Tumour pathology 2

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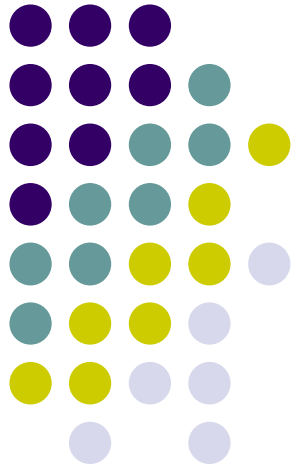
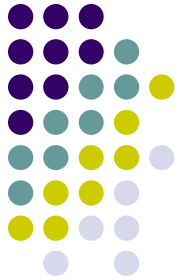
Dept. of pathology



Objectives

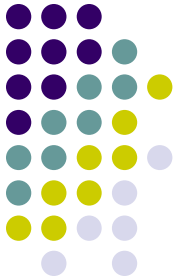
- Describe the characteristics of a neoplasm
- Describe the clinical aspects of neoplasia

Characteristics of neoplasms



1) Rate of growth
2)Clinical features
3)Gross features
4)Microscopic features
5)Local invasion(Direct spread)
6) Metastases (Distant spread)

1)Rate of growth

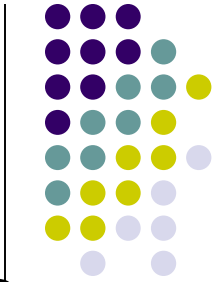


- Tumor cells proliferate more rapidly than normal cells
- Malignant tumors proliferate faster than benign tumors
- Rate of growth depends on
  - Doubling time of tumour cells
  - Fraction of cells in replicative pool
  - Rate at which tumour cells die/shed
- Malignant tumors –High mitotic rate (proliferative rate)
  Cell death rate is relatively low

Rate of growth cont.

- Growth fraction decide the response to cancer therapy
- Tumours with low growth fraction will have only few cells to respond to therapy
- Surgical debulking/radiotherapy will shift the resting cells to enter the cell cycle
- Tumours with high growth fraction responds well to chemotherapy (eg- High grade lymphoma)

Rate of growth cont.



- Regulation of a rate of growth of a tumor is under the influence of growth factors secreted by the tumor cells
  - EGF , FGF , PDGF , CSF

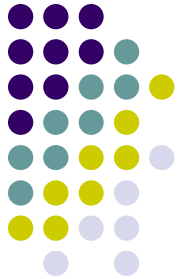
- Degree of differentiation correlate well with the growth of a tumor
- Poorly differentiated tumors have a rapid growth rate

Rate of growth cont.

Cancer stem cells

- ‘Stem cell like cells’ in the cancers
- Ongoing research into the properties of these stem cell like cells in cancers
- These follow the same genes and pathways as the normal cells
- So new drugs are tested to target these pathways at different levels

Characteristics of neoplasms



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2)Clinical features of neoplasia

A) Local effects

B) Hormonal effects

C) Cancer cachexia

D) Paraneoplastic syndrome

A) Local effects

- Benign tumours- Compress and destroy the surrounding tissue

  - Pituatory adenoma- hypopituatarism
- Malignant - Infiltrations and destruction
- Obstructive features

  Gut – intususception
- Ulceration
- Secondary infection
- Malena and haematuria (Gut and Urinary)

B) Hormonal effects

- Seen with benign and malignant tumours
- More commonly with benign tumours
- Non-endocrine tumours producing hormones (Paraneoplastic syndrome)

C) Cancer cachexia

- Progressive loss of body fat and lean body mass
- Weakness
- Anorexia
- Anaemia

- Not due to nutritional demands of the tumour
- In cancer the basal metabolic rate is increased

C)Cachexia

- Cytokines are the main contributory factor

TNF –

- Produced by macrophages / tumour cells
- Mobilize fat
- Supress appetitie

C) Cachexia

- Others – IL-1
  IF-gamma
  Proteolysis inducing factor
  Lipid-mobilizing factor

- In cancer cachexia the homeostatic mechanisms tilt towards cachectic factors

D) Paraneoplastic syndrome

Definition

- Symptom complexes that cannot be explained by local spread,distant spread or by elaboration of hormones indigenous to the tissue from which the tumour arose
- Why is it important
  - first manfectation of an occult tumour
  - Could have lethal effects
  - Misdiagnosed

D) Paraneoplastic syndrome cont

a)Endocrinopathies – ectopic hormone production

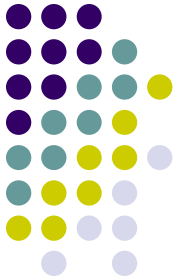
Cushing syndrome	**ACTH /ACTH like substance**	**Small cell carcinoma**
SIADH	ADH	Small cell carcinoma
Hypercalcaemia	PTHRP/TGF/IL	SCC of lung Breast carcinoma
Hypoglycaemia	Insulin / insulin like substance	Ovarian cancer
Cacinoid syndrome	Serotonin/ Bradykinin	Hepatocellular
Polycythemia	Erythropoietin	Gastric , renal, hepatocellular

D) Paraneoplastic syndrome cont

b) Nerve and muscle syndromes (immunological)

- Myesthenia
- Peripheral neuropathy
- Cortical cerebellar degeneration

D) Paraneoplastic syndrome cont



c)Dermatological

- Acanthosis nigricans (immunological)

  Grey-black hyperkeratotic patches

  Gastric , lung

- Dermatomyositis (immunological)

d) Hypertrophic osteoarthropathy(unknown)

- Periosteal new bone formation, arthritis and clubbing
- In 1-10% of ronchogenic carcinoma

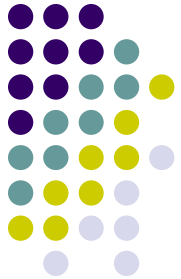
D) Paraneoplastic syndrome cont

e) Vascular and haematological manifestations

- Thrombosis (mucin induced clotting)
- Migrating thrombophlebitis (pancreatic , bronchogenic)
- Disseminated intravascular coagulation (Leukaemia and prostate carcinoma)
- Nonbacterial thrombotic endocarditis

(hypercoagulability mucin producing adenocarcinomas)

Characteristics of neoplasms



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3) Gross features

- Colour and consistency of tumors differ from the surrounding tissue
- Macroscopic appearance – Papillary
  fungating
  Infiltrating
  Ulcarative
  Cystic
- Areas of necrosis and haemorrhages

2) Gross features cont.

Benign tumors	Malignant tumors
Spherical / ovoid	Irregular
Encapsulated/ circumscribed	Poorly circumscribed Extends to the surrounding tissue
Firm ,Uniform consistency	Firm- hard,
May get haemorrhage / infarctions	Necrosis , haemorrhage

Fibroadenoma of the breast

Well circumscribed margin - A feature of benign tumor

Bronchial carcinoma

Infiltrating edges

Osteosarcoma

Tumor extending to the bone and surrounding soft tissue

Melanoma

Irregular margin
Pigmented lesion

Well differentiated liposarcoma

Fatty appearance is maintained

Characteristics of neoplasms

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4)Microscopic features

- Important for classification and grading

- ***A) Microscopic pattern***
- ***B) Cellular features***
- C) Angiogenesis
- D) Inflammatory reaction

3)Microscopic features cont.

A) Microscopic pattern

- Epithelial tumours –acini
  Sheets
  Cords
- Mesenchymal tumours- Bundles of cells
  Matrix –Hyaline
  cartilagenous
  osteoid

B)Cellular features

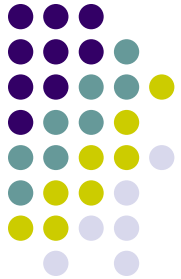
- Differentiation-

  Morphological and functional resemblance to normal cells
- Benign tumors closely resembles the normal cells
- Malignant tumors

  Well differentiated – resembles to some degree

  Poorly differentiated –poor resemblance to normal cells

B)Cellular features cont.



