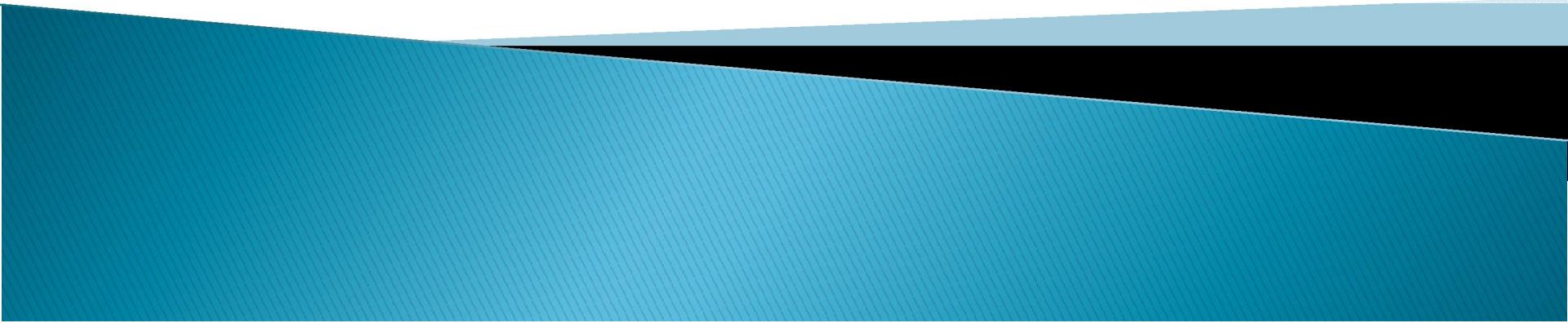


Tumors in animals



SPREAD OF NEOPLASM

The neoplasm spreads by-

- I) Invasion
- II) Metastasis

These are hall marks of malignant tumour.

Metastasis can occur by -

1. Implantation
2. Haematogenous spread
3. Lymphatic spread
4. Perineural spread

➤ **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.**

SPREAD OF NEOPLASM

The neoplasm spreads by-

I) Invasion -

The malignant neoplasms are infiltrated or invaded the surrounding tissue.

Penetration of the basement membrane and invasion of the surrounding tissue.

It occurs in **three steps.**

A. Binding to the extracellular matrix. The tumor cells firstly bind to the extracellular matrix as laminin, proteoglycans and collagen through surface receptors.

B. Degradation of the extracellular matrix through secretion of enzymes that degrades the matrix as proteinases, collaginases and cystein proteinases.

C. Movement through interstitial tissue through the help of proteolytic enzymes or proteases. The malignant cells require locomotion, which enhanced through secretion of autocrine motility factors and lack of cohesiveness facilitate the process of invasion.

SPREAD OF NEOPLASM

The neoplasm spreads by-

II) Metastasis -

- Metastasis refers to the spread of malignant cells from one site to another
- It occurs following invasion of the surrounding tissue.
- The malignant cells invade the blood and lymphatic vessels in the same way that they invade parenchymal tissue.

The metastasize occurs through -

1. **Blood (hematogenous metastasize)** or through
2. **Lymph (lymphatic metastasize)** and through
3. **Seeding of body cavities and surfaces (transcoelomic spread) or implantation**

SPREAD OF NEOPLASM

1. 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.

2. Hematogenous metastases -

- 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.

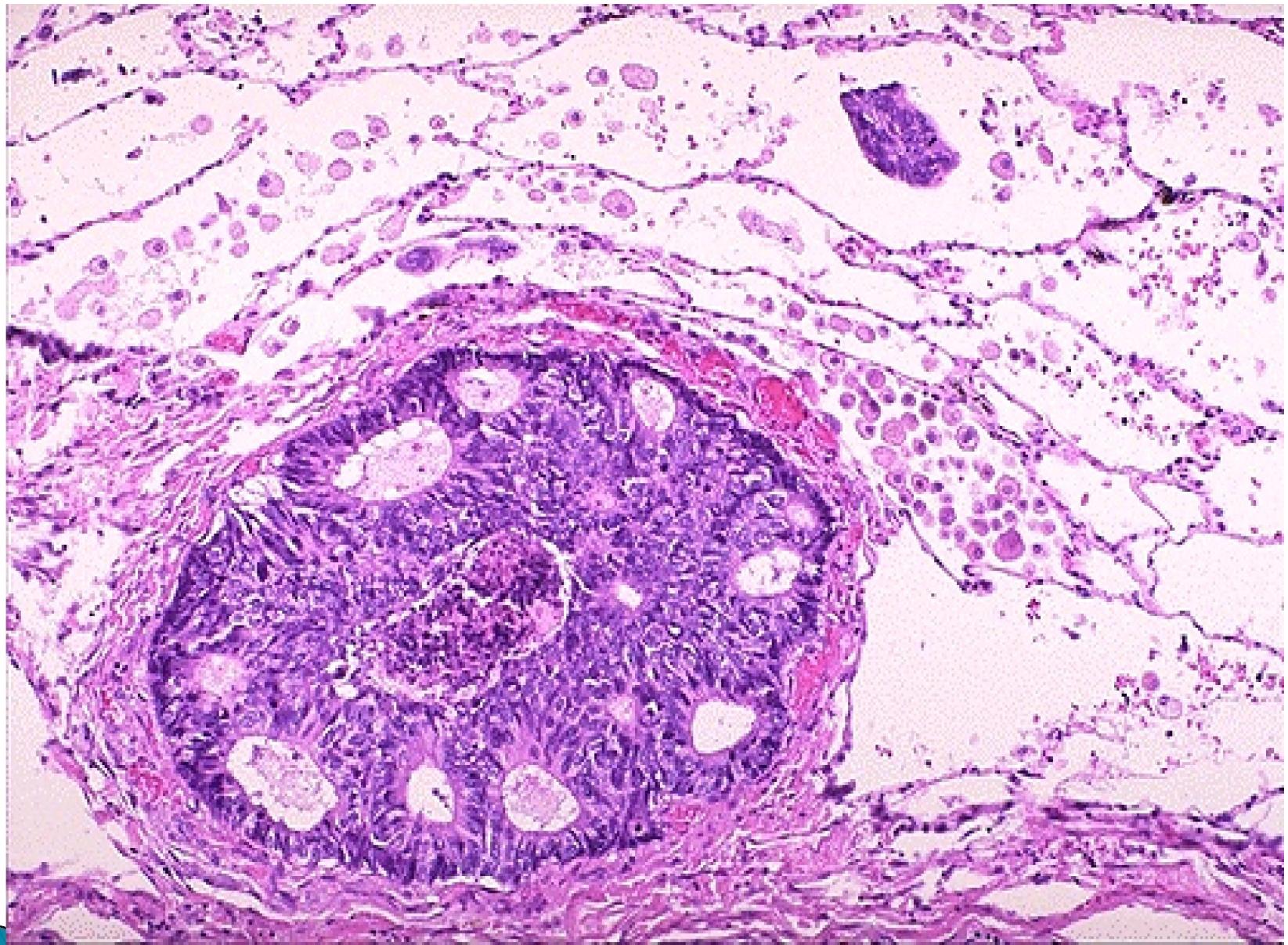


Fig. A breast carcinoma has spread to a **lymphatic** within the lung.

