

# **Infectious Disease and Cancer in Africa – A medical and Demographical Reality**

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## **Lecture manuscript**

Throughout history mankind has been afflicted by infectious diseases but improvement in sanitation and development of vaccines especially for diseases caused by viruses, have played a central role in controlling these diseases.

By and large infectious diseases are no longer serious public health problems in the developed world. However in Africa they are still prevalent and are killing and maiming millions every year. The trio of malaria, tuberculosis and HIV/AIDS are devastating the continent.

### **Malaria**

The World Health Organization (WHO) estimates that 300 to 500 million Africans are infected with malaria each year causing 1.5 to 2.7 million deaths. More than 90% of these deaths occur in children under 5 years of age. This means that in Africa a child dies every 45 seconds of malaria. The estimated annual direct and indirect costs of malaria to Africa were US\$800 million in 1987 and about US\$1.8 billion in 1995.

### **HIV/AIDS**

Sub-Saharan Africa is more heavily affected by HIV and AIDS than any other region of the world. An estimated 22.4 million people are living with HIV in the region - around two thirds of the global total. In 2008 around 1.4 million people died from AIDS in sub-Saharan Africa and 1.9 million people became infected with HIV. Since the beginning of the epidemic, more than 14 million children have lost one or both parents to HIV/AIDS. Of the 22.4 million people in Africa currently infected with HIV, only 30% of the 7 million people in immediate need of treatment are receiving it.

### **Tuberculosis**

Globally, TB is second only to HIV/AIDS as a cause of illness and death of adults, accounting for nearly nine million cases of active disease and two million deaths every year. Although it has only 11% of the world's population, Africa accounts for more than a quarter of this global burden with an estimated 2.4 million TB cases and 540,000 TB deaths annually. There is resurgence of TB in Africa due to the link between TB and HIV/AIDS. In Africa, TB is the leading killer of people living with HIV/AIDS. About 30% of the inhabitants of Sub-Saharan Africa are latently infected with *Mycobacterium tuberculosis* and these people at greater risk of developing active TB if they are also immunologically weakened by a concurrent HIV infection. HIV-positive people are also more likely to develop TB when newly infected or re-infected with *M. tuberculosis*.

Africa is said to have a double burden of diseases. One may say Africa has a triple burden of disease. Firstly, non communicable diseases (NCDs) such as heart disease, hypertension and stroke that are affected by lifestyle are increasing on the continent. The World Heart Federation (WHF) estimates that 17.1 million people die every year from heart disease and stroke and 80% of these deaths occur in

developing countries. The total projected deaths due to chronic NCDs in Africa in 2005 were about 2.5 million. Over the next 10 years in WHO Africa Region 28 million will die from chronic diseases.

Secondly, the continent has not been able to deal with many of the infections and communicable diseases, including childhood diseases that are no longer prevalent in the developed world.

Thirdly, whilst the world is focused on controlling the spread infections such as of HIV/Aids, tuberculosis and malaria and raising awareness on some non-communicable diseases such as hypertension and stroke in Africa the increasing onslaught of cancer has been largely overlooked and ignored.

In 2002, there were 6.7 million cancer deaths worldwide with less than 5% of these in sub-Saharan Africa. According to the World Health Organization (WHO), by 2020, African states will account for more than a million new cancer cases per year out of a total of 16-million cases worldwide and that should present trends continue Africa is expected to have the highest incidence of cancer by 2030 (1, 2, 3).

The irony of the situation is that infectious agents play a role in the development of many of these cancers. The growing evidence of the role of infectious agents oncogenesis led the WHO to estimate in 1996 that up to 84% of cases of cancer are attributable to viruses, bacteria, and parasites and that worldwide more than 1.5 million (15%) new cases each year could be avoided by preventing the infectious disease associated with them (4, 5, 6). In Africa it is estimated that 26.3% of new cases could be prevented with appropriate measures.

The link between infectious disease and cancer dates back to the beginning of the last Century. In 1911, Peyton Rous used cell-free filtered extract of a chicken sarcoma to establish an association between cancer and an infectious agent – the Rous sarcoma virus (7, 8). Recent developments in techniques used to detect microbial genomes and investigate their biological properties have led to a definitive role for viral, bacterial and parasitic infection in human carcinogenesis.

### **How infectious agents cause cancer**

The major mechanisms by which infectious agents can promote and maintain tumor formation can be divided broadly into three main categories:

1. Induction of chronic inflammation as a result of a continuing immune response to a persistent infection.
  - a. Hepatitis B virus (HBV), associated with liver cancer, which continually replicates in the liver, setting up a chronic state of inflammation leading to cirrhosis and cancer;
  - b. Chronic inflammation of the bladder mucosa by the blood fluke *Schistosoma haematobium*
  - c. Infection of the stomach mucosa by the gram-negative bacterium *Helicobacter pylori* can both directly contribute to cancer formation through persistence within the host causing chronic inflammation.
2. Second, oncogenesis can occur through virus-induced transformation. This is due to the persistence of the viral genome in a latent form in an infected cell, either without replication, as with Epstein-Barr virus (EBV), which infects B lymphocytes, or through integration of the viral genome into a host-cell chromosome, as with human papillomavirus (HPV), the cause of cervical cancer.
3. The third mechanism is the chronic suppression of the immune system by the infectious agent, such as the immunodeficiency (AIDS) caused by HIV infection. A compromised immune system can result in an increased incidence of infection-driven tumors by weakening the immune control especially immunosurveillance for cancer cells.