Anaplasia

- Feature of most malignant tumors

a) Loss of polarity

Orientation along the basement membrane is lost due to loss of adhesion molecules

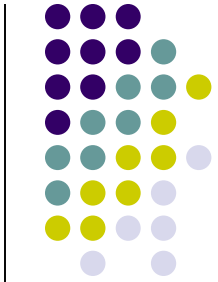
b) Pleomorphism

Variation in cell and nuclear size and shape

c) N:C ratio (Nuclear cytoplasmic ratio)

Increased (1:1 instead of 1:5)

B)Cellular features cont.



d)Anisonucleosis

- Variation in size and shape of nuclei

e)Hyperchromatism

- Nuclear chromatin increased
- Coarsely clumped chromatin
- Darkly staining nuclei
- Irregular nuclear membrane

f)Nucleolar changes

- Prominent nucleolus/nucleoli

B) Cellular features cont.

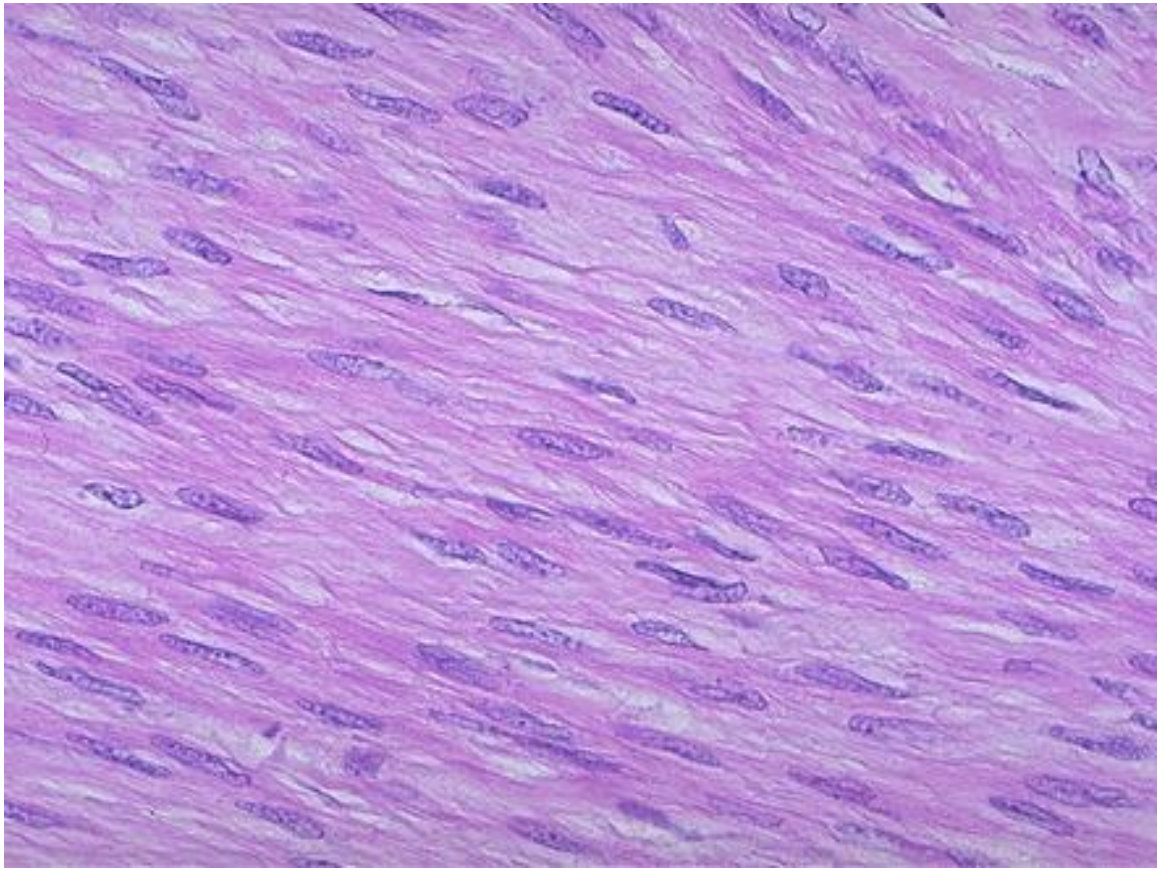
g)Mitotic figures

- Increased number of normal/ abnormal mitosis
- Abnormal forms are important in malignant tumours– Tripolar , quadripolar , multipolar

h)Tumour giant cells

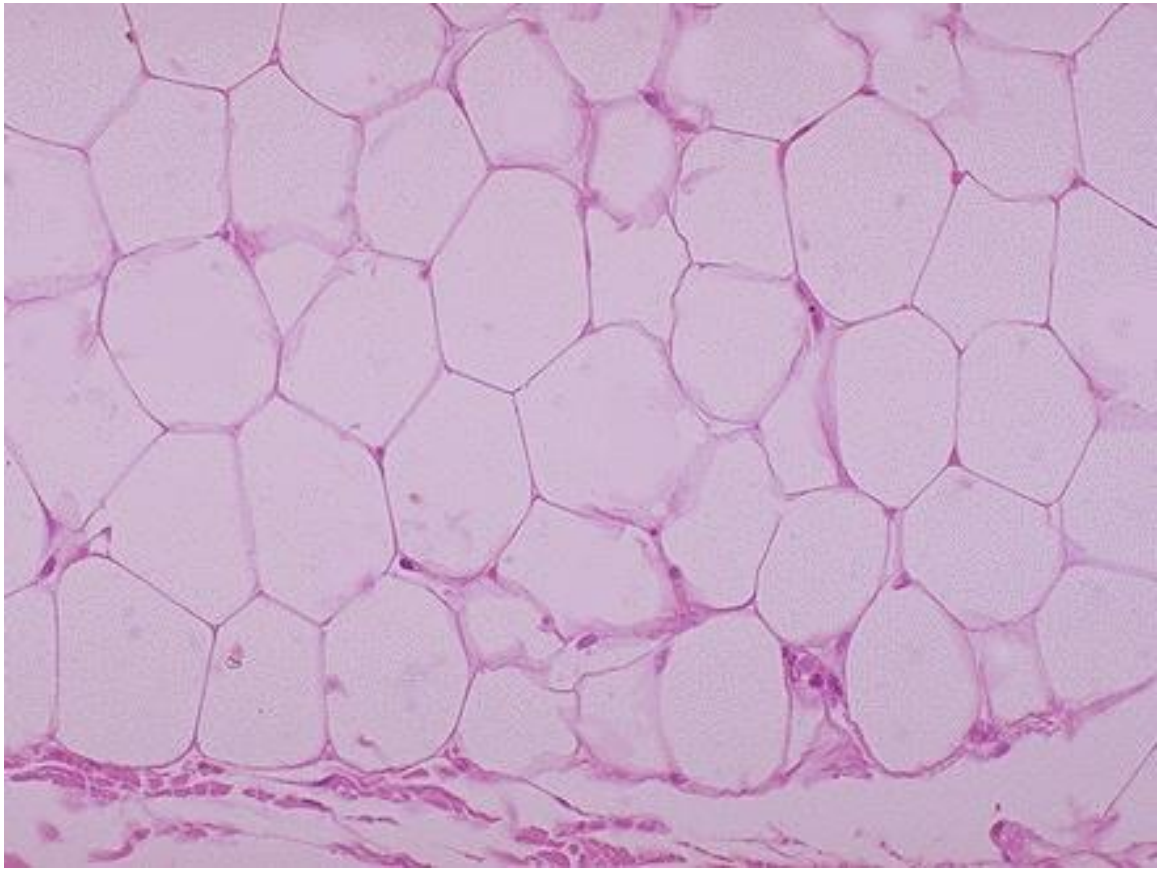
i)Cytoplasmic features

- Benign tumors - Collagen , keratin in cytoplasm
- Well differentiated tumors may have normal constituents
- Poorly differentiated tumors do not have normal cytoplasmic material



