The carcinogenesis or oncogenesis

A. Bensalem, MD

✉ *Corresponding Author: Dr. Assia Bensalem, MD*
Medical Oncology, Constantine, Algeria
E-mail: assiabensalem@yahoo.fr

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Introduction

Despite the large number of body cells, their proliferation is a physiological process controlled strictly. Among this large number of cells, one no longer obeys the organization proliferates unchecked and unbalanced is installed. This uncontrolled monoclonal proliferation will tend to persist, to grow, to destroy the other surrounding tissue, thus giving rise to the term cancer.

Cancerous disease caused by a disturbance monoclonal anarchic generally acquired and transmitted, control mechanisms of proliferation and the situation of cells in the body. What defines the tumor phenotype. This inheritance at the cellular level suggests the existence of genetic abnormalities at the base of the neoplastic process.

However, despite their monoclonal origin, cancer cells often do not maintain a homogenous phenotype and genotype in a single primary tumor.

Because of high genomic instability, many chromosomal rearrangements cause activation or inactivation of different genes.

Five classes of genes may be involved in the genesis of a neoplasm: oncogenes (/ Hyper-expression of HER2 amplification of the oncogene c-erb-B2 and causing abnormal cell growth), anti-oncogenes (/ The protein P53: guardian of the genome and whose mutation causes a lifting of the permanent locking it exerts on cell division), genes sharing the DNA, the genes of carcinogen metabolism genes and susceptibility to certain cancers.

A/ Definition :

There is no simple definition of the word cancer.

Cancer is the uncontrolled proliferation of some normal body cells, which escape the normal mechanisms of differentiation and regulation of their proliferation.

In addition, these cells are able to invade surrounding normal tissue, by destroying it, and then migrate away to form metastases.

Carcinogenesis: is the set of events leading to the neo-angiogenesis, the formation of cancer.

Stages of carcinogenesis

A/ Cell Cycle :

A cell, between his birth and his division, through a number of steps that constitute the cell cycle. S phase: DNA synthesis and M phase: Mitosis. These two phases are interrupted by G1 (between M and S) and G2 (between S and M). Cycle time Tc is the sum of these phases. A tumor cell divides more slowly than a normal cell.

Thus, the normal cell can either proliferate or differentiate, or to otherwise leave the cell cycle and have a quiescent state.

After a limited number of division cycles defined for each cell type, the cell dies through a process of programmed cell death (apoptosis), with an active enzymatic process.

There is therefore a mechanism for positive and negative regulation of cell proliferation that is the basis of tissue homeostasis.

This is the alteration of this control system, especially an imbalance between proliferation and programmed cell death that characterizes cancer.

B/ Evolution of Cancer from normal tissue to cancer metastasis**:**

Within 10 to 30 years before the emergence of clinical cancer is sometimes observed. This is so the average time between onset of intoxication of smoking onset lung cancer. Similarly, leukemia and cancers occurred 10 to 35 years after the explosion of atomic bomb survivors in Nagasaki and Hiroshima.

Cases of cancers of epithelial origin where it is possible to conduct regular surveillance, cancers of the uterus for example, have helped define the development stages of this cancer.

Thus, there are four phases.

1. Dysplasias

Dysplasia Is A complex lesion Characterized by cellular dedifferentiation and mitotic activity Hyperplasia With Increased.

In fact, the number of cell layers is higher than in the surrounding mucosa.

2. Carcinoma in situ

After a slow onset (5-10 years), and fickle, may appear carcinoma in situ with an uncontrolled proliferation of the entire mucosa, but without invading the underlying tissues and, in particular, crossing the basement membrane.

3. Invasive Cancer

In some cases, the previously observed cytological malignancy associated malignancy histologically characterized by the crossing of the basement

membranes but it still takes 1-5 years for the tumor reaches a size sufficient to be diagnosed by clinical examination.
The invasive process is characterized by two phenomena: a decrease in the expression of adhesion molecules between tumor cells and the cells of their microenvironment and loss of contact between these cells.

4. Metastatic
It is characterized by a spread of the malignant cell with remote development of new tumor foci; metastasis.

C/ Stages of Carcinogenesis : We can distinguish schematically three stages in the genesis of cancer, including the first two are known only by the experimental models and study the epidemiology of human tumors:

- **Initiation** is rapid and irreversible damage of DNA after exposure to a carcinogen (physical, chemical, viral, etc..)
- **Promotion** is prolonged exposure, repeated or continuous, a substance that maintains and stabilizes the lesion initiated
- **Growth** is the acquisition of properties incontrolled proliferation, acquisition of independence, loss of differentiation, local invasion and metastasis.

A1/ Initiation :

The cell becomes «immortal» after exposure to carcinogens

1/ Physical Carcinogens : RX Radioactivity (-sensitive tissue: Thyroid> Breast> Colon - Latency:> 5 years - Dose-effect-type of energy - Genetic susceptibility), UV (Main Mechanism: Mutagenesis)

2/ Chemical Carcinogens :
» Tobacco, alcohol
» Chemicals (arsenic, asbestos, aromatic hydrocarbons ...)
» Drugs (oestrogens, anti-mitotic, Immuno-depressant ...)