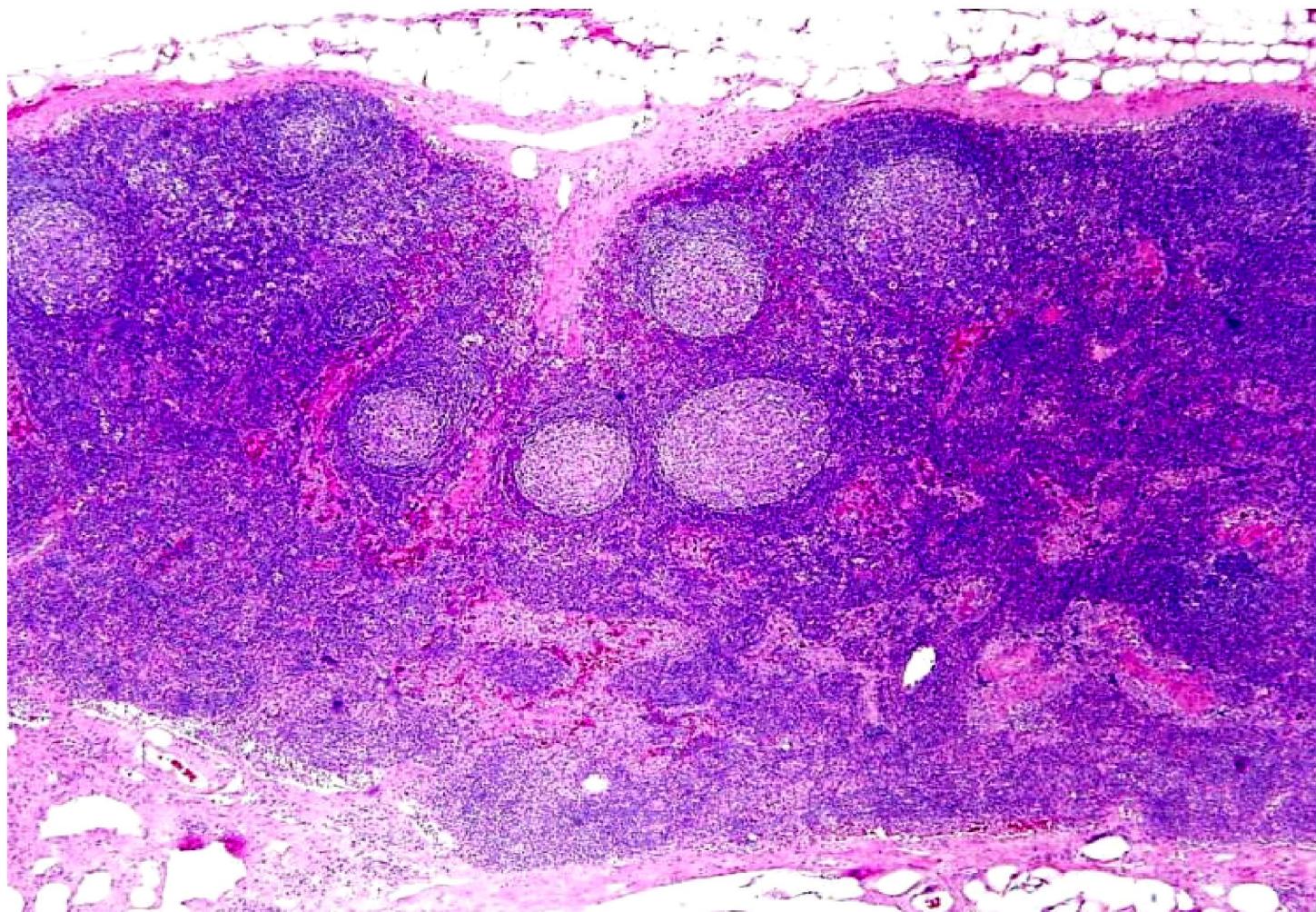
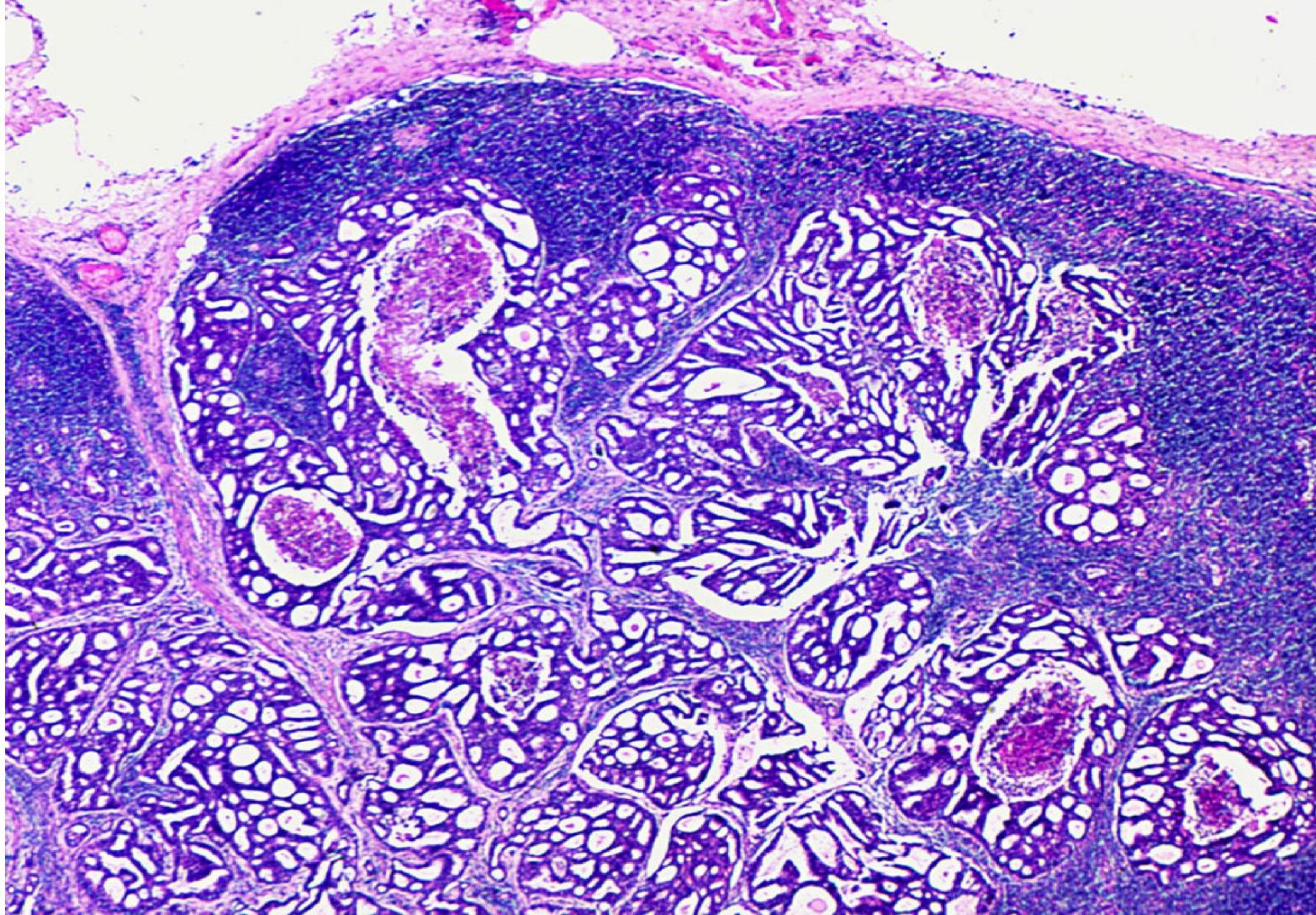


