CHAPTER 16

Cancers in the Tropics

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16.1 INTRODUCTION

Of an estimated total world population of 6.2 billion, some 2.5 billion people, or more than 40% are said to reside in the tropics. This broad geographic band, encompassing the entire circumference of the world between 23degrees, 30 minutes on either side of the equator is a vast terrain, with diverse climatic and topographic features. There is a wide diversity in demographic aspects with numerous ethnic groups expressing a profusion of social and cultural practices. It is clear then that "Cancer in the Tropics" cannot be condensed into a single chapter. Even an entire book solely devoted to the subject would barely scratch the surface of a study of malignant diseases tending to afflict almost half of the entire world population!. This short chapter will merely attempt to summarize some aspects of more commonly recognized neoplasms having a proclivity for occurrence in the tropics.

Many tropical countries are part of what was formerly termed the "third world", now more correctly referred to as "developing" nations, as apposed to "developed", or "first world" (mainly Western) nations. This dichotomy can result in a marked disparity in the distribution of the common cancers occurring in the two settings. The appellation "developing" nation usually carries the implication of poverty, often resulting from over population with exploitation of human resources, attended by overcrowding, inadequate housing, and poor standards of education resulting in unemployment, ignorance, poor hygiene and malnutrition. Medical facilities are frequently meagre. Cancer sufferers often present with very advanced disease, usually in an incurable stage. This contrasts with Western societies, where malignancy is frequently diagnosed in the early and often curable stage. The strategy of "screening" programs for detection of common cancers is widely employed in affluent, developed countries, resulting in early identification of cancer sufferers, and probable enhanced survival. Sadly, such facilities are rarely available in many tropical regions.

Many types of cancer in the tropics, and sub-tropics have a strong association with chronic infections. For instance schistosomiasis with squamous cell carcinoma of bladder, intestinal parasites with Mediterranean lymphoma and hepatitis B virus infection with liver cancer, to mention only a few. Genetic and environmental factors also play a significant role in tropical tumourigenesis.

16.2 INFLUENCE OF ACQUIRED IMMUNODEFICIENCY SYNDROME.

The relatively recent phenomenon of acquired immunodeficiency syndrome (AIDS), due to human immunodeficiency virus (HIV) has obviously had a profound influence on the incidence

and types of malignant diseases in tropical countries. For instance, the patterns of malignant lymphoma have been markedly affected by this “paradigm shift”.

HIV is a retrovirus of the lentivirus class, and occurs in two forms: HIV-1, which is the most widespread, and HIV-2, originally confined to West Africa, but now tending to global extension. HIV is spread by homo- or hetero- sexual intercourse, blood or blood products as in transfusion or intravenous drug abuse, or by vertical transmission from mother to infant through parturition or breast feeding. Transmission methods are similar for hepatitis C virus (HCV) and hepatitis B virus (HBV). The prime target cell of the HIV virus is helper T lymphocytes (CD 4 cells). Over time, lysis of helper cells results in reversal of the helper to suppressor (CD 8 cells) ratio which is normally above 1.5.Following infection, there is a prodromal period of about 6 weeks, during which the viral load is very high and may approach 10^7 RNA copies per ml. In the course of disease, CD 4 counts decline from normal being above 1000 lymphocytes per microlitre to less than 200 per microlitre, in the advanced stages[1]. The Centers for Disease Control (CDC) have defined the progression of HIV infection in terms of four categories, or stages[2]:

Group 1: Acute infection resembling infectious mononucleosis.
Group 2: Asymptomatic phase with positive serology. Cytopaenias may occur.
Group 3: Persistent generalized lymphadenopathy (PGL).
Group 4: Acquired immunodeficiency syndrome (AIDS).
Group 4 is further subdivided into two categories:
Group 4A: AIDS related complex (ARC): Constitutional symptoms with weight loss, fever, diarrhoea, malaise, and various neurological disorders.
Group 4 B: Full blown AIDS: Severe opportunistic infections and/or neoplasia.

The commonest tumours are Kaposi sarcoma, non- Hodgkin’s lymphoma, primary lymphoma of the central nervous system, Hodgkin’s disease and squamous cell carcinoma of the oral or anorectal mucosa. Adenosquamous lung carcinoma, and cervical intraepithelial carcinoma are also said to be more frequent in Group 4. Additionally, any common malignant disease presenting at an inappropriately young age, should arouse a suspicion of AIDS.

NOTE : RISK OF INFECTION WITH SERIOUS VIRAL DISEASE FOLLOWING OCCUPATIONAL EXPOSURE (NEEDLE STICK INJURY).
(Adapted from Olmsted RN. Am J Infect Control, 1996, 24, 411.)

HIV : 0.4 % risk of infection. Very low risk. (Least infective).
HCV : 4.0 % risk of infection. Low risk. (Medium).
HBV : 40 % risk of infection. High risk. (Most infective).

16.3 RETICULOENDOTHELIAL AND HAEMATOLOGICAL MALIGNANCY

Burkitt’s Lymphoma is the archetypal tropical cancer. Although lymphomatous growths of the jawbones in childhood had long been recognized in Central and East Africa, it was Denis Burkitt who literally put it on the map[3]. His seminal epidemiological contribution plotted an African “lymphoma belt” across tropical Africa. The disease is also endemic in Papua New Guinea. The

geographical and climatic distribution suggested an association with an infectious agent, especially, chronic malaria, which shares the same distribution. A cell line of the tumour was propagated, leading to the discovery by Epstein, Achong and Barr of a hitherto unknown herpes virus which bears two of their names: EBV, also now known to be the causative agent of infectious mononucleosis[4]. It has been suggested that chronic infection by malaria, and possibly other parasitic, or even bacterial or viral agents such as HIV, may lead to a hyperimmune state, with polyclonal B cell activation, setting the scene for malignant transformation. Central to the malignant potential of the tumour, is amplification of the oncogene c-myc, which is usually manifest as reciprocal translocation of chromosomes 8 and 14, i.e. t (8:14). There is usually a high tumour burden at presentation, with widespread organ infiltration, by B cell lymphoma of small, non-cleaved cell type. Jawbone involvement is characteristic of this endemic or "African" variety of the disease (Figure 1). It shares many similarities with non-endemic or "American" type Burkitt's lymphoma, which has a widespread distribution, being a common form of childhood lymphoma in Western countries, with a tendency to bulky abdominal disease centred on lymphoid tissue in the ileo-caecal area. A third form of Burkitt's lymphoma is that which complicates HIV infection, and mainly involves peripheral lymph nodes.

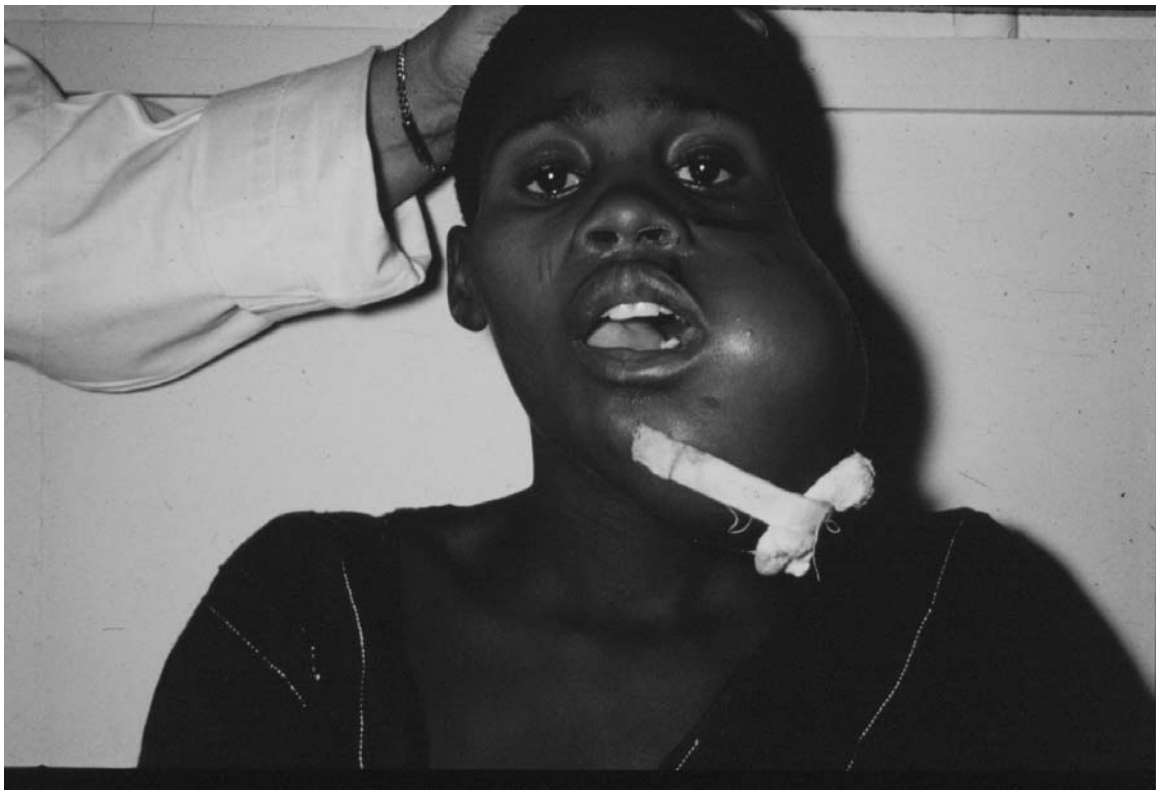

Figure 1. Burkitt's lymphoma (African type).

The virus replication by EBV appears to involve two phases: an initial productive cycle in oropharyngeal epithelium, followed by infection of B lymphocytes which become transformed or " immortalised " to undergo cellular proliferation. It was initially thought that only

oropharyngeal epithelium and B lymphocytes possessed the EBV receptor (CD 21). However, there is now evidence that other cells, including some T cell subsets may have appropriate epitopes.

