# PREVENTION AND EARLY DETECTION OF PAEDIATRIC CANCERS

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In 190, President Theodore Roosevelt proclaimed, "A new century is a time for both celebration and reflection". However, we in the sub-Saharan Africa have only an opportunity to reflect on the little progress made with respect to our children's health and also on many challenges that we as part of the global community face in this new century. May I remind you that on September 19-21st 2001 we participated with other people of the world in the United Nation's special session for children. There have been also several activities geared towards children's health in our community since then.

We have seen some remarkable success in Kenya during the last decade in the practice of paediatric oncology. In the one particular case of Burkitt's lymphoma, some form of mapping has been done; there is also baseline, if not fully adequate but nonetheless some, information of the ranking of childhood cancers at our national and referral hospital, the Kenyatta National Hospital.

Certainly oncology in general has been placed rightly in the minds of many medical personnel and the students at the medical colleges clearly know he existence of a discipline of oncology. However, gigantic challenges still face us. This is more glaring in the all-important activity of prevention and early detection of cancer.

Prevention is the ultimate goal in the control of disease. Disease is a reaction of the organism to noxious stimuli. Hence the occurrence of disease can be prevented by avoidance of the stimulus or the protection of the organism against the stimulus. This is primary prevention. Early detection and institution of therapeutic measure is secondary prevention.

An effective program of prevention has two essential components: public education, creating an informed motivated population, and availability of medical health delivery system that is adequate and acceptable to the population.

Avoidance of carcinogenic stimuli in the environment involves either individual or public decisions. Of course these are based upon education of people leading to awareness, motivation and appropriate actions.

Primary cancer prevention involves the medical person in education and couselling. Perharps in the days ahead vaccines and other protective measures against cancer will extend this responsibility.

Secondary prevention also requires informed, motivated public and informed medical personnel whose suspicions are promptly followed by appropriate diagnostic and therapeutic actions

It is important to place childhood cancer in the broader perspective of cancers at all ages. In terms of numbers of deaths rate, the problem of childhood cancer is dwarfed by the problem of cancer in adult life, although there are small peaks during childhood years. Also the cancers seen in children are not the same cancers as those in adult life.

## Genetics

Perhaps this component in cancer play's a much greater role in children while the effects of environmental manifest more in adults. Genetic forms also tend to occur earlier than environmental forms: for example familial cases of retinoblastoma occur at a much earlier age than do he non-familial cases. Similar phenomenon is also seen in the age distribution of patients with skin cancer. Cancers occur earlier in patients with xeroderma pigmentosum than people without this condition. It is possible to verify that in the instances when we have diagnosed squmous cell carcinoma in childhood it has been on the background of xeroderma pigmentosum, a genetic disorder. However, there is hope that even in this genetic disorders certain environmental manipulations may bring potential benefit in the future as exemplified by feeding of children of phenylketonuria with diet low on phenylalanine

Aspects of epidemiology of cancers give very important clues as to the associated aetiological factors of cancer. For example, the age pattern for Hodgkin's disease shows trimodal distribution with a peak in mid childhood, the twenties and another peak in older life. This suggests that several factors may be involved and these may be different diseases.

Studies to elucidate agents in the etiologic role of cancer have looked into radiation, drugs, chemicals and viruses. Susceptibility to these agents may be modified by certain demographic characteristics or by genetic constitutions. It has to be stated rightly that most of these factors do interact particularly environmental ones. Identification of high-risk individuals aids early cancer diagnosis and prevention by elimination of carcinogens and by genetic counselling.

## Environmental Cancer Risk Factors

### Ionising Radiation

Aspects of ionising radiation activity have been associated with carcinogenesis. It is uncertain whether the developing foetuses are unusually susceptible to radiation

carcinogenesis, despite the fact that several investigations having reported that prenatal exposure to approximately 1 rad of diagnostic x-ray was associated with a 50% increase in the risk of acute leukemia and perharps other cancers during the first years of life. Parental radiation exposure before conception has the same carcinogenic effect. In addition Diamond and co-workers found that an excess of childhood radiation was associated with an excess of childhood leukemia in whites, a corresponding deficit of leukemia in blacks and an overall rate that was in accord with expectation.

The modifying effects of age and sex on genetic constitution are seen in some cancers. For example, radiation associated breast cancers develop primarily in females.

The influence of age is suggested by the higher relative risk of acute leukaemia among atomic bomb survivors exposed before 10 years of age as compared with exposed adults. Also rate of thyroid cancers after partial or whole body radiation are higher among persons exposed in childhood.

Increased susceptibility to radiogenic malignacy may be due to genetic susceptibility in patients treated for bilateral retinoblastoma and medulloblstoma associated with basal cell nevus syndrome. After unusually short latent period, these patients have developed a greater than expected number of sarcomas following treatment for the eye tumour and skin cancers in the field of radiation of medulloblastoma. Host factors also predispose patients with xeroderma pigmentosum to develop skin cancers at sites exposed to sunlight; these cancers result from an inherited defect in repair of ultraviolet radiation induced DNA damage. Patients with ataxia-telangiectasia have a corresponding defect in repair of ionising radiation injury and are susceptible to lymphoreticular neoplasms and acute radiation toxicity.

## Drugs

A variety of drugs have carcinogenic activity in animals while the causal role of many of these agents in the development of human cancers has not been established (69). However, precaution needs to be taken when administering these drugs. Particularly the alkalating agent therapy may be indicated for selected patients with life-threatening childhood disorders such as cancer, chronic hepatitis, rheumatoid arthritis and renal failure, and a few patients have subsequently developed leukemia.

