Biology and Kinetics of Tumors

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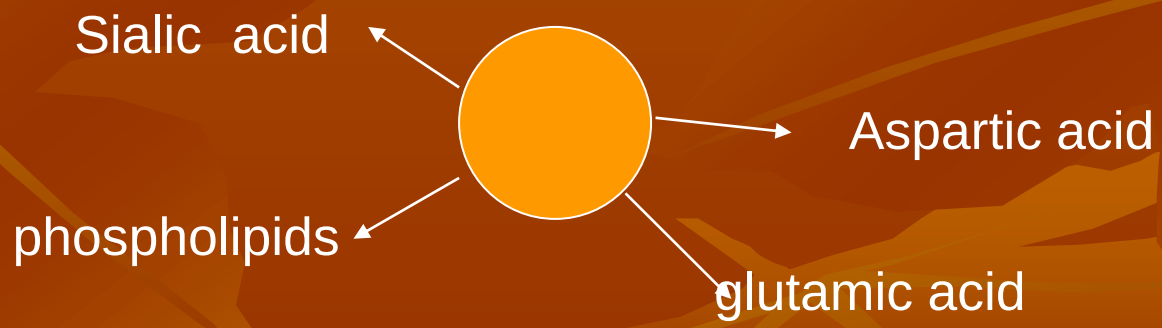
Biology and Kinetics of Tumor

- Definition of tumors
  - Malignant change in the target tissue
  - variation in size, shape,staining ability, nucleo-cytoplasmic ratio, no of nucleoli increases and the no of mitochonderia dercreases
  - Tumor cells may resemble normal cell in abnormal places

Behavioral characters of cancer cells:



Clonality of tumors

- The genetic hypothesis of cancer: a tumor mass results from the clonal expansion of a single cell that sufferd a genetic damage (i.e. tumors are monoclonal)

