Neoplasia(2)

- Definition
- Nomenclature
- Benign and malignant tumors

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Definition of neoplasia

- Neoplasia =neoplasm =tumor
- Abnormal mass of tissue, with uncontrolled (uncoordinated) growth of *genetically altered cells*.
- Purposless, autonomous, it grows without respect for the needs of the host as a whole

Definitions

Neoplasm – „new growth” abnormal mass of tissue, the growth of which exceeds and is uncoordinated with the normal tissues

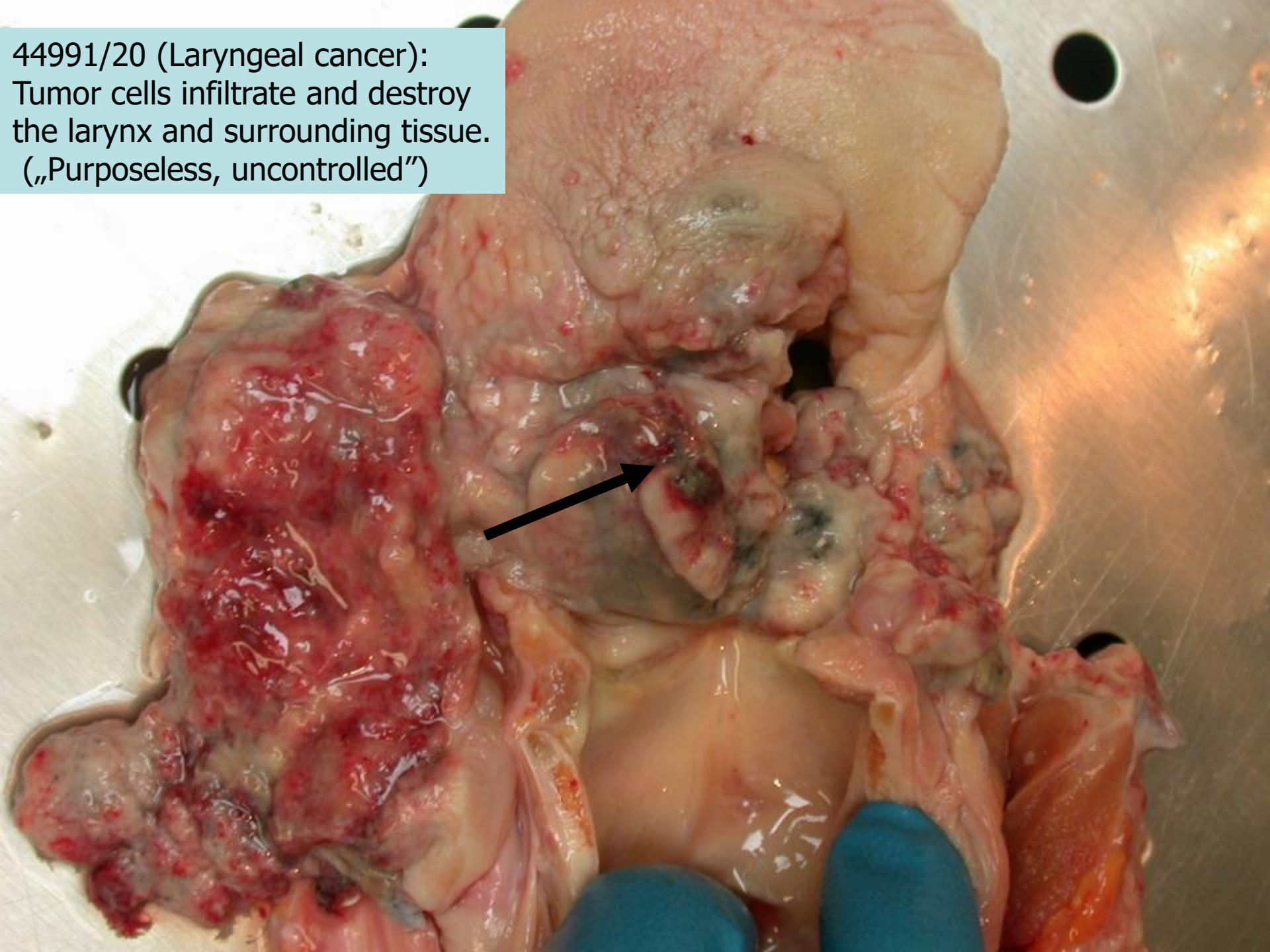
Tumor - a non-specific term meaning lump or swelling. Often synonym for neoplasm

Cancer - any malignant neoplasm or tumor

(Hippocrates- „crab”)

Metastasis - discontinuous spread of a malignant neoplasm to distant sites


44892/13 (Liver metastasis):
Uncontrolled growth of tumor cells
The normal tissue of the liver is
destroyed.


44991/20 (Laryngeal cancer):
Tumor cells infiltrate and destroy the larynx and surrounding tissue.
(„Purposeless, uncontrolled”)

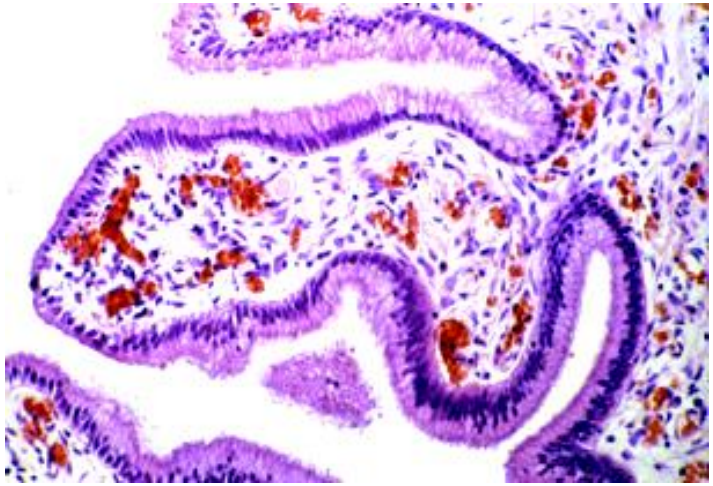
Nomenclature of various growth processes (“plasias”)

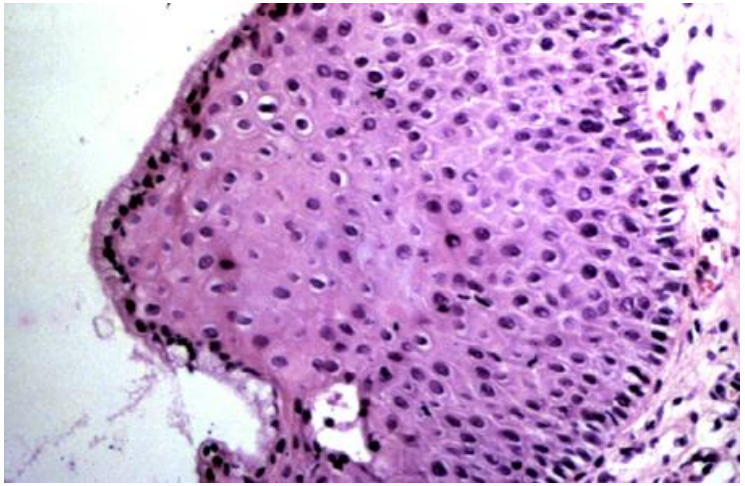
- Hyperplasia
- Metaplasia
- Dysplasia
- Neoplasia
- Desmoplasia

Metaplasia

an adaptive substitution of one type of mature tissue to another type of adult tissue

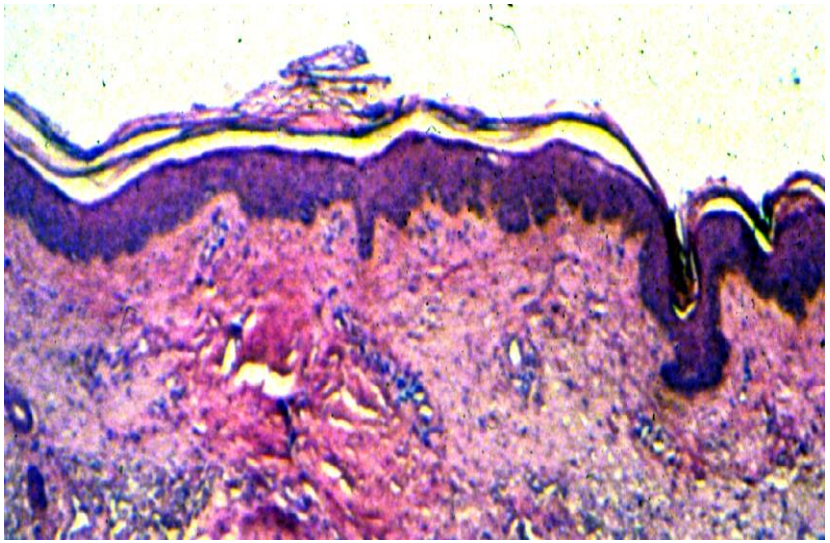
under stress a more vulnerable type of tissue will be replaced by another more capable of withstanding stress

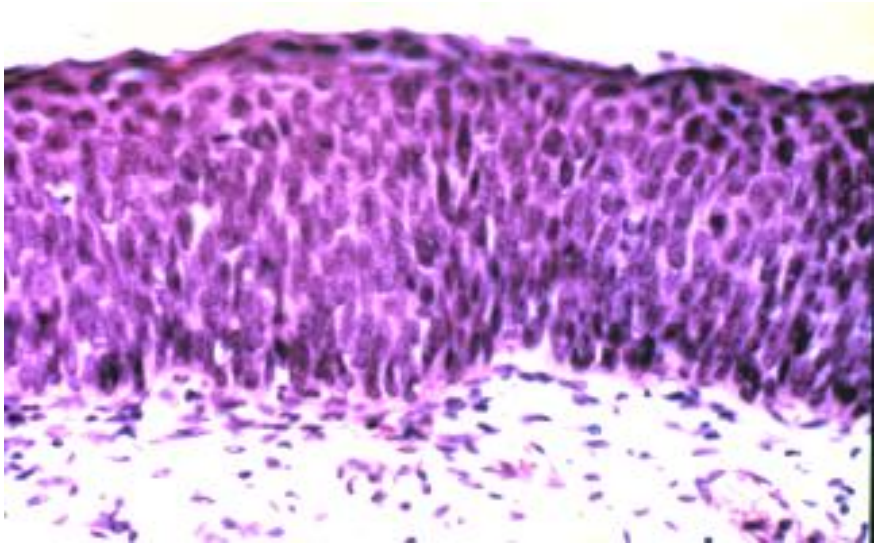




Dysplasia

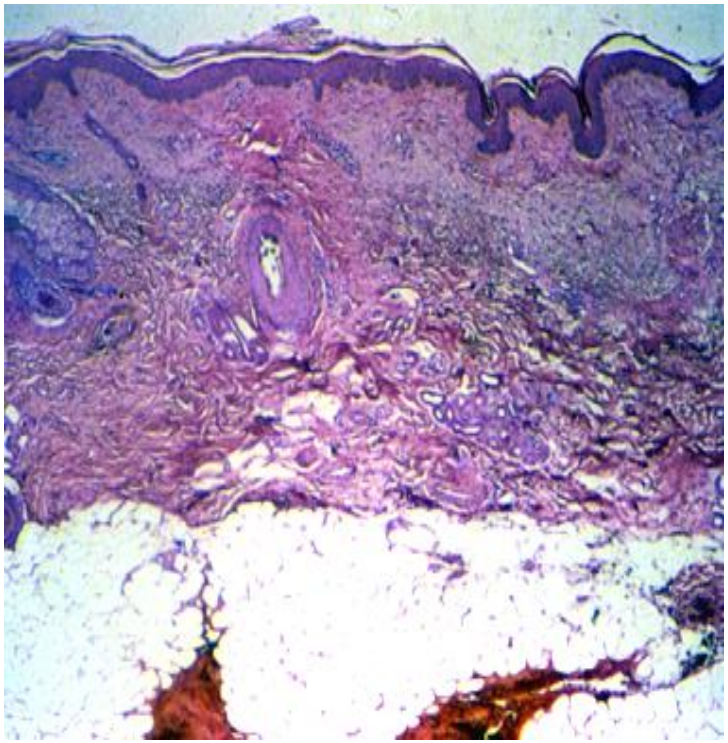
An abnormality in cell size, appearance, with or without a disorganized growth pattern