## Viruses

Only a few viruses that infect human cells actually cause cancer. Worldwide, the WHO International Agency for Research on Cancer estimated that in 2002, 17.8% of human cancers were caused by infection, with 11.9% being caused by one of seven different viruses. The viruses linked to cancers in humans in sub-Saharan Africa are the Epstein-Barr virus (EBV), associated with Burkitt's lymphoma, hepatitis B virus (HBV) and hepatitis C virus (HCV), both associated with cancer of the liver, human papillomaviruses (HPV), associated with cancer of the cervix, human T lymphotropic virus type 1 (HTLV-1) associated with adult T-cell leukemia, and human herpesvirus 8 (HHV-8), associated with Kaposi sarcoma.

### Epstein Barr Virus

Epstein-Barr virus (EBV) also known as Human Herpesvirus 4 (HHV4), is a member of the herpesvirus family of DNA viruses and one of the most common viruses in humans. EBV is named after Michael Epstein and Yvonne Barr, who, together with Bert Achong, discovered the virus in 1964, in cells cultured from the tumor specimens sent to them from Mulago Hospital in Uganda.

EBV is found in all regions of the world. The Centers for Disease Control (CDC) estimates that 95 percent of all adult Americans between the ages of 35 and 40 years have been infected, and is more prevalent in adults than children and adolescents. In Africa, however, most children have been infected by EBV by the age of three years old. Once EBV infects a person, it remains in the human body for (9). The primary site of Epstein-Barr virus (EBV) infection is the oropharyngeal cavity. Children and teenagers are commonly afflicted usually after oral contact.

In infected persons Epstein-Barr virus establishes a latent growth-transforming infection of its main target cell, the B lymphocyte. The growth of latently-infected B cells is normally controlled by the host immune response, particularly the T cell response, and so the great majority of people are able to carry this potentially dangerous virus all their life without any ill effect. Under certain conditions, especially in the immune-compromised state as may be caused by malnutrition and malaria in tropical Africa long-term virus carriage can result in the appearance a number of EBV-positive tumours such as Burkitt's lymphoma and nasopharyngeal carcinoma. Of particular importance in Africa is Burkitt's lymphoma.

Burkitt's lymphoma was first described in 1957 by Denis Parsons Burkitt, an Irish surgeon (10). It is a type of Non-Hodgkin's lymphoma and is most common in equatorial Africa, in the so-called "lymphoma belt," a region that extends from West to East Africa between the 10th degree north and 10th degree south of the equator and continues south down the Eastern coast of Africa. This belt corresponds to malaria endemic areas of Africa. In these endemic areas the annual incidence is 6–7 cases per 100 000 and with peak incidence at 6 or 7 years of age. It is responsible for 50% of cancer deaths in children in Uganda and central Africa. Burkitt's lymphoma is the most common childhood cancer in many African countries. In Ghana it represents 37% of all childhood tumors. The rates for other countries are: Nigeria 45.4%, Ethiopia, 25.4% and Kenya 56.5% (11, 12, 13, 14).

The endemic form of Burkitt's lymphoma is characterized by rapid enlargement of the patient's jaw, loosening of the teeth, protruding eyeballs, or an abdominal tumor in the region of the kidneys or ovaries.

Malaria and Epstein-Barr virus (EBV) are known cofactors in its development of Burkitt's lymphoma (15). Research suggests that *P. falciparum*-derived proteins can lead to a direct reactivation of EBV during acute malaria infection, increasing the risk of Burkitt lymphoma development for children living in malaria-endemic areas. Burkitt's lymphoma commonly affects the jaw bone, forming a huge tumor mass. It responds quickly to chemotherapy treatment, namely cyclophosphamide, but recurrence is common.

### Hepatitis B virus (HBV), Hepatitis C virus (HCV) and Liver Cancer

Hepatitis B (HepB) is a major public health problem worldwide. Approximately 30% of the world's population, or about 1.8 billion persons, have serologic evidence of hepatitis B virus (HBV) infection. Of these, an estimated 350 million have chronic HBV infection and at least

625 000 chronically infected persons die each year from liver cancer and cirrhosis. Liver cancer is the third most common cancer in the world.

Liver cancer is one of the commonest cancers in Africa. In Ghana liver cancer is the number one cause of cancer deaths in males and the third in females. In The Gambia for example, liver cancer is the commonest form of cancer among males and the second commonest in females. The age-adjusted rates are: 34 per 100,000 and 11 per 100,000 in males and females respectively. The commonest histological type of liver cancer in sub-Saharan Africa is hepatocellular carcinoma (HCC) and it is associated with persistent infection with Hepatitis B virus (HBV) and Hepatitis C virus (HCV) (16). Again in The Gambia case-control studies showed that HBV infection is universal and chronic carriage of the virus is in the range of 15-20%. This classifies the country among the highly endemic areas for HBV infection. Alcohol abuse is also an important contributing factor. All of these diseases cause continual damage to the liver, which can result in cirrhosis that then leads to cancer.

