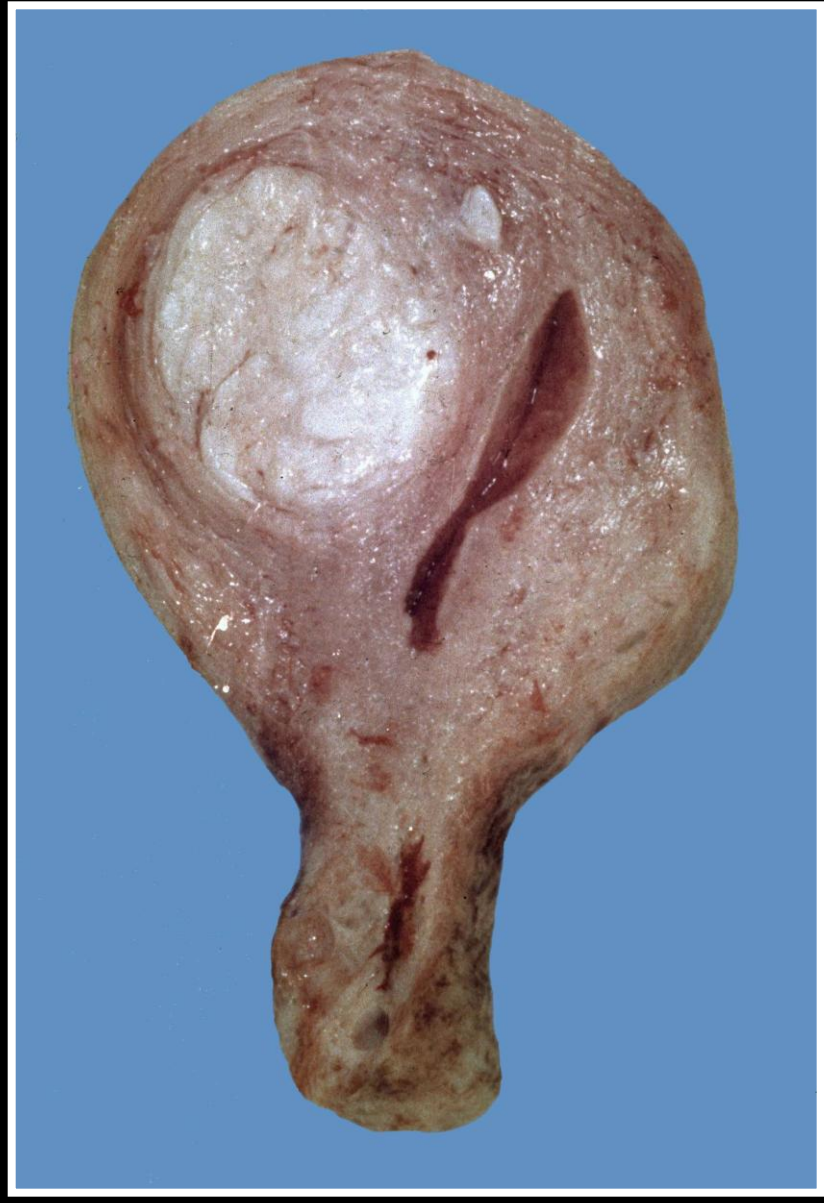
General Pathology

Histogenetic Classification of Neoplasms

Mesenchymal Neoplasms



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Histogenetic Classification of Neoplasms

Mesenchymal Neoplasms - contents

- Histogenetic classification – meaning
- Terminology
- Epidemiology of the mesenchymal tumours
- Pathogenesis
- Most frequent representatives & methods of diagnostics

NEOPLASIA

Definition - pathogenetic:

DNA disease

- Stepwise accumulation of genetic abnormalities
- Escape of immunological clearing systems

NEOPLASIA – *classification*

according to various criteria:

- Organ (system)
- Biology behaviour
- Histogenetic (cell of origin) – the main part of tumor definition in TYPING
- ...

COMBINED - WHO classifications

Histogenesis

formation of different tissues from undifferentiated cells.

Three primary germ layers

- endoderm
- mesoderm → mesenchyme: soft tissues, muscles, adipocytes, vessels, bone and cartilage , blood cells*
- ectoderm

** subject of a separate lecture*

NEOPLASIA – *classification*

HISTOGENETIC (cell of origin)

- mesenchymal
- epithelial
- neuroectodermal
- mixed
- germ cell
- mesothelioma

Mesenchymal tumours

Soft tissue tumours

- fibroblastic and myofibroblastic differentiation
- adipocytic differentiation
- smooth muscle differentiation
- rhabdomyocellular differentiation
- vascular tumours

Bone and cartilage tumours

Tumours of uncertain histogenesis

Undifferentiated sarcomas

Blood cells derived tumours*

** subject of a separate lecture*

Mesenchymal tumours – *general characteristics*

- Epidemiology
  - benign – common *(lipoma, leiomyoma, hemangioma…)*
  - malignant rare *(1-2% of neoplastic mortality in population)*

- Location
  - superficial (more frequently benign)
  - deep (retroperitoneum, intramuscular) – more risky for uncertain biology behaviour or malignancy

Mesenchymal tumours – *general characteristics*

- Etiopathogenesis - mutations
  - translocations (frequent also in haematology malignancies)
  - germ cell mutations of tumor supressor genes

- Behaviour
  - benign – borderline - low grade sarcomas - high grade sarcomas

- Tendency for haematogenous spread in malignant

Mesenchymal tumours – *growth*

Benign - expansive, complete excision curing

Low grade sarcomas - slowly growing, locally destructive, recurrences

Malignant - locally aggressive, hematogenous

METASTASES

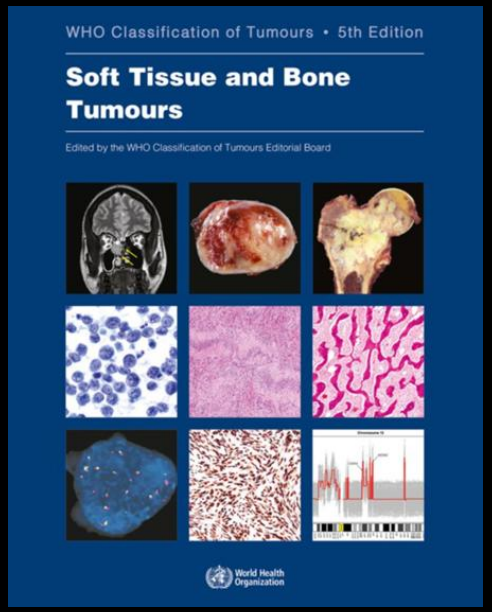
(secondary neoplastic foci in the distant places)

Metastases - pathways

- *seeding (body cavities)*
- *lymphatic spread*
- *haematogenous spread*

Mesenchymal tumours – diagnostics

- Macroscopy (imaging)
- Histopathology / cytopathology
- Immunohisto(cyto)chemistry
- Molecular pathology
- WHO 2022 more than 130 nosology units

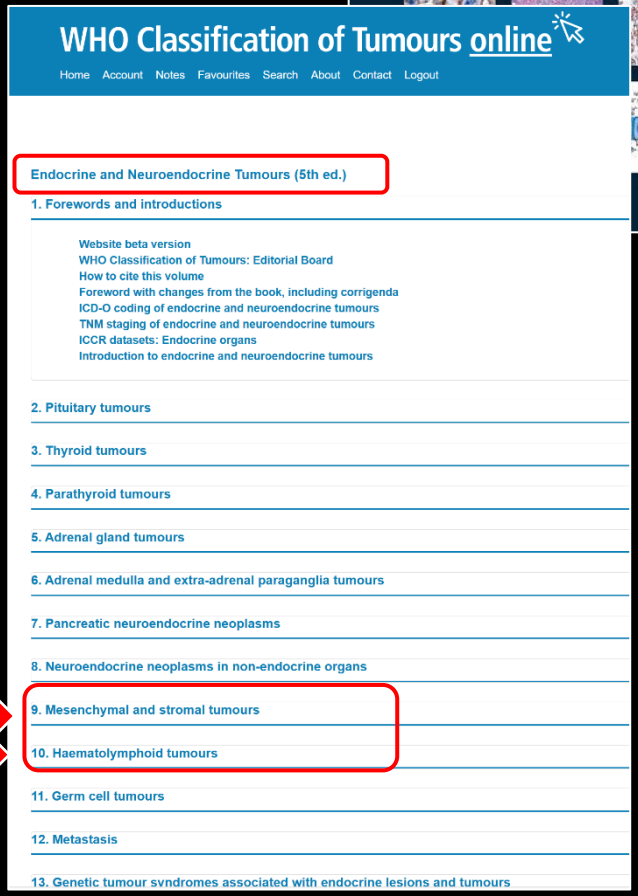


Mesenchymal tumours – diagnostics

- possible location in many other organ systems, like e.g. endocrine
  diff. dg. !

- Histopathology / cytopathology
- Immunohisto(cyto)chemistry
- Molecular pathology

Chapters on mesenchymal & haematolymphoid tumours in classifications of many other organ systems



Mesenchymal tumors – *macroscopy*

- Whittish / grayish mass
- yellow nodule — lipoma, ~~clear cell renal cell tumor, adrenocortical adenoma~~
- red nodule — hemangioma
- ~~brown nodule~~ — ~~nevocellular nevus, melanoma, pigm. basalioma~~
- organ enlargement — leukemia
- organ softening – necrosis — mostly sarcomas
- organ hardening - bone and cartilage tumors

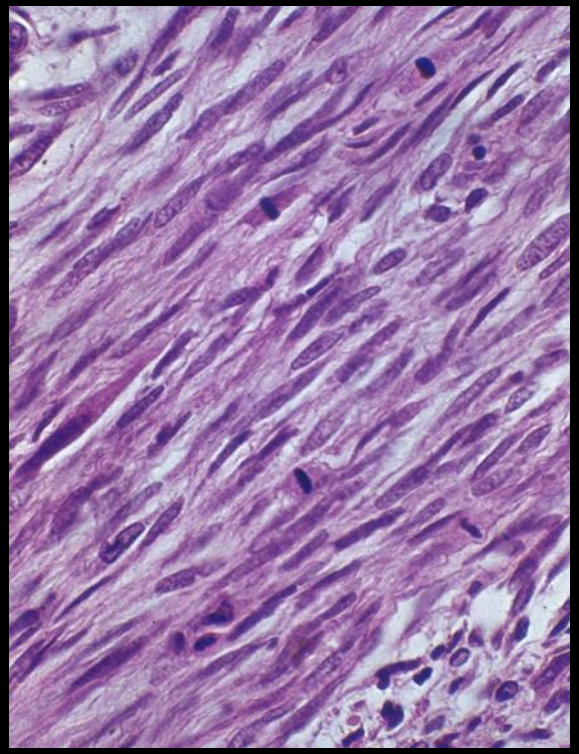
- ~~branched outgrowth~~
- ~~cystic (cystopapillary)~~

~~Other histogenesis~~

Mesenchymal tumours – *histological architecture*

Benign

similar to nonneoplastic



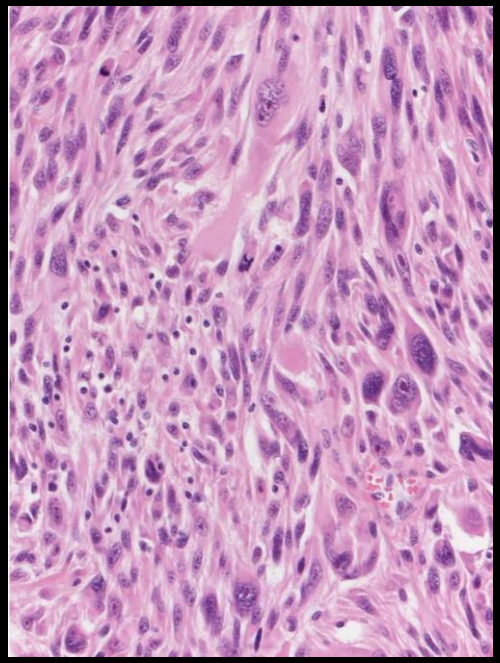
solid

~~glandular~~

~~papillary~~

~~papillary~~

dissociated



Mesenchymal tumours – *cytology*

Benign similar to nonneoplastic

Malignant cellular pleomorphism

NUCLEAR FEATURES:

hyperchromasia
(polyploidy, aneuploidy)
rough chromatin structure
irregular nuclear outline
large and/or multiple nucleoli, mitoses (incl. atypical)

Elongated (fusiform), round, polymorphous cells
or undifferentiated monotonous cellularity or small round cell tumour

Mesenchymal neoplasms

Terminology

Named after the cell of origin

(Greek or Latin)

- *benign - suffix -oma*
- *borderline - suffix -blastoma*
- *malignant – suffix -sarcoma*

exceptions not rare…

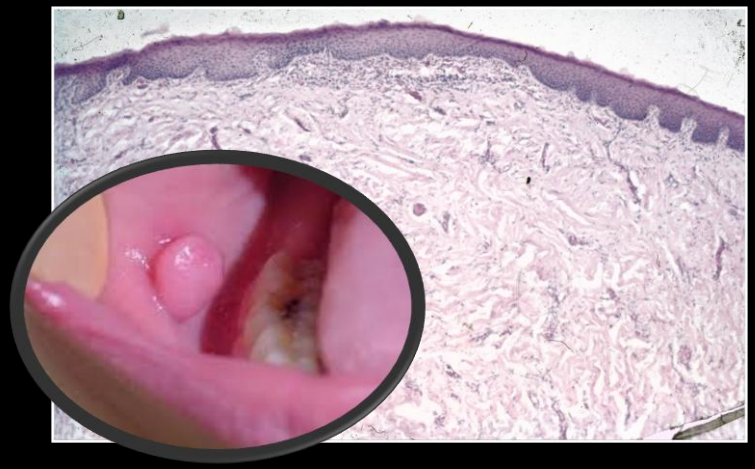
Mesenchymal neoplasms

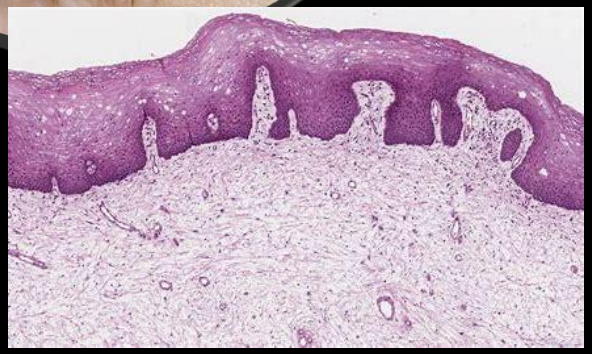
Benign	Borderline	Malignant
fibroma	fibromatoses	fibrosarcoma
lipoma	lipoblastoma	liposarcoma
leiomyoma	atypical smooth muscle cell tumors	leiomyosarcoma
rhabdomyoma		rhabdomyosarcoma
hemangioma	hemangioendothelioma	hemangiosarcoma
lymphangioma		lymphangiosarcoma
chondroma	chondroblastoma	chondrosarcoma
chordoma		*invasive* chordoma
osteoma	osteoid osteoma <2cm osteoblastoma >2cm	osteosarcoma
!!!		lymphoma/leukaemia

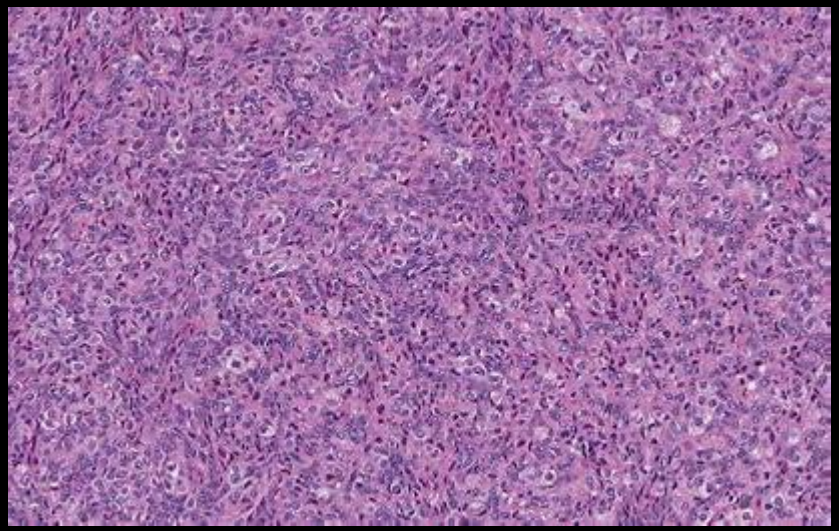
Fibroma

True fibroma does not exist – the term is used to denote:

- reactive lesion in the oral cavity – „irritation fibroma“
- skin tag
- skin dermatohistiocytoma
- ovarian fibrothecoma
- fibroma of tendon sheet



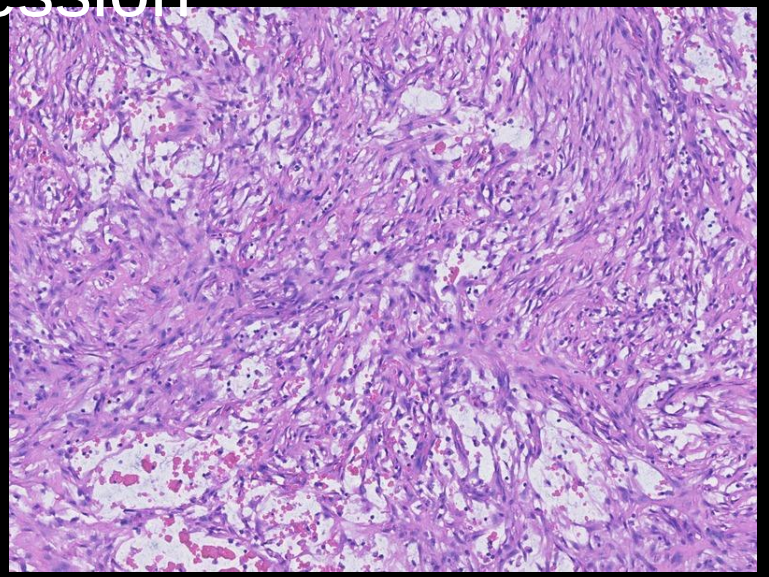




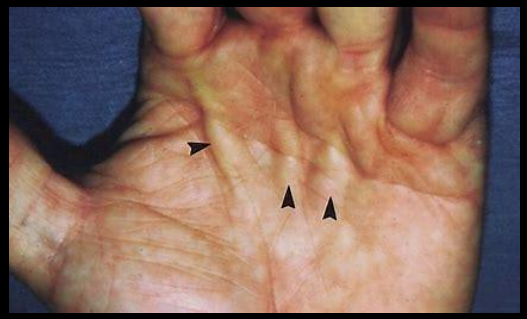
Nodular fasciitis M 8828/0

- benign clonal – t (17;22) - proliferation of fibroblasts & myofibroblasts
- subcutaneous or deep intramuscular location
- high (regular only) mitotic activity
- sometimes spontaneous regression

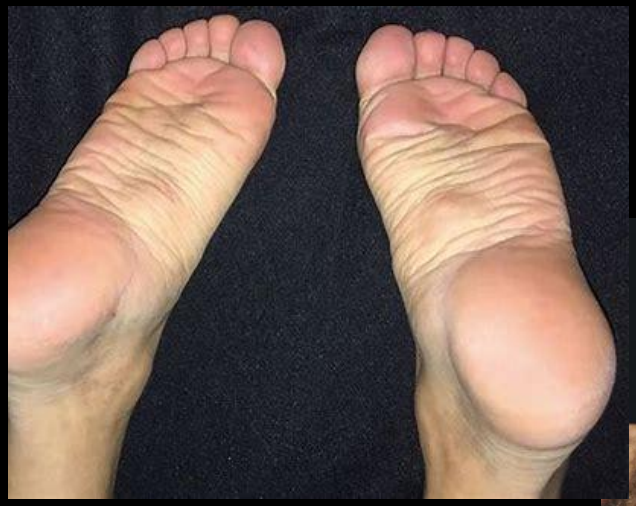
Risk of overdiagnosis!

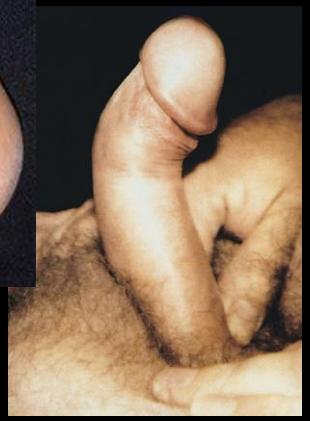


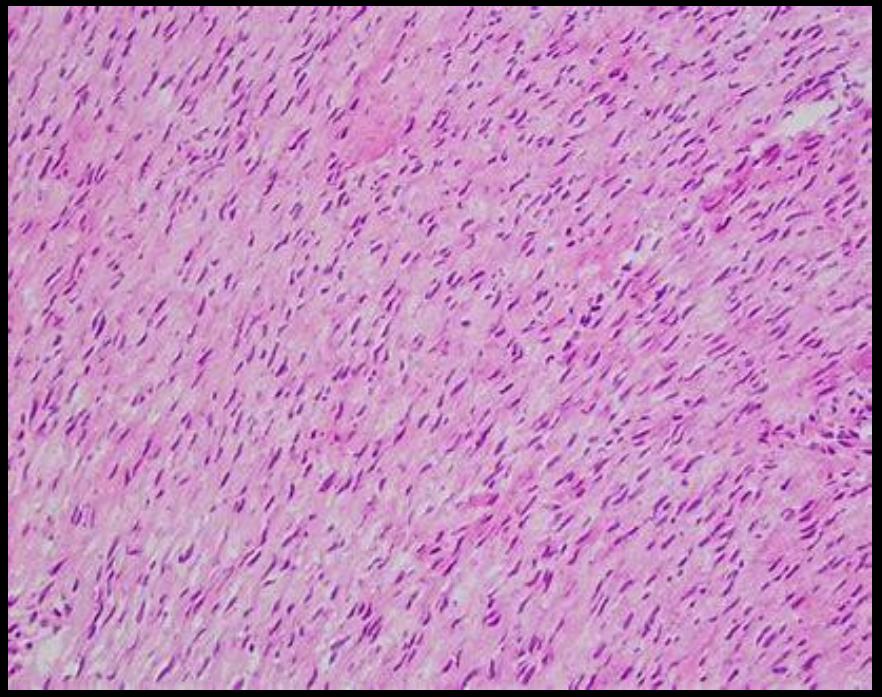
Fibromatosis 1/2



- superficial
  - palms (Dupuytren contracture),
  - soles of feet (both condition can coexist)
  - penile - m. Peyronie – induratio penis plastica – curved painful erection & stricture of urethra

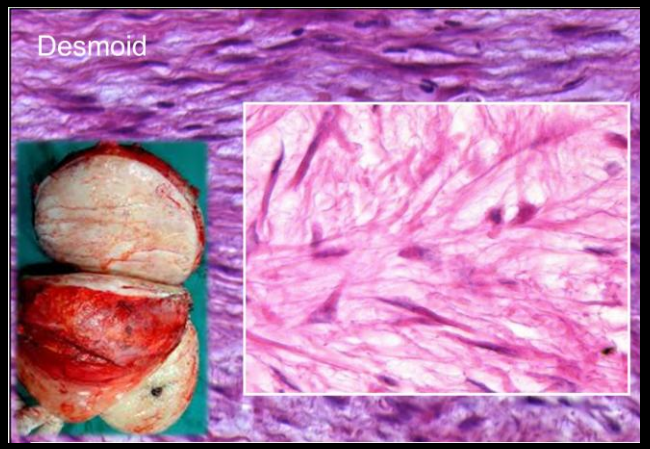






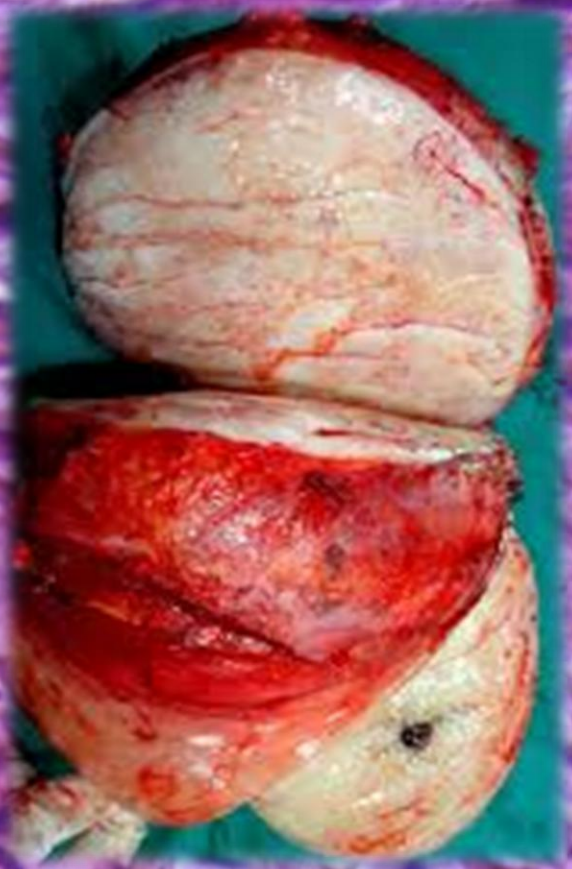
Fibromatosis 2/2

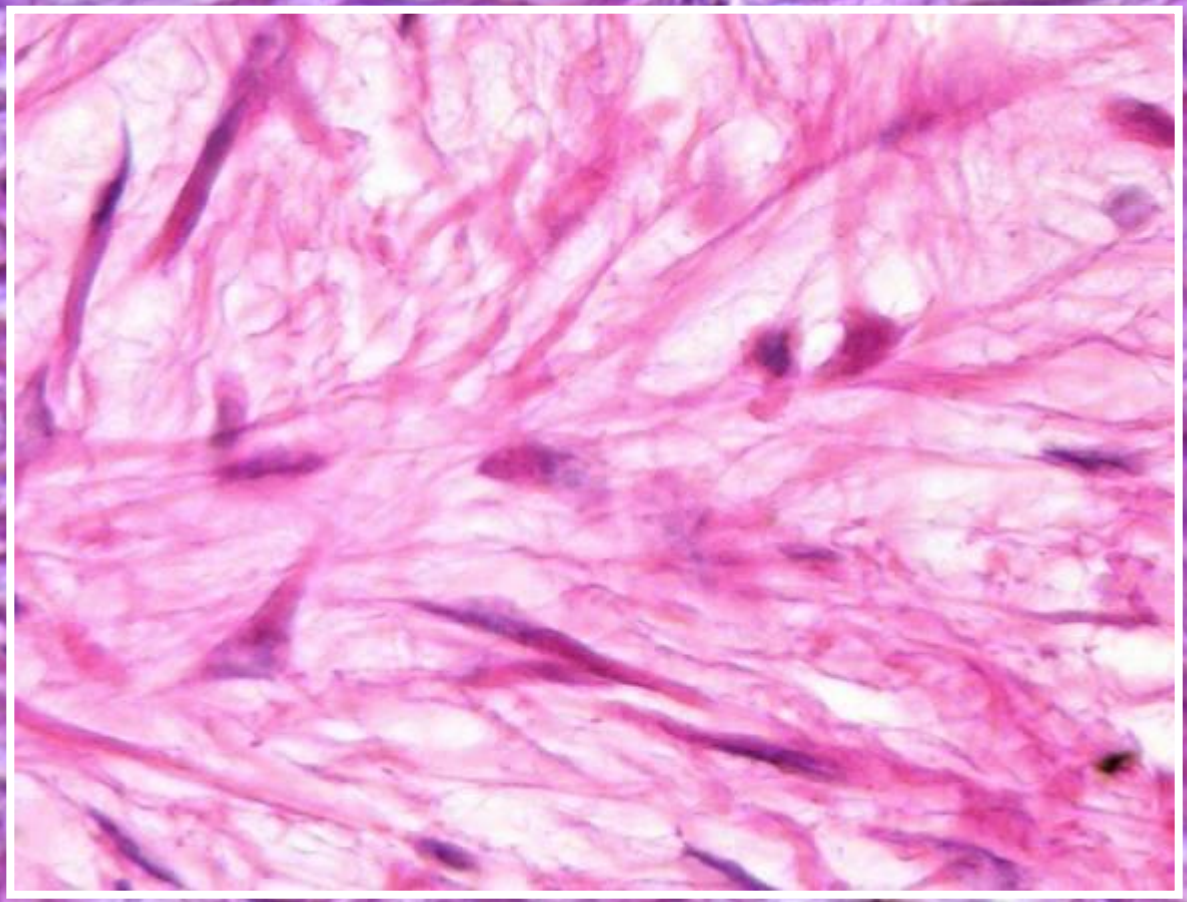
- deep: desmoid fibromatosis M 88211
  - abdominal, intraabdominal extraabdominal (chest, head / neck, extremities)
  - infiltrative growth, propensity for local recurrence
  - rare
  - age/sex predisposition F, middle age
  - gross level: strictures / large infiltrative masses
  - fibroblast like fusiform cells (β-catenin)
  - mass



The majority (90–95%) of sporadic desmoid tumours result from three different point mutations in two codons (41 and 45) of exon 3 of the gene that encodes β-catenin (*CTNNB1*).

