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Leicester Warwick Medical School

Neoplasia II

Invasion, Metastasis and Effects of Tumours

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WHAT IS INVASION?

Ability of cells to break through basement membrane and then spread.

- Into surrounding tissue
In-Situ Carcinoma → Invasive Carcinoma
- In lymphatic/vascular channels

Characteristic of malignant cells



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HOW DO CELLS INVADE AND SPREAD?

Complex mechanism involving various factors.

- Malignant cells do not adhere (stick) to the same extent as normal cells
- Malignant cells show a change in their interaction with surrounding stroma
- Factors produced that help cells spread (“scatter factor”)
- Altered synthesis of enzymes that breakdown basement membrane and stroma



ALTERED CELL ADHESION

CADHERINS are calcium dependent glycoproteins present at cell membrane.

They interact between cells, and within each cell with the actin cytoskeleton through catenins, maintaining polarity.

Reduced expression and alterations in interactions in cancer cells, allowing cells to move apart.



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ALTERED CELL ADHESION

INTEGRINS are cell surface glycoproteins composed of two subunits.

They are receptors for different components of the basement membrane eg. fibronectin.

Reduced expression of integrins in malignant cells modifies the contact between the cell and stroma allowing movement.



ALTERED ENZYME SYNTHESIS AND INTERACTION

Different enzymes can modify stroma allowing cells to break through basement membrane and spread