- **Cancer Arises from Damage to DNA**
- **The Damage to DNA Is Acquired**

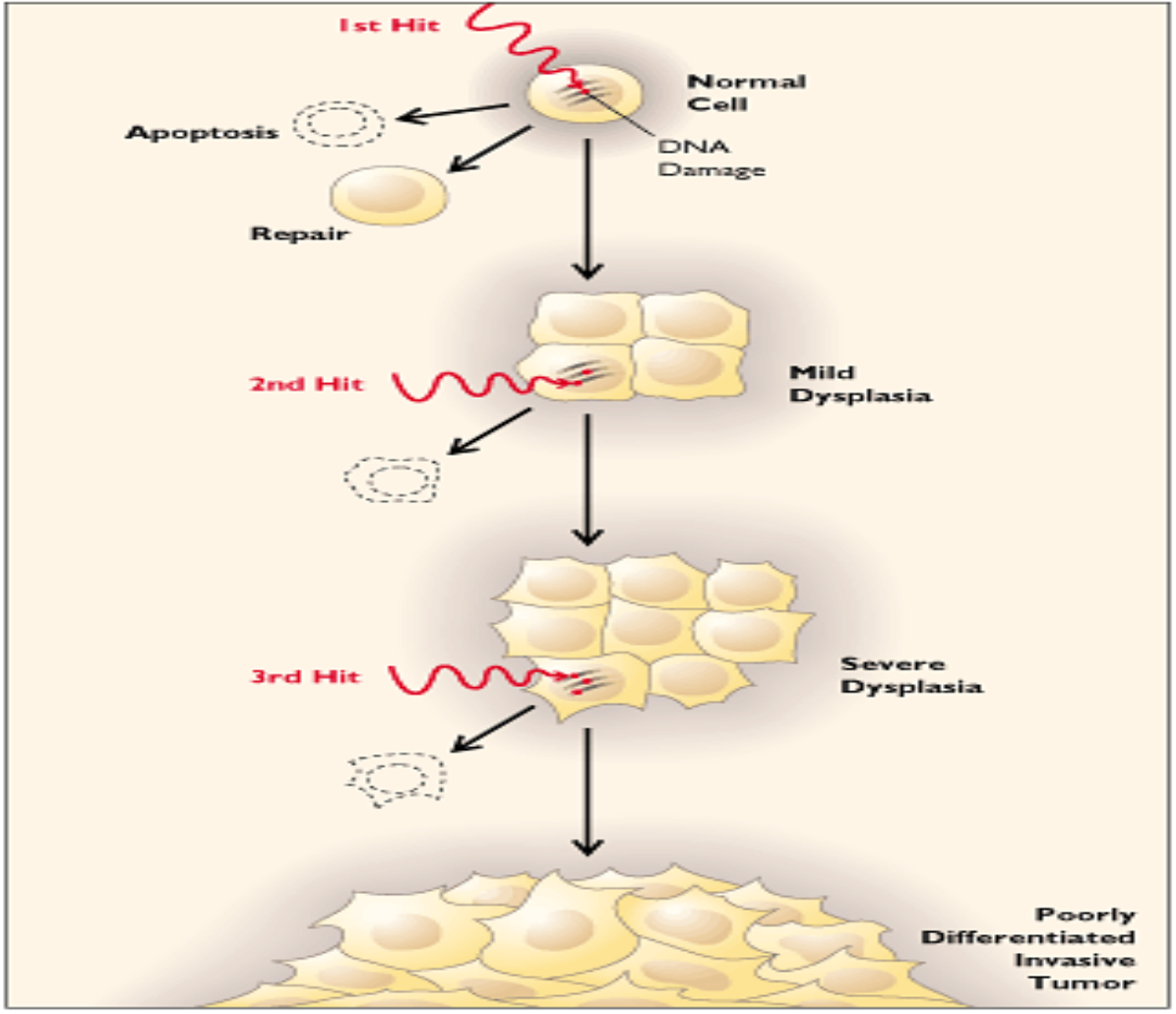


Figure 1. Multistage pathogenesis of a cancer begins when a normal cell suffers a "hit"—that is, damage to DNA. The cell may die from the damage or by the cellular suicide called apoptosis; it may succeed in making repairs; or, most rarely, it may survive unrepaired and dysplastic, and perhaps with a growth advantage. Among its clonal offspring, a cell eventually suffers a second hit, with much the same range of consequences, including the possibility of continued survival with severe dysplasia. Among the offspring, a further hit may be the one that creates a frank malignancy (sometimes by enabling prior mutations to take effect).

Regulatory Genes

- Growth-promoting Proto oncogenes (dominant genes)

- Growth-inhibiting cancer-suppressor genes (recessive genes)

- DNA repair genes

Cellular locations of tumor suppressor genes

- Cell surface
- Under plasma membrane
- Cytoskeleton
- Cytosol
- Nucleus

Functions of tumor suppressor genes

- Growth inhibition
- Inhibition of signal transduction
- Regulation of cell cycle
- Nuclear transcription
- promote DNA repair genes

P53 Gene

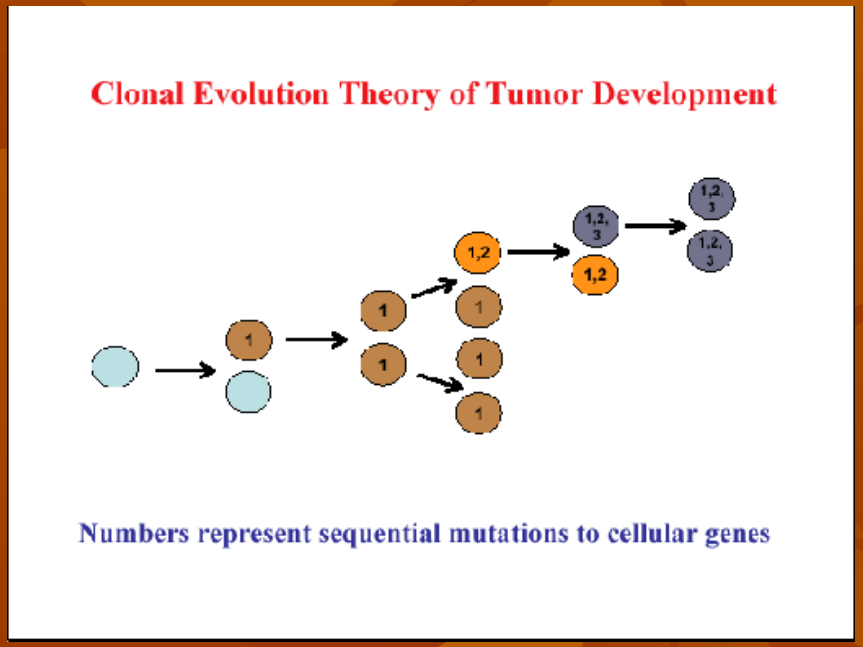
- located on chromosome 17p13.1
- single most common target for genetic alteration in human tumors (>50% of cancers)
- Function:cell cycle arrest and apoptosis in response to DNA damage

BRCA-1 and BRCA-2 Genes

- Located on chromosome 17q12-21 and 13q12-13 respectively
- BRCA-1 breast,ovary,prostate and colon
- BRCA-2 male and female breast ,ovary prostate,pancreas and larynx
- 5-10% of breast cancer is familial and mutations in these genes account for 80% of the familial cases
- Function: regulation and DNA repair

Growth and proliferation of cancer cells

- Growth is continuous process even no stimulus (unhealed wound)
- Growth and proliferation is not necessarly faster than normal
- Initial proliferation is exponentional



