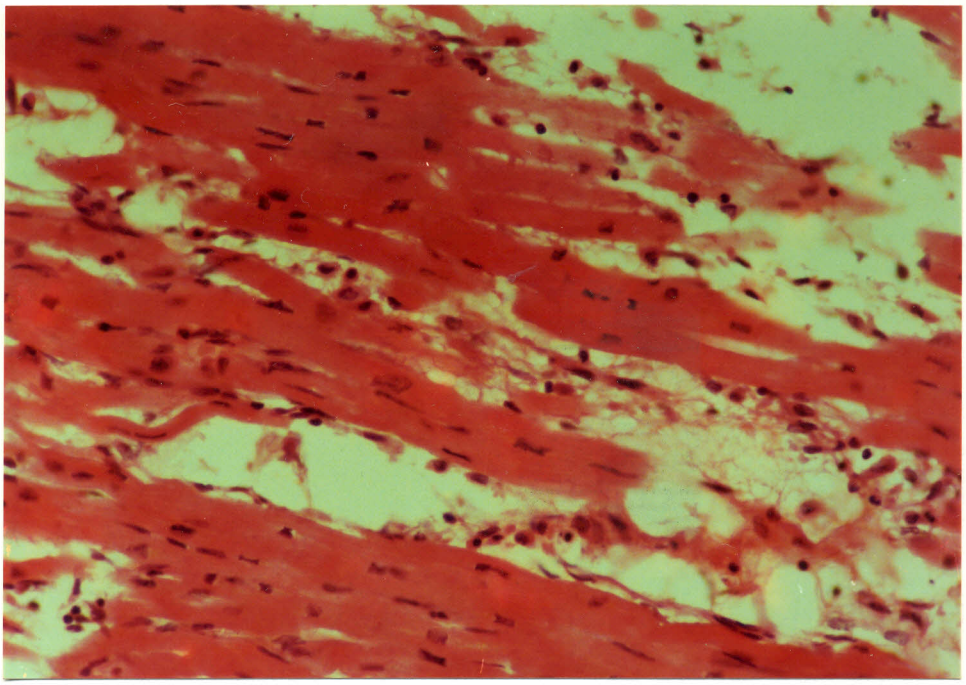
1. On average autopsies were performed three to four days following death due to reluctance of person/persons with custody of the bodies consenting to postmortem examination. In addition, the interval between death and transfer from the ward to the morgue varied from case to case as did daily ambient temperatures, and the storage compartments were not all at the same temperature this being complicated by the opening of the compartments during removal or rearrangement of corpses. All these factors were attended by variable degrees of autolysis which was taken into account during histological assessment necessitating the omission of some specimen from the analysis.
2. The autopsies required alot of time and care in an effort to avoid incidental and accidental infection.
3. The postmortem rate of 2% at KNH as a teaching hospital is abysmally low.
4. There is a fear of performing invasive diagnostic procedures in patients with AIDS.
5. Due to technical and financial constraints it was not possible to determine T4 T8 ratios.



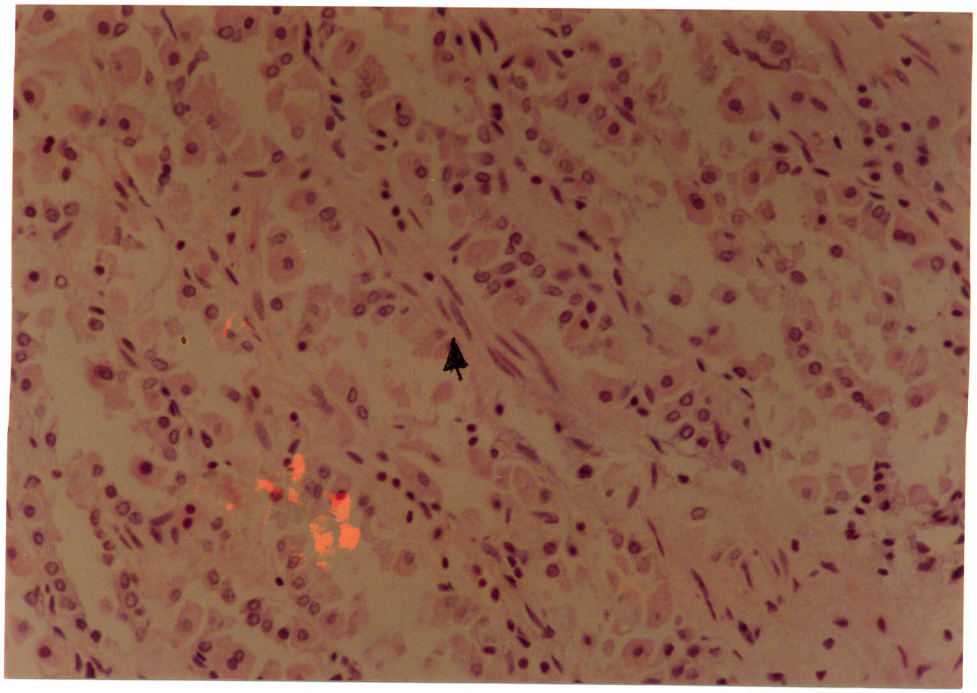
3. Kaposi's sarcoma in the lung (H&E x 100)