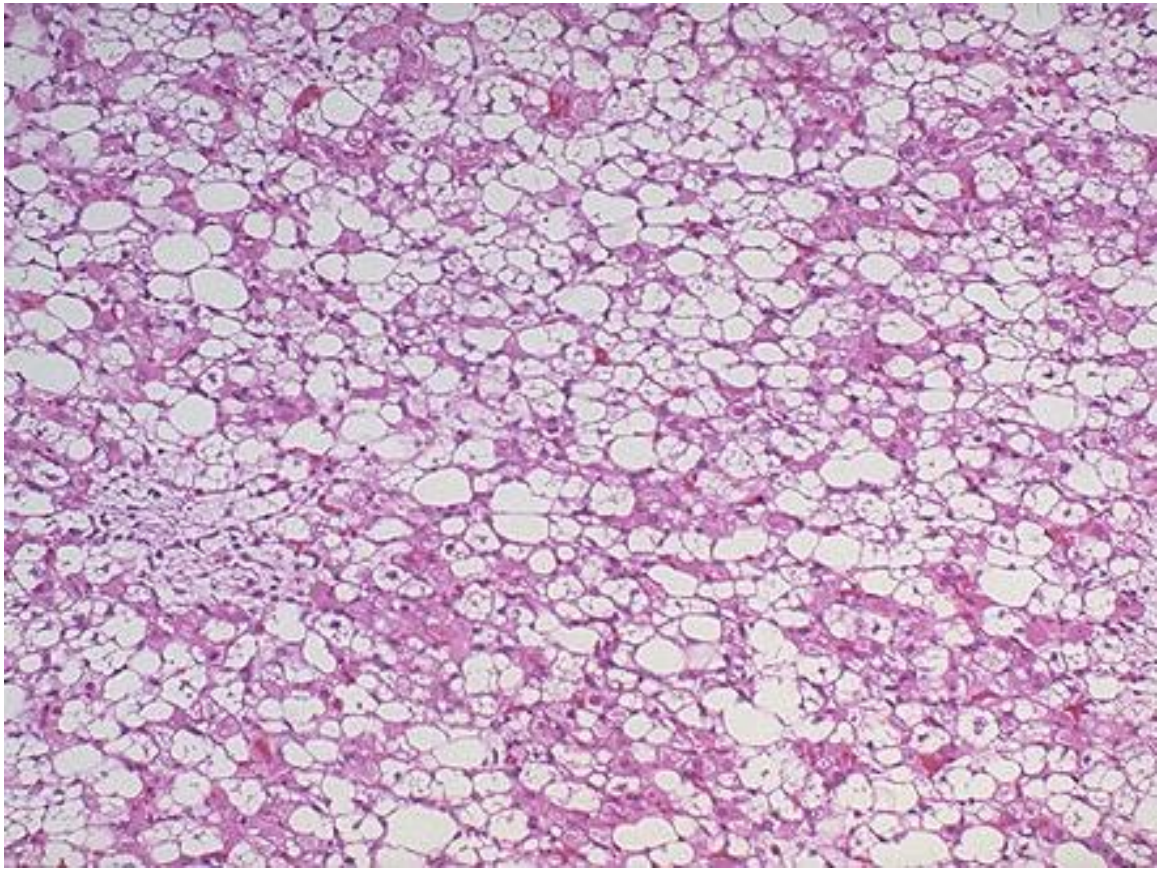
Leimyoma

Tumor cells resembles smooth muscle cells



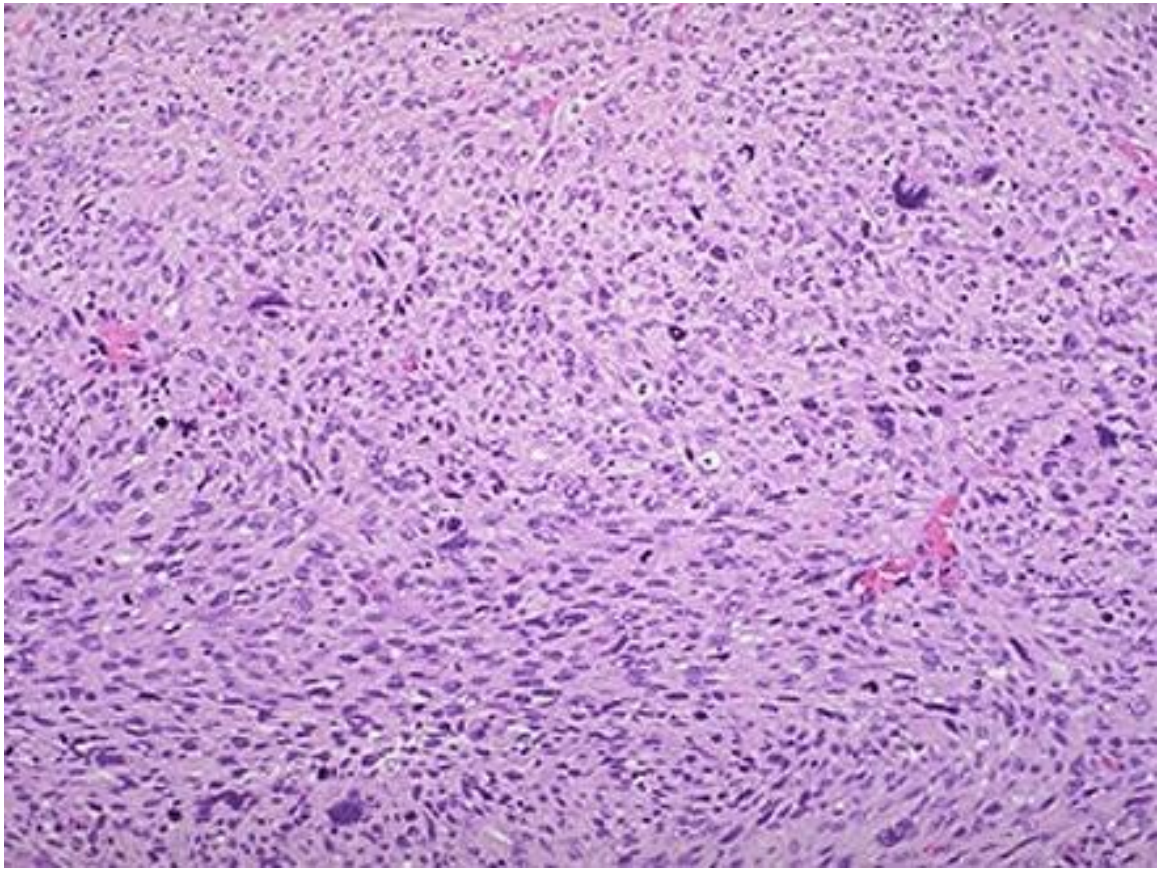
Lipoima

Cells resemble mature adipocytes



Well differentiated liposarcoma

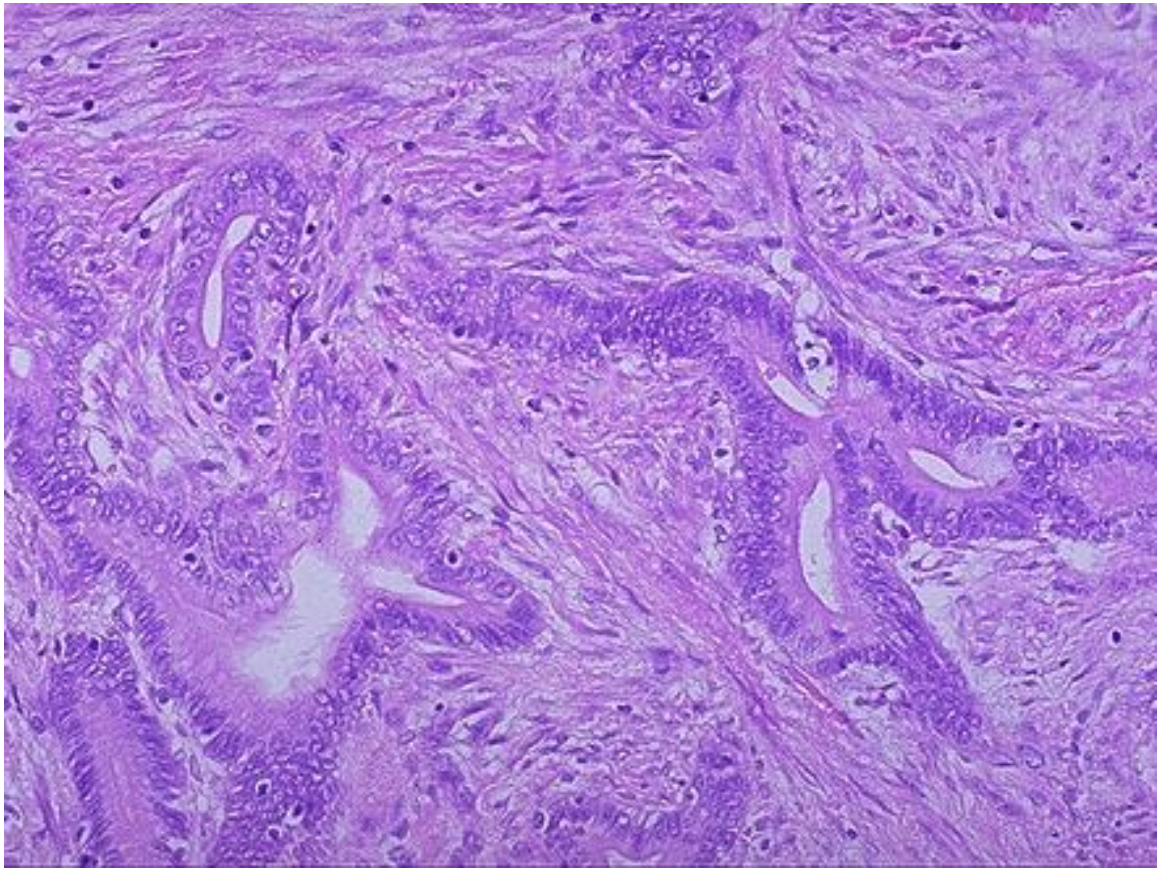
Fat cells are evident



Sarcoma

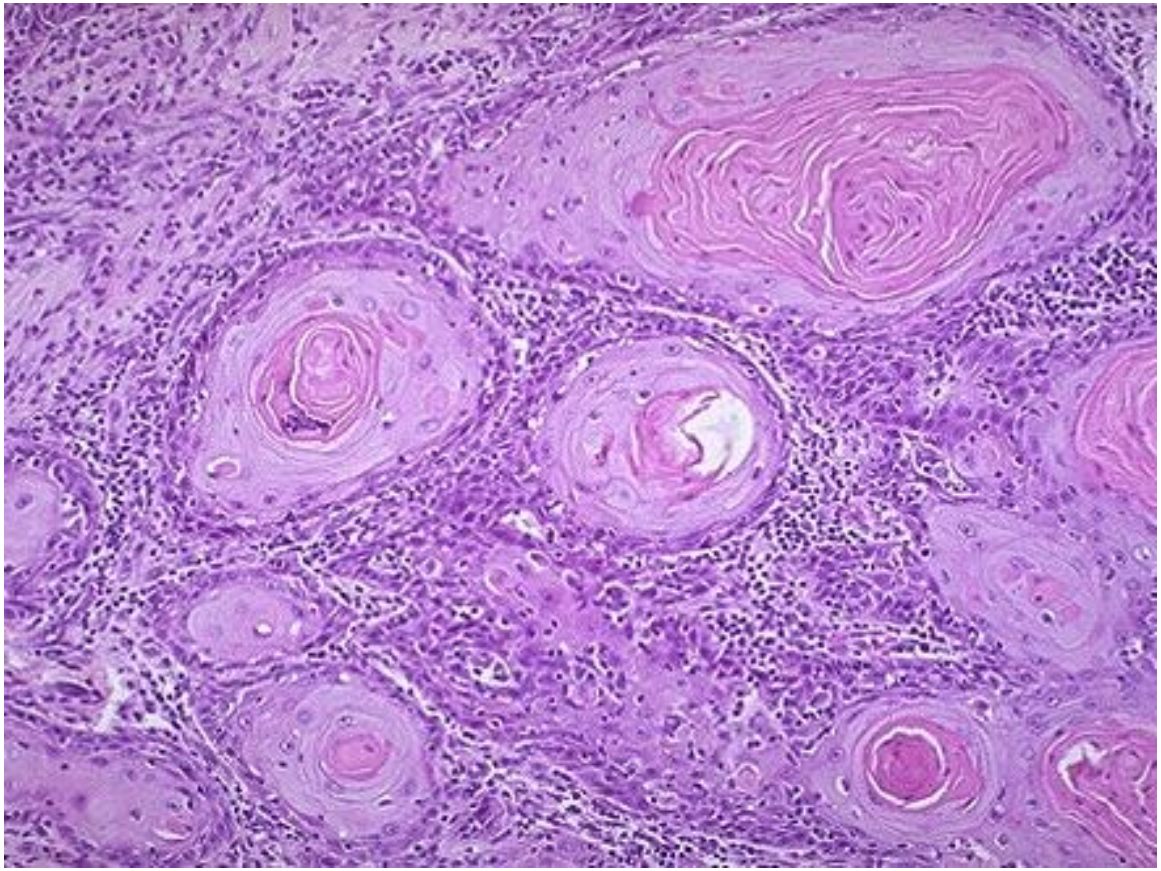
Pleomorphic spindle cells

Arranged into bundles