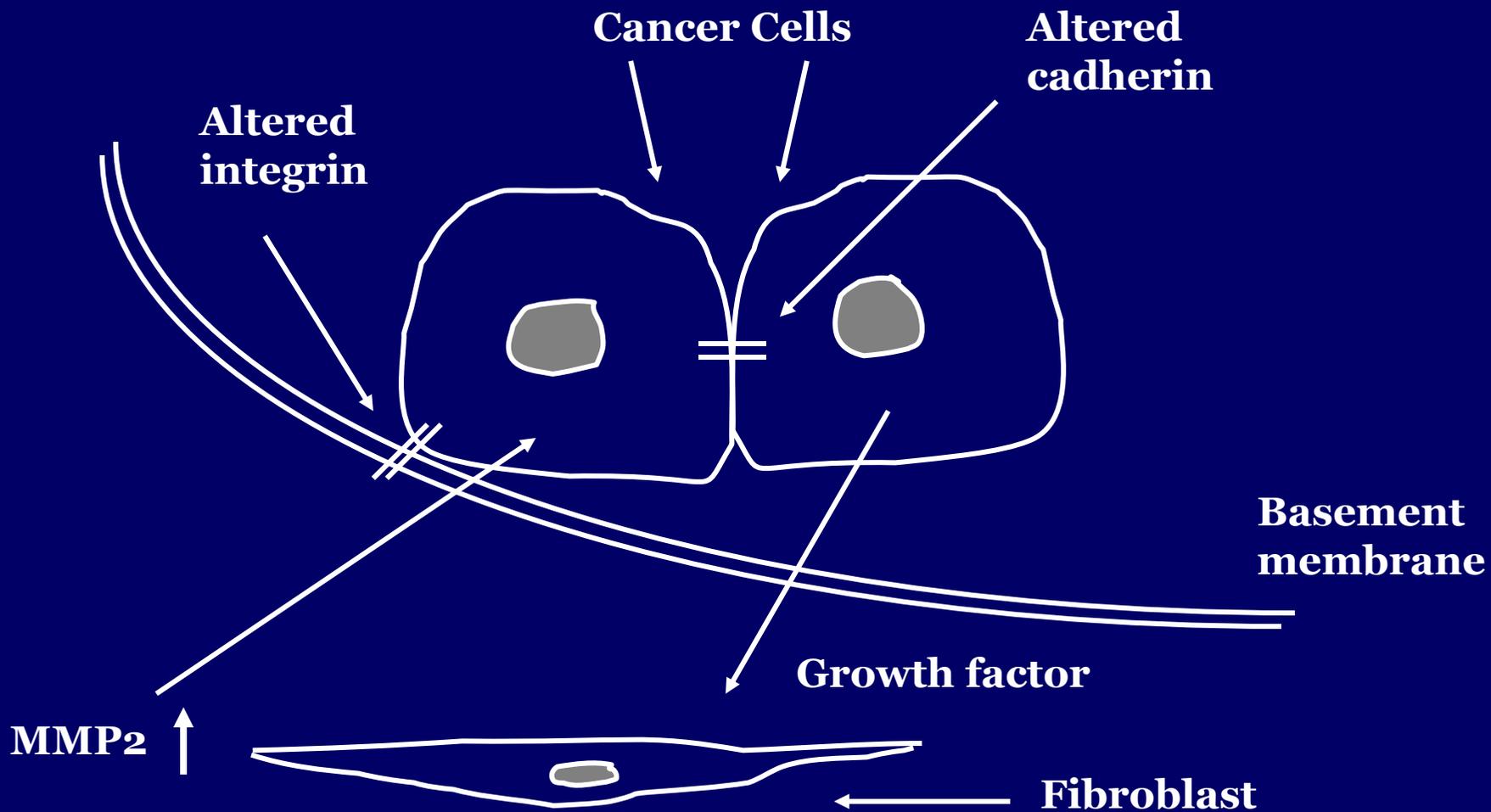
eg. Metalloproteinases

MMP2 and MMP9 - collagen IV

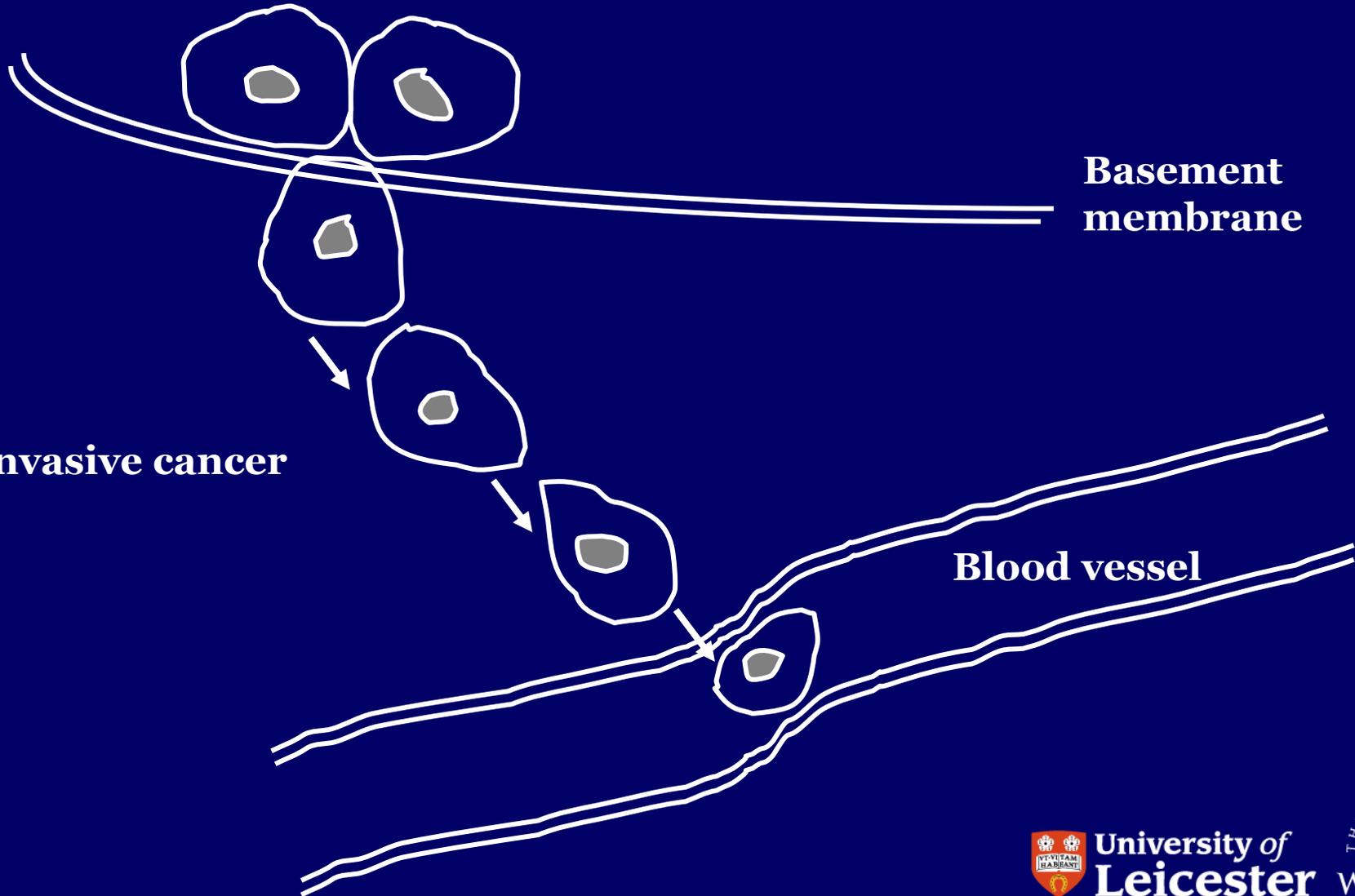
MMP1 - collagen I

ALTERED ENZYME SYNTHESIS AND INTERACTION

Malignant cells synthesise factors that stimulate stromal cells (fibroblasts) to synthesise more enzymes. Enzymes eg. MMP2 bind to malignant cell and allow it to break through basement membrane.



In Situ Cancer



Invasive cancer

**Basement
membrane**

Blood vessel



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WHAT IS METASTASIS?

Ability of malignant cells to invade into lymphatics, blood vessels and cavities and spread to distant sites.

Cells must be able to invade out of channels and grow at distant site.

Not all circulating cancer cells will settle at a distant site and be able to grow.

WHY DON'T ALL MALIGNANT CELLS METASTASISE?

Cells may invade and circulate.

May get to distant site but environment may not be appropriate for growth of those cells.

- Incorrect receptors
- Metabolic factors
- Failure of angiogenesis

“Seed and Soil”



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ANGIOGENESIS

Formation of small new vessels needed to maintain growth of cells.

Due to various growth factors produced by cancer cells.

Can aid invasion – more vessels with thin walls.

Aids growth of metastasis.



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METASTASIS

Primary = the site where the malignant neoplasm arises eg. breast, stomach.

Secondary = metastasis eg. breast carcinoma that has spread to another organ.

WHAT ARE THE ROUTES OF METASTASIS?