Desmoid





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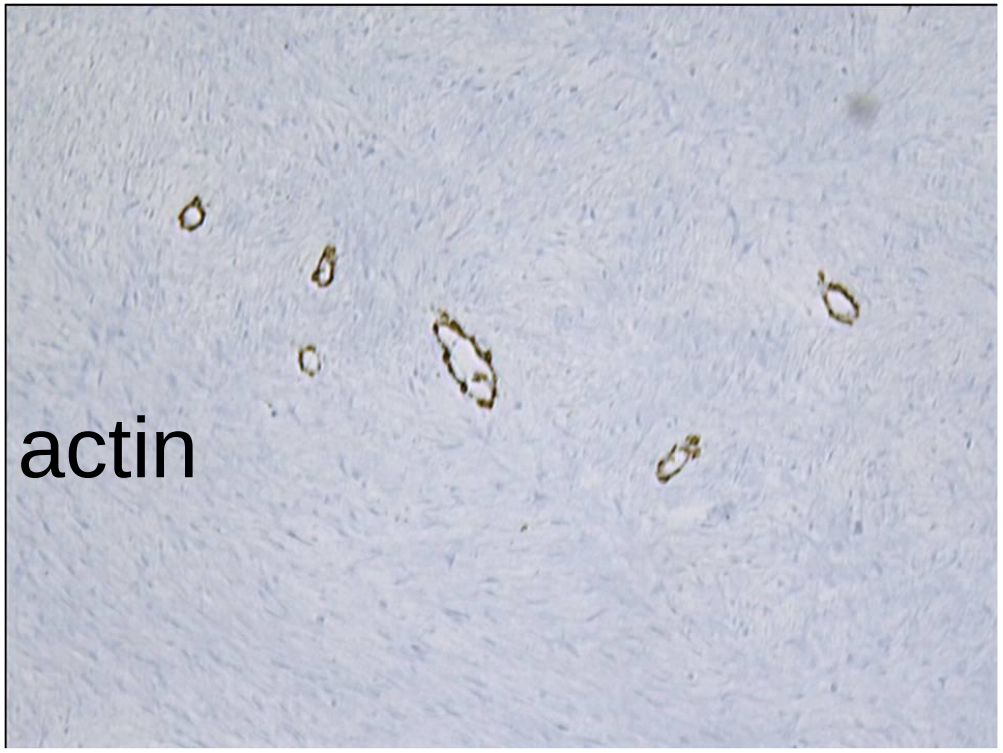
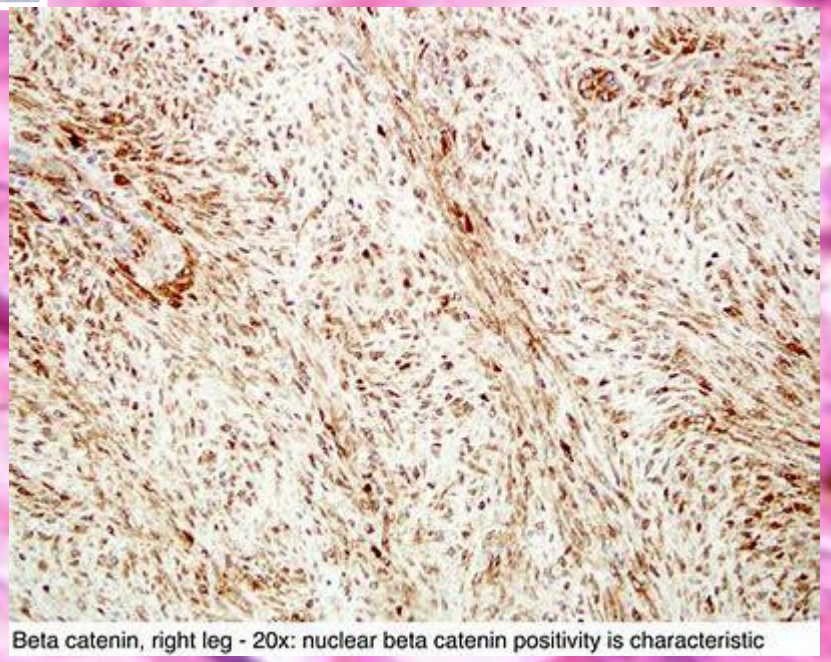
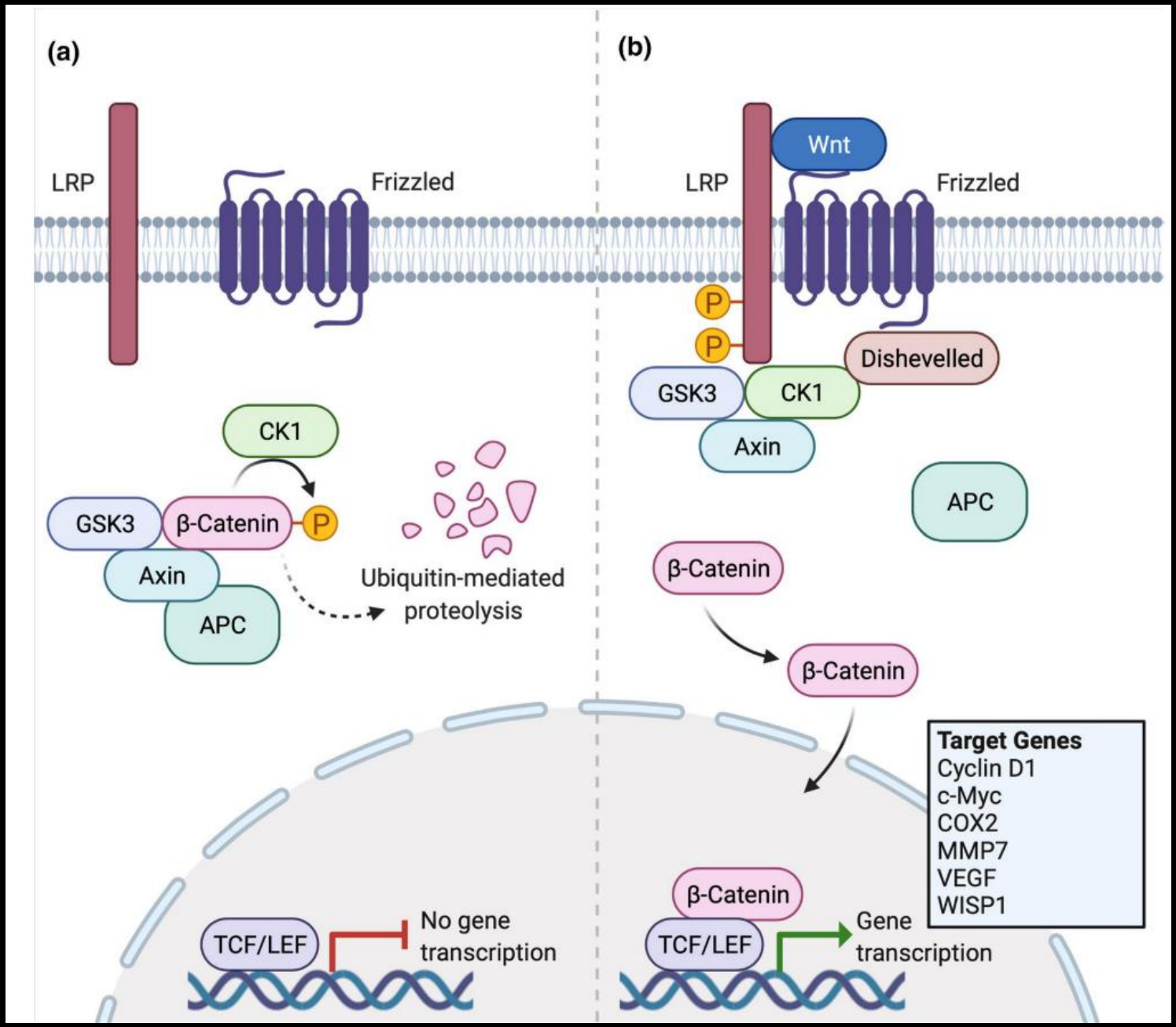


Desmoid



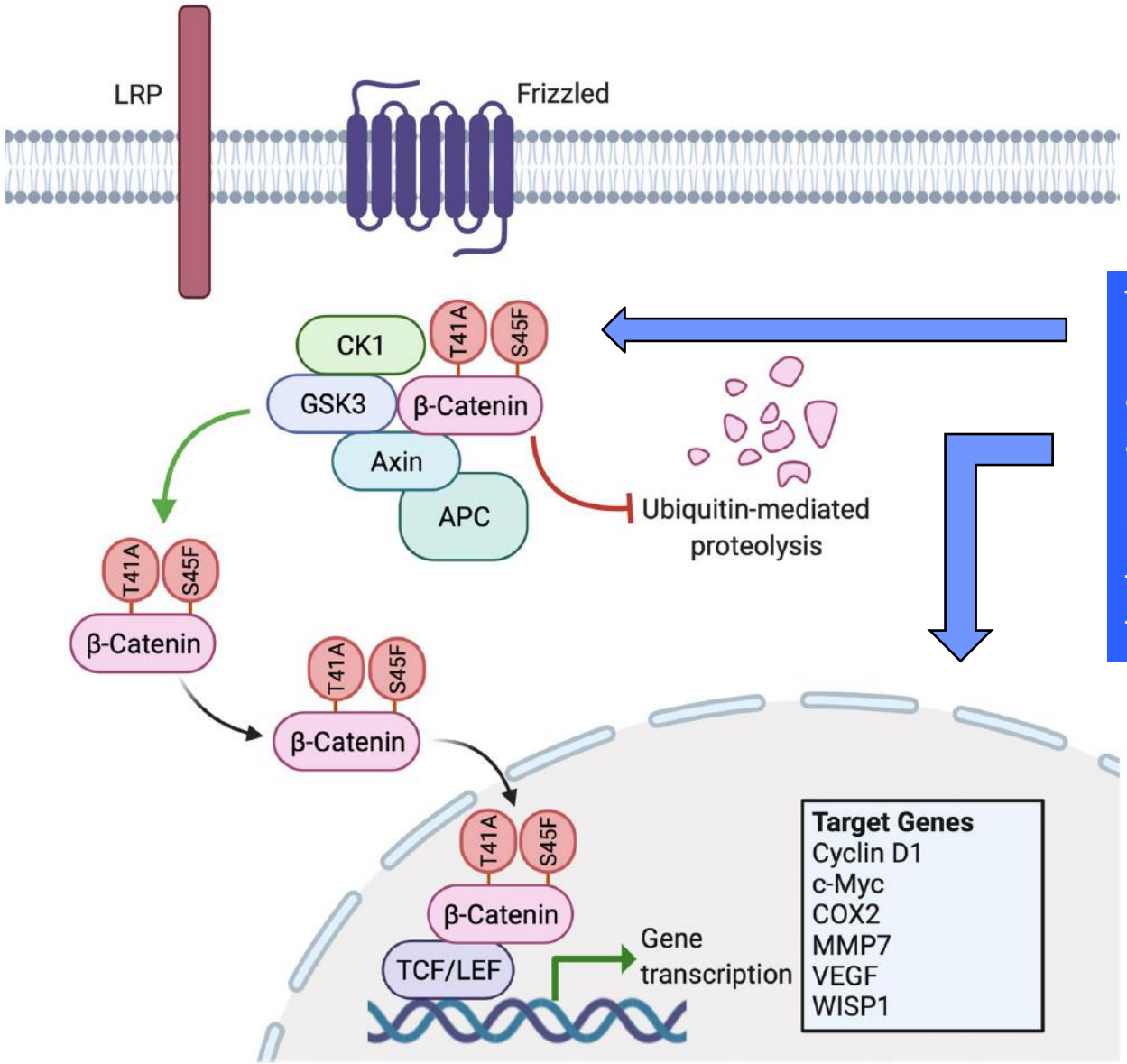
Beta catenin, right leg - 20x: nuclear beta catenin positivity is characteristic

Desmoid
pathogenesis



McLean TD, Duchi S, Di Bella C: Molecular Pathogenesis of Sporadic Desmoid Tumours and Its Implications for Novel Therapies: A Systematised Narrative Review. Target Oncol 2022, 17:223-52.

Desmoid
pathogenesis

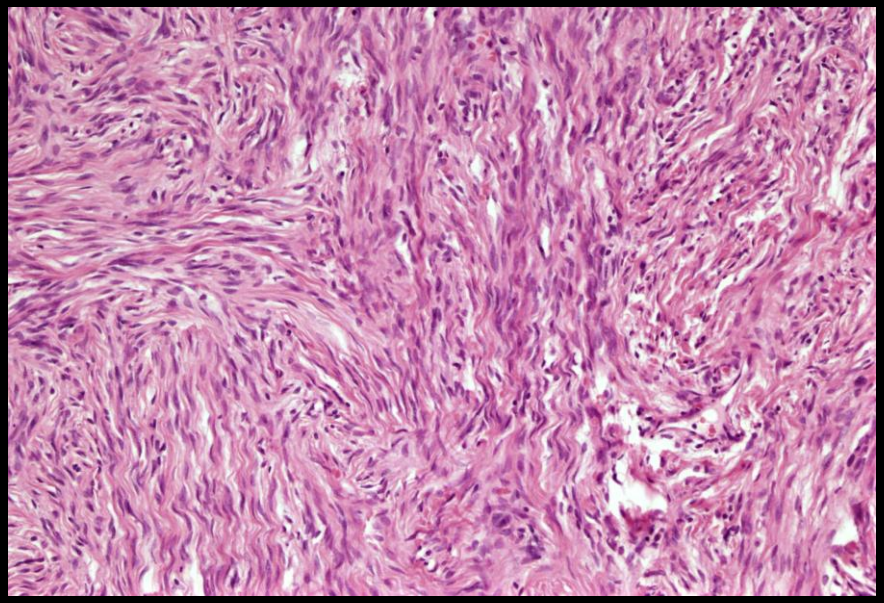


The mutated β-catenin is not marked for degradation, allowing it to accumulate and translocate into the nucleus where it promotes the unregulated transcription of specific target genes.

McLean TD, Duchi S, Di Bella C: Molecular Pathogenesis of Sporadic Desmoid Tumours and Its Implications for Novel Therapies: A Systematised Narrative Review. Target Oncol 2022, 17:223-52.

Solitary fibrous tumour - SFT

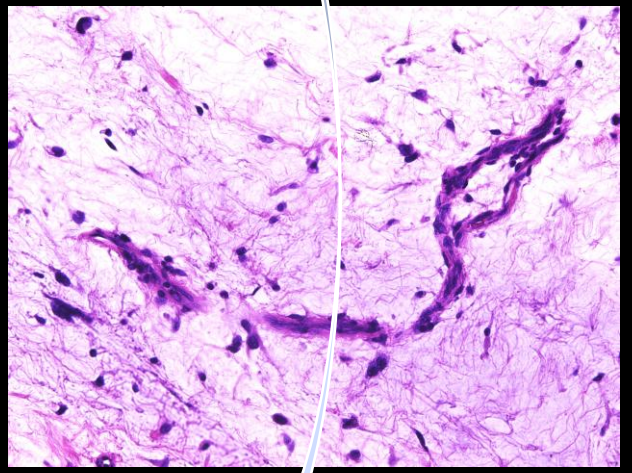
- Patternless proliferation of fusiform cells with staghorn vasculature
- CD34 and bcl 2 positivity
- NAB2::STAT6 fusion - ihch



Uncertain biology behaviour – mostly benign , but aggressive / metastatic forms do exist

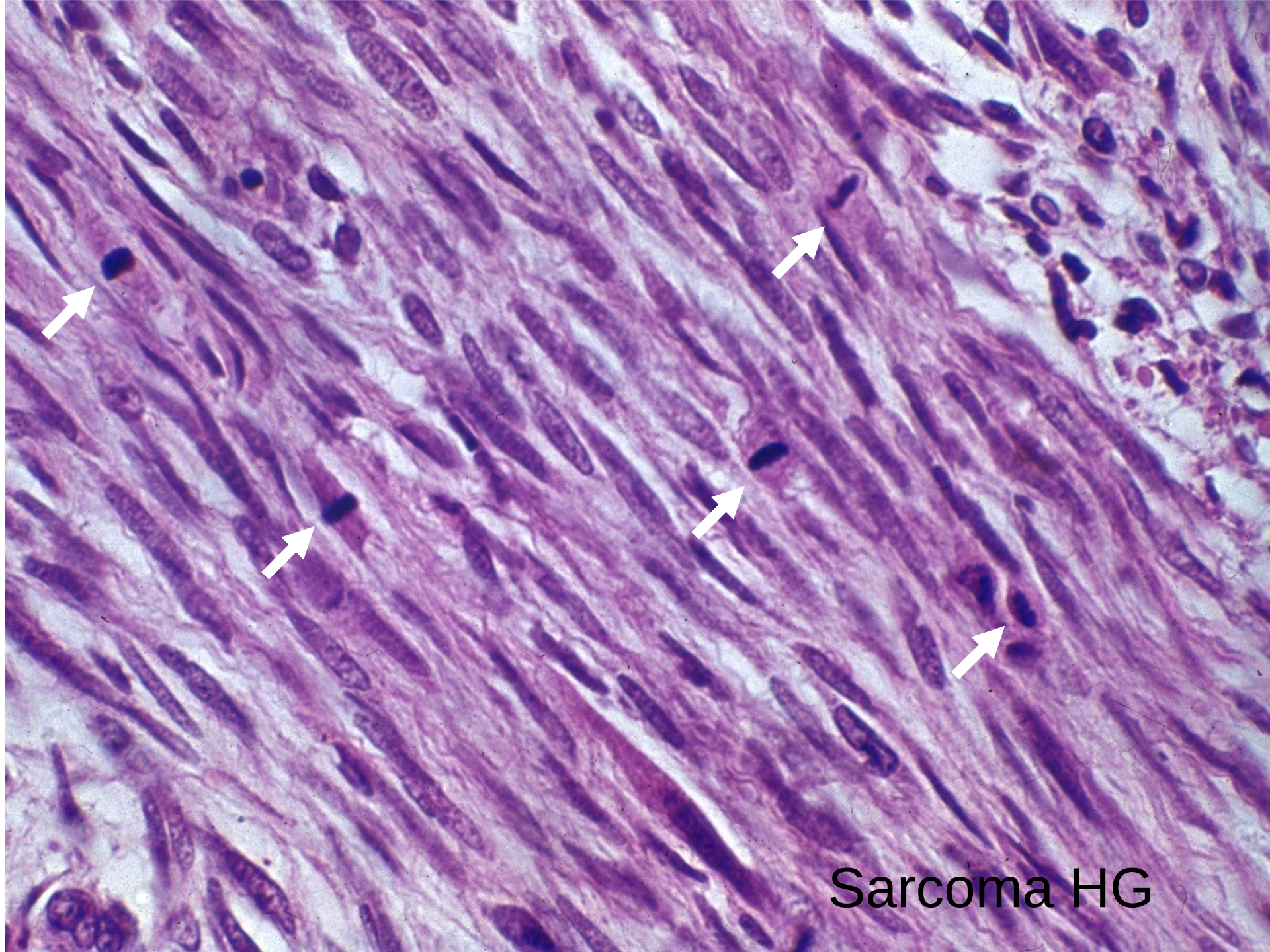
Fibrosarcoma (family)

- derived from fibroblasts & myofibroblasts
- age/sex predisposition M
- soft tissue – deep locations
- clinical symptoms: mass
- gross level view: fish flesh look
- fusiform cells, mitoses,
- hematogenous spread

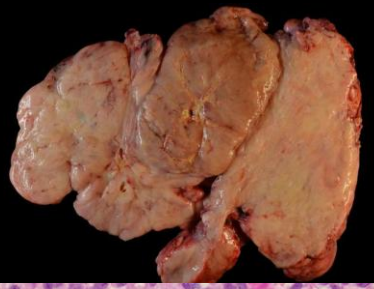


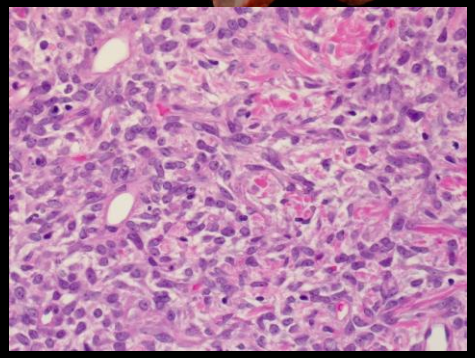
TP53 (46%; most frequently mutated), *RB1* (18%), and *CDKN2A*/*CDKN2B* (16%) tumour suppressor gene mutations are more common than *CDK6*, *CCND1*,and *MDM2* amplifications

Myxoinflammatory fibroblastic sarcoma
Infantile fibrosarcoma
Adult fibrosarcoma
Myxofibrosarcoma
Low-grade fibromyxoid sarcoma
Sclerosing epithelioid fibrosarcoma


Sarcoma HG

Myofibroblastic tumors



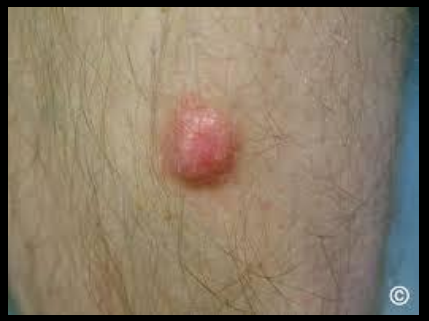


- solitary fibrous tumor
  - **ICD-O coding :**
    - 8815/0 Solitary fibrous tumour, benign
    - 8815/1 Solitary fibrous tumour NOS
    - 8815/3 Solitary fibrous tumour, malignant

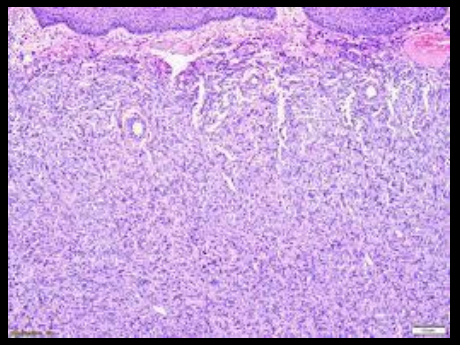
–(CD34+, bcl +, translocation with a fusion gene - stat 6+)

- myxofibrosarcoma (LG , HG)

Dermatofibroma



- cutaneous fibrous histiocytoma
- storiform architecture (myofibroblasts)



Dermatofibrosarcoma protuberans – LG sarcoma

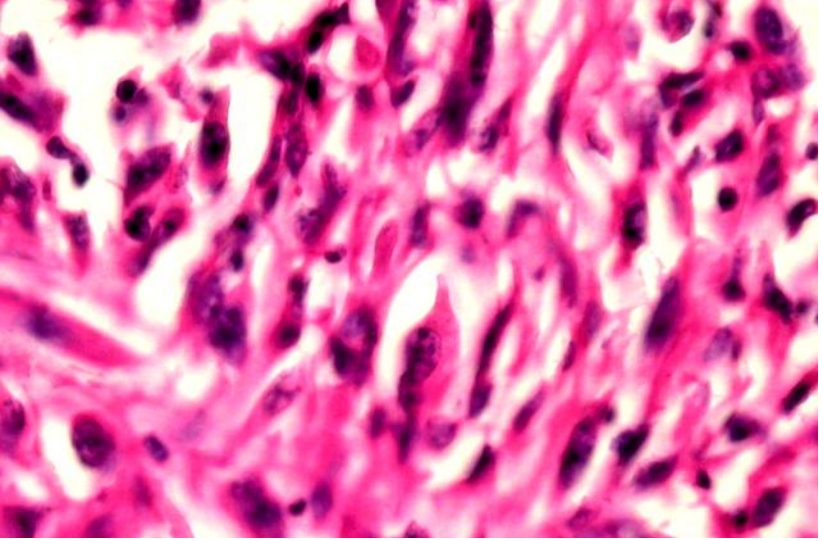
- borderline – ulceration & recurrences
- increased cellularity & atypiae

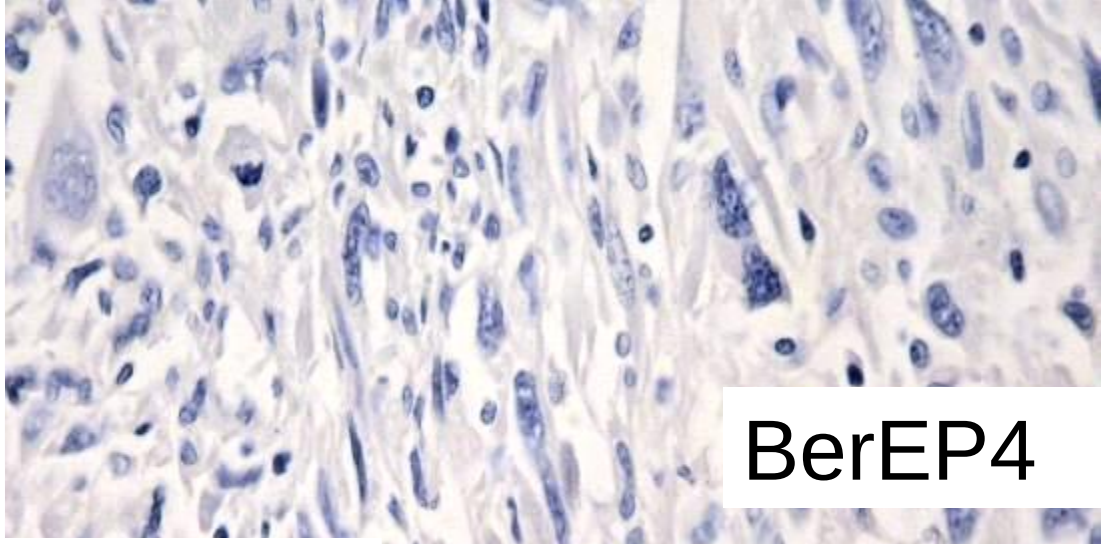
Fibrous Histiocytoma

- benign (pigmented villonodullar synovitis)

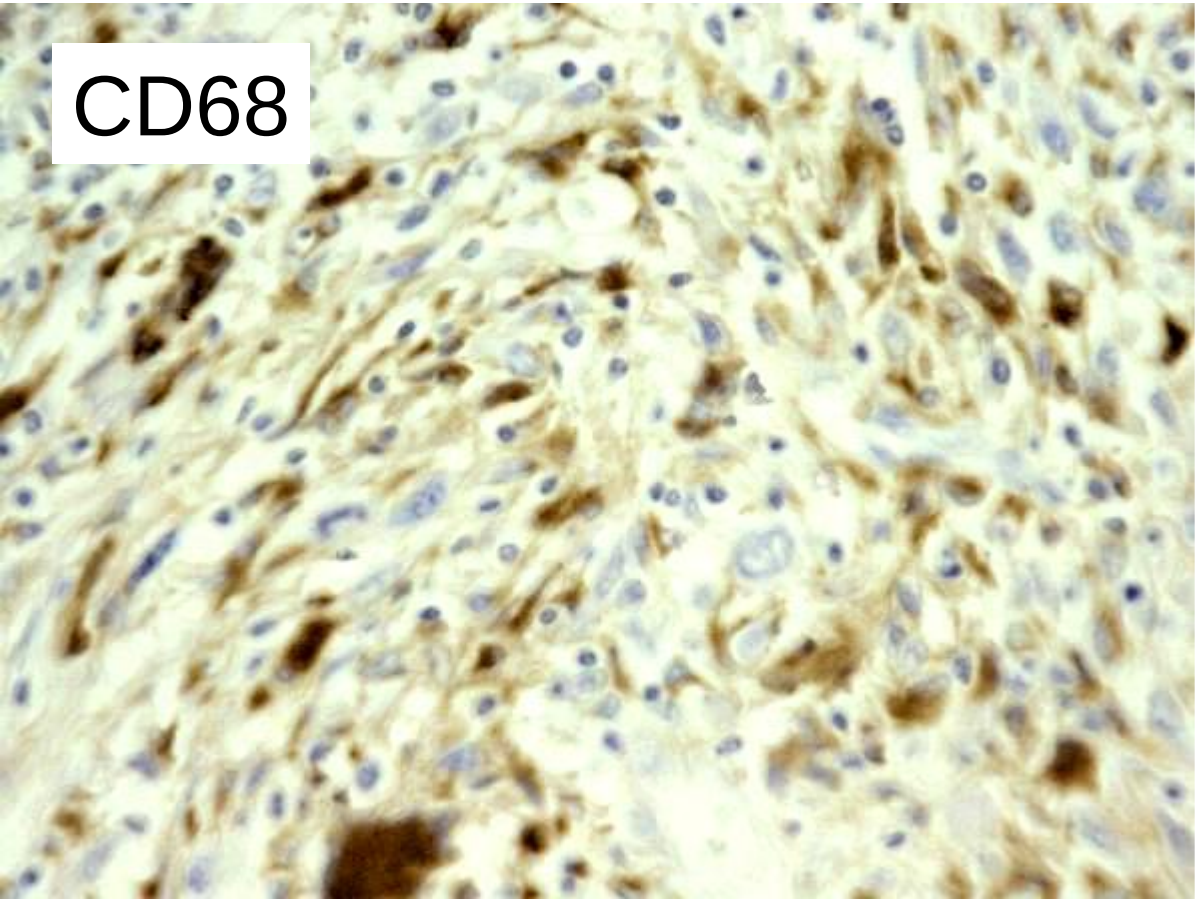
„Malignant Fibrous Histiocytoma“ –
a cancelled unit substituted recently with other molecular pathology defined

poorly differentiated sarcomas





BerEP4



CD68

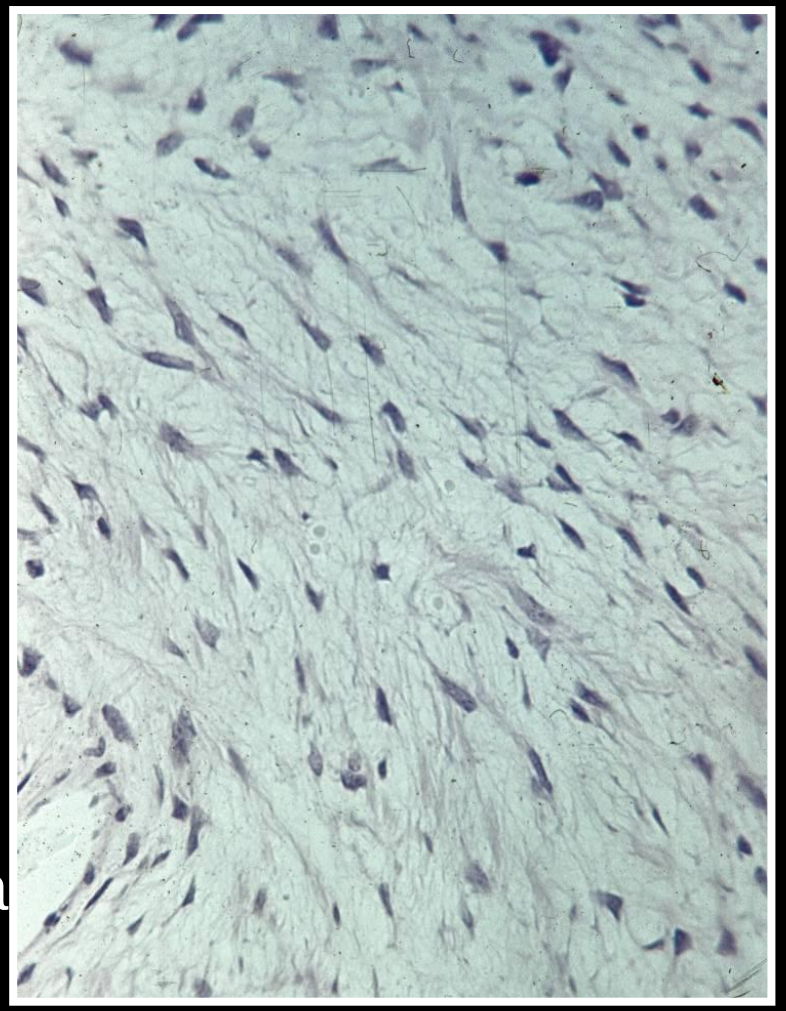
Poorly differentiated sarcoma

(thyroid)

