MODULE-16: NEOPLASIA-I

Learning objective

- Neoplasia is dealt in two lessons. In this module, the learner will learn about what is neoplasia?; its characteristics, classifications, differences between benign and malignant neoplasms and causes of neoplasia.

NEOPLASM

Neoplasm (G. neo-new; plasia- development or formation)

Definitions

The simple meaning of neoplasia is new growth. Out of many definitions offered, the following definition given by Mallory (1914) is satisfactory.

"A neoplasm is a new growth of cells which

- Proliferate continuously without control
- Bearing a considerable resemblance to the healthy cells from which they arise
- Have no orderly structural arrangement
- Serve no useful function
- Have no clearly understood cause (Now a few causes of neoplasms have been identified)".

Sastry (1986) added that neoplasm continues to grow even after the cessation of the stimuli which evoked the growth response. Tumour the term meaning swelling is currently restricted to neoplasms. The term cancer is used to indicate malignant tumours.

CLASSIFICATION OF NEOPLASM

- Tumours are classified based on histogenesis (Cell of origin) and behavioral pattern (Dangerous to life or not). Based on histogenesis, the neoplasms are classified as simple tumours (Involvement of one cell type), mixed tumours (Involves more than one cell type arising from a single germinal layer) and compound tumours (Cells arising from all germinal layers). Tumours are further classified based on behavioral pattern as benign (not ordinarily fatal) and malignant (usually fatal).

Nomenclature

- The nomenclature of neoplasm has two components: an initial part (Prefix) that indicates the type of cell (Histogenesis) and the following part (Suffix) indicates the benign or malignant nature of neoplasm. All benign tumours have the suffix –oma, while malignant tumours originating from epithelial cells carry the suffix carcinoma and mesenchymal cells carry the suffix sarcoma.

S. No.	Histogenesis	Behaviour	
		Benign	Malignant
I.	Simple tumours: Epithelial cells Mesenchymal cells Others	-oma -oma -oma	-carcinoma -sarcoma -oma
I I.	Mixed tumours	Benign mixed tumour	Malignant mixed tumour
I I I.	Compound tumours	Mature teratoma	Immature teratoma

Histological classification of neoplasms

	Benign	Malignant
Epithelial		
i. Epidermis	Papilloma	Squamous cell carcinoma
ii. Basal cell (Skin adnexae)	-	Basal cell carcinoma
Adnexae		
i. Hair follicle	Trichoepithelioma	Adenocarcinoma
ii. Sebaceous/Sweat/Perianal gland	Adenoma of respective gland	Adenocarcinoma
Non glandular epithelium	Papilloma	Carcinoma
Glandular surface	Polyp	Adenocarcinoma
Glandular epithelium	Adenoma	Adenocarcinoma

Mesenchymal		
i. Fibrocyte	Fibroma	Fibrosarcoma
ii. Mucoid connective tissue	Myxoma	Myxosarcoma
iii. Adipose connective tissue	Lipoma	Liposarcoma
iv. Cartilage	Chondroma	Chondrosarcoma
v. Bone	Osteoma	Osteosarcoma
Blood vessel	Angioma or haemangioma	Haemangiosarcoma
Lymph vessel	Lymphangioma	Lymphangiosarcoma
Smooth muscle	Leiomyoma	Leiomyosarcoma
Striated muscle	Rhabdomyoma	Rhabdomyosarcoma
Histiocyte	Histiocytoma	Malignant histiocytoma or histiocytic sarcoma
Mast cell	Mastocytoma	Malignant mast cell tumour or mast cell sarcoma
Haemopoietic tissue		
i. Lymphocyte	Lymphocytoma	Lymphosarcoma
ii. Plasma cell	-	Myeloma
iii. Monocyte	-	Monocytic leukemia
iv. Granulocyte	-	Myelogenous leukemia or granulocytic leukemia
v. Reticulum cells	-	Reticulum cell sarcoma
vi. Erythroblasts	-	Erythroid leukemia
vii. Myoloblast	-	Myeloid leukemia
Mesothelium		
i. Synovial membrane	Synovioma	Synovial carcinoma
ii. Meninges	Meningioma	Meningioma or invasive meningioma
iii. Bronchial epithelium	-	Bronchogenic carcinoma

