1. write on the cancer epidemiology in Africa generally,and Nigeria in particular.
2. Critically examine the involvement of angiogenic genes in the development and progression of osteosarcomas.

**BY**

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16/MHS03/022

ANA 404

HISTOPATHOLOGY

AN ASSIGNMENT SUBMITTED TO THE

DEPARTMENT OF ANATOMY,

FACULTY OF BASIC MEDICAL SCIENCES,

COLLEGE OF MEDICINE AND HEALTH SCIENCES,

AFE BABALOLA UNIVERSITY,ADO-EKITI,

EKITI STATE,NIGERIA

IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR

THE AWARD OF THE DEGREE OF

BACHELOR OF SCIENCE (B.Sc)

IN ANATOMY

1. write on the cancer epidemiology in Africa generally,and Nigeria in particular?

Answers

Cancer has received low priority for health care services in Sub-Saharan Africa. The reason is undoubtedly the overwhelming burden of communicable diseases, as illustrated by the proportions of deaths by major categories.Africa and for the whole world, made by the World Health Organization (WHO) of the percentages of deaths due to different causes in the year 2002 ([WHO 2004](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).From a purely objective point of view, therefore, concentration on health problems in Africa that have been largely solved in the developed world (infant and child mortality, maternal mortality, infectious diseases) appears eminently reasonable. Unfortunately, these "old" diseases coexist in Africa with the emergence of new ones, most prominently the acquired immune deficiency syndrome (AIDS), but also some of the noncommunicable diseases, such as hypertension, diabetes, accidents and violence ([Motala 2002](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Reza, Mercy, and Krug 2001](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Seedat 2000](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Walker et al. 2000](https://www.ncbi.nlm.nih.gov/books/NBK2293/)), and cancer. Cancer is not a rare disease in Africa. Even ignoring the huge load of AIDS-related Kaposi's sarcoma, the probability that a woman living in present-day Kampala or Harare will develop a cancer by the age of 65 years is only about 20 percent lower than that of her sisters in Western Europe. Yet the facilities for providing treatment for cancer cases in most of Africa are minimal, as illustrated by the sparse distribution of radiation therapy services in Africa ([Levin, El-Gueddari, and Meghzifene 1999](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

The noncommunicable diseases, such as cancers, are emerging health problems that need to be dealt with appropriately to sustain public health advances that have already been achieved. Increases in the prevalence of tobacco consumption and immunosuppression induced by the human immunodeficiency virus (HIV), coupled with such existing risk factors for cancer as alcohol; the high prevalence of cancer-associated infectious agents like human papillomaviruses (HPV), hepatitis B viruses (HBV), and human herpesvirus-8 (HHV8); and environmental exposure to toxins, such as aflatoxins, will have an important impact on future cancer patterns and incidence. Even despite declining overall life expectancy as a result of the HIV epidemic, Africans will continue to age, which will contribute to cancer's becoming an increased burden on health services, both in relative and absolute terms.

Until quite recently, knowledge of cancer patterns was based primarily on clinical and pathological case series from the 1950s and 1960s, which were the subject of several reviews that drew together information on the relative frequency of different types of cancer in different areas in order to piece together an overall picture ([Clifford, Linsell, and Timms 1968](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Cook and Burkitt 1971](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Oettlé 1964](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). Statistics on disease mortality are particularly sparse. Only about 0.25 percent of the population of Sub-Saharan Africa is covered by accurate death registration systems. The countries that have reasonably accurate death registration include islands like Mauritius and the Seychelles, which are unlikely to be representative of the region, and no country on the mainland of Sub-Saharan Africa has data of sufficient quality for the estimation of national mortality rates ([Mathers](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2005](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). Hence, reliance has to be placed on indirect measures of mortality and on the few cancer registries that do exist across Africa, now covering roughly 8 percent ([Parkin](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2003](https://www.ncbi.nlm.nih.gov/books/NBK2293/)) of this population. An exception to this has been South Africa, which until 1990 had almost complete death notification for whites, mixed race "coloureds," and Asian Indians, comprising about 20 percent of the population. Population group identifiers on death notification forms were removed in 1991 but reintroduced in 1998. National coverage of deaths in South Africa across all populations has now increased to over 90 percent ([Dorrington](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2001](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

Since the 1990s there has been a resurgence of interest in cancer incidence in Africa, and data from cancer registries from Sub-Saharan Africa have been published from West Africa in The Gambia ([Bah](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2001](https://www.ncbi.nlm.nih.gov/books/NBK2293/)), Mali ([Bayo](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 1990](https://www.ncbi.nlm.nih.gov/books/NBK2293/)), Guinea ([Koulibaly](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 1997](https://www.ncbi.nlm.nih.gov/books/NBK2293/)), and Côte d'Ivoire ([Echimane](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2000](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). Data from East Africa are available from cancer registries in Kampala, Uganda ([Wabinga](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2000](https://www.ncbi.nlm.nih.gov/books/NBK2293/)), and from southern Africa from the Zimbabwe Cancer Registry in Harare ([Chokunonga](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2000](https://www.ncbi.nlm.nih.gov/books/NBK2293/)), and the Malawi Cancer Registry in Blantyre ([Banda](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2001](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