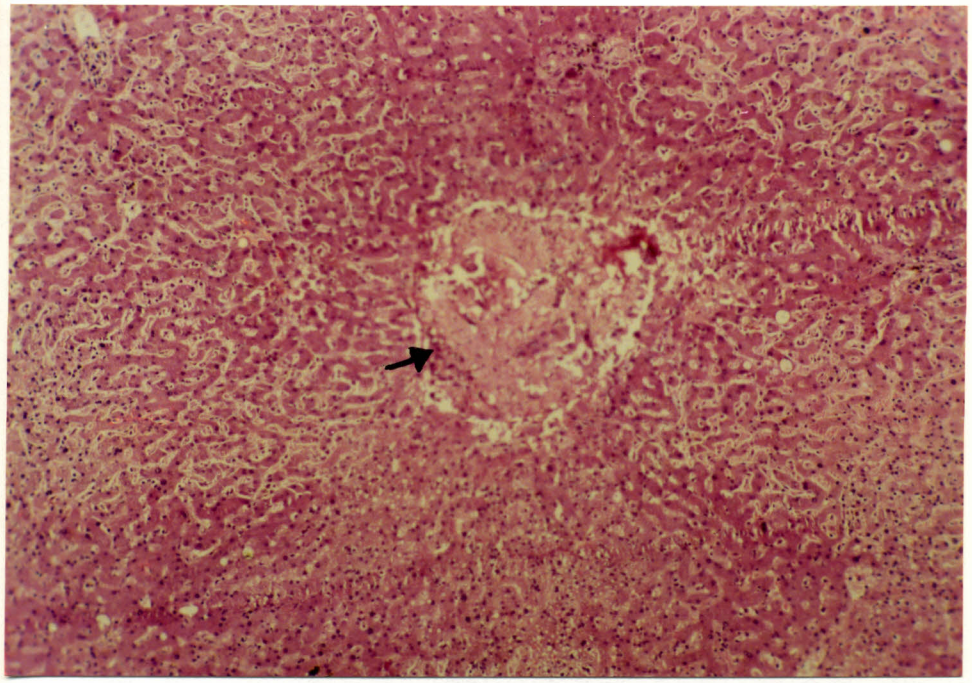
4. Skeletal muscle atrophy with hyalinisation and fibrosis (H&E x 400)



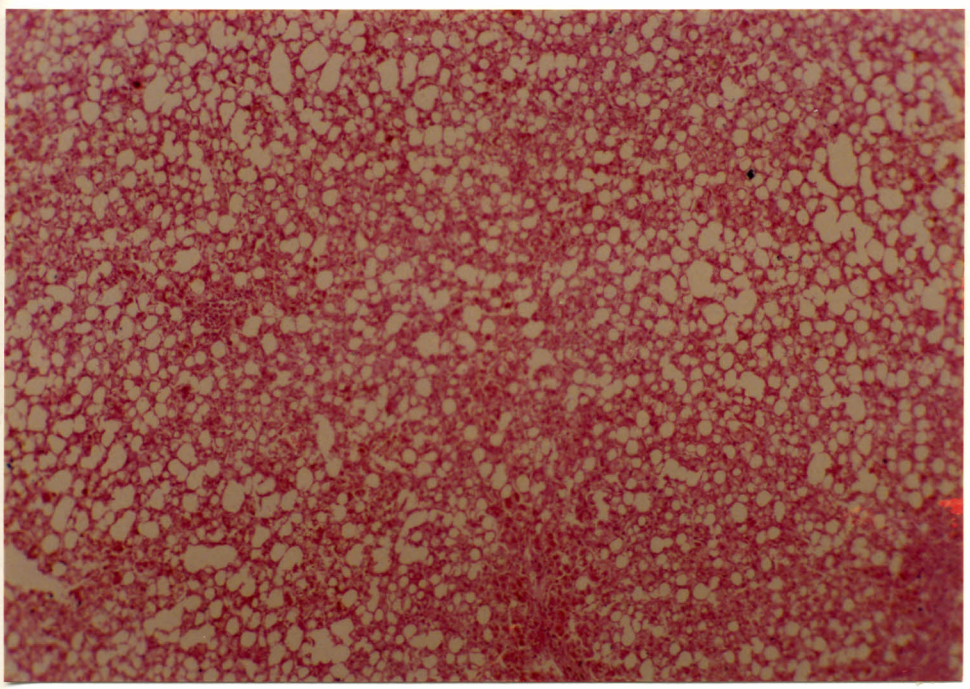
5. Myocardiolysis (H&E x 400)



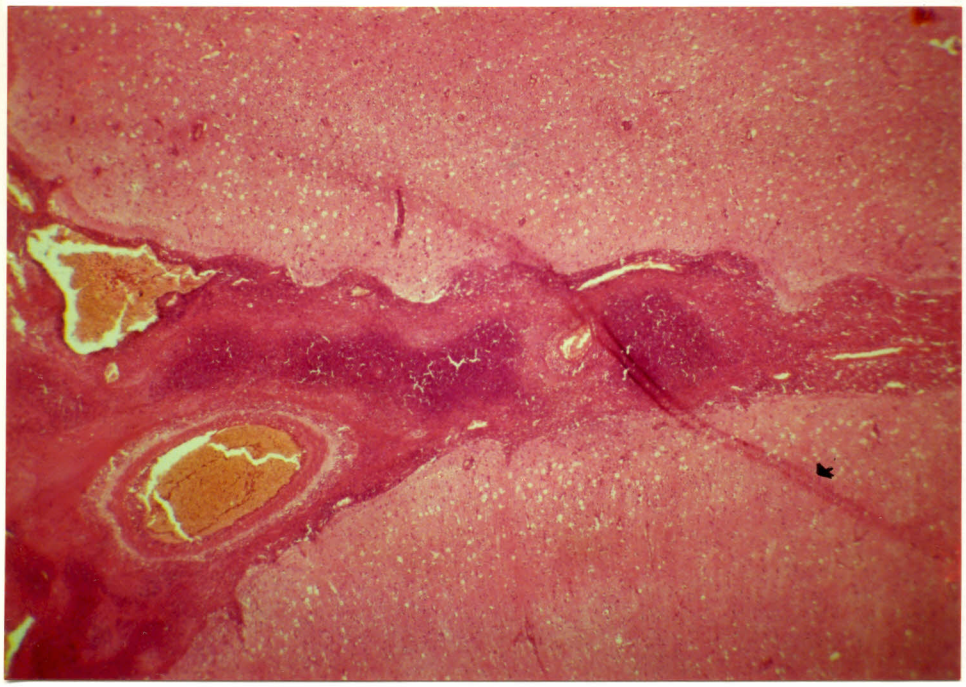
• Linear streaming of spindle cells in gastric mucosa (H&E x 400)