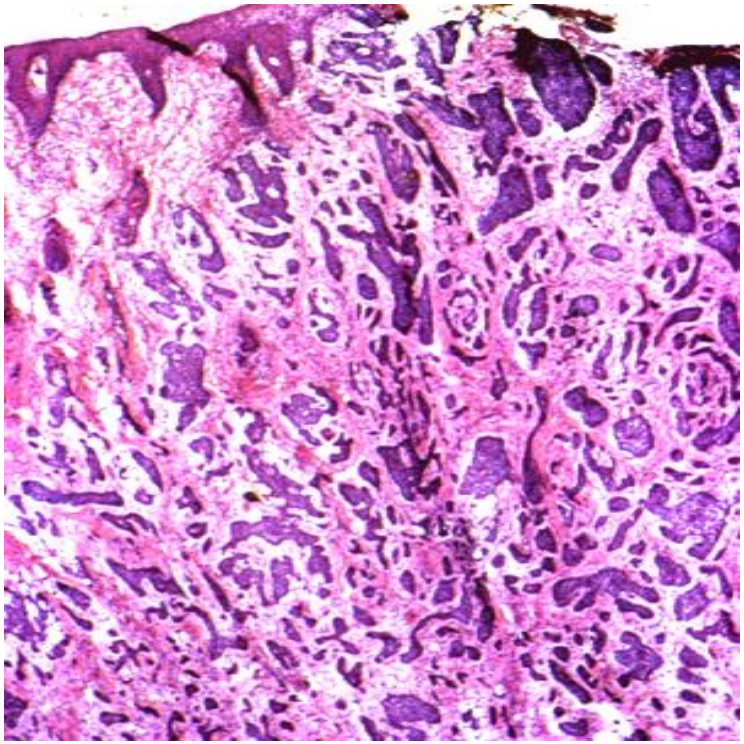




Desmoplasia

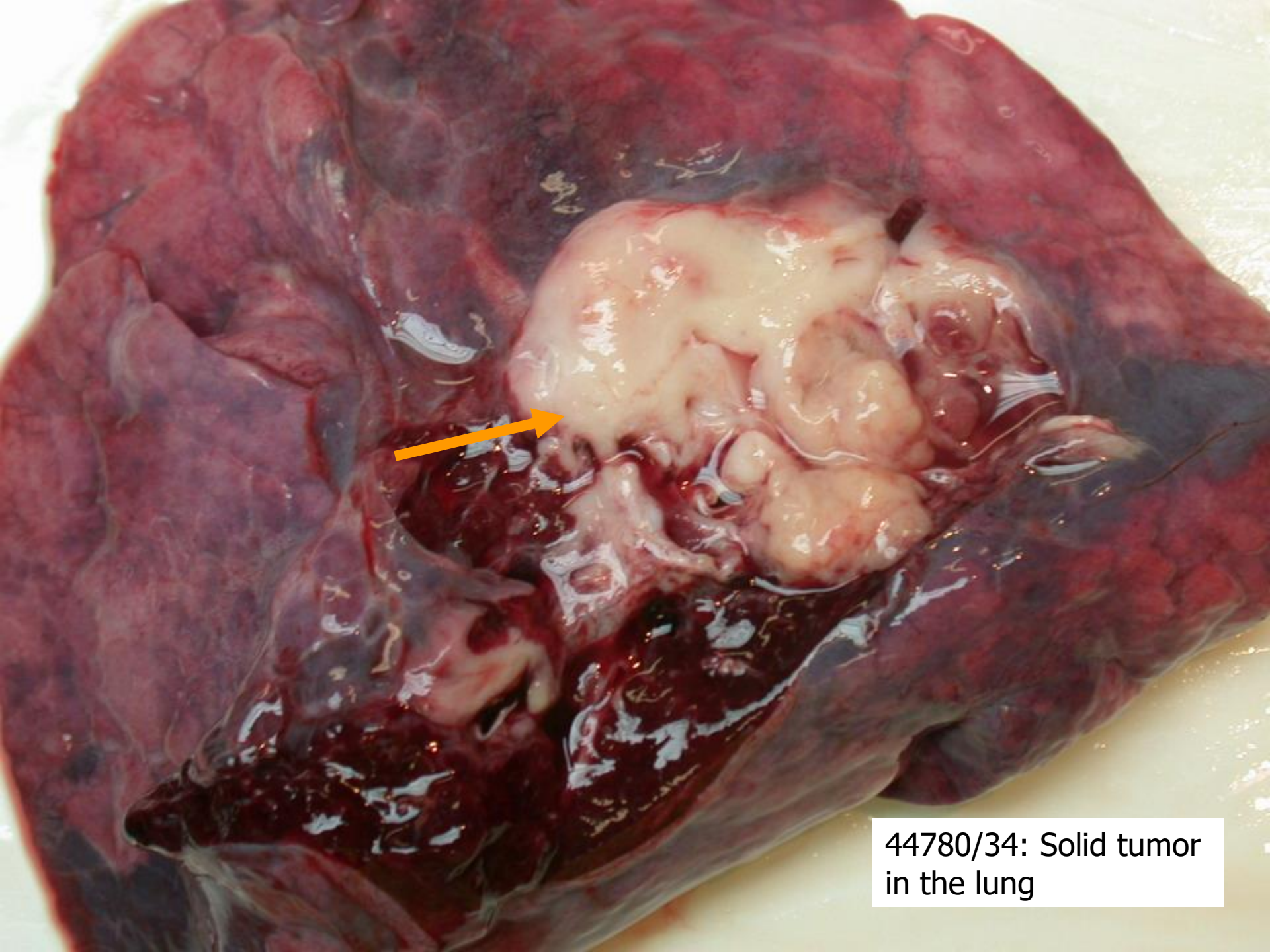
The formation and proliferation of connective tissue in response to neoplastic growth





Nomenclature (1)

- Parenchyma: proliferating neoplastic cells
- Stroma: „supporting" connective tissue and blood vessels (desmoplasia, scirrhous, medullar etc)
- Suffix „-oma" (fibroma, melanoma, carcinoma, sarcoma etc)
- Cancer: common term for all malignant tumor
- „Solid" tumor: tumor that does not derive from blood cells (leukemias and lymphomas are not considered solid tumors because the cells do not usually form cohesive masses with a vascular stroma)



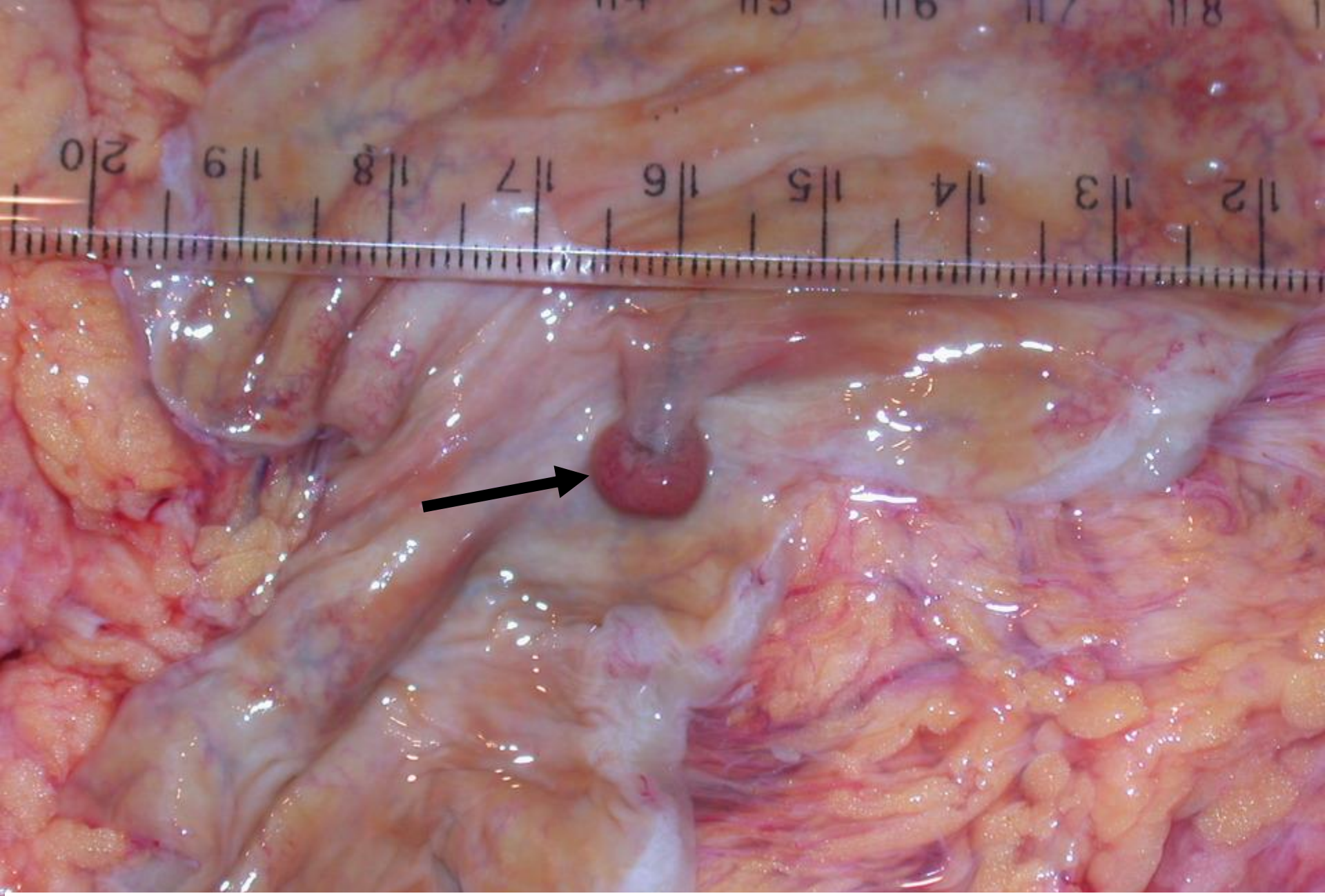
44780/34: Solid tumor in the lung

Nomenclature (2): Benign and Malignant tumors

- Benign: well differentiated structure, grows slowly, *expansive* growth, well circumcised, capsule (usually, not always), non-invasive, never metastasize, contact inhibition of growth. But: they may still be dangerous!
- Malignant: atypical structure, lose contact inhibition of growth, rapid growth with many mitoses, no true capsule (or infiltrate capsule), *infiltrative* growth, tend to form metastases

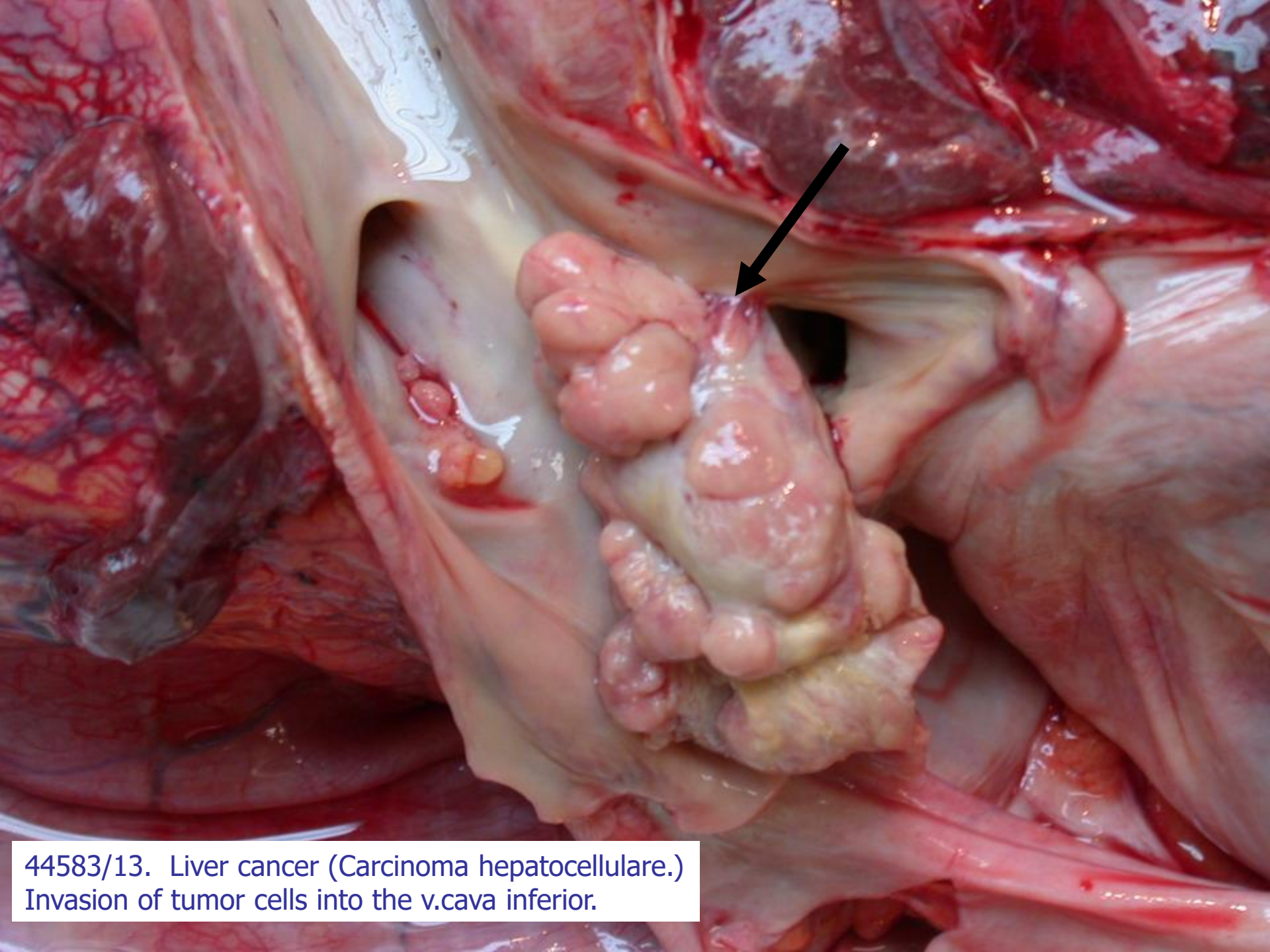
Classification Criteria and Associated Biologic Behavior

Characteristics	Benign	Malignant
Growth pattern	expansive	infiltrative
Rate of growth	slow	fast
Differentiation	well	poor (...)
Metastasis	absent	typical