Cancer registration in economically underdeveloped populations, such as all the countries of Sub-Saharan Africa, is a difficult undertaking for a variety of reasons ([Parkin](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2003](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). The major challenge is to ensure that all new cases of cancer are identified. Cases can be found only when they come into contact with health services: hospitals, health centers, clinics, and laboratories. When resources are restricted, the proportion of the population with access to such institutions may be limited, and the statistics generated will thus not truly reflect the pattern of cancer. The ease with which the cases can be identified also depends on the extent of medical facilities available and the quality of statistical and record systems already in place (for example, pathology request forms, hospital discharge abstracts, treatment records, and so forth). It is impossible to know, without an extensive population survey, what proportion of those with cancer never come into contact with modern diagnostic or treatment services, instead making use only of traditional healers or receiving no care at all.

In the past, studies have suggested that some sections of the population may have been underrepresented in hospital statistics, particularly older women and young men, both of whom were more likely to return to their rural homes to seek care ([Flegg Mitchell 1966](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). However, currently, this underrepresentation is probably rather rare in contemporary urban Africa. Most cancer patients will, eventually, seek medical assistance, although often at an advanced stage of disease. The situation in rural areas may be quite different, but almost all the present-day cancer registries are located in urban centers. From an epidemiological point of view, one must guess at how well the cancer profile from the urban areas reflects that in the country as a whole, given what is known of urban–rural differences in cancer patterns in other areas of the world.

The International Agency for Research on Cancer (IARC) has published the available data on cancer incidence and other cancer data from a variety of sources ([Parkin](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2003](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). Such data have also been used to prepare a set of estimates of incidence and mortality at the national level for the year 2002 ([Ferlay](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2005](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). These sources are extensively used in this chapter. We also draw upon the few available series from which it is possible to make some inferences about temporal trends in cancer incidence: the two cancer registries with data available in the 1960s—Kampala (Uganda) and Ibadan (Nigeria)—and the mortality data sets from South Africa referred to earlier.

According to the 2002 estimates of cancer incidence for the Sub-Saharan Africa region, about half a million (530,000) new cases of cancer occurred annually, 251,000 in males and 279,000 in females. world-standardized cancer rates were estimated to be 133 per 100,000 females and 136 per 100,000 males

**Cervical cancer**

Cancer of the cervix is the leading cancer in women in Sub-Saharan Africa with an estimated 70,700 new cases occurring in 2002 (the total in the whole continent was 78,900 cases). 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), but the reasons for this difference are unclear. In many developed countries, such as the United Kingdom and Sweden, mortality from cancer of the cervix declined between the early 1900s and the 1960s and then declined further as a result of the introduction of national screening programs ([Bergstrom, Sparen, and Adami 1999](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). However, in Bulawayo between 1963 and 1977 and in Kampala in the 1960s, 1970s, and 1990s, cancer of the cervix has appeared to increase in incidence over time ([Skinner](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 1993](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Wabinga](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2000](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). No increases over time were observed in Nigeria and South Africa ([Parkin](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2003](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

It was noted early that cervical cancer has quite marked differences in incidence according to classical demographic variables (social class, marital status, ethnicity, religion). Later, epidemiological studies (mainly case-control studies) showed a consistent association between risk and early age at initiation of sexual activity, increasing number of sexual partners of females or of their sexual partners, and other indicators of sexual behavior. These findings were strongly suggestive of a causative role for a sexually transmitted agent. It is now recognized that certain sexually transmitted oncogenic human papillomaviruses constitute the necessary cause of cervical cancer. However, additional independent risk factors include increasing number of pregnancies, exposure to oral contraceptives, smoking, and specific dietary patterns.

At the onset of the AIDS epidemic, cancer of the cervix was classified as an AIDS-defining cancer by the U.S. Centers for Disease Control and Prevention ([CDC 1993](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). But it is far from clear that HIV infection really increases the risk of invasive cervical cancer. No change in cervical cancer incidence has been demonstrated in some centers like Harare, where HIV/AIDS has been endemic for some time ([Chokunonga](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 1999](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). In Kampd to adjust for the fact that, for obvious reasons, women infected by HIV were very often also infected by HPV (with a consequently high risk of CIN). Careful adjustment for such confounding suggests that HIV has an independent effect on risk of CIN but that it is small; there is an interaction between the effects of HIV and HPV, as might be expected, if the role of HIV is indirect, through creation of immune suppression and dysfunction ([Mandelblatt](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[, 1999](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

