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Received on 03/01/2012;

Revised on 19/01/2012;

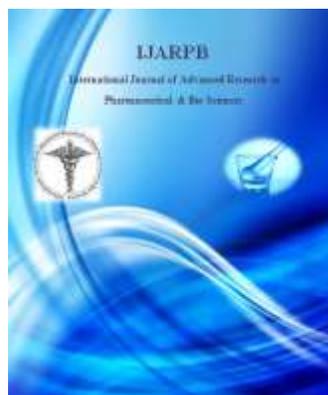
Accepted on 23/01/2012.

Introduction to Neoplasm : a Review Article

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ABSTRACT:

Neoplasm is an abnormal mass of tissue as a result of neoplasia. Neoplasia ("new growth" in Greek) is the abnormal proliferation of cells. Prior to neoplasia, cells often undergo an abnormal pattern of growth, such as metaplasia or dysplasia. However, metaplasia or dysplasia do not always progress to neoplasia. The growth of neoplastic cells exceeds and is not coordinated with that of the normal tissues around it. The growth persists in the same excessive manner even after cessation of the stimuli. It usually causes a lump or tumor. Neoplasms may be benign, pre-malignant (carcinoma in situ) or malignant (cancer). In modern medicine.

KEY WORDS: Tumor Cell, Proliferation of Cells, Apoptosis, Tumor Angiogenesis.

(Review Article)**INTRODUCTION**

Each cell contains a copy of the genetic plan for our growth, development and health. This genetic plan comes in the form of the genes, located on chromosomes that we inherit from our parents. The genes contain the information for the body to make all the necessary structural components and chemicals to ensure normal function. There are two copies of every gene, one inherited from our mother and one inherited from our father. As we go through life our cells are continually growing and being replaced. New cells are formed from existing cells by a process called cell division. Each time a cell divides it has to make a copy of all of its contents, including its genes, so that the new cells have the same genes or information as the old. A number of different genes act together to instruct each cell how to copy its genes properly, and how to divide and grow in a controlled and orderly manner (ie. growth control genes). Different growth control genes work in the cells of different organs and tissues in the body ie. growth control genes that are active in the cells of breast tissue may be different to growth control genes that are active in the cells of the bowel.

Cancer occurs when cells in the body become abnormal and grow out of control and they have the ability to spread to other parts of the body (metastasis). Cancer is a result of uncontrolled cell division and growth.

Uncontrolled cell division and growth leading to cancer can occur in any tissue or organ in the body. Cancer is named according to the place where it starts growing: for example, when it

occurs in the breast it is called breast cancer. A group of cells that has resulted from uncontrolled cell division and growth is called a tumour.

- Tumours can be benign (not cancer) or malignant (cancer)
- Metastatic cancer occurs when cancerous cells spread into other surrounding tissues, or enter the circulatory system and travel to other parts of the body, producing new tumours¹.

How do cancer cells grow and spread?

The human body is made up of billions of cells. Cells are the tiny building blocks of our tissues and organs. We all started life as a single cell. That cell made an internal copy of itself (replication) and then divided into two cells.

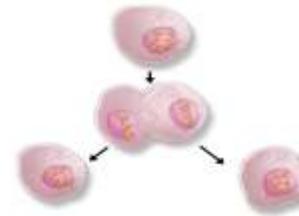


Fig:1 Replication of Cancer cells

Those two cells then also replicated and divided, so the two cells became four cells. The four cells replicated too and divided into eight cells, and so on.

Cells specialise to perform particular tasks. Some cells will cluster together to form a finger, for example. Others create skin and heal the skin when it is wounded. Cells get old and die after a certain amount of time (“programmed cell death”, or apoptosis), and replication ensures that new cells are made to take their place.

When they are acting normally, cells “know” which other cells to join up with and stick to – and

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they also know when to stop replicating and die. Each type of cell has a particular role and set of knowledge or instructions in their DNA (genes). Our cells know how to make the right number of fingers on our hand for us (and they know that fingers should only grow on our hands).