Nervous tissue		
i. Astrocyte	Astrocytoma	Astrocytoma
ii. Oligodendroglia	Oligodendroglioma	Oligodendroglioma
iii. Ependyma	Ependymoma	Ependymoma
iv. Schwann cells	Schwannoma (neurilemmoma)	Neurilemmoma
v. Nerve cell	Neuroblastoma or Ganglioneuroma	Malignant neuroblastoma or Malignant ganglioneuroma
vi. Chromaffin paraganglia (adrenal medulla)	Pheochromocytoma	Malignant pheochromocytoma
vii. Non chromaffin paraganglia (Carotid body, aortic body)	Chemodectoma or Non chromaffin paraganglioma	Malignant chemodectoma or Non chromaffin paraganglioma or meduloblastoma
Others		
i. Neuroectoderm- Melanocyte	Melanoma	Malignant melanoma
ii. Renal epithelium	Renal tubular adenoma	Renal cell carcinoma
iii. Urinary tract epithelium (Transitional)	Transitional cell papilloma	Transitional cell carcinoma
iv. Placental epithelium (Trophoblast)	Hydatidiform mole	Choriocarcinoma
v. Spermatogonic epithelium (Testicular epithelium; germ cells)	Seminoma	Seminoma or Embryonal carcinoma

vi. Kidney	Nephroblastoma	Malignant nephroblastoma
vii. Islet cell	Insulinoma (β cell adenoma)	Malignant insulinoma
viii. Liver ix. Sertoli cell	Hepatoma Sertoli cell tumour	Hepatocellular carcinoma Sertoli cell tumour

DIFFERENCE BETWEEN BENIGN AND MALIGNANT TUMOURS

S. No.	Features	Benign	Malignant
1	Occurrence of nodule or mass	Single	Single or multiple
2	Shape of nodule	Round, elliptical or wart-like and pedunculated	Irregular
3	Encapsulation	Present	Absent
4	Rate of growth	Slow	Rapid
5	Growth	Limited	Unceasing
6	Spontaneous regression	Occurs	Do not occur
7	Invasion	Absent	Present
8	Metastasis	Absent	Present
9	Basement membrane	Intact	Broken
10	Blood vessel formation	Moderate	Numerous
11	Degenerative and necrotic changes	Absent as the blood supply is adequate	Present because of inadequate blood supply
12	Recurrence	Do not recur	Recurs after apparent removal
13	Destruction of adjacent tissues	Little	Extensive
14	Cell structure	Typical to adult tissue	Not typical to that of adult tissue
15	Anaplasia	Absent, resembles cells from which they originate	Present

16	Polarity	Maintained	Lost
17	Cellular pleomorphism	Absent	Present
18	Anisokaryosis	Absent	Present
19	Number of nucleus	Not altered	Multiple (Tumour giant cell)
19	Nucleolus	No change	Enlarged, prominent and multiple
20	Nucleolar to nucleus ratio	Not altered	Increased
21	Cytoplasm to nuclear ratio	Not altered	Decreased
22	Mitosis	A few in number; Typical	Abundant, some are atypical
23	Death	Do not occur except if the tumour involves vital organs like heart, brain	Usually occurs depending on the invasion, metastasis and tissue destruction

CAUSES / ETIOLOGY OF NEOPLASMS

Predisposing causes	Definite causes
• Hereditary • Breed • Age • colour • Hormones	• Physical • Chemical • Biological

Predispoing causes

Hereditary

- Hereditary predisposition is observed for some tumours.
- Certain strains of mice are highly susceptible to mammary and liver tumours. e.g. C3H. This is due to simple recessive Mendelian factor.
    - Human e.g. - Neuroblastoma, retinoblastoma and colon, ovarian, prostate, mammary and uterine cancer.
    - Lymphoid leucosis in poultry

Age

The period of life at which cancer appears is called cancer age. The malignant tumours usually occur in old age.

Species	Cancer age
Dog	5 years
Cattle	8-10 years
Human	50 years

- Older age
    - This may be attributed to exposure to carcinogen and accumulation of somatic mutations. Epithelial neoplasms are common in old age. However some tumour occurs at young age. e.g. sarcomas
    - Congenital e.g. nephroblastoma

Colour (Pigmentation)

- Melanin pigment produced by melanocyte protects skin against UV rays of sun. Hence, lack of pigmentation may lead to occurrence of tumours.
- eg. Grey and white horses - malignant melanoma (especially old age); Hereford cattle - ocular squamous cell carcinoma

Hormones

- Hormones like estrogen and progesterone may play a role to predispose animals to cancer. e.g. Estrogen - Mammary tumour, ovarian carcinoma. Progesterone - Mammary tumour in dogs ans cats.