The epidemiology of EBV is complex. Based on VCA-IgG titres, it appears that in Third World countries, there is almost universal infection of young children who exhibit a very high prevalence of IgG antibodies by four years of age. Infectious mononucleosis is very unusual in indigenous inhabitants of Africa. By contrast the prevalence of infection in young children is very rare in Western countries, where infectious mononucleosis is common in adolescents and young adults.

Two strains of EBV have been described. Type A with a world wide distribution, and Type B occurring mainly in tropical Africa, and Papua New Guinea; thus corresponding with the distribution of endemic Burkitt's lymphoma. The coexistence of the two strains has been recorded.

A rare fatal form of infectious mononucleosis (Duncan's disease) may occur as a fulminant lymphoproliferative disorder affecting male members of susceptible kindreds, as an X -linked condition.

Human herpes virus type 6 (HHV 6) has also been causally related to an identical syndrome to infectious mononucleosis thus raising the intriguing possibility that it too, may have malignant potential. HHV 6 has been established as the causal organism of roseola infantum (exanthem subitum).

Another EBV related tumour, with defined geographical distribution is the nasal form of angiocentric NK/T cell lymphoma occurring in South East Asia, especially southern China and parts of South America. Alaskan Inuit people are also susceptible. There is also an association of EBV, with other forms of lymphoma such as occurring in immunodeficiency states, such as HIV related, and post transplant large cell lymphoma, and Hodgkin's disease, which however do not exhibit any specific propensity for a tropical distribution. However, while nodular sclerosing Hodgkin's disease is the commonest form in Western countries, prognostically less favourable subtypes, such as mixed cellularity or lymphocyte depleted varieties predominate in many tropical areas, (as well as in AIDS sufferers). Primary effusion lymphoma, (body cavity based lymphoma), related to human herpes virus type 8 (HHV8 or Kaposi sarcoma herpes virus-KSHV) is confined to HIV positive patients, and may be associated with Kaposi sarcoma[5]. Castleman's disease of multifocal plasma cell type is also related to HHV8, and over represented in AIDS patients. Pyothorax associated large B cell lymphoma, a rare entity, is said to be a complication of secondarily infected pneumothoraces induced artificially in the treatment of tuberculosis. Presumably then, this has the same distribution as tuberculosis.

Non Hodgkin's lymphoma frequently complicates HIV infection. These are usually aggressive B cell lymphomas, and fall into three major categories, centroblastic and/or immunoblastic lymphoma (classified as diffuse large B cell by the World Health Organisation or WHO system), Burkitt's lymphoma, and primary central nervous system lymphoma. Lymphoid interstitial pneumonia (LIP) in childhood may be a manifestation of AIDS, but is rare in adult patients. HIV

related LIP, appears to be a benign polyclonal pulmonary lymphoid infiltrate in the spectrum of chronic interstitial pneumonia. However the terminology is confusing, as LIP in the setting unrelated to AIDS is regarded as a potential precursor to low grade lymphoma, now termed BALT (bronchus associated lymphoid tissue) lymphoma. The premalignant phase, BALT hyperplasia, of nodular or diffuse type, appears to be synonymous with LIP. LIP may also occur in the fulminant lymphomatous disease termed angioimmunoblastic lymphadenopthy with dysproteinemia[6].

Lymphomatoid granulomatosis, or so called angiocentric immunoproliferative lesion is an angiocentric, angiodestructive lymphoma of B cell type accompanied by a prominent reactive T cell component. This rare disorder involves clonal expansion of EBV positive B cells, in an immunocompromised host, such as a patient with AIDS. The disorder usually involves the lung, but may occasionally occur in brain, skin or kidney. Increasing numbers of large cells correlate with increasing aggressiveness.

Chronic lymphocytic leukaemia presenting in young adults may rarely be a manifestation of HIV infection.

Plasmablastic lymphoma of the oral cavity is another rare, HIV associated lesion of the mouth or jaw, with EBV usually present in the tumour cells.

There do not appear to be major differences in the absolute incidence of other types of acute or chronic leukaemia, according to geography. However, there may be differences in the subtypes between developed and underdeveloped countries. The leukaemias may be subclassified immunophenotypically, cytogenetically and morphologically (French, American and British, or FAB method). For instance, the favourable common acute lymphoblastic leukaemia of childhood (precursor B, usually morphologically FAB type 1) is less common in Africa, where the less prognostically favourable (T cell, often FAB type L 2) variety is more frequent[7]. The FAB subtype termed L 3, which is closely related to Burkitt lymphoma, is universally uncommon.

Adult T cell leukaemia- lymphoma is a subacute lymphoproliferative disorder, mainly confined to Caribbean countries, South West Japan, as well as black Americans. However it also occurs in South America, West Africa and India. It is caused by human T cell leukaemia-lymphoma virus (HTLV-1). This agent was the first retrovirus to be known to cause human malignancy. Transmission is by exposure to blood or blood products, as in transfusion or intravenous drug abuse, sexual intercourse and breast feeding. Only about 5% of infected people develop clinical manifestations. When it develops, the T cell leukaemia- lymphoma is aggressive, with poor prognosis. Lymphadenopathy, hepatosplenomegaly, cutaneous infiltrates, osteolysis and hypercalcemia are usual. The leukemic phase is characterized by large lymphoid cells with polylobate, convoluted nuclei. The tumour cells are: CD 4 +, CD 3 + and TdT - . HTLV-1 is also the etiological agent of tropical spastic paraparesis, also termed HTLV associated myelopathy. A related retrovirus, HTLV-2 was isolated from a case of hairy cell leukaemia, but this was probably only a chance association. HTLV-3 was the former designation of HIV.

Kaposi sarcoma involving lymph nodes of young black African children, is a well recognized lymphoma- type condition in tropical Africa, and is unrelated to AIDS. Hepatitis C virus (HCV)

has recently been causally incriminated as a potential cause of a form of B cell splenic marginal cell lymphoma termed splenic lymphoma with circulating villous lymphocytes[8]. The relationship of viruses to lymphoma has been reviewed [9].

The gram negative bacillus, Helicobacter pylori, a close relative of Campylobacter jejuni, is strongly linked to non-ulcer dyspepsia/ gastritis and peptic ulceration, and associated with poor socioeconomic conditions. H. pylori induced gastritis, may be a precursor lesion of extranodal marginal zone B-cell lymphoma of mucosa associated lymphoid tissue (MALT lymphoma, or MALTOMA). This group of small cell B cell lymphoma is considered to originate in a putative follicular marginal zone, surrounding benign reactive germinal centres associated with a chronic mucosal inflammatory reaction Other examples of this low grade lymphoma may involve salivary glands in Sjogren's syndrome, thyroid in Hashimoto thyroiditis, lung, ocular adnexae and skin. A variant of MALTOMA, immunoproliferative small intestinal disease (IPSID), also known as alpha chain disease or Mediterranean lymphoma, involves small bowel, & and colon, and is an IgA producing B cell lymphoma of lymphoplasmacytic-lymphoplasmacytoid type It may transform to high grade, large cell lymphoma. IPSID is a disease of under privileged young adults in the Middle East, but also occurring in the Far East parts of South America, Nigeria and the Cape region of South Africa. Malabsorption, diarrhoea, abdominal pain, fever , weight loss and eventual finger clubbing are among the symptoms. Like gastric MALTOMA, early disease can be cured with antibiotics. MALTOMA cells are typically CD20+, CD79a+, and CD5- . On occasion, gastric MALTOMA progresses to an aggressive, high grade large cell variant.

Multiple myeloma is the commonest lymphoid malignancy in the American black population, and much more frequent than it's occurrence in whites. This is probably a reflection of higher immunoglobulin levels in black people. Osteosclerotic myeloma is a rare variant which has mainly been recorded in Asia, and is also known as Crow-Fukase or POEMS syndrome. The acronym indicates some features of the disorder ie polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes .The prognosis is said to be more favourable than regular myeloma.

Other haematological disorders, such as myelodysplastic and myeloproliferative syndromes seem to have a similar incidence in tropical and temperate climes. People with chronic haemolytic anaemia, such as sickle cell disease, or thalassemia, and those with immunodeficiency states such as AIDS, are susceptible to severe haemolytic crises if exposed to parvovirus B19. This single stranded DNA virus is the cause of the mild childhood exanthem termed erythema infectiosum (also known as fifth disease, or "slapped - cheek" rash), and may cause arthropathy in adults. The virus replicates in erythroid precursor cells, hence its ability to cause anaemia when red cell survival is shortened by hemolysis

16.4 CUTANEOUS MALIGNANCY

Fair skinned residents living in tropical climes are subject to a variety of skin cancers which are related to solar damage resulting from excessive exposure to ultra violet light. These skin tumours include basal cell carcinoma, squamous cell carcinoma, and malignant melanoma. Basal cell carcinoma (BCC) is the commonest cutaneous malignancy, accounting for about 70% of all

skin cancers, with a predisposition to occur in the head and neck region. The tumour is usually slow growing, and does not tend to metastasize, but may be locally aggressive, with a tendency to ulcerate (“rodent ulcer”) .By contrast, a diagnosis of squamous cell carcinoma (SCC), which is the second commonest skin cancer in Caucasians, implies the potential to metastasize, especially to regional lymph nodes, although this is unlikely in thin tumours, less than 3 mm thick, which clinically behave similarly to BCC. Those examples of SCC arising on the lip or ear are at particular risk of giving rise to metastatic disease. Invasive SCC arising in sun damaged skin usually evolves from a preceding, pre-invasive phase of squamous cell carcinoma in situ. Depending on the extent of dysplasia, precursor lesions encompass a spectrum of histologically defined entities which include solar keratosis, Bowenoid solar keratosis, and Bowen’s disease. Chronic exposure to inorganic arsenic may result in “ rain-drop “ pigmentation, and subsequently to development of keratoses of palms and soles, so called arsenical keratosis (Figure 2). Arsenical keratosis may also be considered a pre-malignant condition, especially as a precursor of SCC. The therapeutic or medicinal use of arsenic is no longer practiced, resulting in chronic arcenicism now being extremely rare in developed countries. However, the association of arsenic with many ores, such as gold, still poses a threat to persons involved with the mining industry. This risk is especially high where labour practices are unsafe, such as might occur in the Third World. Arsine gas can escape into the atmosphere from smelting plants posing a hazard to the nearby population.