- Lymphatics
- Blood vessels
- Coelemic spaces



LYMPHATICS

Spread to local and distant lymph nodes

Frequent route of spread of carcinomas

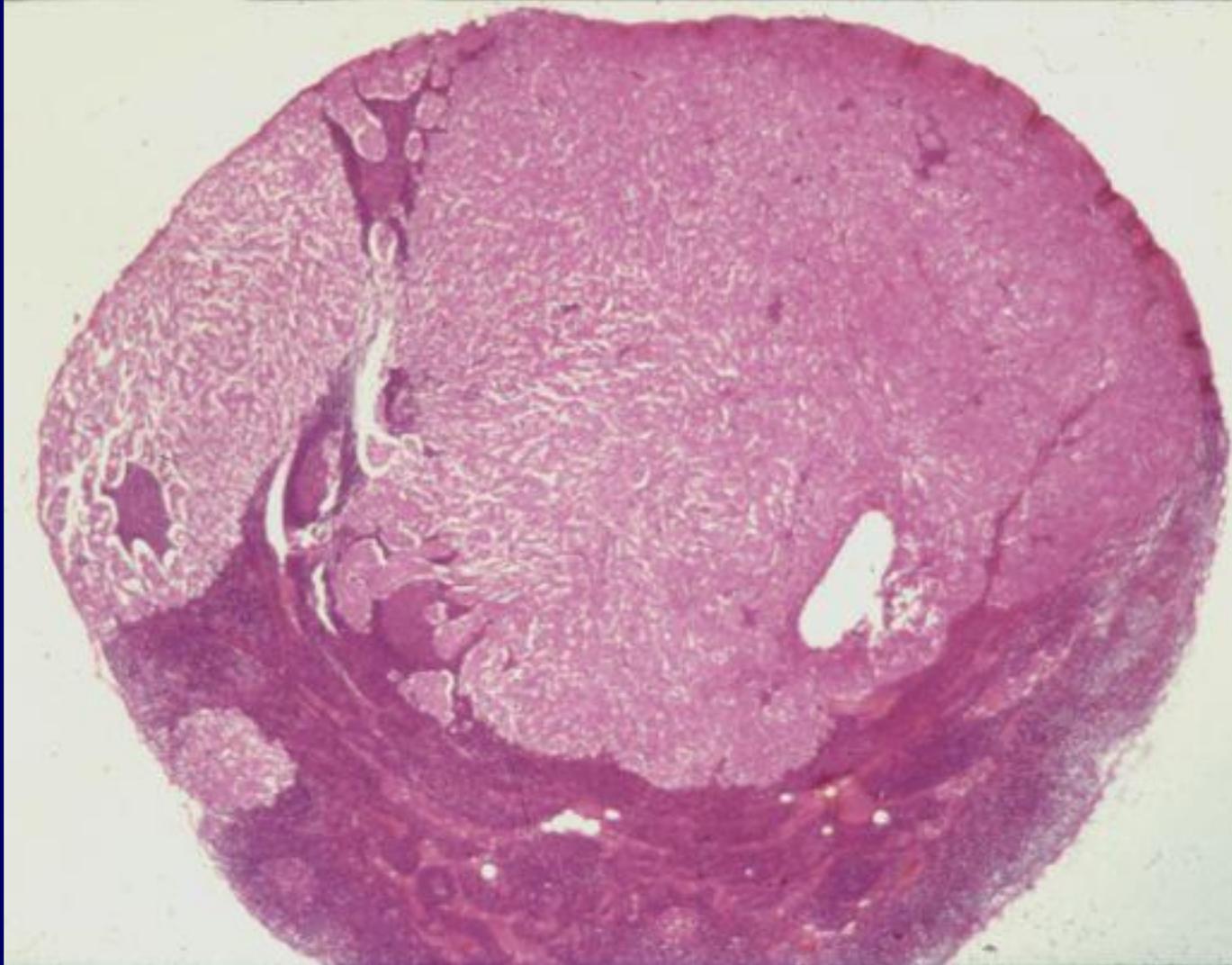
Can involve lymphatics of lung



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VASCULAR SPREAD

Spread through capillaries and veins to various organs.

Common sites are lung, liver, bone and brain.

VASCULAR SPREAD

To Lung

Can occur with a wide range of malignant neoplasms.

Sarcomas eg. Osteosarcoma

Carcinomas eg. breast, stomach, large intestine

Kidney (cannonball)

Testis eg. malignant teratoma



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VASCULAR SPREAD

To Liver

Common site for carcinomas of large intestine (portal vein).

Bronchial carcinoma.

Breast Carcinoma.



