

DEFINITION

1. Cancer is a term which embraces a large number of different diseases, the common feature of which is malignant tumour. This is a growth (neoplasm) which is not circumscribed but which infiltrates the surrounding tissues and metastasises (spreads to other sites in the body, thereby producing secondary deposits). Any tissue in the body may be affected.
2. Cancers are classified according to the tissue of origin. **Carcinoma** arises from epithelial tissue and **sarcoma** from connective tissue. The suffix-**blastoma** implies a tumour of embryonic origin.
3. Malignant melanoma of the eye is a malignant tumour which arises in the uveal tract, that is the iris, ciliary body or choroid. The tumour may or may not be pigmented. It spreads locally or by the blood stream.

CLINICAL MANIFESTATIONS

4. Malignant melanomas of the eye are single and unilateral. They occur most commonly between the ages of 40 and 60.
5. The clinical manifestations vary with the site of onset.
 - 5.1. malignant melanoma of the **iris** may arise from a developmental naevus which is visible as a dark brown spot on the iris. Malignant transformation is suggested by an increase in its size. More commonly it appears as an isolated rapidly growing nodule. It may penetrate the cornea or sclera and perforate the globe of the eye.
 - 5.2. malignant melanoma of the **ciliary body** or **choroid** usually presents with visual impairment following by secondary glaucoma. This is followed by extraocular extension and retinal detachment. Finally there may be metastases in any part of the body. These stages are not always followed and the condition may present with glaucoma.
6. Sometimes the tumours necrose and remit spontaneously. There may be a long time interval between the earlier stages and the development of metastases.

AETIOLOGY

7. Cancer is not one disease but a group of widely different diseases. While some aetiological factors may be common to a number of different types of cancer, each type should be recognised to be an individual disease with its own specific aetiology.

8. The common feature of all cancers is the loss of control over normal cell division and differentiation. Cell division proceeds by a complex sequence of events. For this to be maintained in a normal way it must be strictly controlled. It has been found that certain regions of the chromosomes are vital to this control. These regions are called oncogenes. While the oncogenes perform normally, cell division and differentiation remain under control.
9. The process whereby oncogenes lose control of cell division and differentiation is known as activation. When this occurs cell division and differentiation become chaotic and neoplasia (carcinogenesis) ensues. The factors which activate oncogenes are numerous and varied, some being endogenous, others environmental. There is evidence that in most types of cancer a number of different factors play a part at different stages of the neoplastic process.
10. Some types of cancer are strongly genetically determined with a family history, for example retinoblastoma. In other types of cancer an external agent is the dominant factor, for example aniline dyes, which will cause carcinoma of the bladder in 100% of cases following sufficient exposure.
11. Some individuals are **genetically determined** to be more likely to develop cancer and there is a strong history of a certain type of cancer in their family of origin. Some cancers are more common in one sex than the other.
12. During life many **constitutional factors** are present which may activate oncogenes. These include humoral factors, immunological factors and the normal ageing process during which spontaneous changes affect the genes (somatic mutations).
13. For the most part, cancer is commoner at the extremes of life. This may be because the immune system is relatively less efficient in the young and the elderly. In addition, with increasing age, the summation of naturally occurring somatic mutations and any exposure to carcinogens may become sufficient to activate oncogenes.
14. **Environmental factors** play a part in the aetiology of some types of cancer. The following groups of factors have been identified:
 - 14.1 **Chemical**, for example aniline dyes and carcinoma of the bladder.
 - 14.2 **Physical** agents, for example asbestos and mesothelioma.
 - 14.3 **Ionising radiation** which when a certain dose is exceeded will cause cancer in some, but not all, tissues.
 - 14.4 **Ultraviolet radiation** which may cause cancer of the skin. Its tissue penetration is limited and so it does not cause cancer in the deeper tissues.
 - 14.5 Some specific **viruses** have been identified which play a part in the causation of particular types of cancer, for example hepatitis B and primary carcinoma of the liver.

- 14.6 It has been suggested that a wide variety of other environmental factors may cause certain types of cancer. Many of these suggestions have been based on animal studies, in vitro experiments or on epidemiological studies with small samples or inadequate controls. These contentions are still at the stage of speculation.
15. The aetiology of malignant melanoma of the eye is unknown. There is growing evidence of a strong constitutional element. The natural history of the condition, including the occasional spontaneous remission or long interval before the development of metastases, suggests that the host immunological status may be important.
16. The principal environmental risk factor which has been identified for malignant melanoma of the skin is exposure to ultraviolet light. This is supported by the latitudinal gradient in the incidence rates. Epidemiological research amongst Caucasians in the USA and other countries has shown that the frequency of the tumour depends upon the latitude and hence on the degree of exposure to sunlight. That a similar factor might be involved in the aetiology of malignant melanoma of the eye is suggested by the fact that there is a common cell of origin and that dark skinned populations have a much lower prevalence of both tumours.
17. However no latitudinal gradient has been observed with malignant melanoma of the eye. Some recent studies have addressed the issue of ultraviolet light exposure as a risk factor for malignant melanoma of the eye. At present these must be considered to be exploratory. The available evidence is not sufficient to raise a reasonable doubt that ultraviolet light exposure is aetiologically related to malignant melanoma of the eye.
18. Malignant melanoma of the eye is not caused by climatic extremes, trauma, physical or mental stress or lowered resistance arising from hardship or other diseases. Its progress is independent of external factors other than medical treatment.

CONCLUSION

19. Malignant melanoma of the eye is a malignant tumour, the aetiological factors of which are described above. The course of the condition is unaffected by environmental factors other than those involved in its treatment.

REFERENCES

Harnden D G, Lorenzen J, Pusztai L and McGee J O'D. Carcinogenesis. In: (Eds) McGee J O'D, Isaacson P G and Wright N A. Oxford Textbook of Pathology. 1992. Oxford. Oxford University Press. p633-678.

Doll R and Peto R. Epidemiology of Cancer. In: (Eds) Weatherall D J, Ledingham J G G and Warrell D A. Oxford Textbook of Medicine. 2nd Ed. 1987. Oxford. Oxford University Press. p4.95-4.123.

Doll R. Epidemiology of Human Neoplasia. In: (Eds) McGee J O'D, Isaacson P G Wright N A. Oxford Textbook of Pathology. 1992. Oxford. Oxford University Press. p679-694.

Higginson J, Muir C S and Munoz N. Human Cancer: Epidemiology and Environmental Causes. 1992. Cambridge. Cambridge University Press. p433-434.

Magus I A. Photopathology. In: (Eds) McGee J O'D, Isaacson P G and Wright N A. Oxford Textbook of Pathology. 1992. Oxford. Oxford University Press. p759-770.

Miller S J H. Parsons' Diseases of the Eye. Edinburgh. 1990. Churchill Livingstone. 18th Ed. p273-278.

Tucker M A, Shields J A, Hartge P et al. Sunlight exposure as a risk factor for intraocular malignant melanoma. N Eng J Med 1985;313:13:789-792.

Lee J A H. Melanoma and exposure to sunlight. Epidemiol Review 1982;4:110-136.

February 1995