Mammary tumour - Dog - Primary tumour

Definite causes

Physical

- Solar radiation- cutaneous tumours
- It is associated with areas where sunlight is intense, light skinned animals and exposure of the area.
- UV radiation (UVB 280-320 nm) causes pyrimidine dimers injuring DNA causing mutation and tumours.
- **Xeroderma pigmentosum** - a genetic disease of human in which enzymes required for DNA repair are lacking, hence exposure to UV ray of sunlight results in dry pigmented skin. Whole body radiation can cause leukaemia
- Radiation includes elctromagnetic radiation (UV rays, X rays and gamma radiation and particulate radiation (α, β, proton and neutrons) which are carcinogens.
- X ray - skin tumour
- I^{131} - thyroid adenoma
- Radium - osteosarcoma and leukaemia (painters of watches and clocks)

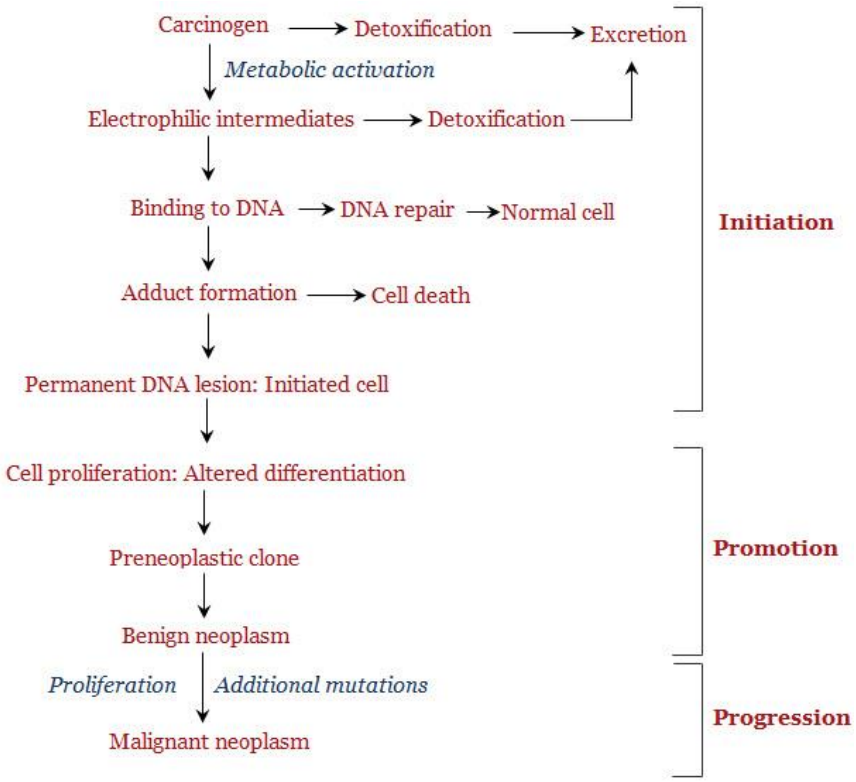
Chemicals

Sir Percival Pott (1775) was the first scientist to identify chemical agent to cause of cancer. In 1915, Yamagiwa and Itchikawa produced cancer in rabbit ears with repeated application of coal tar i.e. experimental carcinogenesis. Kenneway and Cook purified the carcinogen 3, 4 - benzapyrene from crude tar. Other potent chemical carcinogens are benzanthracene, methylcholanthracene (Chlorinated hydrocarbons).

Examples of major chemical carcinogens

- **Direct acting**
  - Alkylating agents - β propiolactone, Dimethylsulfoxide
  - Aceylating agents - 1 acetyl imidasone
- **Indirect acting or procarcinogen** - It requires metabolic conversion to become ultimate carcinogen to induce cancer.
  - Polycyclic and heterocyclic hydrocarbons - benzanthracene
  - Nitrosoamines and nitrosoamides - vinyl chloride, aldrin, dieldrin

Mechanism of chemical carcinogenesis



Initiation promotion model

S.No.	Initiator	Promoter	Tumour produced
1	Aflatoxin B1	Methyl sterculate	Hepatocellular carcinoma in trout
2	Benzapyrene	Croton oil	Squamous cell carcinoma inn mouse skin