In Africa because of the association of liver cancer with hepatitis B, the disease usually develops in people in their 30s and 40s, as opposed to other areas of the world, where they are in their 60s and 70s. This is because it generally takes about 30 years of chronic damage to the liver before the cancer grows large enough to become obvious.

Hepatitis B can be transmitted through contaminated blood products or used needles or sexual contact but it is frequently transmitted from mother to child at birth or even biting among children at play. In Africa cases of liver cancer occur in individuals who have been infected with chronic hepatitis B virus most of their lives.

Transmission of hepatitis C infection usually requires direct contact with infected blood, either from contaminated blood products or needles. HCV is also associated with the development of liver cancer but because the prevalence of hepatitis C in Africa is about 3% on the average, the percentage of cases of liver cancer attributable to hepatitis C infection alone may be small.

### **Human Immunodeficiency Virus (HIV) and Cancer**

According to WHO World Health Reports, sub-Saharan Africa is more heavily affected by HIV and AIDS than any other region of the world. The average prevalence rate is 6.1%, but it ranges from less than 1% to over 20% depending on the area in Africa. An estimated 22.4 million people are living with HIV in the region - around two thirds of the global total. In 2008 around 1.4 million people died from AIDS in sub-Saharan Africa and 1.9 million people became infected with HIV. Since the beginning of the epidemic, more than 14 million African children have lost one or both parents to HIV/AIDS.

Many people infected with HIV have a substantially higher risk of being infected with other viruses that increase the risk of certain cancers (17). The following are the most important of these cancer-causing viruses:

- Human herpes virus 8 (HHV8), also known as Kaposi Sarcoma-associated herpes virus (KSHV) is the cause of Kaposi sarcoma.
- Epstein Barr virus (EBV) causes some subtypes of non-Hodgkin and Hodgkin lymphoma.
- Human papillomavirus (HPV) causes cervical cancer and some types of anal, penile vaginal, vulval and head and neck cancer.
- Hepatitis B virus (HBV) and Hepatitis C virus (HCV) both can cause liver cancer.

Three of these cancers are usually referred to as "AIDS-defining cancers" or "AIDS-defining malignancies" (18): These are Kaposi sarcoma, non-Hodgkin lymphoma and cervical cancer. Diagnosis of any one of these cancers marks the point at which HIV infection has progressed to AIDS.

Other, less common types of cancer that may develop in people with HIV/AIDS are Hodgkin lymphoma, angiosarcoma, anal cancer, liver cancer, mouth cancer, throat cancer, lung cancer, testicular cancer, colorectal cancer, and multiple types of skin cancer including basal cell carcinoma, squamous cell carcinoma, and melanoma. These are termed non-AIDS-defining cancers and may occur even if patients take HIV medications and have healthier immune systems.

The introduction of highly active antiretroviral therapy (HAART) in the mid-1990s greatly reduced the incidence of Kaposi sarcoma and non-Hodgkin lymphoma among people infected with HIV. It has,

however, not reduced the incidence of cervical cancer, which has essentially remained unchanged. Moreover, the incidence of several non-AIDS-defining cancers, particularly Hodgkin lymphoma and anal cancer, may have been increasing among HIV-infected individuals since the introduction of HAART.

### **Human papillomaviruses (HPVs)**

These are a group of more than 100 related viruses. They are called papillomaviruses because certain types may cause warts, or papillomas, which are benign tumors which grow on hands and feet. Others cause growths in the throat or genital area. HPV types 6 and 11 cause genital warts and are not associated with increased cancer risks. HPV types 16, 18, 31, 33, and 35 are linked to cervical cancer. HPV types 16 and 18 account for 70% of cases of cervical cancer (19).

HPV types associated with genital infections are transmitted sexually, primarily through skin-to-skin contact during sexual activity. HPV can also be spread through oral sex. The prevalence HPV infection in sexually active young women is as high as 40%.

Cancer of the cervix is the leading cancer in women in Sub-Saharan Africa with an estimated 70,700 new cases occurring in 2002. Estimated rates for eastern and southern Africa of 30 to 60 per 100,000 are higher than those found in the rest of Sub-Saharan Africa (20 to 35 per 100,000). Worldwide there are more than 274,000 deaths from cervical cancer each year with 80% occur in developing countries. Africa has nine times the incidence of cervical cancer compared to the USA, but 24 times the mortality. The incidence of cervical cancer appears to be increasing in the developing world, whereas incidence is falling in developed nations, largely due to systematic screening activity and vaccination program targeted at girls aged 10-12 years.

Two vaccines (Cervarix and Gardasil) are available to protect females against HPV types 16 and 18 which cause most cervical cancers. Protecting African women against the virus requires vaccinating young women aged 10-12 three times in six months. This exercise may present a unique challenge in Africa, where girls of this age may not be in school, where immunization is easiest. At the cost of US\$360 a course per girl the current HPV vaccines are expensive and beyond the reach of African countries. It will be critical to reach agreement over means of providing affordable vaccines throughout Africa.