Case-control and descriptive studies on cancer of the cervix in Africa have shown associations of the disease similar to those observed in Western ala the increase in cervical cancer incidence began before the advent of AIDS ([Wabinga](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2000](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). With respect to cervical intraepithelial neoplasia (CIN), most studies failecountries with respect to number of partners, level of education, high parity, and steroid contraceptives; however, genital hygiene, vaginal discharge, alcohol, and male circumcision were also found in certain studies to be important ([Parkin](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2003](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). HIV was found to be associated with cervical cancer in case-control and cohort studies in South Africa and Uganda (Mbulaiteye et al., forthcoming; [Newton](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2001](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Sitas](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)* [2000](https://www.ncbi.nlm.nih.gov/books/NBK2293/)) with odds ratios between 1.6 and 2.4; however, such a weak association could easily be due to confounding by sexual activity, and other studies have shown no association ([Newton](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[, 1995](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Sitas](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[. 1997](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Meulen](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 1992](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). With regard to HPV, subtypes 16, 18, and 31 appear to be the leading ones, but other sexually transmitted infections causing chronic cervico-vaginal inflammation may increase the risk of cervical cancer.

Before the introduction of screening programs in the 1960s and 1970s, the incidence in most of Europe, North America, and Australia and New Zealand was much as we see it in Africa today: it was 38 per 100,000 in the Second National Cancer Survey of the United States, for example ([Dorn and Cutler 1959](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). National screening programs have been responsible for the further decline in the incidence of cancer of the cervix. Pap test screening, with coverage of over 80 percent of the female population over 35 years of age appears to be the most effective method in reducing the incidence of cervical cancer. For example, if women were offered screening three times in their lifetime (at about ages 35, 45, and 55) the incidence of cancer of the cervix would be halved ([Miller 1992](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

Given the complex organization of screening programs, no organized national cervical cancer screening program exists in Africa. Reasons for this include lack of good quality cytology services, difficulty of long-term follow-up in many communities, lack of education, and lack of postal facilities and infrastructure. But many countries in Sub-Saharan Africa do not have the ability to diagnose or treat CIN. In other countries some attention has been given to the value of screening by visual inspection after acetic acid impregnation of the cervix ([University of Zimbabwe/JHPIEGO Cervical Cancer Project 1999](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). The high negative predictive value of this approach suggests that few significant lesions will be missed. If appropriately and safely treated by effective, affordable methods like cryotherapy ([Chirenje](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2001](https://www.ncbi.nlm.nih.gov/books/NBK2293/)), then this method may provide a useful alternative to the conventional Pap test, not least in that treatment is provided during the same visit as the screening test, thus dispensing with the requirement to recall women for diagnosis and therapy.

Vaccines against the leading HPV serotypes have now been developed, and programs may be implemented for women before they become sexually active. However, it is unclear how long the protection will last and whether the vaccine will also be effective in reducing the incidence of cancer of the cervix among women who are infected. The ongoing trials are expected to clarify such issues. As men are also carriers of HPV, future studies ought to measure any added effectiveness of vaccination in this group.

**Breast cancer**

Breast cancer is the second most common cancer among women in Sub-Saharan Africa, accounting for 16.8 percent of all female cancers. Central, West, and East Africa appear to have lower incidence rates than southern Africa, the latter estimated at 33.4 per 100,000. An estimated total of 48,600 cases occurred in Sub-Saharan Africa in 2002.

Worldwide, risk factors for female breast cancer include menstrual and reproductive factors, high body mass index (BMI), family history of breast cancer, and certain genetic mutations, including BRCA1/2. Other suggested risk factors include, to a much lesser extent, high alcohol consumption, contraceptive use, and the use of certain postmenopausal hormone replacement therapies. Reproductive and hormonal factors appear to be the most important, with risk being increased by early menarche, late menopause, late age at first birth, and low parity ([Henderson, Ross, and Bernstein 1988](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

Studies in Sub-Saharan Africa have also found reproductive and hormonal factors to be important, reporting increased risk with advanced age at first pregnancy and delivery, low parity, and late age at menarche ([Adebamowo and Adekunle 1999](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Coogan](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[, 1996](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Shapiro](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2000](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Ssali, Gakwaya, and Katangole-Mbidde 1995](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

In Sub-Saharan Africa, higher incidence rates and relative frequencies of breast cancer have been reported in association with urban than with rural residence ([Oettlé and Higginson 1966](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Schonland and Bradshaw 1968](https://www.ncbi.nlm.nih.gov/books/NBK2293/)), but data are sparse. The incidence of breast cancer is much higher among white women in Africa than among black African women; for example, in Harare between 1993 and 1995, the incidence was 127.7 per 100,000 in whites and 20.4 in blacks ([Chokunonga](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.,](https://www.ncbi.nlm.nih.gov/books/NBK2293/)* [2000](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). These differences may be a reflection of the distribution of lifestyle factors thought to be important in the development of breast cancer, for example, low parity and high body mass.