3/ Viral Carcinogens : Leukemia and HTLV-1, EBV and Burkitt's lymphoma and nasopharyngeal cancer, hepatitis B or C and hepatocellular carcinoma-, Herpes Virus, HPV and cervical cancer ...

4/ Genetic Carcinogens : predispositions
Several processes occur when: accumulation of mutations, clonal proliferation and irreversibility.
The increase in cancer is seen mainly in the constitutional and acquired immunodeficiency.

Agents	Exposition	Cancer	Co-factors
Aflatoxin	Food	*Hepatoma*	HPV
Alcohol	Drink	VADS, Hepatoma	Tobacco
Alkylating	Latrogenic	Leukemia	?
Amines Arom.	Dyes	Bladder	
Asbestos	Insulation	Mesothelioma	Tobacco?
Benzene	Petrochemistry	Leukemia	
Chrome	Industry	Lungs	Tobacco?
Ion Radiation.	Mining, Nuclear	Nbx	
Wood	Carpentary	ADK ENT	
Vinyl	Plastics	Liver angiosarcoma	

Family	Type	Cancer	Co-factors
Hepadnavirus	HBV	Hepatoma	Aflatoxin, Alcohol
Herpes	EBV	UCNT, Burkitt THE Immunobastique	Malaria, Nitrosamines, Immunodeficiency
HPV	16, 18, 33, 39, 5, 8, 17	Ano - genital Skin	?, UV, Genetics,
Retrovirus	HTLV-1	The T Cell	

***B1/ Promotion*:**
A clone of cells acquired the characteristics that will enable him to create a cancer. It is the uncontrolled cell proliferation is the subclinical phase and the long phase.
During the various stages that characterize the malignant cell transformation, the cells will accumulate genetic alterations leading to different manifestations of both morphological and biological weapons.

The characteristics of cancer cells include :

1.. **Deformities :** They include :
» Inequalities in cell size (anisocytosis)
» Abnormal kernel: unequal size and shape (anisokaryosis)
» Increased cytoplasmic nucleoplasmic
» Chromosomal abnormalities: quantitative (aneuploidy), qualitative (trans-locations)
» abnormal mitotic figures and many
» Abnormal Nucleoli,
» Abnormal membrane or cytoplasmic

2.. **Laboratory abnormalities :** They are :
» Abnormal cell behavior: loss of adhesion, loss of dependence / anchor, loss of inhibition of contact;
» Loss of specific cells.
» Functional disorders: Genetic instability, Tumorigenicity, Immortality

C1/ Progression **:**

This step involves local invasion, lymphatic invasion and metastatic spread.

1/ **The local invasion** : It is the ability qu'acquièrent cells to invade surrounding tissue gradually. They divert their benefit, directly or by stimulating neighboring cells, the normal mechanisms of tissue remodeling. They lose their cohesion (dependent on surface proteins) and invade surrounding tissue (proteolysis).
Break and cross the basement membrane represent a criterion for identifying invasive cancer in situ cancer

2/ **Lymphatic invasion** : After reaching the lymphatic wall, cancer cells are removed quickly by the lymph flow to the cortical sinus of the first relay node. When cells arrive at the lymph nodes, there is often a «reactive state» in the form of chronic nonspecific lymphadenitis.
At the node, the cancer cells :

- Can be destroyed,
- Can bind remaining quiescent,
- set in the ganglion, multiply to give a palpable lymph node metastasis, and possibly lead to important underlying stasis of lymph,
- through the ganglion, and win the relay node following, either in the normal sense of the current or against the current, if lymphatic stasis.
- infiltrate the route of lymphatic vessels (lymphangitis carcinomatosis).

The prosecution, step by step, invasion of lymphatics leading to the release of cancer cells into the circulation via the thoracic duct.

An intermediate step is the frequent presence of a left supraclavicular lymph node (called ganglai Troisier), the last relay before the general circulation, and signs and circulation throughout the body next to the cancerous process.

3/ **The invasion of metastatic** : Some cancers are poorly developed locally and metastasize very quickly. Conversely, others may occur years after the apparent recovery of the original cancer. Metastases may occur by:

- intravasation,
- Circulating tumor,
- extravasation,
- reimplantation,
- neovascularization.

Metastases can be :

Metastasis revealing cancer	10-15% of cancers are found by metastases from the outset, the location of metastases often citing the location of the original cancer
Synchronous metastases cancer	discovered either because of clinical symptoms, either at the staging systematic
Late onset of metastases	after delays of months or years. Metastases become rarer as and as time passes (except for breast and kidney). Late metastasis may be unique and respond well to topical therapy

It may, in case of metastasis revealing, developing an array of research of the primary tumor, according to the seat of metastasis.

Metastasis revealing	Primaries
Liver	Gastrointestinal tumors, breast, ovary, lung
Lung	Breast tumor, digestive, bronchus, testis, Kaposi
Bone	Breast, prostate, kidney, thyroid, bronchus
Brain	Bronchus, Sein, digestive tract