Neoplasms (Tumours)

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Lecture outline

1. Definition of terms
2. Cancer epidemiology
3. Classifications of neoplasms
4. Nomenclature of neoplasms
5. Characteristics of neoplasms
6. Predisposing factors to cancer
7. Molecular basis of cancer (carcinogenesis)
8. Clinical aspects of cancers
9. Diagnosis of Cancer

Introduction

- Cancer is the second cause of death worldwide
- But more agonizing than the mortality rate about cancer is the emotional and physical suffering inflicted by the disease.
- It was a rare disease in Zambia, but now it is one of the common diseases we encounter in our daily practice.

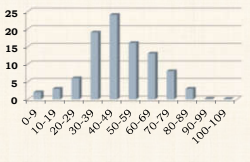
Epidemiology of neoplasms

- Worldwide, about 20% of all deaths are cancer-related.
- In Zambia, cancer cases are on the increase
- Every year CDH receives about 2,700 new patients
- **About 60** in a week **and about 240** in a month

Years	No. of Pts.
2006	35
2007	719
2008	1204
2009	1285
2010	1282
2011	1302
2012	1828
2013	2049
Total	**9800**

Top 10 cancers for Both Males & Females in Zambia in 2013

Cancers	# of Pts	%
Cervical	665	32
Breast	188	9
Kaposi's sarcoma	151	7
Prostate	102	5
Lymphomas	100	5
esophagus	51	2.5
Colorectal	39	2
keloids	30	1.5
Hepatocellular	18	1
Eye	15	1



Cervical cancer (32%) has always been on top of CDH disease chart, then breast (9%) , and a fluctuation between Kaposi's sarcoma, prostate and lymphomas.

Males

Prostate	102	15 %
Kaposis sarcoma	100	14.6%
Lymphomas	64	9%
Oesophagus	34	5%
Colorectal	26	4%
Penis	17	2.5%
Hepatocellular	12	1.8%
Stomach	11	1.6%
Rhabdomyosarcoma	11	1.6%
Bladder	11	1.6%

Females

Cervix	650	48%
Breast	182	13.5%
Kaposis	51	3.7%
Lymphomas	35	2.6%
Eye	20	1.5%
Oesophagus	18	1.3%
Vulva	14	1%
Bladder	12	0.9%
Melanoma	11	0.8%
Uterus	11	0.8%

Definition of terms

- **Neoplasm means "new growth"**
- **Neoplasm** is also referred to as a **tumour**
- **Neoplasia** is a process of forming a tumour
- A **tumor** is an abnormal growth of cells that serves no purpose
- **Oncology (oncos** – tumor**, log** - study**)** is the study of tumors or neoplasms.

Definition of terms.....

- A **neoplasm** is an **abnormal mass** of tissue **the growth** of which **exceeds and is uncoordinated with that of the normal tissue** and **persist in the same excessive manner** after the cessation of the stimuli which evoked the change. (Willis)

Classifications

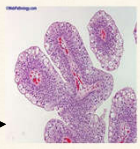
- Two (2) classifications - **benign** and **malignant** tumours.
- **A benign tumour** is considered to be innocent.
- Suggesting that it will remain localized and will not spread to other sites.
- While a **malignant tumour (cancer)** attack and destroy neighbouring structures and spread to other sites (metastasize) causing death.

Nomenclature (Naming of tumors)

- Names of tumors are derived from the components of a tumor.
- Basically, there are **two components**
  - **Parenchyma** AKA **proliferating cells**
  - **Stroma** AKA **connective tissue and vessels**
- The stroma supports the proliferating tumour cells
- Tumours get their names from the parenchyma, however, the stroma is crucial to the growth

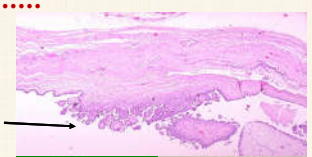
Nomenclature of Benign Tumours

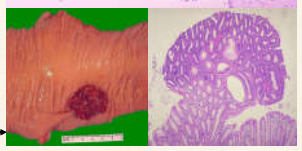
- In general, the name of a benign tumour, often ends with – **oma**. e.g.
  - Fibrous tissue (fibrocytes) is a **fibroma**
  - Cartilaginous tissue (chondrocytes) is a **chondroma**.
- However, naming of **benign epithelial tumors** is a complex one
- Those that produce microscopic finger-like branches is called a **Papillomas**



Nomenclature .....