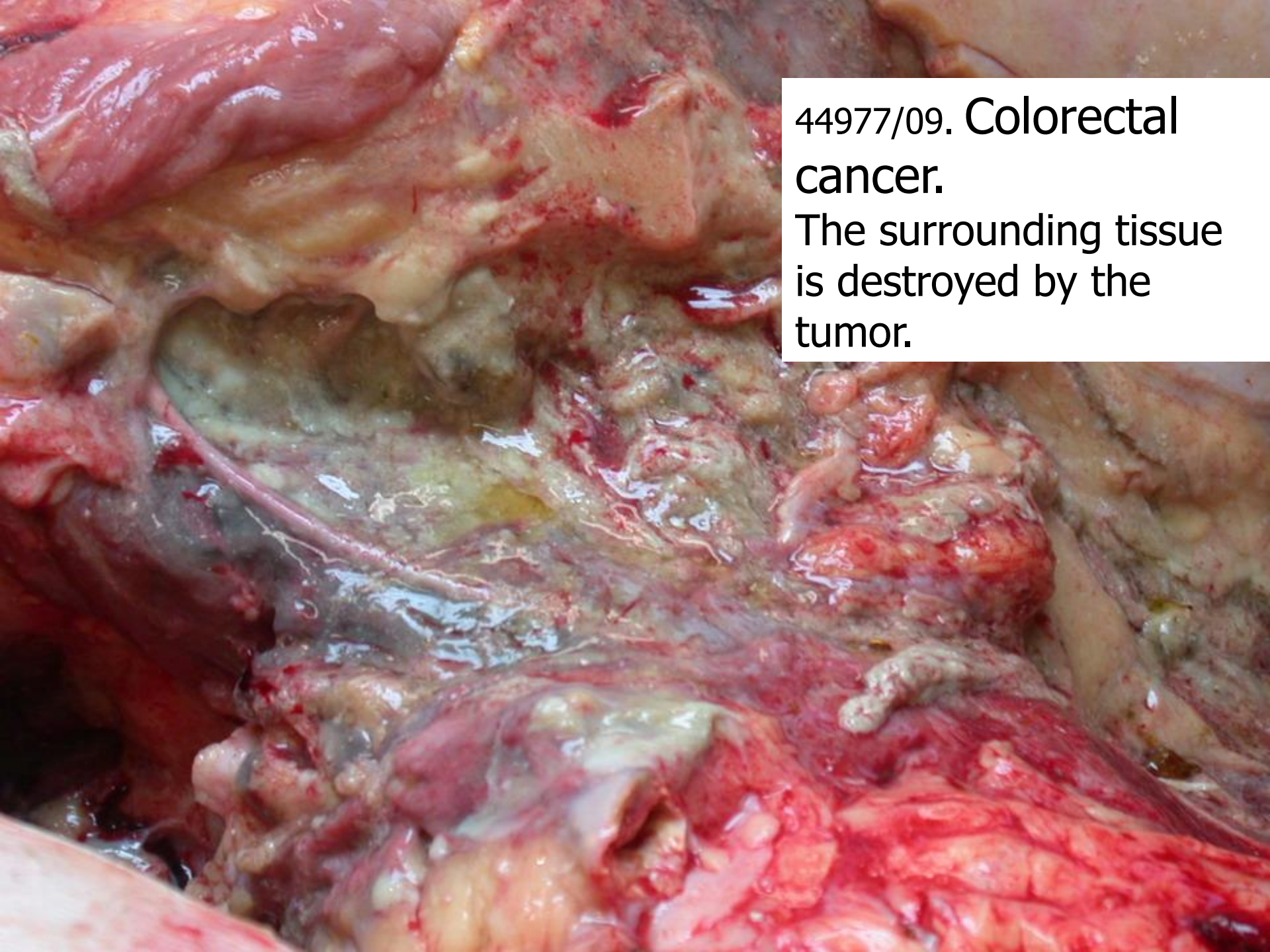


44909/06: **Polypus coli**
Pedunculated benign epithelial tumor of glandular origin.

45065/06: Colorectal cancer (Adenocarcinoma recti.)
Malignant polypoid tumor infiltrating the wall of the rectum.



44583/13. Liver cancer (Carcinoma hepatocellulare.)
Invasion of tumor cells into the v.cava inferior.



44977/09. Colorectal cancer.
The surrounding tissue is destroyed by the tumor.

„Dangerous aspects” of tumors

- Benign:
  - Positional (brain tumors etc)
  - Necrosis, hemorrhage
  - Excessive production of a material (such as hormones)
- Malignant
  - Progressive growth and metastasis
  - Necrosis, hemorrhage
  - Infection
  - Cachexia (role of TNF and IL-1)
  - Various products such as hormones, enzymes, oncofetal Ags (CEA, AFP etc- diagnosis!). Paraneoplastic syndromes

Paraneoplastic syndrome (PNSy)

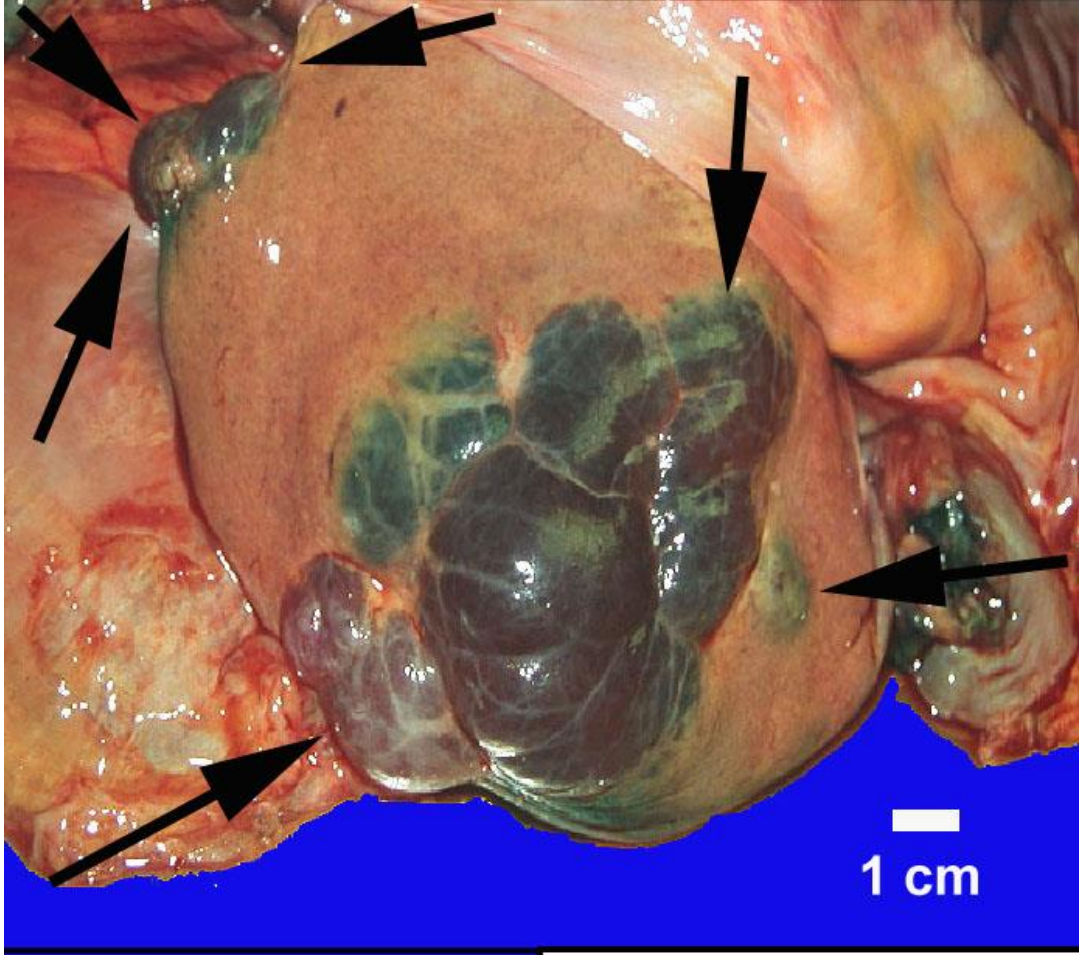
- Definition: PNSy is the combination of signs and symptomes in a patients with cancer that cannot be attributed to either (1) the location of the primary tumor or its metastases or (2) to the secretion of hormones indigenous to the tissue from which the tumor is derived.
- Examples:
  - Production of ACTH or ACTH like substances by a small cell (oat cell) cc of the lung
  - Hypercalcemia; possibilities: (1) cc induces osteolysis (not a paraneoplastic sy!), (2) tumor produces parathyroid hormone (PTH) or –like substances (squamous lung cc)
  - Migratory venous thrombosis (Trousseau's thrombophlebitis) – secondary to a poorly undertstood „hypercoagulable state" (pancreas cc)
  - DIC: simultaneous thrombogenesis and thrombolysis (any type of advanced cancer)
  - Carcinoid syndrome: in patients with carcinoid tumors (secretion of serotonin, histamin- hyperperistalsis, diarrhea, bronchospasm, cardiac valve fibrosis) etc.....

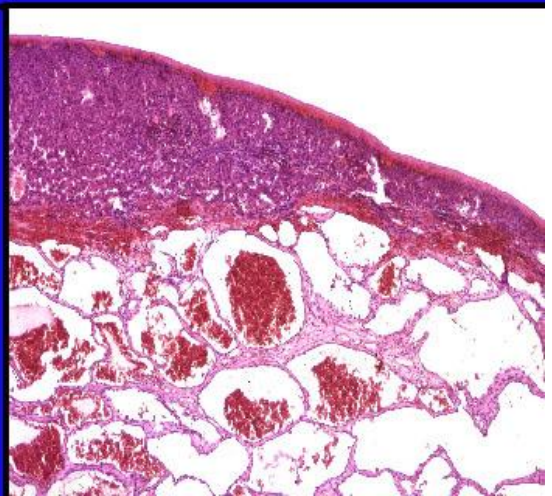

Pozitron Diagnosztika
Ref.: SOTE
Biograph 6
A

Nomenclature (3): Benign and Malignant tumors

- Benign:
  - One parenchymal cell type:
    - (1) mesenchymal: fibroma, lipoma, chondroma, myoma, haemangioma etc
    - (2) epithelial: papilloma, adenoma, naevus etc
  - More than one cell type (mixed): fibroadenoma, pleomorphic adenoma etc
  - Teratogenous (more than one germ layer): mature teratoma, dermoid cyst
- Malignant:
  - One parenchymal cell type:
    - (1) mesenchymal: fibrosarcoma, liposarcoma etc....,
    - (2) epithelial: squamous cell carcinoma, basal cell cc, adenocc, malignant melanoma etc
  - Teratogenous: immature teratoma, teratocarcinoma
  - More than one cell type: Wilms tumor (kidney), etc

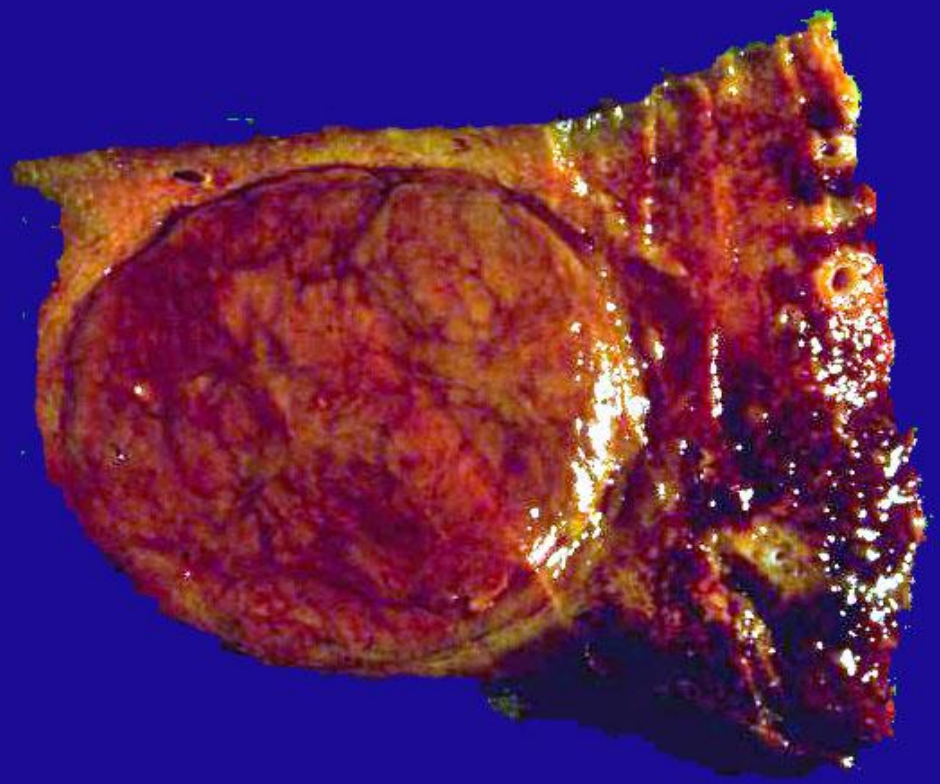
Haemangioma hepatis (giant).
Benign tumor: well circumcised,
No metastasis.