MYXOMA component in:

(WHO Soft tissue tumours 5th. ed.:)

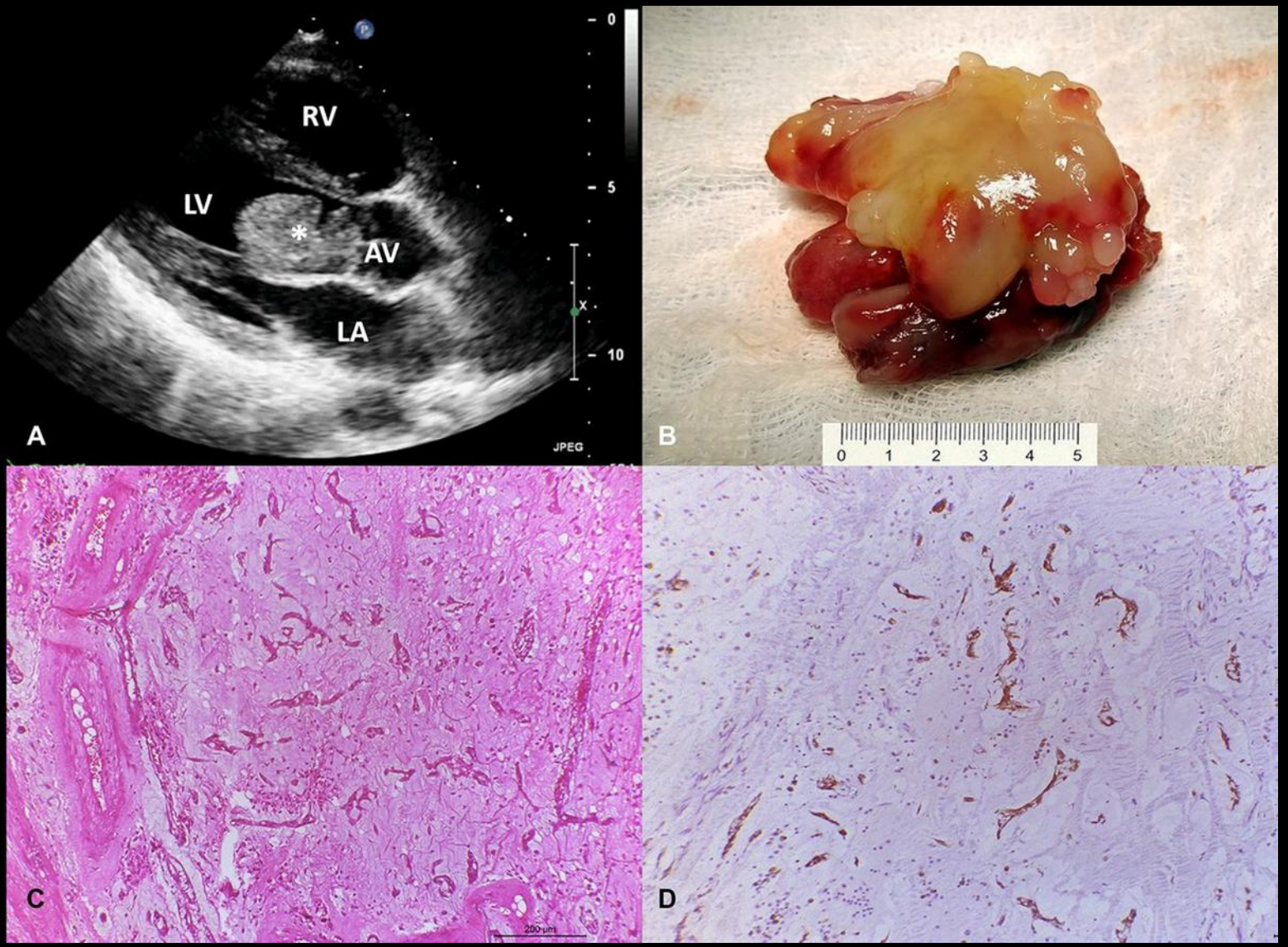
- acral fibromyxoma
- dermal nerve sheet myxoma
- intramuscular myxoma
- juxta-articular myxoma
- deep (aggressive) angiomyxoma
- osteochondromyxoma…



Scanty branching cells irregularly distributed in an abundant clear matrix.

M 88400

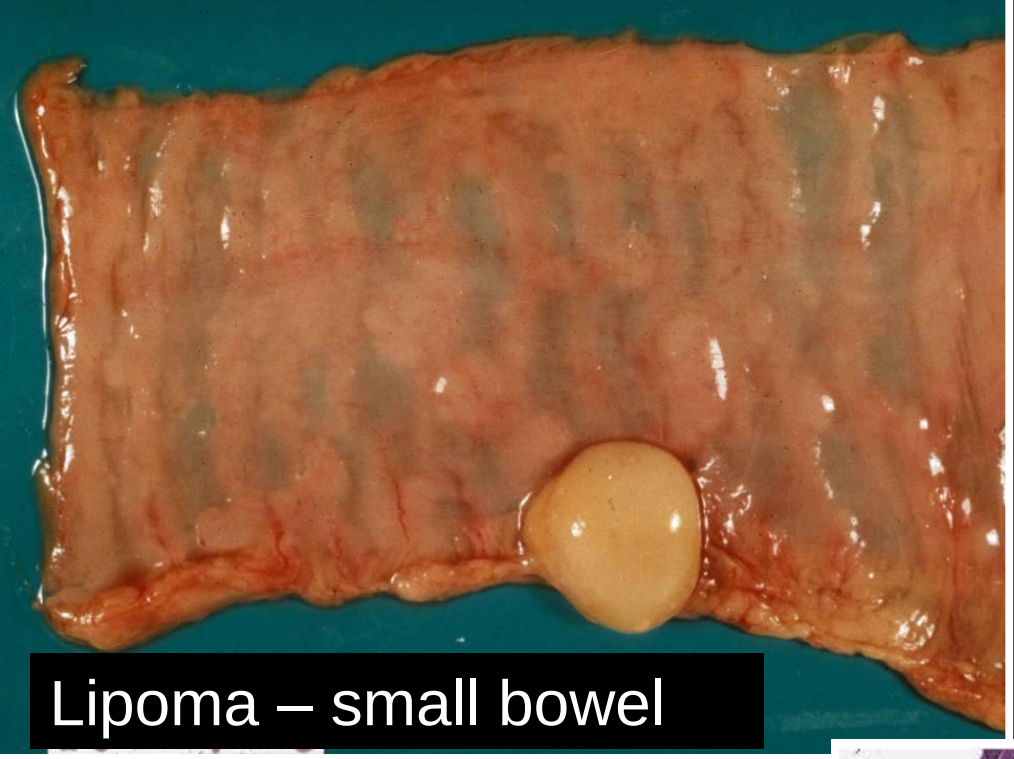
Cardiac Myxoma



Sambaturu V Kartik et al. Postgrad Med J 2018;94:725-726

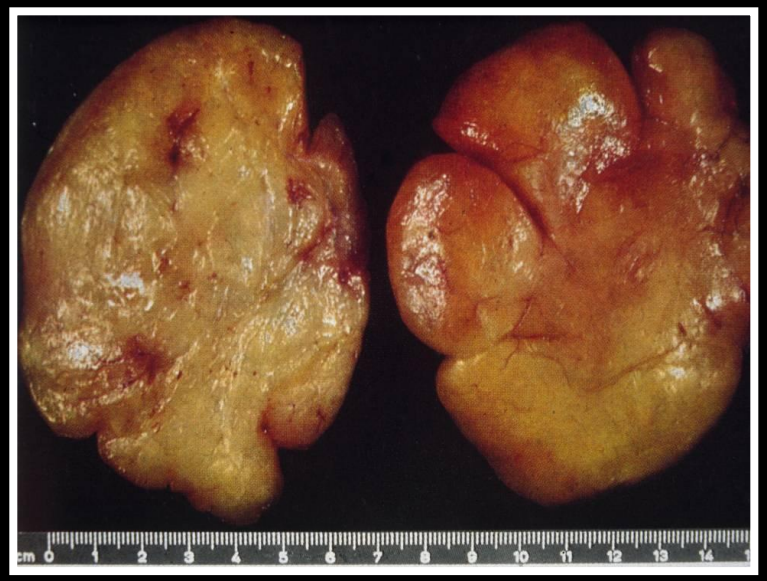
Mesenchymal neoplasms

Benign	Borderline	Malignant
fibroma	fibromatoses	fibrosarcoma
lipoma	lipoblastoma	liposarcoma
leiomyoma	atypical smooth muscle cell tumors	leiomyosarcoma
rhabdomyoma		rhabdomyosarcoma
hemangioma	hemangioendothelioma	hemangiosarcoma
lymphangioma		lymphangiosarcoma
chondroma	chondroblastoma	chondrosarcoma
chordoma		*invasive* chordoma
osteoma	osteoid osteoma <2cm osteoblastoma >2cm	osteosarcoma
!!!		lymphoma/leukaemia



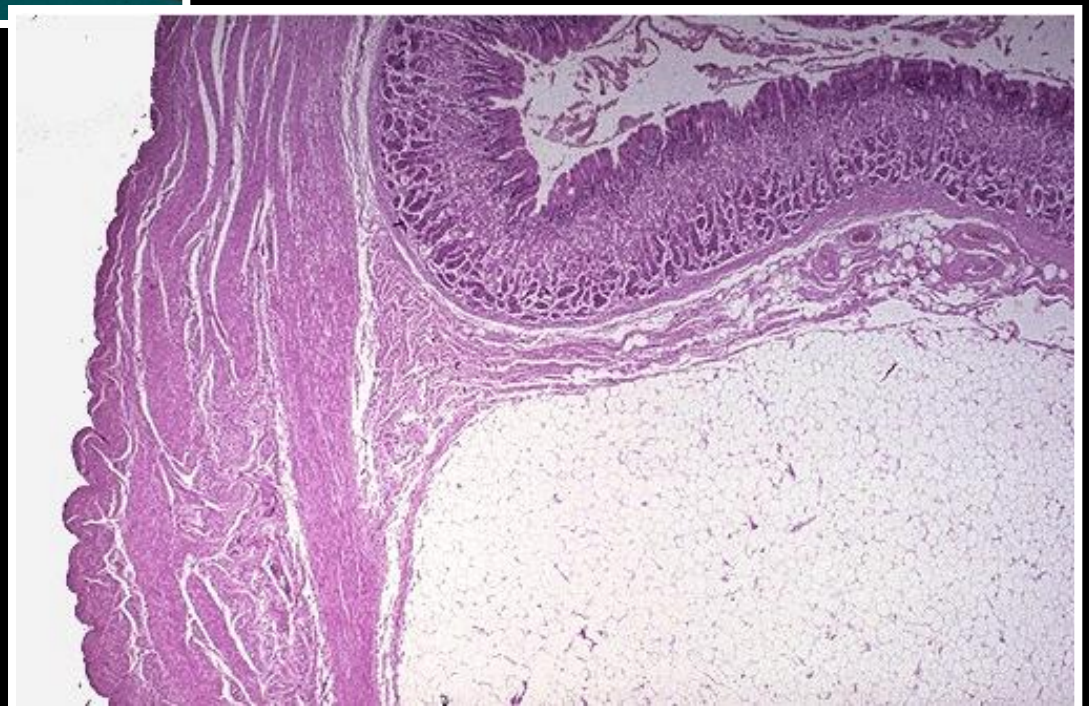
Lipoma – small bowel

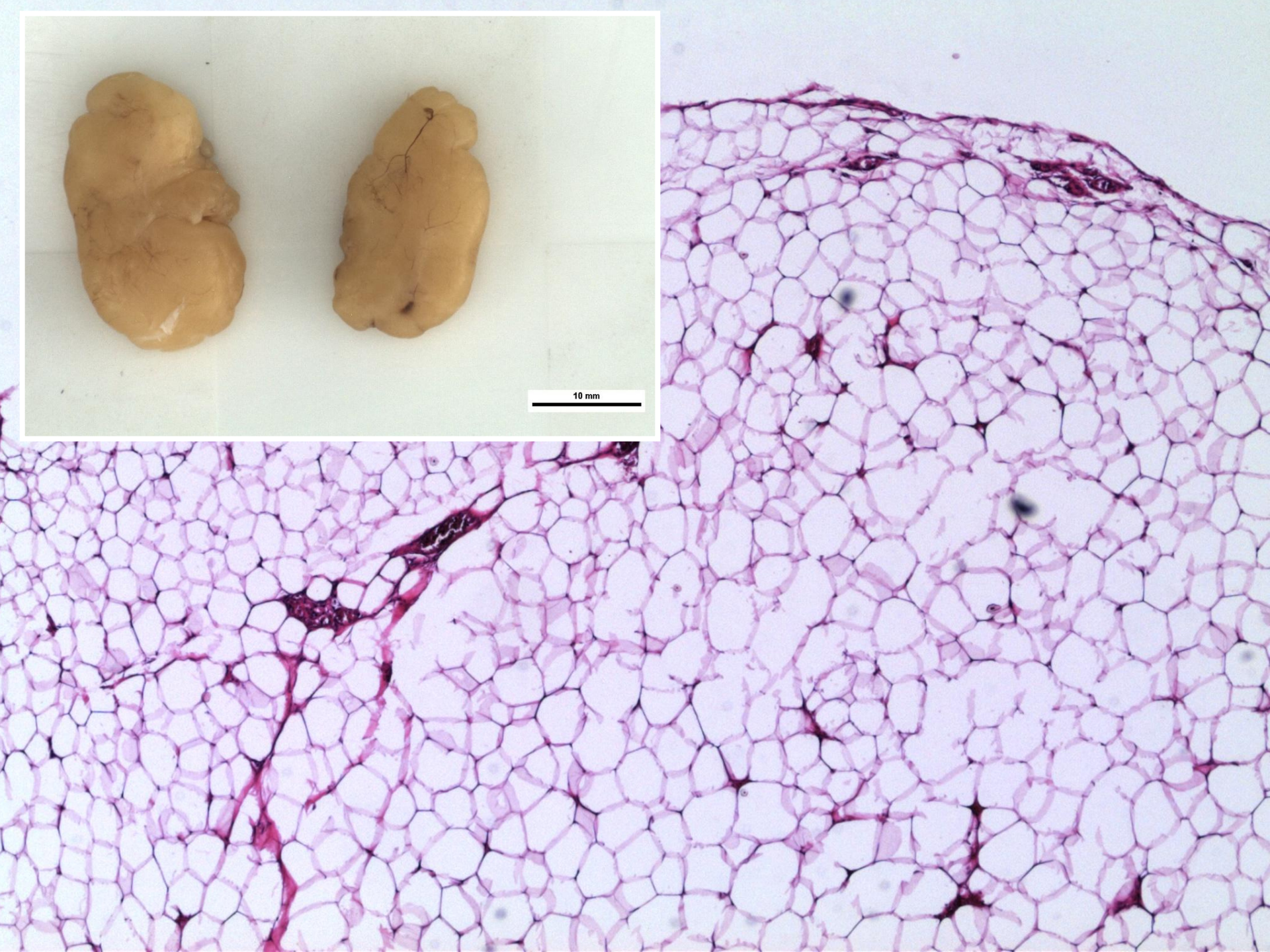
Lipoma - subcutaneous

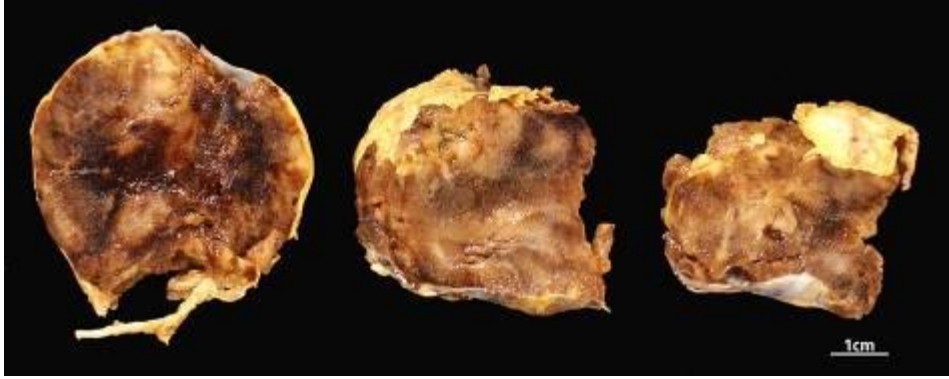


M 88500

Lipoma - stomach

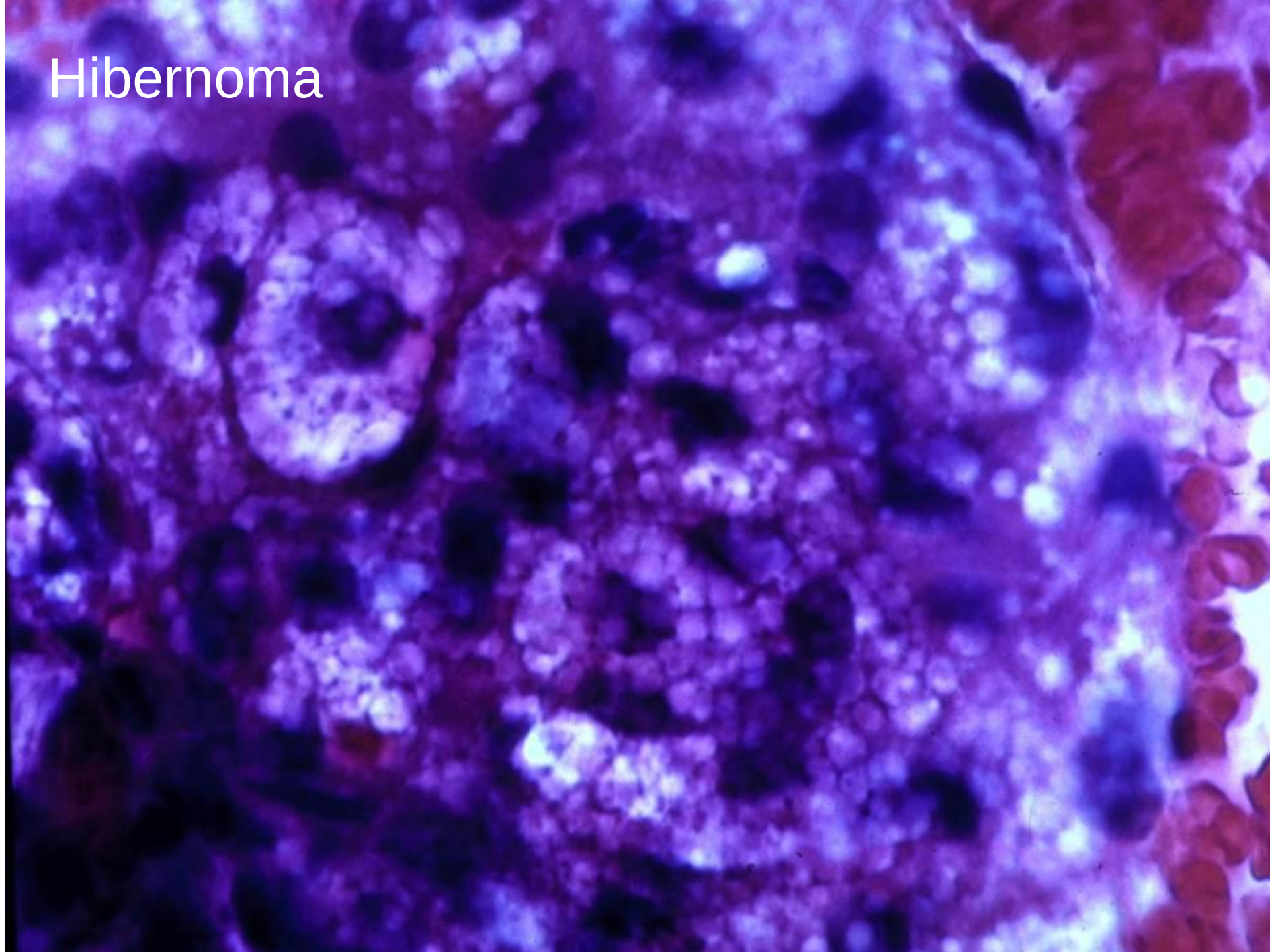


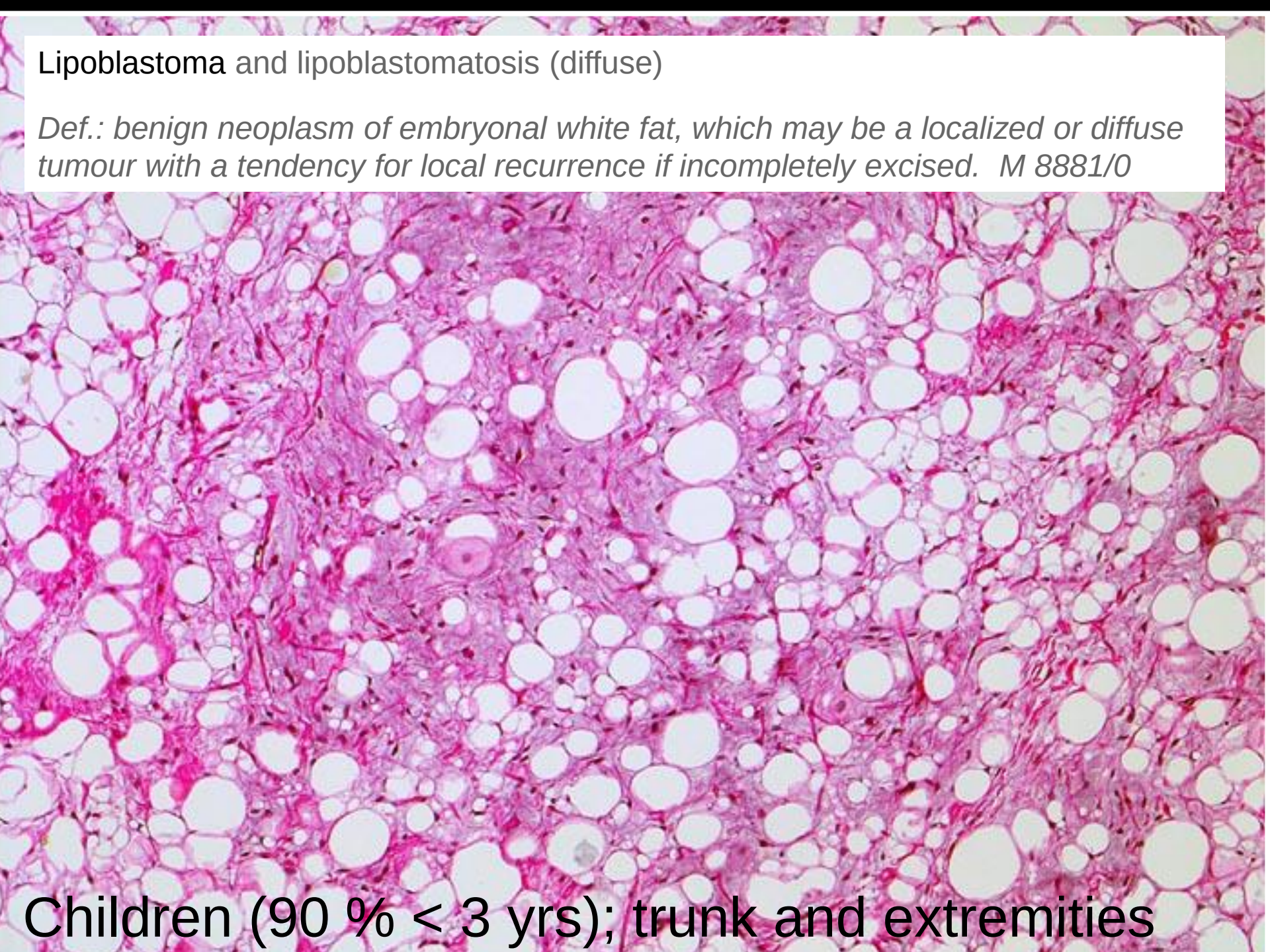

10 mm



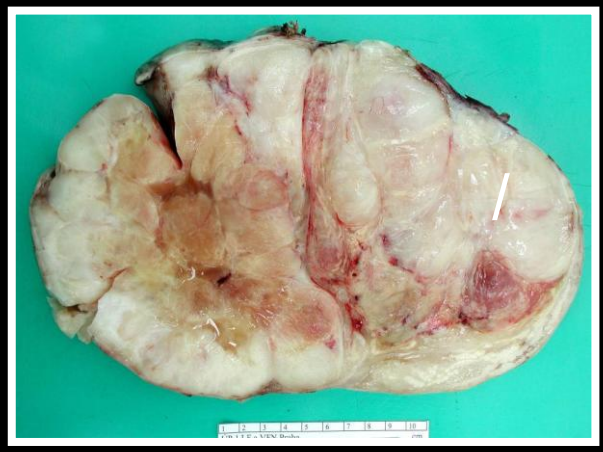
Myelolipoma adrenale

Hibernoma




Lipoblastoma and lipoblastomatosis (diffuse)
Def.: benign neoplasm of embryonal white fat, which may be a localized or diffuse tumour with a tendency for local recurrence if incompletely excised. M 8881/0
Children (90 % < 3 yrs); trunk and extremities

Liposarcoma



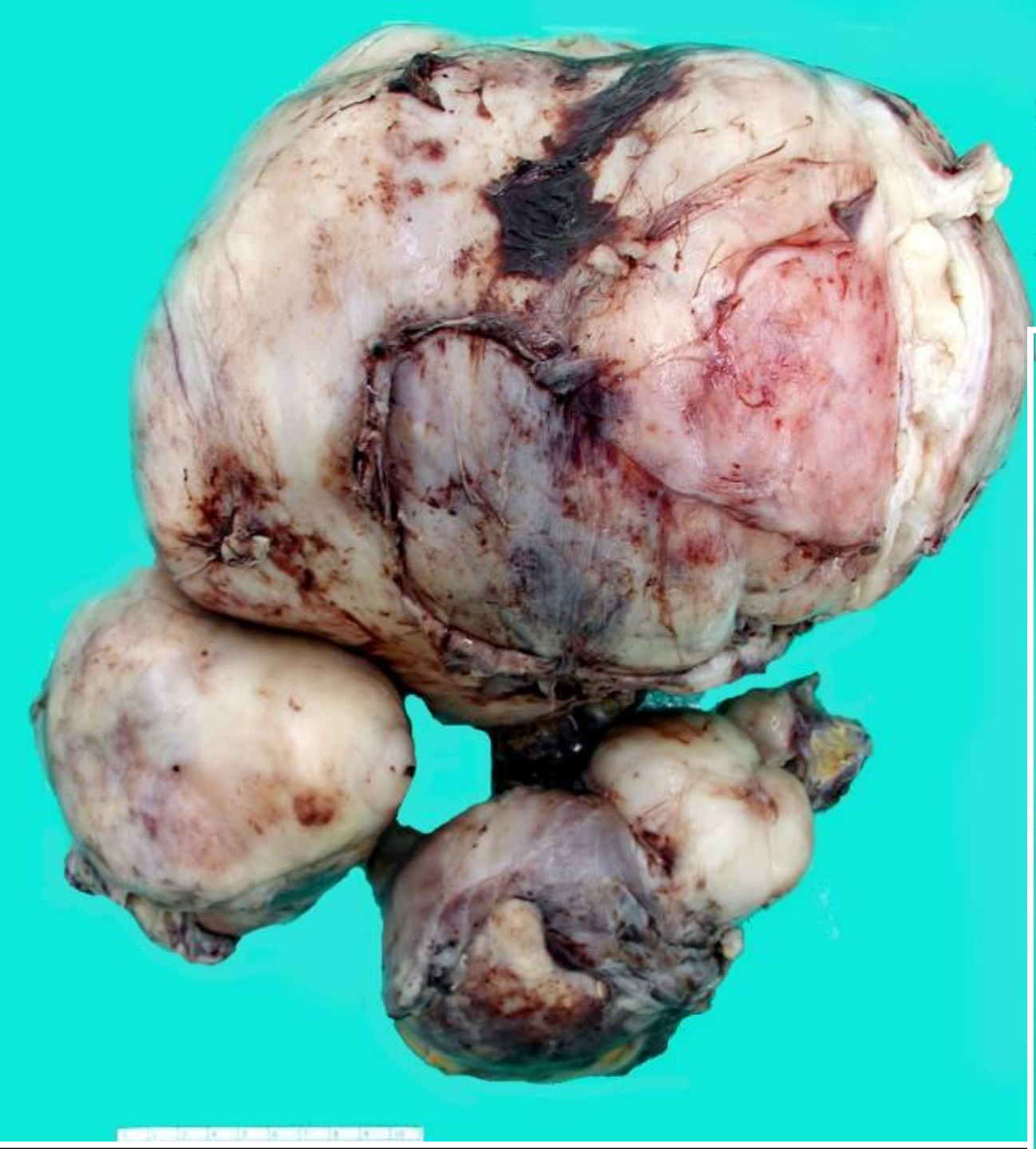
- Atypical lipomatous tumour M 8850/1 well-differentiated liposarcoma M 8851/3
- Dedifferentiated liposarcoma M8858/3