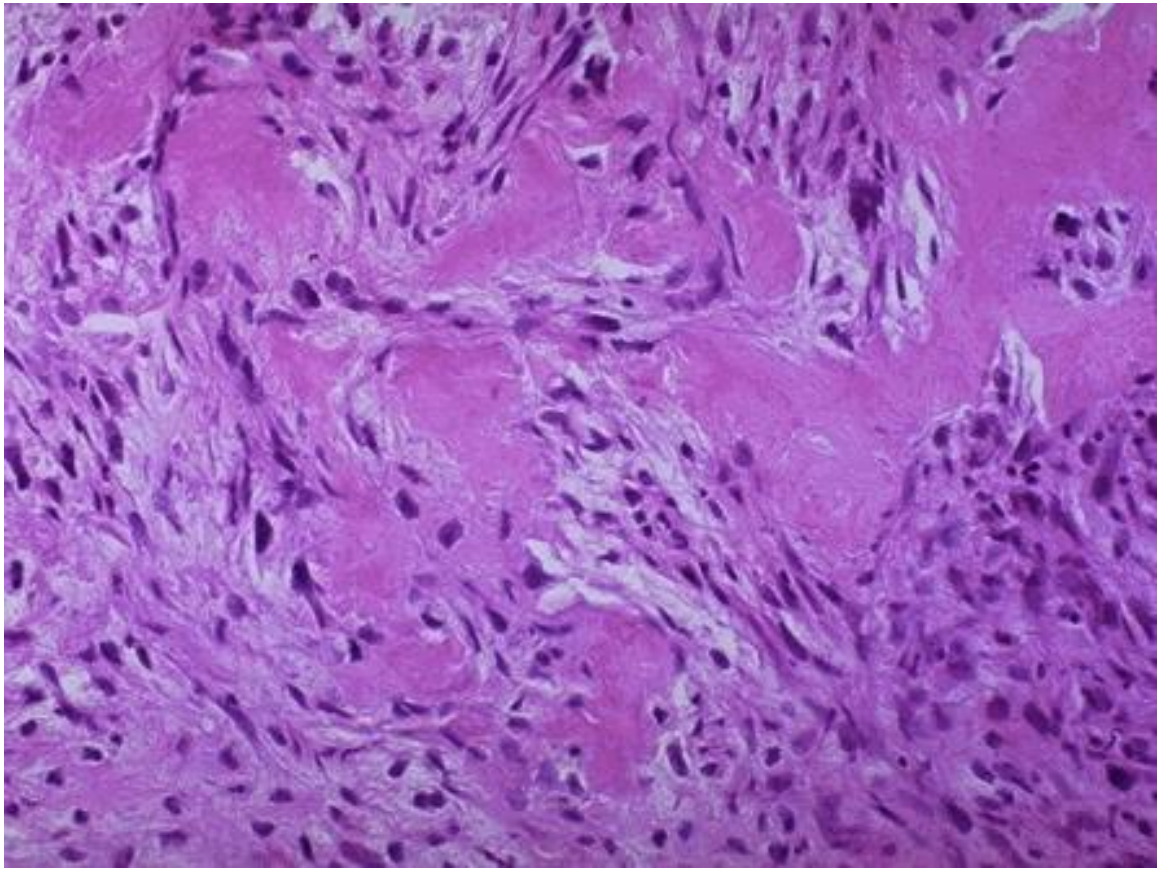
Adenocarcinoma

Irregular glands infiltrating the stroma



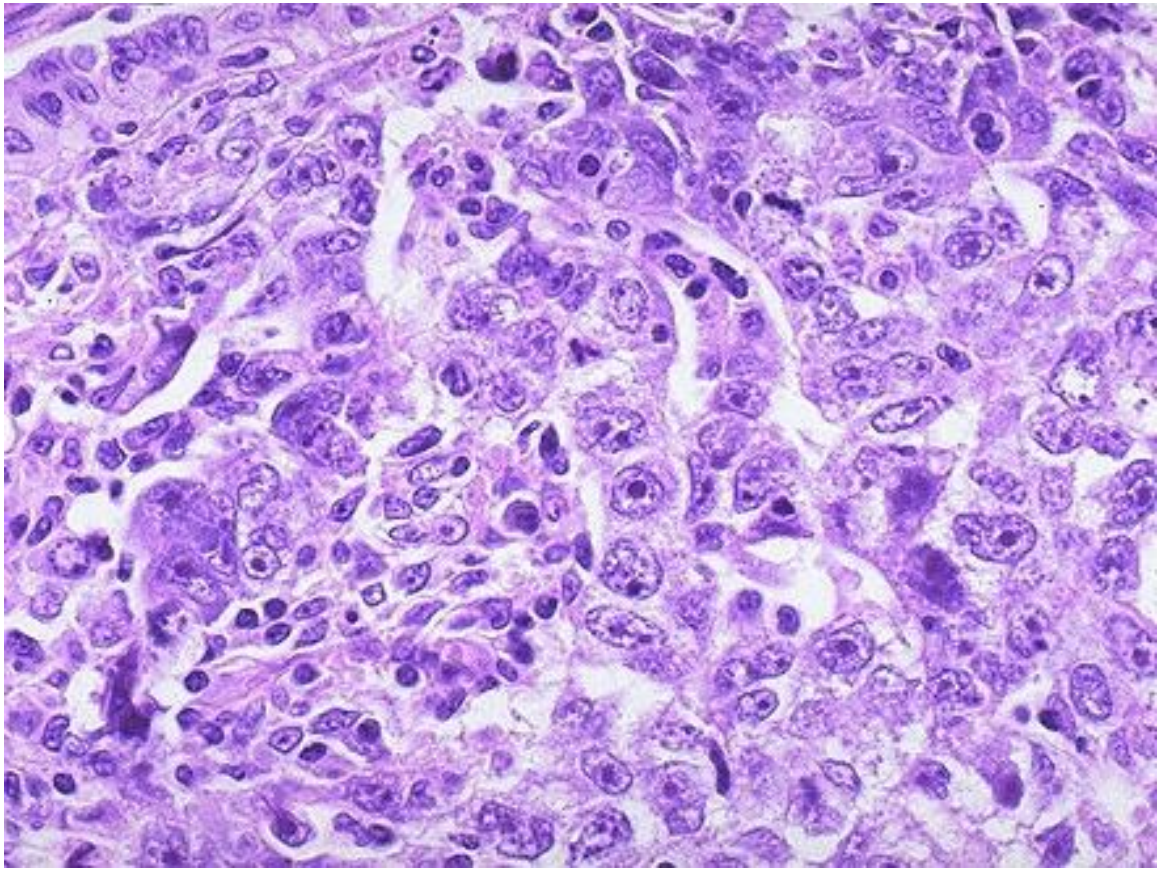
Squamous cell carcinoma

Well differentiated tumor producing keratin



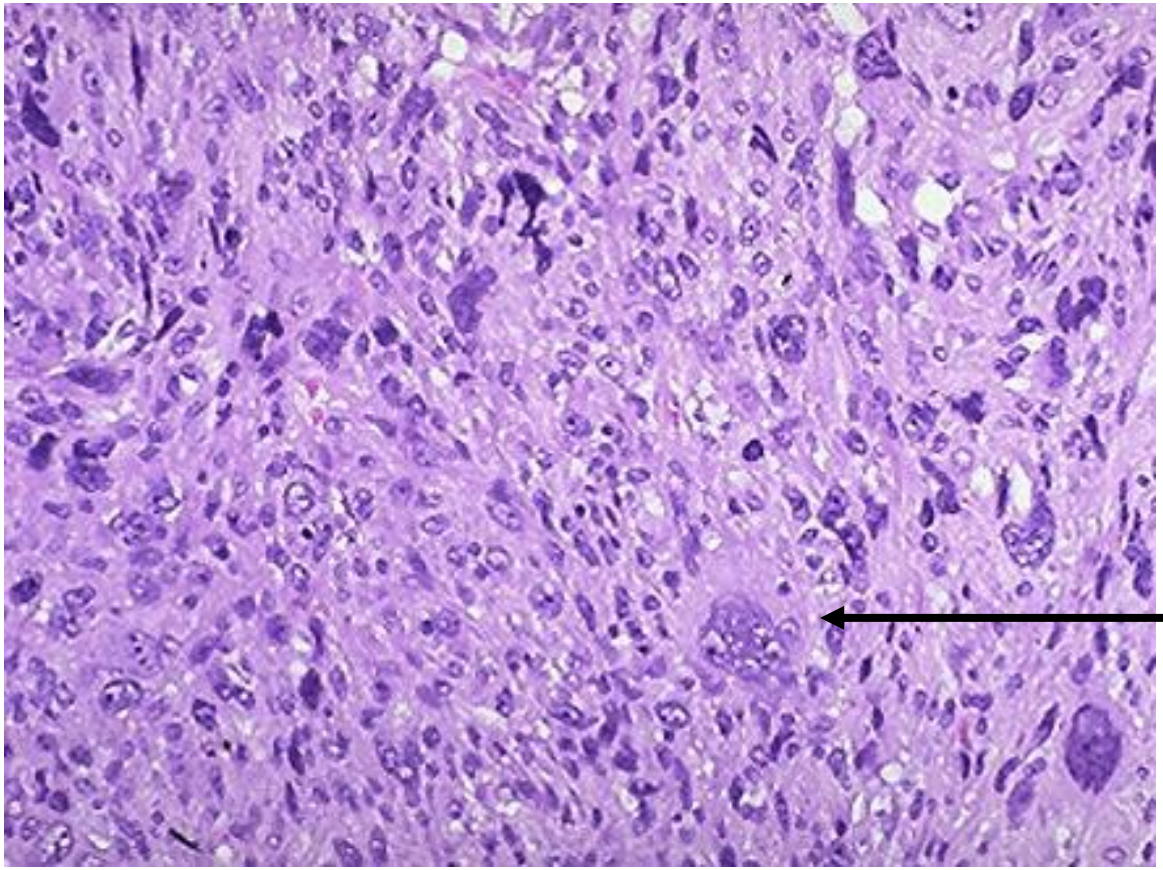
Osteosarcoma

Osteoid production by tumour cells

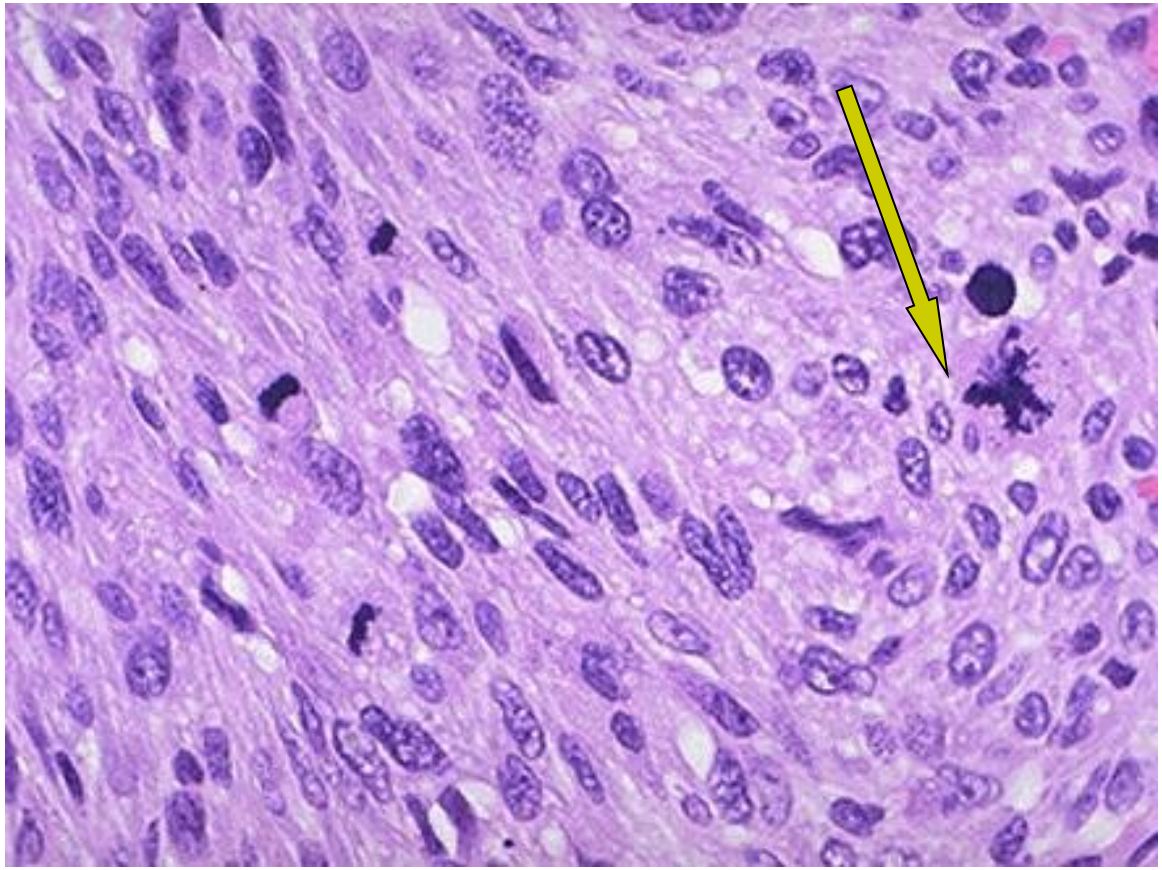


Malignant tumor

Pleomorphism , nuclear changes



Tumor giant cells