Adenoma hepatocellulare

Well circumcised, surrounded by capsule
No infiltration

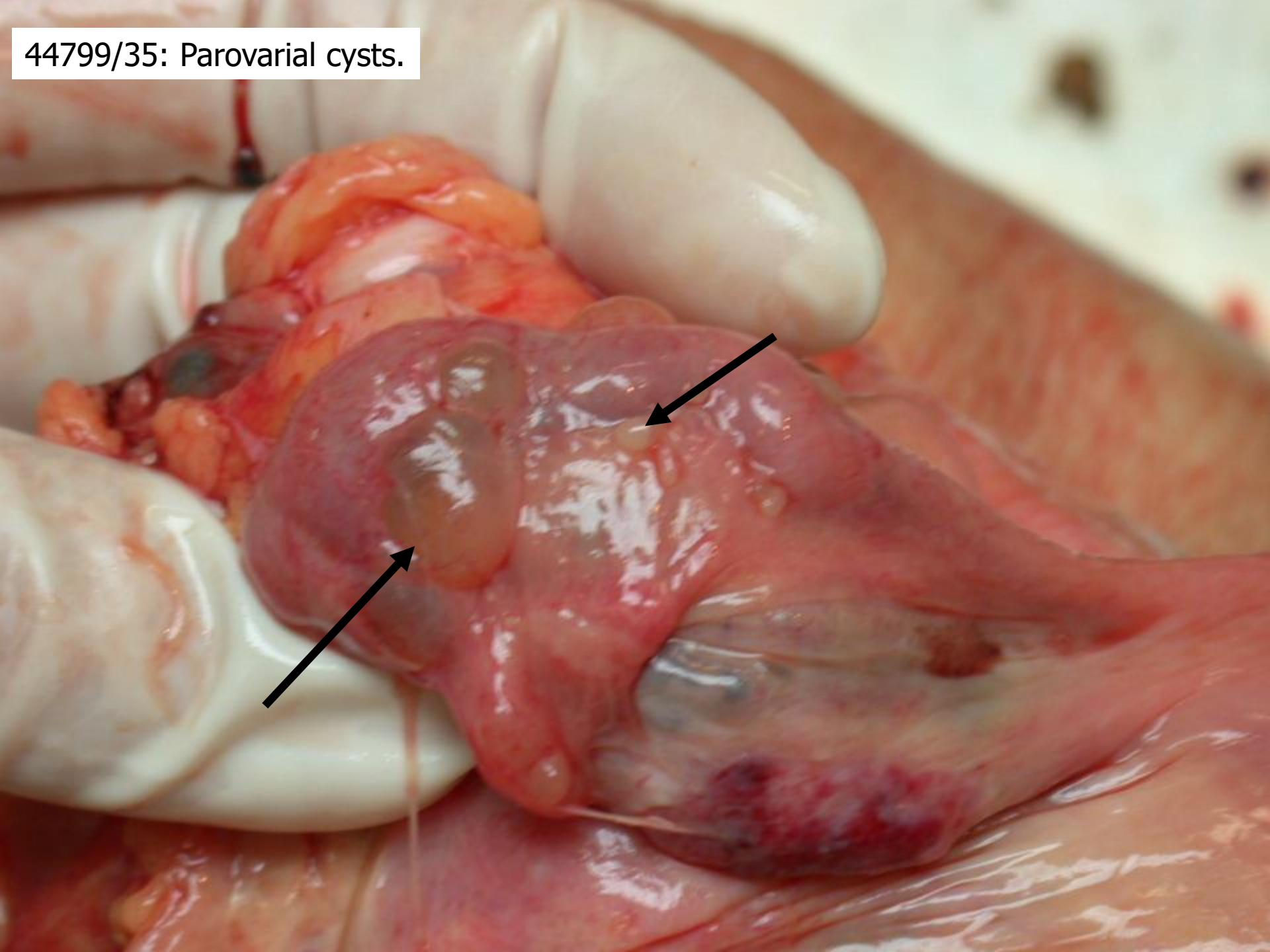


Nomenclature (4): Benign and Malignant tumors (examples)

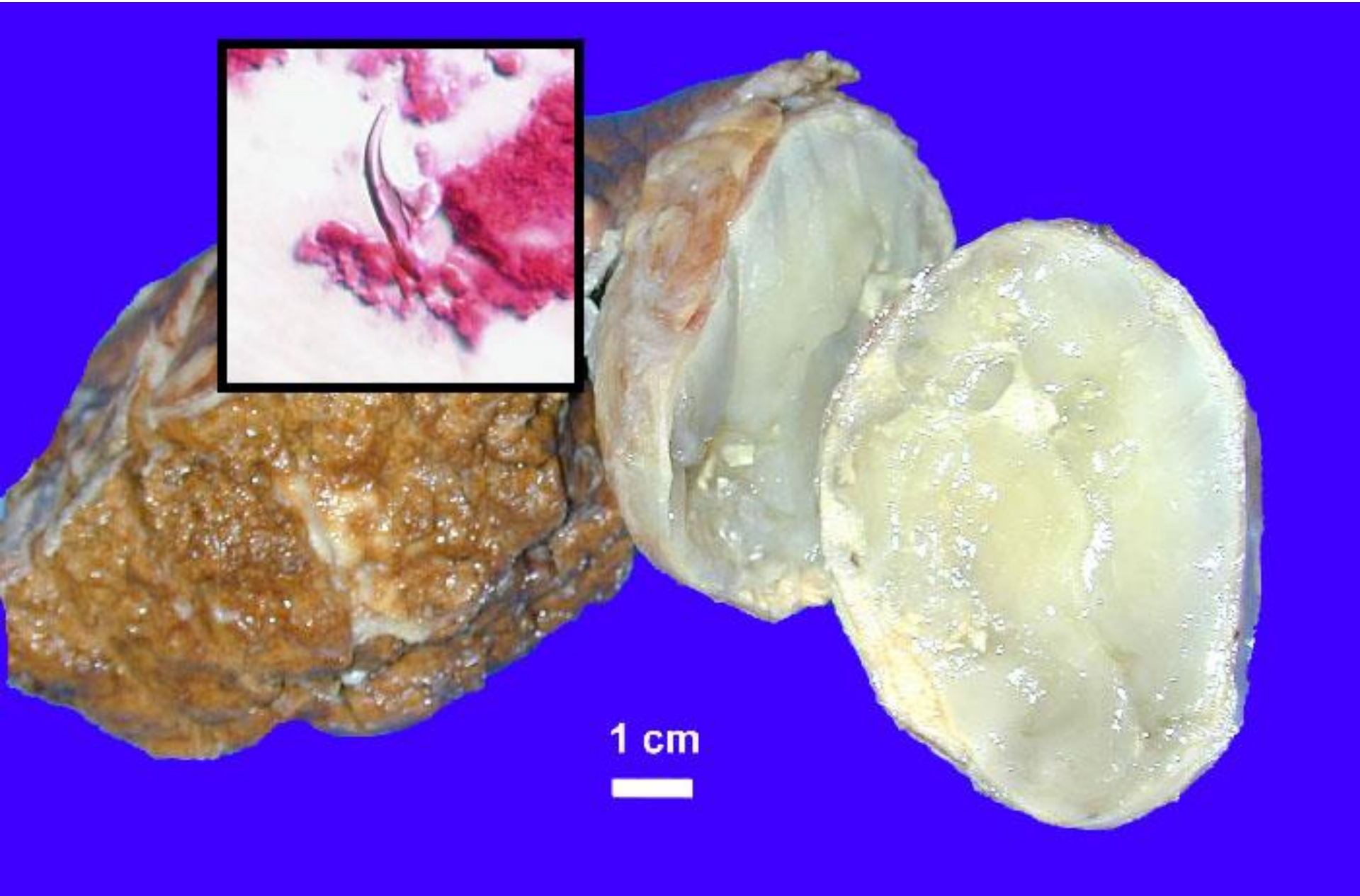
- Adenoma: a benign tumor arising from glandular or secretory epithelium (liver, adrenals, kidneys, salivary glands, pancreas etc)
- Cystadenoma: cystic mass in an adenoma (differentiation of cyst, cystoma, pseudocyst! Ask your tutor!)
- Papilloma: a benign tumor arising from non-secretory epithelium (finger-like, warty projections) (skin, oral cavity, esophagus, vagina, urothelium etc), verruca, condyloma
- Polyp: macroscopocally visible (pedunculated or sessile) projection above a mucosal surface and projects into the lumen (intestinal, gastric, cervical etc. Benign, but polypoid cancer !!!)
- Carcinoma: a malignant neoplasm of epithelial stem cell origin (squamous cell or epidermoid cc, basal cell cc, adenocc etc)
- Sarcoma: a malignant neoplasm of mesenchamal stem cell origin (fibrosarcoma, oseteosarcoma, rhabdomyosarcoma etc)

Nomenclature (5): Benign and Malignant tumors

- Teratoma: neoplasm containing cells derived from more than one germ layer. They might contain fragments of bone, cartilage, epithelium, fat, nerve, muscle etc. Teratomas may be benign (mature teratoma) or malignant (immature teratoma)
- *Hamartoma: mass of disorganized tissue indigenous to a specific site (mesenchymal hamartoma of the liver etc)*
- *Choristoma: heterotopic rest, developmental lesion where non-neoplastic tissue is located at an abnormal site*
- Cystoma: a cystic tumor, where the cyst is lined by tumor cells (cystadenoma of the ovary etc)
- Cyst: a cyst lined by non-tumorous epithelial cells (retention, obstruction etc) (biliary, kidney, follicular etc)
- Pseudocyst: a cyst not lined by epithelial cells (follows necrosis; brain infarct, necrotizing pancreatitis etc)


44799/35: Parovarial cysts.

Ecchinococcus cyst (parasitic cyst)

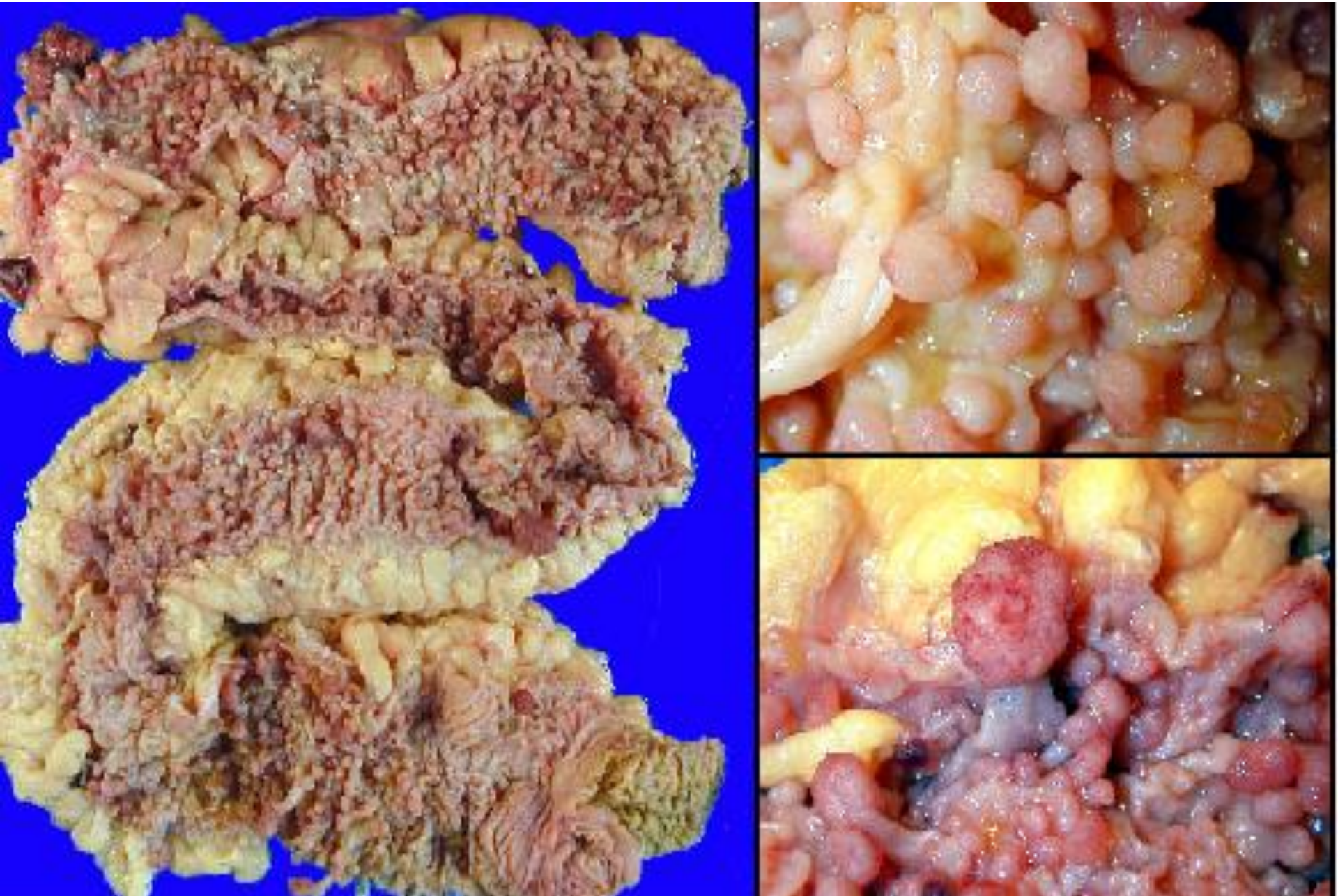


Mesenchymal hamartoma of the liver

Benign tumor in childhood. Several cysts.