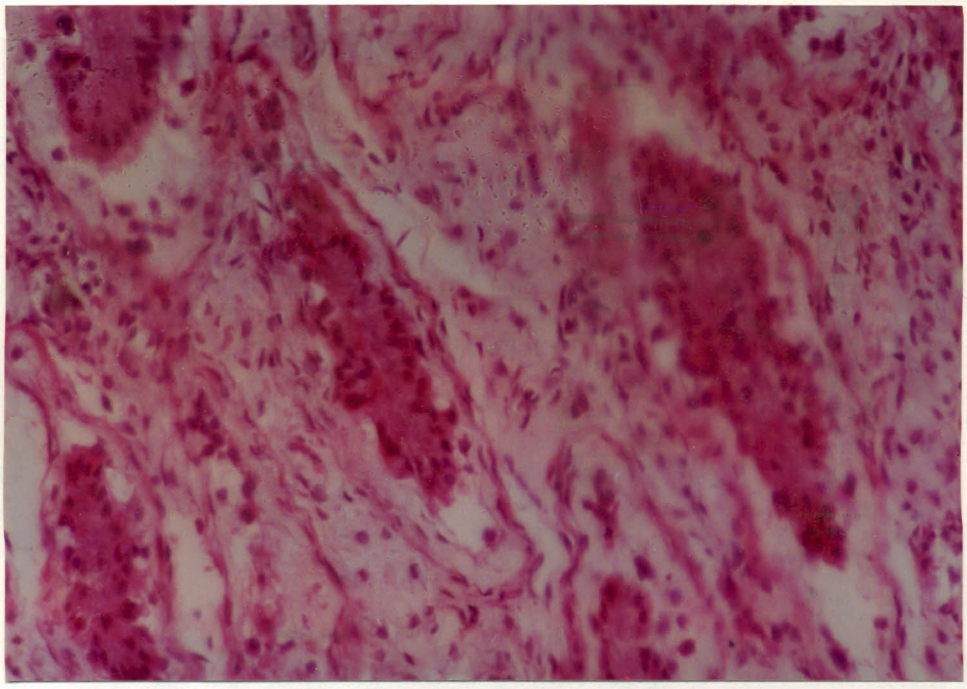
7. Hepatolysis with lakelisation (H&E x 100)



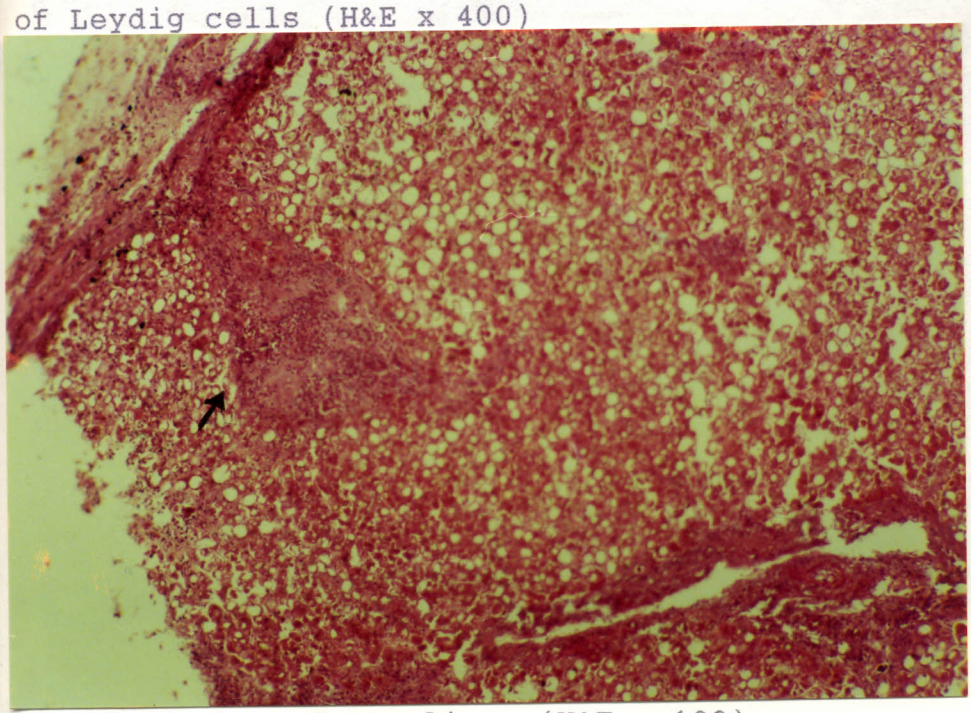
8. Fatty change in liver (H&E x 100)