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VASCULAR SPREAD

To Bone

Can cause destruction of bone

- Bronchial carcinoma
- Breast carcinoma
- Thyroid carcinoma
- Renal carcinoma

Cause production of dense bone (osteosclerosis)

- Prostate





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VASCULAR SPREAD

To Brain

Can cause problems within the brain and the meninges

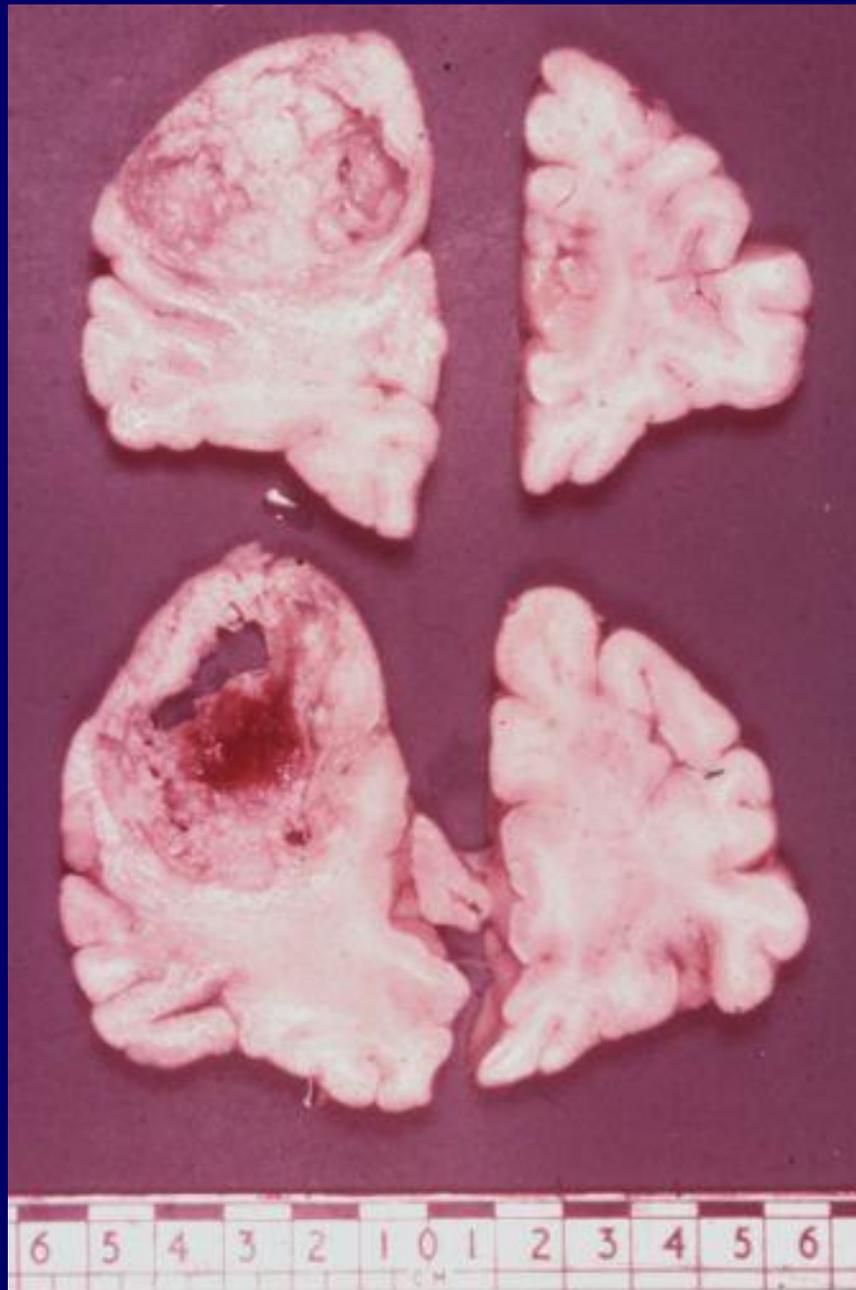
Metastasis from eg.

- Bronchial carcinoma
- Breast carcinoma
- Testicular carcinoma
- Malignant melanoma



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WHAT EFFECTS DO TUMOURS HAVE?

Depends on:

- site of tumour
- extent of local spread
- site of metastasis
- extent of metastatic spread
- functional effects

WHAT EFFECTS DO TUMOURS HAVE?