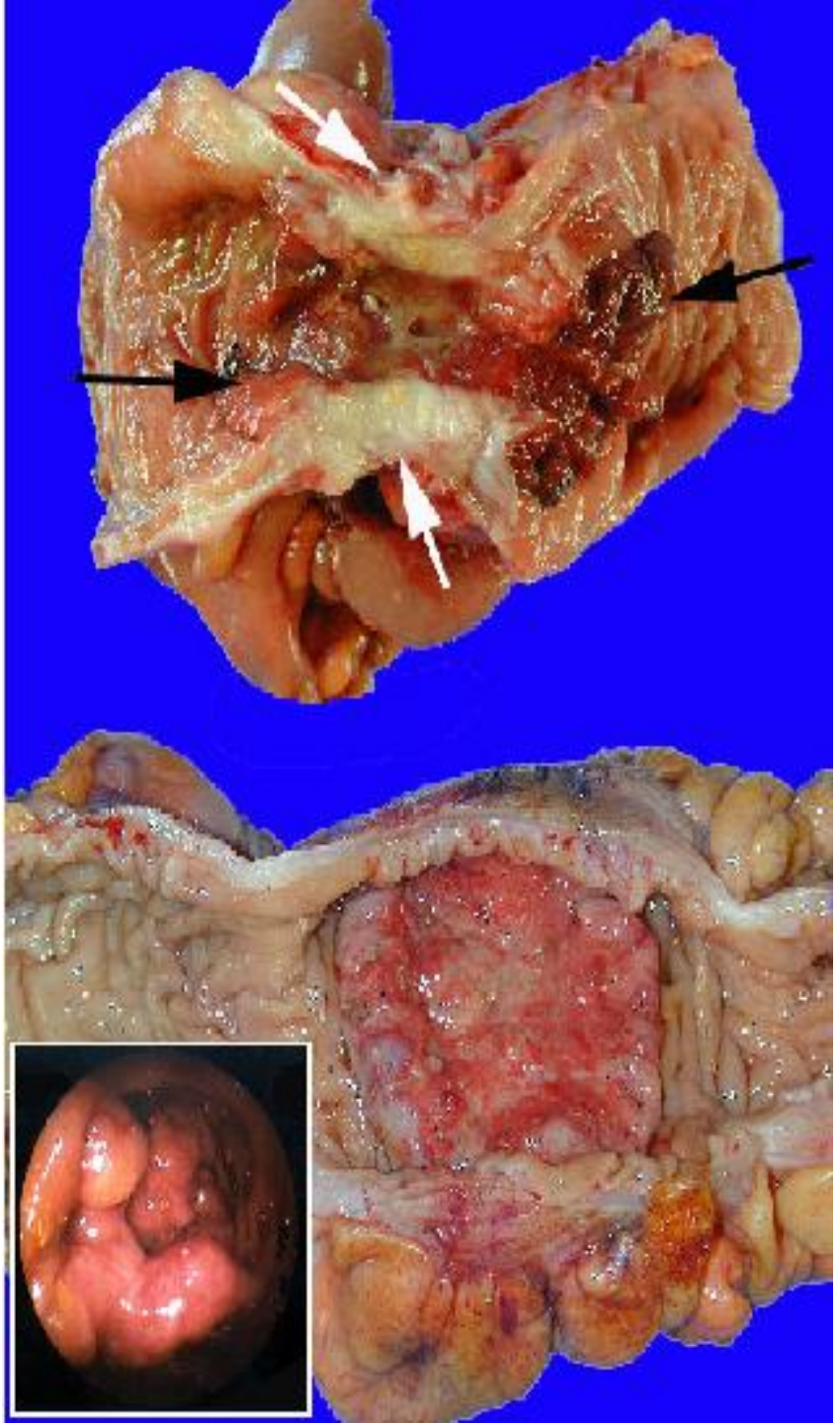
Polypus adenomatosus villosus coli (sessile, villous).

Familial adenomatous polyposis coli. The surface is covered by innumerable polypoid adenomas. (Kopper-Schaff:Fig.16.38)



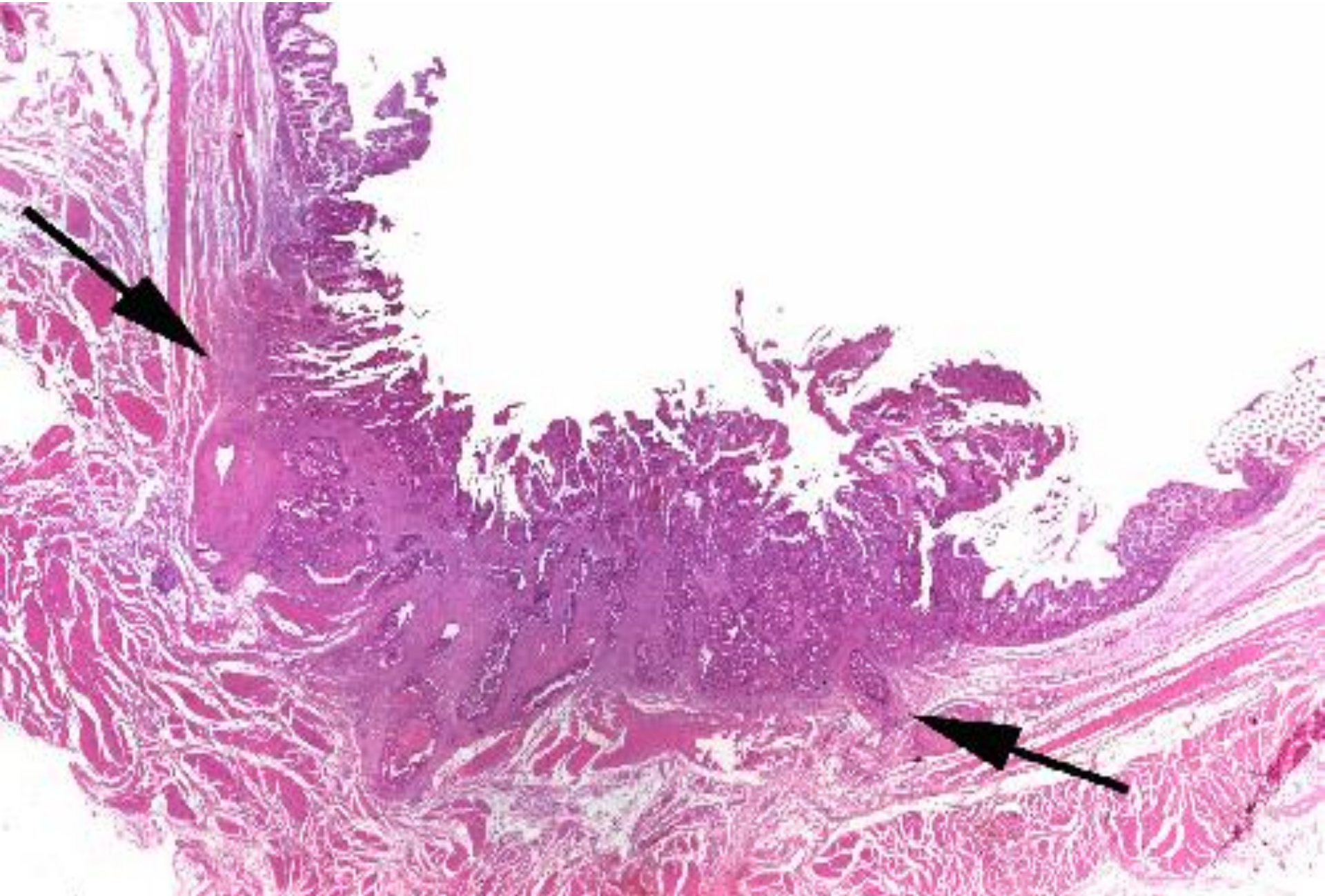
Adenocarcinoma coli. Infiltration

Of the wall (upper), ulceration,
Exophphytic growth pattern (down)
(Kopper-Schaff: Fig.16.41.)



Endoscopic picture of a
Colorectal exophytic cancer
(prof.J.Papp)

Small- size rectal cancer. (Kopper-Schaff Fig.16-44)



Characteristics of benign and malignant neoplasms(1)

- Differentiation：extent to which cells resemble normal adult cells from which neoplasm is derived; this includes both morphological and functional characteristics.
  - Terms: „well differentiated" and „poorly differentiated" tumors. (Benign tumors: well differentiated, malignant: less differentiated (from well to poorly!)
- Anaplasia: lack of differentiation: the more anaplastic the less differentiated and the less like the normal adult tissue of origin; increasing anaplasia usually means increased growth rate. A „hallmark" of malignant transformation.
  - Characteristics:
  - pleomorphism, anisocytosis: variation in size and shape of cells; increased anaplasia usually means increased pleomorphism.
  - Hyperchromasia: increased nuclear staining
  - Increased mitosis rate, Atypical, bizarr mitotic figures
  - Giant cells , Changes in orientation, polarity, architecture

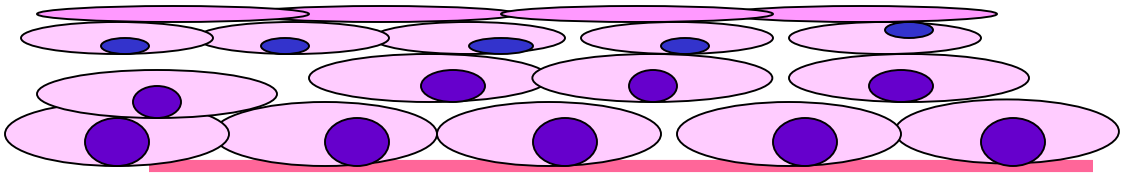
Classification According to Cellular Features (1)