### **HHV-8**

HHV-8 is a type of rhadinovirus. It is also known as Kaposi's sarcoma associated herpes virus (KSHV) and is responsible for causing diseases such as Kaposi's sarcoma (KS), lymphoproliferative disorders, primary effusion lymphoma (PEL), and multicentric Castlemans disease (MCD) (20). This virus only attacks immunocompromised individuals. KSHV is uncommon in the general population of the US and northern Europe (less than 3%). Higher infection rates are seen in Mediterranean and Middle Eastern countries (5%--20%). The highest rates are found in sub-Saharan Africa and in some Amazonian populations (more than 50%).

### **Kaposi Sarcoma (KS)**

Kaposi's sarcoma was originally described by Moritz Kaposi a Hungarian dermatologist practicing at the University of Vienna, Austria in 1872. It became more widely known as one of the AIDS defining illnesses in the 1980s. The viral cause for this cancer was discovered in 1994 by Yuan Chang and Patrick Moore at Columbia University in New York City who isolated genetic pieces of a virus from a KS lesion which they subsequently showed was the eighth human herpesvirus (HHV-8) (21). In the United States and Europe, sex between men may be an important route of transmission. There is no strong evidence of sexual transmission of HHV8 in Africa. Rather research results from South Africa strongly suggest that transmission of HHV-8 in Africa is mostly from mother to child and between siblings.

Four clinically different KS forms are now recognized:

- a) Classical or sporadic KS (CKS) originally described as a slow growing, indolent tumor mostly developing in the extremities of elderly males of eastern and Mediterranean Europe.
- b) Endemic KS (EKS) was predominant in eastern and central sub-Saharan Africa before the AIDS epidemic and clinically similar to CKS. In these areas, such as Zimbabwe, KS is the most

frequently reported cancer. A more fulminant and fatal form is seen in children where it is often lymphoglandular with or without skin involvement.

- c) Acquired immunodeficiency syndrome (AIDS)-associated KS (AKS), the most frequent tumor of human immunodeficiency virus type I (HIV-I) infection and the most aggressive and rapidly growing form of KS in AIDS, with early dissemination in the skin and viscera.
- d) Iatrogenic KS (IKS), seen in drug related immunosuppressed patients, e.g. transplant patients, emphasizing the importance of immune disturbance as a co-factor in the pathogenesis of IKS and AKS, and possibly also EKS.

Kaposi sarcoma tumors are divided into three groups, based on appearance, with much overlap: nodular, infiltrating and lymphatic lesions.

On the average, endemic African Kaposi sarcoma accounts for 10% of cancers in Africa with a male-to-female ratio of 15:1. The disease is more prevalent in East Africa and there has been a significant increase in the incidence of Kaposi sarcoma in the era of AIDS. In Uganda, Kaposi sarcoma makes up almost one half (48.9%) of cancer cases in men and 17.9% in women. The incidence is 30.1 cases per 100,000 for men and 11 cases per 100,000 for women. Again in Uganda lymphadenopathic Kaposi sarcoma accounts for 12% of total cases of Kaposi sarcoma but is responsible for 42% of childhood cases. In Zambia Kaposi sarcoma represents 25% of childhood cancers and 80% of patients are HIV seropositive (22, 23).

### **Prostate Cancer & viral infection**

Prostate cancer is the predominant genitourinary tumour, accounting for nearly two-thirds of cases (24). In Ghana it is the second commonest of cancer mortality after liver cancer (25). There is growing evidence that xenotropic murine leukemia-related virus (XMRV), a gammaretrovirus similar to viruses known to cause cancer in animals may be responsible for aggressive prostate cancer. Researchers at Columbia University and the University of Utah found the virus in more than a quarter of some 300 prostate cancer tissue samples, especially in malignant cells. Other workers in Cleveland clinic, Ohio have reported that both human semen and one of its major components, acid phosphatase, increase XMRV infectivity for prostate cells 100-fold. They also found the virus in prostatic secretions of men with prostate cancer. This finding suggests that XMRV is sexually transmitted (26, 27, 28).

### **Bacteria**

#### **Buruli Ulcer disease**

Clinical features of Buruli ulcer as we know it today dates back to 1897 when, Sir Albert Cook, a British physician working at the Mengo Hospital in Kampala, Uganda, described skin ulcers that characterized the disease. In 1948, Professor Peter MacCallum and his colleagues in Australia provided a detailed description of the disease among six patients from the Bairnsdale area near Melbourne (29).

In the 1960s, many cases of the disease were seen and reported from the in Buruli County (now called Nakasongola District) in Uganda, giving rise to the most widely used name for the disease – Buruli ulcer. Over the last two decades Buruli ulcer disease has emerged rapidly in several parts of the world, particularly in West Africa.