- Those forming **cystic masses** are called **Cystadenomas** typically **seen in the ovary**.
- Those forming **gland patterns** and those **derived from glands** are called **Adenomas**





Nomenclature of Malignant Tumours

- **Malignant Tumors** – use **embryonic origin of tissue**
- **3 tissues -** (ectoderm, **mesoderm** and Endoderm)
- For **epithelial** and **glandular tissues** (ectoderm and Endoderm) - **Carcinomas**
- **Carcinomas may be classified further.**
- Those which **forms glandular pattern** - ***adenocarcinomas*****,** from **squamous cells** are called ***squamous cell carcinomas*****.**
- Those forming cysts are ***cystadenocarcinoma.***

Nomenclature .....

- For **connective tissue** (mesoderm), **muscle**, **nerve, bone** - **Sarcomas**
- Hence, cancer of the fibrous tissue is called **fibrosarcoma**
- And a malignant tumour composed of chondrocytes is a **chondrosarcoma**.
- Osteocytes - **Osteosarcoma**

Some exceptions

- Although, there is a broad generalisation regarding nomenclature, there are **some exceptions to this concept apply**:
  - **Melanoma** for cancer of the melanocytes
  - **Hepatoma** for cancer of the hepatocytes
  - **Lymphoma** for malignant tumour of the lymphoid tissue
  - **Seminoma** for malignant tumour of the testis
  - **Leukaemia** for cancer of blood forming cells

Special categories of tumours

- Some tumours defy the generalisation given above e.g.

I. Mixed tumours

- **Adenocarcinoma** and **squamous cell carcinoma** mostly affecting **endometrium**.
- **Two types of tumours combined** in one tumour - ***Adenosquamous cell carcinoma***

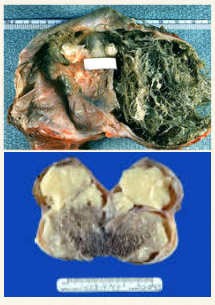
Special categories of tumours .....

II. Teratomas

- These tumours arise from **totipotent cells** and are made up of a mixture of various types of tissue
- In these tumours you can find **skin** (ectodermal), **intestine - like** and **bronchial-like structures** (endodermal), and tissues such as **bone or cartilage** (mesodermal) all intermixed in a haphazard manner.
- Most common sites for teratomas are **ovaries** and **testis**

Special categories of tumours .....

- **Teratomas** may be **benign** (**mature)** - most of ovarian Teratomas or
- **Malignant (immature)** most of testicular Teratomas.
- All age groups are affected



Special categories of tumours .....

III.Blastomas or **embryomas** are malignant tumours arising from **embryonal cells** which **normally form organs** and **tissue** during embryogenesis

- **Nephroblastoma** (Wilms' Tumour), **Retinoblastoma**, **Medulloblastoma**, **Pulmonary Blastoma**.
- Occurs in children less than 5 years

Characteristics of Neoplasms

- There are four fundamental features by which benign and malignant tumors can be distinguished.
- These are;
  - Differentiation and anaplasia
  - Rate of growth
  - Local invasion and
  - Metastasis

1. Differentiation and anaplasia

- **Differentiation** refer to the extent where **tumour cells resemble the normal cells morphologically** and **functionally**.
- **Anaplasia** refer to lack of differentiation

With regard to differentiation;

- **Benign tumours** are composed of **well-differentiated cells** that closely resemble their normal counterparts.

Differentiation and anaplasia .....