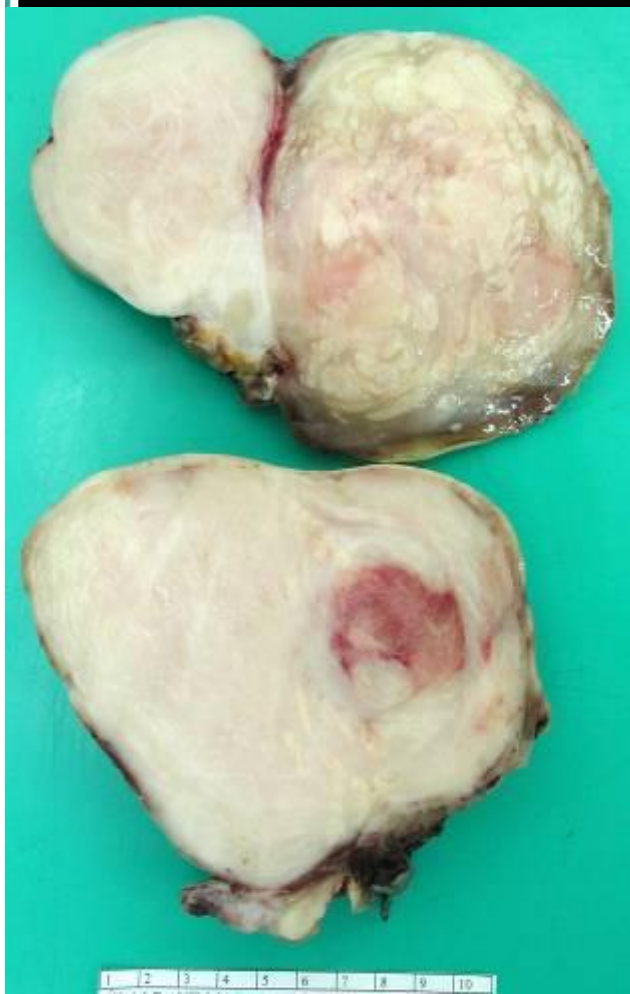
- Middle aged adults
- Pathogenesis: both entities are characterized by consistent amplification of MDM2 and CDK4 (12q14-q15)

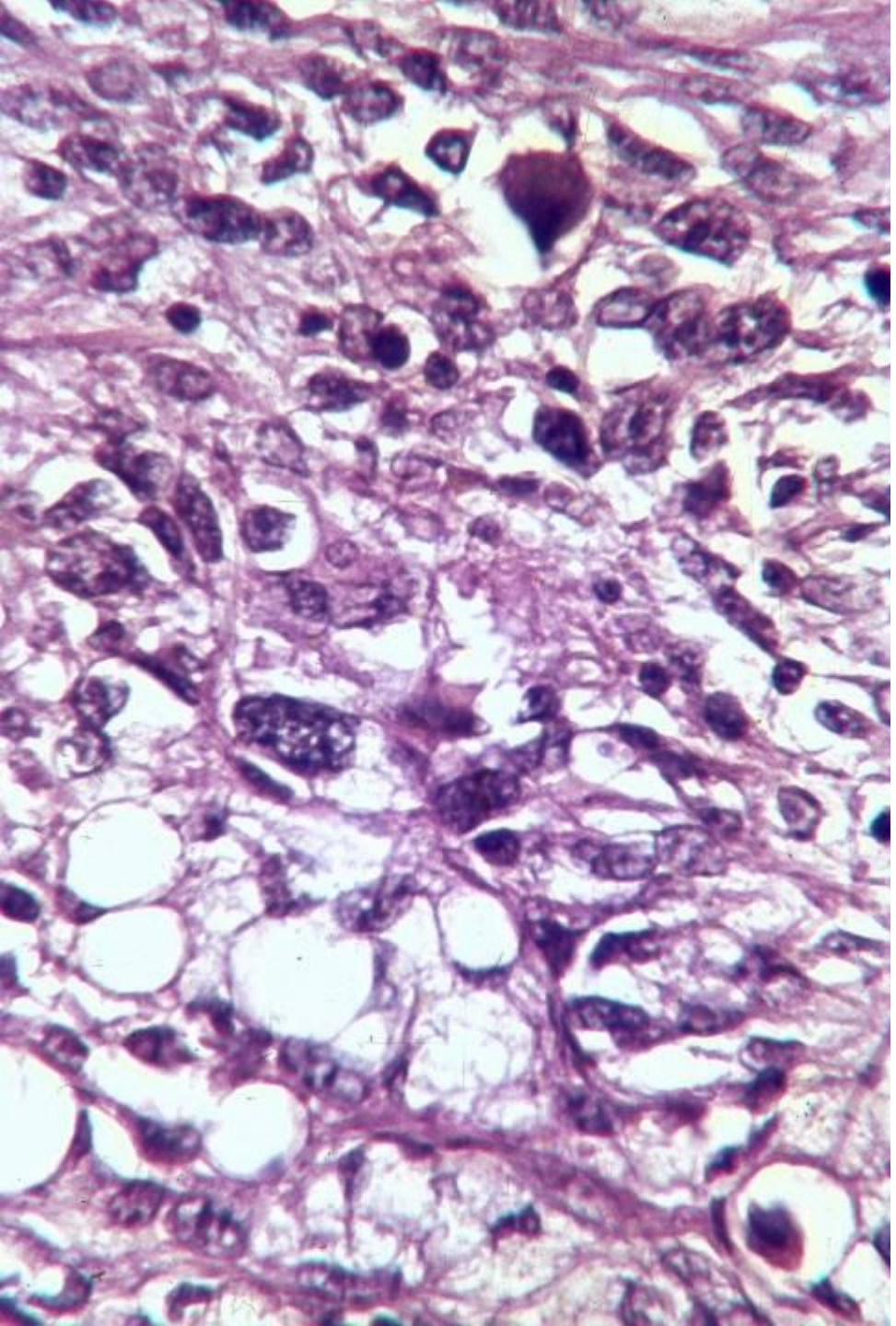
- Lesions located in surgically amenable anatomical regions do not recur after complete excision.
- Tumours occurring in deep anatomical sites such as retroperitoneum, spermatic cord, or mediastinum tend to recur repeatedly and eventually cause death as a result of uncontrolled local effects or less often as a result of systemic spread subsequent to dedifferentiation.

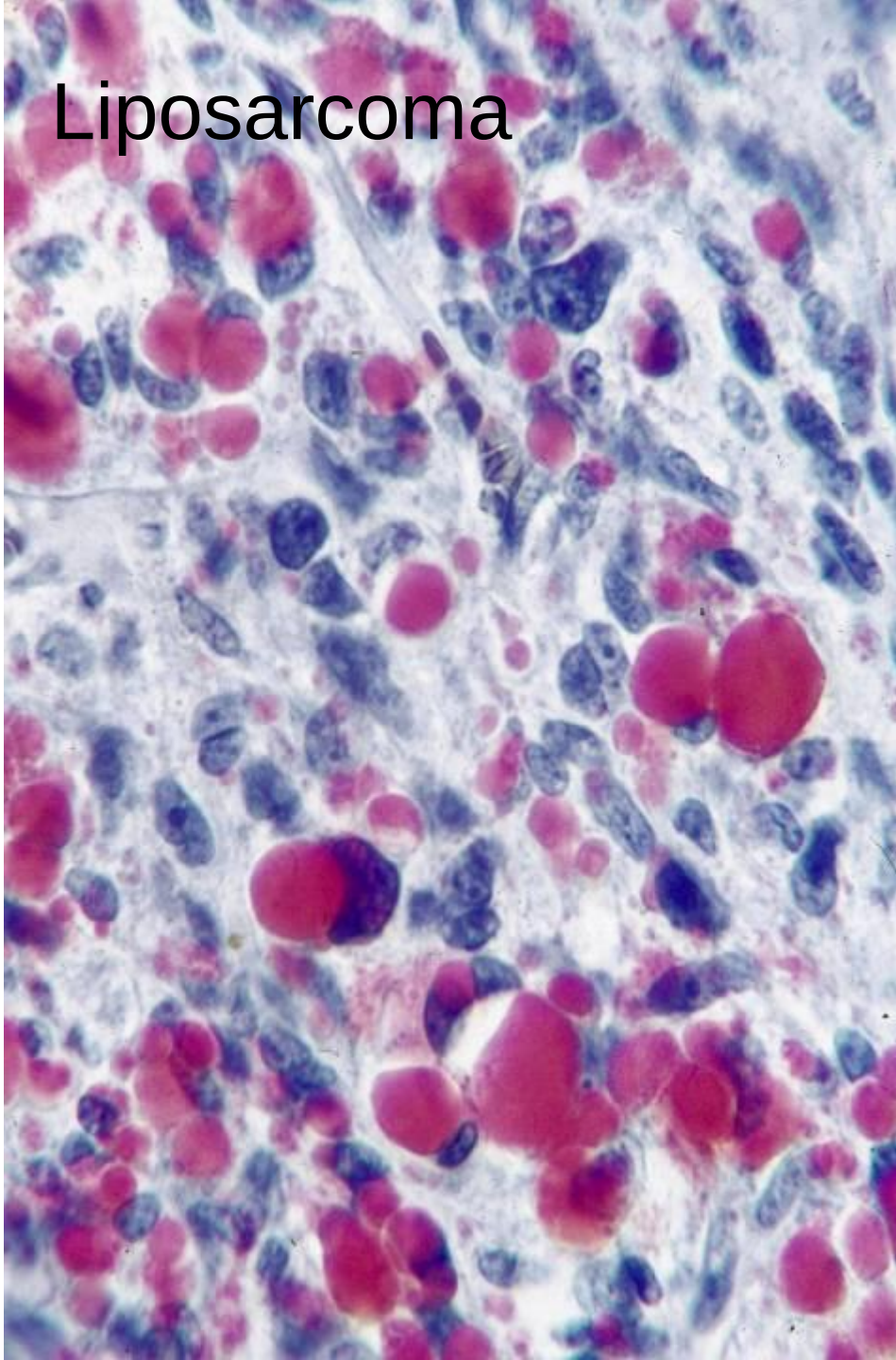
- Myxoid liposarcoma
- Pleomorphic liposarcoma

Liposarcoma (recurrence)





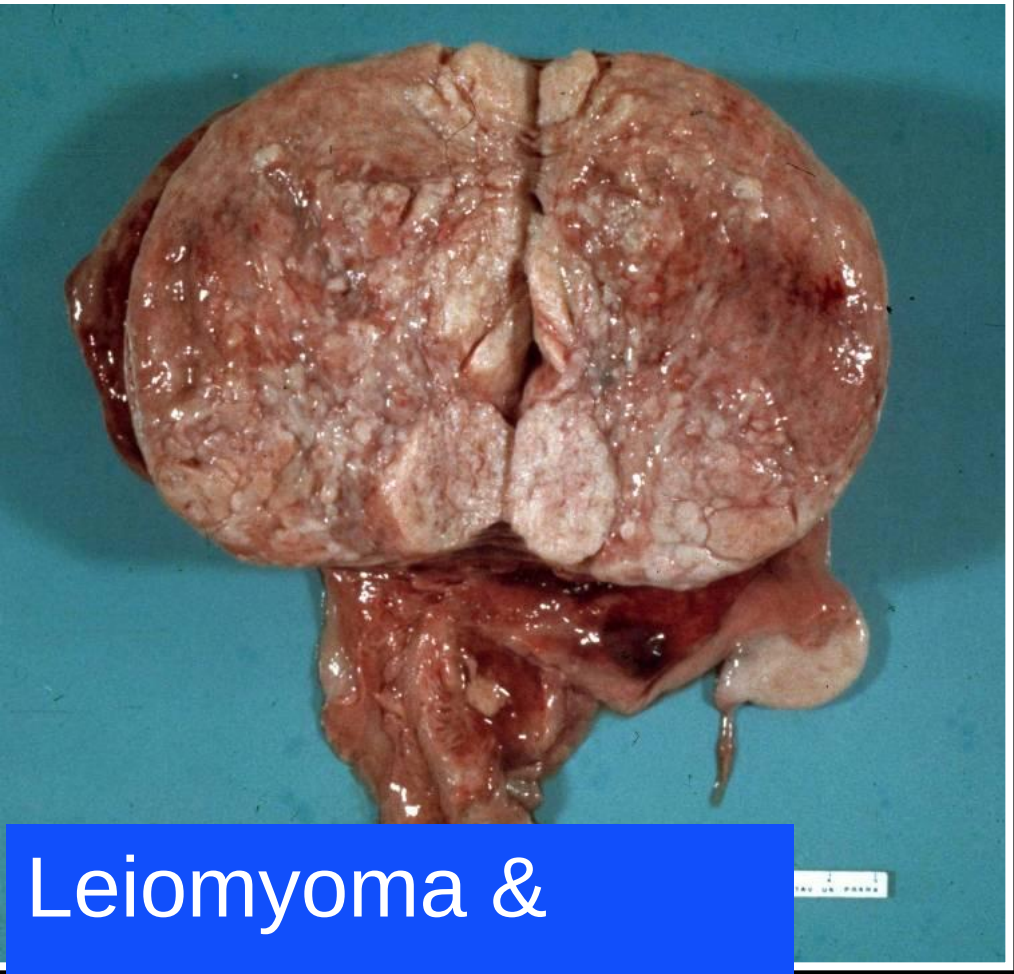




Liposarcoma

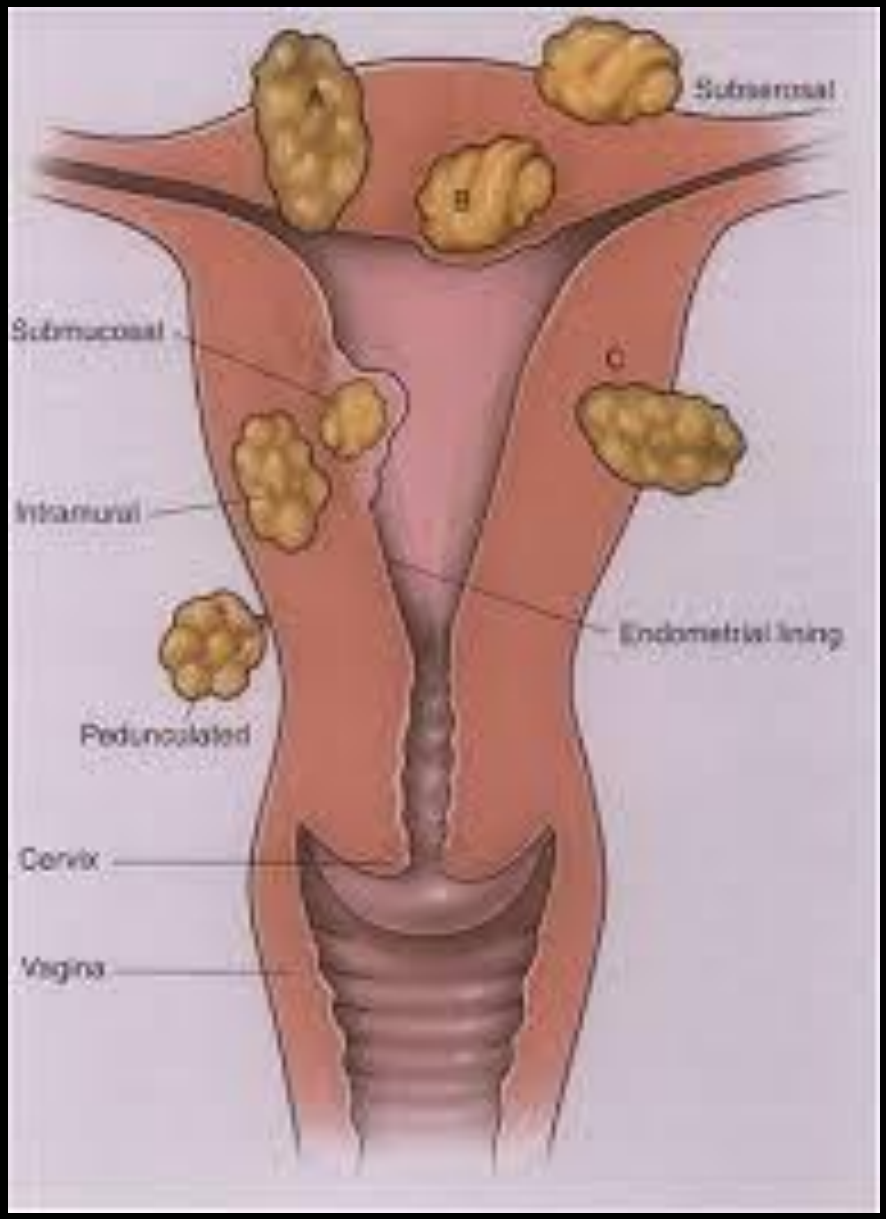
Mesenchymal neoplasms

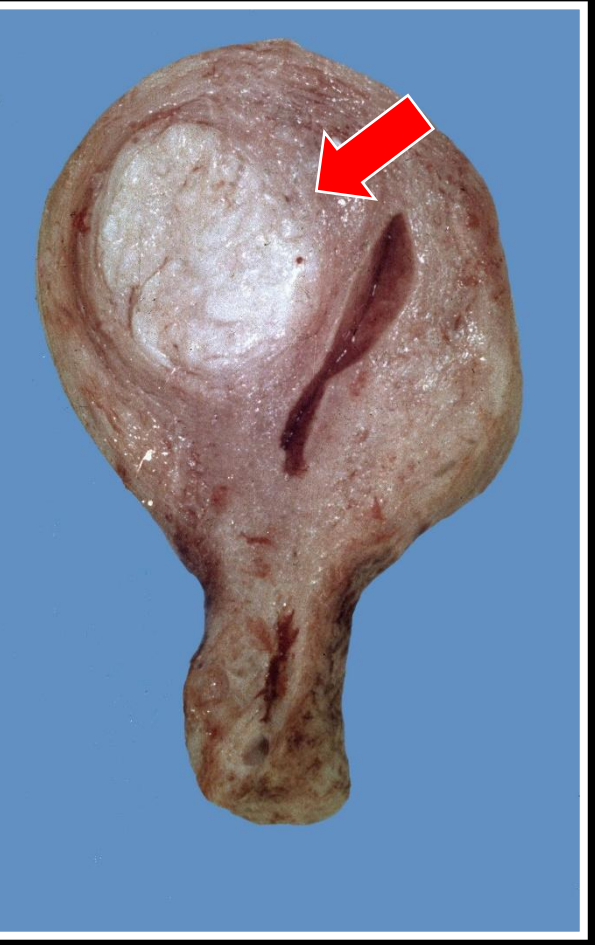
Benign	Borderline	Malignant
fibroma	fibromatoses	fibrosarcoma
lipoma	lipoblastoma	liposarcoma
leiomyoma	atypical smooth muscle cell tumors (STUMP)	leiomyosarcoma
rhabdomyoma		rhabdomyosarcoma
hemangioma	hemangioendothelioma	hemangiosarcoma
lymphangioma		lymphangiosarcoma
chondroma	chondroblastoma	chondrosarcoma
chordoma		*invasive* chordoma
osteoma	osteoid osteoma <2cm osteoblastoma >2cm	osteosarcoma
!!!		lymphoma/leukaemia