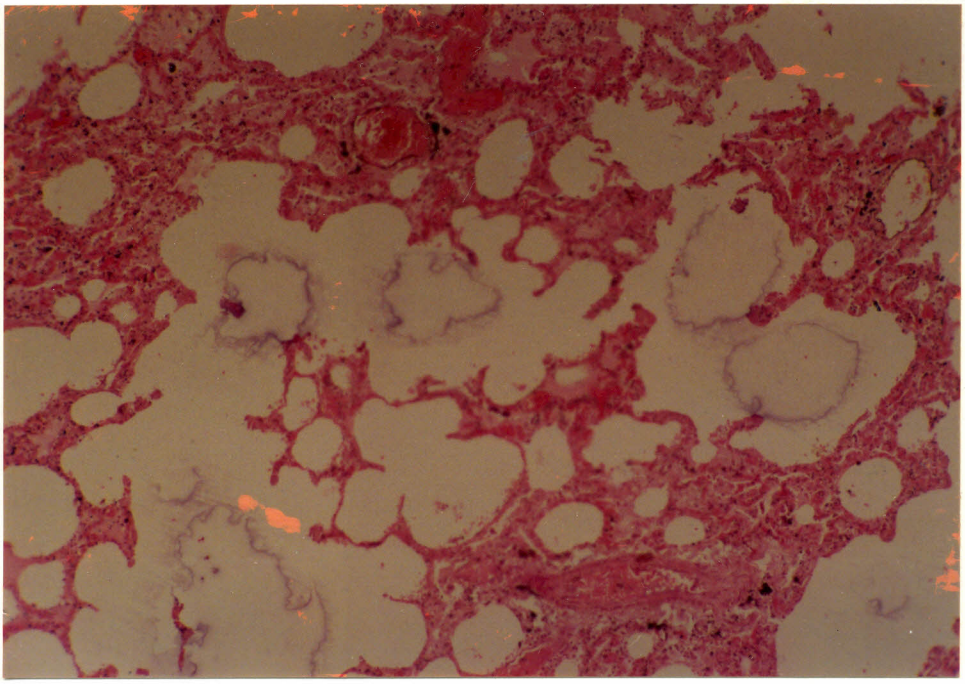
9. Necrotising leptomeningitis with parenchymatous edema (arrow artifact) (H&E x 100)



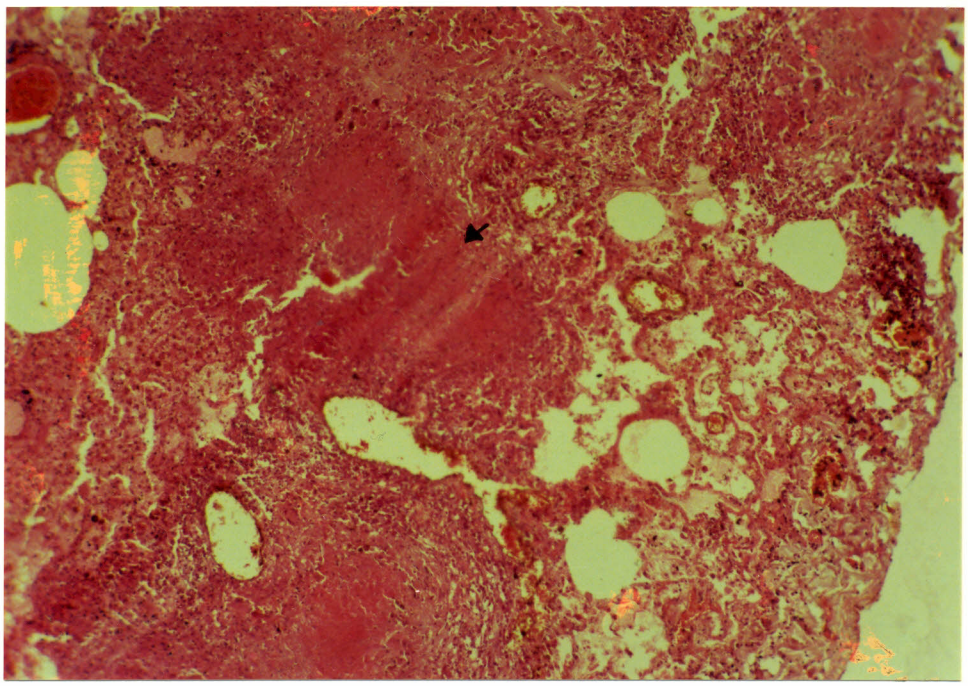
0. Testicular atrophy. Note interstitial fibrosis and paucity of Leydig cells (H&E x 400)



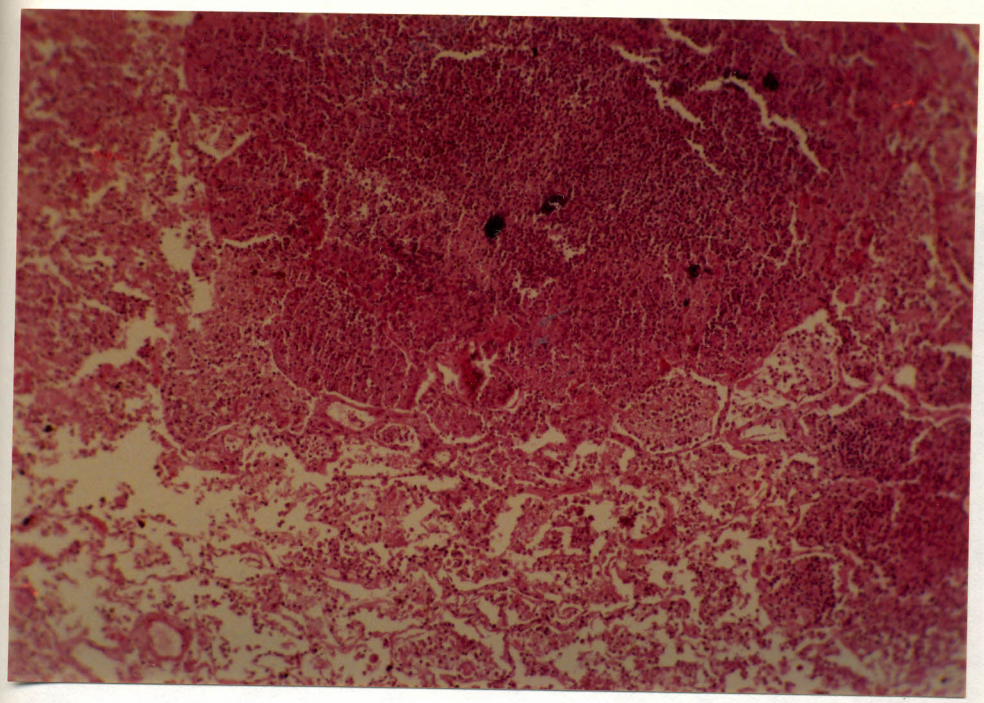
. Granuloma in a fatty liver (H&E x 100)