Biological causes

- **Bacteria**: *Helicobacter pylori* – gastric cancer and lymphoma in man; *Helicobacter hepaticus* – hepatocellular carcinoma in mice
- **Parasites**
  - *Spirocera lupi* - Oesophageal fibrosarcoma and osteosarcoma in dogs
  - *Cysticercus fasciolaris* – fibrosarcoma in rat liver
  - *Eimeria stiedae* – bile duct tumour in rabbits
  - *Schistosoma haematobium* – bladder cancer in man
- **Viruses**
  - **DNA viruses** – Papova, Shope papilloma, canine oral papilloma, bovine papilloma, human papilloma
    - Pox viruses – fibroma, myxoma in rabbit
    - Herpes virus – Marek's disease chicken
  - **Oncogenic RNA viruses**
    - Retroviruses – Lymphoid leucosis
    - Rous sarcoma virus – Tumours in poultry

Ellerman and Bang (1908) were the first to demonstrate viral carcinogenesis and later by Rous. Peyton Rous (1910) produced similar results with fowl sarcomas. Gross (1953) induced leukaemia with cell free filtrate in mice.

MODULE-17: NEOPLASIA-II

Learning objective

- In this module, the learner will learn about spread of neoplasms, tumour and immunity, clinical effects of neoplasia, diagnosis and stages and grades of neoplasia.

SPREAD OF NEOPLASM

The neoplasm spreads by

- Invasion
- Metastasis

These are hall marks of malignant tumour.

Metastasis can occur by

- Implantation
- Haematogenous spread
- Lymphatic spread

The invasion and metastasis are characteristic features of malignant neoplasm. Invasion is defined as movement of neoplasm directly through tissue planes. Implantation is establishment of neoplasm on new surfaces especially body cavities. Metastasis is defined as spread of neoplasm from primary to a distant site. Invasion of neoplasm into an adjacent tissue is facilitated by breaking of basement membrane by proteolysis (collagenases) and migration through interstitial tissue through the help of proteolytic enzymes or proteases. Increased negative charges on plasma membranes, decreased calcium ion content and lack of cohesiveness facilitate the process of invasion.

Infiltration of neighbouring tissues: The malignant tumour infiltrates and invades the adjacent tissues because of rapid multiplication of cells, neoplastic cell motility (amoeboid movement of fibroblast due to lack of contact inhibition and cohesiveness) and accumulation of metabolites (e.g. Lactic acid) and enzymes like hyaluronidase which hydrolyse cementing substance.

Infiltration

- Infiltration into tissue spaces
    - Invasion depends upon the type of tissue. Soft and loose tissue can be infiltrated easily while it is difficult to infiltrate hard tissues.
- Intracellular infiltration
    - Tumour cells can also traverse cell. e.g. Penetrate muscle fibres

Lymphatic spread

- This occurs by emboli formed by clumping of neoplastic cells. Permeation can also occur wherein the tumour cells extend along lymphatics by growing along endothelium. Neoplastic cells reach regional lymph nodes and are trapped in the cortical sinuses and following proliferation of cells lead to secondary tumours. Carcinomas spread by lymphatics.

Blood spread

- Neoplastic cells frequently invade veins and capillaries. Tumour emboli involving portal vein induces tumour in the liver and those spread through systemic vein produce metastases in lungs.

Transcoelomic spread (Spread in body cavities)

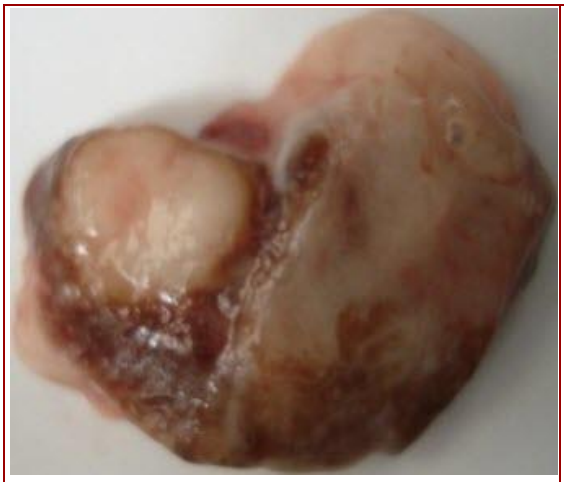
- In implantation, the lack of cohesiveness of neoplastic cells favours implantation into the surrounding body cavities i.e. transcoelomic spread or soil theory or seeding into pericardial, pleural, peritoneal and subarachnoid membranes. e.g. Cancer of ovary and stomach

