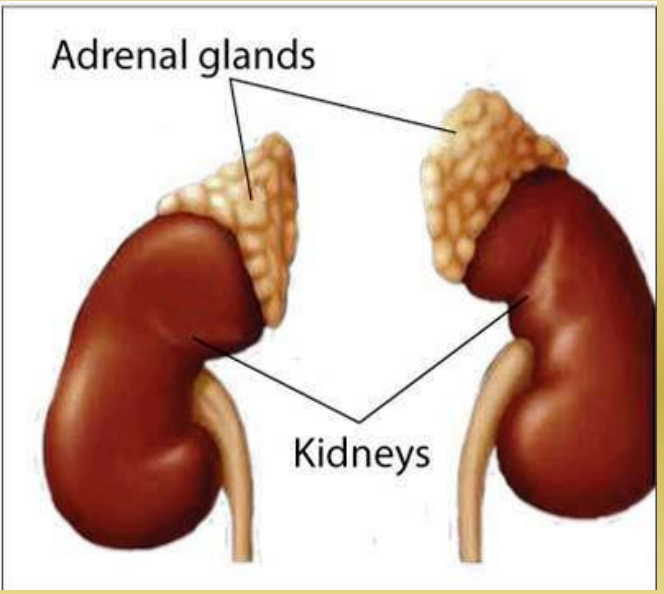


Lecture 6

Tumors of adrenal gland

By Dr.Esraah Alharris
PhD(path), MSc(path), MBChB

Objectives

- To understand
  - The classification of adrenal tumors
  - Tumors of adrenal cortex
    - Benign
    - Malignant
  - tumors of the adrenal medulla
    - Pheochromocytom
- To show the approach to a case of adrenal tumor

Case presentation

A 34-year-old woman presents with recurrent episodes of severe headaches, palpitations, tachycardia, and sweating. A physical examination reveals her blood pressure to be within normal limits; however, during one of these episodes of headaches, palpitations, and tachycardia, her blood pressure is found to be markedly elevated. Workup finds a small tumor of the right adrenal gland. Which of the following is most likely to be increased in the urine of this individual?

1. Acetone
2. Aminolevulinic acid (ALA)
3. Hydroxy-indoleacetic acid (HIAA)
4. N-formiminoglutamate (FIGlu)
5. Vanillylmandelic acid (VMA)

Adrenocortical neoplasms:

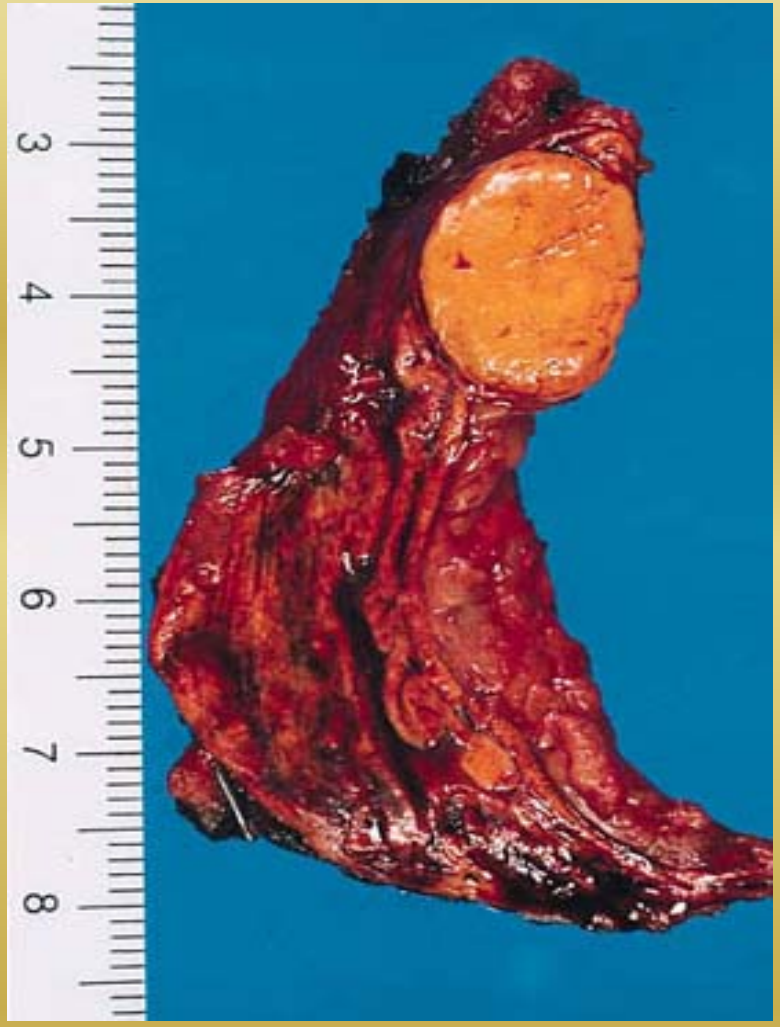
A- Adenomas:

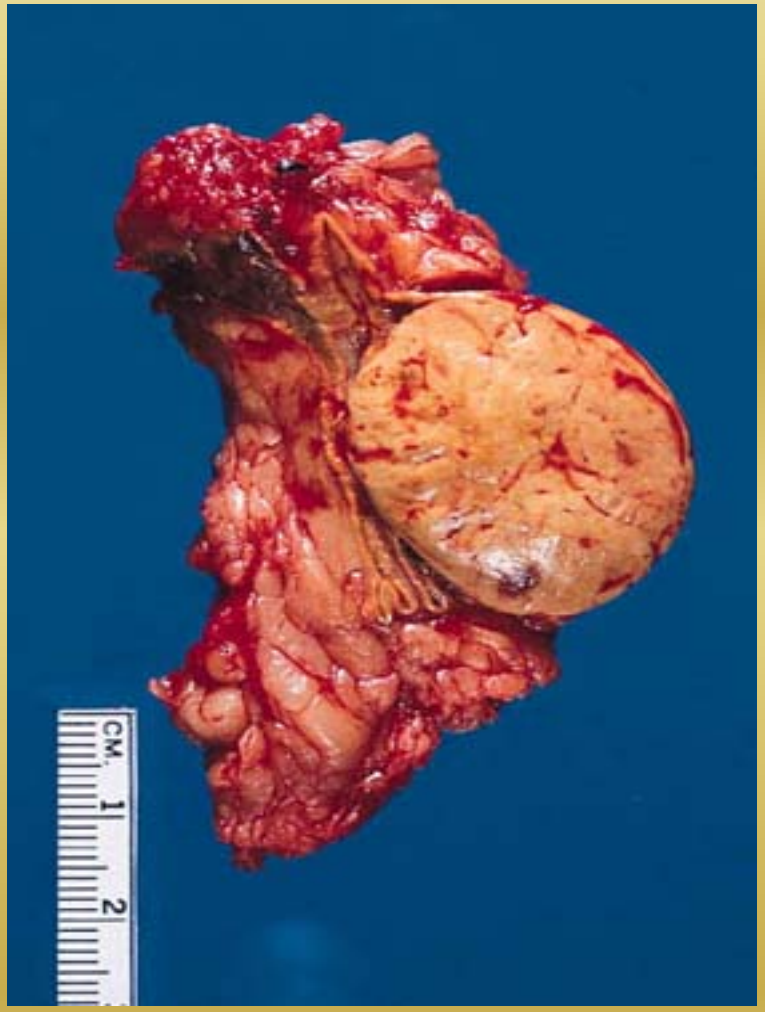
Functioning or non- functioning

(same gross and microscopic features)