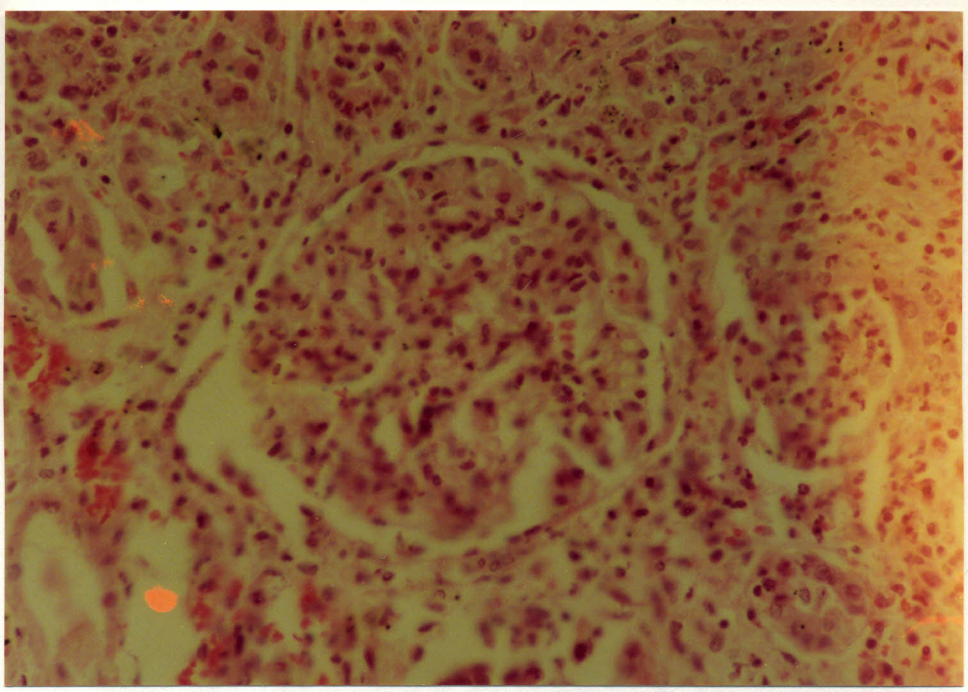
2. Interstitial pneumonitis (H&E x 100)



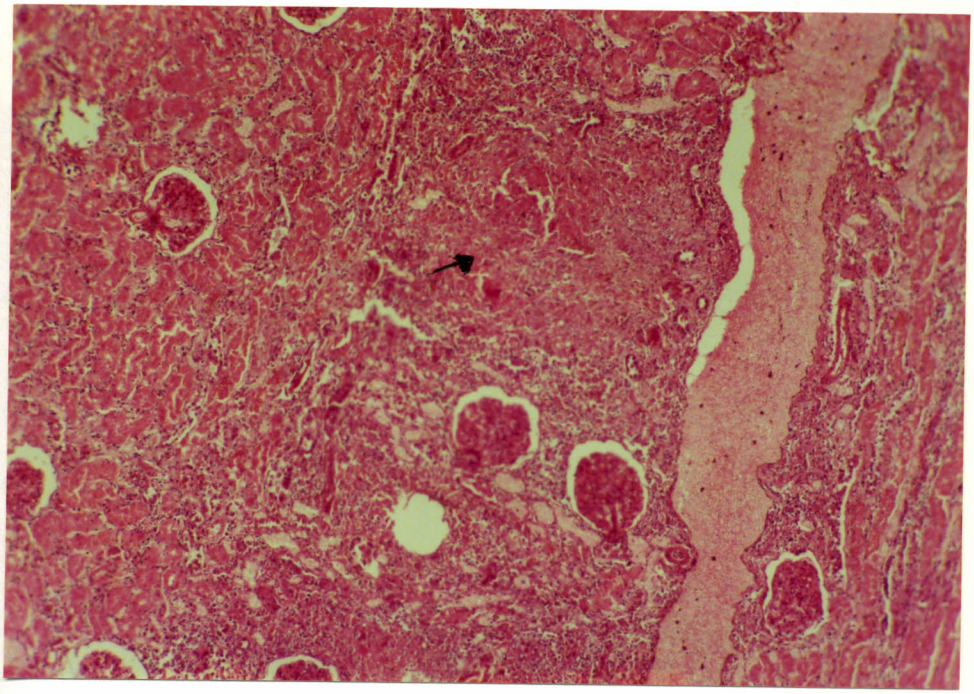
. Areactive necrotising bronchopneumonia (H&E x 100)