Breast cancer risk has been associated with socioeconomic status, with women of higher social class (as measured by education, income, housing, and so forth) having a higher risk ([Kogevinas](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[, 1997](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). Once again, such differences are most likely a reflection of different prevalences of risk factors among social classes (for example, parity, age at menstruation and menopause, height, weight, alcohol consumption).

The effect of oral contraceptive hormones on the risk of breast cancer has been the subject of much research. There appears to be a small but detectable risk in women currently using oral contraceptives, but this diminishes when contraception ceases, and after 10 years, none of the excess risk remains ([Reeves 1996](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). A case-control study in South Africa found that combined oral contraceptives may result in a small increase in risk, confined to women below the age of 25 years, but that injectable progesterone contraceptives did not increase risk ([Shapiro](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2000](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

Dietary fat appears to be correlated with the risk of breast cancer in interpopulation studies ([Prentice and Sheppard 1990](https://www.ncbi.nlm.nih.gov/books/NBK2293/)), but the association has been difficult to confirm in studies of individuals ([Hunter](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[, 1996](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). However, obesity in postmenopausal women has been identified as a risk factor in Europe ([Bergstrom et al., 2001](https://www.ncbi.nlm.nih.gov/books/NBK2293/)) as well as in Sub-Saharan Africa ([Adebamowo and Adekunle 1999](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Walker](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 1989](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). Although traditional diets in Africa are typically low in animal products, especially fat, and high in fiber ([Labadarios](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 1996](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Manning](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[, 1971](https://www.ncbi.nlm.nih.gov/books/NBK2293/)), this pattern is being modified by urbanization and Westernization of lifestyles, which may lead to an increase in breast cancer incidence in African populations. A case-control study in Cape Town did not find a protective effect of breastfeeding on breast cancer ([Coogan](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)* [1999](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). However, in a meta-analysis of 47 studies from 30 countries breastfeeding appears to be protective; based on a reanalysis of about 50,302 cases and 96,973 controls, two-thirds of the difference in rates between developed and developing countries were estimated to be attributed to breastfeeding ([International Collaboration on HIV and Cancer 2002](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

At least part of the familial risk of breast cancer is mediated through the major susceptibility genes BRCA1 and BRCA2 (about 2 percent of breast cancer cases in Europe). Very little is known of the prevalence of these mutations in African populations, although family history of breast cancer is also a risk factor in this setting ([Rosenberg](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2002](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

About 1 percent of all breast cancer cases occur in men, with the male-to-female ratio being higher in black and African populations than among white populations ([Parkin](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2003](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Sasco, Lowels, and Pasker de Jong 1993](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

A review of the literature indicates a deficit of studies on breast cancer risk in Sub-Saharan Africa, and further research could be beneficial. As certain groups become more Westernized and urbanized, with associated changes in diet, later childbirth, and reduced parity and periods of breast-feeding, breast cancer incidence may increase. Public health campaigns should encourage breastfeeding unless there are good reasons not to (for example, HIV-infected mothers where milk powder and sterile water are freely available). There is no organized mammography screening program in Sub-Saharan Africa.

**Karposi’s sarcoma**

Prior to the HIV/AIDS era, Kaposi's sarcoma was a rare cancer in Western countries, seen mainly among immigrants from the Mediterranean littoral and African regions and in immunosuppressed transplant recipients. Meanwhile, in Africa, the incidence of Kaposi's sarcoma varied 100-fold, being most common in central and eastern Africa and rare in northern and southern Africa ([IARC 1996](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Oettlé 1962](https://www.ncbi.nlm.nih.gov/books/NBK2293/)); in certain parts of central and eastern Africa, Kaposi's sarcoma was as common as cancer of the colon was in the West ([Cook-Mozaffari](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 1998](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). There appears to be some geographical association with the prevalence of human herpes virus-8, now regarded as a necessary cause for the development of Kaposi's sarcoma ([Dukers and Rezza 2003](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). The incidence of Kaposi's sarcoma has increased over 1,000-fold in populations at high risk of HIV in some Western countries ([Biggar](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 1984](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Rabkin, Biggar, and Horm 1991](https://www.ncbi.nlm.nih.gov/books/NBK2293/)), but in the rest of the population the tumor still remains relatively rare ([Grulich, Beral, and Swerdlow 1992](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Rabkin, Biggar, and Horm 1991](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). In Africa, since the 1980s, areas like Malawi, Swaziland, Uganda, and Zimbabwe, where Kaposi's sarcoma was relatively common before the era of AIDS, the incidence of Kaposi's sarcoma has increased about 20-fold, such that it is now the leading cancer in men and the second leading cancer in women. In these cancer registries, overall age-standardized rates have increased by about 15 percent, mainly as a result of HIV-associated Kaposi's sarcoma (for example, [Bassett](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 1995](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Wabinga](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[, 1993](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Wabinga](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.,](https://www.ncbi.nlm.nih.gov/books/NBK2293/)* [2000](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