Abnormal mitosis

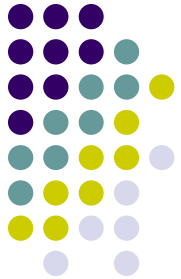
C)Tumour angiogenesis

- Tumors develop new vessels
- Microvascular density is used as a marker to assess the growth of a tumor
- If a tumor growth exceeds the blood supply necrosis occurs

D) Inflammatory reaction

- Adjacent tissue shows a chronic inflammatory response
- Ulceration may produce acute inflmmation

Characteristics of neoplasms



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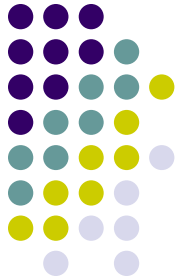


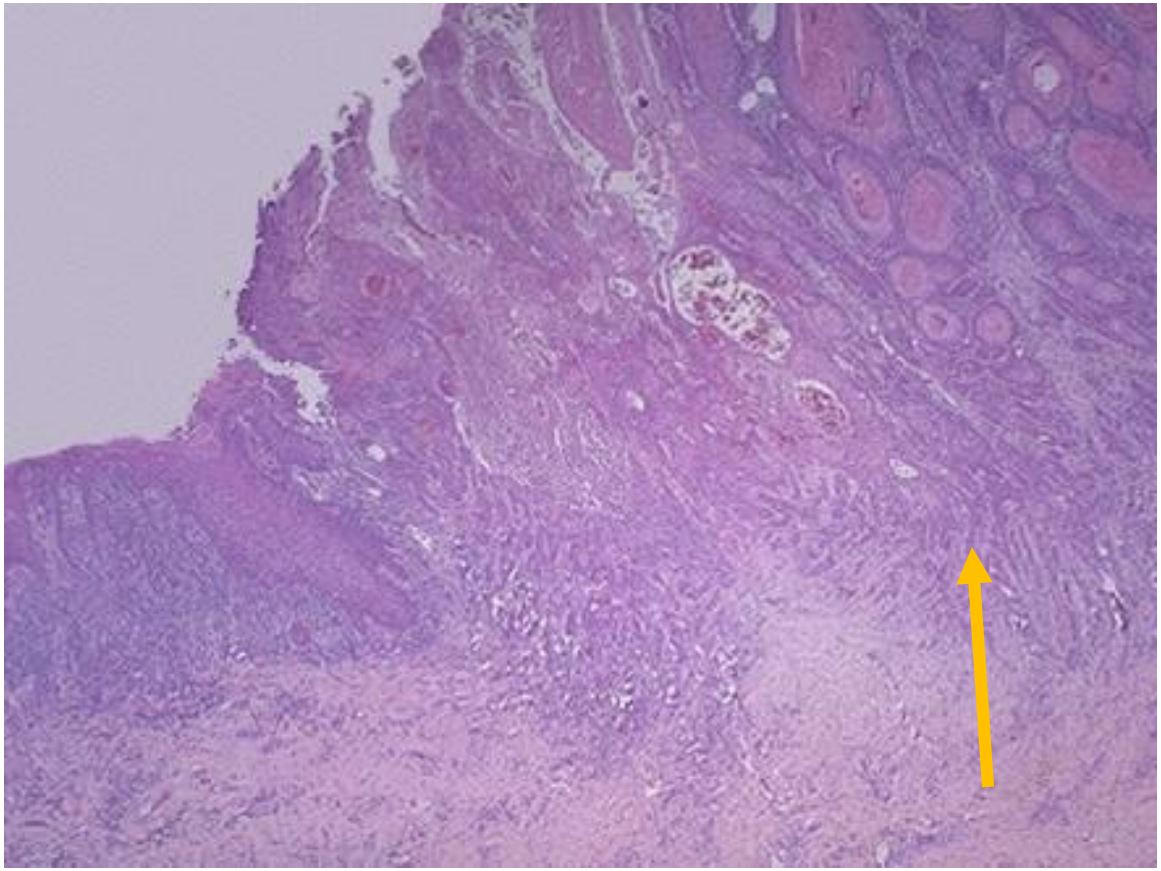
Benign tumours – encapsulated / circumscribed

- Expand and push the surrounding structures

Malignat tumours

- Expand
- Invade
- Infiltrate
- Destruction of the surrounding structures
- Usually via least resistant tissue spaces invasion occurs

