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ANA404 ASSIGNMENT

INTRODUCTION TO HISTOPATHOLOGY

LECTURER: MR EDEM

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

1. 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). It is 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.

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. Dietary fat appears to be correlated with the risk of breast cancer in interpopulation studies (Prentice and Sheppard 1990), but the association has been difficult to confirm in studies of individuals (Hunter et al. 1996). However, obesity in postmenopausal women has been identified as a risk factor in Europe (Bergstrom et al. 2001) as well as in Sub-Saharan Africa (Adebamowo and Adekunle 1999; Walker et al. 1989). A case-control study in Cape Town did not find a protective effect of breastfeeding on breast cancer (Coogan et al. 1999). 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). 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 et al. 2003; Sasco, Lowels, and Pasker de Jong 1993).

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. 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 et al. 1999; Wabinga et al. 1993)

A total of 13,800 cases of stomach cancer in males and 10,700 in females was estimated in Sub-Saharan Africa in 2002. Age-standardized incidence rates in males varied, per 100,000, from 3.4 in western Africa to 7.4 in eastern, 8.2 in southern, and 13.4 in central Africa. In western Africa, where the incidence of stomach cancer is the lowest, the male-to-female ratio is 0.9 to 1; however, there is a male predominance in all other areas. Despite the generally low incidence rate in Africa, some populations have a particularly high incidence rate. Clusters of high

incidence exist among the South African mixed race, or coloured, population of 98 per 100,000. A high incidence rate is also reported in the Great Lakes region that includes Burundi, Kivu Province of the Democratic Republic of Congo, Rwanda, northwestern Tanzania, and southwestern Uganda. In Rwanda the age-standard incidence rate was found to be 13 per 100,000 males and 15 per 100,000 females (Newton et al. 1996). In western Uganda, stomach cancer was the second most common cancer, accounting for 12 percent of all male cancers and 6 percent of all female cancers (Wabinga et al. 2000). Bamako in Mali was another area with a high incidence rate: 18.5 per 100,000 males and 15 per 100,000 females (Bayo et al. 1990). *Helicobacter pylori* infection is now recognized as an important risk factor for cancer of the stomach (IARC 1994); however, smoking and diets low in fruit and vegetables and vitamin C, and high in salts appear to play an important role.

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 et al. 2005). 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). In Zimbabwe (defined as being part of eastern

Africa), rates for whites and blacks were 70 versus 25 per 100,000 (Parkin et al. 2003). 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 et al. 2005). High rates are observed in other places with populations that are descended from West Africa (for example, the Bahamas, Barbados, Trinidad).

Nigeria recorded 102079 cases of cancer, out of which 27,304 (26.7%) cases were for breast cancer, 14089 (13.8%) for cervix uteri, 12,047 (11.8%) for liver and 11,944 (11.7%) for prostate cancer as incidence. (Globocan,2012). A 5-year prevalence study in Nigeria also showed almost the same trend. breast cancer being the leading cases with 87,579 (37.7%), followed by cervix uteri 35,644(15.4%), prostate 31062 (13.4%) and then liver 8,447 (3.7%).

The mortality as recorded by Globocan (2012) showed that breast cancer caused 13,960 (19.5%) deaths, cervix uteri 8,240 (11.5%) deaths, liver 11,663 (16.3%) deaths and prostate 9628 (13.5%) deaths in Nigeria.

2. Osteosarcoma (also called osteogenic sarcoma) is the most common type of cancer that starts in the bones. Sarcomas are mesenchymal-derived cancers. This heterogeneous group of tumors depends on new blood vessel development, also known as angiogenesis, for tumor growth and metastasis. Angiogenesis is the process of new blood vessel development, which is critical in both physiological development and pathological processes, such as tumor progression, wound healing, and cardiovascular, inflammatory, ischemic, and infectious diseases (Carmeliet P. 2005). Angiogenesis plays a key role in osteosarcoma (OS) development and progression. Angiogenesis is a pivotal process in osteosarcoma (OS) development and progression (Zhu L et.al 2013). In response to hypoxia, tumor tissues produce and release angiogenic growth factors, such as vasculo-endothelial growth factor (VEGF), the acidic and basic fibroblast growth factors (aFGF and bFGF), and the platelet-derived endothelial cell growth factor (PD-ECGF) to recruit new blood vessels by angiogenesis and vasculogenesis (Niu G and Chen X, 2010).

Expression of VEGF has been used as a more objective means of evaluating the prognostic importance of angiogenesis in osteosarcoma. VEGF is a key tumor-derived angiogenic factor that has multiple functions, including stimulation of angiogenesis, vasculogenesis, inflammation, and vascular permeability, which

constitutes the most important signaling pathways in tumor angiogenesis. There are a number of different VEGF molecules (VEGFA through VEGFE) that bind to VEGF receptors (VEGFR1-3). VEGFA binds to VEGFR2 and initiates a number of divergent signaling pathways (Shibuya M, Claesson-Welsh, 2006). Among the proteins that are upregulated upon VEGF activation are the matrix metalloproteinase (MMP) and plasmin proteases (Carmeliet P, 2005), which act on the vascular network by breaking down the extracellular matrix (ECM) and allow for tumor cell invasion, as well as the migration of the precursor cells that give rise to vascular structures: pericytes and endothelial cells. Additionally, VEGF signaling also induces the expression of the anti-apoptotic factors Bcl-2 and survivin, as well as the ERK/NF- κ B and PI3K pathways (Steeg, 2006). These effectors promote tumor cell proliferation and survival. Angiogenesis-related factors other than VEGF have also been evaluated as possible markers of prognosis in osteosarcoma.

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