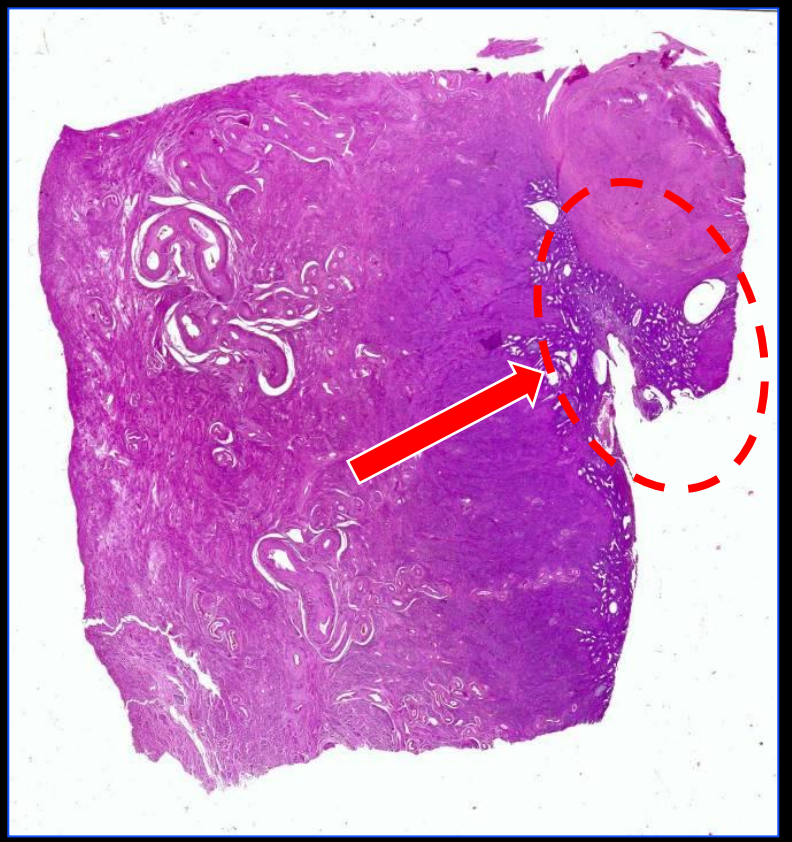
Leiomyoma &

myomatous uterus

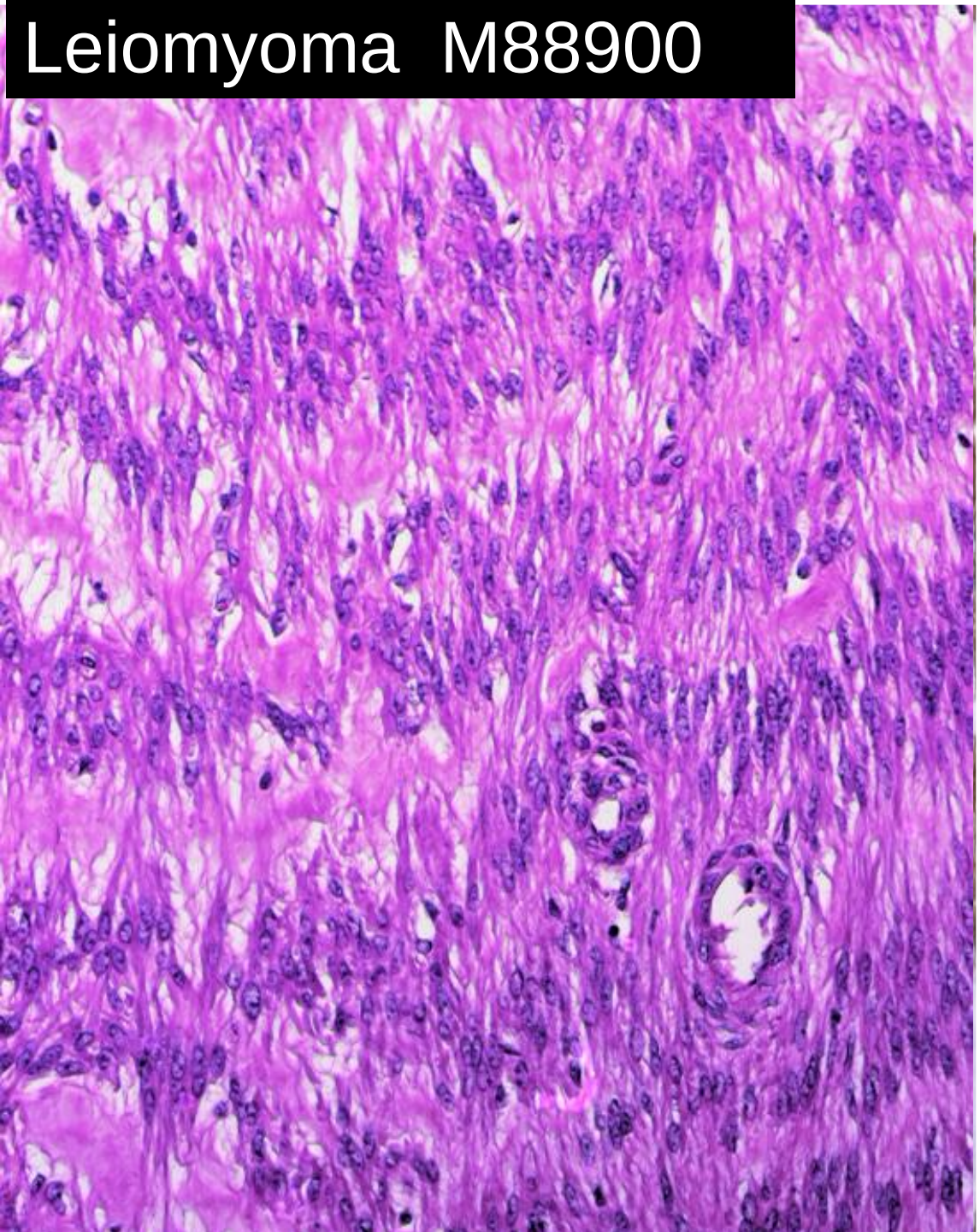


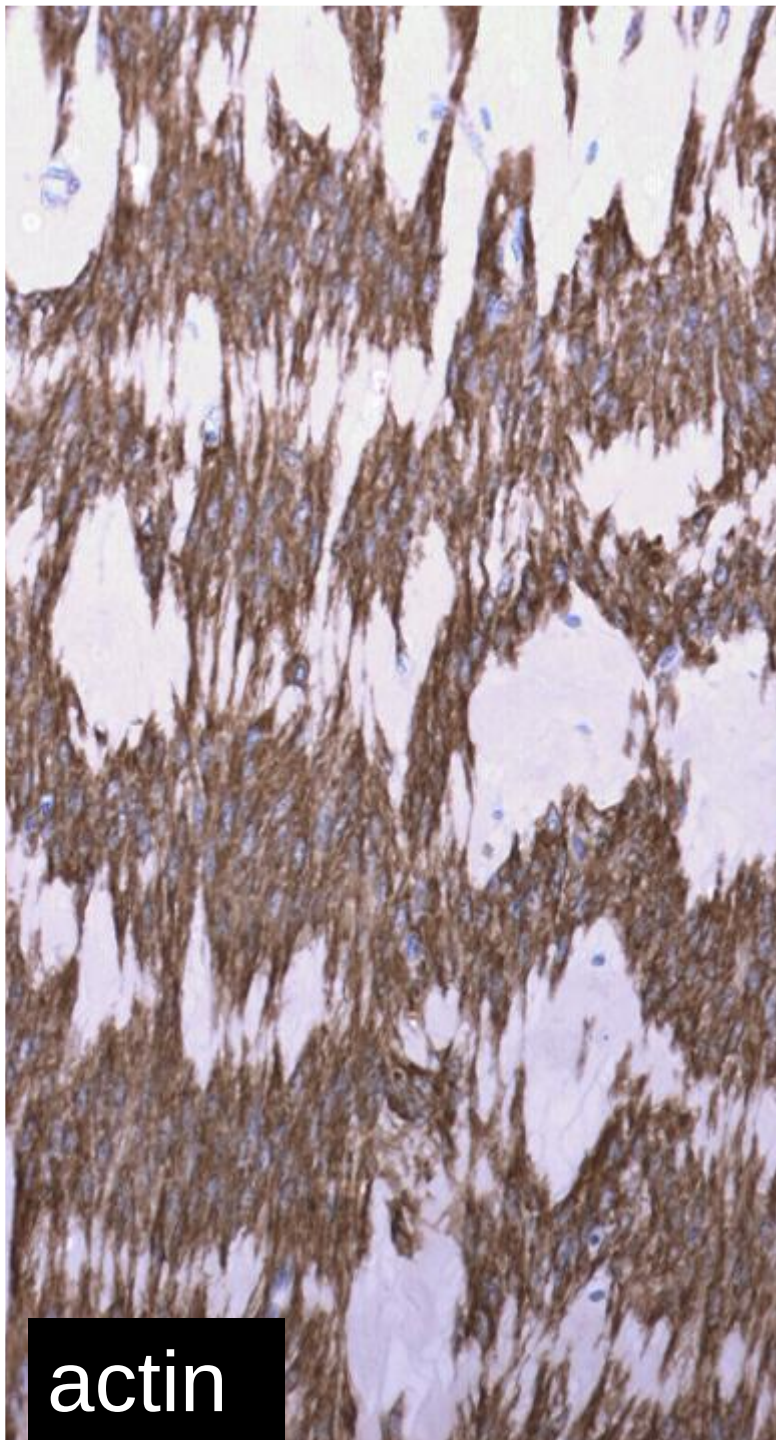


Intramural leiomyoma

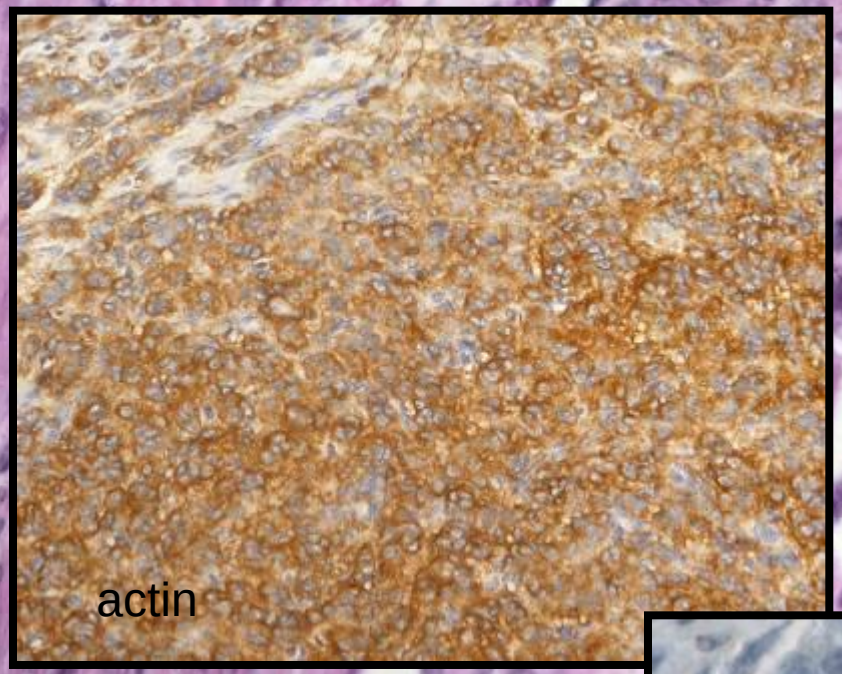


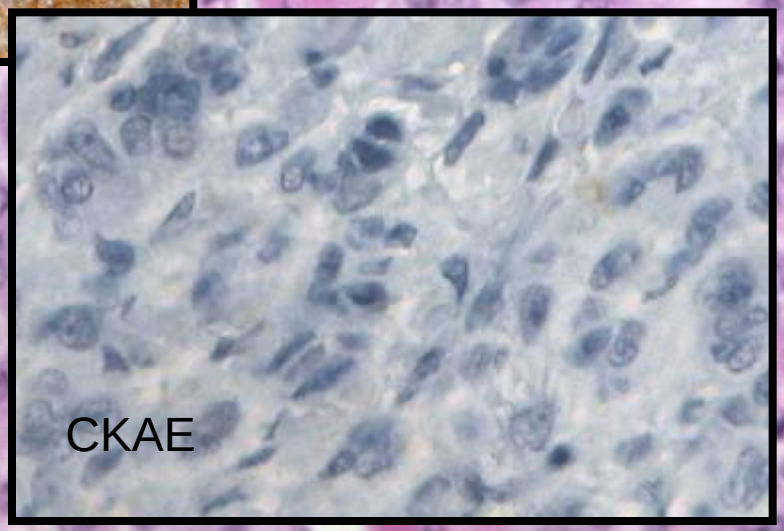
Submucose leiomyoma


Leiomyoma M88900


actin

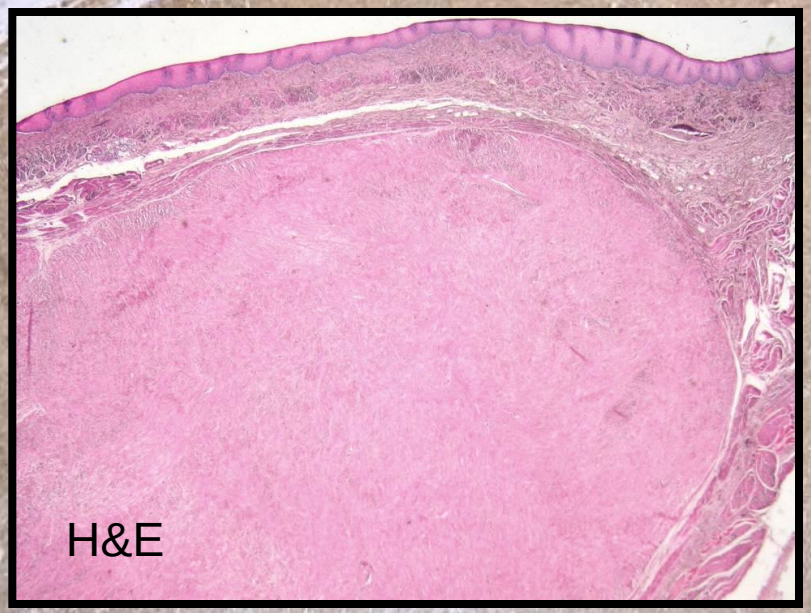
Leiomyoma - epithelioid – and many more histopathology subtypes – *mitotically active, pleomorphic, myxoid…diff. dg.!*

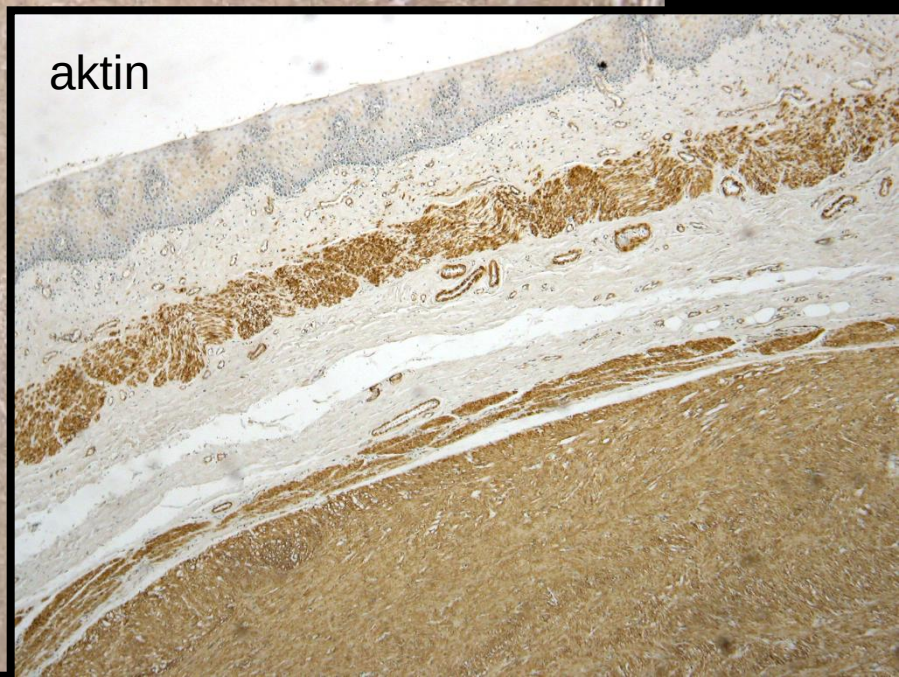




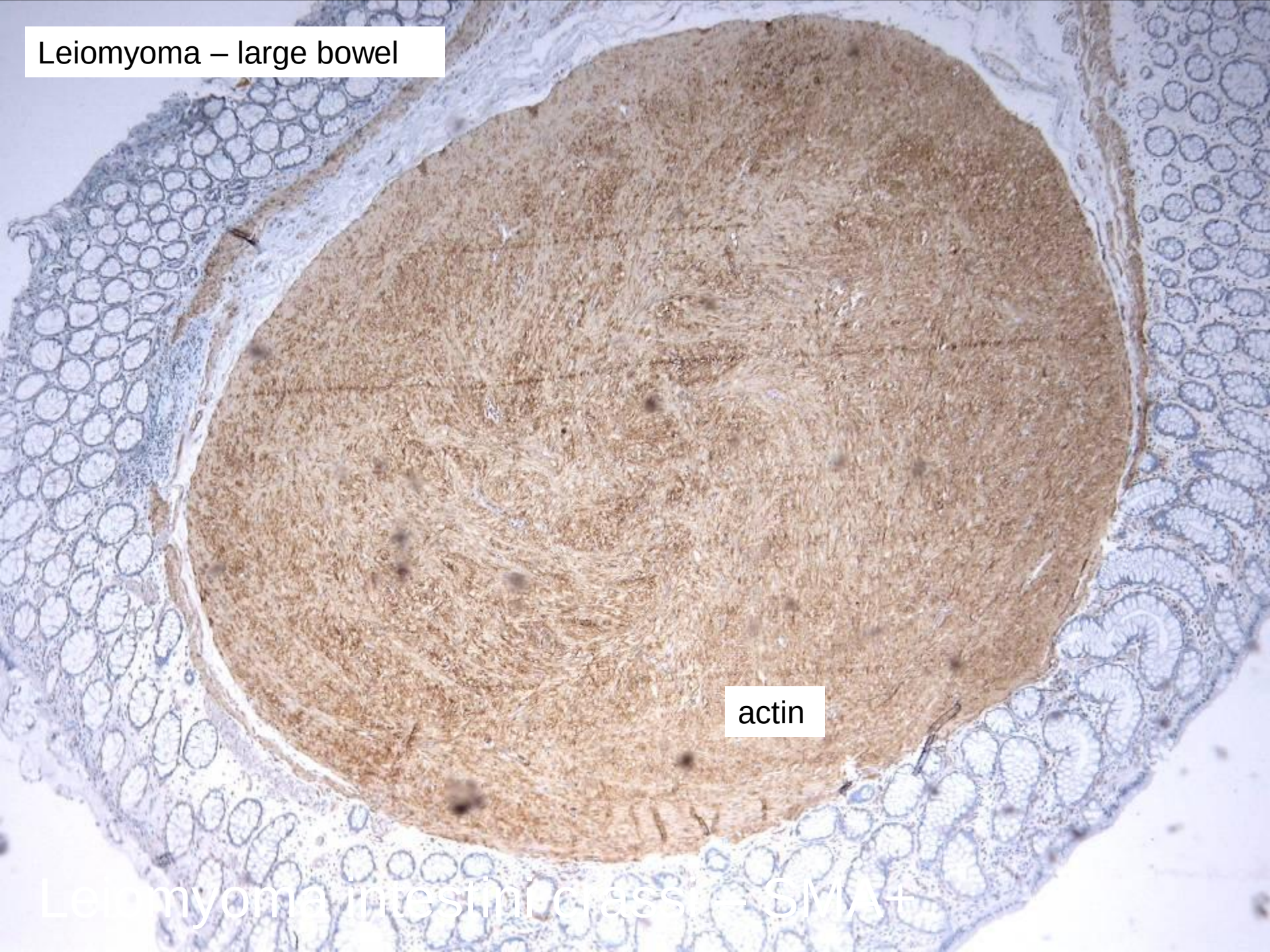
Leiomyoma oesophagi

aktin



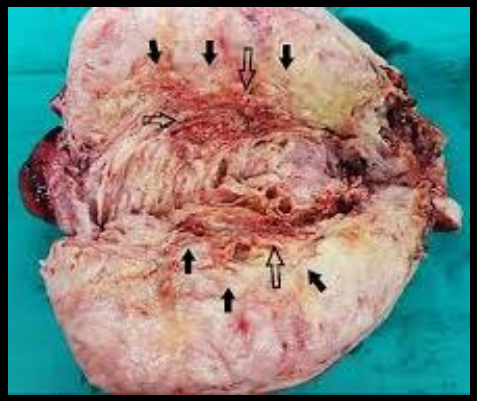


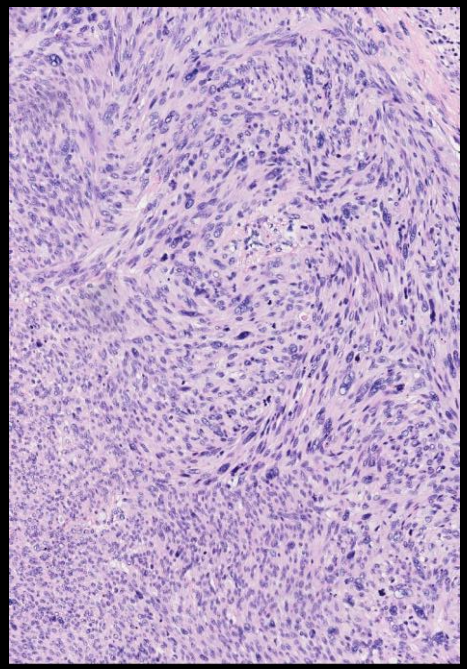
Leiomyoma – large bowel



Leiomyoma intestinal tissue, SMA+

Leiomyosarcoma –malignant tumour of smooth muscle cells M88903





- uterus (mostly de novo), deep soft tissues
- large, necrotizing, haemorrhages
- Micro: cytology atypia, mitoses – variable amount needed in relation to the subtypes

Mesenchymal neoplasms

Benign	Borderline	Malignant
fibroma	fibromatoses	fibrosarcoma
lipoma	lipoblastoma	liposarcoma
leiomyoma	atypical smooth muscle cell tumors	leiomyosarcoma
rhabdomyoma		rhabdomyosarcoma
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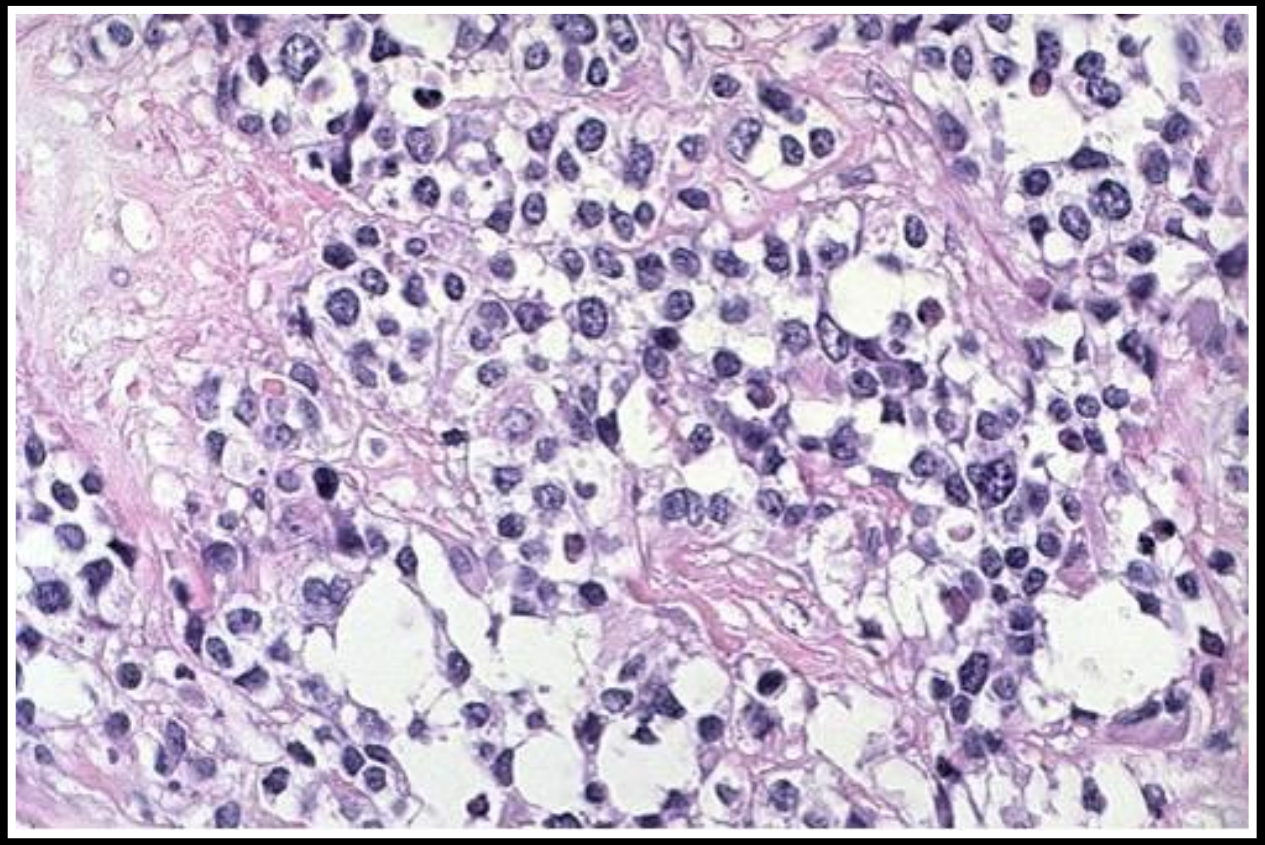
chondroma	chondroblastoma	chondrosarcoma
chordoma		*invasive* chordoma
osteoma	osteoid osteoma <2cm osteoblastoma >2cm	osteosarcoma
!!!		lymphoma/leukaemia

Rhabdomyosarcoma - embryonal (mostly children), alveolar - adolescents, pleomorphic – adults)



grape-like mass, solid

nasopharyngeal region
urogenital tract
extremities…

Markers: desmin, actin, MyoD1, myogenin…

Mesenchymal neoplasms

Benign	Borderline	Malignant
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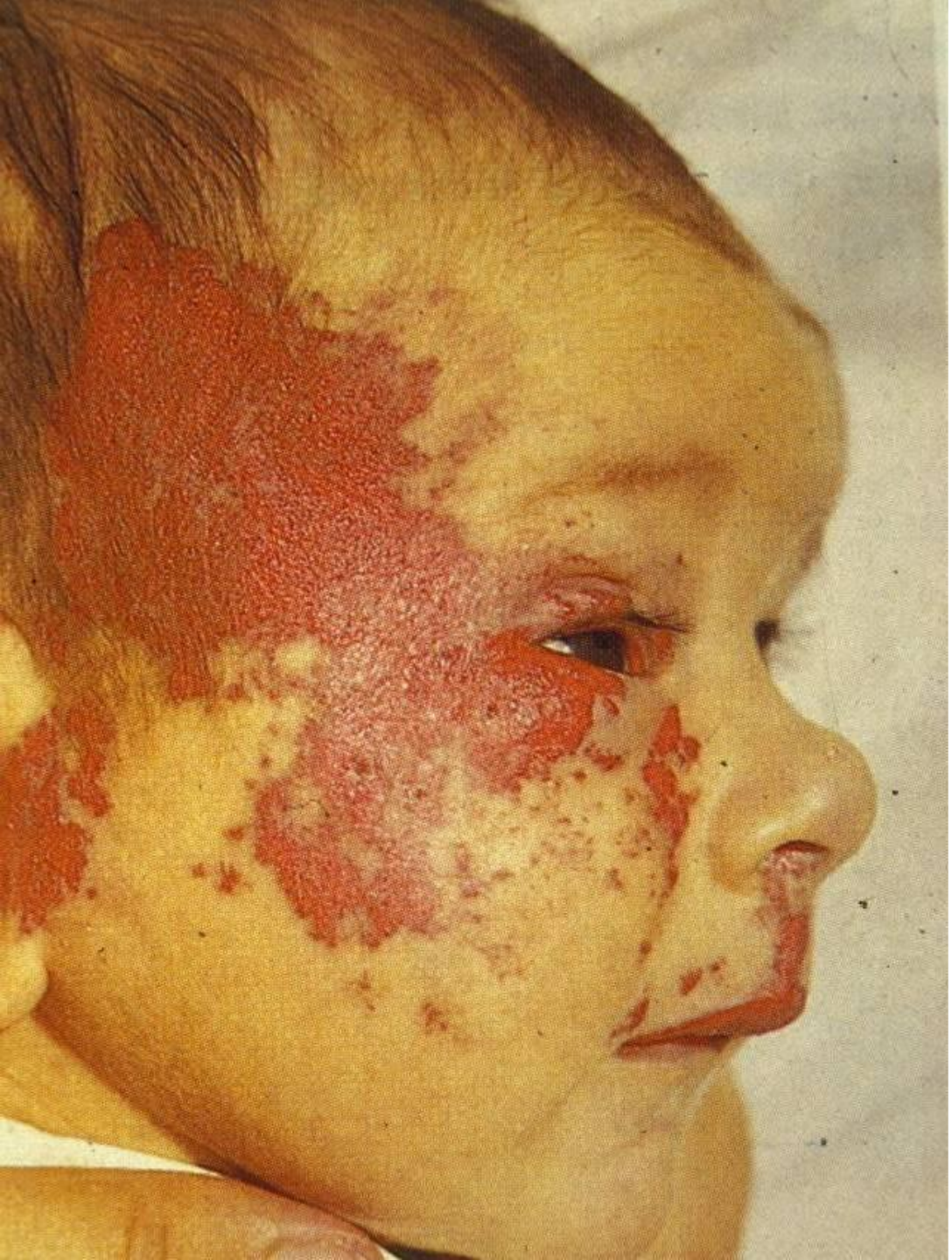
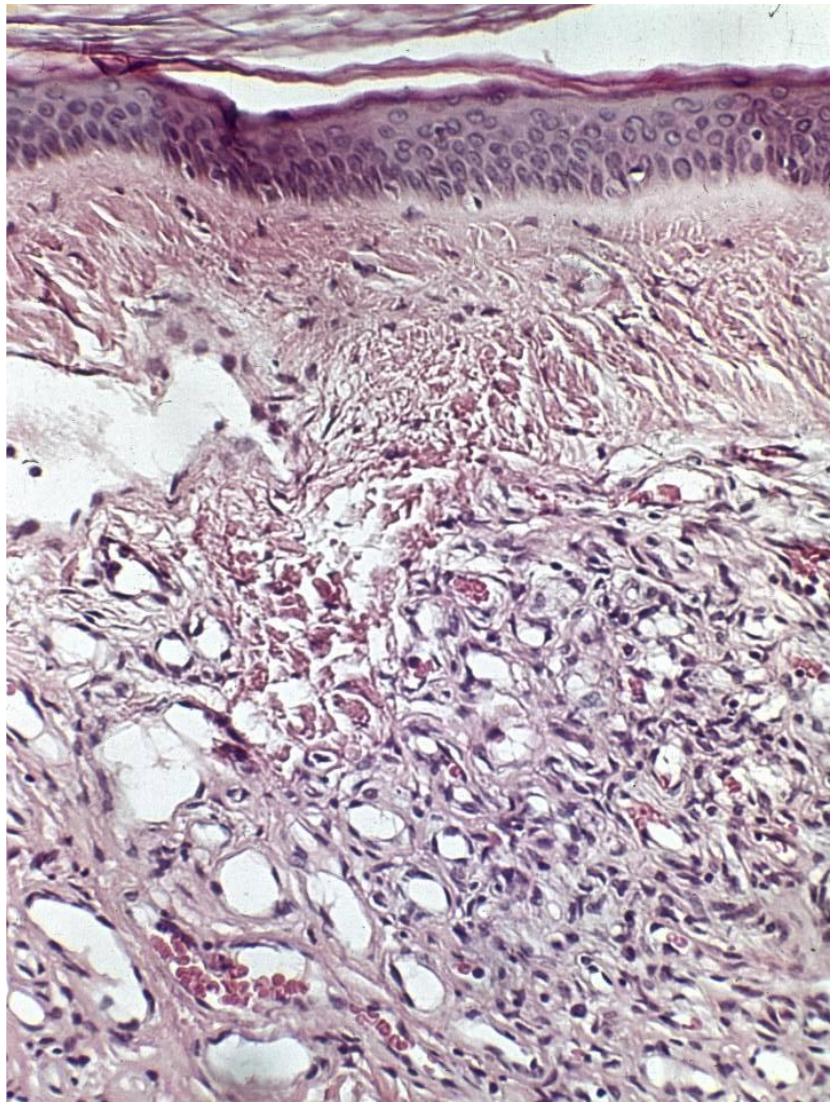
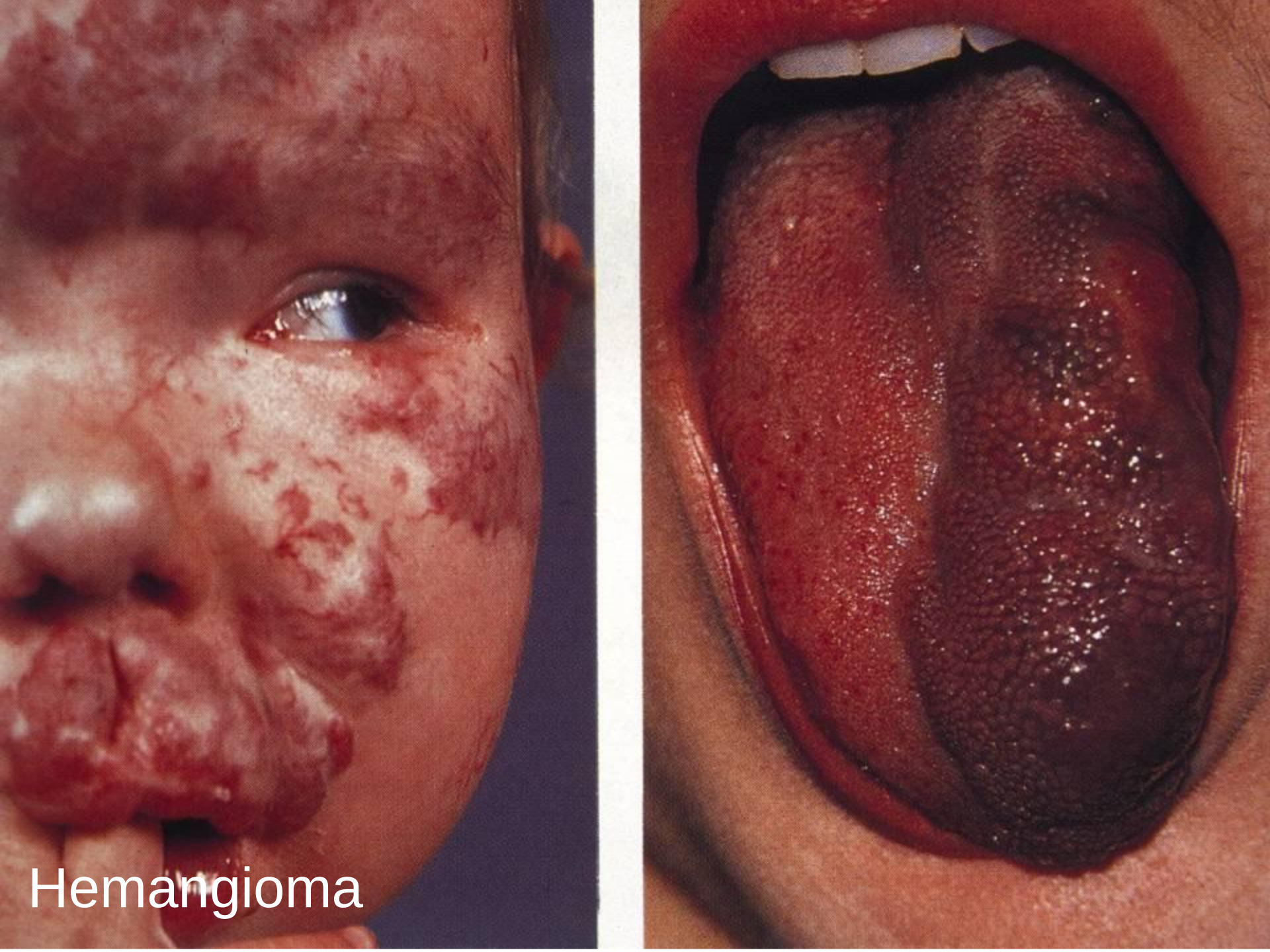
chordoma		*invasive* chordoma
osteoma	osteoid osteoma <2cm osteoblastoma >2cm	osteosarcoma
!!!		lymphoma/leukaemia