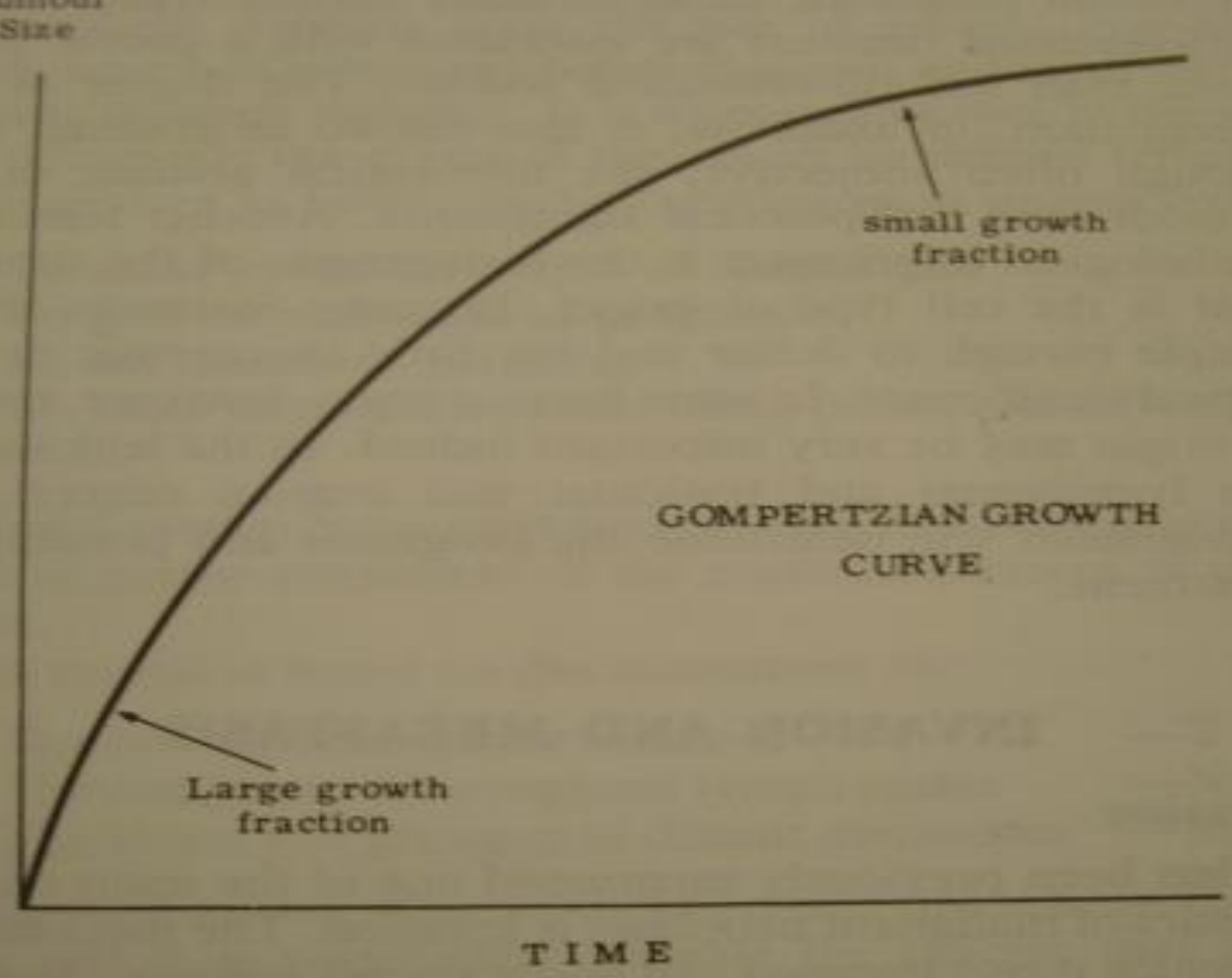


Fig. 11.4 Growth kinetics of tumours. As tumours increase in size their growth rate slows. Initially the tumour has a large growth fraction, but as the tumour volume increases, this is reduced.