#### **Prevalence**

Buruli ulcer is endemic in most parts of Africa. In West Africa Buruli ulcer is currently endemic in Benin Republic, Cote d'Ivoire, Ghana, Guinea, Burkina Faso, Liberia, Nigeria, Sierra Leone, Benin and Togo. In these countries the incidence of Buruli ulcer is steadily rising and is now the third leading cause of mycobacterial infection in healthy people, after tuberculosis and leprosy. In Côte d'Ivoire, approximately 24 000 cases were recorded between 1978 and 2006. In Benin, nearly 7000 cases were recorded between 1989 and 2006; in Ghana more than 11 000 cases have been recorded since 1993(30). A survey by Amofa and associates at the Ministry of Health in Ghana gave an overall crude national prevalence rate of active lesions as 20.7 per 100,000, but in the most disease-endemic district the rate was estimated to be 150.8 per 100,000.

## Cause & Transmission

Buruli Ulcer is an infectious disease by *Mycobacterium ulcerans*. Its mode of transmission is not known with certainty but evidence suggests that aquatic insects of the order Hemiptera (Naucoridae and Belostomatidae), which harbour the *Mycobacterium ulcerans* in their salivary glands may be involved. Trauma to contaminated skin sites appears to be the means by which the organism enters the body. Once introduced into the subcutaneous tissue the organism proliferates and elaborates a toxin called mycolactone. Mycolactone has both immunosuppressive and cytotoxic properties, which explains the lack of host symptoms, such as fever, malaise, or adenopathy. Mycolactone is responsible for the extensive tissue necrosis seen in Buruli ulcers. There is no evidence of transmission from person to person.

## Clinical Features

The resulting necrosis then provides a favourable milieu for further proliferation of the organism. The early stage of infection is characterized by a painless dermal papule or subcutaneous nodule. As the disease progresses these papules or nodules break down to form non-pyogenic, necrotizing lesions with extensively undermining edges developing in the skin, and occasionally extending to adjacent bones. Lesions heal with scarring, which is a significant source of morbidity.

Hypertrophic scars and keloids may develop at infection and surgical sites including skin graft donor sites. Squamous cell carcinoma (Marjolin's ulcer) may appear in an unstable scar or persistent ulcer many years after initial infection with *M. ulcerans*. The disease is more severe in impoverished inhabitants of remote rural areas. All ages and sexes are affected, but about 70% of patients are children under the age of 15 years. Mortality due to the disease is low, but morbidity is high. Complications include contracture deformities, amputation of limbs, and involvement of the eye, breast and genitalia. In some localities 20–25% of those with healed lesions are left with disabilities that have a long term social and economic impact. The current economic and social burden imposed by Buruli ulcer is enormous. In Ghana, the average cost of treatment per patient is estimated to be US\$ 780.

## *Helicobacter pylori* infection and cancer

*Helicobacter pylori* (*H. pylori*) is a gram negative, spiral shaped bacterium that can inhabit various areas of the stomach, particularly the antrum. It was first discovered in the stomachs of patients with gastritis and stomach ulcers in 1982 by Dr. Barry Marshall and Dr. Robin Warren in Australia. *H. pylori* secretes urease, an enzyme that converts urea to ammonia. Ammonia reduces the acidity of the stomach, making it a more hospitable home for *H. pylori*. *H. pylori* is thought to be spread either through contaminated food and water or through direct mouth-to-mouth contact. In most populations children living in crowded conditions and with a lower socioeconomic status as is the case in most African communities are more likely to become infected. It is estimated that more than 90% of people in sub-Saharan Africa have the bacterium. In the developed world this figure is about 40 to 50%. Despite the high prevalence rate only about 2% to 20% of people infected with *H. pylori* will develop ulcers.

*H. pylori* causes a chronic low-level inflammation of the stomach lining that leads to the development of stomach cancer (31, 32).

Gastric cancer is the second most common cancer worldwide, with an estimated 930 000 new cases diagnosed with 700,000 deaths each year and almost two-thirds of these occurring in the developing countries. Five-year survival statistics in gastric cancer are poor (less than 5%).

Countries with high *H. pylori* infection rates normally have higher gastric cancer incidence, as is seen in Asian countries. However, although *H. pylori* infection is quite common in Africa gastric cancer incidence is not as frequent as expected. This anomaly has been referred to as the 'African enigma'.

Apart from non-cardia gastric cancer, some evidence links *H. pylori* to other neoplasms such as gastric mucosa-associated lymphoid tissue (MALT) lymphoma, and perhaps pancreatic cancer and also to cardiovascular disease such as coronary artery disease (33)

## **Chlamydia trachomatis**

*Chlamydia trachomatis* is a relatively common gram-negative bacterium that can infect the female reproductive system. It is spread through sex. Most infected individuals have no symptoms but studies suggest that women whose blood test results show past or current *Chlamydia* infection are at greater risk for cervical cancer than are women with a negative blood test. There is, however, no evidence that *Chlamydia* by itself can cause cancer. But it may work with HPV in some way that promotes cancer growth. Researchers found that women who had *Chlamydia* along with HPV were more likely to still have HPV when they were re-tested later than the women who had not had *Chlamydia* (34, 35). *Chlamydia* seems to affect how long cancer-promoting HPV stays in the cervix.