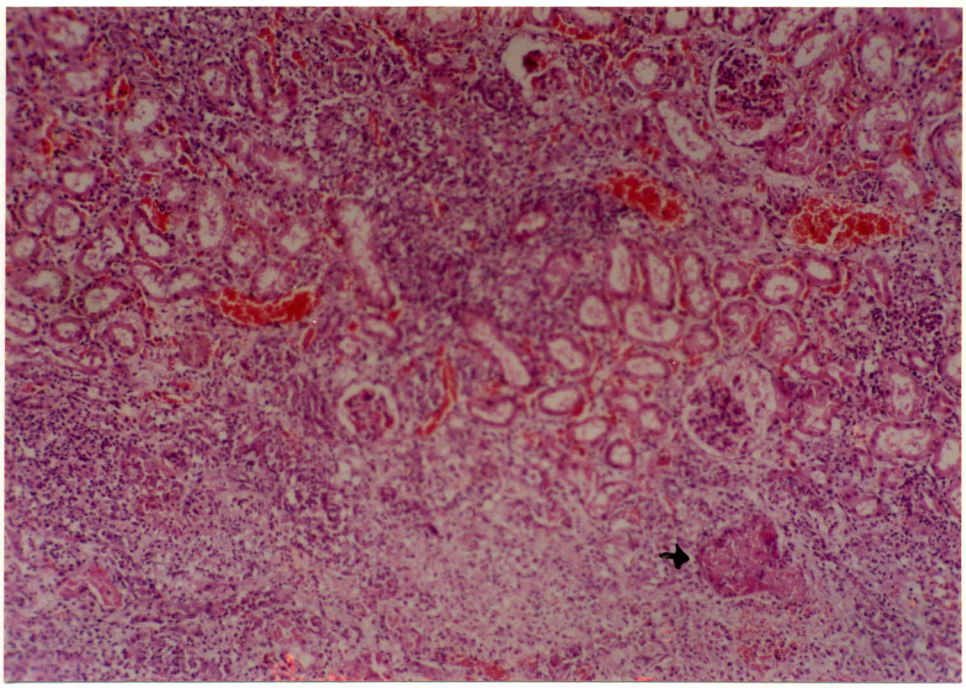
4. Lung abscess. Note paucity of inflammatory cell infiltrate in surrounding lung tissue (H&E x 100)



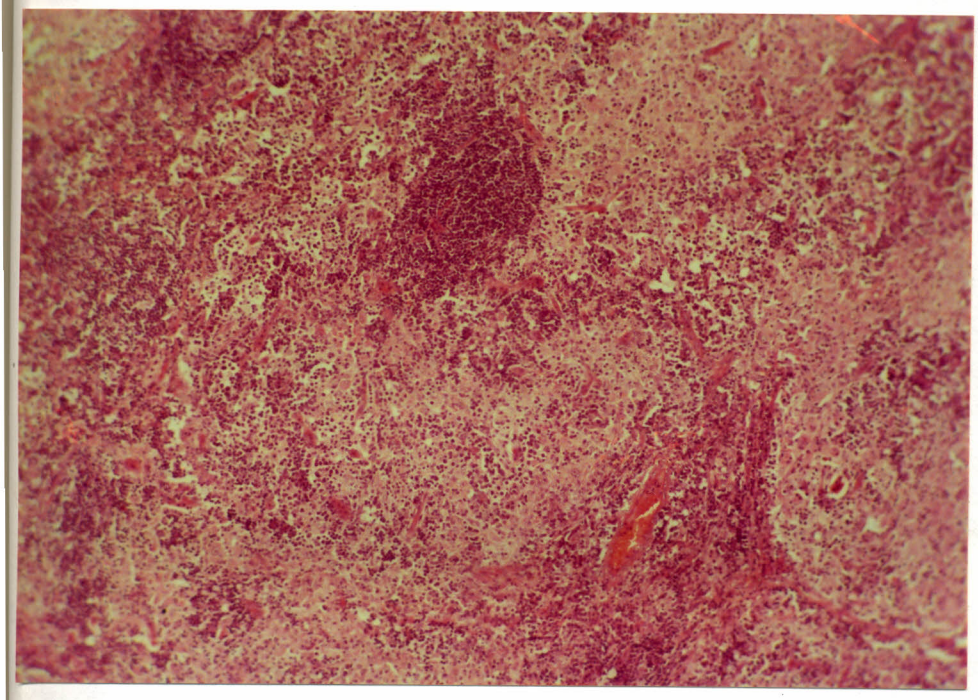
5. Focal segmental proliferative gromerulonephritis (H&E x 400)



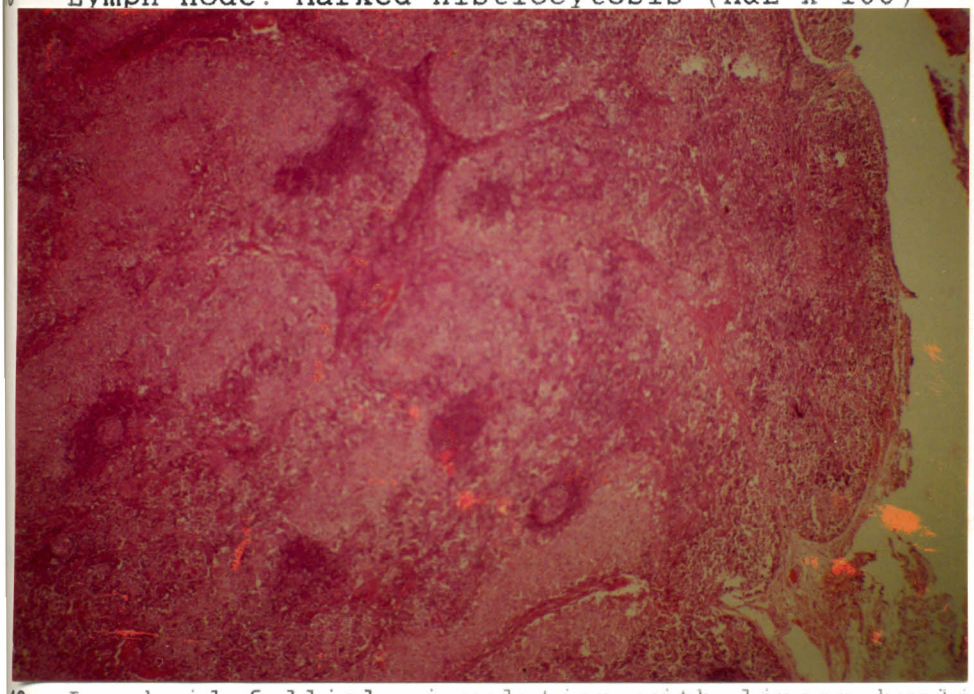
Coagulative necrosis of renal parenchyma (arrow) (H&E x 100)