Fig. Nomal histology of a Lymph Node



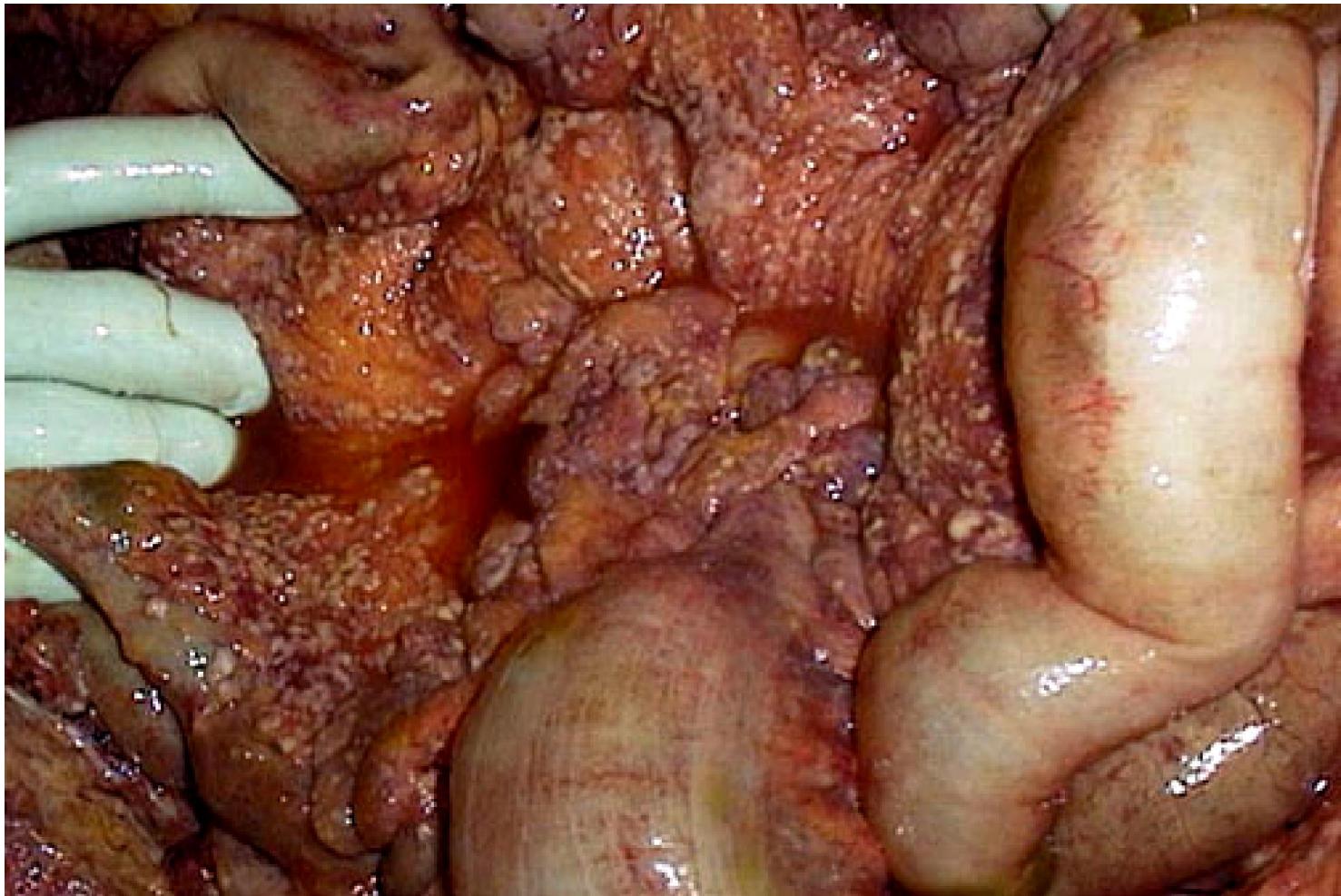
Metastatic Carcinoma Lymph Node

Carcinomas will often invade the lymphatic system and colonize in the local lymph nodes. Initially, the cancerous cells will appear as collections of epithelial cells in the lymph node but over time they will resemble the tissue or organ from which they derived. In this image metastatic adenocarcinoma from the breast, note the extensive glandular tissue that is similar to glands of the breast.

SPREAD OF NEOPLASM

3. Implantation or Seeding of body cavities and surfaces (transcoelomic spread) –

- It means separation of malignant cells from its primary site and implant in the adjacent tissue without migration through blood or lymph. It is usually occurred in serous cavities. **OR**
- In implantation, the lack of cohesiveness of neoplastic cells favours implantation into the surrounding body cavities i.e. transcoelomic spread or seeding into pericardial, pleural, peritoneal and subarachnoid membranes.
- **The commonest example of implantation is seen in the peritoneal cavity** in cases carcinoma of the colon may penetrate the wall of the gut and re-implant in the wall of peritoneal cavity. e.g. Cancer of ovary, stomach and mesothelioma.



Fg.Tumor nodules seen over the peritoneal surface of the mesentery

SPREAD OF NEOPLASM

Ways of 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 (TVT) of dogs gets transmitted by this way.

4. Perineural spread - eg prostatic carcinoma, Gall bladder carcinoma.

Perineural tumor spread refers to the **migration of tumor cells along nerve** tissues. It worsens the prognosis, increases the recurrence rate, and diminishes 5-year survival by up to 30%. Eg. Head and neck neoplasms by the cranial nerves.

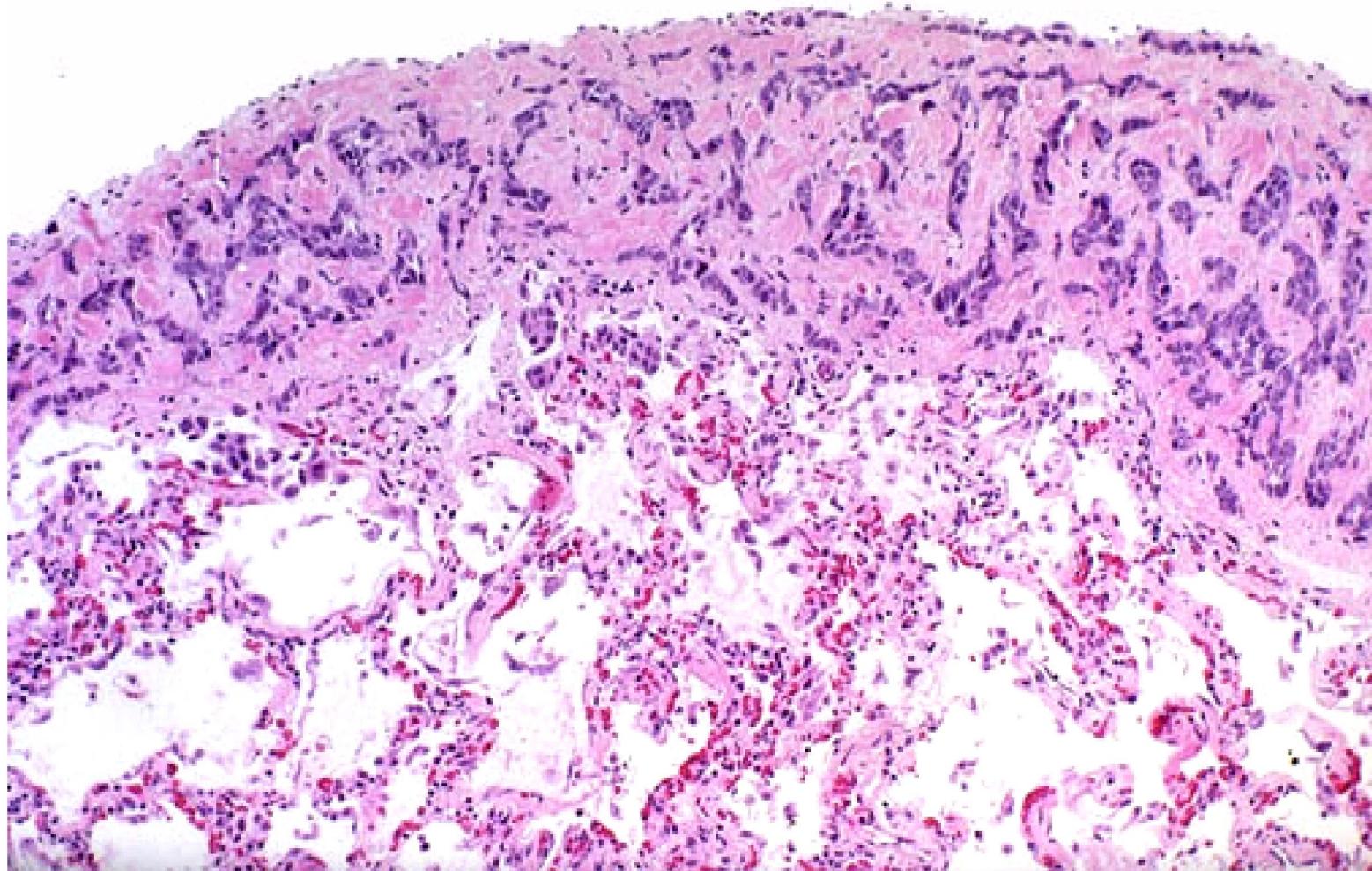


Fig. **Metastatic breast carcinoma** is present along the pleura overlying the lung.