In certain sites a small tumour can have devastating effects

People can survive for some time with very extensive metastatic spread



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LOCAL EFFECTS OF NEOPLASMS

BENIGN

Cause compression - pressure atrophy
- altered function eg.
pituitary

In a hollow viscus cause partial or complete obstruction.

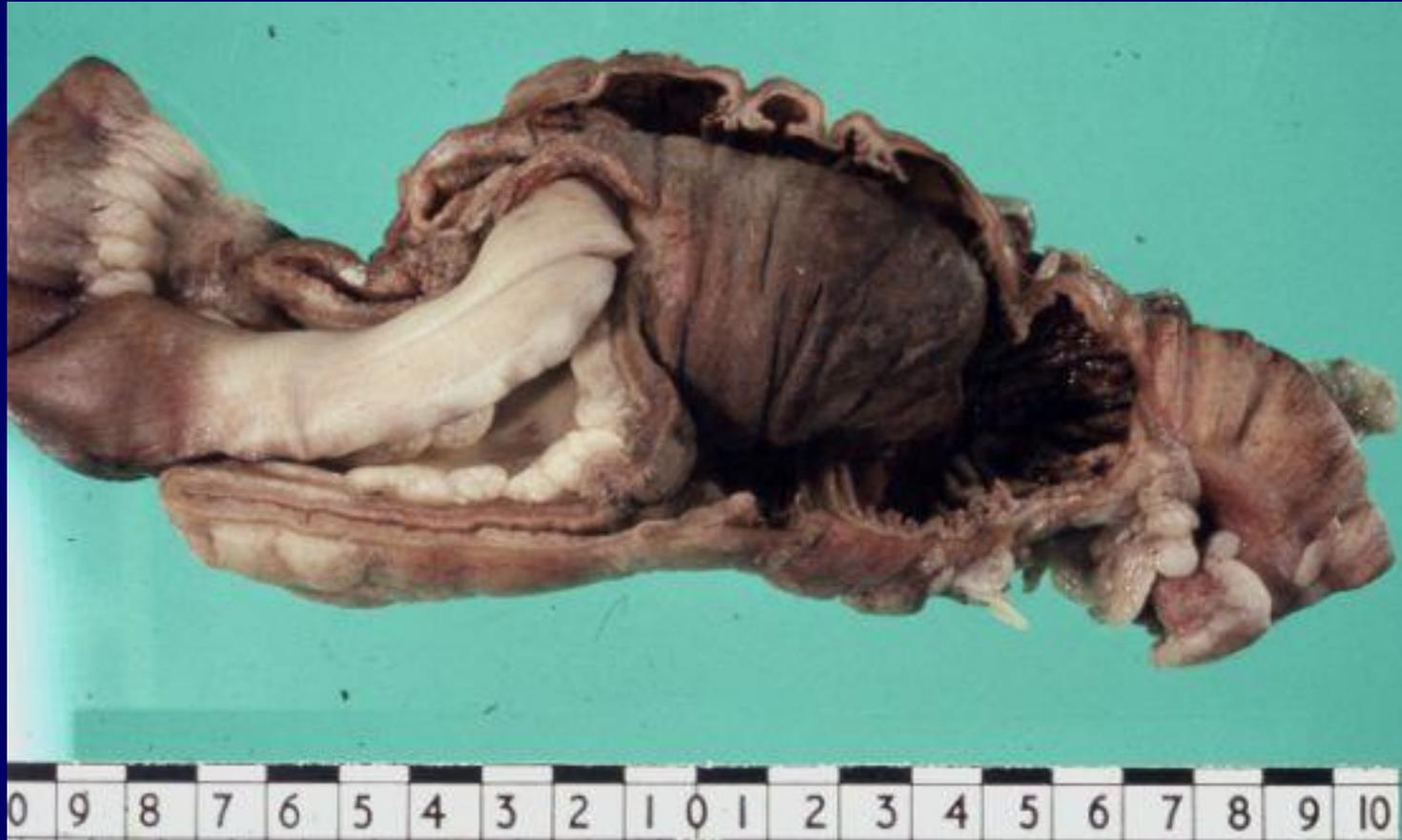
Ulceration of surface mucosa.