B- Carcinomas

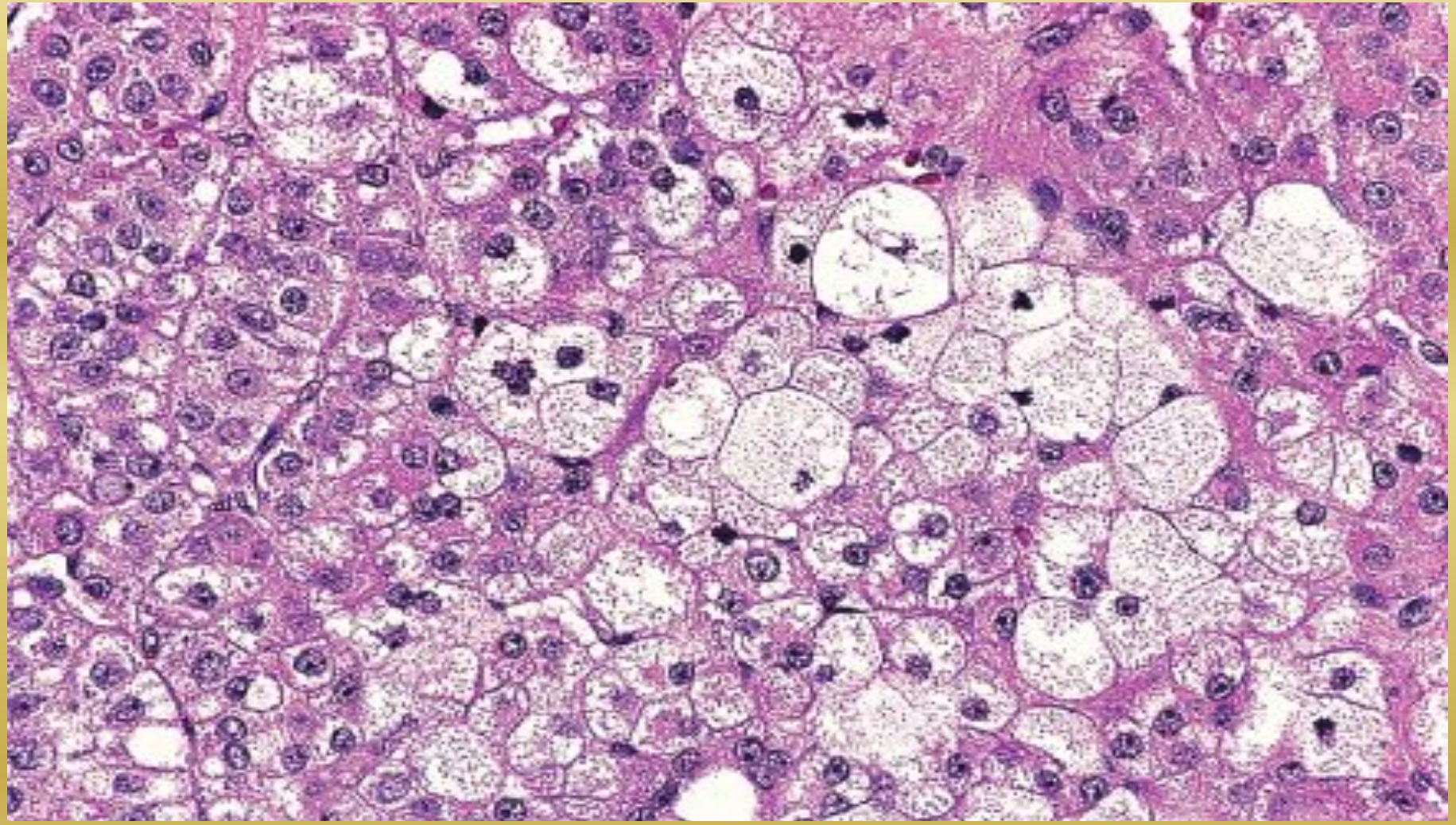
Adrenocortical adenoma



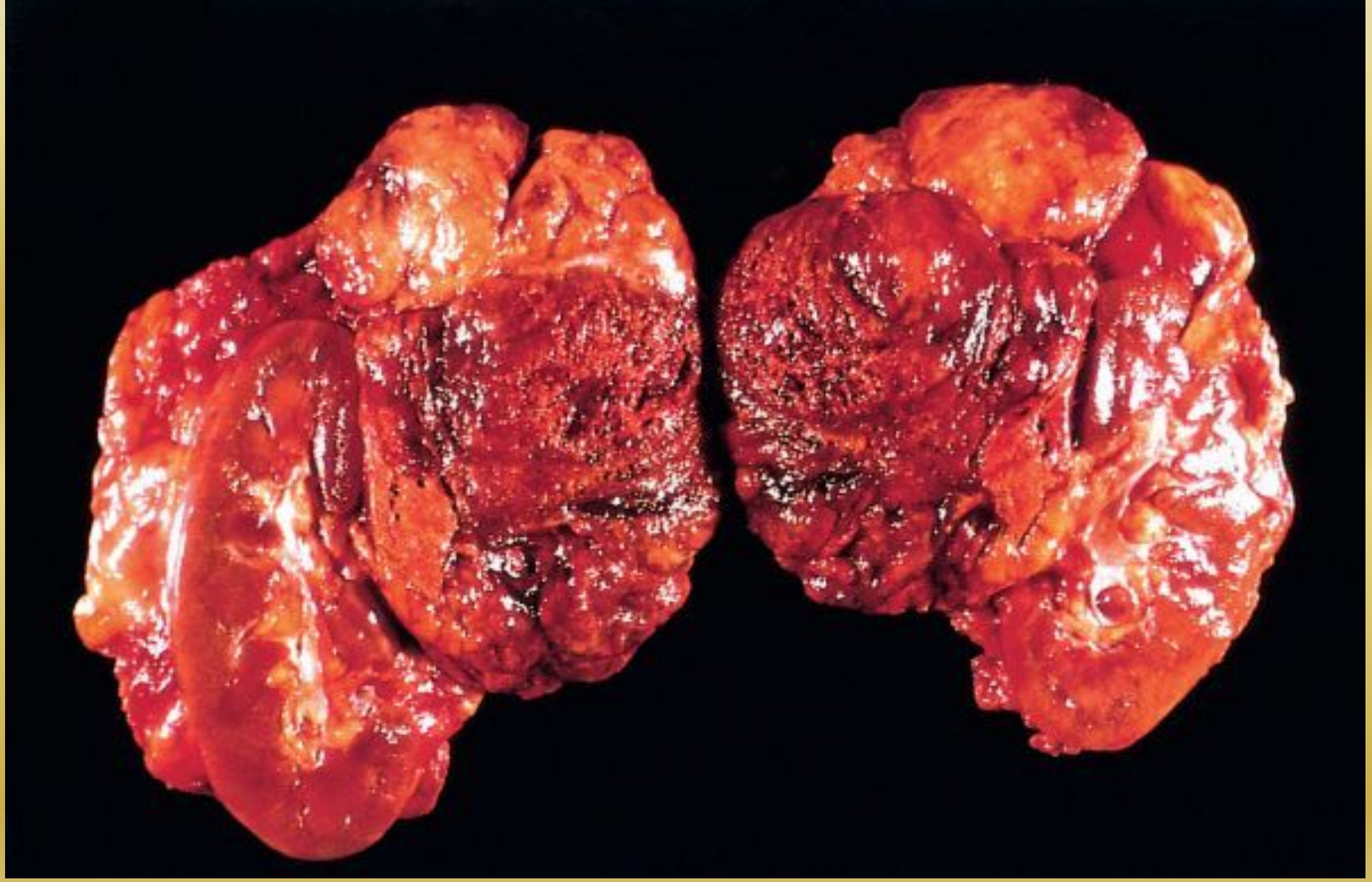


A and B, Gross appearance of adrenal cortical adenoma. Both tumors are well circumscribed, of homogeneous appearance, without hemorrhage or necrosis. They are typically golden yellow in color