Transplacental chemical carcinogenesis in humans was first demonstrated when seven young women developed clear cell adenocarcinomas of the vagina and cervix after maternal ingestion of the drug diethеylstlbestrol (DES) during early gestation. Among prenatally exposed women, the risk of developing this cancer in early adulthood is approximately 1 per 1000. Longer follow up will determine whether or not these patients will develop other forms of DES associated neoplasia in later life.

In isolated reports, other childhood cancers have developed in patients whose mothers used estrogens during pregnancy and neuroblastoma has developed in at least four patients with foetal hydatoid syndrome.

With regards to chemical carcinogens, children can be exposed by contamination of the air, soil, food and other articles in their environment. Mesotheliomas, for example, have developed in adults who lived near asbestos mines during childhood or who were exposed to asbestos carried home on a parent's work clothes. One study has reported a high risk of cancer associated with employers of the fathers in hydrocarbon related industries at the time of conception.

Exposures during childhood may have a role in the development of a variety of neoplasms in later life. Therefore, preventive mechanisms should be adopted so as to forestall such an eventuality.

## Infectious Agents

Several viruses have been shown to induce cancers in animals; a similar oncogenic effect in humans has been difficult to demonstrate. However, African Burkitt's lymphoma may in part result from infections with Epstein -Barr virus (EBV).

## Host Susceptibility

Observations, mainly clinica,l have identified unusual susceptibility to cancer in children with certain heritable diseases, chromosomal disorders or constitutional syndromes. Such include:-

Fanconi's Anaemia with resulting acute leukemia, Wiskot Aldrich syndrome associated with brain tumours, Hodgkin's lymphoma and soft tissue sarcoma, while Beckwith-Wiedermann syndrome is associated with Wilm's tumour of the kidney.

## Familial Associations

Some childhood cancers have been reported to aggregate within families. Recent data for children are consistent with the estimated risk estimates e.g sibs of a child with cancer have approximately twice the risk of a childhood neoplasm, often of the same type. If two siblings develop cancer during childhood the risk to other sites may be even higher.

## Some Examples Of Cancers And Associated Risk Factors:-

## Leukaemia

Persons with certain constitutional or acquired chromosomal abnormalities have a greater than normal risk of acute leukemia. These include Bloom's syndrome,

Fanconi's anaemia and ataxia-telangiactacia, while Down's syndrome (trisomy 21) is a constitutional chromosomal abnormality associated with at least a 10-fold increased risk of leukemia durir.g the first decade of life.

### Lymphomas

In childhood, Burkitt's lympoma is found in association with t(8,14), t(8,22) and t(4,8). Studies reveal geographical differences in disease rates and clinical features. High risk populations have diverse ethnic and tribal backgrounds and dissimilarities in diet. These findings have suggested the possibility of an etiological interaction between malaria infection and other etiologic influences such as an oncogenic virus.

### Hodgkin's Disease

Familial aggregation of Hodgkin's disease has been described in several instances. International studies identify four distinct epidemiologic patterns that correlate with the regional level of socio-economic development.

### Wilsms' Tumour

It is the most common malignant kidney tumour of childhood, usually occurs in those aged between one and three years in world literature. It is the second most common tumour in our series.

About 15% of patients have congenital anomalies (15%) including sporadic aniridia, genitourinary tract malformation accompanied in some patients with a nephron disorder, harmatomas of the skin, hemihypertrophy and the Beckwith-Wiedermann syndrome (visceral organomegaly, megaloglsia and omphalocele)

### Retinoblastoma

5 to 10% of cases have a family history. Approximately 30% of patients without family history may also have herediarty retinoblastoma as the consequences of new germinal mutation.

Genetic counselling in these families may need consider risk for other cancers as well as for retinoblastoma.

### Kaposi's Sarcoma

As we start the third decade of the AIDS epidemic, it is apparent that neoplastic complications of HIV infections are increasingly recognised as major causes of morbidity and mortality in our patients. These neoplasms include Kaposi's sarcoma. In general, AIDS-associated neoplasms have been known for their aggressiveness and shortened survival when compared to similar tumours in those who are HIV-seroenegative.

*Table:* **Pediatric cohort**

| | HIV +ve | HIV -ve | Total | Significance |
|---|---|---|---|---|
| **Oral:** | | | | |
| Normal | 8 | 2 | 10 | p<.005 |
| Abnormal | 0 | 5 | 5 | |
| **Respiratory:** | | | | |
| Normal | 7 | 3 | 10 | p<.06 |
| Abnormal | 1 | 4 | 5 | |
| **Cutaneous disease:** | | | | |
| Normal | 5 | 1 | 6 | p=.06 |
| Abnormal | 3 | 6 | 9 | |

From this table, the following are notable:

- Significantly greater oral mucosal involvement
- Significantly greater abnormal chest radiographs
- Tendency to more respiratory symptoms and cutaneous involvement.

### Challenges:-

- For prevention of cancers, proper national register will be necessary.
- Centre for research on features of common paediatric cancers as to tease out early detection and preventive measures is necessary.
- The establishment of cancer centres outside Nairobi will enhance understanding of cancer with the community concepts.
- The genetics and environmental associated risk factors in cancer are not elucidated in our cancer cases yet there is general agreement that demographic features of our paediatric cancers differ from those seen in the western part of the world.