Each finger is covered with skin and each finger has a fingernail. If we cut our finger, the skin cells will start replicating and create new skin to heal the wound. If we lose a fingernail, our cells can grow a new one. But the cells will not create extra fingers, even if we lose one. The rules are clear for those cells, and they keep to the rules.

The role of hormones and the lymphatic system

Our hormones carry messages to our cells, triggering the cells to take action. These messages are carried by our blood through our vascular system (arteries, veins and capillaries). The blood carries the other things that cells need to function too. Our cells need oxygen and glucose to keep them alive, for example. Our blood vessels also carry away waste products and oxygen-poor blood once the cells have used the oxygen in the blood. Our lymphatic system helps to clean and drain what we do not need. The lymphatic system is a part of our body's defence system (immune system), and it drains away bacteria and germs. You can read more about the lymphatic system here.

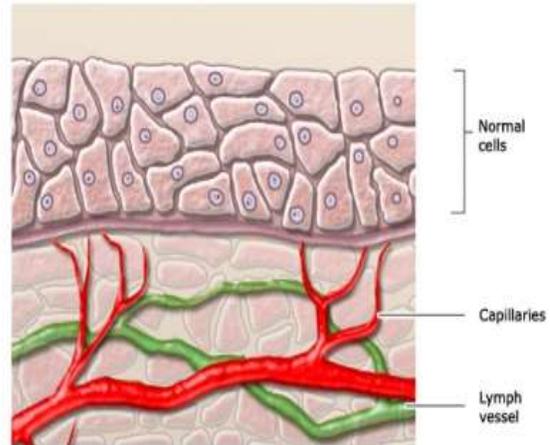


Fig:2 lymphatic system

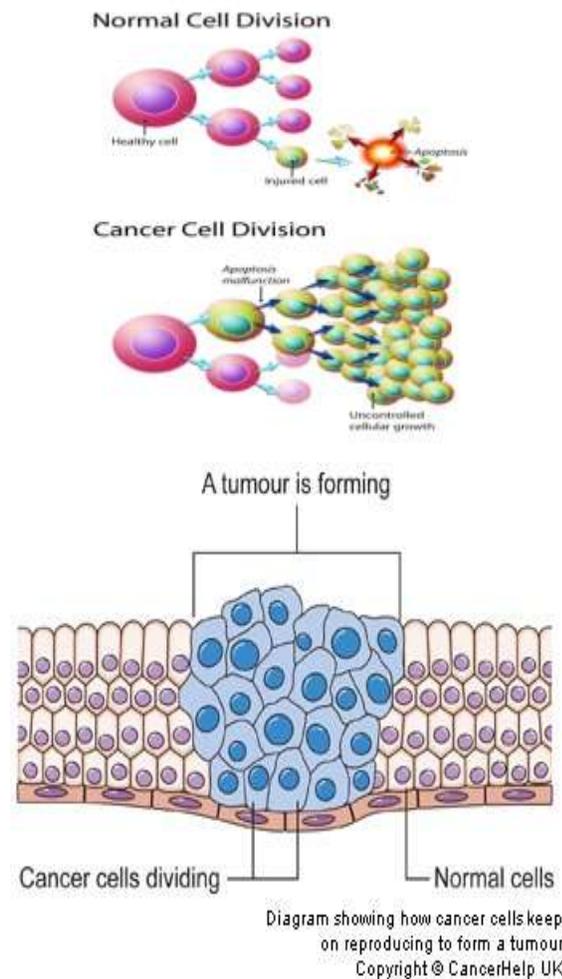
Benign and malignant growth

Cells become abnormal if their DNA - and therefore their "knowledge" - becomes damaged. As long as there are very few abnormal cells and they are kept under control by our immune system, they will not harm us. It is only when these cells start to divide uncontrollably, forming lumps or growths, that we have one of the more than 200 diseases called cancer. Growths like this are called tumours. The main differences between malignant (cancerous) and benign (non-cancerous) tumours are that malignant ones can

- 1) spread into the surrounding tissue,
- 2) destroy the surrounding tissue, and
- 3) cause other tumours to develop.