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

1. Invasion of extracellular matrix -

Extracellular matrix is divided into two types

- I. Basement membrane
- II. Interstitial connective tissue

Invasion of extracellular matrix by tumour cell is an active process involving -

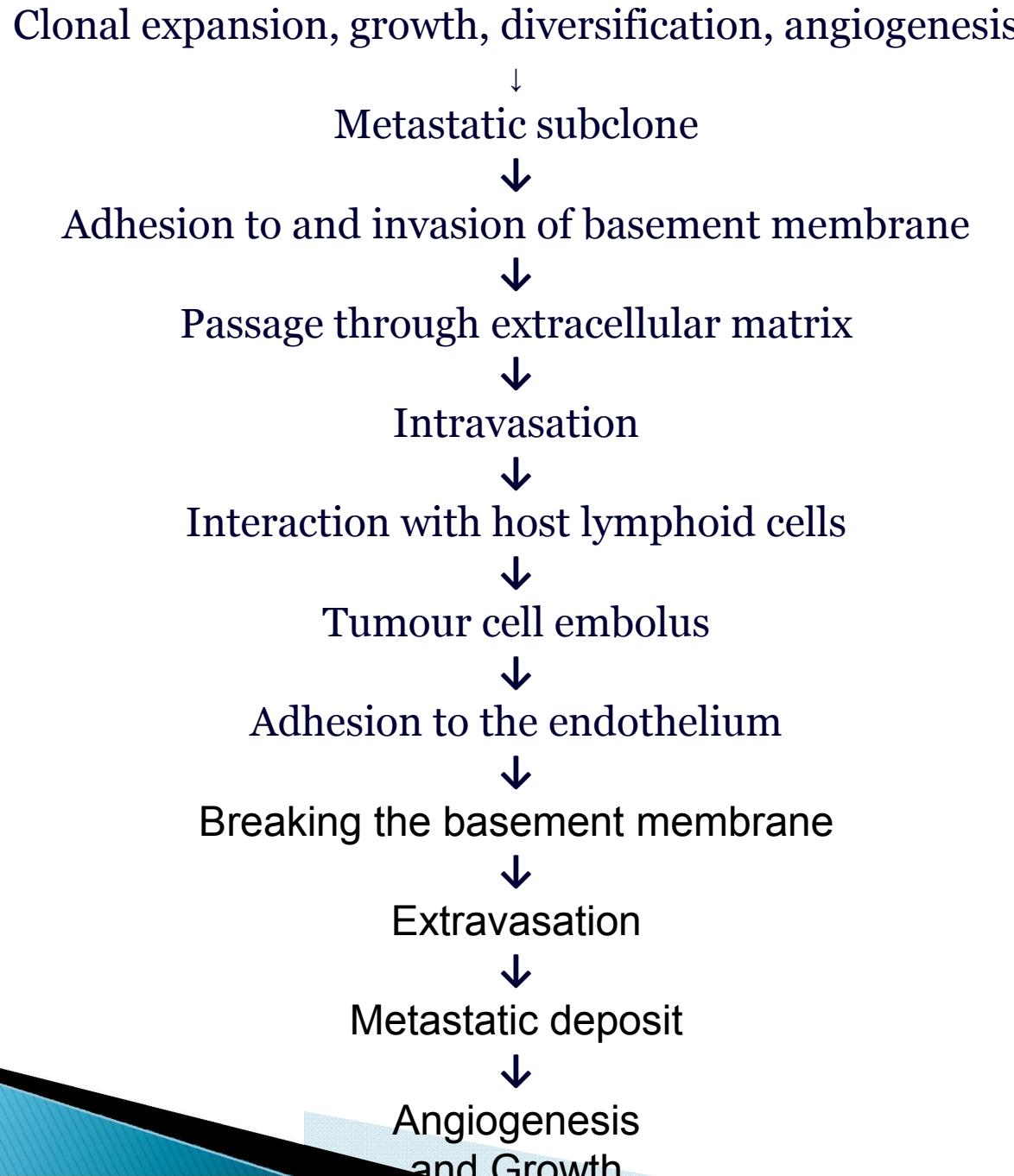
- Detachment of tumour cells from each other
- Attachment of tumour cells to matrix
- Degeneration of extracellular matrix
- Migration of tumour cells

MECHANISM OF INVASION AND SPREAD

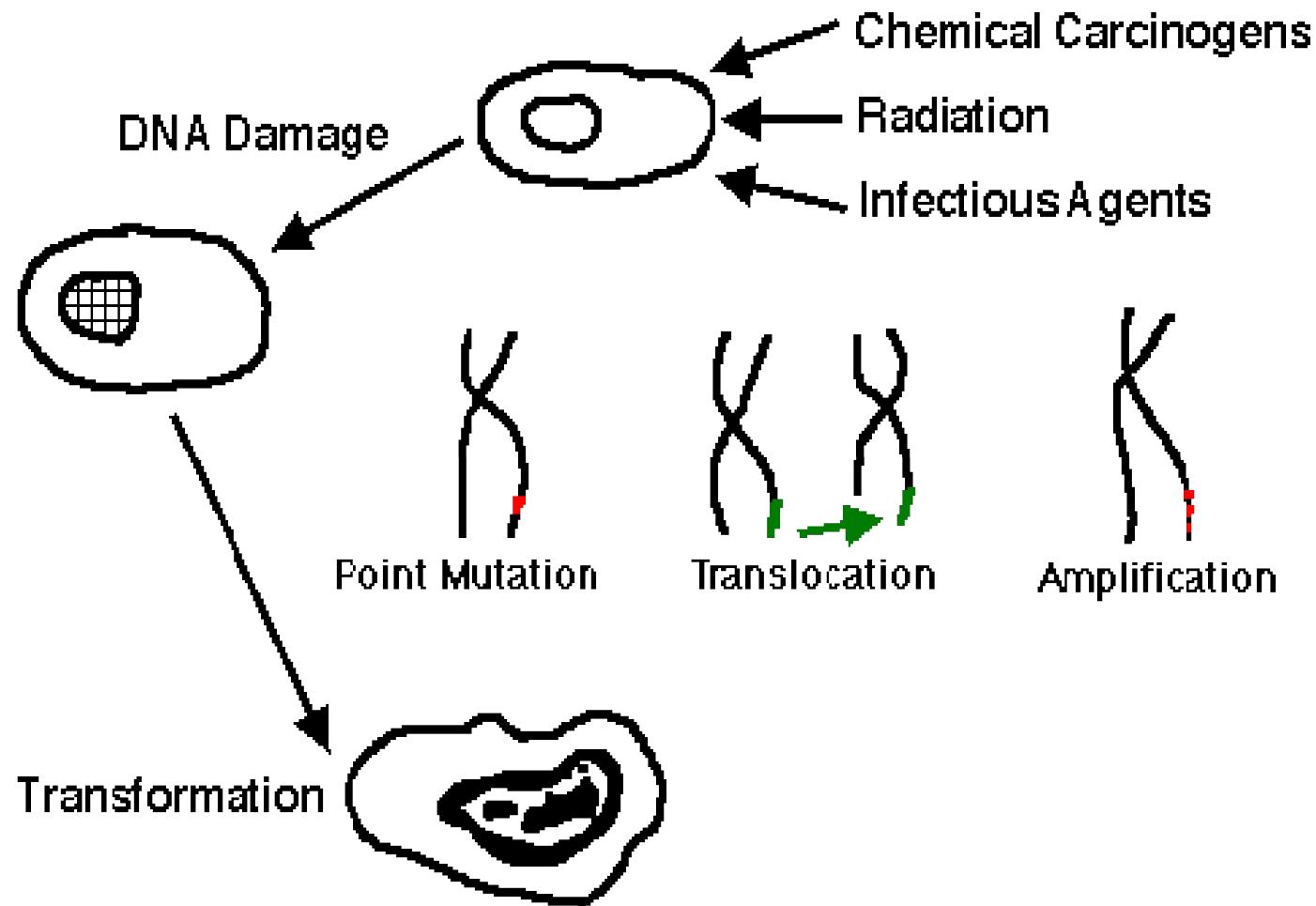
2. Vascular dissemination and homing of cells -

- 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.
- Example. Lung cancer spreads to adrenals and do not affect skeletal muscle. This phenomenon is called **homing of tumours**.