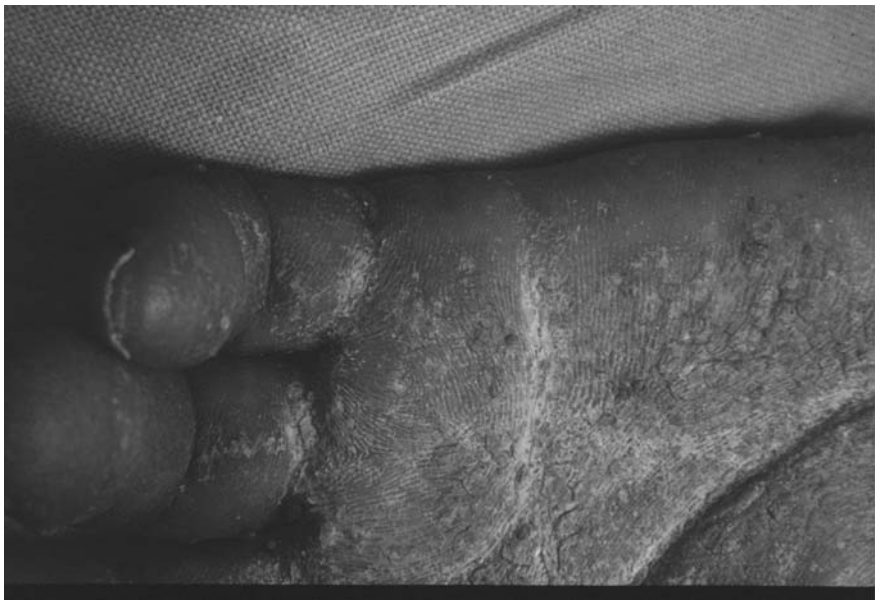

Figure 2. Arsenical keratosis (palm of hand).

Malignant melanoma is the third commonest, but potentially the most serious form of skin cancer. About half of all melanomas are of so called superficial spreading type. Other types of melanoma include lentigo maligna melanoma, nodular melanoma, acral lentigenous melanoma, desmoplastic-neurotropic melanoma and rare miscellaneous forms. While most melanomas arise in chronically sun exposed areas, a number of superficial spreading melanomas occur with a truncal distribution, in normally clothed parts of the body. These cases have been attributed to acute sun exposure or sunburn usually occurring in childhood, often acquired during vacation in

a hot climate. The prognosis of melanoma is related to the thickness of the tumour at presentation. Thickness is traditionally defined by the Clark's level, or accurately measured as the Breslow's maximum tumour thickness. The latter is considered more reproducible, and accurate. Thin melanomas less than 0.76 mm thickness have an excellent prognosis Intermediate melanoma is between 0.76 and 1.5 mm in thickness, and thick melanoma exceeds 1.5 mm. Metastases usually involve regional lymph nodes, but are rare with primary tumours less than 1mm in thickness, while those tumours exceeding 4mm have a rate of nodal metastases greater than 50 %.This stage may be followed by widespread distant metastases. Invasive melanoma is frequently preceded by an in-situ phase, with tumour confined to the epidermis (Clark's level 0). So called dysplastic nevi may also be precursor lesions.

By contrast, dark skinned inhabitants of tropical climes are afforded pigmentary protection against solar damage, thus basal cell carcinoma, squamous cell carcinoma, and truncal melanoma is rare. Exceptions however occur. Oculocutaneous albinism, an autosomal recessive condition, is common in tropical Africa, especially sub-Saharan Africa, and affected individuals are at extreme risk of suffering both BCC, and SCC (Figure 3). Paradoxically, there does not appear to be much increased incidence of melanoma, in this group of individuals.

A rare autosomal recessive condition is the genodermatosis, xeroderma pigmentosum, with fairly high gene frequency rates in Africa, especially North Africa, where consanguinity rates are also high, leading to increased expression of the disorder. These children are prone to all forms of skin cancer: basal cell carcinoma, squamous cell carcinoma, and malignant melanoma. An aggressive form of SCC, the so called Marjolin's ulcer, is common in underdeveloped countries. In this case the carcinoma develops in a pre-existing scar, which is often the result of a burn (Figure 4). Epileptic patients are at particular risk, when exposed to unprotected cooking fires. Malignant melanoma does occur in black races, but tends to occur in anatomical sites containing little pigment, namely palms of hands, and soles of feet, with a strong predisposition to involve the soles of the feet (Figure 5). The disease is usually advanced at presentation, with thick, ulcerated primary acral tumours, and secondary deposits in regional, inguinal lymph nodes.

A frequently encountered skin tumour in Africa is Kaposi sarcoma, a condition in which tumour nodules are composed of proliferating small vascular channels admixed with spindle cells. This tumour is related to Human Herpes virus type 8, and occurs in three differing forms[5]. Endemic adult African Kaposi sarcoma, is a cutaneous nodulo-ulcerative process tending to involve the distal extremities, especially the lower leg and foot (Figure 6). There is a strong male predilection. The disease usually follows a chronic, indolent rather benign course, but rarely may manifest as an aggressive condition, with associated visceral involvement. Clinically, the skin tumours must be differentiated from elephantiasis, chromomycosis, and ulcero-osteolytic neuropathy, which may appear clinically similar[10]. Endemic African infantile, or juvenile nodal Kaposi sarcoma, by contrast, is more aggressive, and is almost entirely confined to peripheral lymph nodes, with little, or no, skin involvement. Epitrochlear & groin nodes are usually enlarged (Figure 7). The most aggressive form of the disease is the epidemic, HIV related AIDS-Kaposi sarcoma in which cutaneous lesions are accompanied by widespread visceral and mucosal deposits. A related, but distinct vascular cutaneous lesion which may complicate AIDS, is bacillary angiomatosis. This vascular-proliferative disorder is caused by inappropriate skin infection by *Bartonella bacilliformis* (formerly termed *Rochalimaea henselae*) in an

immunocompromised setting. Clusters of the Gram negative bacilli can be demonstrated in the epitheliod endothelial cells using the Warthin- Starry silver stain. *Bartonella bacilliformis* is the causative organism of cat scratch fever. Although this condition is a pseudotumour, and not a malignancy, it is potentially fatal if visceral spread takes place. Usually however, the condition responds to erythromycin treatment. This shares some similarity with mycobacterial spindle cell pseudotumour, a leiomyoma - like lesion, in which masses of acid fast bacilli (*Mycobacterium avium-intracellulare* complex) can be demonstrated by the Ziehl-Neelsen stain. Various mycobacteria capable of causing inappropriate human infection in the immuno-compromised host have been termed MOTT (mycobacteria other than tuberculosis).

Other types of skin malignancies, such as malignant appendage tumours and mycosis fungoides-Sezary syndrome and other cutaneous lymphomas do not seem to have an increased expression in the tropics.

Cutaneous neurofibrosarcoma usually arises from malignant change in a neurofibroma, particularly multiple neurofibromata, such as occur in neurofibromatosi (NF). The commonest variety is NF1, or von Recklinghausen's disease (Figure 8). NF1 is inherited as an autosomal dominant disorder. The gene locus is on the long arm of chromosome 17 (17q11.2), and the abnormal gene product is termed neurofibromin. NF1 is characterized by café au lait pigmentation, small hamartomas of the iris termed Lisch nodules, and multiple cutaneous tumours. There is variable penetration with up to about 4% affected individuals developing malignant degeneration. NF1 is common in sub Saharan Africa. By contrast NF 2 is a much less common autosomal dominant condition. It is also termed central neurofibromatosis, and characterized by bilateral acoustic neuromas, glial hamartomas, and gliomas. The gene locus for NF2 is on the long arm of chromosome 22 (22q12). The gene product in NF2 is termed merlin. There are other much rarer forms of NF from NF3 to NF8.

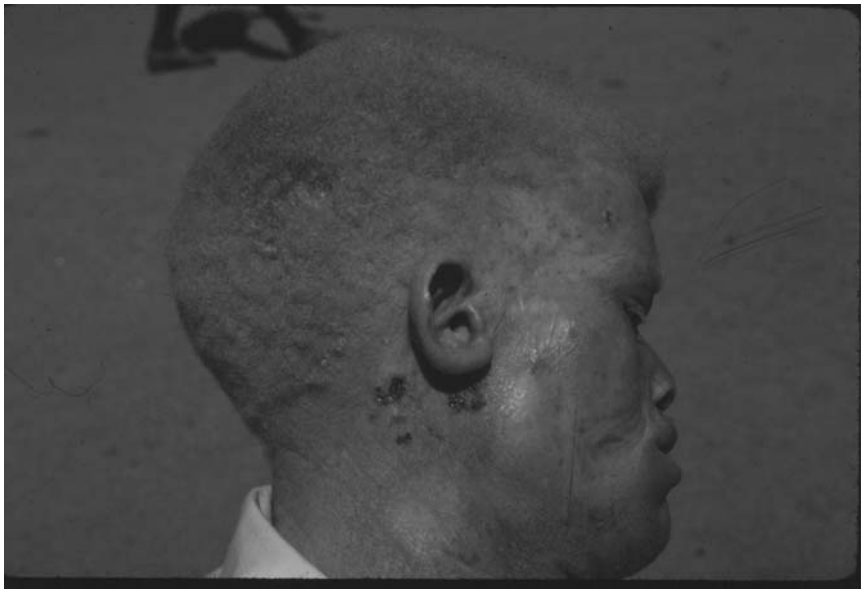

Figure 3. Albinism with basal and squamous cell carcinoma of face.