Adrenal cortical adenoma

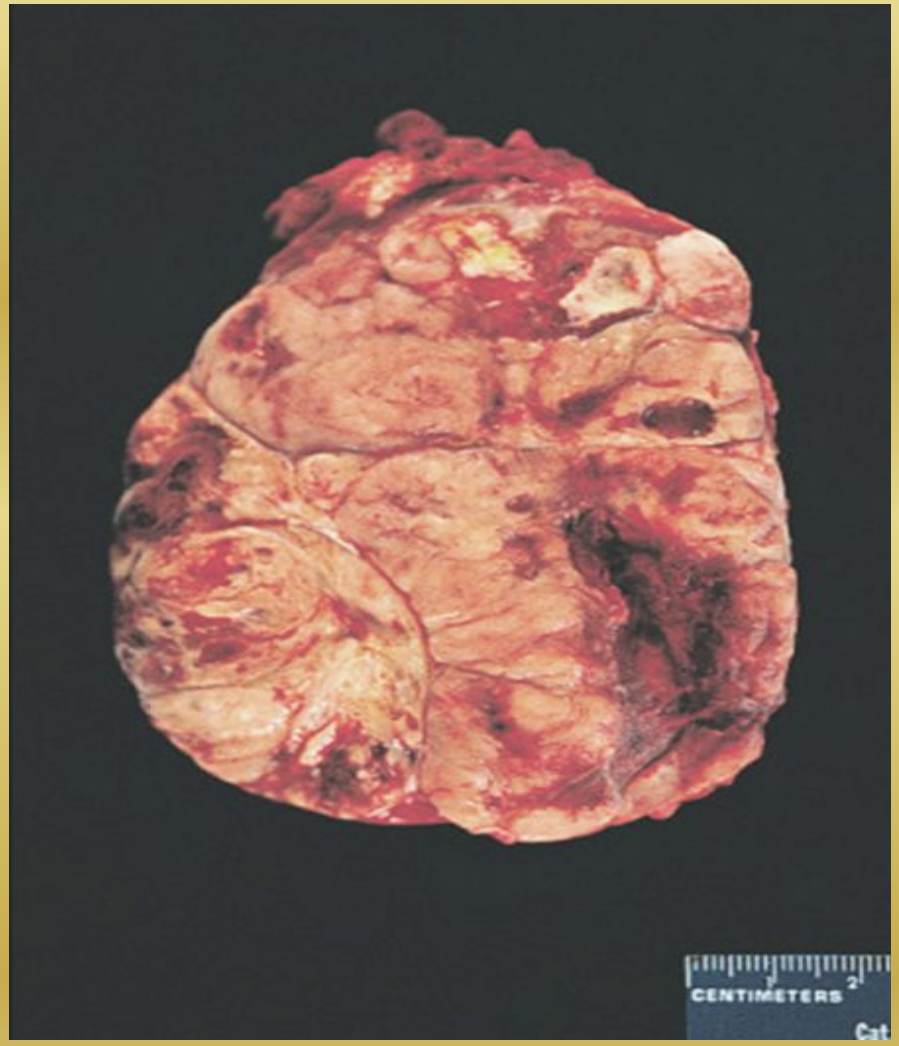


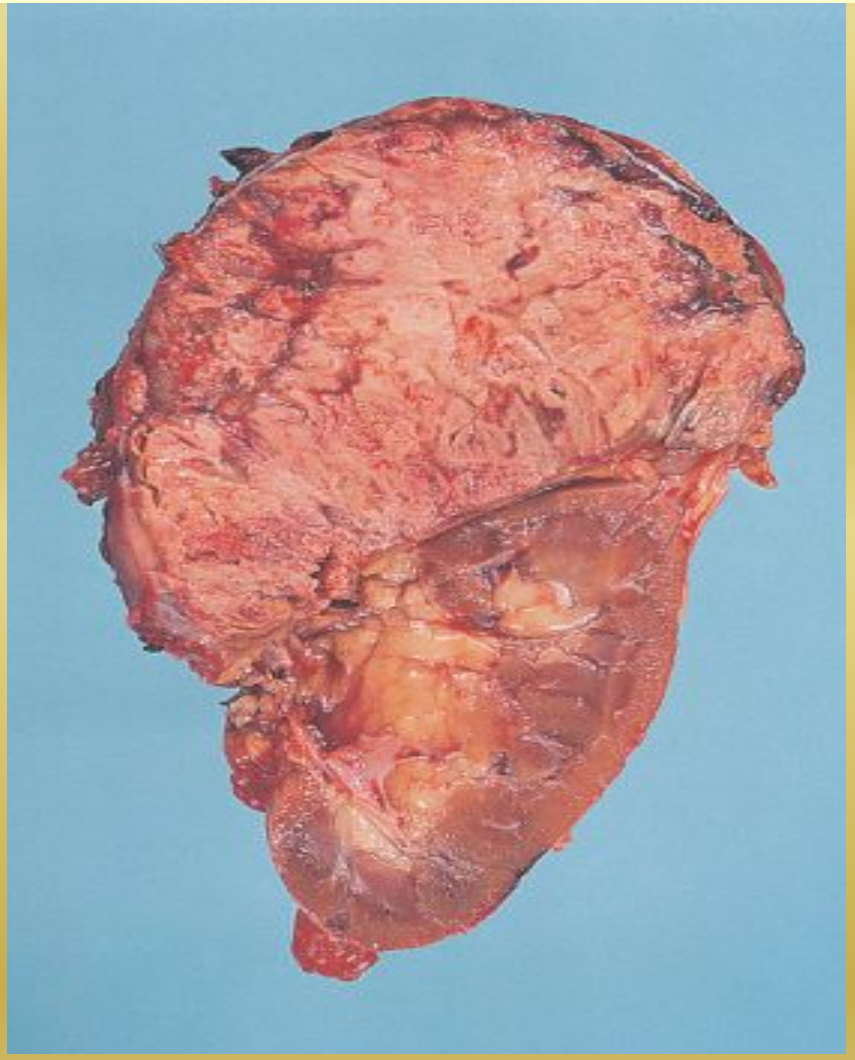
The tumor shows numerous lipid-laden clear cells similar to those of