Mechanism of Neoplasm spread or The metastatic cascade



Mechanism of Neoplasm spread



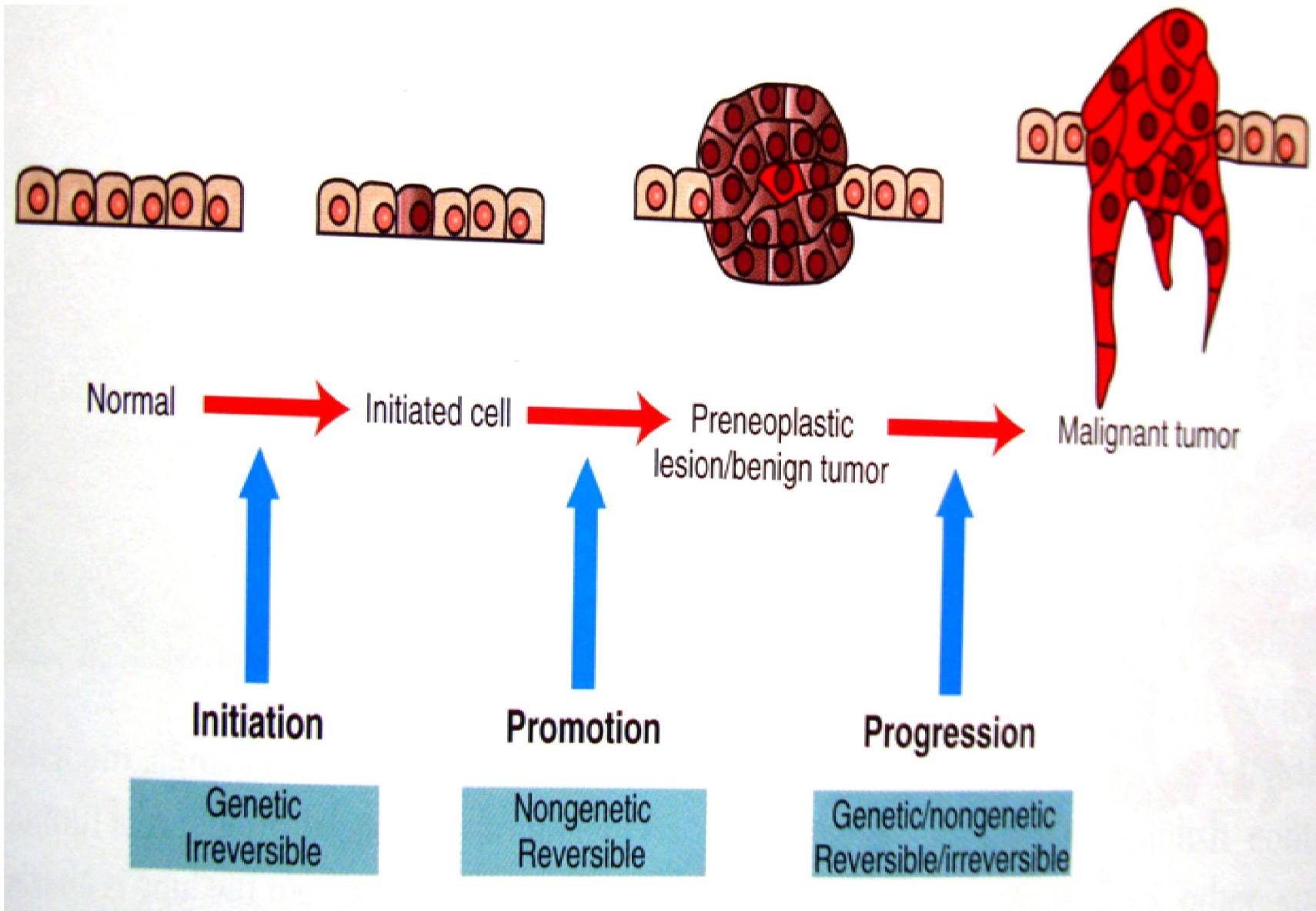
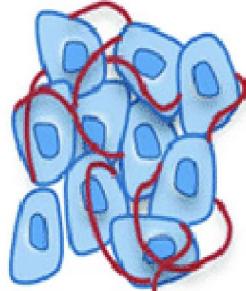


Fig. Illustration of step wise tumor development.