Malignant tumours can be life-threatening. But there are also some kinds of cancer that develop so slowly in older people that they do not lead to any problems in their lifetime.

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metastasis (the medical word for a cancer that is spreading).

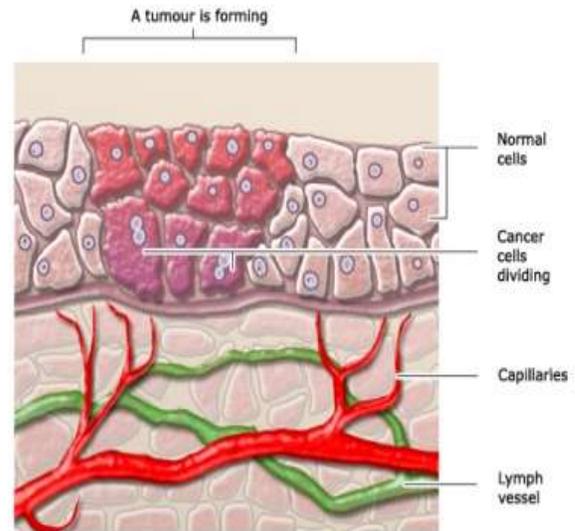


Fig:3 Active Cancer cells

Active cancer cells can enter the bloodstream or lymphatic system and move to other parts of the body to start the process of forming a tumour all over again somewhere else (metastatic or secondary cancer).

The Tumor Cell

The malignant cell is characterized by: acceleration of the cell cycle; genomic alterations; invasive growth; increased cell mobility; chemotaxis; changes in the cellular surface; secretion of lytic factors, etc.

Morphological and functional characteristics of the malignant cell. Morphologically, the cancerous cell is characterized by a large nucleus, having an irregular size and shape, the nucleoli are prominent, the cytoplasm is scarce and intensely colored or, on the contrary, is pale.

Benign tumours usually do not cause much damage and are not normally life-threatening. But there is no guarantee: benign growths can become dangerous if they grow a lot, or they might become malignant after a certain amount of time.

If cancer cells start replicating, they do not behave like normal cells. For example, they do not know when to stop replicating and when to die. And they do not always stick together, so they might break away and move through the vascular or lymphatic system and start growing somewhere else in the body. That is called

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The nucleus of neoplastic cells plays through its changes a main role in the assessment of tumor malignancy. Changes concern its surface, volume, the nucleus/cytoplasm ratio, shape and density, as well as structure and homogeneity. Ultrastructural characteristics are related to nucleus segmentation, invaginations, changes in chromatin, such as heterochromatin reduction, increase of interchromatin and perichromatin granules, increase of nuclear membrane pores, formation of inclusions, etc.

The nucleolus is characterized by hypertrophy, macro- and microsegregation, its movement towards the membrane, numerical increase and formation of intranuclear canalicular systems between the nuclear membrane and the nucleolus.

Mitoses are characteristic of malignant cells. The number of mitoses increases, atypical mitosis forms with defects in the mitotic spindle appear, which results in triple or quadruple asters and dissymmetrical structures and atypical forms of chromosomes².

Proliferation of Cells

Proliferation is the main characteristic of benign tumors and especially malignant ones. Cells grow continuously, without being submitted to the local or general control of the organism. Benign growth is maintained within certain limits, while malignant growth is invasive, with quiet phases, followed by intense and uncontrollable growth phases.

The cell cycle normally develops along four phases²:

- Phase S, the cell synthesizes DNA, in order to prepare mitosis;
- Phase G₂ follows immediately mitosis (phase in which the genome is equally distributed between the two daughter-cells). It occurs between DNA replication and cell division;
- Phase M or mitosis, characterized by the appearance of chromatids migrating separately between the two daughter-cells;
- Phase G₁ is the time interval elapsed between the previous nuclear division and the beginning of DNA synthesis. This phase is very short for bone marrow cells and in enterocytes from intestinal crypts or, in other cases, it can be very long. Cancerous cells have an accelerated cell cycle³.