Squamous-

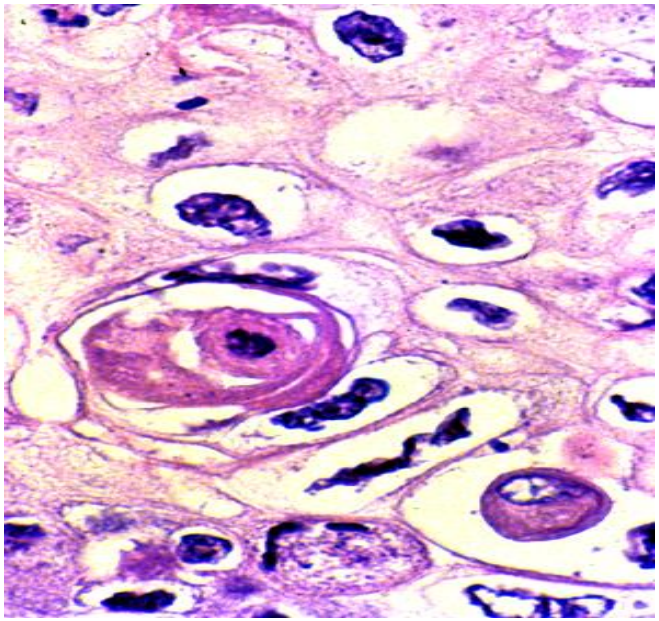
Eosinophillic (pink) abundant cytoplasm

Keratin, keratin pearl

Hyperchromatic (dark) nucleus

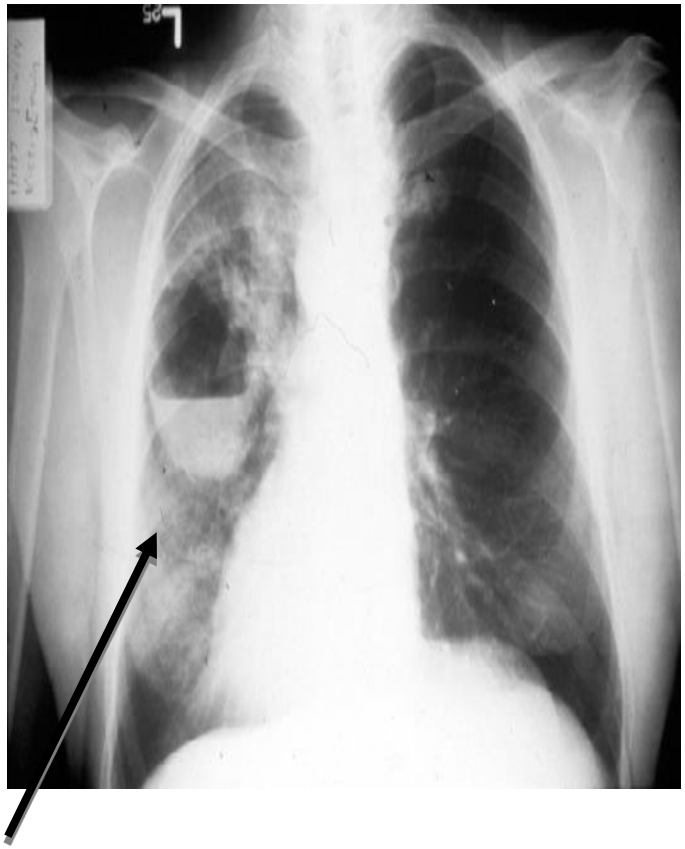


Normal epithelium

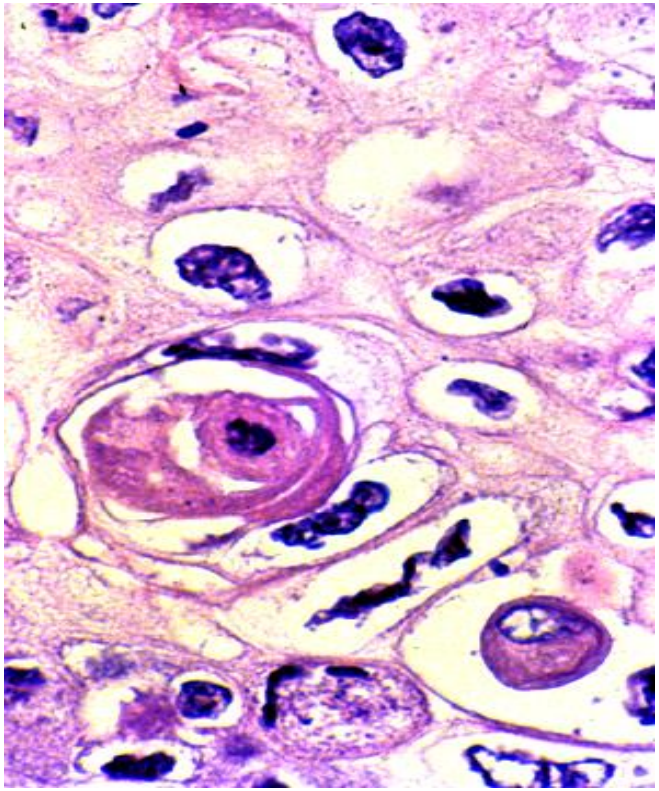


Squamous cell carcinoma

Lung Cancer



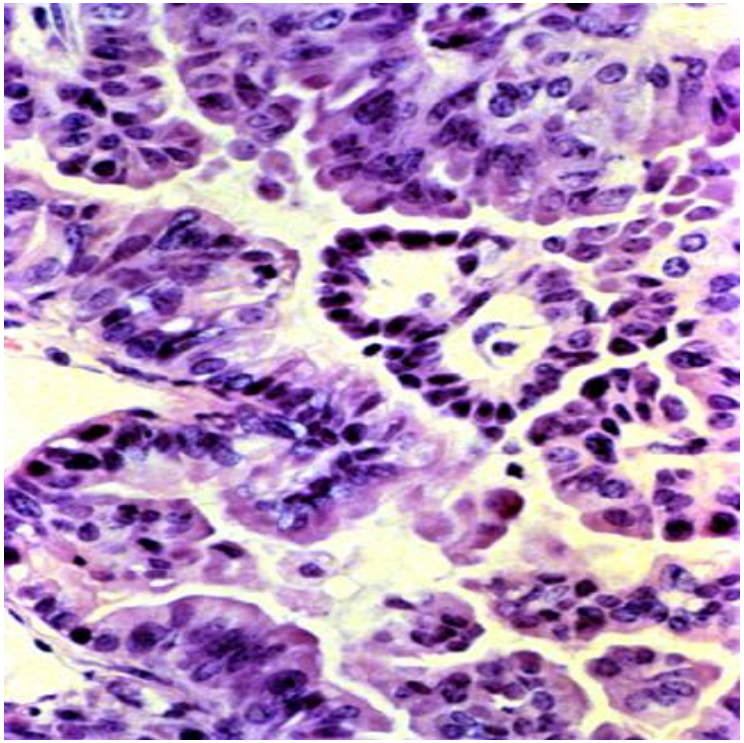
x-ray



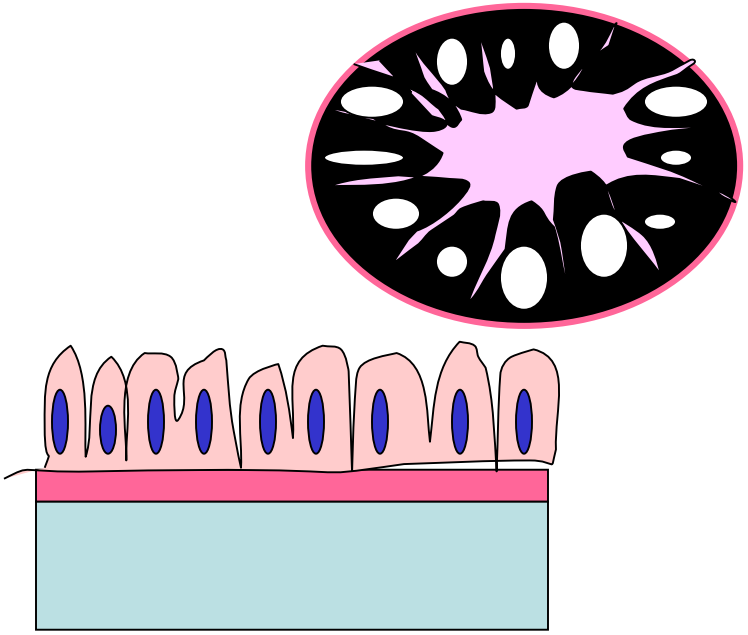
Squamous carcinoma

Classification According to Cellular Features (2)

Adenocarcinoma

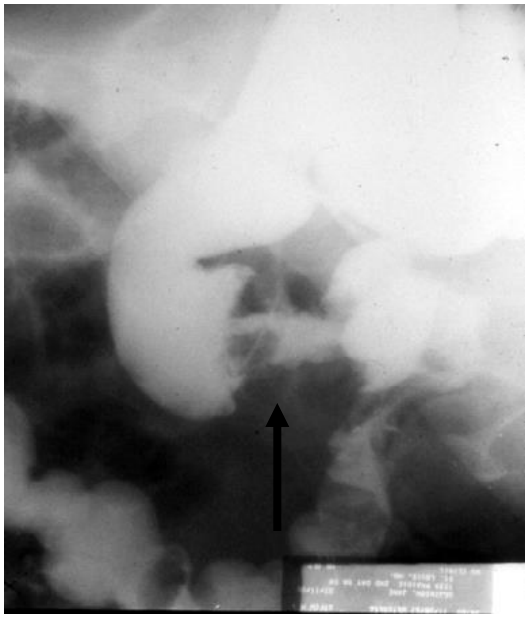


Normal

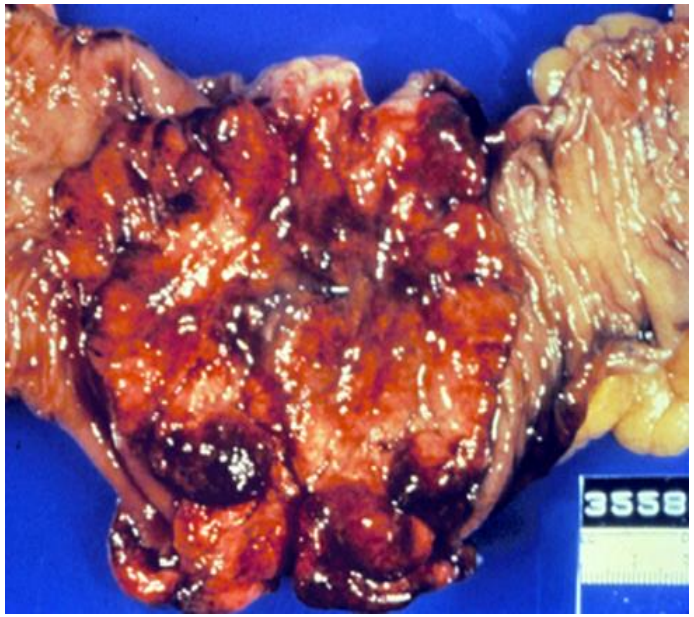


Gland-like spaces
Mucin production, secretory activity

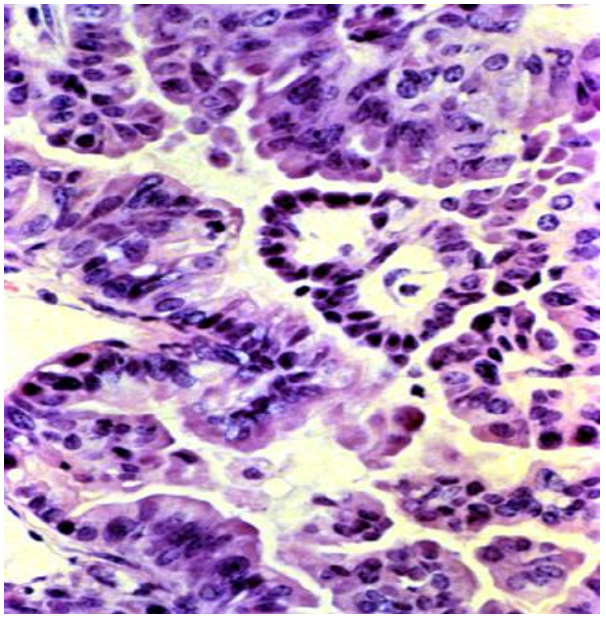
Colon Cancer



X-ray



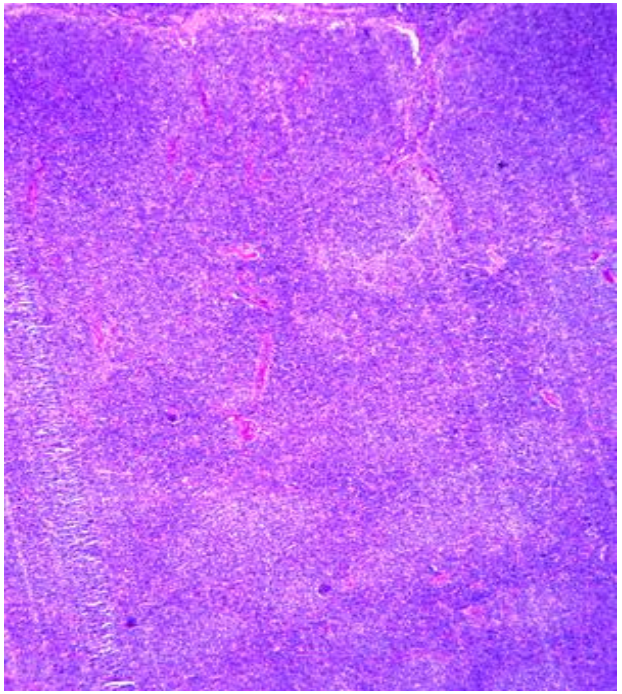
Gross



Microscopic

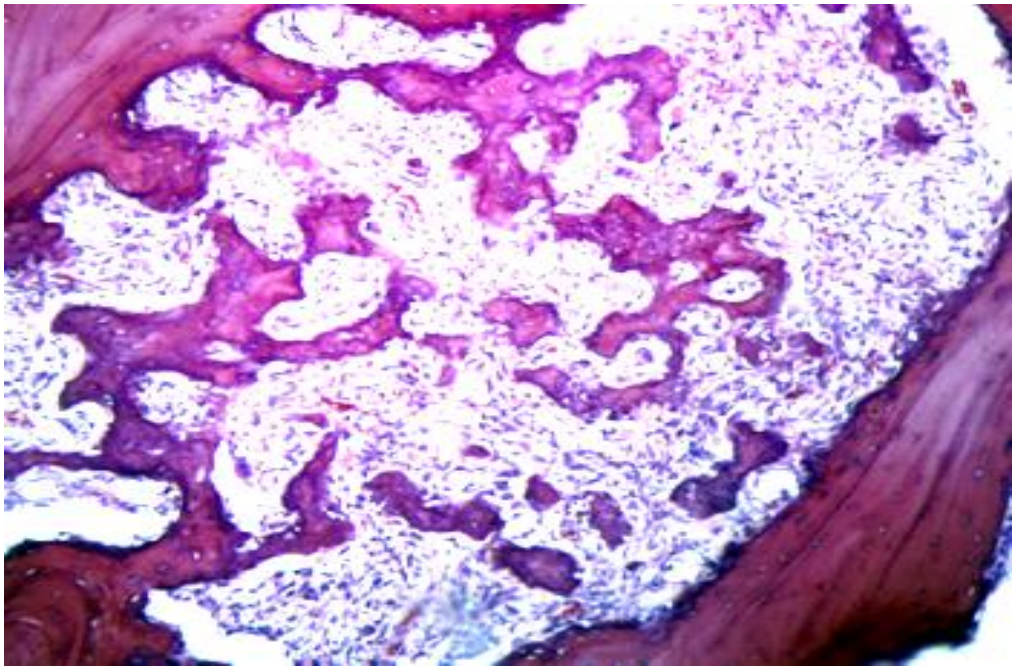
Classification According to Cellular Features (3)

Lymphoma



Classification According to Cellular Features (4)

- Recapitulation of normal features
- Differentiation along mesenchymal pathways



Osteogenic sarcoma

Invasion and Metastasis

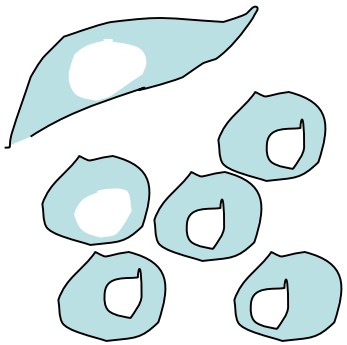
- Characteristics that are unique to malignant neoplasms (cancer)
- The major cause of morbidity and mortality

Invasion

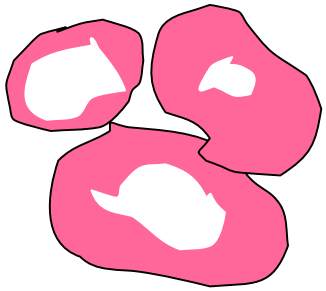
- Local invasion:
  - next to the metastases, invasion is the most reliable feature that differentiates malignant from benign tumors.
- In situ cancer:
  - Cancer often progresses from a precursor (premalignant, preinvasive, in situ) lesion. The dysplastic/anaplastic cells involve the entire epithelial surface (they have the cytological features of malignancy) without invasion of the basement membrane