According to the most recent estimates, 40,000 cases of Kaposi's sarcoma in males and 17,200 cases in females were estimated for 2002 for Sub-Saharan Africa; only 200 male and 65 female cases were estimated to occur in northern Africa. The region most affected is central Africa (age-standardized rates in males of 30 per 100,000) followed by eastern, southern, and lastly western Africa, in line with the background prevalence of HIV in each of these regions. With regard to the effect of HIV infection, three case-control studies from Africa showed increased risks of 30 to 50 in association with HIV, and these risks rise to 1,600 in HIV-positive individuals with high HHV8 antibody titers ([Newton](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[, 2002](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Sitas](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 1997](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Sitas](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.,](https://www.ncbi.nlm.nih.gov/books/NBK2293/)* [1999](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Sitas](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2000](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). HHV8 in adults is associated with increasing age, low educational standard, and increasing numbers of sexual partners ([Sitas](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 1999](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). Antiretroviral therapy for treating HIV in adults has caused a decline in the incidence of Kaposi's sarcoma in Western countries (International Collaboration on HIV and Cancer 2000). HHV8 in children appears to be associated with infected mothers ([Bourboulia](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[, 1998](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). In countries with a high prevalence of HIV, Kaposi's sarcoma is now the leading cancer in children, causing almost a doubling in the childhood cancer incidence ([Chokunonga](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[, 1999](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Wabinga](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 1993](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). Antiretroviral drugs have now become more available in Botswana and recently in South Africa. If their use becomes widespread, then a decline in the incidence of Kaposi's sarcoma would be expected; however, it is unclear whether antiretrovirals (for example, zidovudine [AZT] or nevirapine) issued to mothers during delivery, which proved effective in reducing mother-child transmission of HIV, would cause a decline in Kaposi's sarcoma in children.

**Liver cancer**

Early observations in Africa have always noted the high occurrence of liver cancer (for example, [Oettlé 1964](https://www.ncbi.nlm.nih.gov/books/NBK2293/)), and it is still one of the leading cancer types in men and women, although the relative frequency has been reduced in consequence of the large increase in the number of cases of Kaposi's sarcoma resulting from the epidemic of HIV/AIDS. Liver cancer is now the second leading cancer in men in Sub-Saharan Africa and the fourth leading cancer in women. There were an estimated total of 33,500 cases in males and 15,500 cases in females in 2002. Areas of high liver cancer incidence (mainly hepatocellular cancers) include countries like The Gambia, Guinea, and Senegal in West Africa, where liver cancers comprise a quarter or more of all cancer cases, with incidence rates ranging from 30 to 50 per 100,000 in men and 12 to 20 per 100,000 in women. Similarly, in central Africa, liver cancer is the leading cancer in Rwanda and in the Republic of Congo (Brazzaville); the estimated rate is 15.4 per 100,000 for men and 8.9 per 100,000 for women. Mozambique is reported to have high incidence rates, although the only data are old ([Prates and Torres 1965](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

Few places in Sub-Saharan Africa have information on cancer trends over time. In Ibadan, Nigeria, between 1960–69 and 1998–99, there appears to be no change in incidence, whereas in Kampala, Uganda, between the 1960s and the 1990s there appears to be a decline of liver cancer in men but not in women. However, a decline was noted in liver cancer incidence between the 1970s and the 1980s among Mozambican miners working in South Africa ([Harington, Bradshaw, and McGlashan 1983](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

Chronic carriage of HBV or hepatitis C (HCV), causing cirrhosis, or chronic hepatitis is the leading risk factor for liver cancer. The prevalence of HCV in Sub-Saharan Africa varies between 6.9 percent in central Africa to 0.1 percent in southern Africa. HCV transmission is probably via blood transfusion, unsterile medical and dental procedures, and traditional practices, such as scarification; sexual transmission is thought to be rare ([Madhava, Burgess, and Drucker 2002](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

Persistence of the HBV surface antigen (HbsAg) in blood is an indicator of chronic carriage of HBV infection. The risk of liver cancer in persons with chronic HBV infection, as indicated by the detection of HbsAg in serum, ranges from 6- to 20-fold in different studies, and it is estimated that about two-thirds of liver cancer in Africa is attributed to HBV ([Pisani et al., 1997](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). Prevalence rates in Africa are over 10 percent in central, western, and eastern Africa and between 5 and 10 percent in southern Africa ([Parkin](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2003](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

There are relatively few African studies on the risk of HCV infection on the development of liver cancer. Those that have been conducted give relative risks ranging from 1.1 to 62 ([Parkin](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2003](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). One study ([Kirk](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2004](https://www.ncbi.nlm.nih.gov/books/NBK2293/)) observed that, as has been found elsewhere, the risk of chronic infection by HCV and HBV is additive, suggesting common mechanisms of carcinogenesis.