Implantation

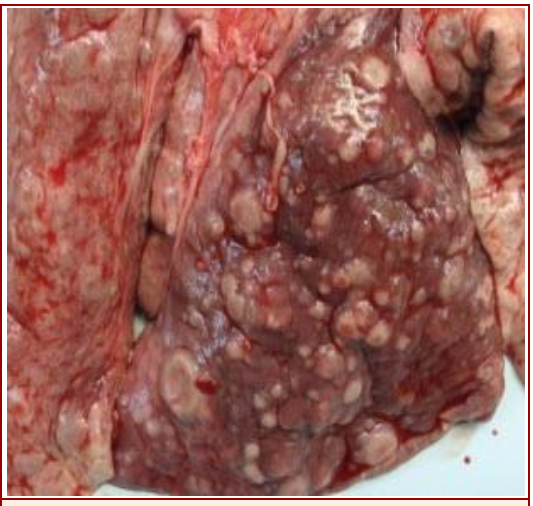
- By natural passages - In hollow organs, the tumour cell casts get and implanted. e.g. Tumour of renal pelvis get washed down in bladder and implanted to form tumours.
- Inoculation - rare hazard in surgery where tumour cell can be implanted in edges of the wound and new tumour develops.
- Coitus - venereal tumour of dogs gets transmitted by this way.

Spread by nerves

- This occurs by permeation through perineural lymphatics with degeneration of nerves.



Mammary tumor - Dog - secondary tumour - Lymph node metastasis



Mammary Tumour - Dog - Metastasis - Lung

Mechanism of invasion and spread

The spread of tumour is divided into two phases.

1. Invasion of extracellular matrix
2. Vascular dissemination and homing of cells

Invasion of extracellular matrix

Extracellular matrix is divided into two types

- Basement membrane
- Interstitial connective tissue

Extracellular matrix is composed of collagen, glycoproteins and proteoglycans. Invasion of extracellular matrix by tumour cell is an active process involving

- Detachment of tumour cells from each other
- Attachment of tumour cells to matrix
- Degeneration of extracellular matrix
- Migration of tumour cells

Detachment of tumour cells from each other which occur due to loosening of tumour cells which lack adhesion molecules. e.g. E-cadherin. Attachment of tumour cells to matrix by proteins like laminin and fibronectin through the receptors. Normal epithelial cells have receptors for basement membrane laminin on basal surface while carcinoma cells have many more receptors. Degeneration of extracellular matrix

occurs due to proteolytic enzymes elaborated by tumour cells. Migration of tumour cells: The locomotion of tumour cell is by amoeboid movement by throwing pseudopodia through the degraded basement membrane.

Vascular dissemination and homing of cells

- Once in the circulation those tumour cells which survive host immunity by binding with circulating lymphocytes and platelets adhere to vascular endothelium and exits through basement membrane. Site of metastasis depends on location of primary tumour and its vascular and lymphatic drainage and organ tropism depends on cellular attraction, etc. e.g. Lung cancer spreads to adrenals and do not affect skeletal muscle. This phenomenon is called homing of tumours.

Spread of tumours

Clonal expansion, growth, diversification, angiogenesis

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Metastatic subclone

↓

Adhesion to and invasion of basement membrane

↓

Passage through extracellular matrix

↓

Intravasation

↓

Interaction with host lymphoid cells

↓

Tumour cell embolus

↓

Adhesion to the endothelium

↓

Breaking the basement membrane

↓

Extravasation

↓

Metastatic deposit

↓

Angiogenesis

↓

Growth

TUMOUR IMMUNITY

- The genetic alteration that occurs during malignant transformation may result in expression of proteins that are regarded as non-self of foreign by the immune system. The immune surveillance mechanism recognises and destroys non-self tumour cells.

Tumour antigens

- The tumour cells may differ antigenically from normal cells and can either gain or lose cell membrane molecules.

- They are of two types
    1. Tumour specific antigen (TSA), present only on tumour cells and not on any other cells
    2. Tumour associated antigen (TAA), present on tumour and also some normal cells

Tumour specific antigens are found in chemically induced tumour of rodents which express unique antigen not shared by other histologically identical tumour induced by the same chemical even in the same animal. Tumour specific antigen is an altered form of normal protein occurring due to mutation of gene. Each mutated protein combines with MHC class I protein to become an antigen. These are recognised by CD8+ cytotoxic T lymphocytes.