Naevus flammeus –

vascular ectasia - pseudotumor

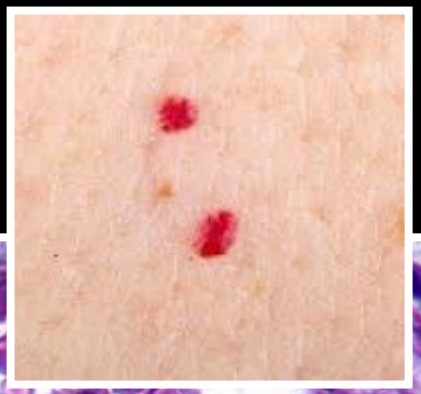


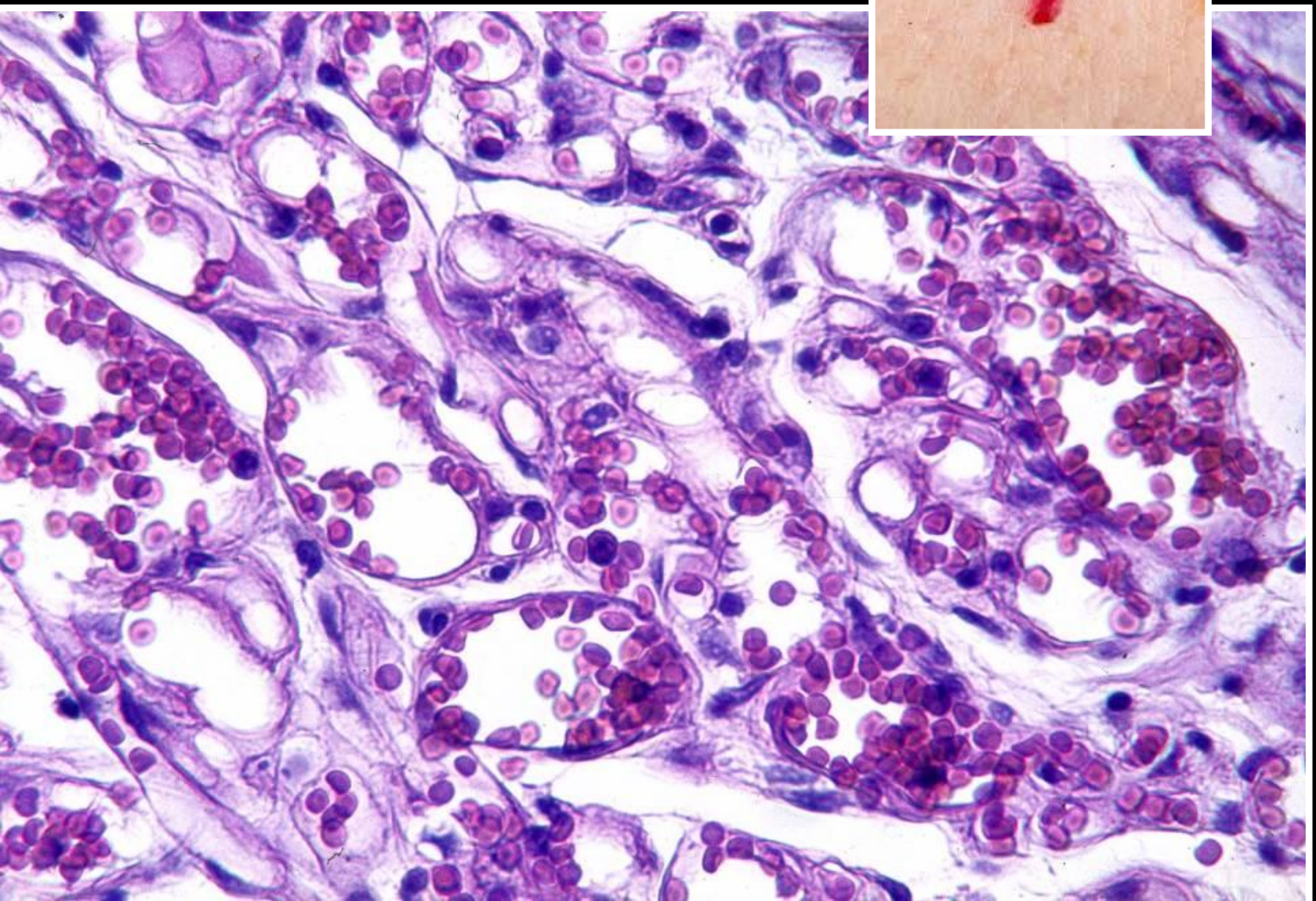



Hemangioma

Capillary hemangioma – cherry hemangioma

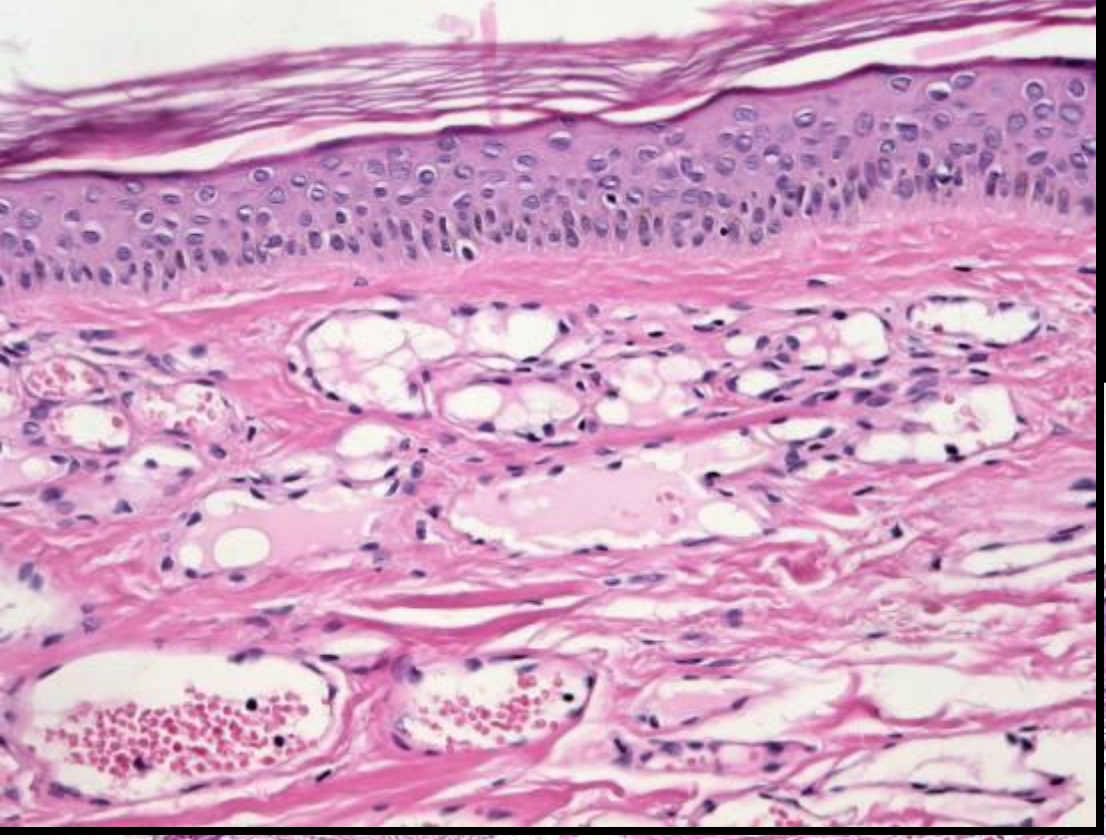
M 9120/0





WHO – skin
5th ed.
17 subtypes

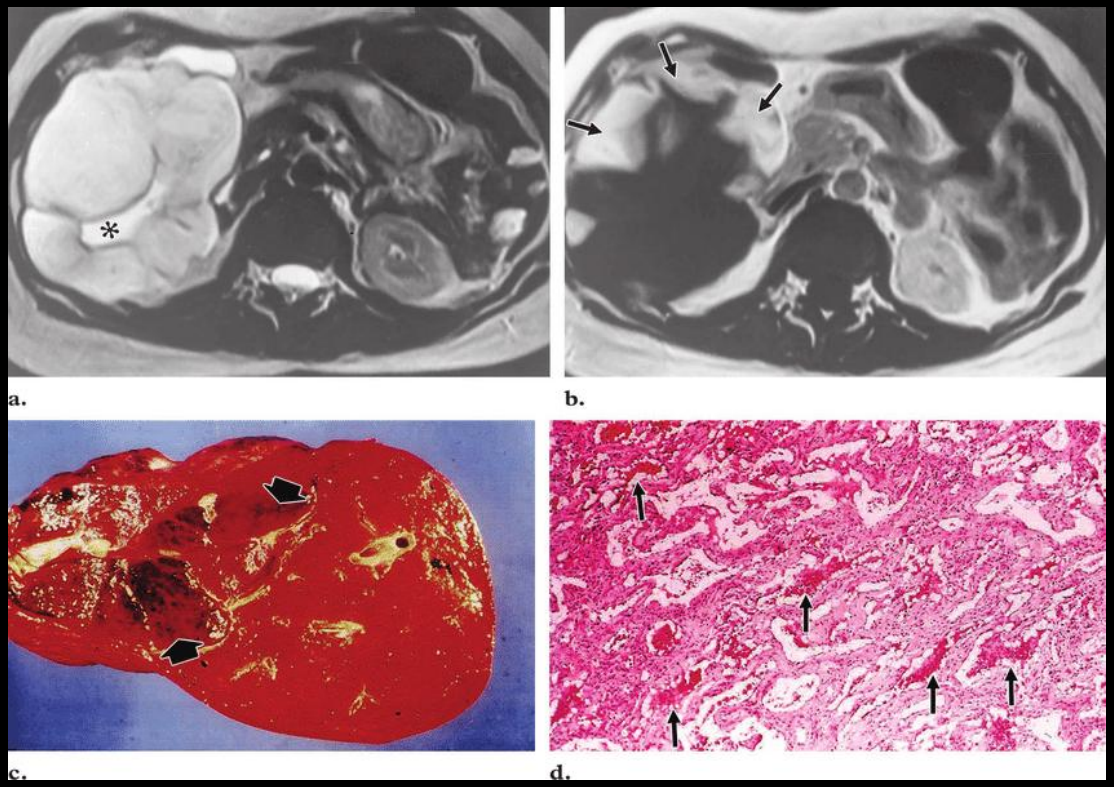
Capillary ectatic hemangioma

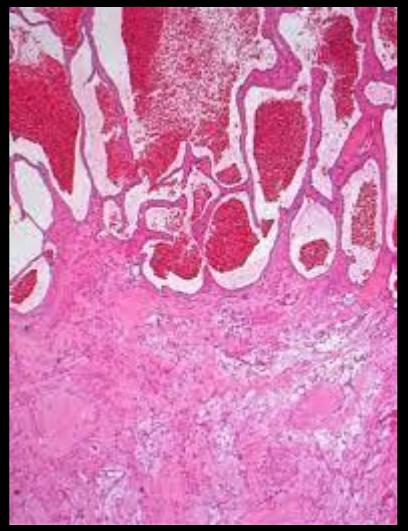


Cavernous hemangioma

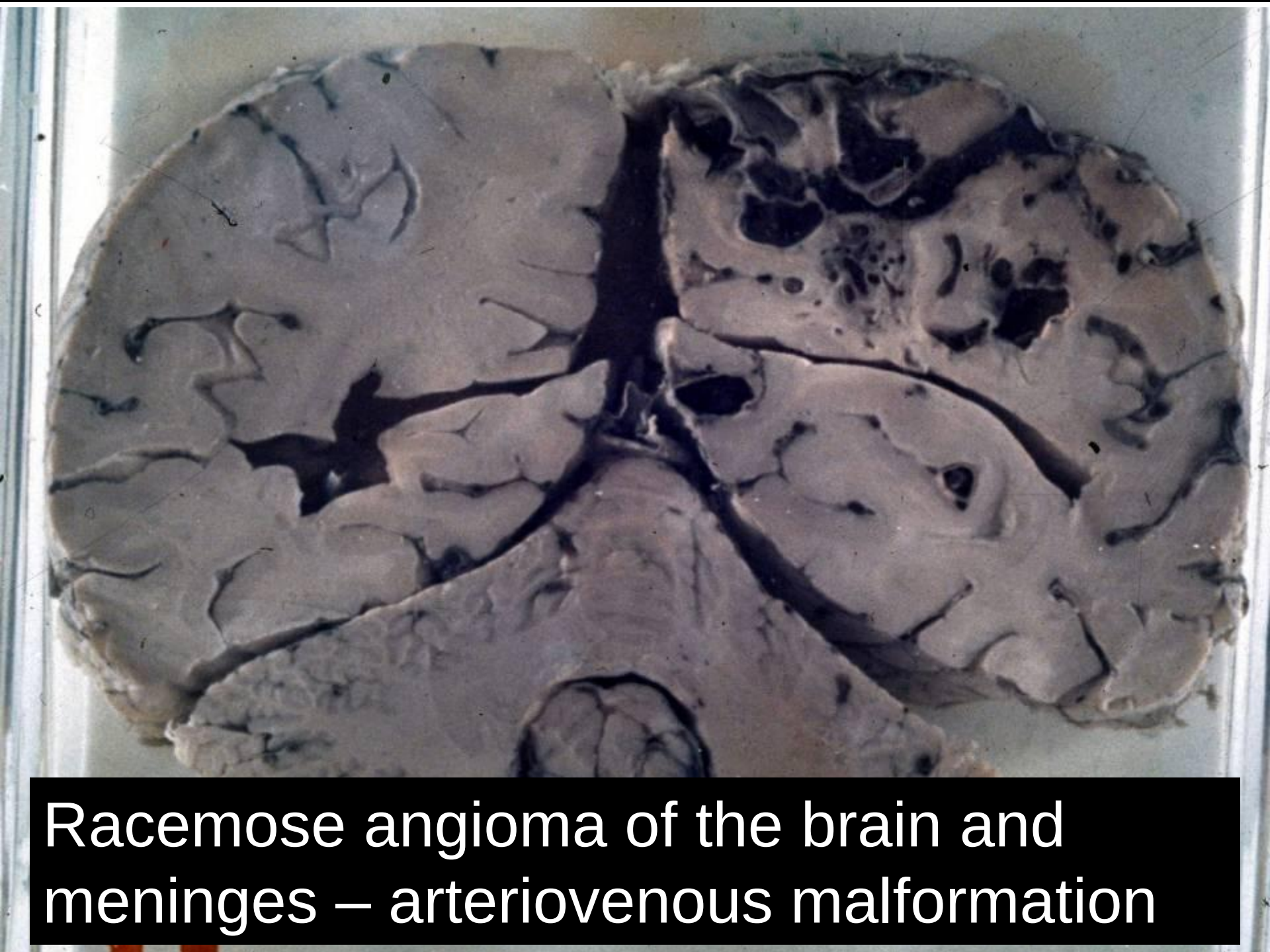
liver, mesenterium, orbita, vertebra….

Thin-walled vessels or blood-filled sinuses lined by a single layer of endothelium. Focal thrombi, fibrosis, hyalinization, calcification…





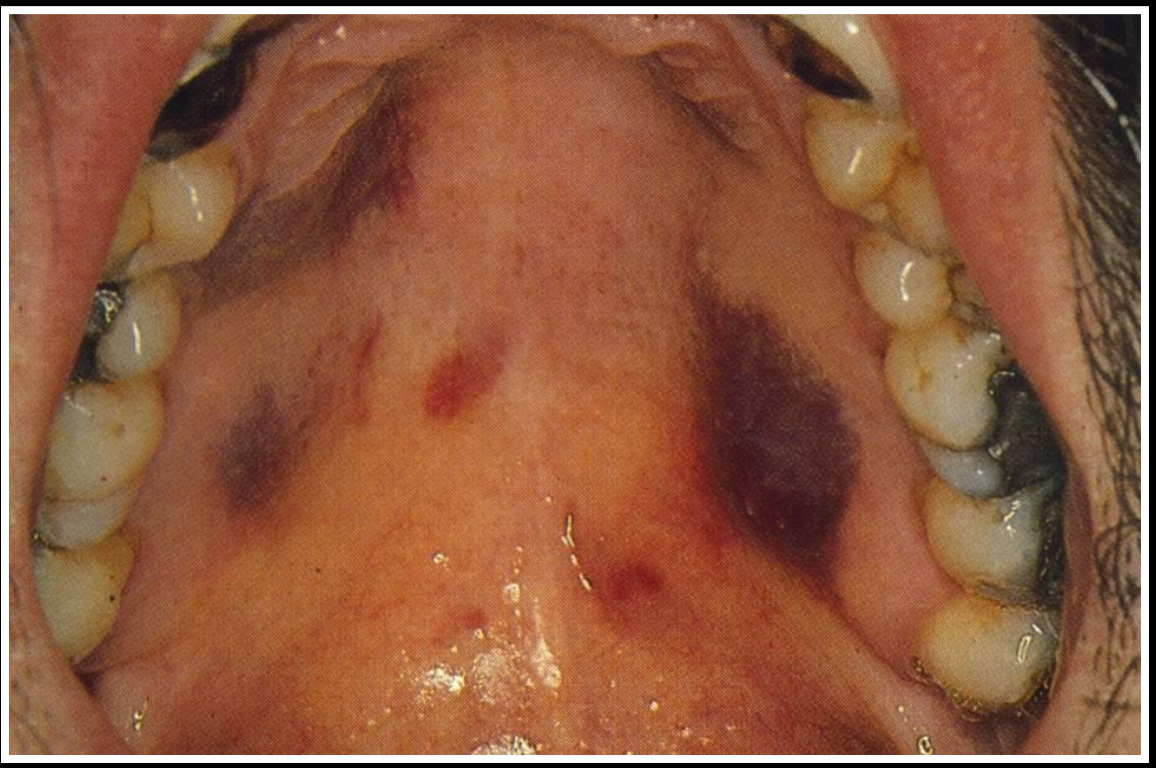
Diff. dg.!
Risk
of bleeding



Racemose angioma of the brain and meninges – arteriovenous malformation

Kaposi Sarcoma – low grade angiosarcoma - locally aggressive

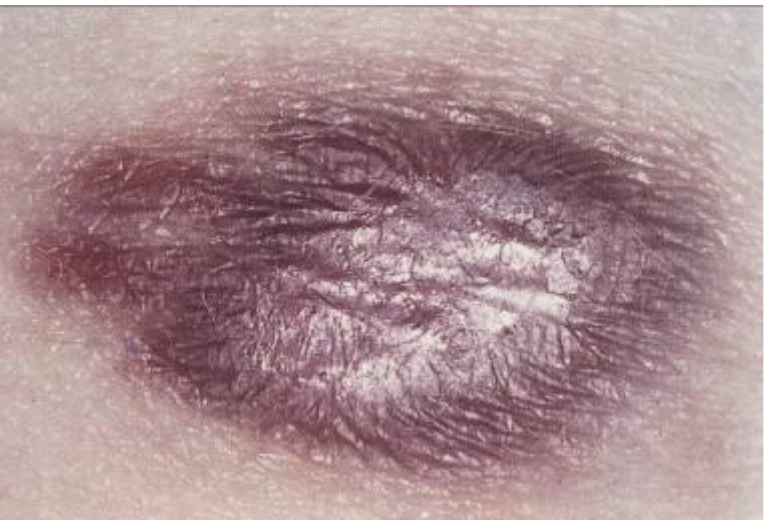
HHV8 - associated, multiple on the skin, lymph nodes and inner organs can be affected



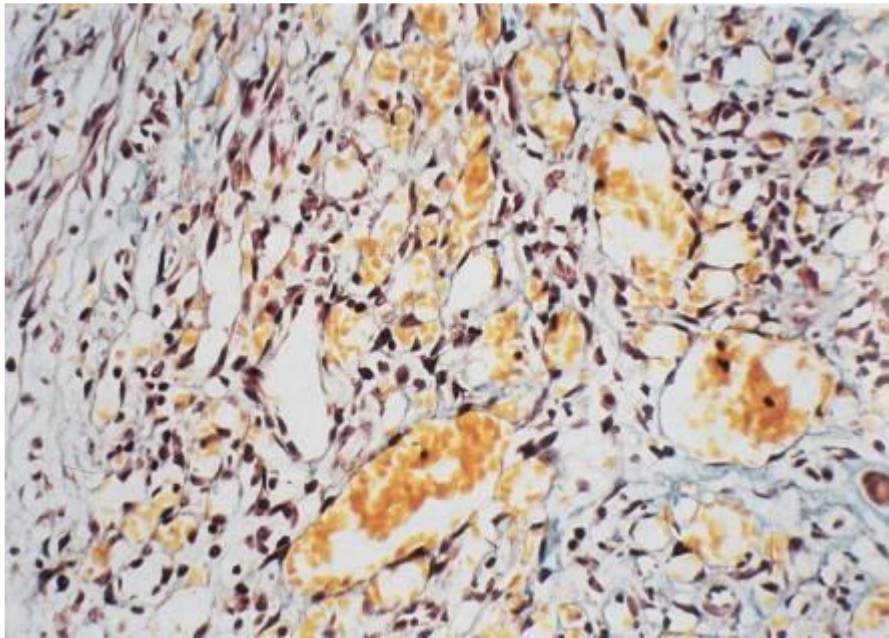
Four clinico-pathological subtypes:

- classic KS
- endemic African KS
- AIDS-associated KS
- iatrogenic (transplant-related) KS.

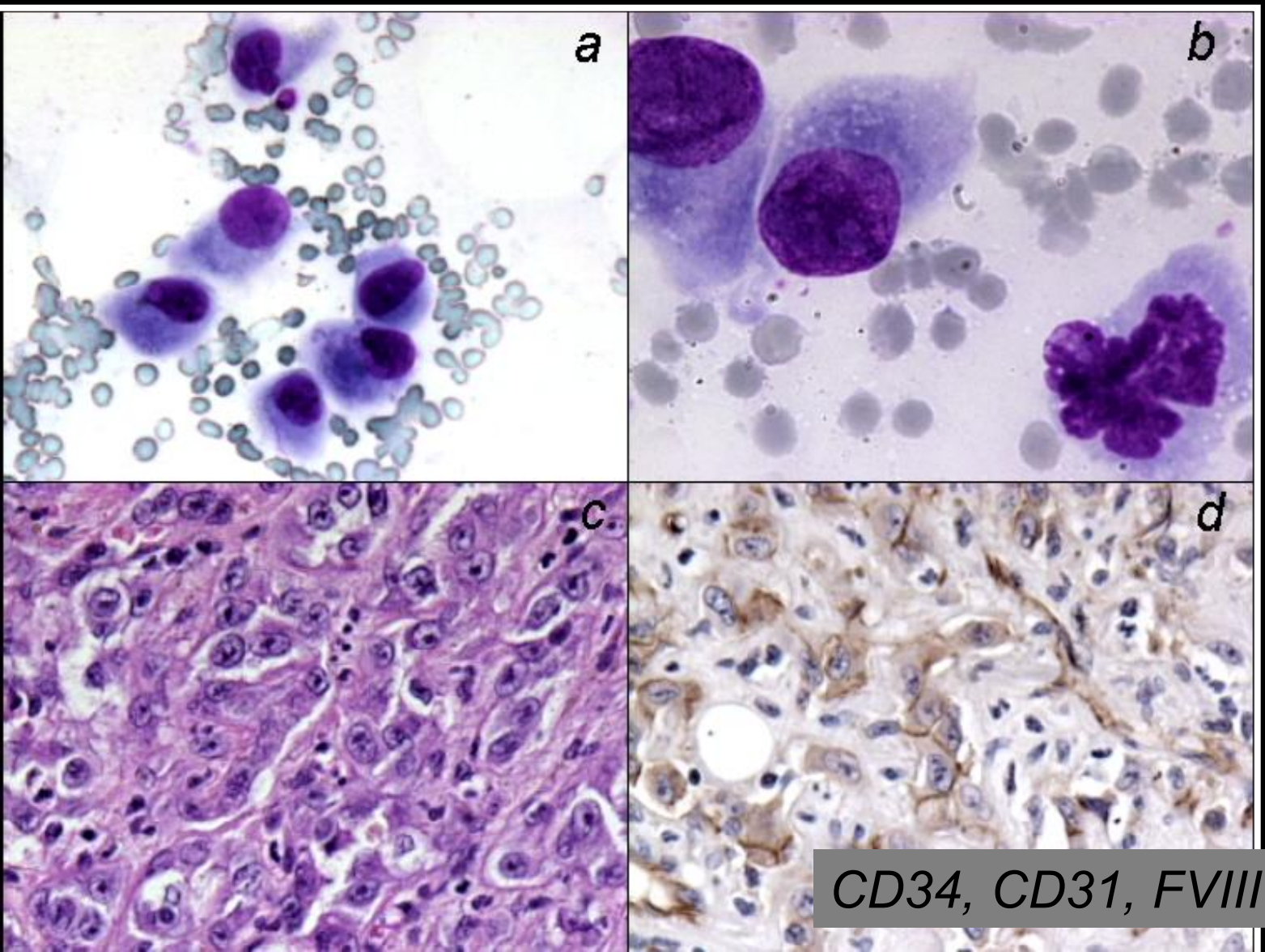
Kaposi sarcoma



HHV-8



Angiosarcoma – high grade endothelial malignancy



CD34, CD31, FVIII…

Mesenchymal neoplasms

Benign	Borderline	Malignant
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lipoma	lipoblastoma	liposarcoma
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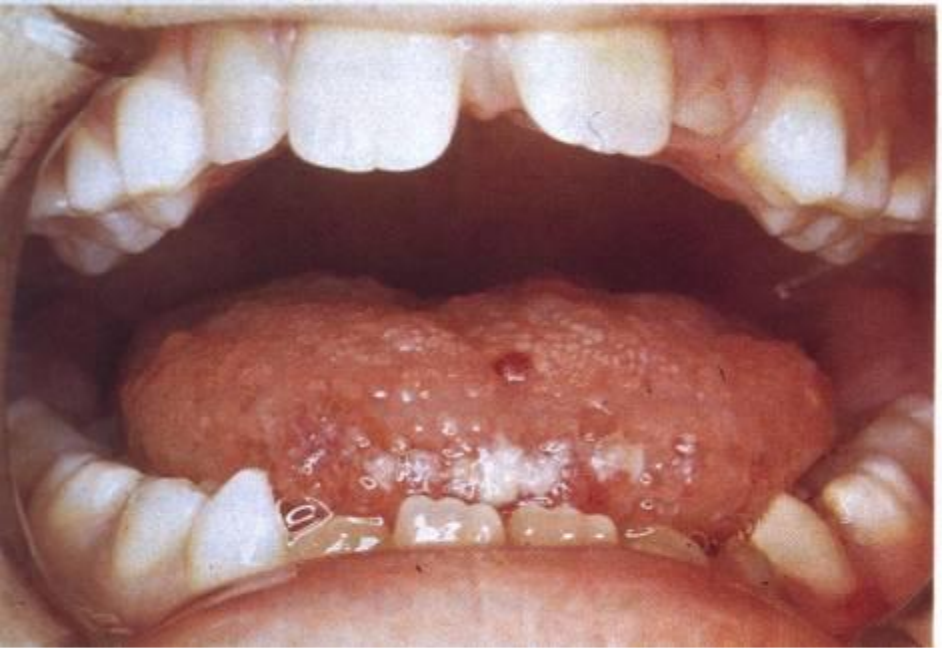
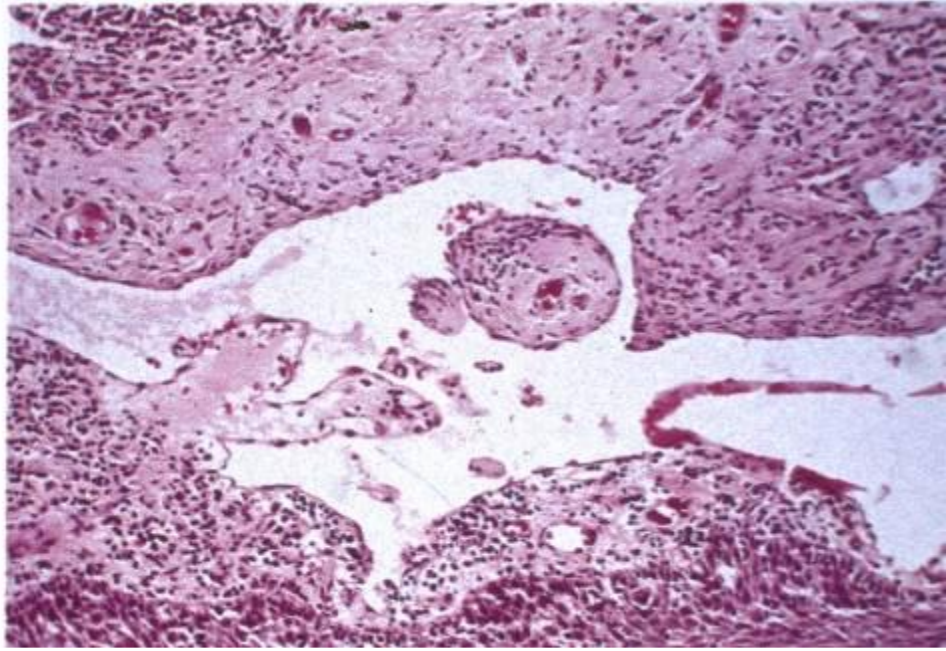
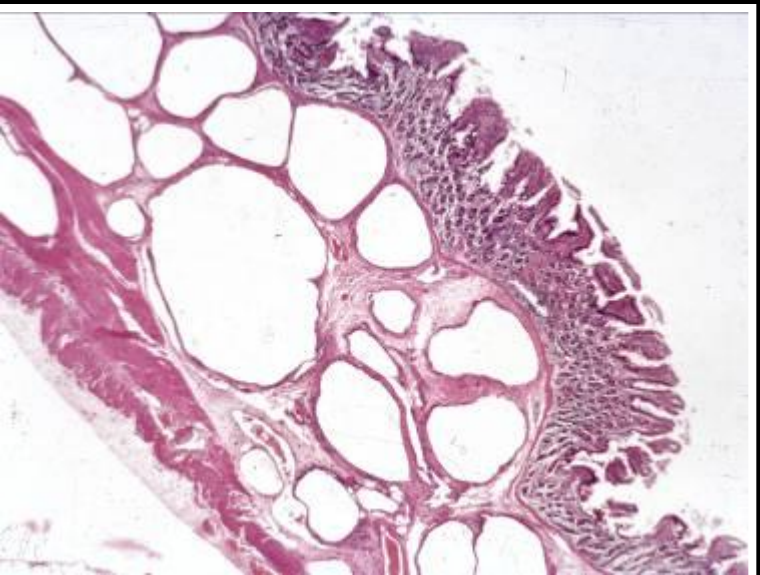