## **Parasites**

### **Schistosomiasis and bladder cancer**

Schistosomiasis is sometimes referred to as "bilharziasis" after Theodor Bilharz who first identified the parasite in 1852. It is a parasitic infection caused by trematodes, also known as flatworms or flukes, of the genus *Schistosoma*. It is the second most socioeconomically devastating parasitic disease after malaria. There are many species of animal schistosomes worldwide, with five responsible for the majority of human infections: *S. haematobium*, *S. mansoni*, *S. japonicum*, *S. intercalatum*, and *S. mekongi*. Infection with schistosomes does not always result in clinical disease, and many infections are asymptomatic.

*S. haematobium*, the cause of urinary schistosomiasis, is the most important schistosome in Africa. *S. haematobium* infection has been endemic in Egypt at least since the time of the ancient Pharaohs, as indicated by the presence of calcified ova in the Egyptian mummies (36). It is a widespread endemic disease currently found in 75 countries. WHO estimates that in sub-Saharan Africa more than 200 million people residing in rural and agricultural areas are infected and that between 500 million and 600 million people are at risk of infection (37). It is estimated that 11,000 men and 2,300 women in sub-Saharan Africa die each year from schistosoma-related cancer of the bladder.

### **Transmission cycle of *S. haematobium***

The eggs of the blood flukes leave the human body in urine, hatch in water and liberate larvae called miracidia that penetrate freshwater snail hosts. After several weeks of growth and multiplication, cercariae emerge from the snails and penetrate human skin during contaminative water contact (wading, swimming, washing and farming). Cercariae transform and subsequently migrate through the lungs to the liver where they mature into adult worms. These adult worms move to the veins of the urinary tract. Approximately six weeks after the initial infection, the females begin to produce hundreds of eggs a day and approximately half of the eggs are excreted in the urine. If the excreted eggs reach freshwater, they hatch into free swimming miracidiae that will infect the appropriate snail species. Further development occurs within the snail and, after three to five weeks, new generations of cercariae emerge from the snail ready to infect other mammalian hosts.

Eggs that are not excreted are trapped mainly in the tissues around the bladder and the host's granulomatous inflammatory response to these eggs is responsible for most of the damage associated with chronic schistosomiasis such as haematuria, ureteric obstruction and bladder cancer.

In North America and Europe, transitional cell carcinoma accounts for over 90% of urinary bladder cancers. In sub-Saharan Africa where infection with *S. haematobium* is prevalent, the overall incidence of bladder cancer is much higher and squamous cell carcinoma (SCC) accounts for approximately 75 percent of cases.

### **Why disease thrives in Africa**

The conditions that allow infectious diseases and cancer to thrive in Africa include the following:

1. Malnutrition- Africa is the only continent where the green revolution has not yet taken place. Consequently, food is scarce in many parts of the continent and protein-calorie malnutrition is

widespread both among adults and children. Malnutrition increases the risk of infection and infectious disease and the development of cancer. The World Health Organization cites malnutrition as the gravest single threat to the world's public health.

2. Access to safe drinking water: more than 60% of Africa's population has no access to safe drinking water. Waterborne diseases claim more than 3 million lives each year, mostly as a result of dysentery and cholera with the highest toll among children.
3. Poverty is a major determinant in the development, spread and management of infectious diseases and cancer in Africa. When people are poor their children are often not vaccinated against childhood diseases. Even though the vaccine may just cost a few cents they are too poor to be able to afford the vaccine or even to afford the cost of transportation to vaccination centres where the vaccines are free.
4. Ignorance & suspicion: The poor and uneducated often do not understand the microbial theory of development of infectious disease or mechanisms of infectious disease transfer and thus cannot take steps to protect themselves and others. Many indigenous African populations attribute diseases, including infections and cancers, to the work evil spirits. Ignorance of the nature of disease is a major factor for the late presentation of illness, especially cancer, to treatment centres.
5. Suspicion due to lack of information and sometimes outright ignorance may prove formidable risk in the control of disease in Africa. A typical example was the rejection of polio vaccine in Nigeria in 2002-2003.

In October 2003 the governors of three states in northern Nigeria - Kano, Kaduna and Zamfara - suspended polio immunization because they believed that polio vaccination was being used as a ploy by Western countries to inject people with certain chemicals to reduce fertility or infect their people with HIV/AIDS in order to reduce the population of Muslims. After several months of investigations the vaccine was found to be safe.

In the meantime, polio, which had been eradicated in almost all of Nigeria made a comeback, not only in Nigeria, but also in and 20 previously polio-free countries across west and central Africa, including Benin, Togo, Ghana, Burkina Faso, Cameroon and Central African Republic, the Horn of Africa, and as far away as Indonesia and Yemen. The outbreaks in these 20 countries resulted in 1,517 cases, and cost upwards of 500 million US Dollars in international emergency outbreak response funds.