Tumour associated antigen are not specific to individual tumour and shared by similar tumour in other animal.

Two types of tumour associated antigen (TAA)

1. **Oncofetal antigen -** Embryonic antigens which are normally expressed in developing embryos. e.g. Alpha fetoprotein,Carcinoembryonic antigen (CEA)
2. **Differentiation antigens** are peculiar to different stage in which cancer cells are arrested and useful differentiator marker in diagnosis of cancer. e.g. Prostatic and lymphoid tumour in man

Since tumour associated antigens are normal self protein they do not evoke immune response but of value in diagnosis of certain and immune therapy.

Anti-tumour effector mechanism

Both cell mediated immunity and hormonal immunity (activation of complement, ADCC) have anti-tumour activities.

- Cytotoxic T lymphocytes (CD8+ T cells)
    - Cytotoxic T lymphocytes are important in chemically induced tumours. It plays a protective role in virus associated neoplasms. The cells destroy the tumour cells by recognising MHC class I antigen expressed on tumour cells.
- Natural killers cells (NK cells)
    - These cells can destroy tumour cells without prior sensitization thereby provides first line of defence against tumour cells. After activation with interleukin 2, natural killer cells can destroy a wide range of animal and human tumours.
- Macrophages
    - Activated macrophages show selective cytotoxicity against tumour cells. T cells, NK cells and macrophages may work together in anti-tumour activity. γ interferon, a cytokine secreted by T cells and NK cells, is a potent activator of macrophage. These cells kill the tumour cells through reactive oxygen species or secretion of tumour necrosis factor (TNF).

- Antibody dependant cellular cytotoxicity (ADCC)
    - It is involving killing those cells that bear receptor for Fc portion of IgG. Target cell coated by antibody are destroyed without phagocytosis or complement fixation. ADCC may be mediated by neutrophils, eosinophils, macrophages and NK cells.

Immunosuppression

- Many oncogenic substances suppress host immune response (chemicals, ionising radiation) and tumours or tumour products e.g. TGF β, potent immunosuppressor

Evasion of immune system (Immunosurveillance)

This may occur through different mechanisms.

- Non expression of new antigens that are immunogenic
- Failure to express host immune stimulatory molecules required for activation of T-cells
- Lack or poor expression of MHC antigen by tumour cells
- Overwhelming the immune system and rapid proliferation of malignant cells or too small tumour cells in initial stage to evoke immune response
- Secretion of immunosuppression molecules
- Expression of death inducing ligands (Fas L, CD95 L)
- Inactivation or mutation of tumour suppressor and apototic genes. e.g. p53, BCL - 2

EFFECTS OF NEOPLASIA

The effects of neoplasia primarily may be due to the size, location and tissue of origin and secondarily due to spread to other organs.

- **Pressure atrophy** - The expanding tumour may cause pressure atrophy of some organs especially through pressure on blood and lymphatic vessels thereby interfering with nutrition and fluid exchanges to tissues.
- **Location** - The tumour may cause obstruction of luminal organs by narrowing luminal space interfering with functional activity.
    - Obstruction Effect
        - Ureter Hydronephrosis
        - Bronchus Collapse of lung
        - Intestine Intussusception
- **Tissue of origin** - If the tumour involves vital organs like heart and brain, it causes death.
- **Cancer cachexia** - It is due to loss of body fat and wasting besides profound weakness. The TNFα plays a role on suppressing the appetite and inhibition of action of lipoprotein. This will lead to excessive protein degradation and negative nitrogen balance.
- **Infection** - Surface tumours may be ulcerated and subsequently infected.
- **Exudate in serous cavities** – Tumour cells deposited on serous membranes incites an inflammatory response with exudation. Eg. Malignant ascites.