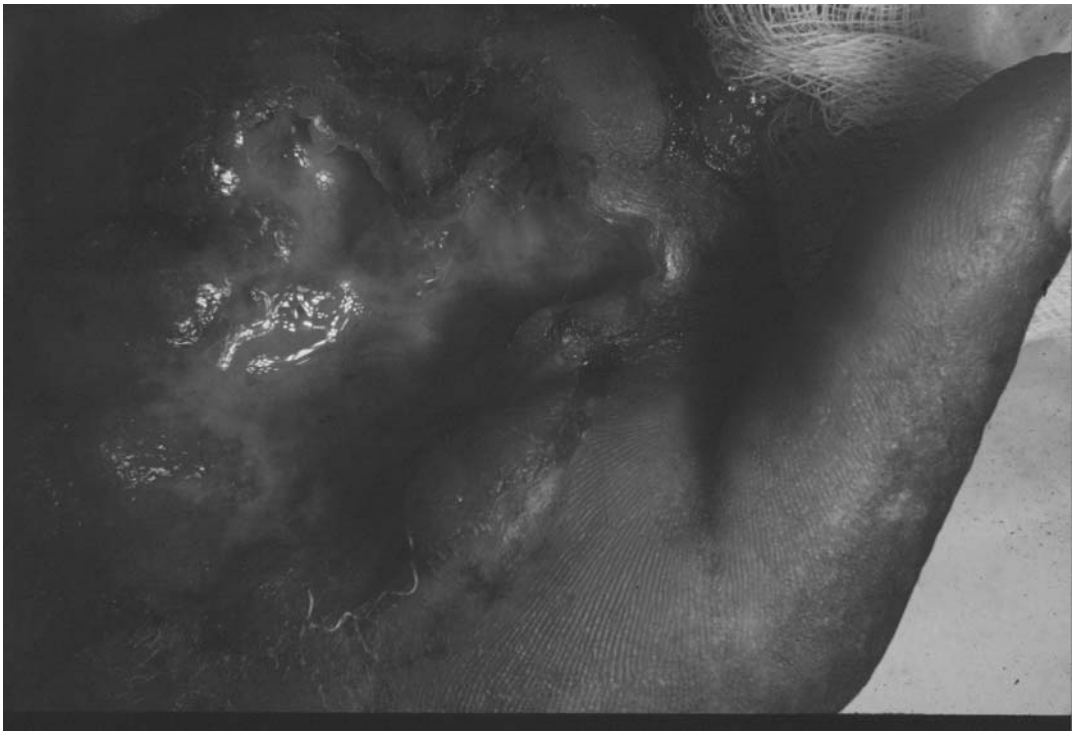

Figure 4.Marjolin’s ulcer in burns scar of palm of hand.

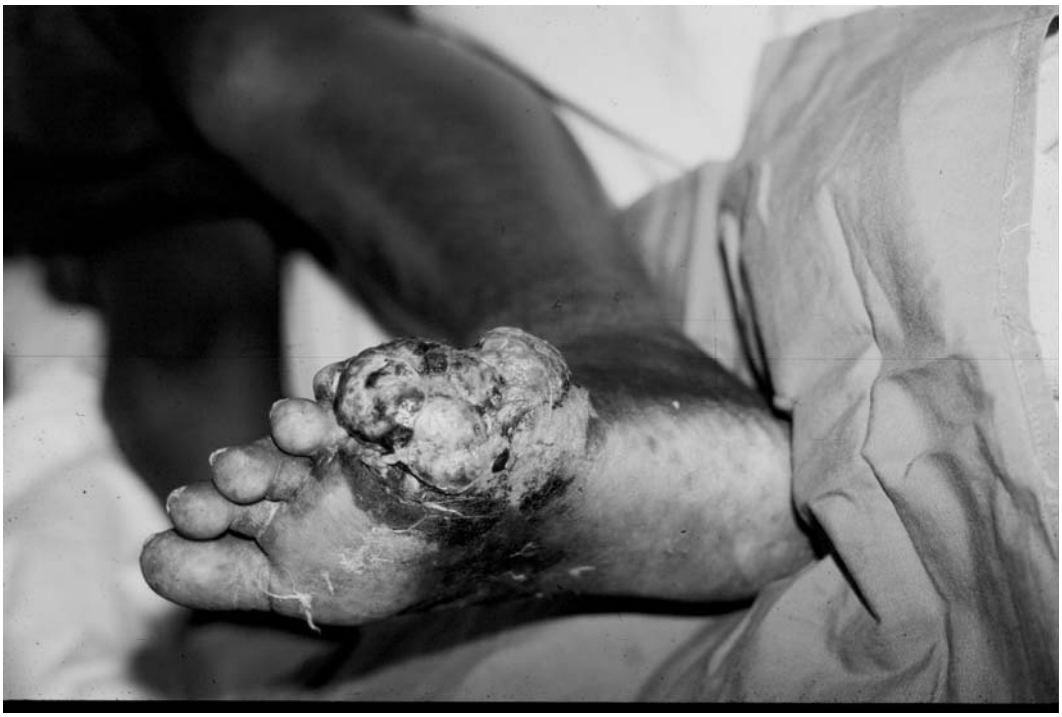

Figure 5. Malignant melanoma on sole of foot.