Aflatoxin B1 (AFB1) is produced by molds of *Aspergillus* sp. that are common contaminants of poorly stored grains. AFB1 is a known liver carcinogen of animals and humans ([IARC 1993](https://www.ncbi.nlm.nih.gov/books/NBK2293/), [2002](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). In Sub-Saharan Africa, high levels of AFB1 contamination are found in groundnuts and, to a lesser extent, corn. Contamination of groundnuts by AFB1 is quite widespread and frequently exceeds thresholds permitted in exports to most developed countries. Several geographical studies have demonstrated correlations between AFB1 levels and the incidence of hepatocellular cancer ([Parkin](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[, 2003](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

Iron overload, derived from food and drink preparation in iron vessels, is a common condition in rural Africa, and there have been several observations that elevated serum ferritin levels are associated with liver cancer. In one small case-control study in South Africa ([Mandishona](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 1998](https://www.ncbi.nlm.nih.gov/books/NBK2293/)), liver cancer cases had higher iron overload levels than controls, corresponding to an odds ratio of 10.6 to 4.1 (depending on the control group used).

Smoking, oral contraception, and alcohol consumption ([IARC 2004](https://www.ncbi.nlm.nih.gov/books/NBK2293/), [1999](https://www.ncbi.nlm.nih.gov/books/NBK2293/), and [1988](https://www.ncbi.nlm.nih.gov/books/NBK2293/), respectively) were also found to be important risk factors for liver cancer. This association, however, has not been extensively examined in Africa.

Early vaccine trials against HBV suggest that 70 to 75 percent of chronic infections could be prevented. A randomized trial to measure the effectiveness of HBV vaccination in the prevention of liver cancer is under way in The Gambia, but it will take many years before results are available. In Taiwan, however, children born after the introduction of mass vaccination had a fourfold lower incidence than those born before its introduction ([Chang](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 1997](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). According to the WHO Web site, by 2002, about a dozen countries in Sub-Saharan Africa had introduced hepatitis B vaccine into their infant immunization system.

Aflatoxin consumption could be reduced by improved education of individuals and farmers by, for example, agricultural extension officers. A trial in western Africa has shown that improved post-harvest storage of groundnuts can significantly reduce aflatoxin exposure in rural populations ([Turner](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[. 2005](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). The public could be educated to avoid contaminated peanuts sold by vendors ([Wild and Hall 2000](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). Companies manufacturing peanut butter could be better controlled by accepting peanuts only from certified farmers and by the testing of their products by independent regulatory authorities

**Prostate cancer**

For the year 2002, a total of 26,800 cases of prostate cancer were estimated, comprising 10.6 percent of cancers of men in Sub-Saharan Africa ([Ferlay](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 2005](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). The relatively high incidence (and mortality) recorded in African populations is reflected in populations of African descent elsewhere. Thus, within the United States, the black population has the highest incidence (and mortality) rates, some 72 percent higher than whites. Southern Africa appears to have the highest rates (40.5 per 100,000). Rates of histologically diagnosed prostate cancer in South Africa are 40.1 per 100,000 in whites versus 14 per 100,000 in blacks, although for blacks, access to diagnostic facilities has been limited ([Parkin](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[, 2003](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). In Zimbabwe (defined as being part of eastern Africa), rates for whites and blacks were 70 versus 25 per 100,000 ([Parkin](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[, 2003](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). Central Africa follows with rates of 24.5 per 100,000. Surprisingly, in West Africa, where the majority of African-American men originated, the incidence rate of prostate cancer was estimated as 19.3 per 100,000 in 2002, compared with about 125 per 100,000 in the United States ([Ferlay](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[, 2005](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). High rates are observed in other places with populations that are descended from West Africa (for example, the Bahamas, Barbados, Trinidad).

Histology of the prostate in elderly men often reveals latent malignant cells, and clearly, advances in diagnostic and screening methods can cause artificial increases in reporting. This is illustrated by a fourfold increase in the incidence of histologically verified prostate cancer among whites in South Africa (most whites were covered by private health insurance) compared with no change in incidence in blacks between 1986 and 1995 ([Sitas, Madhoo, and Wessie 1998](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). Notably, in Cape Town in the 1950s prostate cancer appeared to be more common in blacks than in whites ([Muir-Grieve 1960](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). Increases over time have also been noted in Kampala and in Ibadan, but it is unclear how much of these increases represents a greater risk and how much can be attributed to increased awareness or a greater readiness to perform prostatectomy for urinary symptoms in elderly men ([Parkin](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[, 2003](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

The consumption of fat and red meat has been implicated as a risk factor for prostate cancer in studies in developed countries, even though adjustment for total caloric intake was not always done. Associations with vegetable consumption have been inconclusive. Associations with anthropometric measures or a link with obesity have been inconclusive, and so have associations with numbers of sexual partners and history of sexually transmitted diseases, or STDs ([Hayes](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[, 2000](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Key 1995](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Kolonel 1996](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). In one case-control study from South Africa, prostate cancer was associated with high intake of fat, meat, and eggs; eating out of the house; and a low consumption of vegetables ([Walker](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 1992](https://www.ncbi.nlm.nih.gov/books/NBK2293/)).