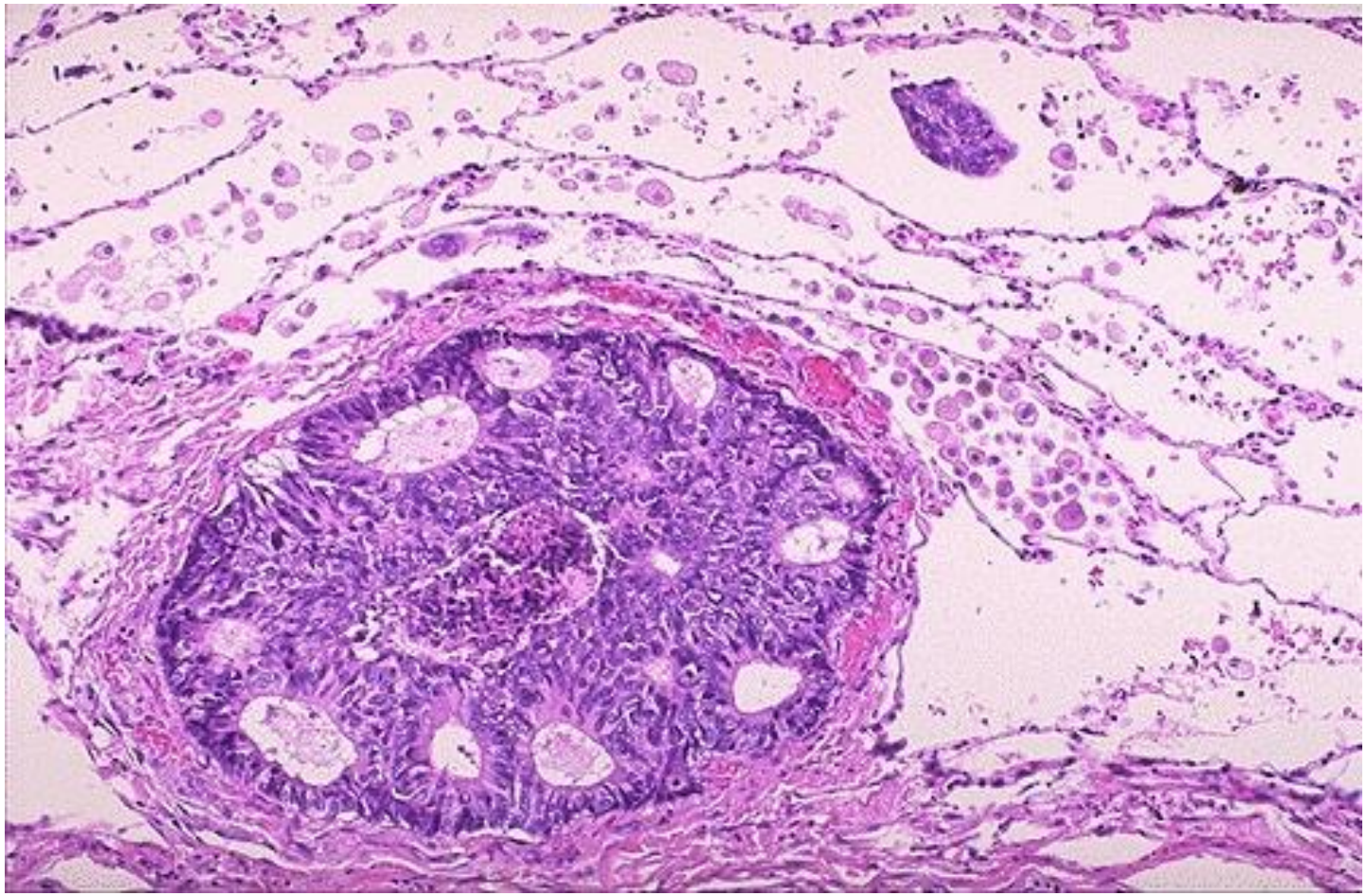
  Lymphatic
  Blood vessels
  Perineural spaces