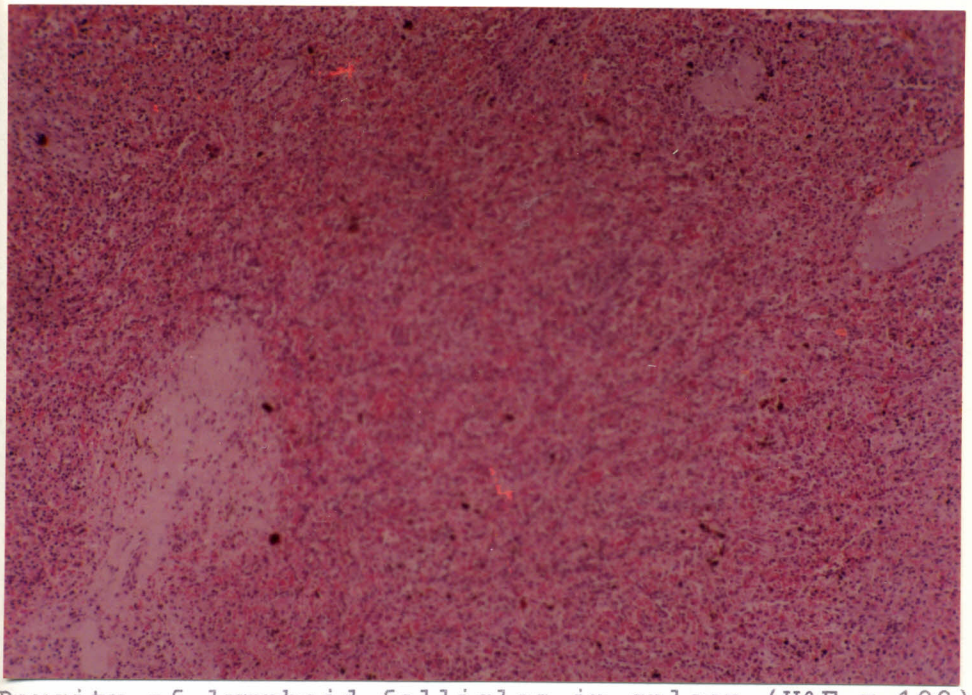
Interstitial nephritis & tubulitis (H&E x 100)



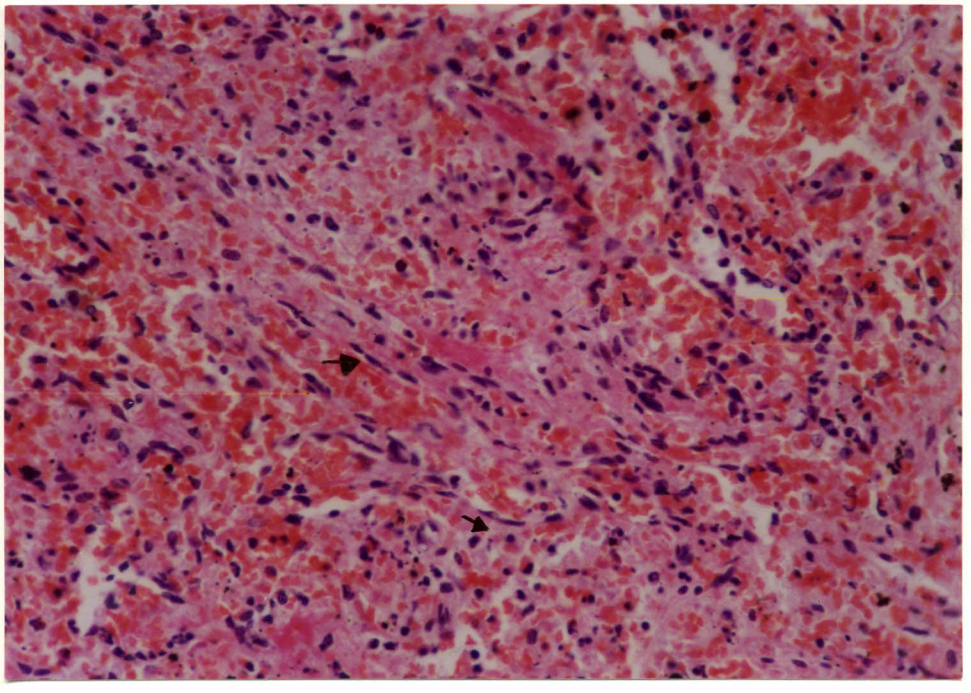
8 Lymph node. Marked histiocytosis (H&E x 100)