Primary
tumor



Detachment



Cancer cell



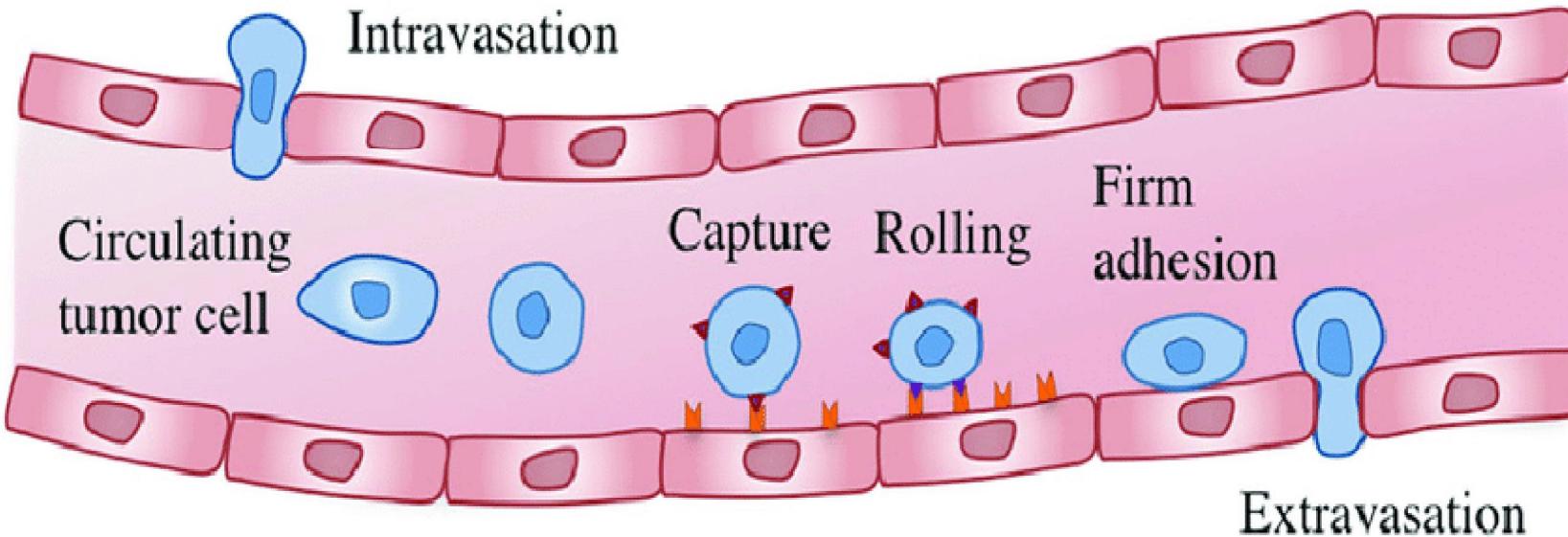
Endothelial cell



CD44

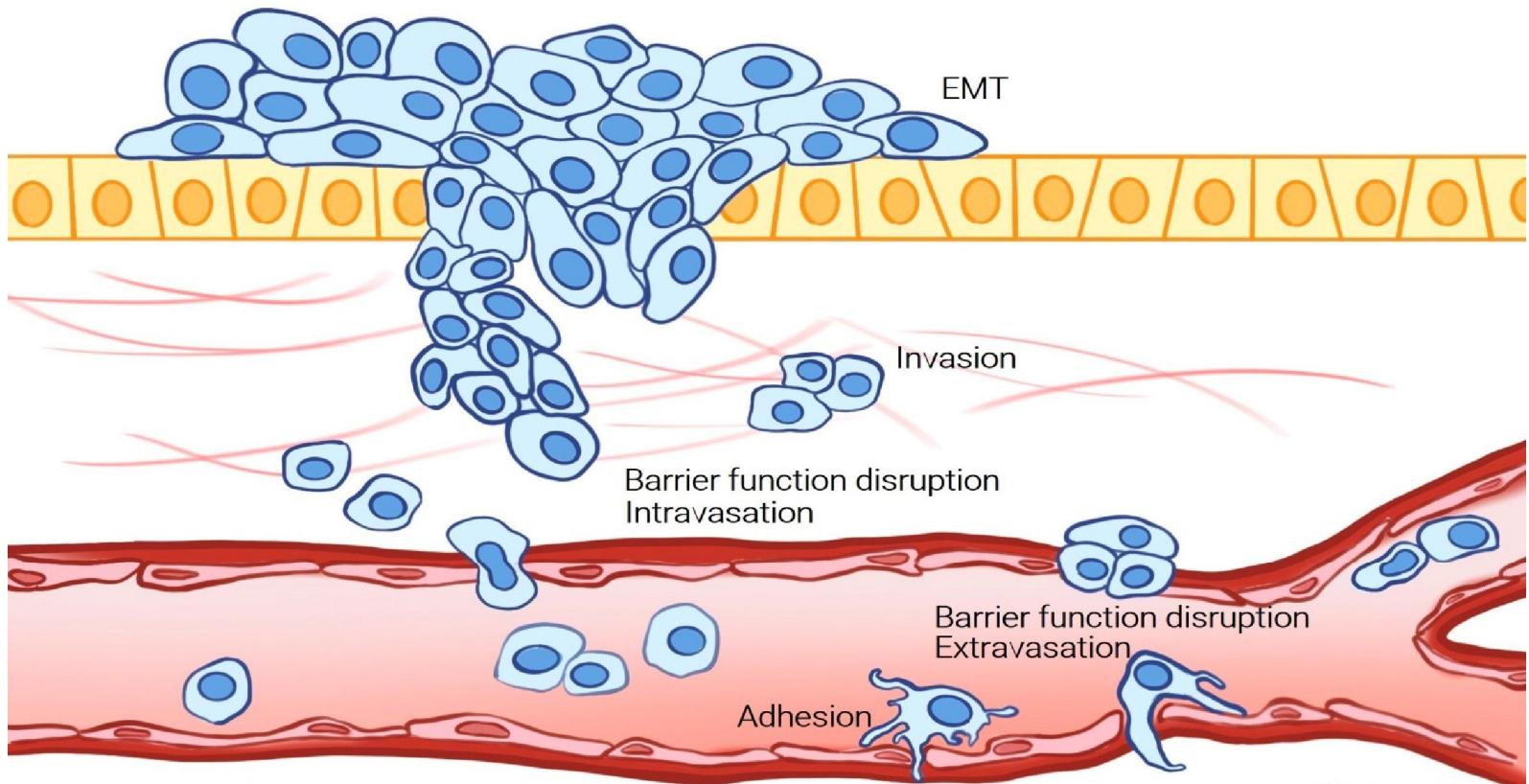


E-selectin



Secondary
tumor





Tumor Cell



Basement membrane



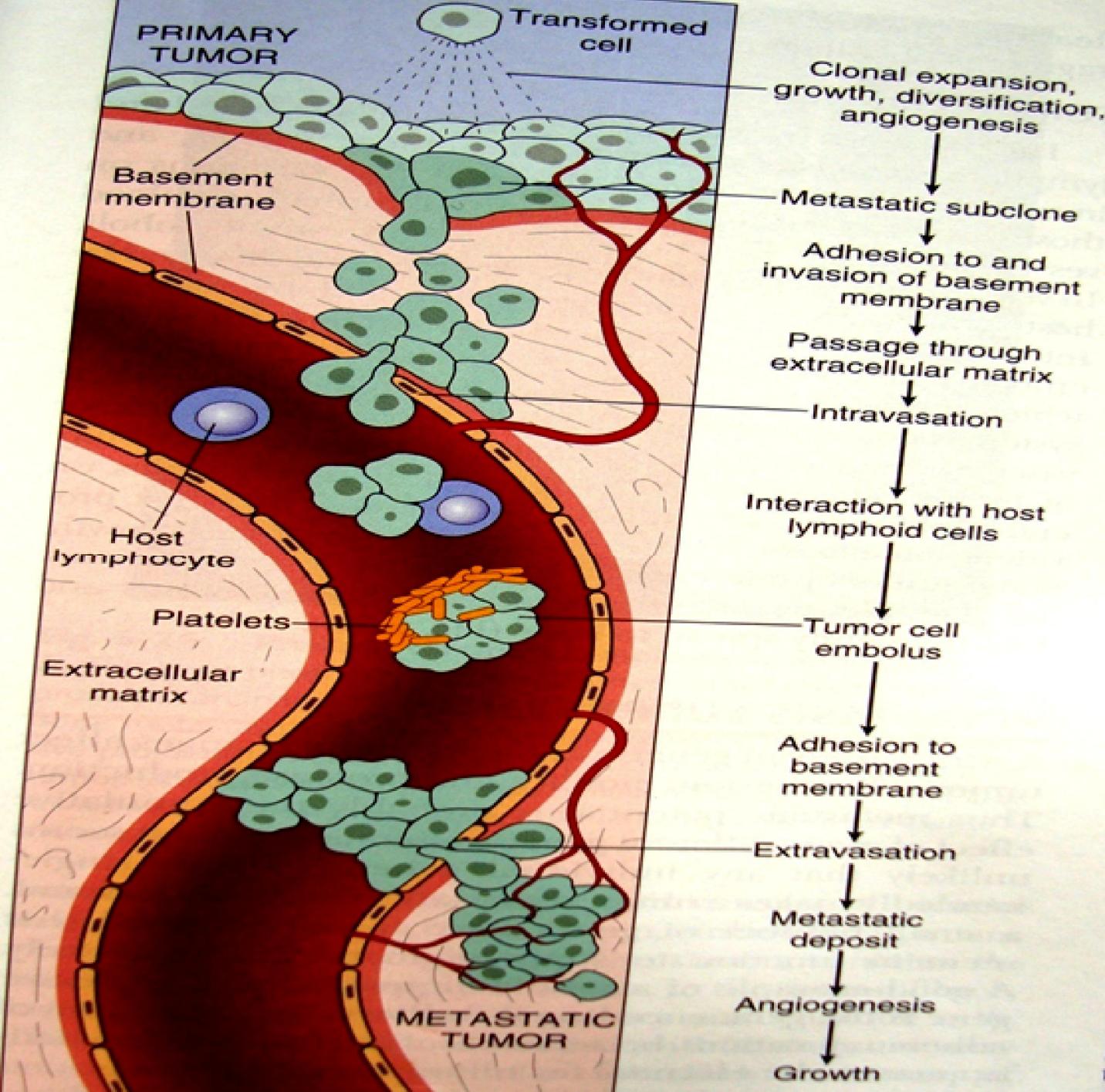
Extracellular matrix



Endothelia Cells



Blood Vessel



The metastatic cascade

In Nut Shell- Invasion and metastasis by tumor cells require sequence of events which are -

1. Loosening or detachment of tumor cells
2. Degradation of basement membrane and interstitial matrix
3. Tumor cell interaction with extracellular matrix proteins
4. Migration of tumor cells through the degraded extracellular matrix into vascular lumen
5. Dissemination of tumor cells through vascular channels
6. Homing of the tumor cells

NOTE –

- The cells which metastasize will have genetic mutations that predicts them for the metastatic spread.
- Multiple genetic abnormalities which are responsible for metastasis in a cell are called “*metastatic signature*”

TUMOURS OF EPITHELIAL CELLS



Papilloma (Warts)

- Benign tumour of epithelial cells projecting from an epithelial surface and is covered by squamous, transitional or columnar epithelium depending on the tissue from which it originates.
- Site – Most common site is skin and buccal mucosa.
Can also arise from mucosa of the intestine and bladder.
Very rarely from the epithelium of the ducts of glands.
- Species – Cattle, dog, horse, rabbit.
- Skin papillomas (warts) – Very common in all animals
In calves, these may be found on the shoulder, head, neck and dewlaps, mostly in clusters.
In horses, either single or multiple
In dogs, papillomas on oral mucosa are common, which are multiple and are infectious (DNA virus).
Multiple papillomas found on skin –of calves and rabbits may also be infectious.

Gross changes:

Small but occasionally large measuring 10 cm in diameter.
Pendunculated or broad base
Surface may be - smooth or rough and horny
Papillomas grow outward away from the basement membrane
but **do not invade underneath it.**

Microscopic changes:

- Tumour growth appears as **finger like papillary projection above the surrounding epithelium and contains connective** tissue core in the centre and keratinized mass on the periphery of the papilla/projection.
- Neoplastic change is found only in the epithelium and not in C.T.
- There is no breaking of the basal layer.
- Most of epithelial cells in the papilla have vacuolated cytoplasm.







Squamous Cell Carcinoma

- Malignant tumour of squamous epithelium
- Usually squamous stratified present on the surface
- Species – Common tumour among cattle in India affecting horn (horn cancer) and eye (eye lid mainly in Hereford breed).
- It is also common in old dogs and in horses (frontal sinuses, eyelids, penis, vulva, external genitalia).
- Dog – eye, skin of external genitalia
- Goat – Anus, vulva
- The affected animals are mostly adults or aged. Found in the areas of the skin of animals where melanin pigment is deficient since melanin is protective against actinic rays of sun. In Broad scars which are deficient in melanin, this tumour has been seen to develop.