Space occupying lesion – brain.



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LOCAL EFFECTS OF NEOPLASMS

MALIGNANT

Tend to destroy surrounding tissue.

In a hollow viscus cause partial or complete obstruction, constriction.

Ulceration.

Infiltration around and into nerves, blood vessels, lymphatics.

Space occupying lesion - brain



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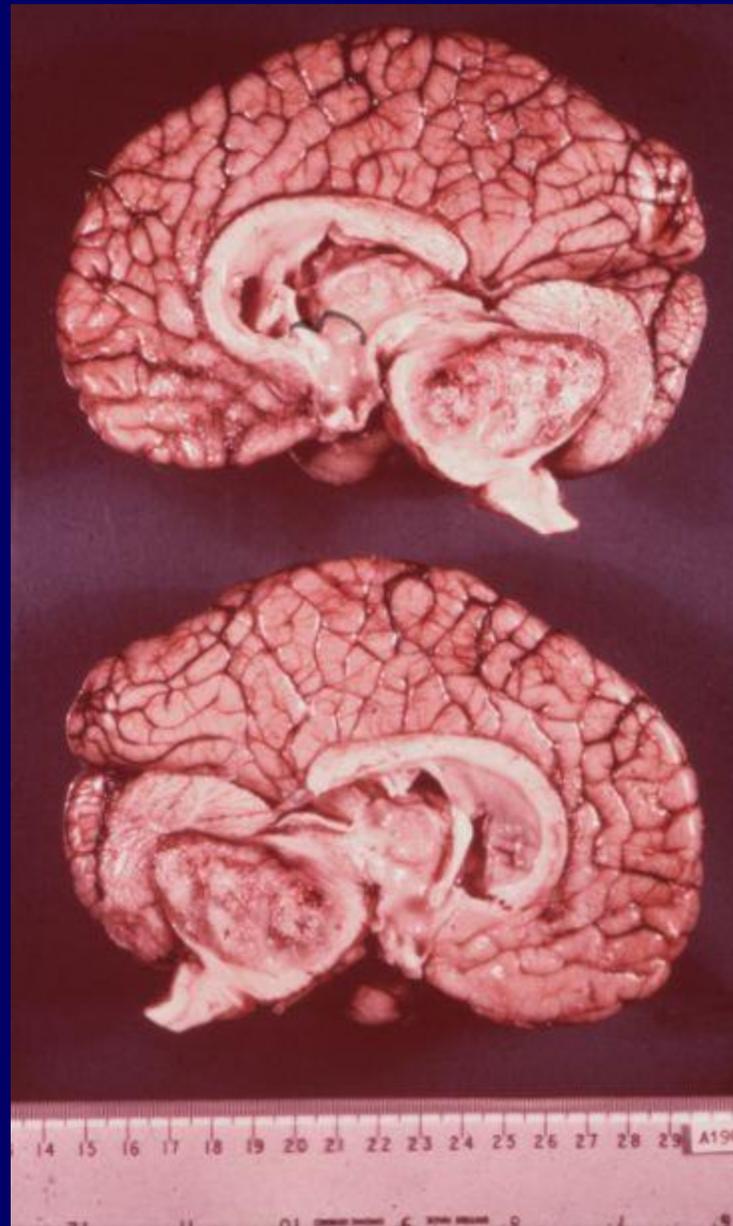
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SYSTEMIC EFFECTS OF NEOPLASMS

Haematological

Anaemia

- due to ulceration (benign and malignant)
- infiltration of bone marrow (leukaemia, metastasis)
- haemolysis