6. Sanitation- More than 75% of Africa's population live in villages or communities with inadequate or no sanitary facilities. Most homes do not have toilets and people tend to use poorly constructed public toilets or open fields. The slightest downpour leading to contamination of water bodies and food items, especially vegetables such as salad leaves, tomatoes, onions and carrots. Increasing level of rubbish and solid wastes in African communities, poor collection and refuse handling services, lack of recycling facilities and inadequate disposal sites all contribute to increase the burden of infectious diseases. Discarded tins, bottles, plastic bags when filled with rain water provide good breeding sites for disease-carrying insects. Pollution of Africa's coastal waters from raw untreated sewage is a key factor in the outbreaks of diarrhoeal diseases, especially cholera.
7. Poor hygienic culture may be as a result of ignorance or lack of infrastructure, especially water supply. Transmission of trachoma, an infectious eye disease can be minimized when infected individuals wash their faces regularly with clean water. But where there is no water this becomes a problem. Most rural and deprived communities in Africa do not have running water. It is therefore virtually impossible for people to wash their hands with water and soap after using the toilet.
8. Lack of scientific and technical capacity- It is always said that the poverty gap is a technology gap. A lot of Africa's problem exist and persist because of lack of technology. Our modern world is essentially driven by technology. Energy, agriculture, medicine and health, clean air and water, transportation, sanitation, management and conservation of natural resources -- all are based

ultimately in science and technology. Any population that lacks the capacity to utilize technology cannot adequately prevent, detect and treat diseases effectively.

9. Disasters either through wars or natural causes, which unfortunately are rife in Africa, often lead to disruption of water and sanitation systems or the displacement of populations to inadequate and overcrowded camps leading to increase the risk of cholera transmission should the bacteria be present or introduced.
10. Enormity of problems- The enormity of a problem can be a serious disincentive to any effort to control a disease. For example unlike the case in many island nations such as Cuba, Singapore and Malaysia, continental sub-Saharan Africa was never a part of the global malaria eradication program. It is thought that the severity of the disease, the density and efficiency of *Anopheles gambiae*, the problem of eradicating the disease over such a large land mass with recurrent reinvasions, high costs, and subsequent maintenance must have all contributed to the lack of will to undertake an eradication program.
11. Overdependence syndrome- Africa in a way has developed developmental inertia. Most sub-Saharan countries on their own do not initiate programs to solve their problems. Almost all the initiatives to combat disease are from the developed world. So long as Africa does not take initiative and work hard with passion to meet its challenges the problems of underdevelopment, malnutrition, infectious disease and cancer and weak health systems will persist.

## **What can be done?**

### **Vaccination**

1. Hepatitis B: At least 85%-90% of HBV-associated deaths are vaccine-preventable (200,000).
2. HPV vaccine: HPV vaccine would eradicate 70% of all known cervical cancers within a generation, saving the lives of almost 200,000 women per annum - the vast majority of whom live in the developing world. In Africa about 90,000 women will be saved

### **Safe drinking water**

1. Safe drinking water will prevent 3 million deaths from diarrhoeal diseases.
2. Keep people, especially children, away from water bodies that will expose them to diseases such as schistosomiasis, Guinea worm, Buruli ulcer, thereby preventing another 20,000 deaths from schistosoma related diseases and more that 200,000 severe physical disability from Buruli ulcer.
3. The average cost of treating a BU case in Ghana was estimated to be US\$ 780 per patient in 1994–1996, an amount which far exceeded per capita government spending on health.

### **Effective control of HIV/AIDS & related diseases**

1. Save 25% of Africa's population from dying
2. Improve human life expectancy by as much as 30 years
3. Save 30 million children in 19 countries from losing their parents
4. Save Namibian nearly 8 percent of GDP, Kenya 14.5% of GDP
5. Zimbabwe Commercial Farmers' Union will no longer lose 50% of production.
6. 6 to 8 percent loss of profits and 5% loss of productivity to AIDS-related costs to African companies such as absenteeism, productivity declines, health and insurance payments, and recruitment and training will be markedly reduced

## Malaria

1. Sub-Saharan Africa loses \$12 billion dollars each year
2. Stunts Africa's economic growth by 1.3% per year
3. Consumes up to 25% of household income in endemic countries
  - a. Nigeria and Kenya spend 13 and 5 percent, respectively, of total household income on malaria