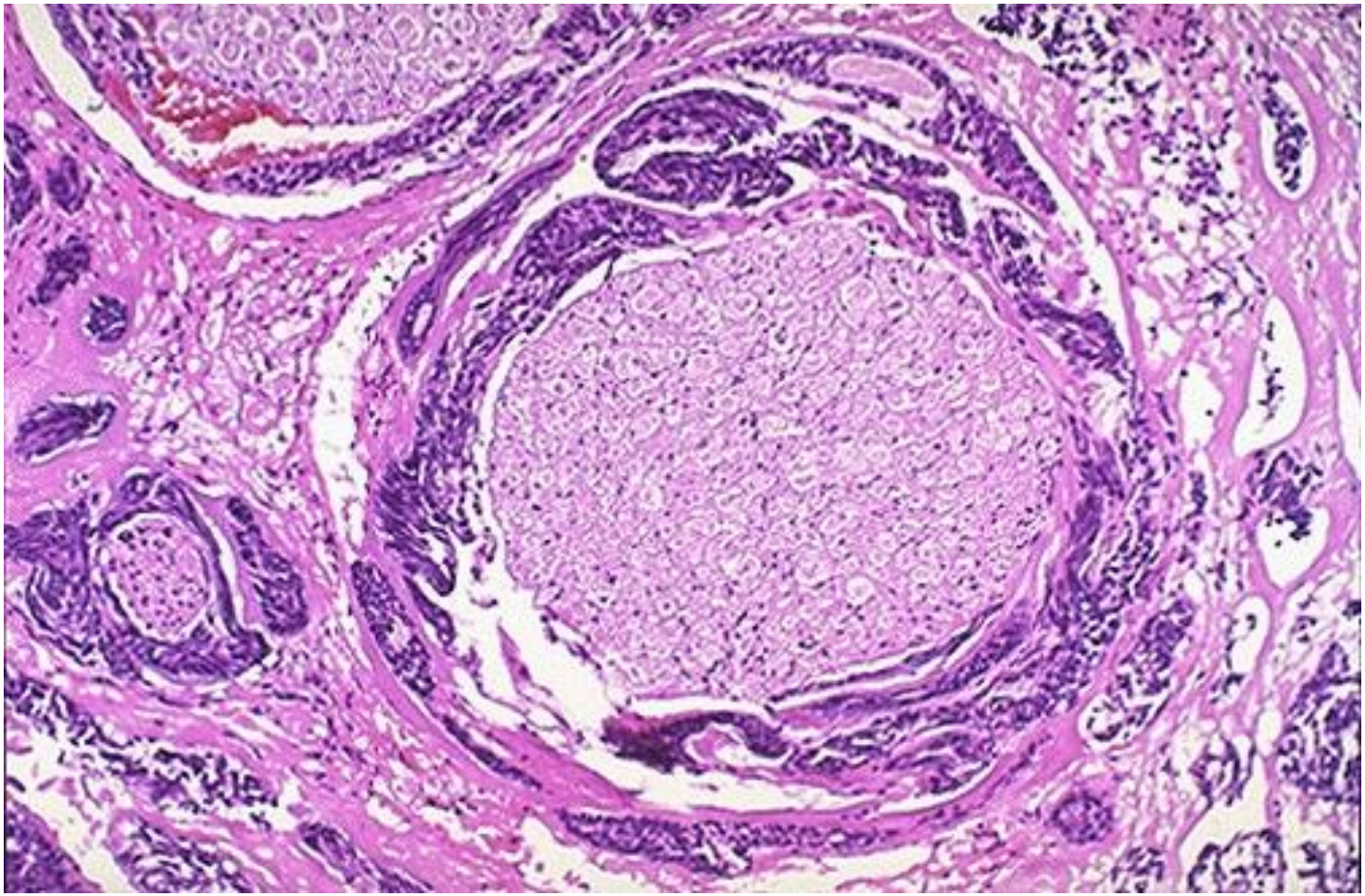
Squamous cell carcinoma

Infiltration seen

Vascular invasion



Perineural invasion



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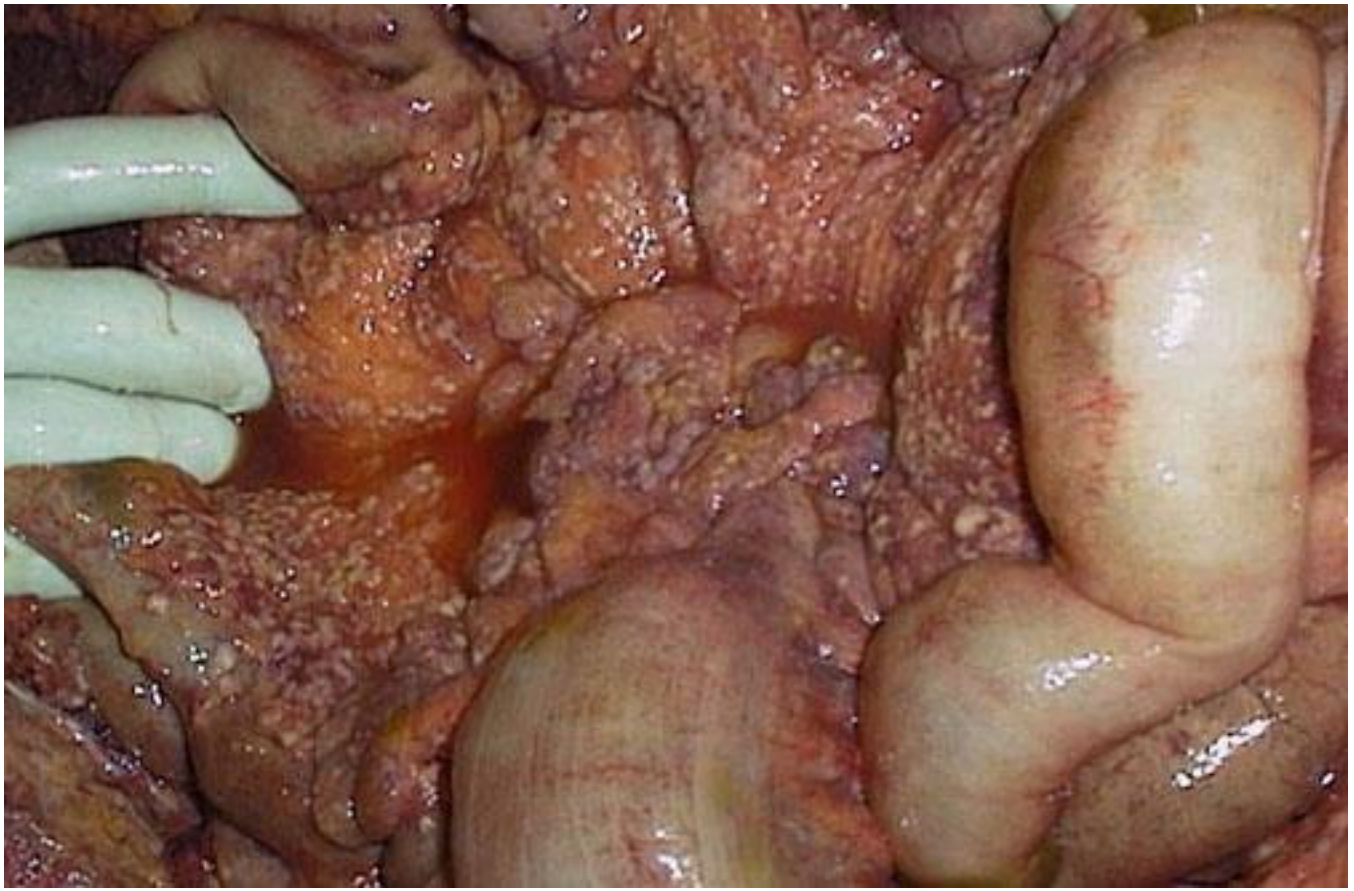
6) Metastasis

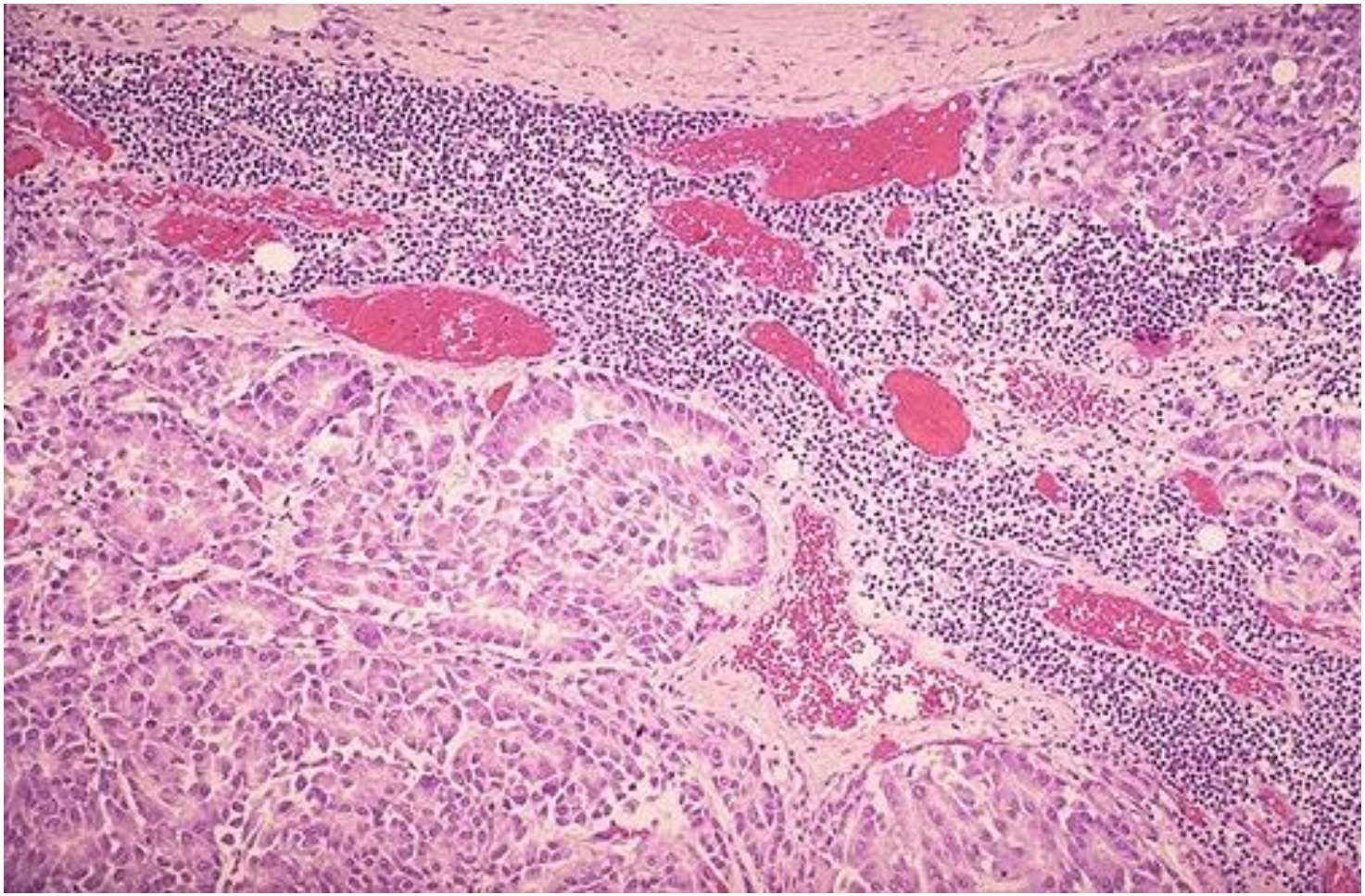
- Formation of discontinuous secondary masses at a distant site
- Lymphatic
- Haematogenous
- Other routes –body cavities

- Most important feature in diagnosing malignant tumours

Peritoneal metastasis



Deposits in a lymph node



- Is this a benign/ malignant tumor
- Tumor originate from smooth muscle.What will you call it