Sex hormones, modulated by polymorphisms on the long arm of chromosome X, play an important role in the development of prostate cancer (for example, [Ross](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[., 1998](https://www.ncbi.nlm.nih.gov/books/NBK2293/); [Shibata and Whittemore 1997](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). Polymorphisms on the androgen receptor gene may vary by ethnic group and may provide some explanation for the geographic variation observed. However, no studies have been done on interethnic variations in androgen receptor polymorphisms in Africa.

**In Nigeria**

 We analyzed data from 2 population based cancer registries in Nigeria, the Ibadan Population Based Cancer Registry (IBCR) and the Abuja Population Based Cancer Registry (ABCR) covering a 2 year period 2009–2010. Data are reported by registry, gender and in age groups. We present data on the age specific incidence rates of all invasive cancers and report age standardized rates of the most common cancers stratified by gender in both registries. Results: The age standardized incidence rate for all invasive cancers from the IBCR was 66.4 per 100 000 men and 130.6 per 100 000 women. In ABCR it was 58.3 per 100 000 for men and 138.6 per 100 000 for women. A total of 3393 cancer cases were reported by the IBCR. Of these cases, 34% (1155) were seen among males and 66% (2238) in females. In Abuja over the same period, 1128 invasive cancers were reported. 33.6% (389) of these cases were in males and 66.4% (768) in females. Mean age of diagnosis of all cancers in men for Ibadan and Abuja were 51.1 and 49.9 years respectively. For women, mean age of diagnosis of all cancers in Ibadan and Abuja were 49.1 and 45.4 respectively. Breast and cervical cancer were the commonest cancers among women and [prostate cancer](https://www.sciencedirect.com/topics/medicine-and-dentistry/prostate-cancer%22%20%5Co%20%22Learn%20more%20about%20Prostate%20Cancer%20from%20ScienceDirect%27s%20AI-generated%20Topic%20Pages) the most common among men. Breast cancer age standardized incidence rate (ASR) at the IBCR was 52.0 per 100 000 in IBCR and 64.6 per 100 000 in ABCR. Cervical cancer ASR at the IBCR was 36.0 per 100 000 and 30.3 per 100 000 at the ABCR. The observed differences in incidence rates of breast, cervical and prostate cancer between Ibadan and Abuja, were not statistically significant. Conclusion: Cancer incidence data from two population based cancer registries in Nigeria suggests substantial increase in incidence of breast cancer in recent times. This paper highlights the need for high quality regional cancer registries in Nigeria and other SSA countries.

**Conclusion**

Over the past century, until about the 1980s (prior to the advent of HIV/AIDS), the average age of most populations in Sub-Saharan Africa has increased because of improvements in the rates of both infant and adult mortality ([Timaeus 1999](https://www.ncbi.nlm.nih.gov/books/NBK2293/)). Since cancer risk is strongly related to age, the aging population has experienced an increase in the numbers of cancers and in crude incidence. Cancer has therefore been an emerging public health problem. The HIV epidemic has arguably caused the biggest change in cancer patterns, with Kaposi's sarcoma now being the leading cancer type in men and the third most common cancer in women. But also, certain cancer types, such as cancer of the lung, breast, prostate, and esophagus, have increased significantly as a result of changing lifestyles and changes in exposures to common carcinogens.

Although the relative importance of many important carcinogens has been described for many cancers in most Western countries, little is known about the distribution of these and the relative importance of the major causes of cancer in Africa. Even in places with existing cancer registries, or well-resourced countries like South Africa, very few cancers or common carcinogenic exposures are being researched in a systematic fashion, and there is therefore wide uncertainty about their relative importance and their evolution over time. The relative importance of cancers and related exposures to them needs to be carefully assessed in order to formulate appropriate health promotion strategies. Given the tremendous variation in the genetics, lifestyle characteristics, and cancer patterns throughout Africa, it may be misleading to extrapolate cancer patterns from one area to the next, so better data from population-based cancer registries and from mortality statistics are needed to provide data of local relevance.

There have, however, been some positive developments. Compared with 1978–82, when no data from population-based cancer registries in Sub-Saharan Africa existed ([Muir](https://www.ncbi.nlm.nih.gov/books/NBK2293/) *[et al.](https://www.ncbi.nlm.nih.gov/books/NBK2293/)*[, 1987](https://www.ncbi.nlm.nih.gov/books/NBK2293/)), the information derived from cancer registries in Sub-Saharan Africa now covers 8 percent of the population. Despite this great achievement most of these registries are staffed by a part-time director and one or two clerks, who do not know whether sufficient support will be forthcoming from their Departments of Health or other potential stakeholders. Given the short time that these registries have existed in Africa the impact of these on cancer incidence is still difficult to quantify. Yet long-term surveillance is necessary to quantify the impact of the epidemics of tobacco and AIDS and to evaluate the efficacy of cancer control measures.