Cancer Grade

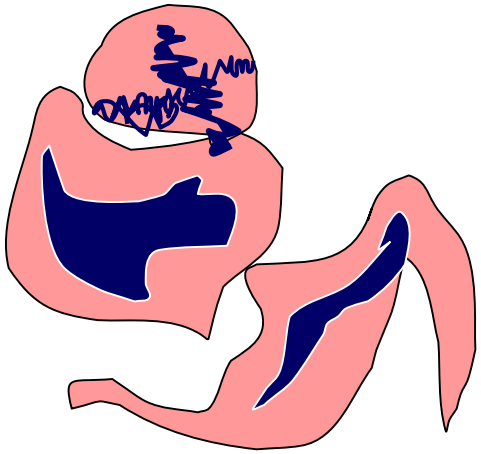
- Alternate term “tumor grade”
- Based on microscopic features (cytology or histology)



low

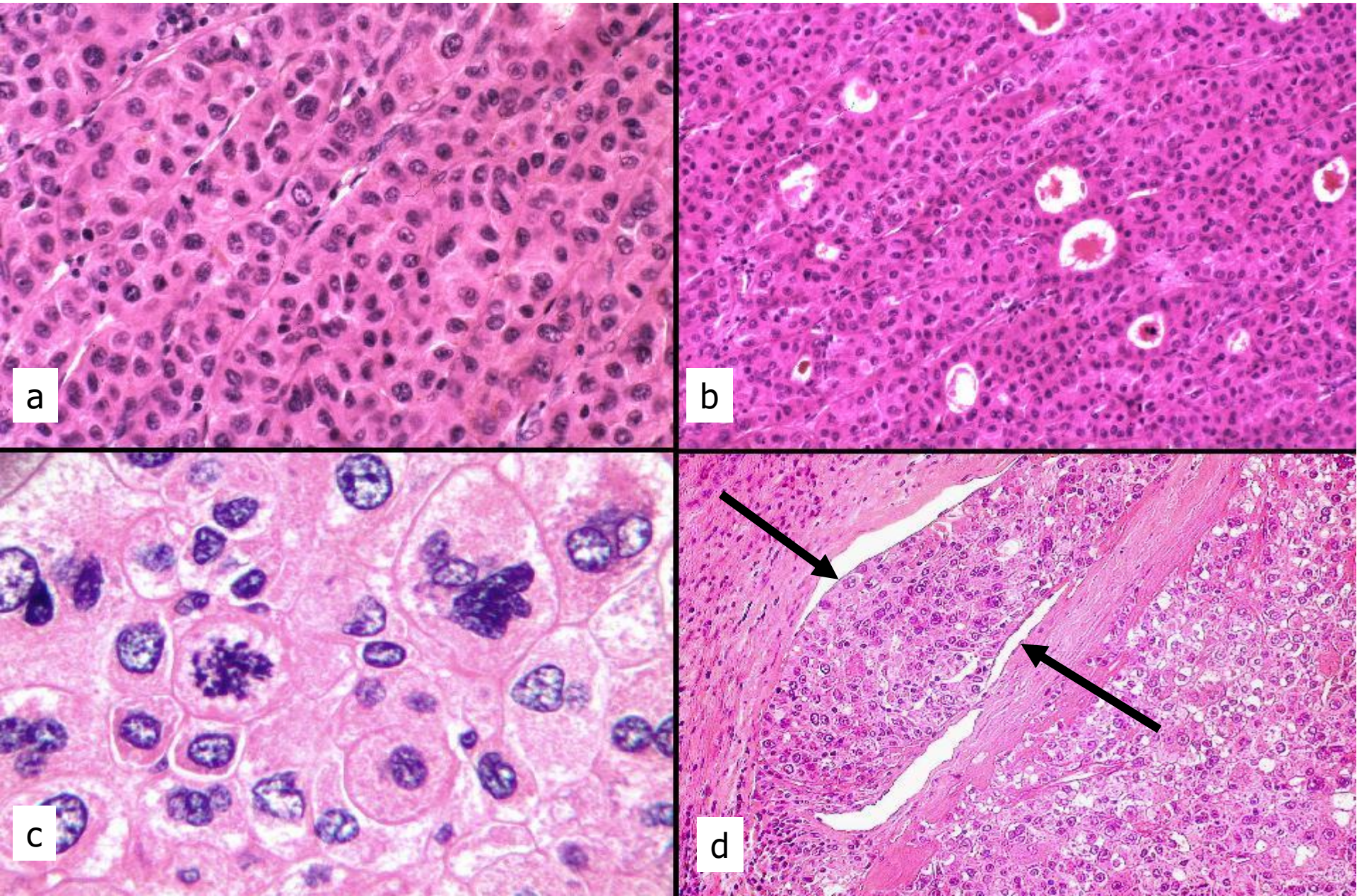


moderate



high grade

Hepatocellular carcinoma. Different growth patterns: a: trabecular, b: glandular/ Acinar, c:anaplastic with giant cells, d: vascular invasion



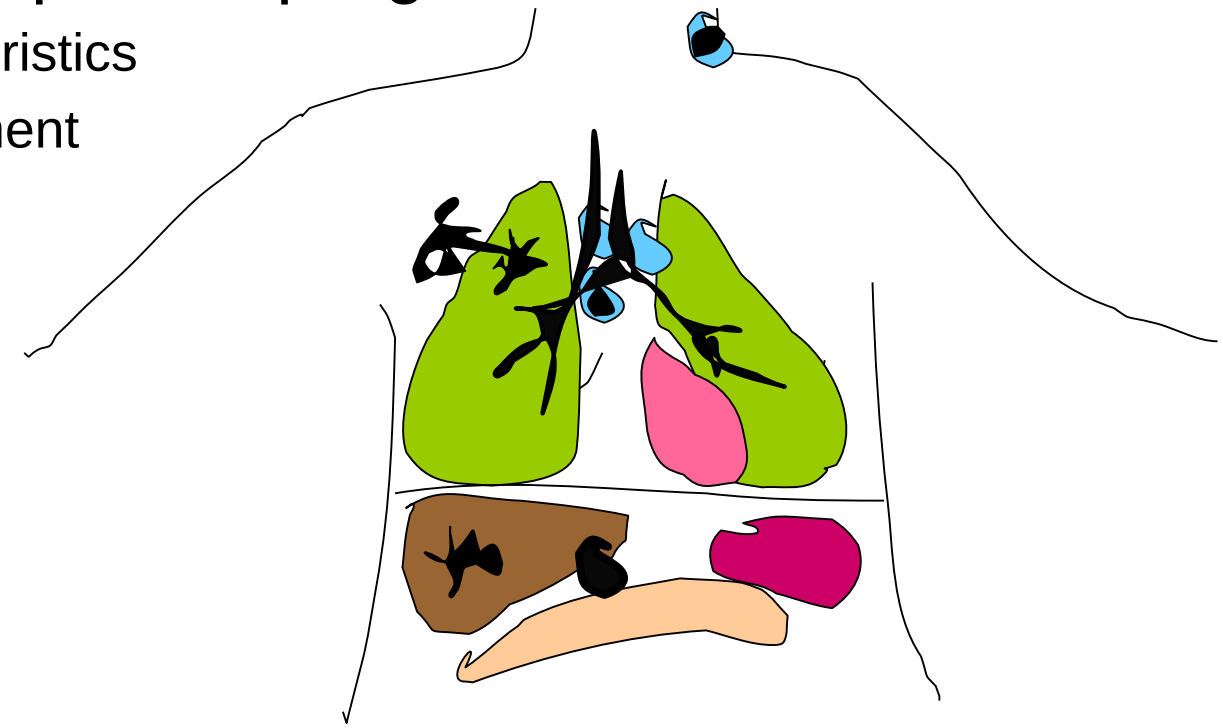
Cancer Stage

- Reflects degree of spread, for an individual cancer patient
- Assigned at the time of diagnosis, may be updated as patient progresses

T Tumor characteristics

N Nodal involvement

M Metastasis

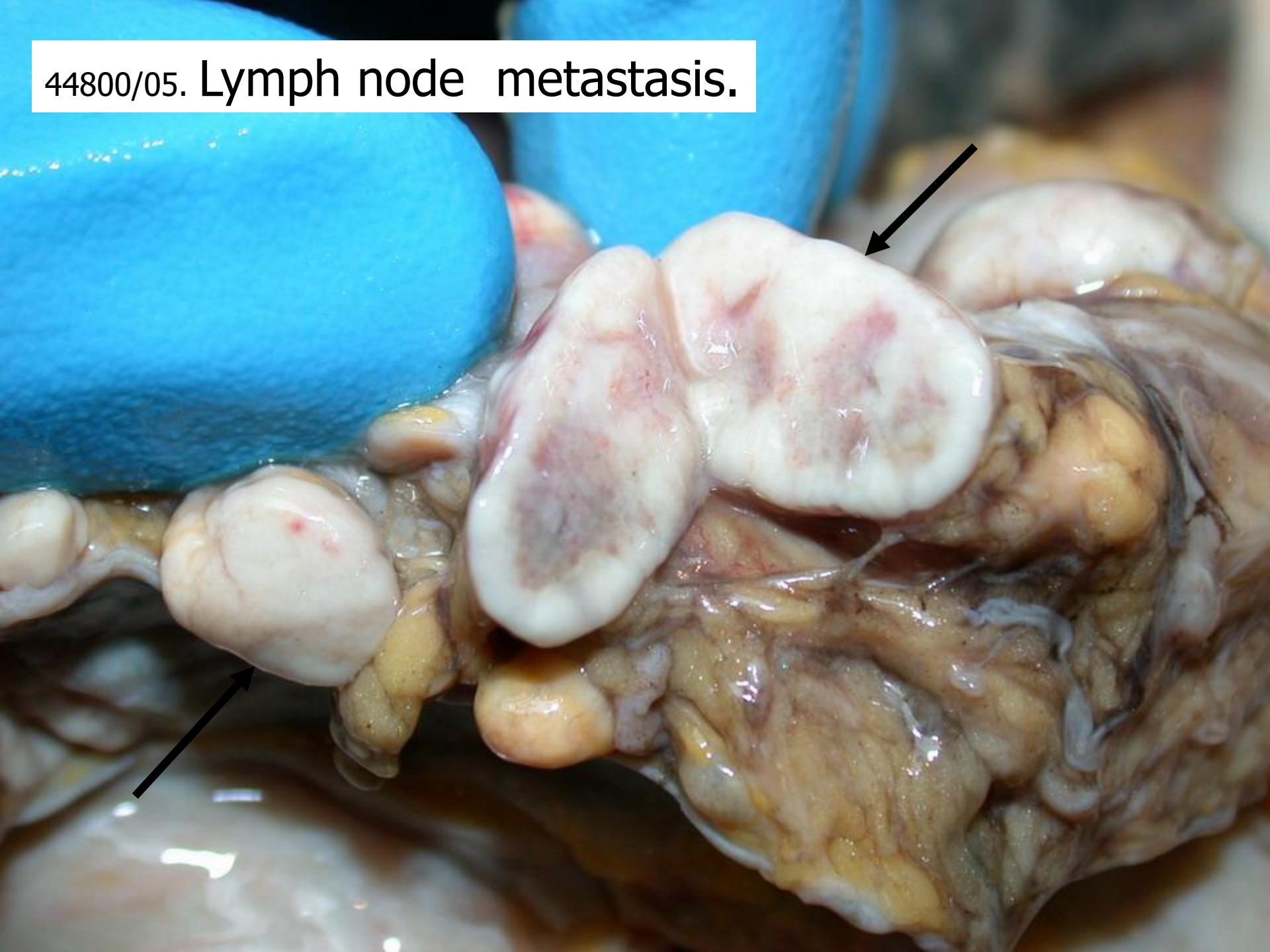


Metastasis

- Definition: evidence of local or systemic dissemination of neoplasm via the lymphatic or blood circulation. Spread to a distant site.
- Metastasis marks a tumor as malignant because benign tumors do not metastasize.
- All cancer (if cancer!!) can metastasize, with few exception (CNS-gliomas, basal cell cc of the skin – but they are invasive!)
- Generally: the larger, more rapid growing cancers more likely metastasize, but: small cancers might metastasize (small lung cc, thyroid cc etc)

Pathways of spread

- Direct seeding of body cavities and surfaces (carcinosis peritonei, pleurae, pseudomyxoma perotonei etc)
- Lymphatic spread:
  - most common for carcinomas, but sarcomas may use it also, interconnections
  - Follows the natural routes of drainage (breast-axillary-sentinel lymph node), regional lymph nodes
- Hematogenous spread
  - typical for sarcomas, but also used by carcinomas
  - Arterial spread (thick wall): after tu cells pass through pulmonary capillaries
  - Venous spread (thin wall):cells follow the venous flow draining the site

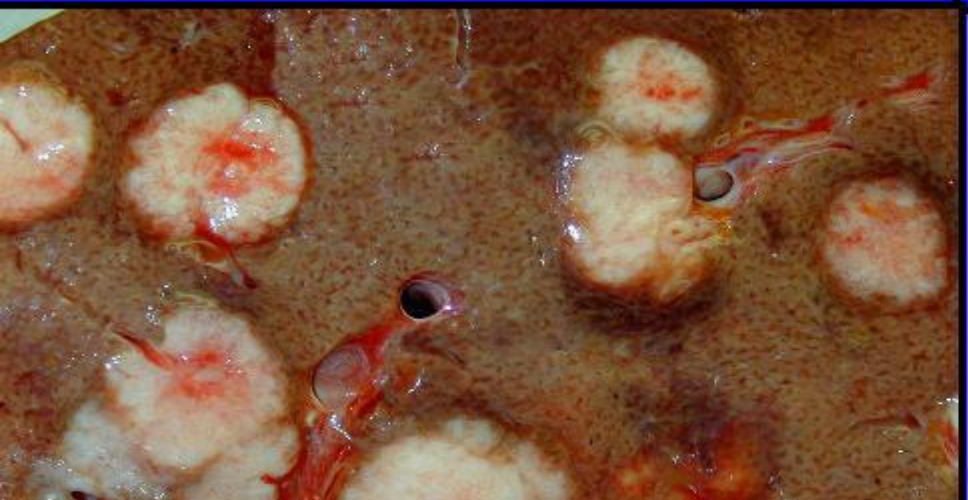

44800/05. Lymph node metastasis.