the normal fasciculata layer.



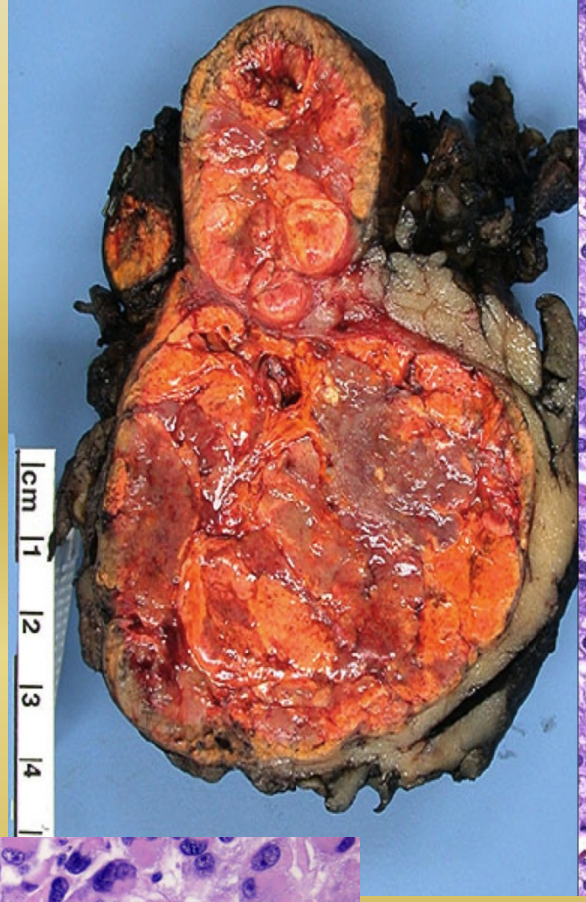
Adrenal carcinoma. The hemorrhagic and necrotic tumor dwarfs the kidney and compresses the upper pole.