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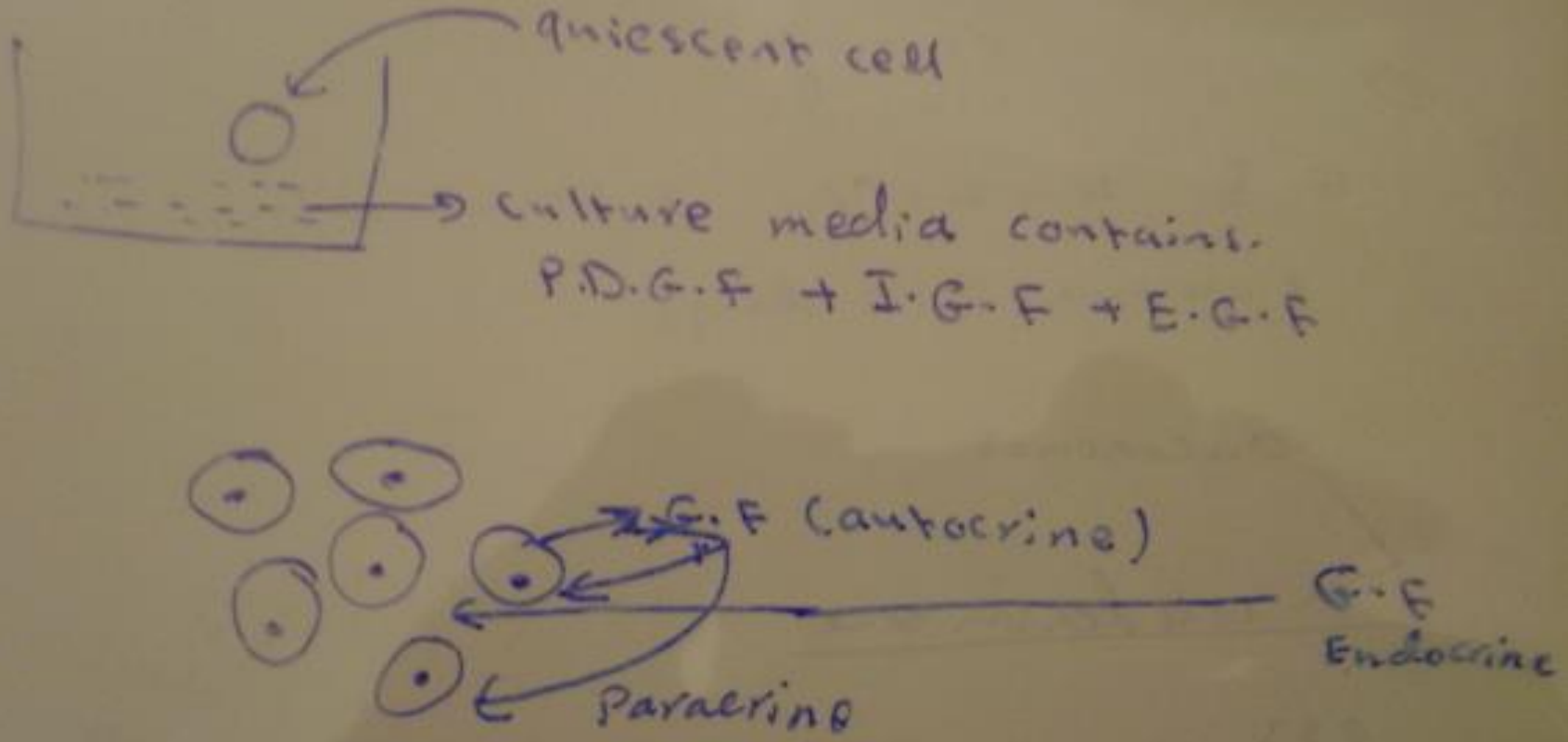
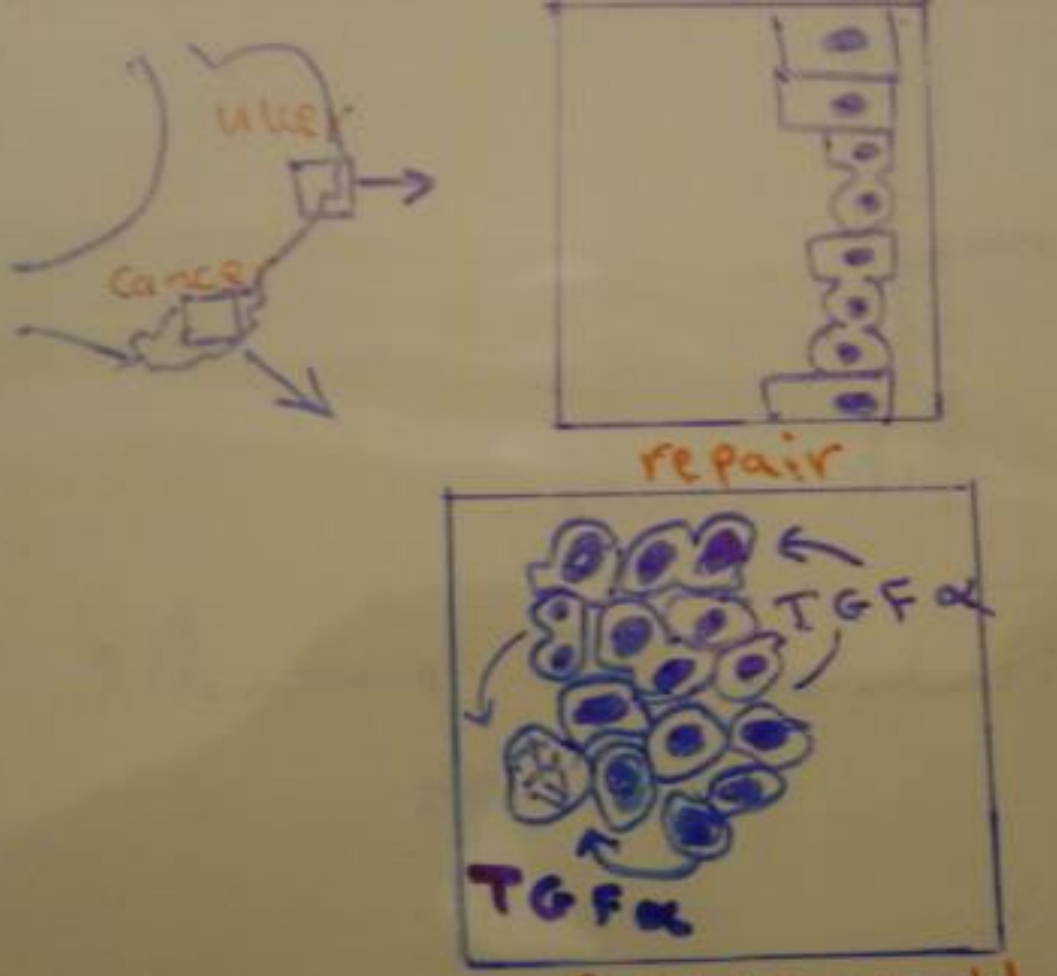
Growth Hormones and proliferation of Ca cells