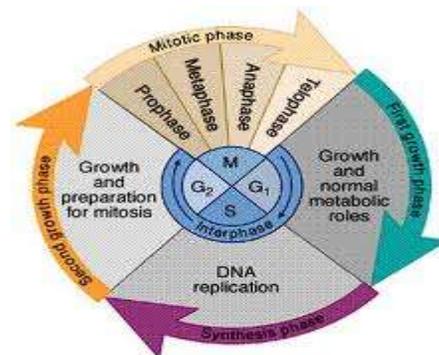


Fig:4 Proliferation of Cells

Apoptosis

Cell death, under the action of external noxious factors, is known as necrosis, and more recently, the term oncosts has been proposed when the cell becomes edematous (oncos = swelling) and represents the first phase of accidental cell

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death, with morphological changes incorporated in the necrosis process⁴.

Apoptosis is the term proposed by KERR et al. (1972), being composed of apo, which means from and ptosis, which means fall. Apoptosis in Greek expresses the fall of leaves or petals. In cell biology, the term suggests the arrest of vital functions and consequently death occurring without the intervention of external factors. The cell has its own biological and chemical mechanisms that are capable of determining cell death. Apoptosis is a physiological process that is triggered by the activation of genetic self-destruction programs existing in the genome of all cells. In this way, the multicellular organism destroys the undesired cells from a tissue⁵.

Apoptosis is an active form of cell death characterized by biochemical and morphological processes, especially by chromatin condensation, poly-nucleosomal DNA fragmentation and the fragmentation of the cell into apoptotic bodies. The apoptotic process plays a central role in the development and functioning of the immune system. Apoptosis can be partly genetically regulated and it can also be related to physiological and nonphysiological signals. Apoptosis can represent a defense mechanism at cellular level against cancer, by the participation of protooncogenes and tumor suppressor genes in the regulation of apoptosis⁶. Each cell receives multiple signals, which by means of specific receptors can induce the cell to enter the cell cycle or apoptosis. The alteration of a specific receptor can lead to the appearance of a malignant clone, due to the imbalanced relation between apoptosis inducing or repressing signals

and proliferation^{7,8,9}. The antiapoptotic Bcl-2 protein may inhibit apoptosis induced by the absence of growth factors, neurotrophic factors and cytokines¹⁰.

Tumor Angiogenesis

Vascularization in normal tissue is essential for its growth and evolution, and in tumor tissue it represents a determining factor for the alert rhythm of development, as well as for the dissemination, the metastasizing of neoplastic cells.

Microvessel density by surface unit is higher in malignant than benign neoplasias, and in highly malignant neoplastic forms, that are intensely anaplastic, the capillary network is denser, having the basal membranes fragmented. These data show the importance of vascularization, neoangiogenesis, in tumor growth and neoplastic cell metastasizing. Tumor neoangiogenesis generates numerous vascular malformations¹².

Cancer therapy aims to remove tumours or limit their growth

There are many different types of cancer treatments that all try to remove the malignant tumour, or at least limit the growth and spread of the cancer. Some cancers can be removed by Surgery. Drugs (Chemotherapy), Immunotherapy or various types of Radiotherapy are also sometimes used to shrink tumours before surgery. Chemotherapy and/or radiotherapy might be used after surgery too, to destroy leftover cancer cells and prevent the cancer from growing back (recurrence).

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If the tumour cannot be removed by surgery, medication and/or radiotherapy may be used. The exact treatment depends on various things, like the type of tumour and the stage of the disease.

You can read more about radiotherapy here. Cancer drugs work in different ways. Some aim to interfere with the cancer growth process by stopping the development of blood vessels that feed the tumour, for example. Other drugs specifically aim to stop the cancer cells replicating or reacting to hormones. Researchers are always trying to find new ways to limit the growth and spread of cancer cells.

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