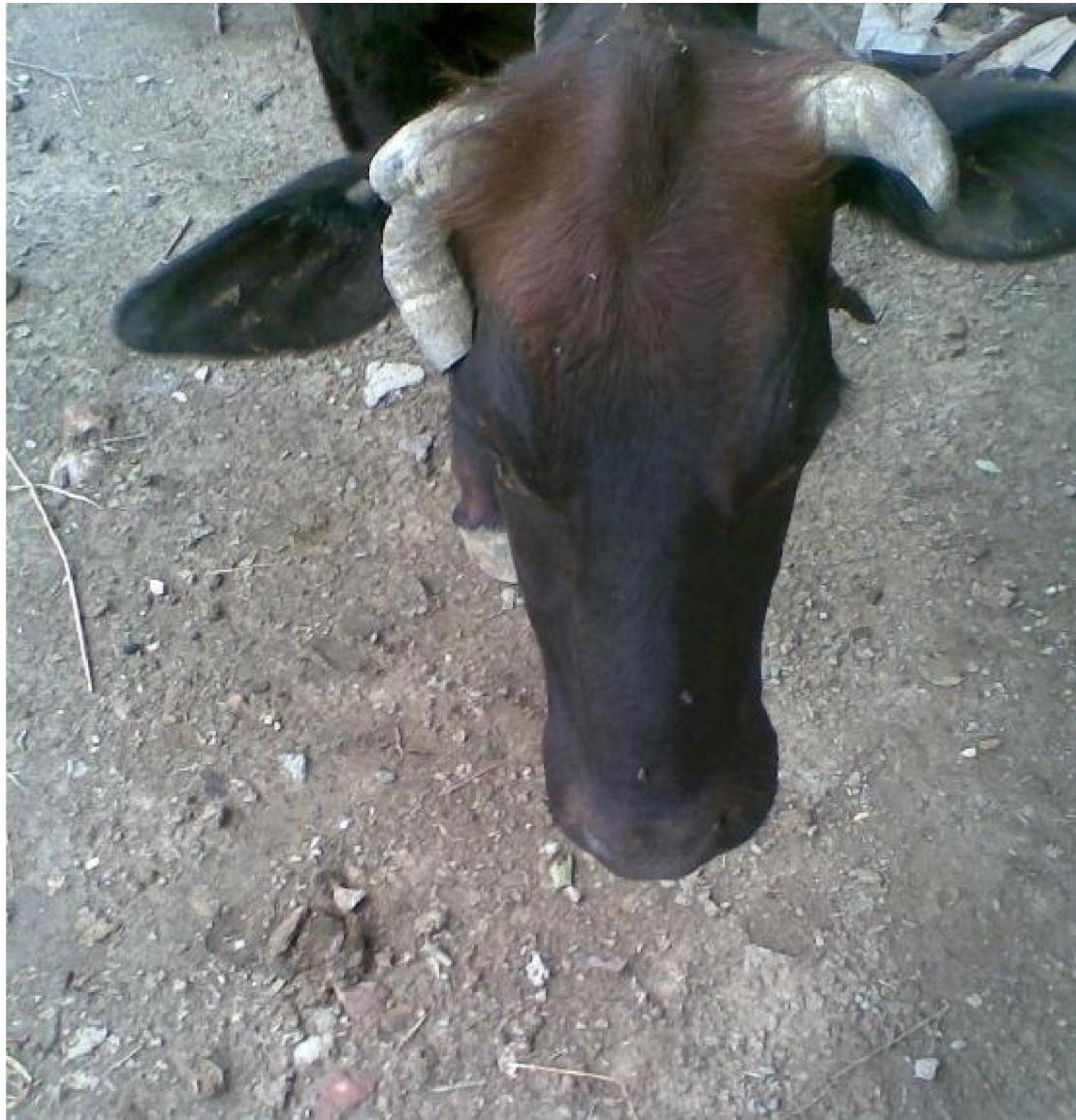
Gross changes: Cauliflower like in appearance having broad base, soft and has grayish or pink colour.

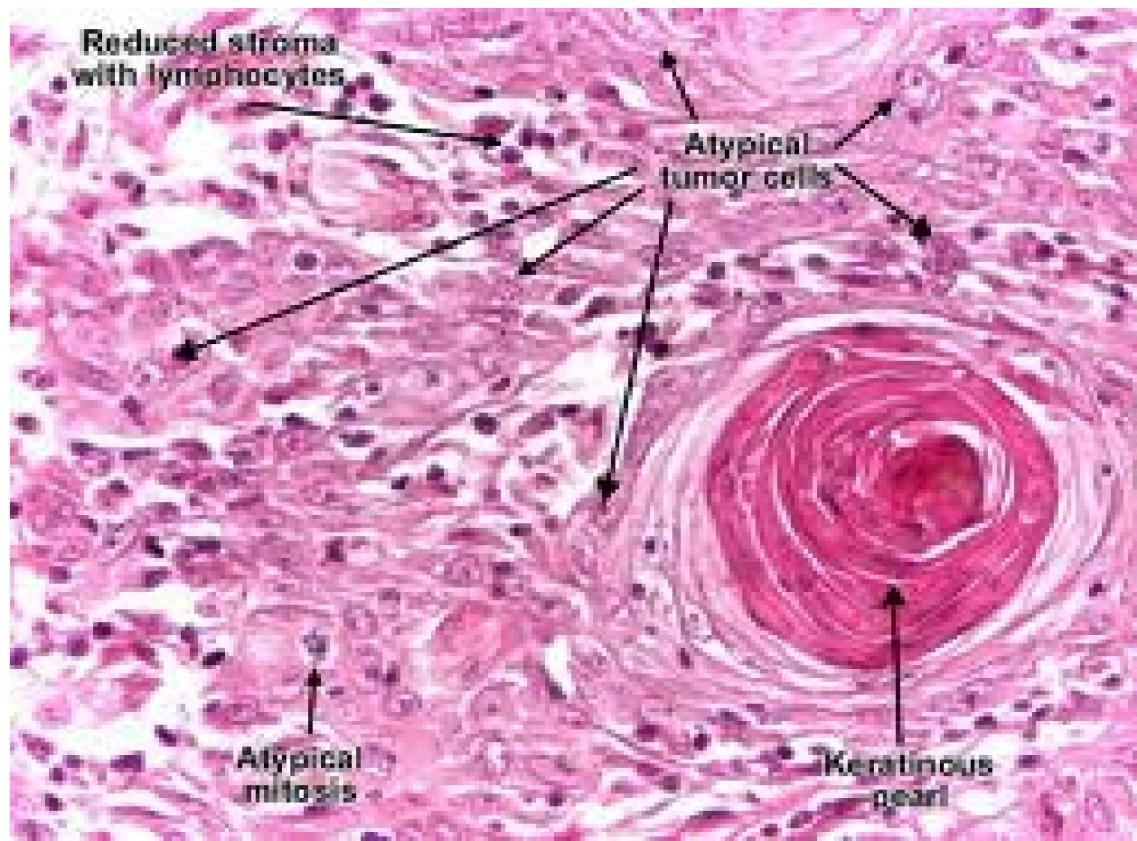
Microscopic changes: The tumour is composed of irregular masses or cords of epidermal cells that proliferate downward and **invade the dermis** and, subcutaneous tissues.

In these masses, keratinized layer of the cells is seen towards centre, than other layers of epidermal cells (prickle cells, stratum germinativum etc.) and at periphery, connective tissue of dermis. In most of the cases, keratin layer is deposited concentrically by the progressive maturation -of the proliferating epithelial cells forming **pearls known as cell nests or cancer/epithelial pearls.**

In more anaplastic type of squamous cell carcinoma, the **cells are found as sheets or islands without differentiation into the different layers.** In this case, the neoplastic cells are having hyperchromatic nuclei and prominent nucleolus. Mitotic figures are numerous.

•Note: In Sq. cell carcinoma, connective tissue stroma may contain macrophages, plasma cells, lymphocytes, erythrocytes (haemorrhages) particularly at the margins of the neoplastic; growth.





Adenoma and Adenocarcinoma

Adenoma is benign tumour and Adenocarcinoma is malignant tumour of glandular epithelium like mammary, sebaceous, prostate, bronchial and thyroid glands.

Gross and microscopic changes:

Adenoma:

Grossly, Nodular and encapsulated and pink in colour.

Firm or soft depending on the stroma and parenchyma

Microscopically, there are papillary projections in the lumen of acini and lining epithelium of acini is usually single layer of the columnar or cuboidal cells which resemble the normal glandular epithelium. Sometimes, the secretions do not drain as there is no duct resulting in cystic dilatation of the glands than known as **Cystadenoma**.

Due to accumulation of secretary fluid in the lumen, there may be **atrophy of lining epithelium at places**.

In between the acini, there is connective tissue stroma.

Note. If the fibrous tissue element also assumes neoplastic character as is found in mammary gland tumours, then tumour is called as fibro-adenoma.

•**Adenocarcinoma:**

Tumour cells are anaplastic, lose their polarity with hyperchromatic nuclei.