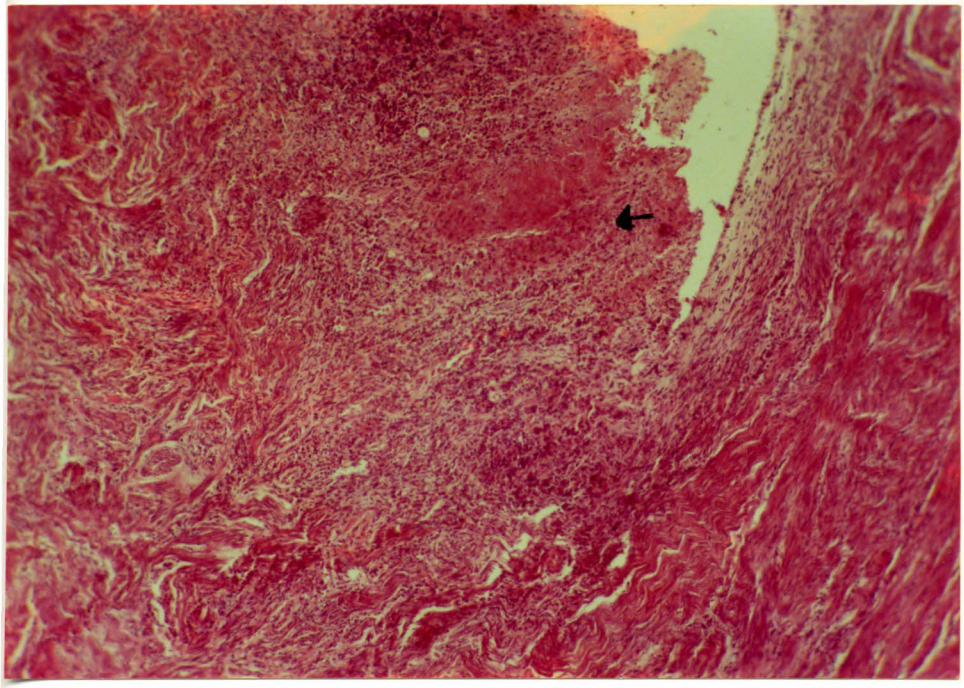
9 Lymphoid follicle involution with linear hyalinisation (H&E x 100)



Paucity of lymphoid follicles in spleen (H&E x 100).



Marked extravasation of red blood cells and linear streaming of spindle cells seen in spleen (H&E x 100)



Section of uterus showing muscle and necrotising endometritis (H&E x 100)

APPENDIX I

PROFORMA

1. Patient's Name.....2. Ward.....

3. Age..... 4. Sex.....

Symptomatology etc	Yes	No
1. Weight Loss		
2. Fever		
3. Night sweats		
4. Neck swelling		

I. Central Nervous System

1. Headache
2. Confusion/Drowsiness
3. Convulsion
4. Behaviorural changes
5. Paralysis
6. Disturbances in vision
7. Weakness
8. Inability to walk

II. Gastro-Intestinal System

1. Sores in the mouth
2. Dysphagia
3. Diarrhoea
4. Bleeding per rectum

APPENDIX II

LABORATORY DATA

I. Haematological

1. Haemoglobin g/dl
2. White Blood Cell Count x $10^9 l^{-1}$

   Differential count

   - Neutrophils %
   - Eosinophils %
   - Monocytes %
   - Basophils %
   - Lymphocytes %

3. Platelets
4. E.S.R.
5. Packed Cell Volume

II. Biochemical

1. Liver function tests

   - Total protein g/dl
   - Albumin "
   - Bilirum umol/l
   - Alkaline Phosphatase K.A. units

2 Renal Function Tests

BUN		mg/dl
Serum	Sodium	meq/l
	Potassium	"
	Creatinine	mg/dl
	Calcium	"
	Uric acid	"
	Chloride	meq/l

3. Others

Creatinine phosphokinase U/l

III. **Microbiology**

1. Stools	a. microscopy	
	b. culture	
2. Sputum	a. microscopy	
	b. ZN staining	
	c. culture	
3. Urine	a. microscopy	
	b. culture	
4. Urethral and vaginal swabs	a. microscopy	
	b. culture	
5. CSF	a. microscopy	
	b. culture	

IV. Immunology

1. T4/T8 ratio

V. Histological Findings

Coding

1. Nervous system

10 - meninges

11 - Brain

2. Alimentary System

20 - mouth and pharynx

21 - oesophagus

3. Respiratory System

30 - Lungs

31 - mediastinum

4. Genito-Urinary system

40 - kidney

41 - prostate

42 - testes

43 - ovary and blood ligament

44 - uretus

45 - vulva and vagina

5. Cardiovascular system

50 - heart

6. Haematopoieitic and Lymphoid tissues

   60 - lymph nodes

   61 - spleen

   62 - tonsils, adenoids, peyer's patches

   63 - bone marrow

7. Endocrine glands

   70 - pancreas

   71 - adrenal glands

8. Skin its appendages and subcutaneous tissues

   Disease conditions

   00 - Normal

1. Inflammatory condition

   10 - Pyogenic

   11 - Non- pyogenic

   12 - granulomatous

   13 - tuberculosis

   14 - parasitic

   15 - fungal

   16 - viral

   17 - leprosy

   18 - other

2. Neoplasms benign

3. Neoplasms malignant (Epithelial)

   30 - Adenocarcinoma

4. Malignant mesodermal tumours

   40 - Kaposi's sarcoma

   41 - Other

5. Tumours of the CNS
6. Degenerative conditions
7. Lymphomas
   - 70 - Hodgkin's disease
   - 71 - Lymphoid tumours
   - 72 - Reticulum cell sarcoma
   - 73 - Histiocytosis X
   - 74 - Myeloma
   - 75 - Burkitts
   - 76 - Obscure
   - 77 - Others
8. Proliferative conditions
   - 80 - regeneration
   - 81 - metaplasia and dysplasia
   - 82 - fibrosis
   - 83 - Other

APPENDIX III

CLINICAL CASE - DEFINITION OF AIDS

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

Major Signs

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

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

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720947

Kenyatta National Hospital
P.O. Box 19676
NAIROBI
KENYA

25/9/89

f:

Dr. C. Mwangi

Dept. of Human Pathology

Dear Dr. Mwangi,

REF: HISTOPATHOLOGY OF VARIOUS ORGANS IN PATIENTS WITH AIDS

This is in response to your letter dated 4th September, 1989. I am glad to inform you that on ethical grounds, you have been cleared to embark on the above study.

Yours sincerely,

DR. D.M. NJAI
Ag. Chairman
Ethical and Research Committee

cc: Director, KNH

Deputy Director, KNH