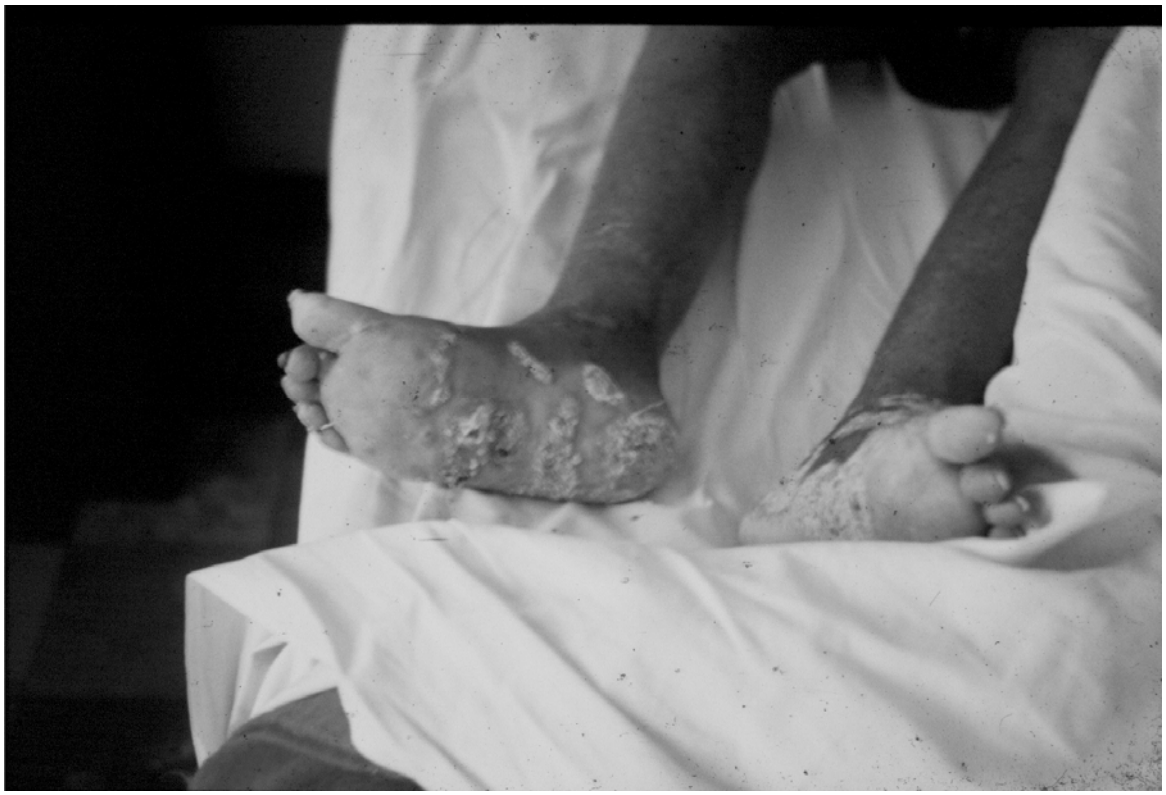

Figure 6. Endemic adult Kaposi sarcoma

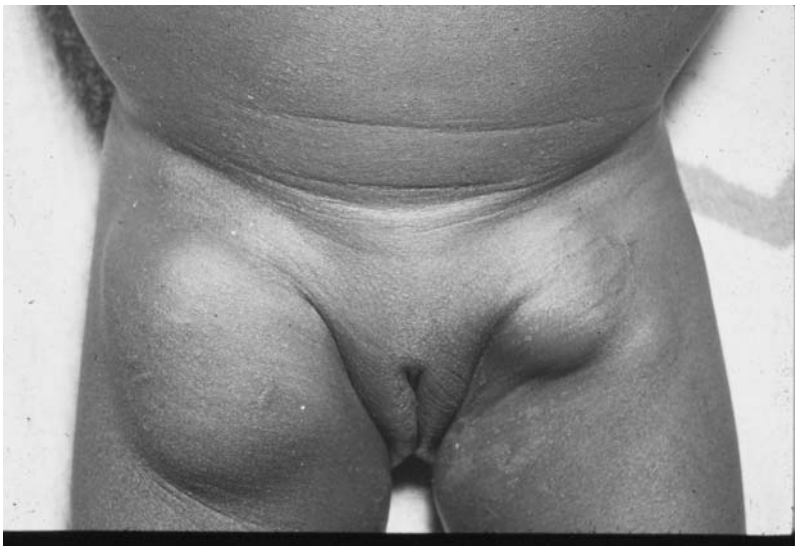

Figure 7. Infantile nodal Kaposi sarcoma

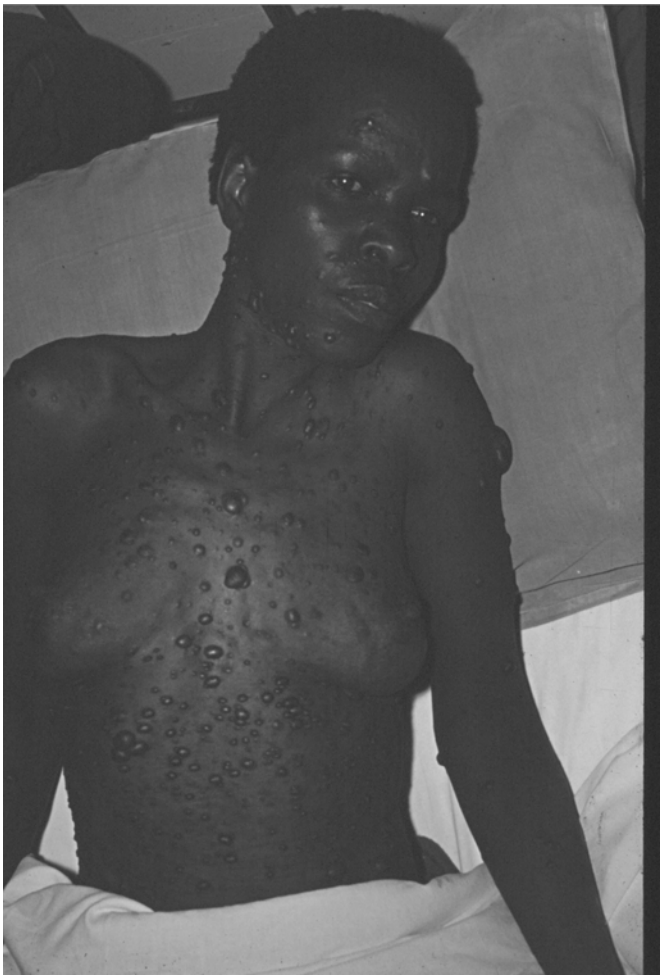

Figure 8. Neurofibromatosis

16.5 CHILDHOOD CANCER

Globally, about 1 in 10,000 children under fifteen years of age develop malignant disease each year. In the Western world, these cancers are made up in roughly similar proportions of brain tumours, other solid tumours and leukaemia-lymphoma i.e. about one third each. However, the distribution of types of tumours can vary between and even within some geographical regions. For instance, in endemic areas, Burkitt's lymphoma can represent up to 40 % of childhood cancer. While the broad classification into Hodgkin's and non- Hodgkin's lymphoma (NHL) remains relevant in childhood, there are many differences from adult disease, particularly in regard to NHL Unlike adult NHL, in childhood , disease is predominantly extra - nodal, and rapidly proliferative, often with an acute leukemic phase Unlike the adult pattern, follicular NHL is an extreme rarity in childhood For these reasons, the Ann Arbor staging system is generally not applicable to childhood NHL, and other methods, such as the Murphy system are preferred. Similarly, histopathological classification as applied to adult cases does not always readily lend itself to childhood NHL. Morphologically, most cases of childhood NHL can be classed as lymphoblastic, small non-cleaved cell (Burkitt's or non- Burkitt's) and large cell lymphoma. Lymphoblastic lymphoma is subdivided into convoluted and non-convoluted cell types. The interface between lymphoma and leukaemia is not as clear cut as in adults, and lymphoma cells frequently morphologically mirror a leukemic counterpart. Thus lymphoblastic lymphoma is usually composed of cells which may be designated by the FAB acute leukaemia classification as either L1 or L2 cell types. Small non-cleaved cell lymphoma has features of the L3 variant. The large cell group is heterogeneous, and morphologically, the appearances may be centroblastic, centrocytic or immunoblastic. Large cell lymphomas may be of B cell, T cell, or true histiocytic origin. Anaplastic large cell or so-called Ki-1 lymphoma falls into this category.

The differential diagnosis of large cell lymphoma includes some variants of Hodgkin's disease, as well as granulocytic sarcoma, malignant histiocytosis, Ewing's tumour and rhabdomyosarcoma. African type Burkitts' lymphoma tends to be centered on jaw bones, and other extra-nodal areas, while the American type is mainly an abdominal tumour. Lymphoblasic lymphoma is usually located in the mediastinum, but a significant number of cases involve peripheral nodes. Large cell lymphoma has a widespread anatomical distribution. Hodgkin's lymphoma is generally classified by the Rye modification of the Luke's and Butler system. Classification of NHL and Hodgkin's lymphoma have recently been refined by the World Health Organization of Tumours (WHO) methodology. The less favourable subtypes of Hodgkin's disease such as mixed cellularity, or lymphocyte depleted variants tend to predominate in the tropics, while the much more favourable nodular sclerosing form is the main type in temperate latitudes. Common acute lymphoblastic leukaemia is relatively less represented in tropical Africa, but this is probably offset by greater numbers of prognostically less favourable forms of acute lymphoblastic leukaemia, such as T cell or lymphoblastic lymphoma. Acute myeloblastic leukaemia is also relatively common in African children in Zimbabwe, and often is associated with, or preceded by granulocytic sarcoma, a form of AML occurring as a localized subperiosteal tumour deposit, usually involving the skull, with a predilection for a peri-orbital location[7] (Figure 9). These tumour masses were formerly termed chloroma, because of green pigmentation. Chronic leukaemia is universally uncommon in children. Chronic myeloid leukaemia (CML), however, is a well recognized, albeit unusual entity in childhood widely distributed through all continents. A specific variety of childhood chronic leukaemia, so called

juvenile chronic myelomonocytic leukaemia is in fact more unusual than typical Ph positive CML in children.. Chronic lymphatic leukaemia is an extreme rarity in children and young adults.

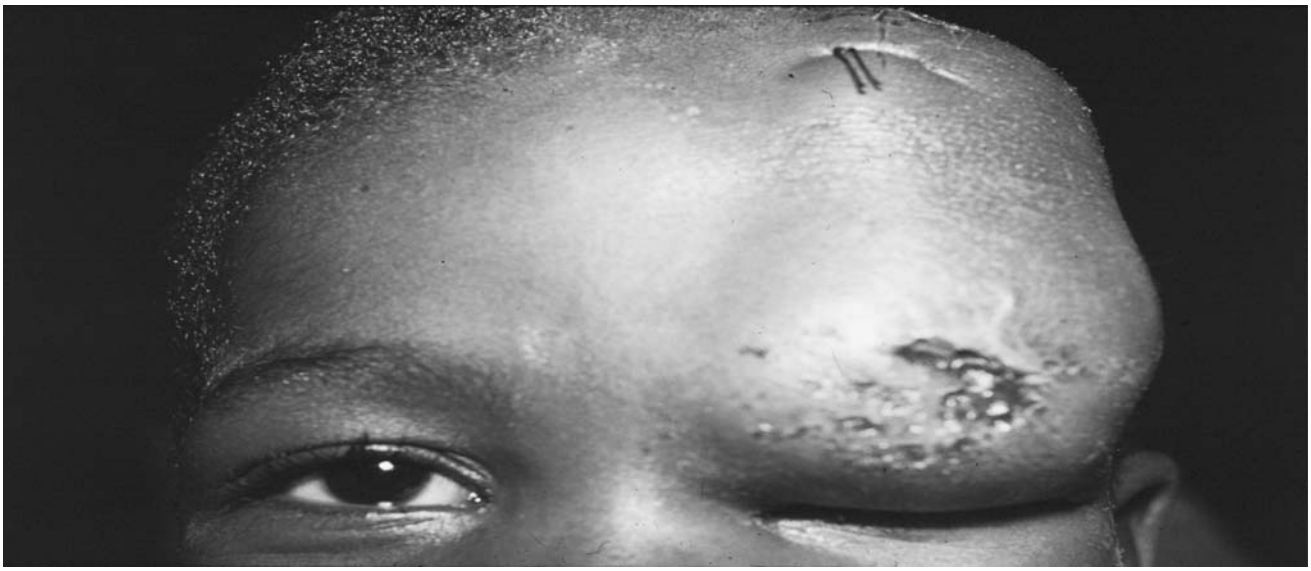

Figure 9. Granulocytic sarcoma of orbit

Most solid tumours of childhood occur with roughly similar frequency in tropical and non tropical areas. An exception is Ewing's tumour which is rare in African blacks. It has been claimed that Wilm's tumour is the commonest childhood malignancy in parts of sub Saharan Africa (i.e. Zimbabwe), and neuroblastoma is exceptionally uncommon in Zaire[11]. However, it is difficult to confirm these findings. Many of the childhood solid tumours are of embryonic origin. These include neuroblastoma, the prototypical small round cell tumour of childhood, nephroblastoma (Wilm's tumour), hepatoblastoma, rhabdomyosarcoma (embryonal and alveolar varieties), medulloblastoma, retinoblastoma and teratoma. These are not a homogeneneous group, but share an embryonic origin.

Neuroblastoma arises from the neural crest and is mostly an abdominal tumour, usually arising in an adrenal gland, but sometimes in sympathetic or dorsal root ganglia. Extra abdominal sites include posterior mediastinum and cervical sympathetic ganglia. Wilms tumour is centred on the kidney. Rhabdomyosarcoma is the commonest soft tissue tumour in children, but may involve nasopharynx and genito-urinary tract ("sarcoma botryoides"). Other genital malignancies involving ovaries or testes are germ cell tumours such as ovarian mature or immature teratoma (also having a proclivity to involve the sacrococcygeal area, brain, testis, and mediastinum), and yolk sac tumour of ovary or testis. Sacrococcygeal teratoma is the most common congenital tumour (Figure 10). Germ cell tumours may also occur extracranially in the head and neck[12]. Hepatoblastoma is a liver cancer of infants and young children.

The differential diagnosis of "small, round, blue cell" tumours of childhood includes

neuroblastoma, rhabdomyosarcoma, Ewing's sarcoma, desmoplastic small round cell tumour, primitive neuroectodermal tumour (P-NET), and lymphoma/leukaemia.