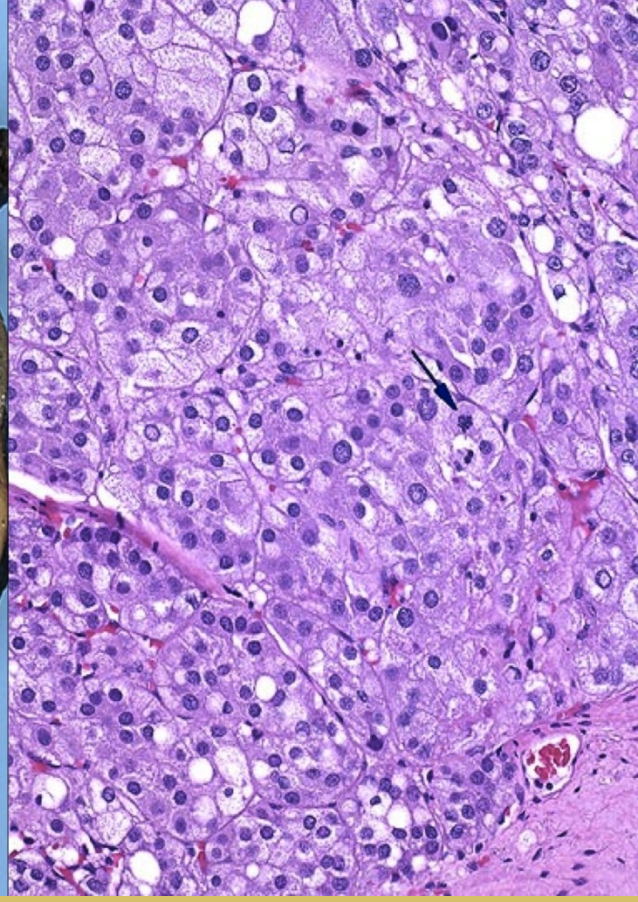
Adrenal cortical ca



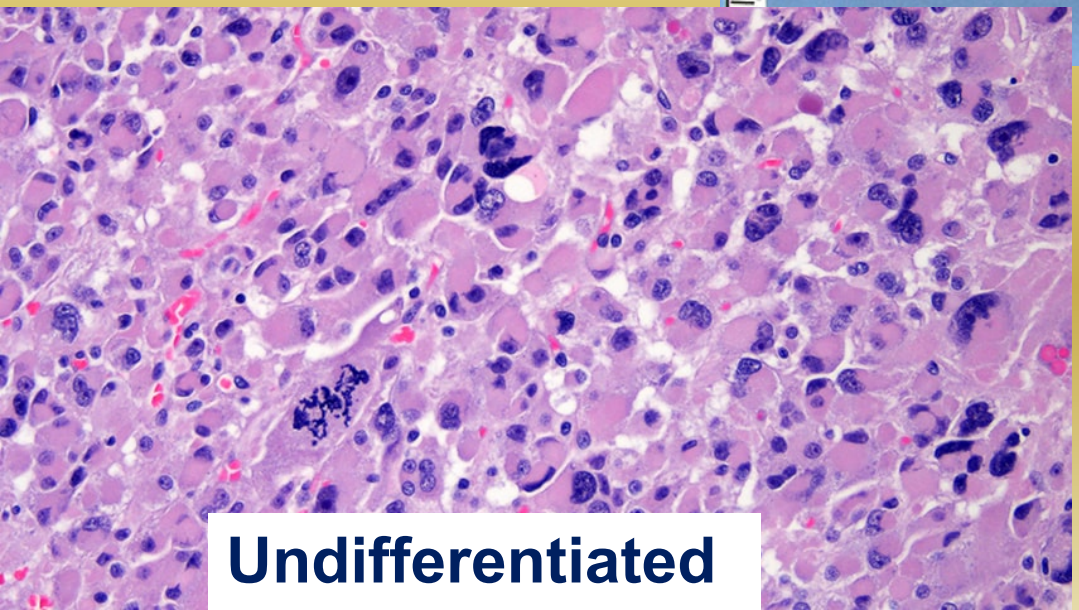


A large tumor that exhibits areas of hemorrhage and necrosis.