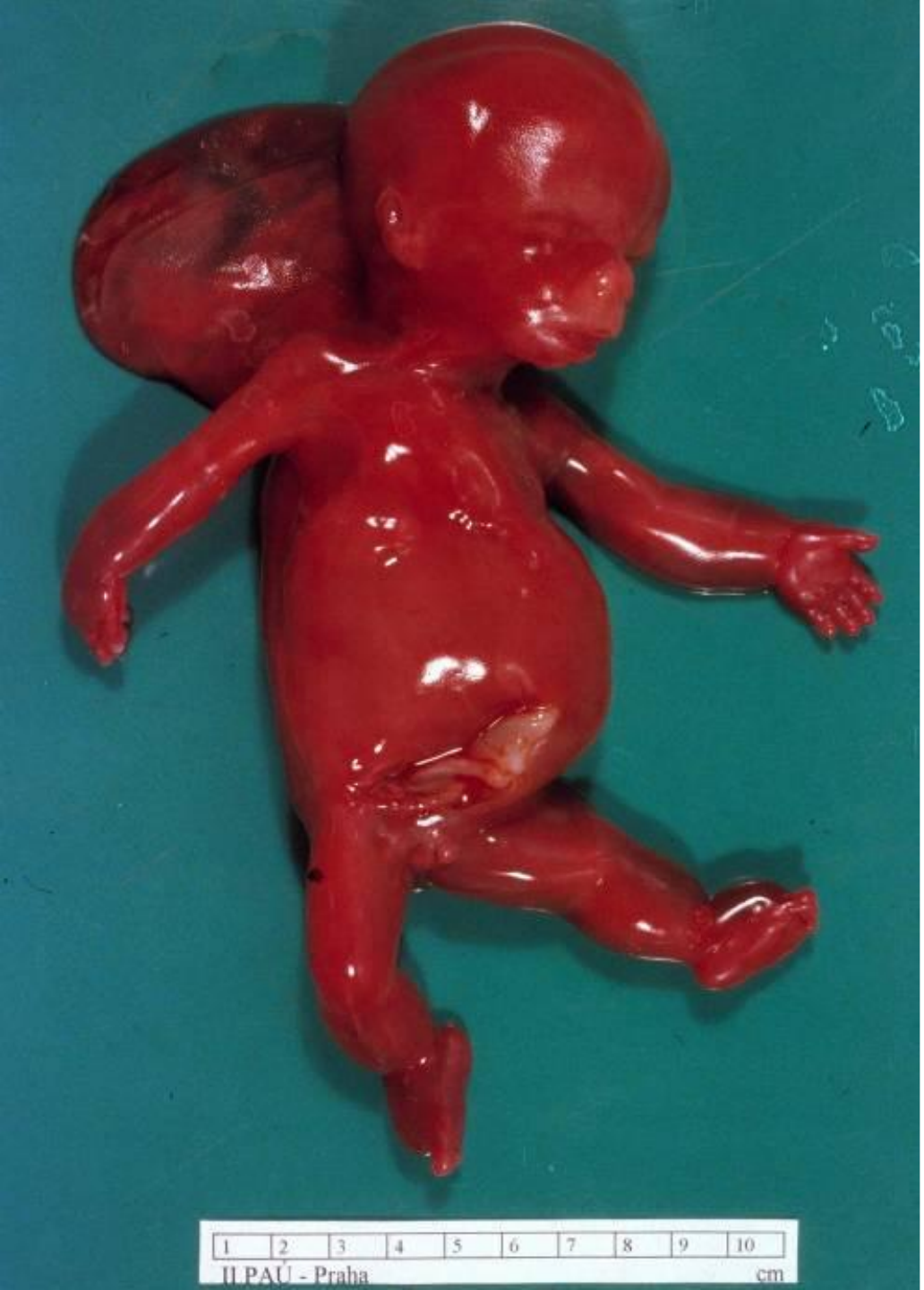


Congenital lymphangioma

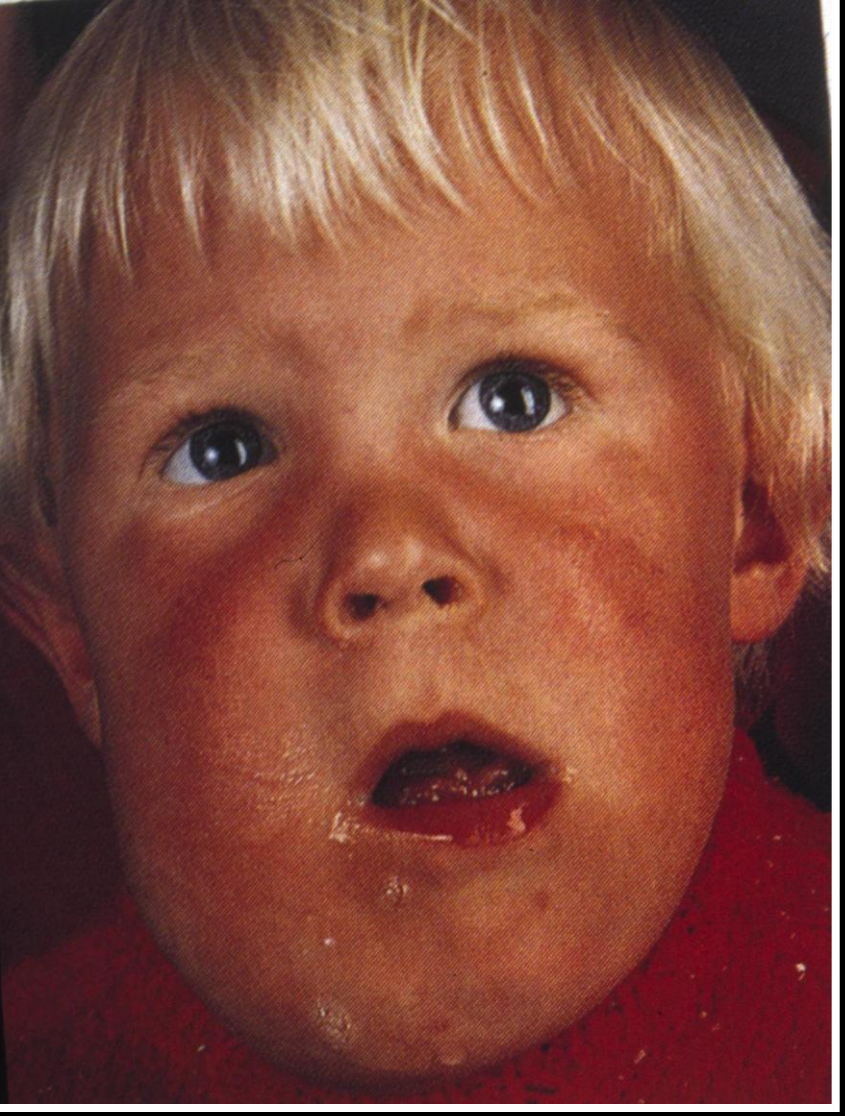


Podoplanin (D2-40) +

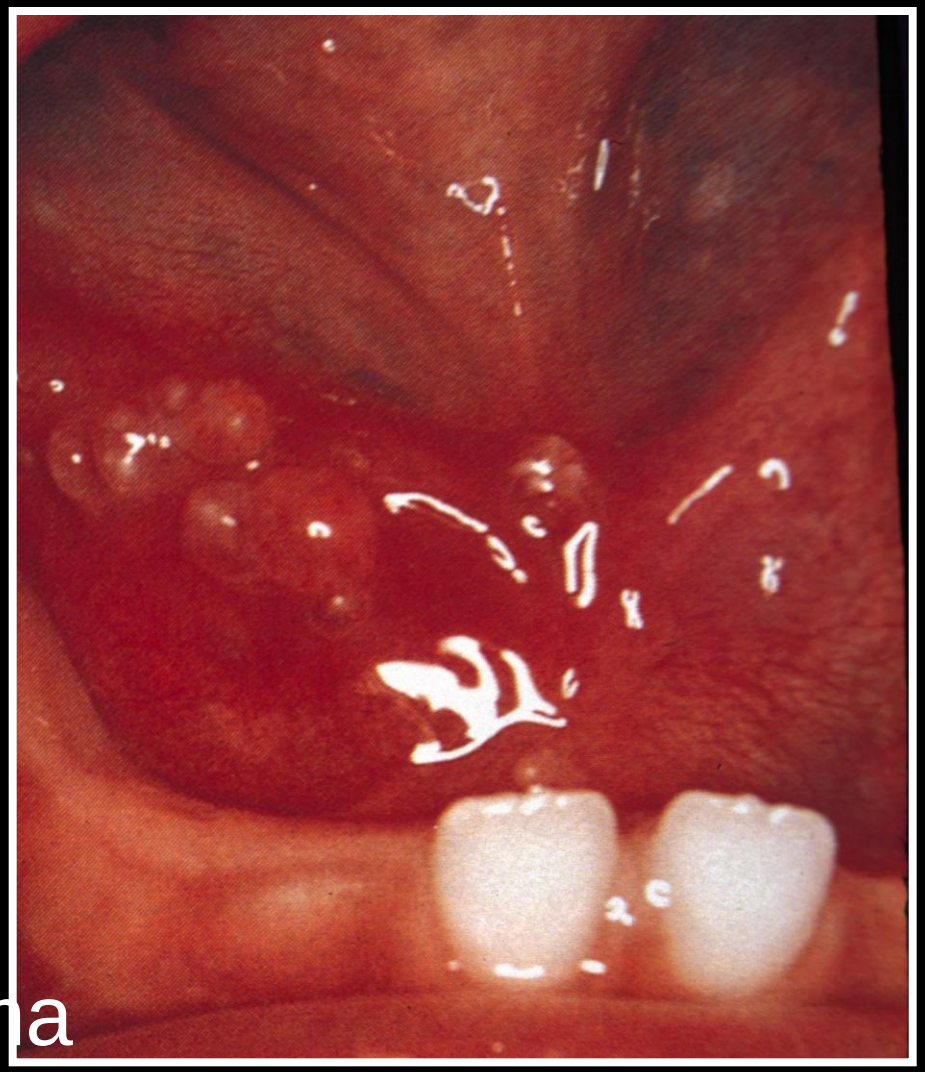
Chylangioma of the small bowel



Hygroma colli cysticum - congenital lymphangioma



Hygroma colli cysticum -



congenital lymphangioma

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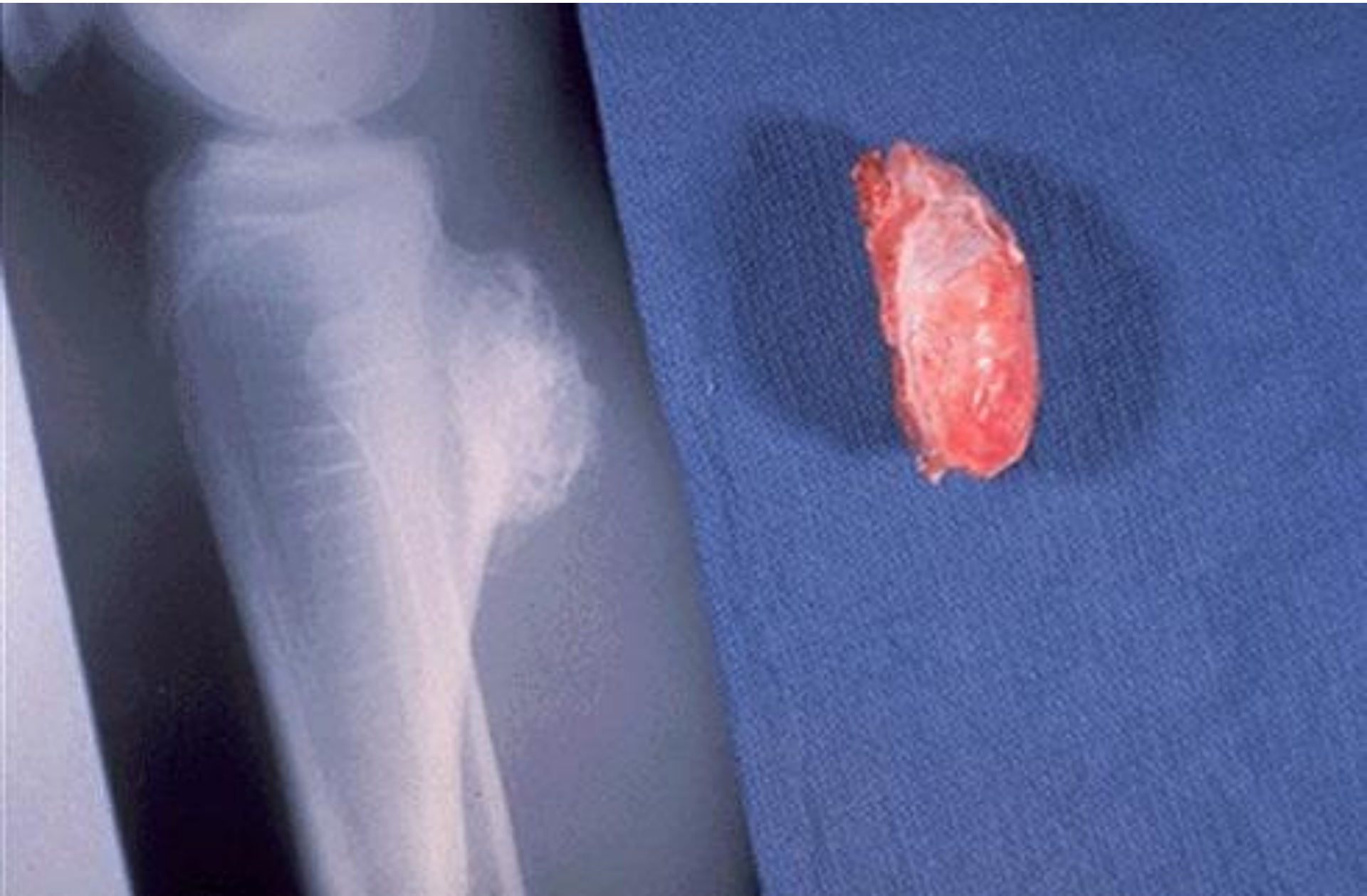
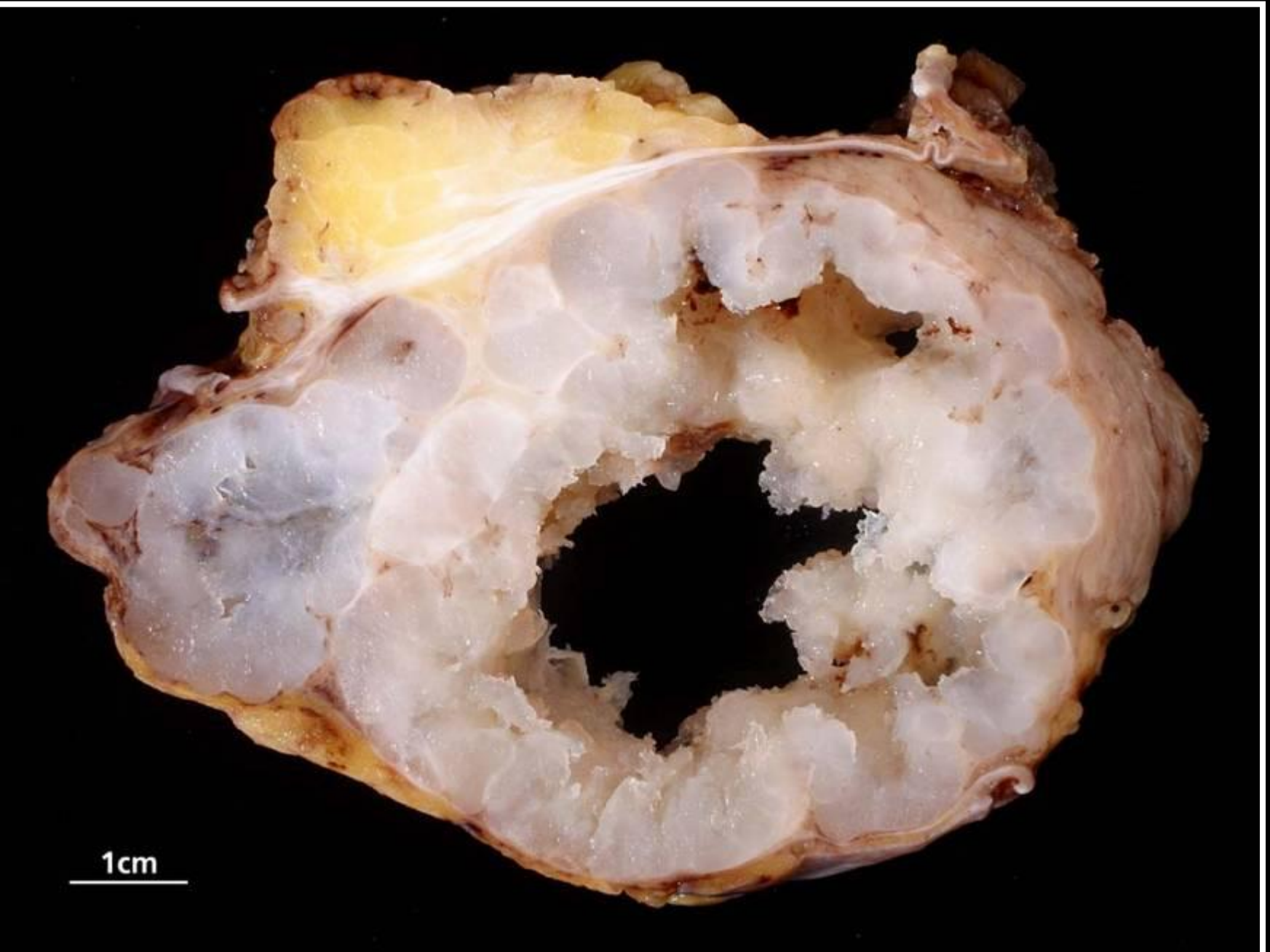
chordoma		*invasive* chordoma
osteoma	osteoid osteoma <2cm osteoblastoma >2cm	osteosarcoma
!!!		lymphoma/leukaemia

Osteochondroma

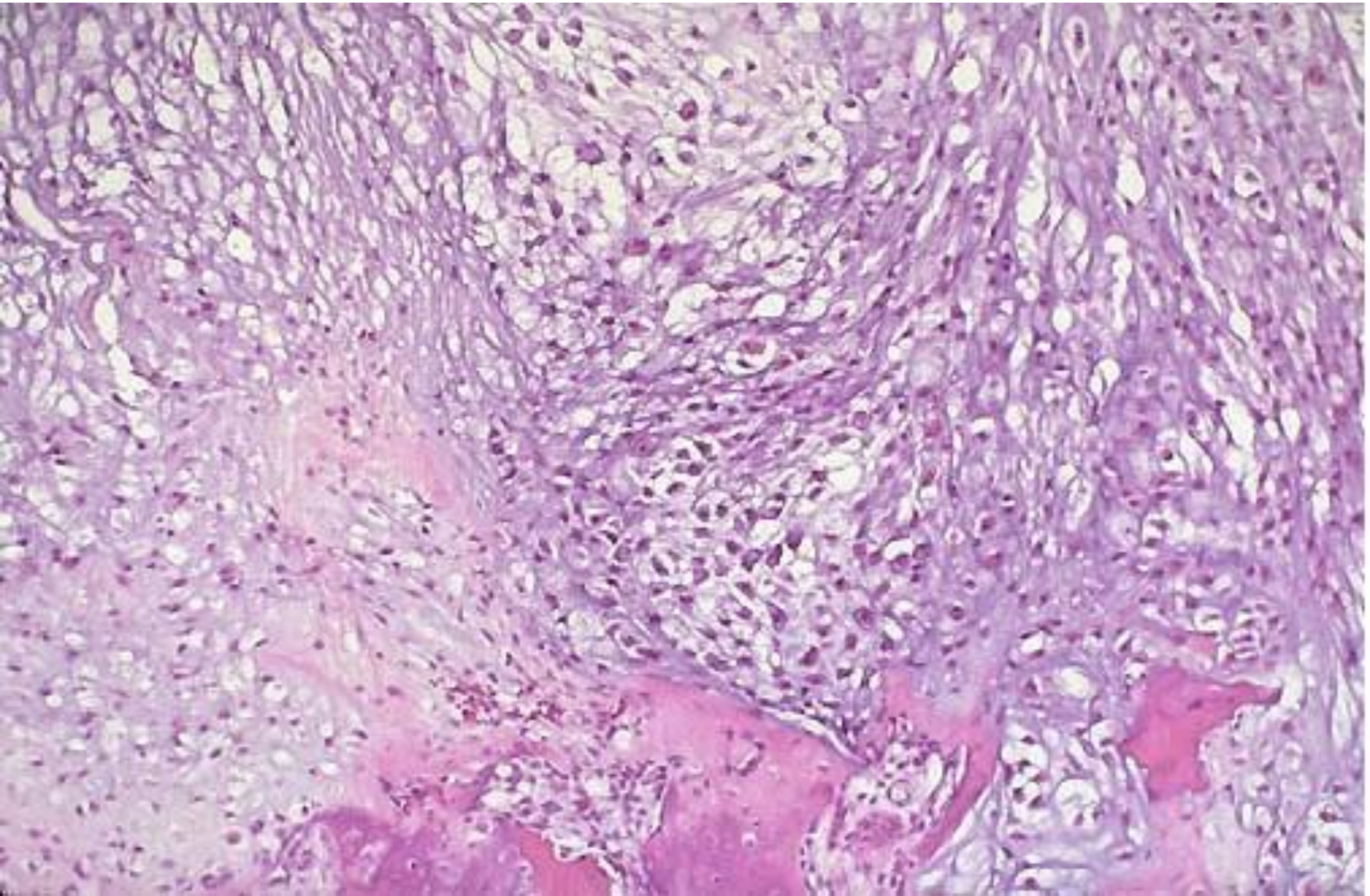


Osteochondroma – benign bone surface tumour of mature bone and cartilaginous cap

Chondrosarcoma G1 abdominal wall (PathoPic Basel)



Chondrosarcoma



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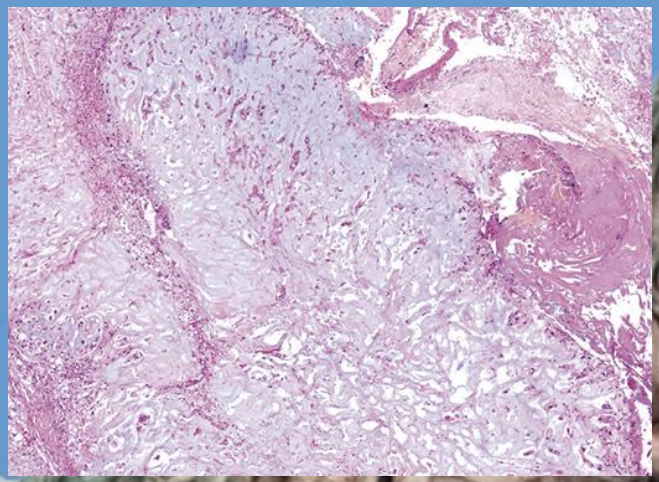
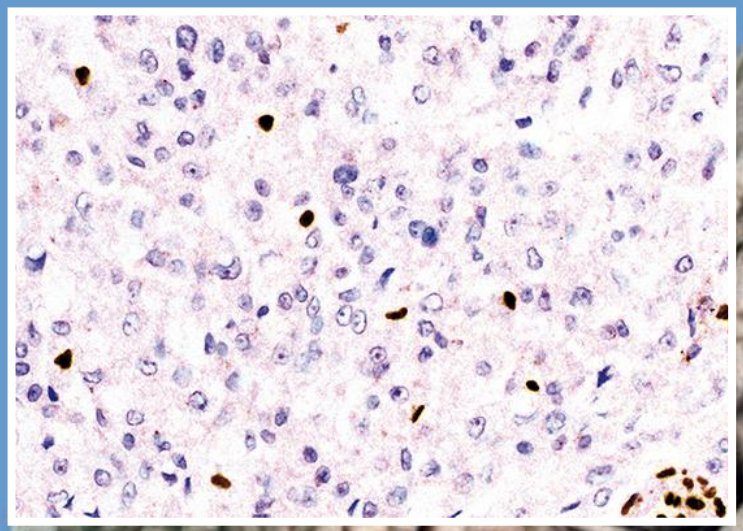
chordoma		*invasive* chordoma
osteoma	osteoid osteoma <2cm osteoblastoma >2cm	osteosarcoma
!!!		lymphoma/leukaemia

Chordoma M 9370/3



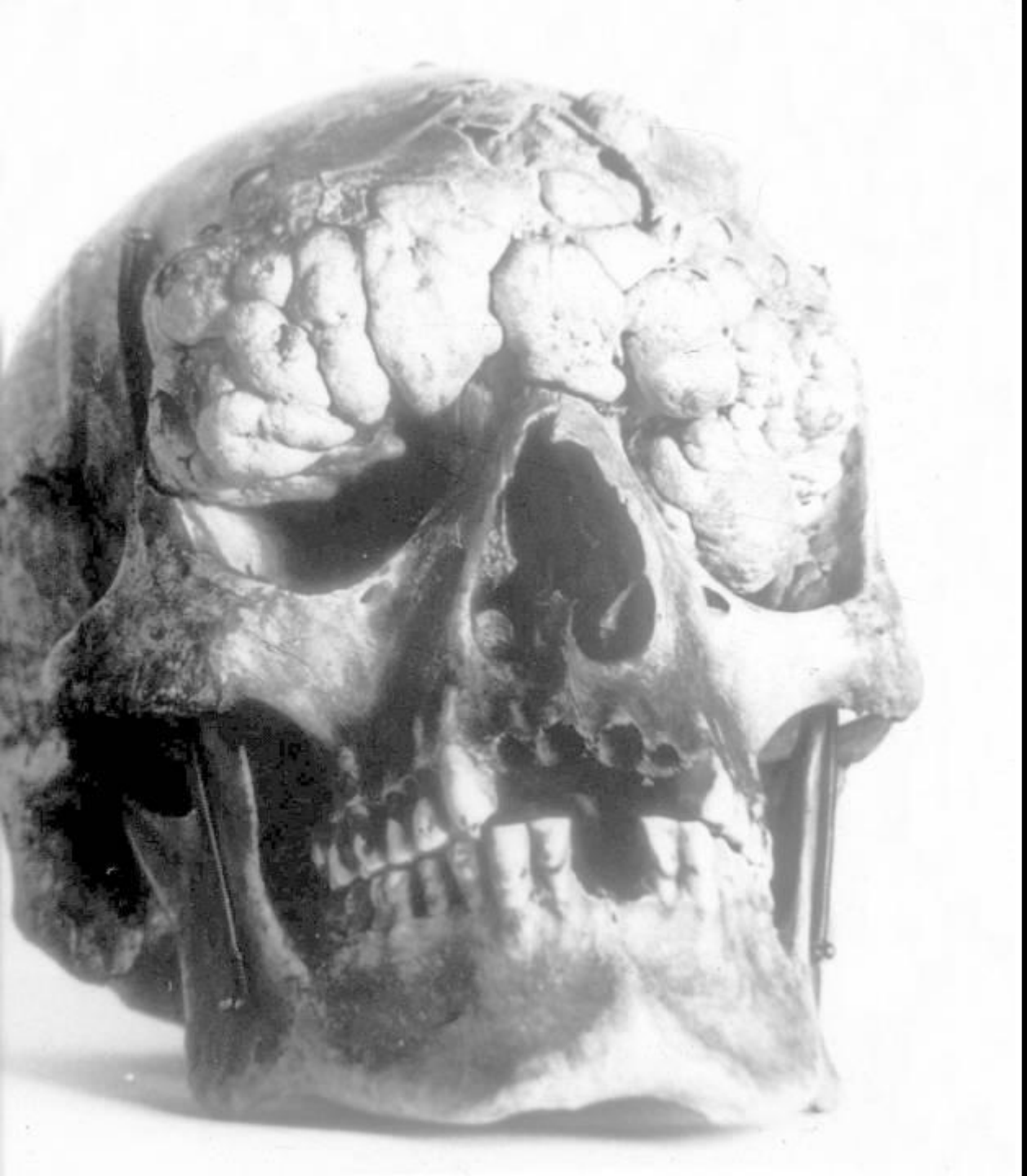
- remnants of notochord
  - sacral 60%
  - sphenooccipital 25%
  - cervical 10%
  - thoracolumbal 5%

Chordoma M 9370/3



- remnants of notochord
  - sacral 60%
  - sphenooccipital 25%
  - cervical 10%
  - thoracolumbal 5%