## References

1. Beaulieu N, Bloom D, Bloom R, Stein R. Breakaway: The global burden of cancer - challenges and opportunities. The Economist Intelligence Unit. 2009.
2. Cancer control opportunities in low- and middle-income countries. Washington, DC: Institute of Medicine of the National Academies, National Academies Press; 2007.
3. Ferlay J, Bray F, Pisani P, Parkin DM. GLOBOCAN 2002: Cancer incidence, mortality, and prevalence worldwide: International Agency for Research on Cancer; 2003.
4. Boyle P, and Levin, B. World Cancer Report 2008. Lyon: International Agency for Research on Cancer; 2008.
5. Kanavos P. The rising burden of cancer in the developing world. *Annals of Oncology* 17 (Supplement 8): viii15–viii23, 2006.
6. Infectious diseases and cancer. 1996. In: *The World Health Report 1996. Fighting disease fostering development*. Geneva: World Health Organization; 1996. p. 59-62.
7. *J Exp Med*. 2005 February 7; 201(3): 320.(Peyton Rous)
8. Rous P. Transmission of a malignant new growth by means of a cell-free filtrate. *JAMA* 1911; 56:198.
9. Longe, J. L. 2006. *The Gale Encyclopedia of Cancer*, 2nd edition. Detroit, MI.: Gale. ISBN 1414403623
10. Burkitt D (1958). "A sarcoma involving the jaws in African children". *The British journal of surgery* 46 (197): 218–23.
11. Akang EE. Tumors of childhood in Ibadan, Nigeria (1973–1990). *Pediatr Pathol Lab Med* 1996; 16: 791-800.
12. Pearce MS, Parker L. Childhood cancer registrations in the developing world: still more boys than girls. *Int J Cancer* 2001; 91: 402-406.
13. Ocheni S, Okafor CO, Emodi IJ, et al. Spectrum of childhood malignancies in Enugu, Nigeria (1999–2004). *Afr J Med Med Sci* 2005; 34: 371-375.
14. RK Gyasi and Y Tettey, Childhood Deaths from Malignant Neoplasms in Accra, Ghana *Med J*. 2007 June; 41(2): 78–81.
15. Evans, A.S., Mueller, N.E. "Epstein-Barr Virus and Malignant Lymphomas." *Viral Infections of Humans: Epidemiology and Control*. New York: Plenum, 1997; 895-933.
16. Chuang WL, Chang WY, Lu SN, Su WP, Lin ZY, Chen SC, et al. The role of hepatitis B and C viruses in hepatocellular carcinoma in a hepatitis B endemic area. A case-control study. *Cancer* 1992; 69:2052-4.
17. Engels EA, Biggar RJ, Hall HI, et al. Cancer risk in people infected with human immunodeficiency virus in the United States. *International Journal of Cancer* 2008; 123(1):187–194.

18. Silverberg MJ, Abrams DI. AIDS-defining and non-AIDS-defining malignancies: Cancer occurrence in the antiretroviral therapy era. *Current Opinion in Oncology* 2007; 19(5):446–451.
19. Parkin DM (2006). "The global health burden of infection-associated cancers in the year 2002". *Int. J. Cancer* 118 (12): 3030–44. Types 16 18
20. Cesarman E, Chang Y, Moore PS, Said JW, Knowles DM. Kaposi's sarcoma-associated herpesvirus-like DNA sequences in AIDS-related body-cavity-based lymphomas. *N Engl J Med* 1995; 332(18):1186-91.
21. Chang Y, Cesarman E, Pessin MS, et al. Identification of herpesvirus-like DNA sequences in AIDS-associated Kaposi's sarcoma. *Science*. Dec 16 1994; 266(5192):1865-9.
22. Wabinga HR, Parkin DM, Wabwire-Mangen F, Mugerwa JW. Cancer in Kampala, Uganda, in 1989–91: changes in incidence in the era of AIDS. *Int J Cancer* 1993;54:26–36.
23. Bassett MT, Chokunonga E, Mauchaza B, Levy L, Ferlay J, Parkin DM. Cancer in the African population of Harare, Zimbabwe, 1990–1992. *Int J Cancer* 1995; 63:29–36.
24. Klufio GO, *West Afr J Med*. 2004 Apr-Jun; 23(2):131-4.
25. Wiredu EK, Armah HB, *BMC Public Health*. 2006 Jun 20; 6:159.
26. *Nature Reviews Urology* 7, 392-402 (July 2010)
27. *PNAS September 22, 2009 vol. 106 no. 38 16351-16356*
28. *Proc Natl Acad Sci U S A*. 2009 September 22; 106(38): 16351–16356.
29. MacCallum P, Tolhurst JC, Buckle G, Sissons HA. A new mycobacterial infection in man. *J Pathol Bacteriol* 1948; 60:93-122.
30. WHO Fact sheet N°199 Revised March 2007
31. Pinto Santini, D. and N.R. Salama, The biology of *Helicobacter pylori* infection, a major risk factor for gastric adenocarcinoma. *Biomarkers Prev*, 2005. 14(8): p. 1853-1858.
32. Parsonnet, J. and P.G. Isaacson, Bacterial Infection and MALT lymphoma. *N Engl J Med*, 2004. 350: p. 213-215.
33. Lehtinen, M., Dillner, J., Knekt, P., *et al.* (1996). Serologically diagnosed infection with human papillomavirus type 16 and risk for subsequent development of cervical carcinoma: nested case-control study. *British Medical Journal* 312, 537 - 539.
34. Hakama, M., Luostarinen, T., Hallmans, G., Jellum, E., Koskela, P., Lehtinen, M. *et al.*, (2000). Joint effect of HPV16 with *Chlamydia trachomatis* and smoking on risk of cervical cancer: antagonism or misclassification (Nordic countries). *Cancer Causes and Control* 11, 783 - 790.
35. Ragheb, M. 1956. Schistosomiasis of the liver: clinical, pathological and laboratory studies in Egyptian cases. *Gastroenterology* 30:631-636
36. Oliveira, G., Guilherme; Rodrigues N.B., Romanha, A.J., Bahia, D. (2004). "Genome and Genomics of Schistosomes". *Canadian Journal of Zoology* 82 (2): 375–90.