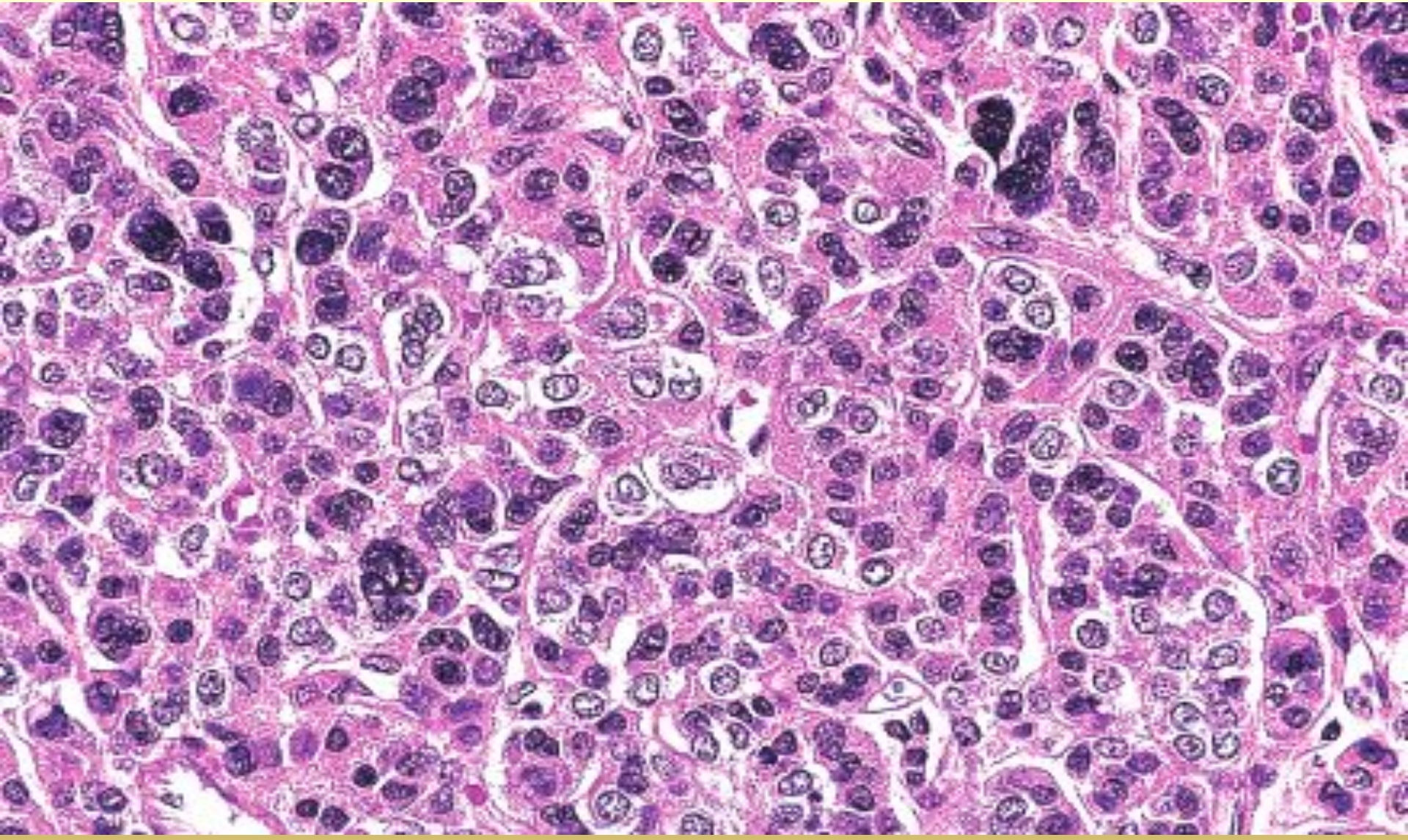


Well differentiated



Undifferentiated

Adrenal cortical ca



There is nuclear hyperchromasia, diffuse pattern of growth, and mitotic activity.

Golden rule

- ✔ In most of endocrine tumours, Malignancy is diagnosed only By presence of Metastases Whatever are the cytological features

- ✔ Adrenal, Parathyroid, Pituitary, Islets of pancreas

Spread:

- Adrenal cancers have a strong tendency to invade the adrenal vein & vena cava.
- Metastases to regional and peri-aortic nodes are common
- Distant hematogenous spread to the lungs & other viscera.

Adrenal medulla

Pheochromocytoma

- uncommon tumors
- Arise from chromaffin cells
- Secrete catecholamines
- Sporadic in 75% of cases
- Familial in 25% of cases (MENI)
- Rule of 10%

Rule of 10

- 10% are extra-adrenal (e.g., organ of Zuckerkandl or carotid body), in which they are designated paragangliomas.
- 10% of sporadic adrenal pheochromocytomas are bilateral (in comparison, 50% of cases associated with familial syndromes are bilateral).
- 10% are biologically malignant (i.e., associated with metastasis); malignancy occurs in 20% to 40% in familial syndromes or in extra-adrenal pheochromocytomas.
- 10% are not associated with hypertension.
- As many as 25% (not 10%, unfortunately) of pheochromocytomas arise in familial syndromes associated with germline mutations in at least one of six different genes, including MEN- 2A and -2B syndromes (RET mutations), type I neurofibromatosis (NF1 mutations), von Hippel- Lindau (VHL) syndrome, and familial para-ganglioma syndromes (mutations in the subunits of the succinate dehydrogenase complex).