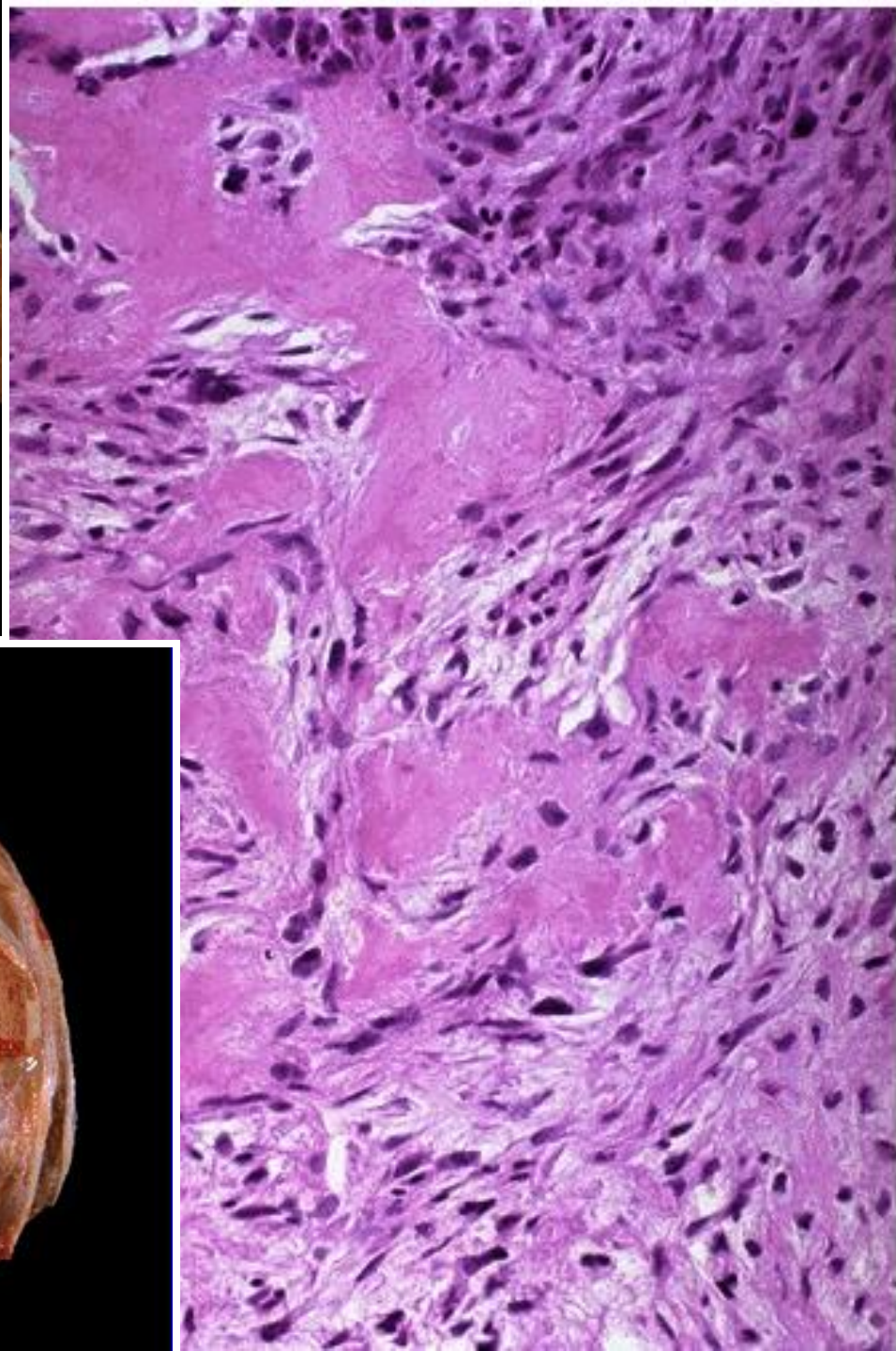
Loss of SMARCB1 (INI1) expression in chordomas results from a homozygous deletion of the *SMARCB1* gene

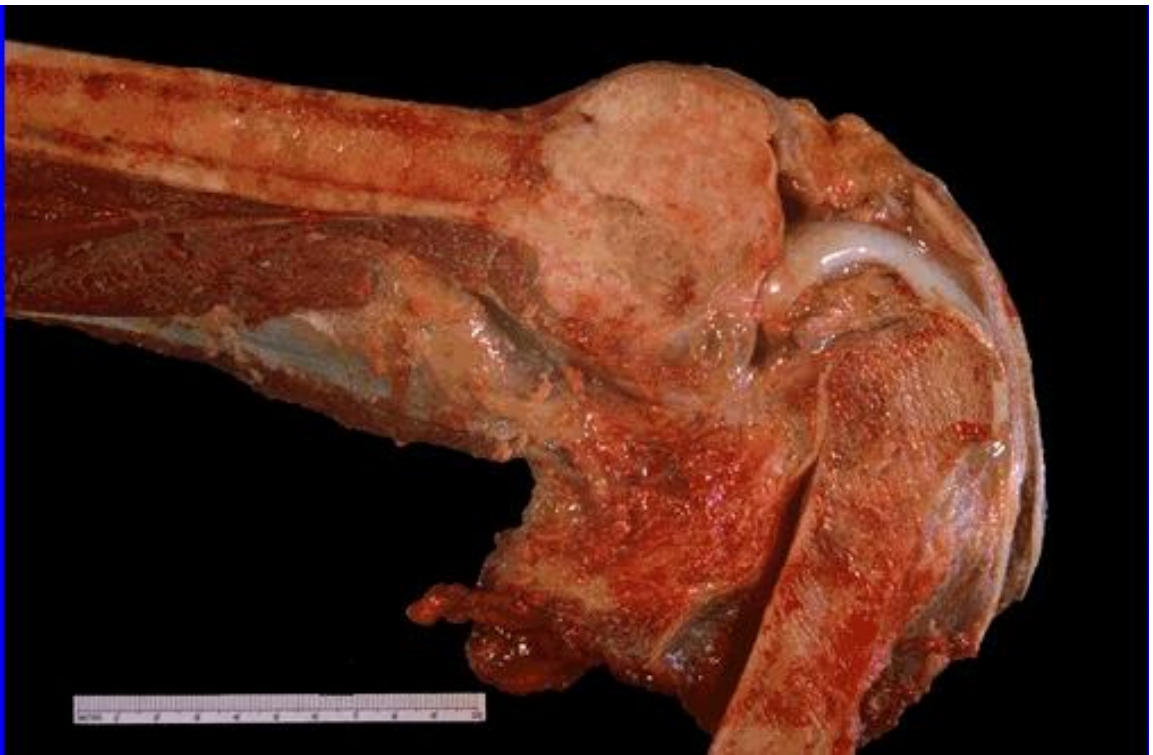


Osteoma

- solitary or multiple
- any age
- associated with Gardner syndrome
  - multiple intestinal polyps
  - supernummerary teeth
  - deep located desmoids
  - autosomal dominant - AD
  - APC gene

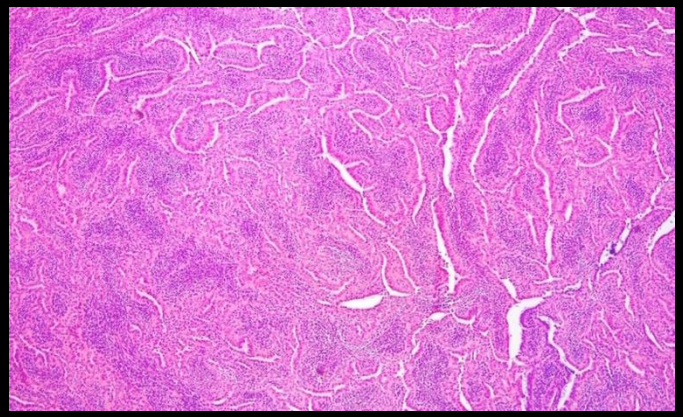
Osteosarcoma





Tumours of uncertain histogenesis

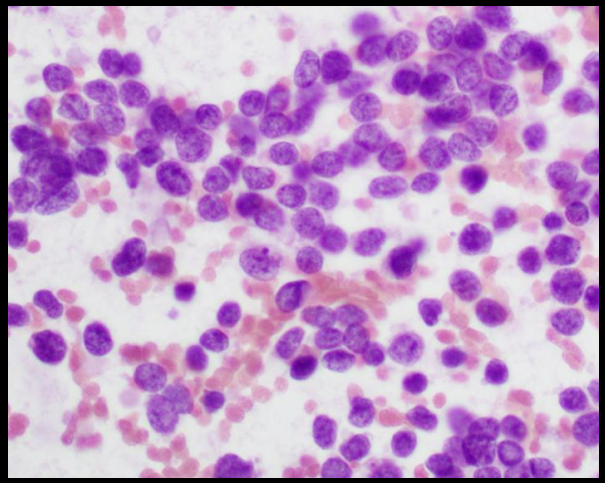
- Synovial sarcoma (a misnomer for high grade neoplasia with biphasic fusiform and epithelioid component (less frequently monophasic) and expression of epithelial (EMA, CKs,) and other (BCl2, CD99) markers in both components
- younger adults, extremities

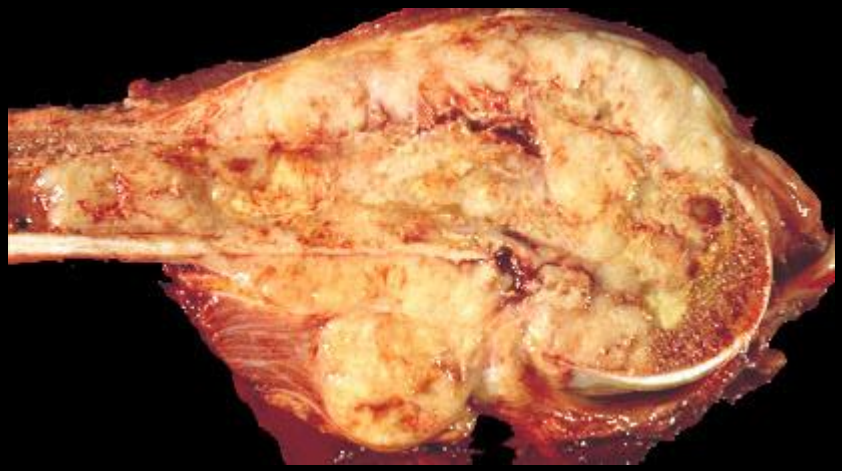


Tumours of uncertain histogenesis

Ewing sarcoma family of tumours

- small round cell tumours with mesenchymal and neuroectodermal features
- young adults, bones and soft tissues
- most frequently translocation t(11:22) - fusion gene EWSR1/FLI1 (and other molecular variants)



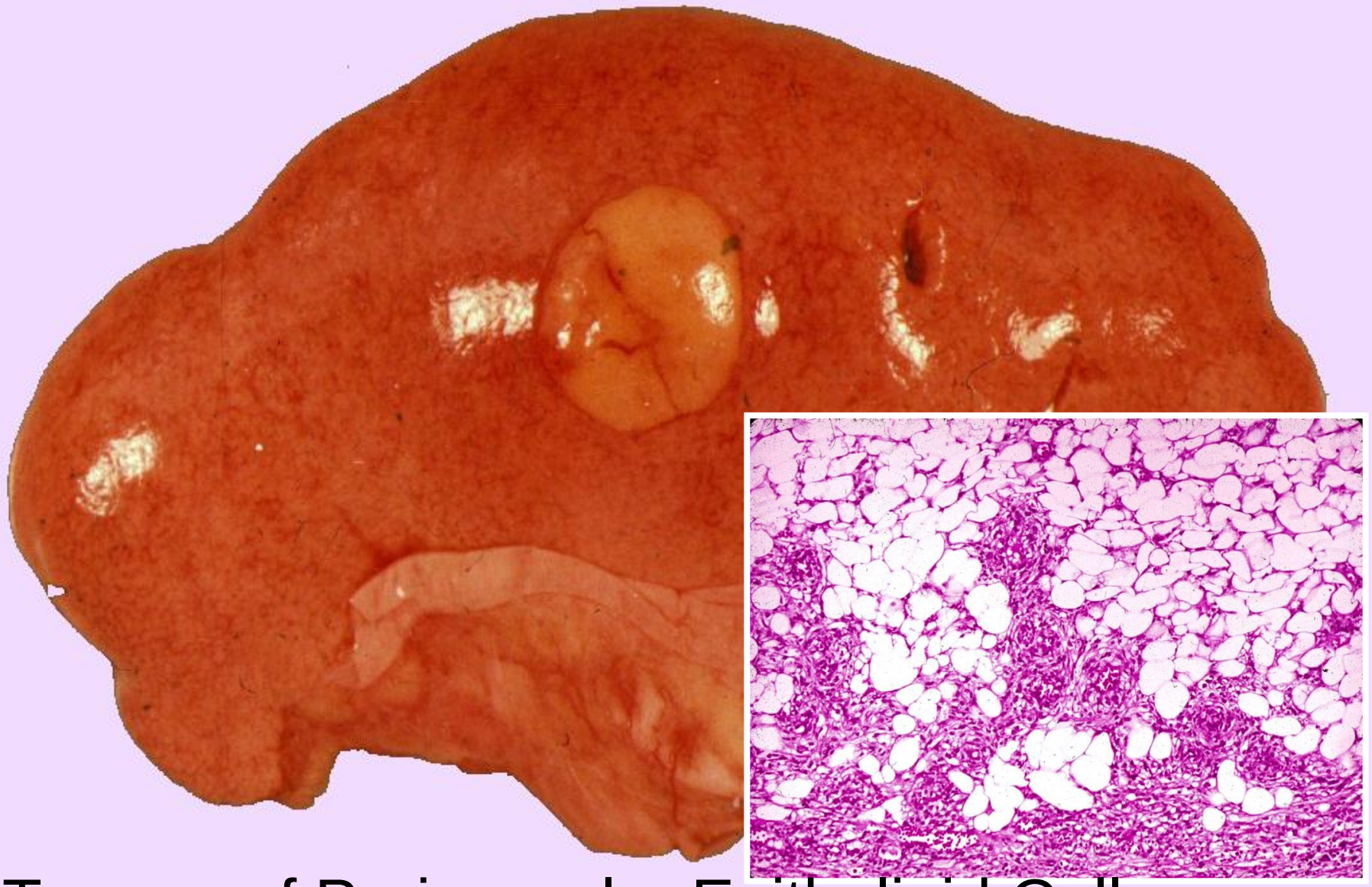


Tumours of uncertain histogenesis

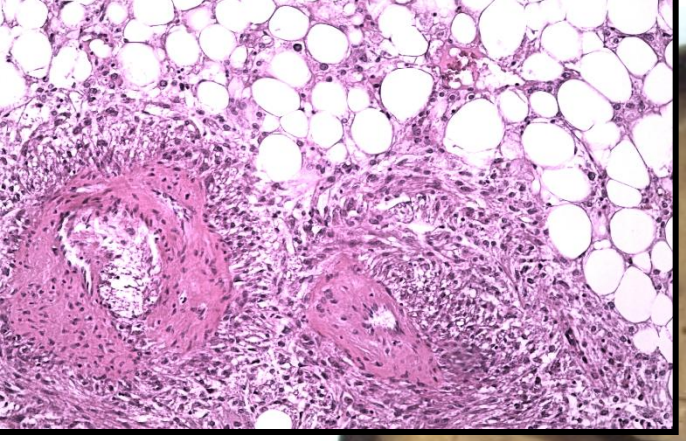
Perivascular epithelioid cells tumours - PEComas

- Neoplasm with myomelanocytic differentiation from perivascular epithelioid cells
- clear cell morphology
- co-expression of muscle and melanocytic markers (actin, HMB45)
- kidney (angiomyolipoma), lung, uterus…
- uncertain biology behaviour

Angiomyolipoma M88600



Tumour of Perivascular Epithelioid Cells – „PEComa“



Risk of bleeding

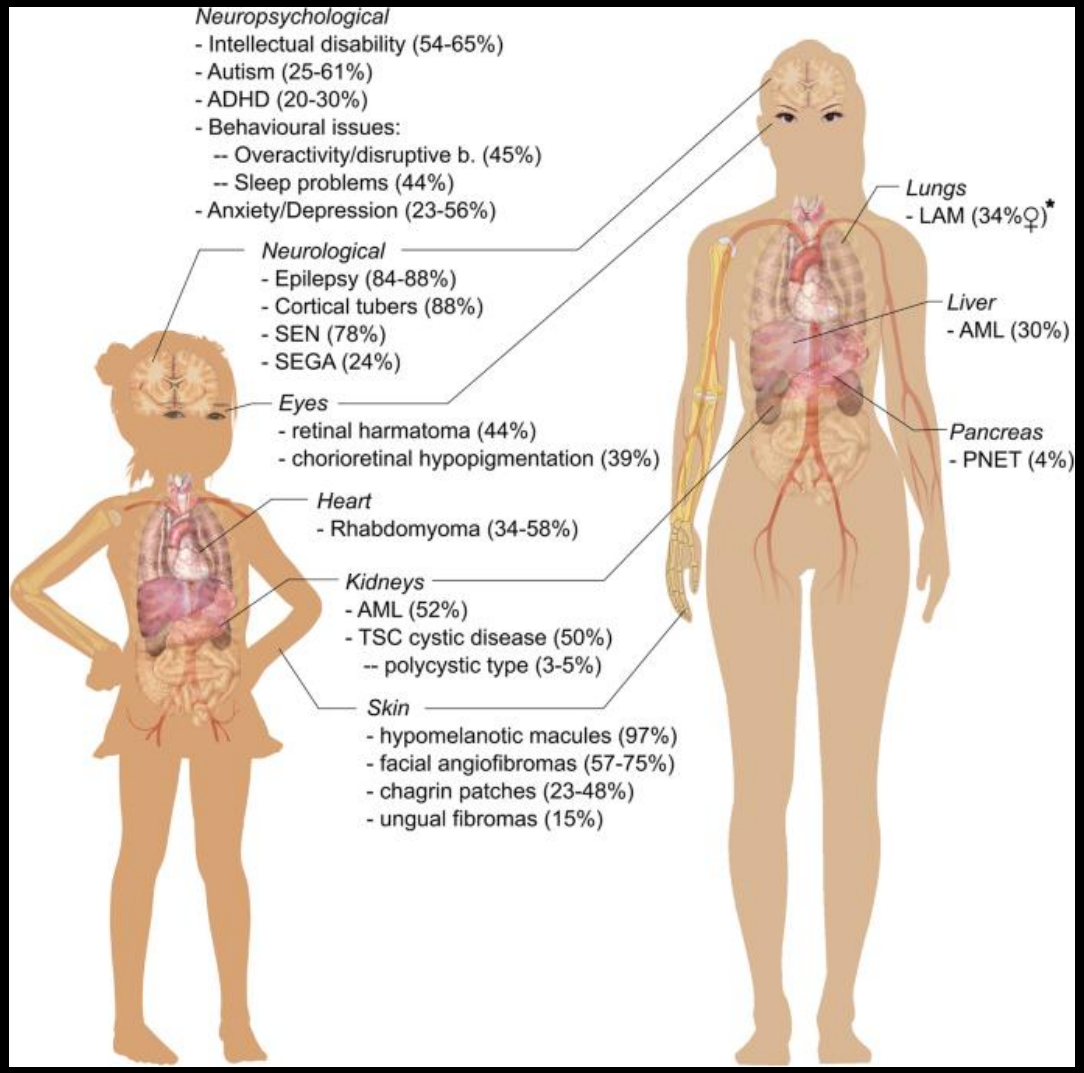
Angiomyolipoma
renis sin.

M 8860/1

50 mm

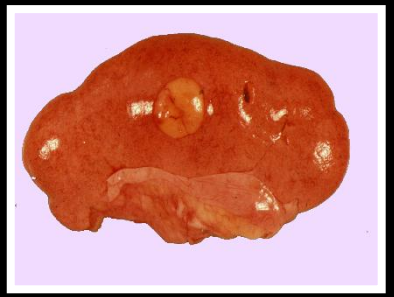
Mesenchymal tumours
can be a part
of
hereditary syndromes

Tuberous sclerosis

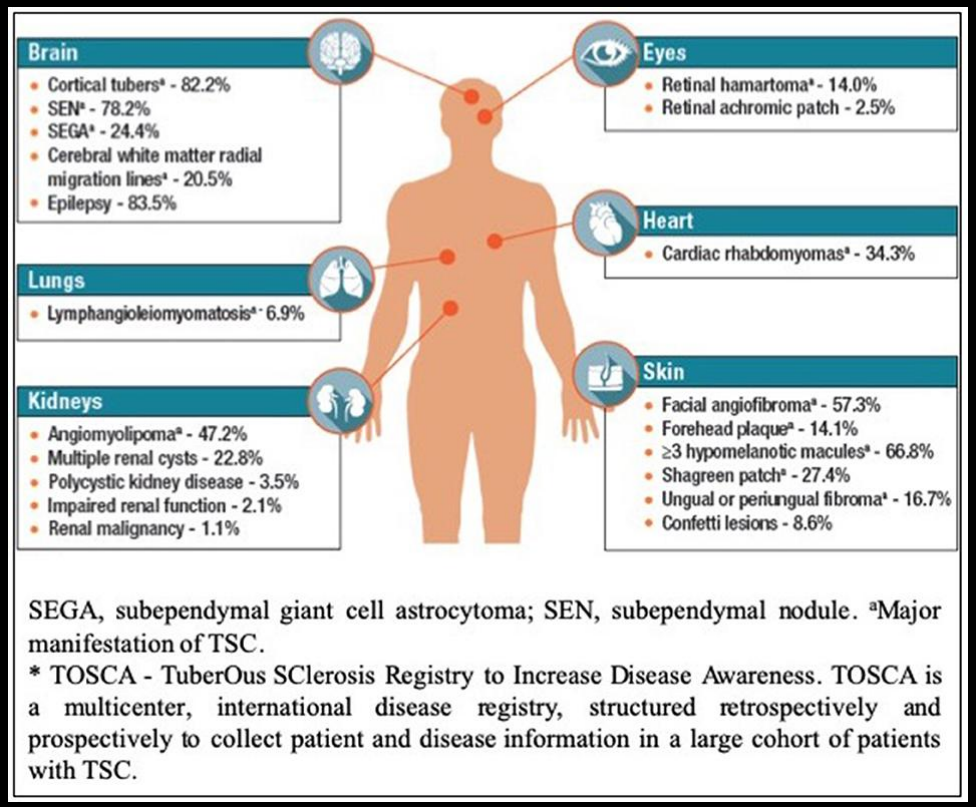


- AD
- 2/3 new mutations
- incidence 1:5800
- mutation of tumor-supressor gene (TSC1/hamartin or TSC2/tuberin).
- clinical manifestation highly variable

Angiomyolipoma
(in TS rather small and multiple, bilat.)

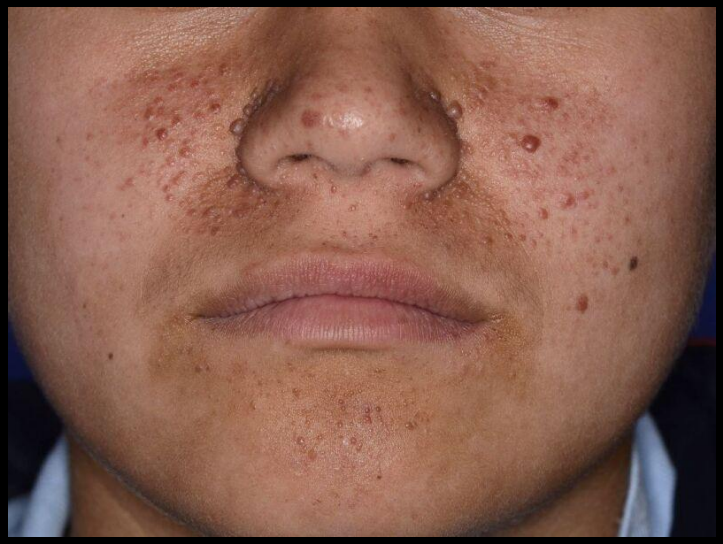


Tuberous sclerosis



SEGA, subependymal giant cell astrocytoma; SEN, subependymal nodule. [a]Major manifestation of TSC.

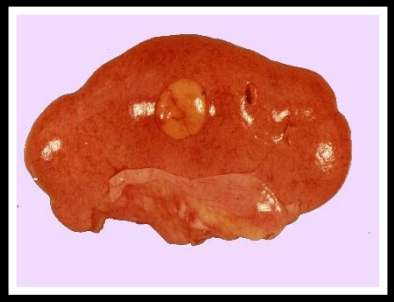
* TOSCA - TuberOus SClerosis Registry to Increase Disease Awareness. TOSCA is a multicenter, international disease registry, structured retrospectively and prospectively to collect patient and disease information in a large cohort of patients with TSC.

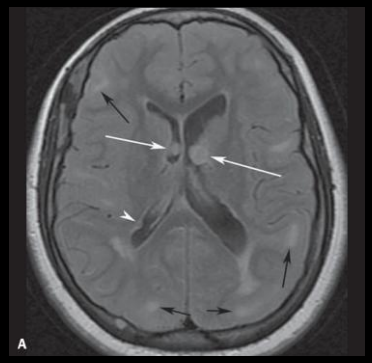


Facial angiofibromas

Sub- & periungual fibromas

Angiomyolipoma



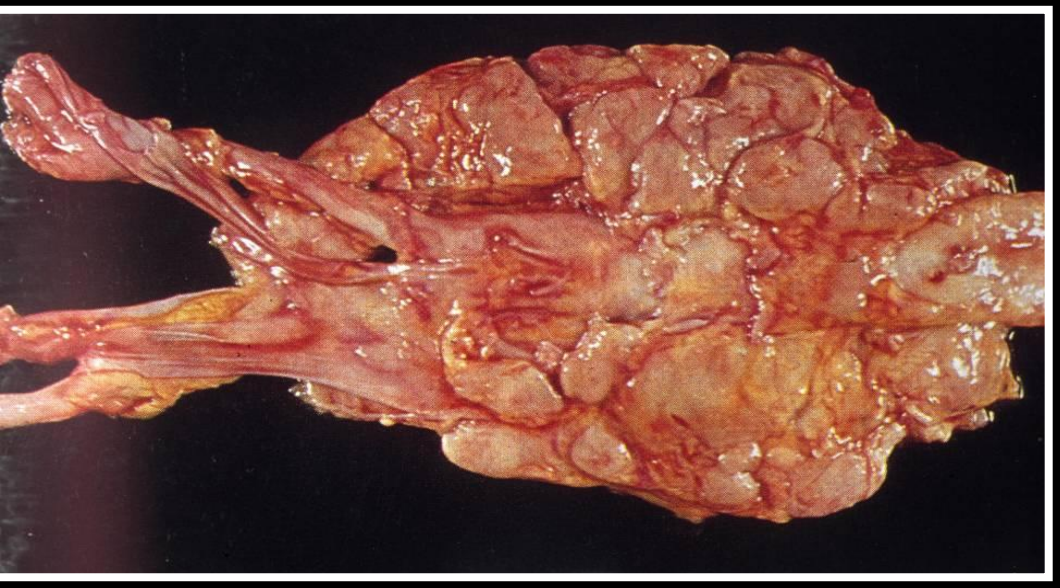


Subependymal nodules

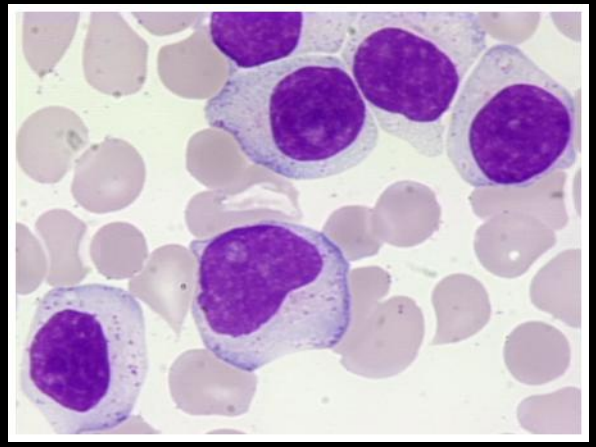
Mesenchymal neoplasms

Benign	Borderline	Malignant
fibroma	fibromatoses	fibrosarcoma
lipoma	lipoblastoma	liposarcoma
leiomyoma	atypical smooth muscle cell tumors	leiomyosarcoma
rhabdomyoma		rhabdomyosarcoma
hemangioma	hemangioendothelioma	hemangiosarcoma
lymphangioma		lymphangiosarcoma
chondroma	chondroblastoma	chondrosarcoma
chordoma		*invasive* chordoma
osteoma	osteoid osteoma <2cm osteoblastoma >2cm	osteosarcoma
!!!		lymphoma/leukaemia

Lymphomas (non Hodgkin, Hodgkin), leukemias



Splenomegalia (CML)

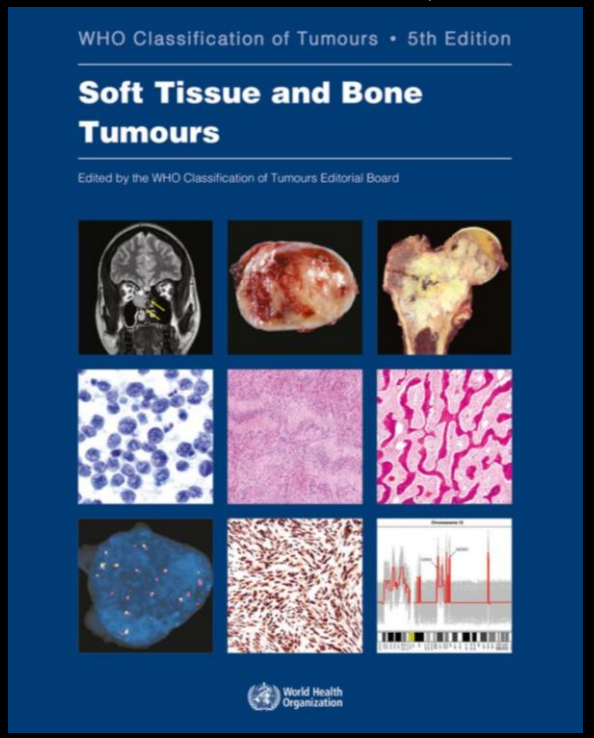


Leukaemia

A special lecture
on general oncology of lymphomas
and leukaemias
will follow ...

NEOPLASIA – description

2022



- definition & ICD-O code
- prevalance
- age/sex predisposition (if any)
- typical (most frequent) locations
- clinical symptoms
- gross level view
- histopathology / cytopathology
  (incl. special diagnostic tools)
- additional methods (*esp. if useful for the diagnosis)*
- *Essential and desirable diagnostic criteria*
- possible complications, prognosis

(in your study focus on green enhanced items…)


Altes
Fetterhaus
RESTAURANT
Thank You