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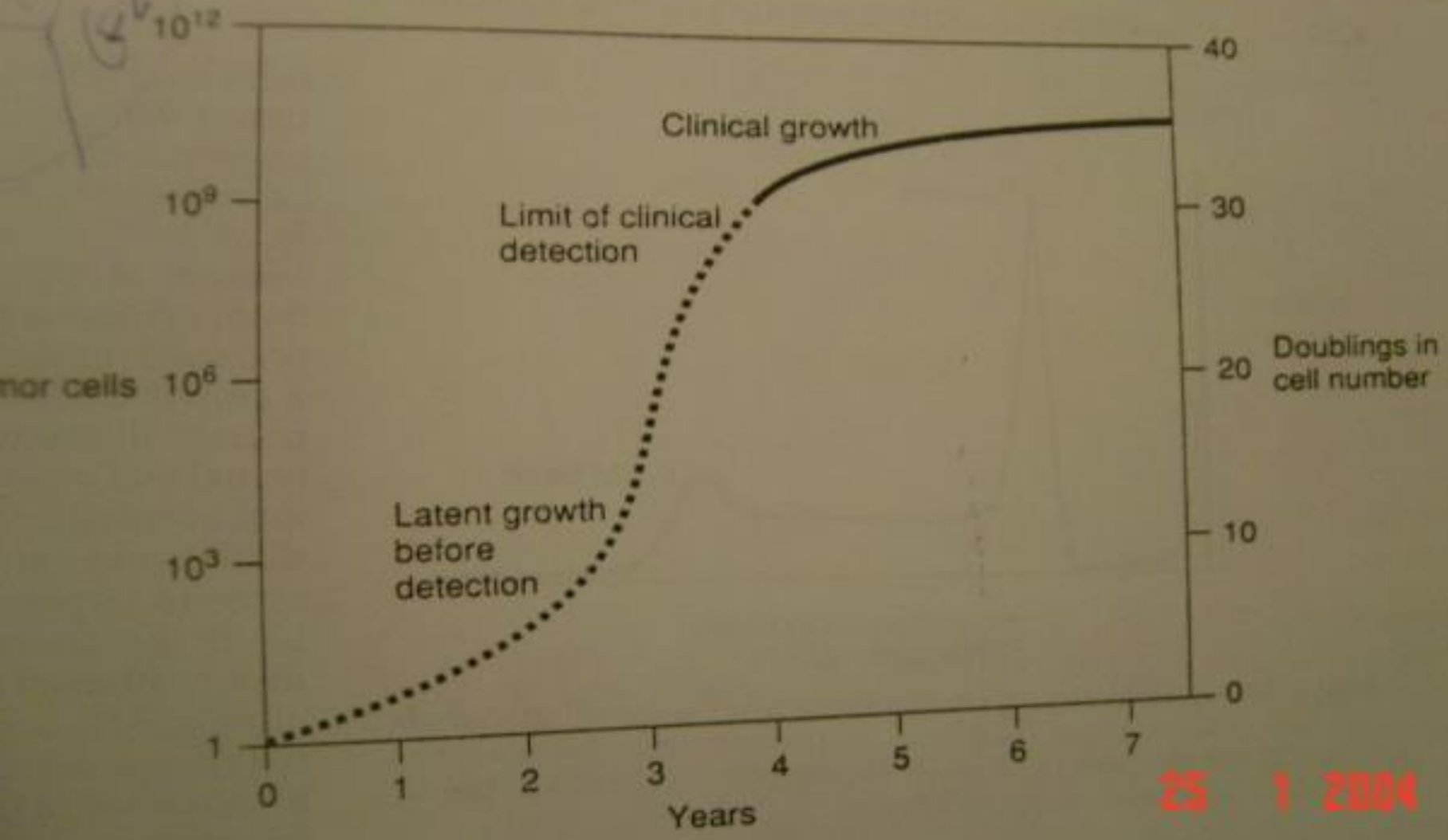

10^{12}
10^{9}
10^{6}
10^{3}
1
mor cells
40
30
20
10
0
Doublings in cell number
Clinical growth
Limit of clinical detection
Latent growth before detection
0
1
2
3
4
5
6
7
Years

Structure of solid tumors

- Parenchyma: proliferating neoplastic cells
- Stroma: made up of connective tissue and blood vessels, supportive.