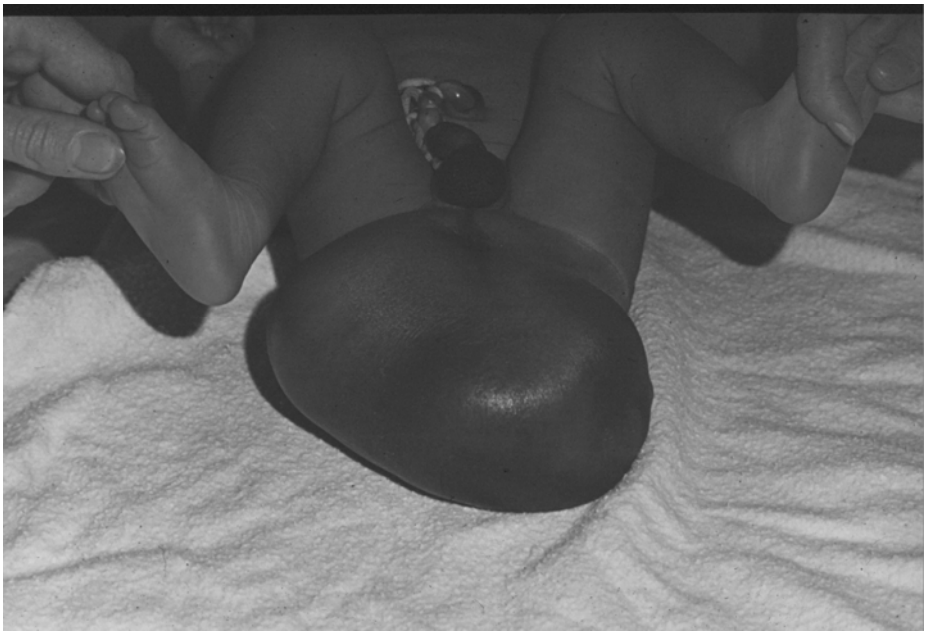

Figure 10. Sacroccocygeal teratoma

Brain tumours too, seem to have a similar incidence in both tropics and elsewhere. Glial tumours (astrocytoma) are the most frequent childhood tumour, followed by neuronal tumours (medulloblastoma). Ependymal tumours (ependymoma) are the third most frequent, with rare miscellaneous tumours also occasionally occurring.

Kaposi sarcoma involving lymph nodes, and unrelated to HIV infection, or immunodeficiency, is a well recognized childhood cancer in tropical Africa. While the disease is aggressive, prognosis is excellent with appropriate chemotherapy[13]. Unlike the situation in adults, neoplasia is unusual in children with AIDS.

16.6 LIVER CANCER

Hepatocellular carcinoma is a common tumour, in Africa, where it parallels the high incidence of chronic hepatitis B virus (HBV) infection. HBV is a blood borne, enveloped, double stranded DNA virus that may be transmitted by blood or its products, as in transfusion, or intravenous drug abuse by sexual intercourse or vertically from mother to newborn. It is the only DNA hepatitis virus. Chronic hepatitis B usually has an early initial replicative phase, which may be accompanied by active hepatitis between two to six months following exposure. The late phase is minimally replicative. Infection in adults by HBV usually results in acute hepatitis. Most adults eliminate the virus within a year, and only about 5% become chronic carriers By contrast,

perinatal infection usually results in an asymptomatic initial phase, but about 90% of cases become chronic carriers. Vertically transmitted neonatal infection is the usual method of spread in many tropical regions, where the prevalence of chronic carriage can be as high as 20% of the population. The high incidence of HBV in these areas may well be a result of unhygienic cultural practices, such as skin excoriation with unsterile implements to induce "*muti* marks", by keloid formation, for instance. Tattooing is also potentially hazardous. The HBV virion, or Dane particle is a complex 42 nanometer double shelled structure with an inner core antigen (HBcAg), and an outer surface antigen (HBsAg).There is also a soluble antigen secreted by the core (HBeAg).Following infection, HBsAg is the first marker to appear, doing so before clinical signs of acute hepatitis. HBeAg, together with HBV DNA appear during the early acute replicative stage. Anti HBcAg IgM is a marker of acute infection. Anti HBcAg IgG is a lifelong indicator of past infection. Persistence of HBeAg indicates a chronic carrier state[14].

Hepatitis D (HDV or delta agent) is a single stranded RNA virus that can only replicate in cells that are infected by HBV, either simultaneously or subsequently. It mainly occurs in the Middle East, parts of Africa and South America as well as Italy, and causes severe liver damage. Hepatitis F, a putative parenterally spread agent has been predicted as causing non A, non B, non C hepatitis. Its status is uncertain. Hepatitis G, a paramyxovirus is a cause of syncitial giant cell hepatitis. Other members of the alphabet are hepatitis A (HAV, or enterovirus 72), and another enterovirus, hepatitis E (HEV), which are spread by the faecal oral route , and do not cause chronic disease. They may rarely result in massive hepatic necrosis, which can lead to post necrotic scarring, macronodular cirrhosis and malignant transformation. HV E is the principal cause of severe hepatitis in many tropical areas, especially India, Africa and the Middle East. Hepatitis C virus (HCV) is spread similarly to HBV. Hepatitis C virus is an enveloped single stranded RNA flavivirus[15]. HCV infection leads progressively to cirrhosis, with many patients' subsequently developing liver cancer. Indeed, cirrhosis, almost always precedes the tumour, which usually has a multifocal distribution within the liver, suggesting neoplastic transformation in areas of nodular regeneration. It is of interest that HCV has been shown to have oncogenic potential in inducing so called splenic lymphoma with circulating villous lymphocytes, a rare B cell tumour of the spleen.

Alcohol probably plays a role in the cirrhosis, in many cases. However, other (potentially carcinogenic) factors are also incriminated in tropical areas. These include the carcinogen, aflatoxin, a metabolite of the fungus *Aspergillus flavus*, which frequently contaminates grain such as maize, a staple food in many parts of sub-Saharan Africa, where the highest incidence is up to 100 new cases per year per 100,000 population. The disease, which has a striking male predominance, is also common in South East Asia. Another important factor is iron overload. The term haemochromatosis has become almost synonymous with genetic, or familial hemochromatosis, an autosomal recessive disorder, largely confined to whites, of northern European origin The term, haemosiderosis, African iron overload or nutritional siderosis is preferable in describing the disorder which is so common throughout most of Africa. The genetics of familial hemochromatosis have recently been well defined[16]. The responsible iron loading gene, HFE is located on the short arm of chromosome 6, closely linked to the HLA locus. The mutation results from a single amino acid substitution from guanine to adenine and is termed C282Y. In a small proportion of cases, the disease represents a complex heterozygous state due to another iron loading gene, termed H63D. Genetic susceptibility has not been clearly

defined in African haemosiderosis .The condition has largely been blamed on consumption of large amounts of iron in maize beer, which has a low pH, and is traditionally brewed in iron skillet pots. This theory seems to be reinforced by the observation that the disorder is declining, as more Africans are taking to commercially brewed beer, and Western style alcoholic drinks. However, Gordeuk et al have demonstrated that there is a genetic component associated with dietary iron overload[17]. This putative iron loading gene is not linked to the HLA locus. Heterozygous carriers of the gene demonstrate elevated serum ferritin and transferrin saturation levels. Other causes of iron overload also exist in the tropics. These include transfusion siderosis, for transfusion dependent anaemia, such as sickle cell disease, other haemoglobinopathies, and thalassemia for instance. Porphyria cutanea tarda, a disease subject to iron overload, is common in Africa.

Membranous obstruction of the inferior vena cava is an unusual condition mainly confined to Southern Africa, and Japan. It is said to result from incomplete resolution of thrombus, leading to hepatic outflow obstruction, cirrhosis and subsequently carcinoma.

There is no evidence that parasitic diseases may be related to liver cancer. In Africa, liver cancer is often at an advanced stage at presentation, with cachexia together with ascites, and oedema due to portal hypertension and hypoalbuminemia. The enlarged, hard knobbly liver is usually palpable (see Figure 11). Tumour rupture with haemoperitonem and shock, obstructive jaundice, pathological fracture due to bone metastases, (often solitary lesions), are among other less frequent manifestations. Bizarre manifestations include a ravenous appetite due to hypoglycemia and polycythemia due to inappropriate erythropoitin production. Other inappropriately secreted hormones which are sometimes associated with liver cell carcinoma, are parathyroid hormone, causing hypercalcemia and chorionic gonadotropin causing feminization and gynecomastia. Characteristically, there is elevation of the serum level of alpha feto protein, an oncofetal antigen, which can act as a tumour marker.

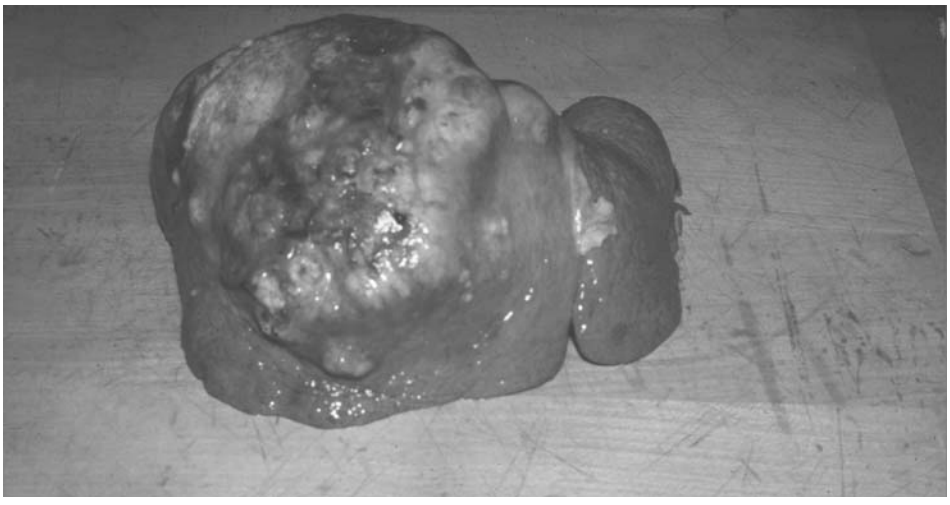

Figure 11. Hepatocellular carcinoma. Appearance of liver at autopsy

16.6 BREAST CANCER

Breast cancer is the commonest malignancy of females in the Western world, where it is the leading cause of female deaths. The lifetime risk of breast cancer in Western women is 1:12. The incidence is intermediate in Mediterranean countries and South America; and is lowest in most of Asia, and the black population of Africa. This contrasts with high rates of breast malignancy in American black females.