Still, despite the dramatic reduction in life expectancy in many populations in Sub-Saharan Africa, age-standardized cancer incidence in these registries has remained the same, and in places where HIV prevalence is high, the overall incidence of cancer seems to have increased by up to 15 percent. This is counterintuitive to the common belief that a reduction in life expectancy due to HIV would cause a decline in chronic disease.

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1. Critically examine the involvement of angiogenic genes in the development and progression of osteosarcomas?

Answer

Angiogenesis is the physiological process through which new blood vessels form from pre-existing vessels,formed in the earlier stage of vasculogenesis. (Santulli 2013). Angiogenesis continues the growth of the vasculature by processes of sprouting and splitting.Vasculogenesis is the embryonic formation of endothelial cells from mesoderm cell precursors, and from neovascularization, although discussions are not always precise (especially in older texts). The first vessels in the developing embryo form through vasculogenesis, after which angiogenesis is responsible for most, if not all, blood vessel growth during development and in disease.

Osteosarcoma is a type of cancer that produces immature bone. It is the most common type of cancer that arises in bones, and it is usually found at the end of long bones, often around the knee. Most people diagnosed with osteosarcoma are under the age of 25, and it is thought to occur more often in males than females.

Osteosarcomas range from low grade tumors that only require surgery to high grade tumors that require an aggressive treatment regimen. Patients with osteosarcoma are best treated at a cancer center where an expert sarcoma team and resources are available to provide specialized and responsive care.

**What causes osteosarcoma?**

Scientists have not discovered the cause of most cases of osteosarcoma. Osteosarcoma can develop as a result of radiation to an area of the body. It can also be associated with specific genetic changes and diseases.

**What are the symptoms of osteosarcoma?**

Most people with osteosarcoma do not feel sick. Patients may have a history of pain in the affected area and may have developed a limp. Often the pain is thought to be related to muscle soreness or &quot;growing pains,&quot; but it does not go away with rest. Many patients only see a doctor when there is some sort of injury to the area or when the tumor weakens a bone so much that it breaks (this is called a pathological fracture).

**How is osteosarcoma diagnosed?**

An x-ray is often the first diagnostic test that osteosarcoma patients receive, and an experienced radiologist may recognize immediately that bone cancer is the likely diagnosis. There are several additional tests that are a critical part of osteosarcoma diagnosis and staging:

An MRI of the entire bone where the primary tumor is located. This test can rule out &quot;skip metastases&quot; (spread of the tumor to other areas of the bone).

A chest x-ray and CT scan of the chest to detect lung metastases

A bone scan of the body to rule out distant spread of the disease

A biopsy of the tumor, which provides a definite diagnosis based on the characteristics of tumor tissue seen under a microscope. The biopsy will also show whether the tumor is high grade (highly malignant, which is the case for most osteosarcomas) or low grade.

In this study three genes were identified with pattern of differential gene expression associated with a phenotypic role in metastasis and invasion. Interestingly all encode for proteins involved in extracellular remodeling suggesting potential roles in osteosarcoma progression. This is the first report on the THBS3 gene working as a stimulator of tumor progression. Higher levels of THBS3 maintain the capacity of angiogenesis. High levels of SPARC are not required for tumor progression but are necessary for tumor growth and maintenance. SPP1 is not necessary for tumor progression in osteosarcoma and may be associated with inflammatory response and bone remodeling, functioning as a good biomarker. (Dalla-Torre, Yoshimoto *et al*., 2006).

The activation of endothelial cells by angiogenic factors leads to the production of proteolytic enzymes, which degrade the extracellular matrix. The degradation of the underlying basement membrane enables endothelial cells to proliferate and migrate to the surrounding tissue to form new vessels. These new vessels provide cancer cells with oxygen and nutrition and play an important role in cancer cell survival and metastasis. (Li, Liu *et al*., 2019).

MicroRNA-29c-3p expression was reduced in OS, and conspicuously associated with distant metastasis and poor prognosis. MicroRNA-29c-3p might inhibit the malignant progression of OS by modulating PIK3R3 expression. (Ma, Wang *et al*., 2020).

Bioinformatics analysis found 70 genes that might be involved in osteosarcoma angiogenesis, and found that SAT1 and VAV3 are closely related to angiogenesis by Gene Ontology (GO) analysis. Bioinformatics analysis and clinical experiments confirmed that LINC00265, SAT1 and VAV3 were overexpressed in osteosarcoma and related to poor prognosis, while miR-382-5p was down-regulated and associated with poor prognosis. It was confirmed that LINC00265 promoted proliferation, migration, invasion and angiogenesis of osteosarcoma cells by targeting miR-382-5p to mediate SAT1 and VAV3. (Fu, Lu *et al.,* 2019).

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