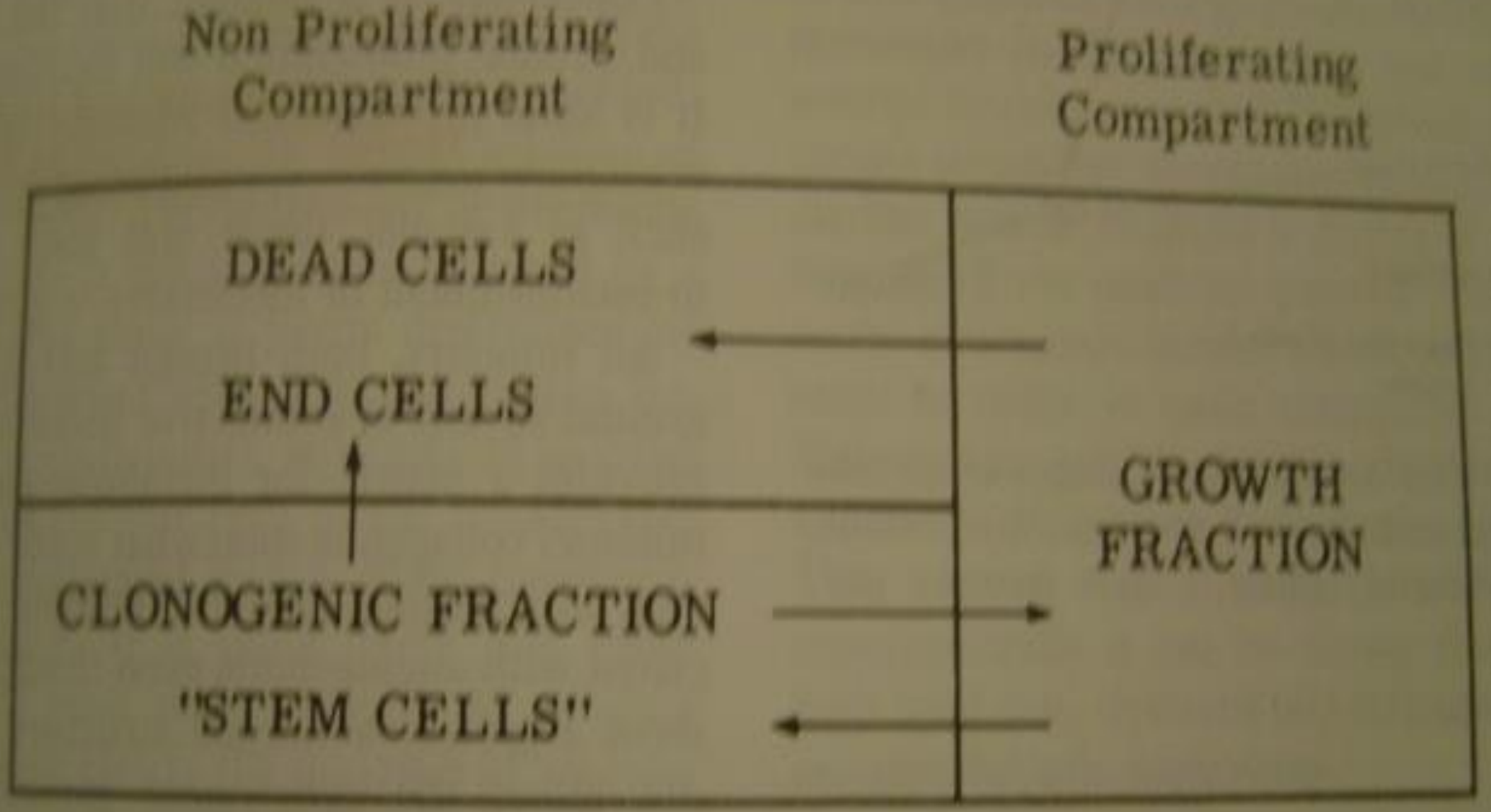
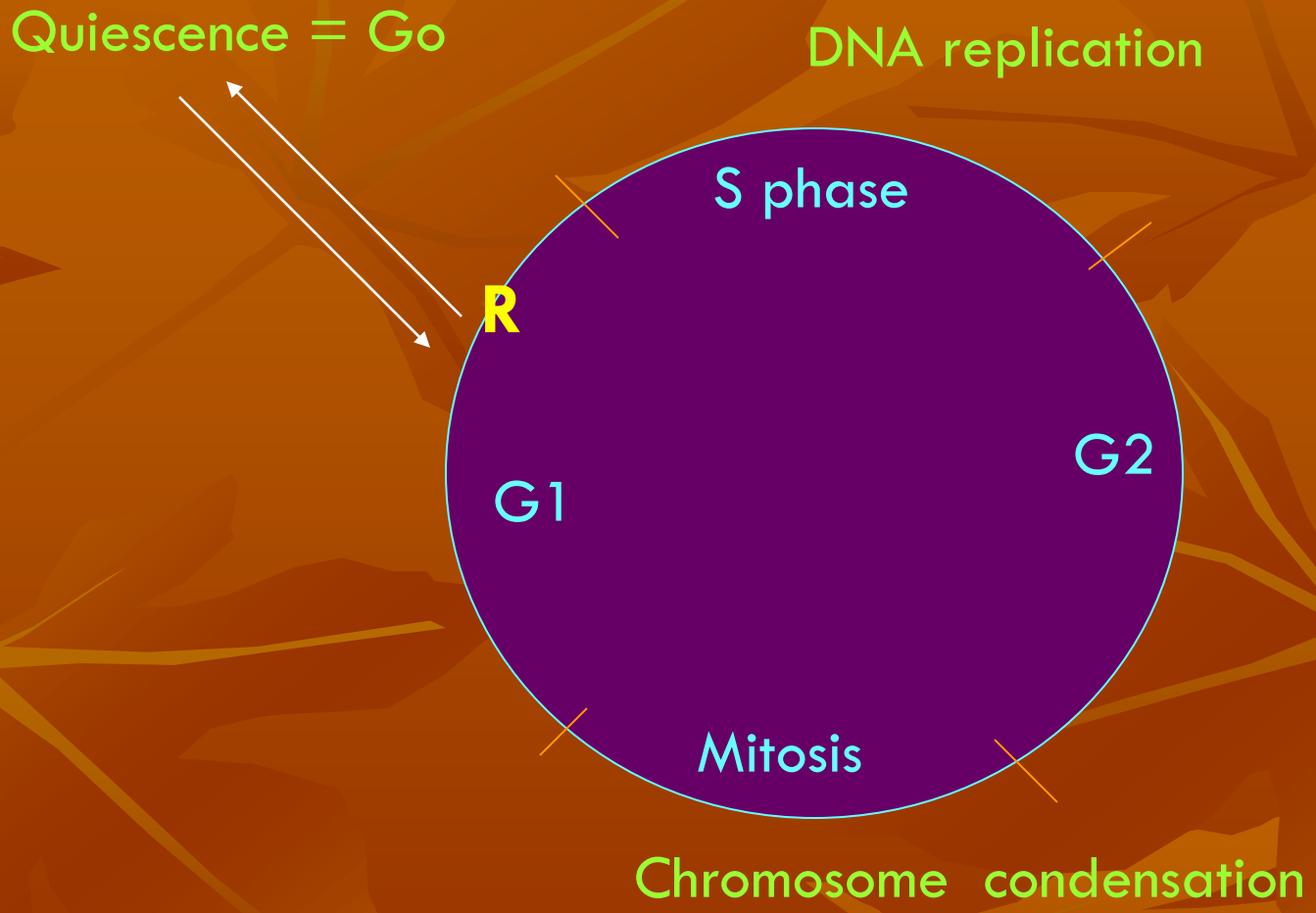