Known protection factors against breast cancer include early age of first sexual contact, high parity, and prolonged breast feeding. These factors tend to prevail under poor social and economic conditions, and go a long way to explaining the low incidence of breast cancer in tropical countries. It is of interest that fibrocystic disease of breast without atypia is common in black African female patients, as an association of fibrocystic disease with subsequently developing carcinoma, has been reported in Western communities. Genetic factors are also important. Two breast cancer susceptibility genes, BRCA1 and BRCA2 have been identified, and cloned. They are located on chromosomes 17 and 13 respectively. Mutations, which may occur at numerous points along these genes, are associated with familial forms of cancer of breast, ovary and prostate[18]. Most breast cancers are, however, sporadic, but are still associated with a strong familial susceptibility. Elucidation of the genetic basis of these sporadic cancers remains elusive.

Fibroadenomas with stromal hypercellularity are more common in African and Indian woman and overlap with phyllodes tumours[19]. This may explain the relatively increased, albeit uncommon, occurrence of breast sarcomas in these population groups (see Figure 12), which may originate in malignant phyllodes tumours (cystosarcoma phyllodes)

16. 8 THYROID CANCER

Endemic, or iodine deficiency goitre, is common in tropical inland areas that do not have access to iodized salt. The development of multi-nodular colloid goitre is often exacerbated by dietary goitrogens. The condition usually presents around the time of puberty, or during first pregnancy, or lactation. It is rare in the male. As most thyroid cancers are of follicular type in the tropics, it seems a reasonable assumption that these are linked to follicular degeneration, and formation of colloid nodules. This opinion however is not universally held. By contrast, papillary carcinoma is by far the commonest form of the disease in iodine depleted Western countries, and the incidence of papillary cancer is said to increase in concert with high iodine intake. The implication of distinguishing these two major forms of thyroid cancer is that papillary tumours have a better prognosis, and tend only to metastasize to regional lymph nodes. By contrast, follicular carcinoma has a proclivity for distant metastases .A study in Zimbabwe demonstrated that all forms of thyroid disease, including the less common forms of malignancy occurred in that country[20] (see Figure 13).

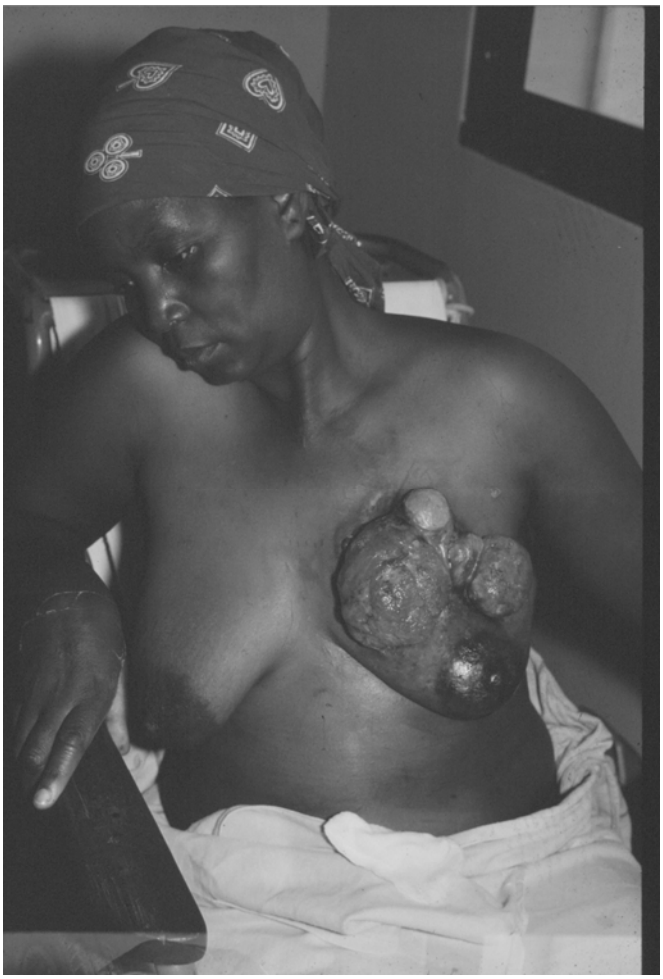

Figure 12. Breast sarcoma

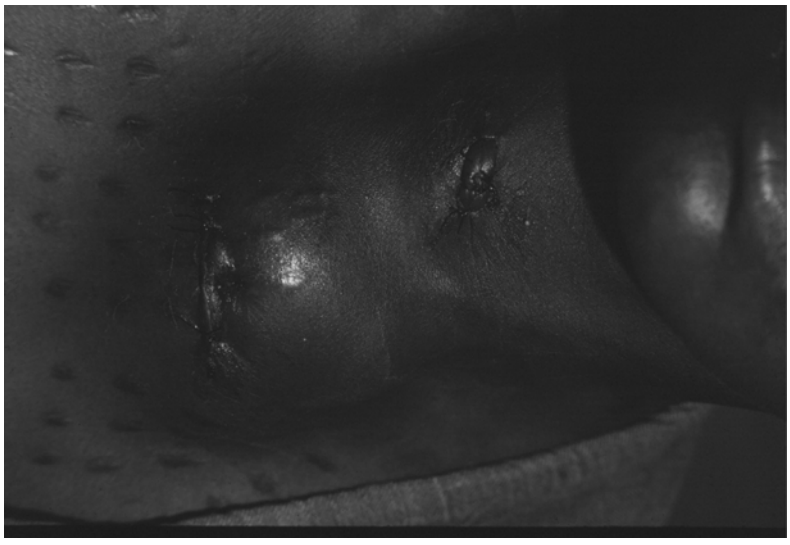

Figure 13. Thyroid carcinoma. Note "*muti* marks" with patterned keloid scars resulting from therapeutic efforts of a *Nganga* ("Witch doctor")

16.8 LUNG CANCER

Primary lung cancer is strongly associated with tobacco consumption, although tumourigenesis is also influenced by genetic and environmental factors. Bronchogenic squamous cell (SCC) carcinoma is especially related to tobacco use, which may also play an albeit lesser role in the evolution of the various forms of primary adenocarcinoma. As cigarette smoking is declining among white Western males, so is the incidence of lung cancer in that group, in whom adenocarcinoma is now more common than SCC. However, this trend is reversed in white Western females and black males universally. Cigarette smoking, if anything, is on the rise in these latter two population groups.

16.10 GENITOURINARY CANCER

16.10.1 KIDNEY CANCER

Renal cell carcinoma is a tumour of adults. It is also termed hypernephroma, or clear cell renal cancer, and is uncommon in indigenous inhabitants of most tropical countries, where in general, it's occurrence is less than a quarter as frequent as in the United States of America (USA). However, in the USA, American whites and blacks exhibit a roughly similar incidence. This implies that environmental factors play a major role. Obesity and industrial pollution have been suggested as possible influences. Renal cell carcinoma is universally much more frequent in males than in females. Other forms of adult kidney cancer, such as papillary renal cell carcinoma, chromophobe renal cell carcinoma and collecting duct carcinoma are uncommon in all population groups. Transitional cell carcinoma (TCC) of the renal pelvis and ureter has been associated with cigarette smoking, exposure to industrial carcinogens and phenacetin abuse. Like renal cell carcinoma, TCC of the kidney appears to be uncommon in the tropics. Childhood kidney cancer, i.e. Wilm's tumour has a similar incidence in both tropical and non- tropical environments.

16.10.2 BLADDER CANCER

In most parts of the temperate world, transitional cell carcinoma (TCC) of the bladder is a common tumour which has been strongly linked to cigarette smoking and exposure to aniline dyes. It is more frequent in males. Squamous cell carcinoma (SCC) is rare in the Western World, only accounting for about 5% of bladder cancers. However, in areas endemic for schistosomiasis, SCC comprises about 75% of bladder neoplasms.

16.10.3 PROSTATE CANCER

Prostatic adenocarcinoma is a leading cause of mortality in the male population of Europe, and the United States. In the USA, black males have a particularly high incidence with 72.3 new cases per year per 100,000 population, which is higher than white American males with an incidence of 46.8 per 100,000. By contrast the incidence is very low in South African black males, with an annual incidence of around 14 per 100,000. Prostatic cancer is relatively

uncommon throughout most tropical regions.

16.10.4 UTERINE CANCER

Endometrial adenocarcinoma reflects rather similar trends in black females to prostatic carcinoma in black males. That is, the condition is quite unusual in the tropics (black females in South Africa having an incidence of 5.9 per 100,000, as apposed to black females in USA at 12.5 per 100,000 and white females in USA at19.3 per 100,000). Uterine leiomyomata are extremely common, occurring in about a quarter of women. However, uterine leiomyosarcoma is universally uncommon.

Cervical cancer is a common tumour in the tropics, for many of the same reasons that breast cancer is uncommon: that is early age of sexual intercourse, often with multiple partners, and high parity[21]. Cervical intraepithelial neoplasia (CIN), is a spectrum of epithelial dysplasia, that usually precedes invasive carcinoma, which is usually of squamous cell type (SCC). Cervical intraepithelial and invasive carcinoma are related to infection with wart viruses, or human papillomaviruses (HPV). These are double stranded DNA papovaviruses. There is a strong association with cervical neoplasia, and HPV types16 and 18.

The term gestational trophoblastic disease encompasses partial and complete hydatidiform mole, chorioncarcinoma, placental site trophoblastic tumour and exaggerated placental site nodule. About 50% of cases of chorioncarcinoma follow complete hydatidiform mole. About 20% of cases follow spontaneous abortion, incomplete mole or normal pregnancy. Complete hydatidiform mole is most common throughout Asia, Latin America, and in the Middle East, and may affect up to 1 in 500 pregnancies, as apposed to Europe where only about 1 in 2000 pregnancies are similarly affected.

16.10.5 OVARIAN AND TESTICULAR CANCER.

Testicular tumours are a rarity in all black populations. Ovarian tumours are also less frequently encountered in black women than white women.

16.11 GASTROINTESTINAL CANCER

Oropharyngeal squamous cell carcinoma (SCC) is strongly linked to tobacco consumption. The rising incidence of mouth cancer in third world countries matches increasing cigarette smoking. Betel and tobacco chewing are also significant risk factors. Oral SCC is also an AIDS related tumour, as is the rare plasmablastic lymphoma of the mouth.