- **Hormonal effects**
  - Parathyroid tumour – Osteoporosis and big head in horses
  - Tumour of sertoli cells – Feminization
  - Hypoglycaemia - Insulinoma
  - Arrhenoblastoma in female - Masculinisation
- **Anaemia** may be due to decreased bone marrow response, haemorrhages and haemolysis
- **Thrombocytopenia** may also occur.
- **Monoclonal gammopathies** occur in plasma cell tumours.
- **Paraneoplastic syndrome** the symptoms that are not directly related to spread of tumour or elaboration of hormones indigenous to the tissue from which tumours arise.
  - Ectopic hormone production or syndrome
    - The production of hormones by the neoplastic cells which are not of endocrine origin.
    - e.g. Lung cancer - ACTH production
    - Fibrosarcoma - insulin production
- **Hypercalcaemia** occurs when neoplastic cell synthesises and secretion of peptides that mimick parathyroid hormones or tumour affecting producing humoral factors and stimulating osteoclasts. e.g. Lymphoma in dogs and cats.

DIAGNOSIS OF CANCER

Early diagnosis of cancer will help in treatment by therapy or surgical intervention.

- Clinical diagnosis
  - Based on the gross features (Papilloma, cystic, fibrotic, nodular tumour)
  - Any nonhealing growth or lesion and growth of profusely bleeding nature are to be suspected for possible cancer.
- Biopsy (histopathology)
  - Reliable method by which diagnosis can be made based on cellular characteristics (microscopically - anaplasia, invasion, mitosis, metastasis, loss of polarity) which indicate malignancy (Also see staging and grading)
- Radiology
  - Radiological examination of viscera and bone may show primary or secondary lesions. However, this is much applicable in small animals and of limited use in veterinary practice.
- Cytology
  - It is examination of cells which can be applied in diagnosing cancer. Cells can be collected most commonly through fine needle aspiration biopsy. Other methods are impression, scraping and brushing. This can be stained by Romanowsky's stains and haematoxylin and eosin stain. Cellular characteristics for malignancy have to be seen.
  - Acridine orange staining - The cytoplasm of malignant cells will show brick red fluorescence and nucleus will show apple green fluorescence.
- Exfoliative cytology
  - Neoplastic cells show loss of cohesiveness and those arising on the surface are easily detached and exfoliated. These cells can be collected and suitably stained for making a diagnosis. This technique is used in human medicine for early diagnosis of cervical, uterine and bronchogenic tumours. Pappanicolaou is considered as father of cytology. This test is known as papa test.

- Chemical and serological tests
  - No such reliable tests are available in veterinary practice. However, in human medicine chemical/enzyme tests are available to diagnose prostatic cancer and bone cancer.
- Molecular methods
  - Polymerase chain reaction (PCR) will be helpful in differentiating monoclonal tumours.
- Flow cytometry
  - This can identify cell population. e.g. immunophenotyping of lymphocytes
- Immunohistochemistry method
  - Immunohistochemistry can be used to identify the type of cell (epithelial cell-cytokeratin marker) and malignancy of tumours.
  - DNA probe analysis, northern, southern and western blot analysis can be used.

Tumour markers

- This is biochemical indicator to identify the presence of tumours. This may be cell surface proteins, cytoplasmic proteins, enzymes and hormones.

Uses

- To confirm diagnosis
- To determine response to therapy
- To indicate relapse after treatment

Markers	Associated tumours
Oncofetal proteins	
Alpha fetoprotein	Hepatocellular carcinoma Germ cell tumour of testes
Carcinoembryonic antigen	Carcinoma of colon, pancreas and stomach
Hormones	
Calcitonin	Thyroid medullary carcinoma
Catecholamines	Pheochromocytoma
Isoenzymes	
Prostatic acid isophosphatase	Prostatic tumour (human)
Specific protein	
Immunoglobulins	Multiple myeloma
Mucin	
CA 125	Ovarian tumour

GRADING AND STAGING OF CANCERS

Based on the extent of malignant features like cellular characters (differentiation and anaplasia), invasion, metastasis and number of mitoses, tumours can be classified as grade I, II, III, IV (grade I for the least and grade IV for the most anaplastic)

Clinical staging of cancer (TNM classification)

This is based on

- Size of the primary tumour -T
- Extent of spread to regional lymph node -N
- Presence or absence of metastasis -M

Clinical staging should be combined with histological analysis such as grading of tumours which is helpful in prediction of survival of cancer patients.

Primary tumour

- T0 – no evidence of tumour
- T1 – tumour confined to primary site
- T2 – tumour invades adjacent tissues

Lymph nodes

- N0 – no evidence of tumour
- N1 – regional lymph node involvement
- N2 – distant lymph node involvement

Metastases

- M0 – no evidence of tumour
- M1 – tumour in same organ or cavity as primary
- M2 – distant metastases