Fig. 11.3 Tumour kinetics. The tumour may be divided into several compartments depending on whether or not the cells are growing (growth fraction), have the capacity to grow (clonogenic fraction) or are end cells.

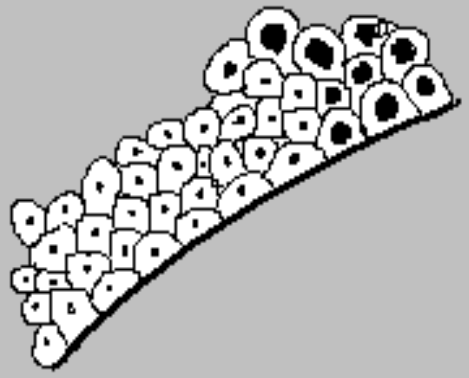
Cell cycle


Quiescence = Go
DNA replication
S phase
R
G2
G1
Mitosis
Chromosome condensation

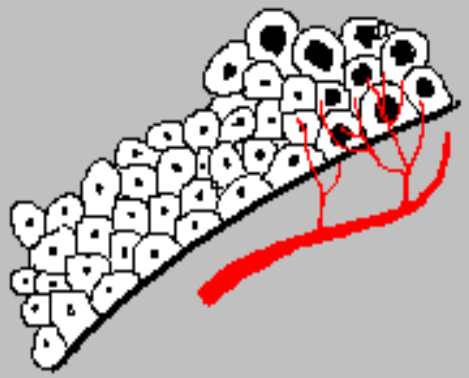
Tumor Angiogenesis

- Most important among factors that modify rate of tumor growth
- Tumors must be vascularized to grow beyond 1-2 mm
- Hypoxia induces apoptosis by activation of p53