Oesophageal SCC shows widespread geographic variation, even within the same country, being common in some non-tropical countries such as parts of Russia, Japan, Northern China and Turkey, while generally uncommon in Western countries. It predominates in poor socio-economic circumstances, and is common in Southern Africa, especially in the Transkaai province of South Africa. There is a marked male predominance in Africa, where clinical presentation is often during advanced disease, with extreme cachexia, and dysphagia. Aetiological factors include alcohol and tobacco consumption, dietary trace element deficiency

(e.g. zinc), and human papilloma virus (HPV) infection. Fungal infection of grain with mycotoxin production, especially by *Fusarium* and *Aspergillus* species is probably an important factor in Southern Africa. A high food content of carcinogenic nitrosamines in geographically dry areas has been related to molybdenum poor pastures, resulting in high nitrate levels in the crops. This effect is probably exacerbated by low ascorbic acid intake, as fruit and green vegetables may be in short supply in hot, dry, arid, regions .The antioxidant, ascorbic acid, acts as a scavenger of nitrates, inhibiting their conversion to nitrosamines. By contrast to SCC, adenocarcinoma of the oesophagus is mainly a disease of Western countries, mainly arising in areas of Barrett's metaplasia, resulting from reflux oesophagitis.

The aetiology of gastric adenocarcinoma is highly complex. Genetic factors (blood group A is a predisposing trait), diet (smoked or preserved food, nitrates and high salt intake increase susceptibility), and socio-economic conditions, especially related to infection by *Helicobacter pylori* are important factors. The prevalence of *H. pylori* infection is over 80% in most developing or third world countries, while the prevalence is much lower in industrialized nations, generally less than 30%.It is probably spread from person to person by oral ingestion under poor, overcrowded, unhygienic conditions. The motile, flagellated, urease producing Gram negative bacillus, *H. .pylori*, has been classed by the WHO, as a group 1, or definite carcinogen. Strains of *H. pylori* that cause human disease are termed type 1 strains, and usually have a virulence marker, or pathogenicity region of the genome containing the cytotoxin associated gene pathogenicity associated island (cagPAI)[22]. One of these numerous genes, cagA, is associated with duodenal ulceration and gastric malignancy. On a separate segment of the genome, is another gene, which encodes for vacuolating cytotoxin(vacA), which may be a marker of aggressive disease, but it's role has not been defined with certainty[23]. Sequelae of infection include non- ulcer dyspepsia, gastric or duodenal peptic ulceration, atrophic follicular gastritis, and gastric adenocarcinoma, or MALT lymphoma. *H. pylori* is uniquely adapted to surviving in the hostile, highly acidic gastric environment. Being motile, it is able to "swim", and remain within the protective thin layer of mucus that coats the stomach lining. As a urease producer, it is able to envelop itself in an alkaline coat of ammonia, produced by catalysing urea into water, and carbon dioxide. The latter is the basis of the breath test, using C13 labelled urea. *H. pylori* infection leads to bacillary or so called type B gastritis, which evolves into atrophic gastritis, with development of intestinal metaplasia, a precursor of adenocarcinoma. Also characteristic of type B gastritis is the accumulation of B cell lymphoid aggregates within gastric lamina propria, forming precursor lesions for MALTOMA.. A paradoxical feature of *H. pylori*, is its self destructive, or "suicidal" behaviour. As atrophic gastritis progresses, achlorhydria develops, leading to progressively decreasing gastric acidity, and regression of the natural habitat of the organism. *H. pylori* tend to be scanty in gastric tumours. A steadily declining incidence of gastric carcinoma in Western countries probably reflects declining infection by *H pylori* due to improved living standards. Stomach cancer was common in Europe during the nineteenth and early twentieth centuries, when it, was referred to as "the captain of the men of death" .It is paradoxical then, that gastric carcinoma has a very low incidence in the indigenous population of Southern Africa. The disease however, is common in parts of South America. It is also common in Japan, China and Finland, where traditional culinary practices, rather than *H pylori* infection are probably responsible.

In general terms, malignant disease of the small intestine is universally uncommon. Primary

small bowel adenocarcinoma is something of a rarity, but said to be more frequent in blacks than whites. Pre-existing Crohn's disease (terminal ileitis), may be a precursor with some cases developing dysplasia. Apart from an increased incidence in Jewish population groups, Crohn's disease does not have any definite geographical preferences, but is rare in blacks in Africa. Similarly, neuroendocrine carcinoma (midgut carcinoid tumour) shows no special distribution. Enteropathy associated T cell lymphoma (EATL), of small intestinal mucosa is a recognized complication of gluten sensitive enteropathy (celiac disease).However, celiac disease is mainly a condition of whites of Northern European and Irish origin. Hence EATL is considered rare in the tropics. By contrast, immunoproliferative small intestinal disease, or so called IPSID, also known as Mediterranean lymphoma, or alpha heavy chain disease, a monoclonal tumour of IgA producing B cells, is a disease with a propensity to affect young adults, living in poor circumstances, in third world countries. The Middle East, Far East, Nigeria, South America, and the Cape Province of South Africa have the highest incidence[24]. The condition is associated with malabsorption, diarrhea, abdominal pain, weight loss and finger clubbing, among other symptoms. IPSID is a form of MALTOMA. The earliest phase is responsive to antibiotic therapy. This lymphoma is of lymphoplasmacytic- lymphoplasmacytoid type. Transformation to aggressive large B cell lymphoma may occur. The disease occasionally involves large bowel. Mediterranean lymphoma is not to be confused with familial Mediterranean fever, an autosomal recessive recessive disorder centered around the Mediterranean littoral. This disease is characterized by intermittent pyrexial bouts of severe abdominal pain, acute peritonitis, arthropathy or pleurisy. Peritoneal adhesions may follow. The condition is regarded as benign ("benign familial polyserositis"). However, amyloidosis is a complication (potentially preventable with colchicine therapy). The amyloid is of AA type, and initially involves nerves, with peripheral neuropathy. It may later become widespread, with extensive visceral involvement, particularly affecting the kidneys, and leading to renal failure.

Large bowel cancer arises in a complex setting of environmental and genetic interactions. It is predominantly a tumour of industrialized Western communities, where it is common, constituting the fourth leading cause of death. Most cases develop in a sequence with adenomata, which become progressively more dysplastic, before evolving into frankly malignant, invasive carcinoma. Some of these develop in a familial setting showing autosomal dominant inheritance, and termed hereditary nonpolyposis colon cancer syndromes. Examples of these are Lynch types 1 and 2 syndromes, and Muir-Torre syndrome. The familial colon cancer syndromes are associated with a variety of extra colonic cancers.. Inflammatory bowel disease, especially ulcerative colitis, and occasionally Crohn's disease may develop focal areas of dysplasia, and develop into areas of flat adenocarcinoma. By contrast with developed Western countries, large bowel cancer is uncommon in developing countries. Indeed, the incidence in South Africa of colo-rectal cancer among black people is among the lowest in the world. Acute appendicitis, diverticulitis, inflammatory bowel disease and colo-rectal cancer are all uncommon in communities that have a bulky, high residue diet. Pre-operative biopsy is sometimes omitted in first world countries, if a large bowel tumour is obviously malignant on clinical grounds. However, confirmatory biopsy is mandatory in tropical areas, as mass lesions occurring with amoebiasis, so-called amoebomas can appear identical to exophytic carcinoma on gross inspection. Squamous cell carcinoma of the anal canal is a well recognized complication of AIDS.

16.12 SUMMARY

About 40% of the world's population live in the tropics. In these areas, many types of cancer are related to chronic infection, and often present in an advanced, incurable stage.

16.12.1 HIV/AIDS

The prevalence of HIV infection in many tropical countries has altered the pattern of malignancy, with full blown AIDS sufferers prone to certain specific tumour types, such as Kaposi sarcoma, aggressive lymphomas, and SCC of oral or anogenital mucosa.

16.12. 2 Lymphoma and leukaemia

Burkitt's lymphoma is the prime example of tropical cancer, and is related to EBV infection. Another is IPSID, a bowel lymphoma, occurring in some tropical areas. There is no major difference in the incidence of acute or chronic leukaemia between tropical and non-tropical areas, but presentation is often much later in many developing tropical areas.

16.12.3 Skin cancer

Dark skinned people have pigmentary protection against common cancers caused by high ultraviolet levels in the tropics. Melanoma, SCC and BCC are thus uncommon in these people although melanoma of non pigmented acral areas of the body, such as the soles of the feet, is, quite frequent, and usually lethal.

16.12.4 Childhood cancer

Unlike adults, malignancy is unusual in children with AIDS. Ewing's tumour is rare in African blacks. Other solid childhood malignant tumours occur with similar frequency in tropical and non tropical countries.

16.12.5 Liver cancer

Hepatitis B, hepatitis C, iron overload, alcohol consumption and food contamination by fungal toxins such as aflatoxin (metabolite of *Aspergillus flavus*I), contribute to the development of cirrhosis, and subsequent evolution of hepatocellular carcinoma, common in many tropical communities. Additionally, in SE Asia, chronic infection with the Chinese liver fluke, *Clonorchis sinensis,* and the related trematode, *Opisthorchis viverrini* has been linked with cholangiocarcinoma, based on epidemiological observations.

16.12.6 Other cancers

Breast cancer in Asia and in the black population of Africa, is much less common than in whites in Western countries. In tropical climes, unlike the First World, follicular thyroid cancer tends to predominate over papillary carcinoma, probably mainly as a consequence of iodine deficiency goitre.

16.12.7 Genitourinary cancer

Renal cell carcinoma is unusual in most tropical countries. In regions endemic for schistosomiasis, SCC is the principal type of bladder tumour. Prostatic, endometrial, ovarian and testicular cancers all tend to be unusual in the warmer climes of the tropics. However, cervical cancer continues to be a frequent entity in tropical latitudes.

16.12.8 Gasrointestinal cancer

SCC of the oropharynx often results from smoking, which appears to be increasing, in Third World countries. Oesophageal SCC shows a very patchy, but focally very common distribution in some tropical areas.

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