Low white cell and platelets

- infiltration of bone marrow, treatment

Thrombosis

- carcinoma of pancreas



SYSTEMIC EFFECTS OF NEOPLASMS

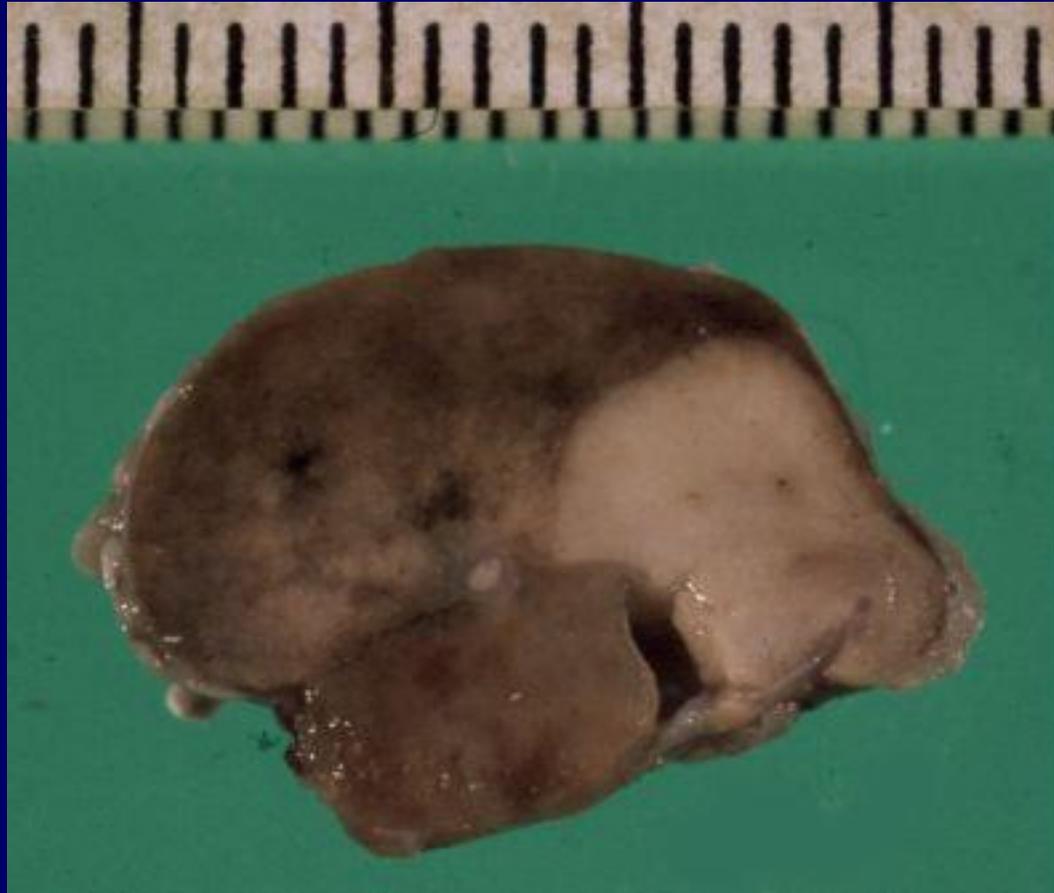
Endocrine

Excessive secretion of hormones -

benign and malignant neoplasms of endocrine glands e.g. parathyroid hormone, corticosteroids

Ectopic hormone secretion -

ACTH by small cell carcinoma of bronchus



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SYSTEMIC EFFECTS OF NEOPLASMS

Skin

Increased pigmentation	many carcinomas
Pruritis (itching)	jaundice, Hodgkin's disease
Herpes zoster	lymphoma
Deratomyositis	bronchial carcinoma





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SYSTEMIC EFFECTS OF NEOPLASMS

Neuromuscular

Problems with balance.

Sensory/sensorimotor neuropathies.

Myopathy and myasthenia.

Progressive multifocal leucoencephalopathy.

Not due to metastasis to brain.

SYSTEMIC EFFECTS OF NEOPLASMS

Cachexia

Malaise

Pyrexia

Mechanisms unknown

WHY DO NEOPLASMS KILL PEOPLE?

Local effect e.g. brain, perforation, haemorrhage

Benign or malignant

Replacement of essential body organs

Malignant