- **Malignant tumours** range from **well differentiated** to **completely undifferentiated**.
- Lack of differentiation is often associated with many other morphologic changes.
  - Nucleus size
  - Staining - hyper
  - Mitotic rates - atypical

2. Rate of Growth

- **Benign tumors** grow slowly, and **malignant tumours** grow much faster.
- There are some exceptions to this generalization.
- Under certain situations, **Some benign tumors** may grow faster than **malignant tumours**
- For example, ***leiomyomas*** (fibroids) are influenced by the circulating levels of oestrogens (↑ in pregnancy ↓ menopause on the other hand CSCC is a slow growing tumour.

Rate of Growth .....

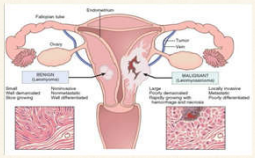
- **The rate of growth for malignant tumors** correlates in general with their level of differentiation.
- In other words, rapidly growing tumors tend to be poorly differentiated.

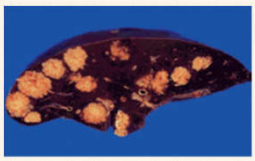
3. Local Invasion

- A benign neoplasm **remains localized** at its site of origin
- It is said to have **a capsule *derived from the stroma*** of the host tissue as the parenchymal cells atrophy under the pressure of the expanding tumor e.g. leiomyoma

Local Invasion .....

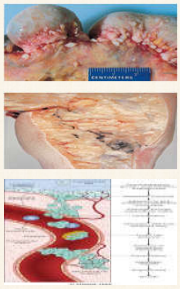
- **Cancers grow** by ***infiltration, invasion and penetration*** of the surrounding tissue.
- Hence, they do not develop well-defined capsules.





4. Metastasis

- The term **metastasis** means development of secondary tumours in remote tissues.
- They disseminate by one of three pathways:
  1. Natural pathways - transcoelomic and seeding within body cavities
  2. Lymphatic spread
  3. Haematogenous spread



Predisposing factors to cancers

- **Familial and genetic factors;** cancers run in families e.g. cancer of the ovary and breast.
- **Racial and geographic factors**. Due to partly genetic composition and largely due to influence of the environment and geographic differences affecting the whole population such as climate, diet, habits, customs etc.

Predisposing factors .....

- E.g. Malignancies of the lung and colon are common in whites while cancer of the penis and cervix common in blacks.
- **Age.** Generally, cancers occur in older individuals above 65 years of age.

Predisposing factors .....

- **Environmental, lifestyle and cultural factors;**

1. **Cigarette smoking** causes cancer of the oral cavity, pharynx, larynx, oesophagus, lungs, pancreas and urinary bladder.
2. **Alcohol abuse** predisposes to the development of cancer of oropharynx, larynx, oesophagus and liver.

Predisposing factors .....

- **Infective agents** e.g. HPV, HIV and Helicobacter pylori

1. **HPV** causes cancer by binding tumour suppressor proteins in the host, thus affecting the cellular cycle of the infected cells and it has been linked to **Cancer of the cervix**.

Predisposing factors .....

- However, CA cervix has been associated to a number of factors such as **age** at **first coitus**, **multiple sexual partners**, **parity** and **HIV status**.

2. **Helicobacter pylori** is associated with cancer of the stomach.

Molecular Basis of Cancer

Characteristics of a normal cell

1. Mortality - Normally, after 50–60 multiplications
2. Anchorage-Dependent Growth and Cell Adhesion
3. Dependence on Growth Factors to Support Proliferation

Cell proliferation is controlled by 4 classes of normal regulatory genes:

i. **Proto-oncogenes:** these are normal genes concerned with the regulation of cell proliferation.