Phases of Metastasis



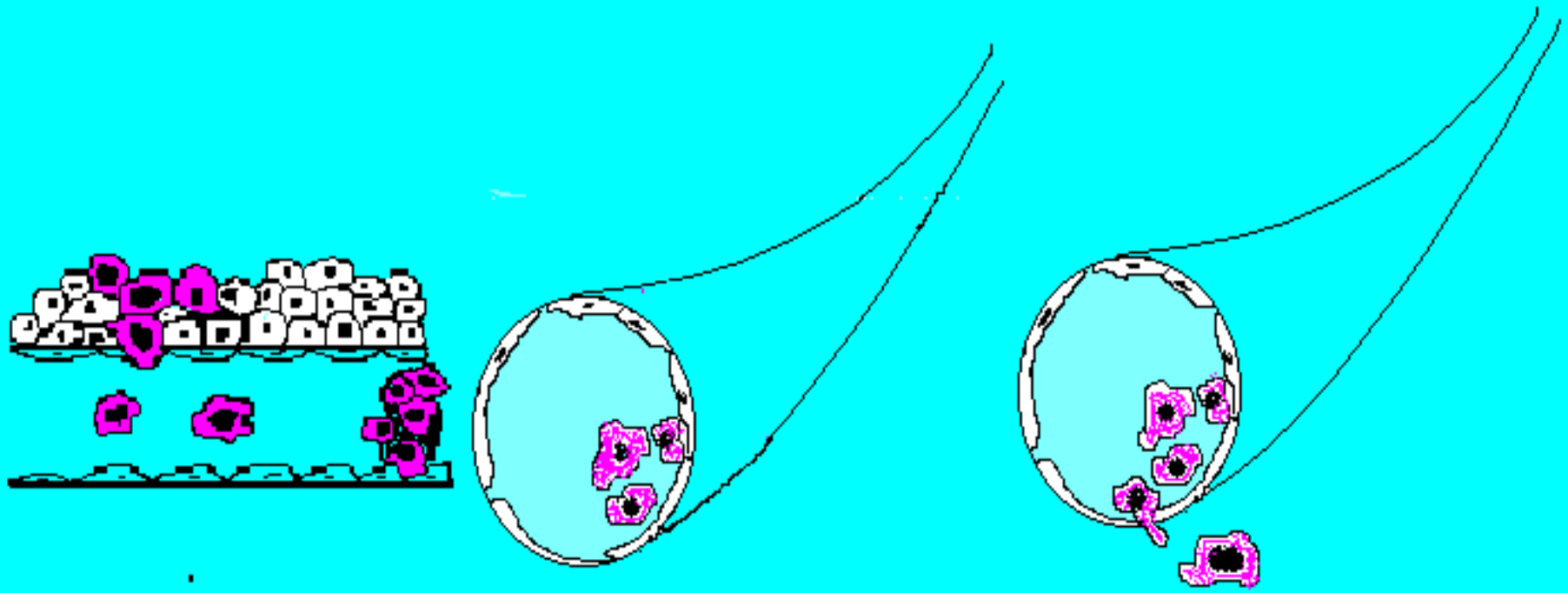
Transformation



Angiogenesis

Detachment Motility / invasion

Phases of Metastasis

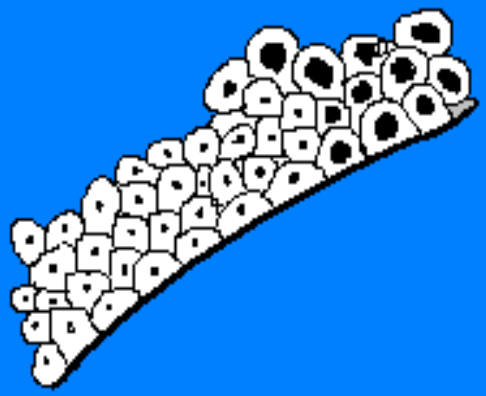


Embolism, Circulation, Survival

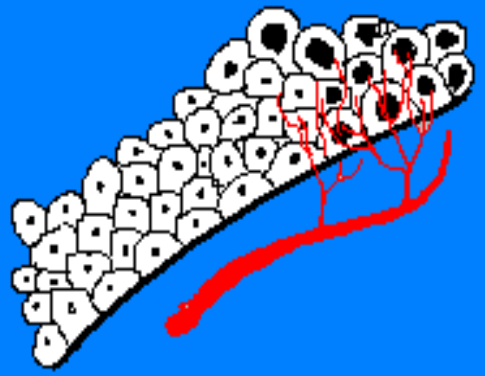
Adherence

Extravasation

Phases of metastasis



Tumor cell proliferation



Angiogenesis

Effect of Neovascularization on tumor growth

- Perfusion supplies nutrients and oxygen
- Newly formed endoth cell stimulate the growth of adjacent tumor cells by secreting polypeptides such as insulin-like growth factors, PDGF, GM-CSF, and IL-1
- Angiogenesis is needed for metastases to occur; it is a necessary biologic correlate of malignancy