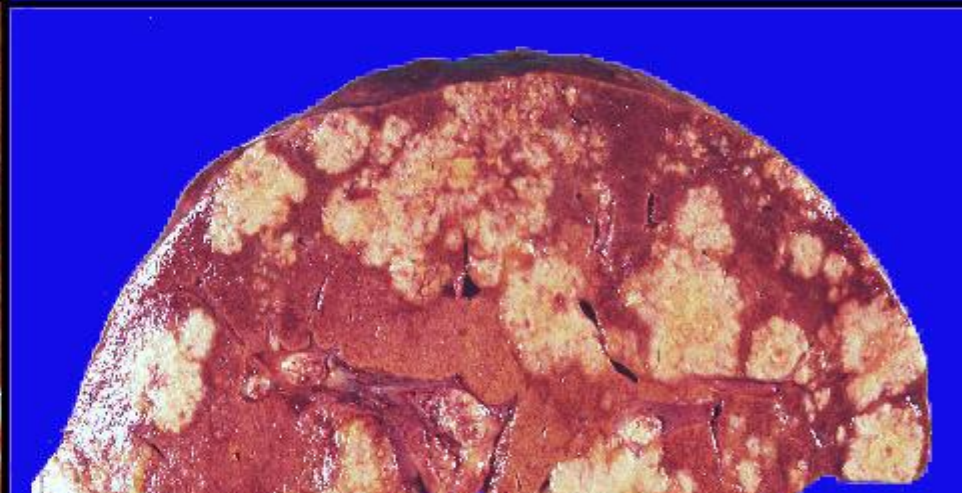
Main routes of metastases
(Walther shemes, 1948 – „metastasis cascade”)

- Vena portae (gastrointestinal) type
- Vena hepatica (liver) type
- Vena cava type
- Vena pulmonalis (lung) type
- Through the Batson venes (paravertebral)

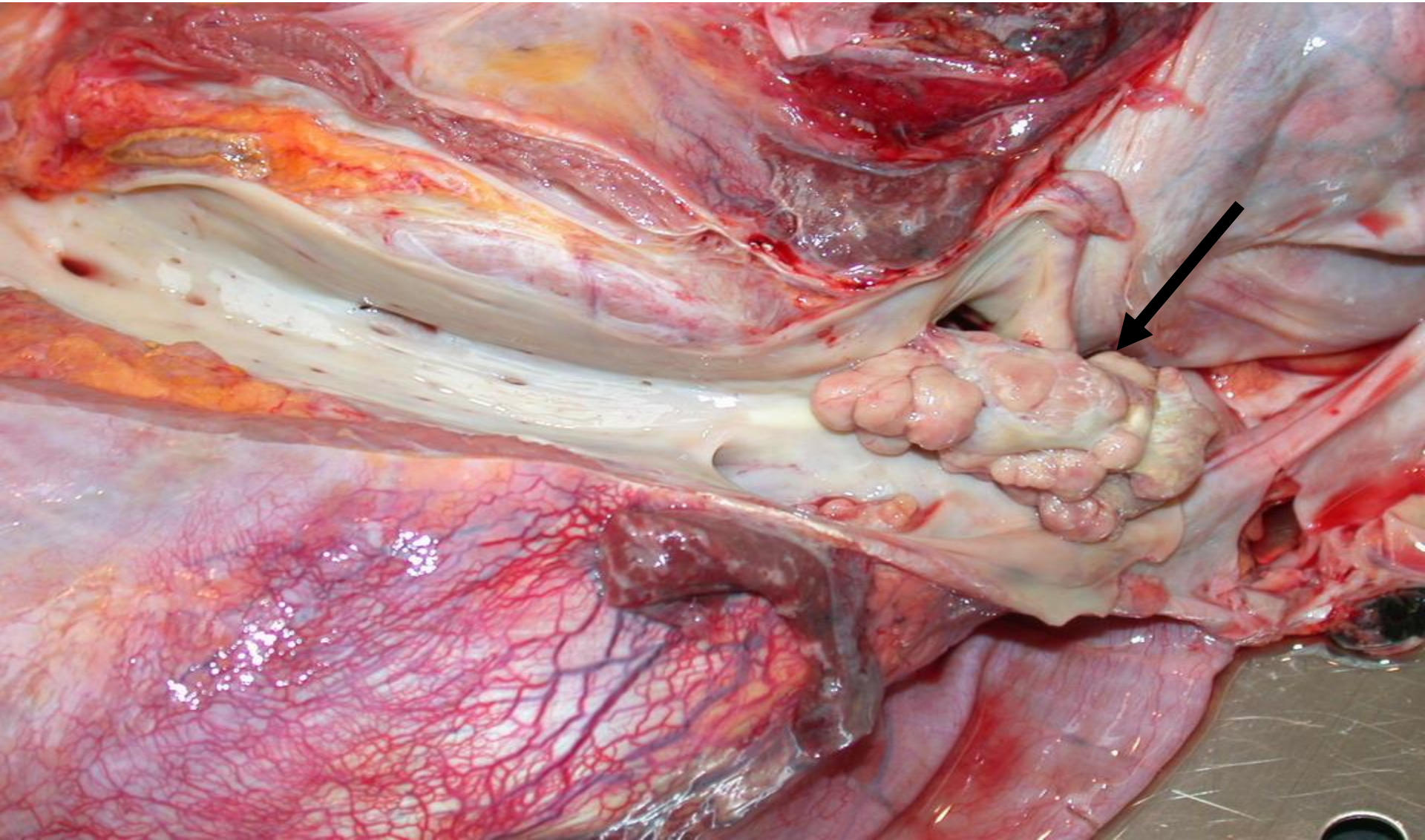
Vena portae type of metastasis.

The primary tumors originated from the gastrointestinal system (stomach, colon, pancreas cancer) and spread through („flow”) the v.portae and metastasize into the liver.

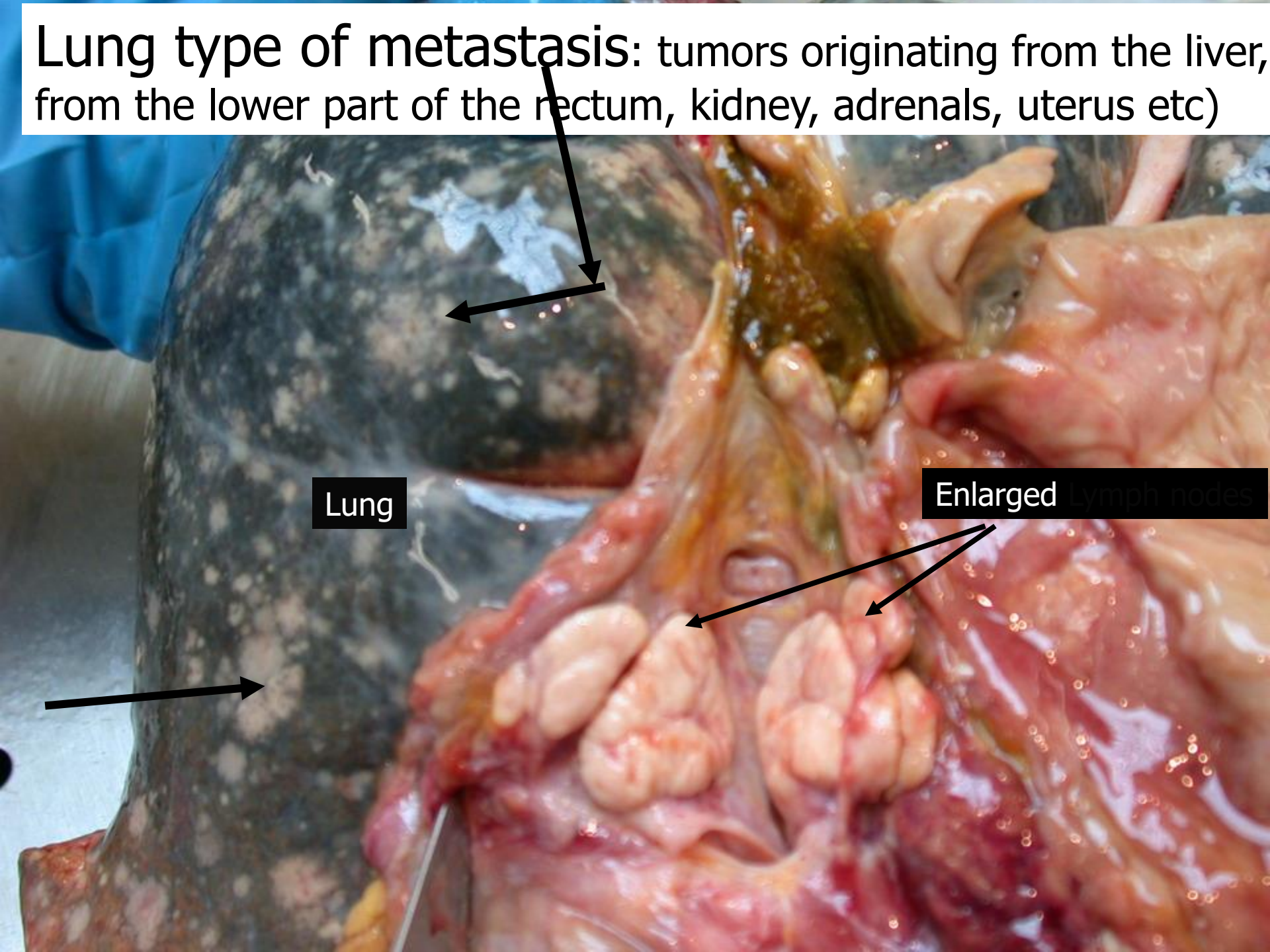


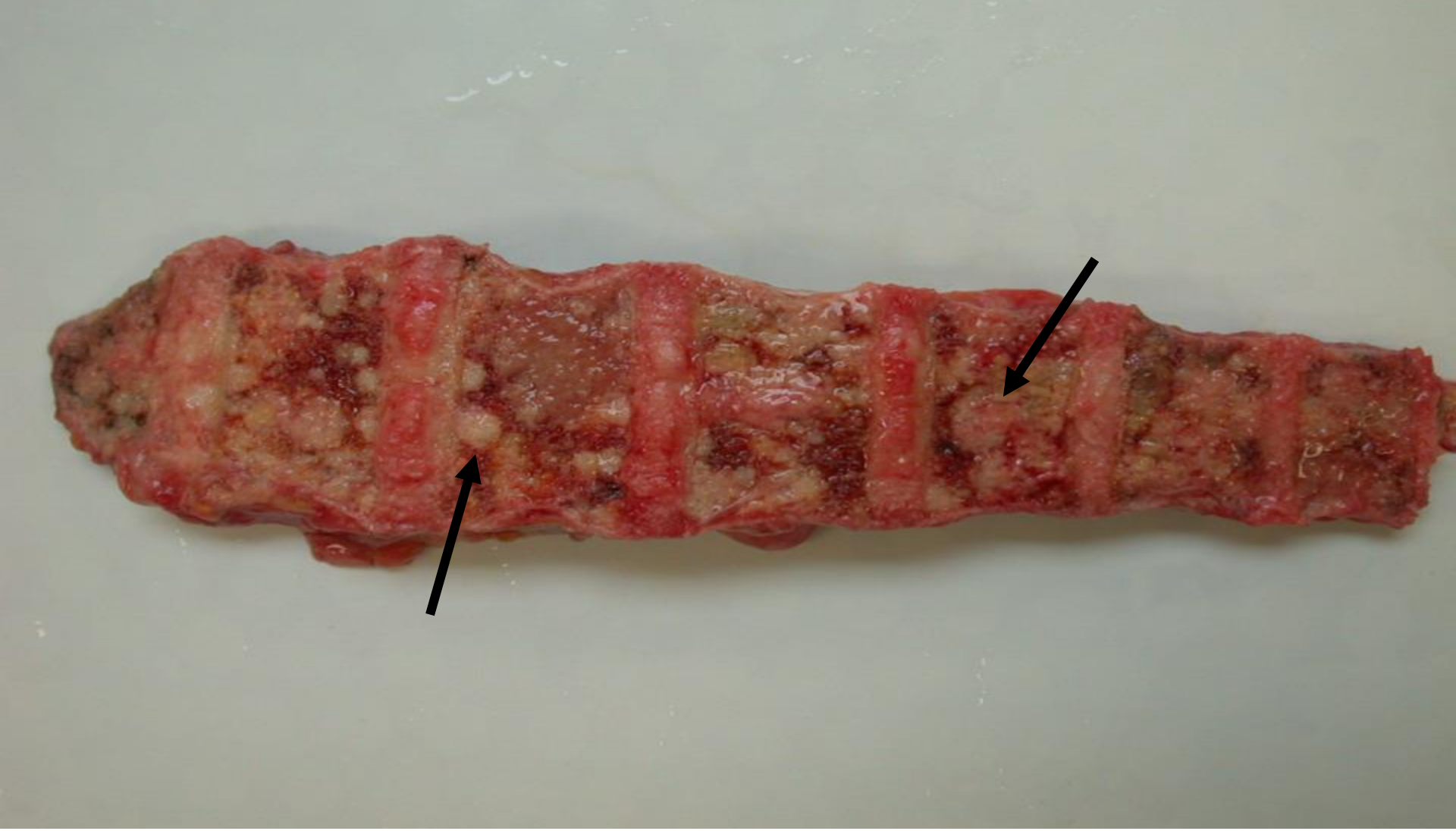


V.Hepatica type metastasis. Tumor cells originated (primary or secondary) from the liver, invade the v.hepaticae, flow to the v.cava and metastases develop in the lung.



Lung type of metastasis: tumors originating from the liver, from the lower part of the rectum, kidney, adrenals, uterus etc)





44800/02. Vertebral metastases of prostate cancer.

Cancers arising in close proximity to the vertebral column often embolize through the paravertebral plexus

Prognosis

- Prediction of Outcome
  - Criteria are different for each cancer type
  - Criteria: Grade, stage, histology
  - Patient „characteristics”
  - Treatment considerations critical

Acquired preneoplastic disorders, Precancerous conditions

- Endometrial hyperplasia- carcinoma (hormonal)
- Cervical dysplasia – cancer (HPV infection)
- Cigarette smoking -Bronchial metaplasia, dysplasia – lung cancer
- Chronic hepatitis/cirrhosis – hepatocellular carcinoma (HBV, HCV, alcohol, aflatoxin, anabolic steroids etc)
- Atrophic gastritis – cancer (H.pylori)
- Solar karatosis – skin cancer (UV)
- Leukoplakia – oral cancer
- Ulcerative colitis – colon cancer

Summary

- Cancer is synonymous with malignant neoplasia
- Precursor/precancerous lesions exist
- Invasion and metastasis are the hallmark of malignancy
- Cancer typing and subtyping is pre-requisite for patient treatment