Important proto-oncogenes:

- **HER-2 gene** - **stimulates cell division**
- The **RAS gene** - involved in ***kinase signalling pathways*** - ***controls transcription of genes***, there by regulating cell growth and differentiation
- **MYC protein** - a transcription factor that controls expression of several genes

ii. **Tumour suppressor genes**: these are normal cells which act as braking signals between ***G1 and S phase of the cell cycle***

- They stop or slow the cell cycle before S phase.
- **A few important tumor-suppressor genes are:**
  - **p53:** regulates cell division and cell death
  - **Rb: alters the activity of transcription factors** and therefore controls cell division
  - **Adenomatous Polyposis Coli (APC):** controls the availability of a transcription factor.

iii. **DNA repair genes** ***code for proteins which correct errors*** that arise during cell duplication in the DNA prior to cell division e.g. **p21.**

- These genes are **active throughout the cell cycle**, particularly **during G2** after **DNA replication** and before the **chromosomes divide**.

iv. **Genes that regulate cell death** (apoptosis) ***BCL-2*** (the anti-apoptotic gene)

Formation of cancer

- Cancer is a multistep process that requires the accumulation of multiple mutations in a single cell.
- Mutation can be due to metabolic activities or environmental factors such as radiation, chemicals or infective agents such viruses.
- 3 things in the cell cycle can go wrong:

i. Mutation of **proto-oncogene** to become an **oncogene** which later stimulates cell proliferation continuously

ii. Mutation of **tumor-suppressor genes** which later stops the ***normal brake mechanism*** resulting in uncontrolled cell growth

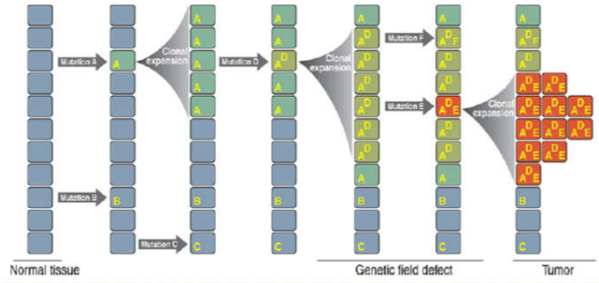
- If the rate of DNA damage exceeds the capacity of the cell to repair it, the accumulation of errors can overwhelm the cell and result in cancer.

iii. Mutations in **DNA repair genes** leading to a failure in repair

Cancer cells therefore display the following characteristics

1. **Immortality**.
2. **Non-dependence** on growth factors to support proliferation.
3. **Non-anchorage-dependent for growth** and cell adhesion – **basis of metastasis**.

Multistep process of cancer in summary



Clinical Features of Neoplasms

- Depends on the ***type, tissue affected*** and ***site***
- Change in bowel or bladder habits
- A sore that does not heal
- Unusual bleeding or discharge
- Thickening or lump in breast or elsewhere
- Indigestion or difficulty in swallowing
- Obvious change in wart or mole
- Nagging cough or hoarseness

Clinical Features of Neoplasms.....

- **Cachexia** defined by progressive loss of body fat and lean body mass, accompanied by
  - Profound weakness
  - Anorexia and
  - Anaemia
- Is caused by release of cytokines by the tumor or host.

Grading of tumours and staging

- Grading of tumors is determined by cytologic appearance and is based on the idea that;
  - Behavior and differentiation are related
  - Poorly differentiated tumors having more aggressive behaviour.
- **Staging** is determined by surgical exploration or imaging and is based on TNM;
  - Size of tumour,
  - Local and regional lymph **node** spread and
  - Distant **metastases**.
- Staging has greater clinical value than grading.

Staging.....

- ***Stage I***: malignant cells are confined to the tissue of origin, no signs of metastasis
- ***Stage II:*** limited spread of cancer in the local area, generally to area lymph nodes
- ***Stage III***: tumor larger or probably has invaded surrounding tissues or both
- ***Stage IV:*** cancer has invaded or metastasized to other parts of the body

Diagnosis of Cancer

1. **Histological Methods**

- Gold standard (biopsy or needle biopsy from the mass), supported with complete clinical and investigative data.

1. **Cytological Methods**
   - Exfoliative cytology, abrasive or fine needle aspiration
2. **Immunohistochemistry**
3. **Tumour Markers (Biochemical Assays)**
4. **Radiological and imaging** (x-rays, US, mammography, CT scan, MRI)

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