The acini may contain many layers of cells which may often show papillary projections in the lumen or as in case of mammary gland tumours

The cells are arranged in tubules of irregular size and shape usually lack secretion and often contain detached cells giving appearance of solid masses or cords of cells. There is dense fibrous stroma. Sometimes, the cells infiltrate under the basement membrane and into the surrounding stroma. Mitotic figures are frequent.

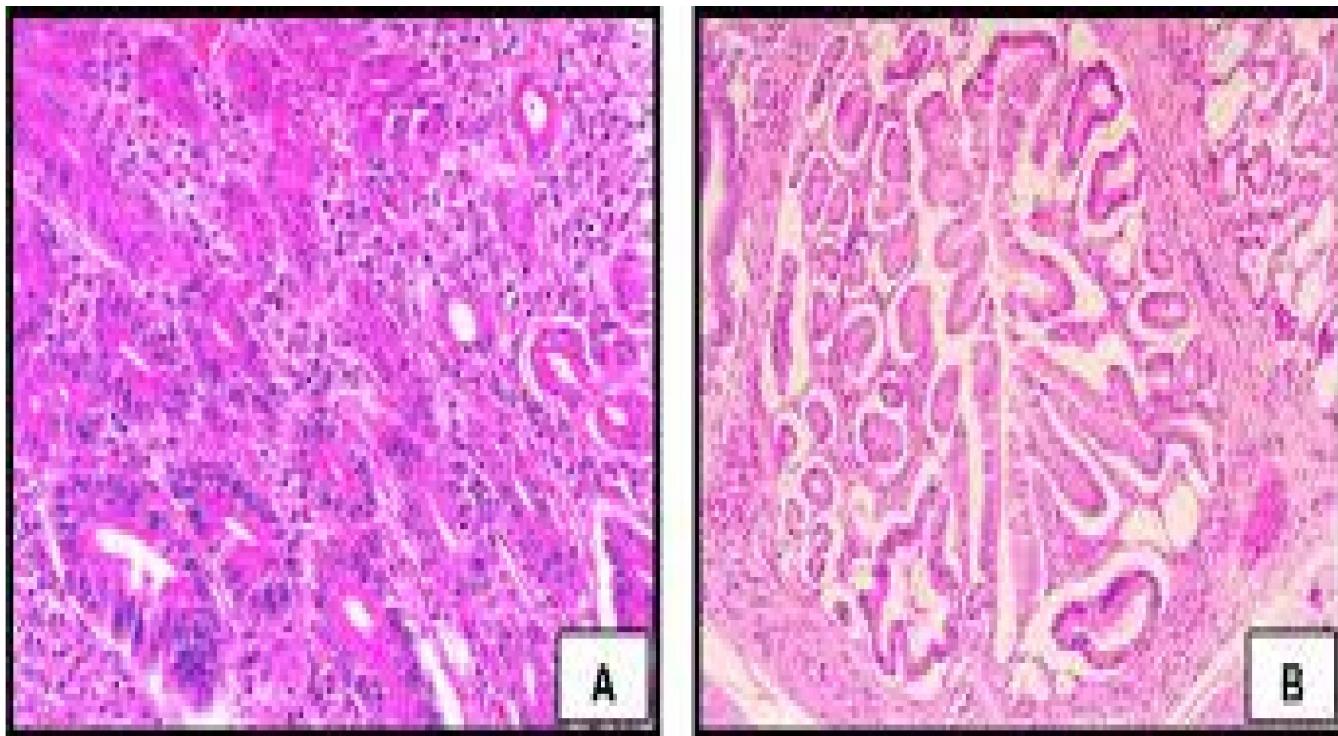
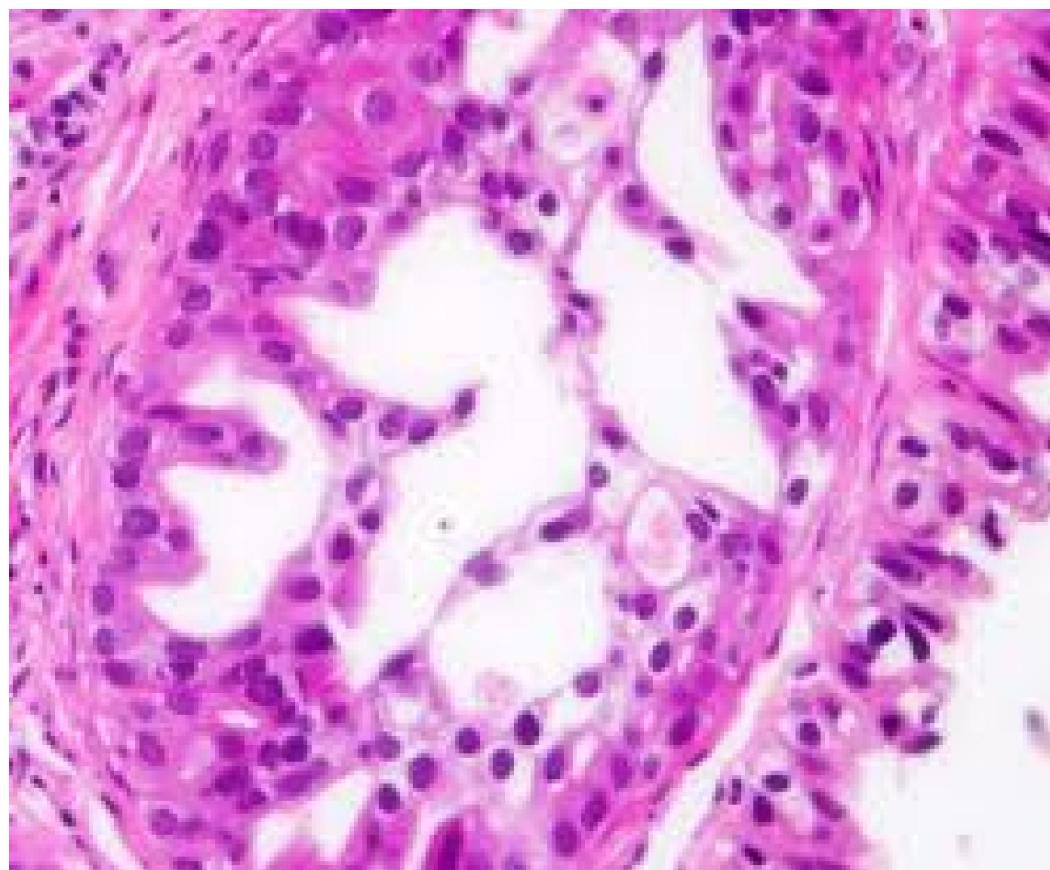


FIGURE 2 – Histology of the lesions in the glandular mucosa. A) Adenocarcinoma characterized by proliferation of glandular structures with cellular atypia. B) Adenomatous hyperplasia characterized by proliferation of glandular structures without cellular atypia











Fibroma and Fibrosarcoma

- ▶ Tumour of fibrous connective tissue cells (fibroblasts)
- ▶ Fibroma – Benign tumour
- ▶ Fibrosarcoma – Malignant tumour
- ▶ Very common tumour especially in horses and dogs.
- ▶ They can occur at any place where connective tissue is present but more often they are found in subcutaneous tissues of the head, neck, shoulder and legs.

▶ **Fibroma:** Size vary from tiny nodules to large.

Depending upon the amount of collagenous fibres, fibroma may be hard (**fibroma duram**) or soft (**fibroma molle**).

In soft fibroma – cells predominate and in hard fibroma – collagenous fibres predominate.

- ▶ Microscopically, fibroma consists of whorls or interlacing bundles of fibrous connective tissue which run in all directions (fibroblasts and collagen fibers). The tumour cells are fusiform or stellate shape and have large, ovoid or elongated (spindle shape) nuclei.
- ▶ Note: Fibroma must be differentiated from granulations tissue which generally has parallel bundles of fibroblasts and collagen fibers with proliferating capillaries running at right angles.

- ▶ **Fibrosarcoma:** Irregular and nodular in shape; poorly demarcated and noncapsulated.
 - ▶ They are firm or fleshy with **soft friable** areas.
 - ▶ Those found on the body surface are ulcerated and emit a foul smell.
-
- ▶ **Microscopically**, arrangement of cells is similar to that of a fibroma but the **cells show features of malignancy** i.e. it consists of interlacing bundles of immature fibroblasts and moderate number of collagenous fibers.
 - ▶ These cells have **hyperchromatic nuclei**.
 - ▶ **Mitotic figures** and **tumour giant cells** are also present.