Clinical Course:-

Sympathetic nervous system hyperactivity

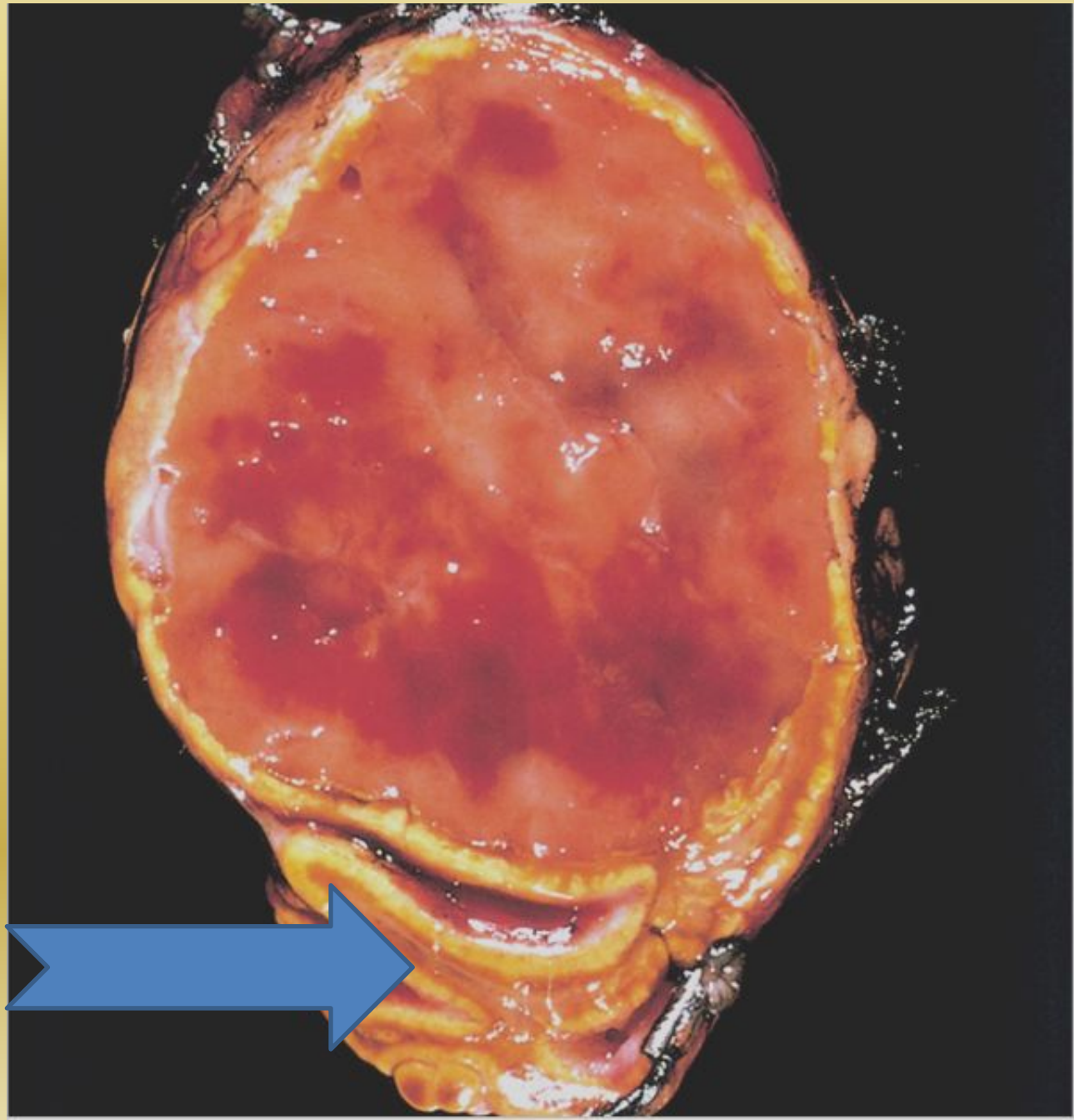
- Skin sensations
- Headaches – most common symptom
- Elevated heart rate (Palpitations)
- Elevated blood pressure,
- Anxiety often resembling that of a panic attack
- Diaphoresis (excessive sweating)
- Pallor
- Weight loss

Laboratory diagnosis is based on increased urinary catecholamines and their metabolites (e.g., vanillylmandelic acid)

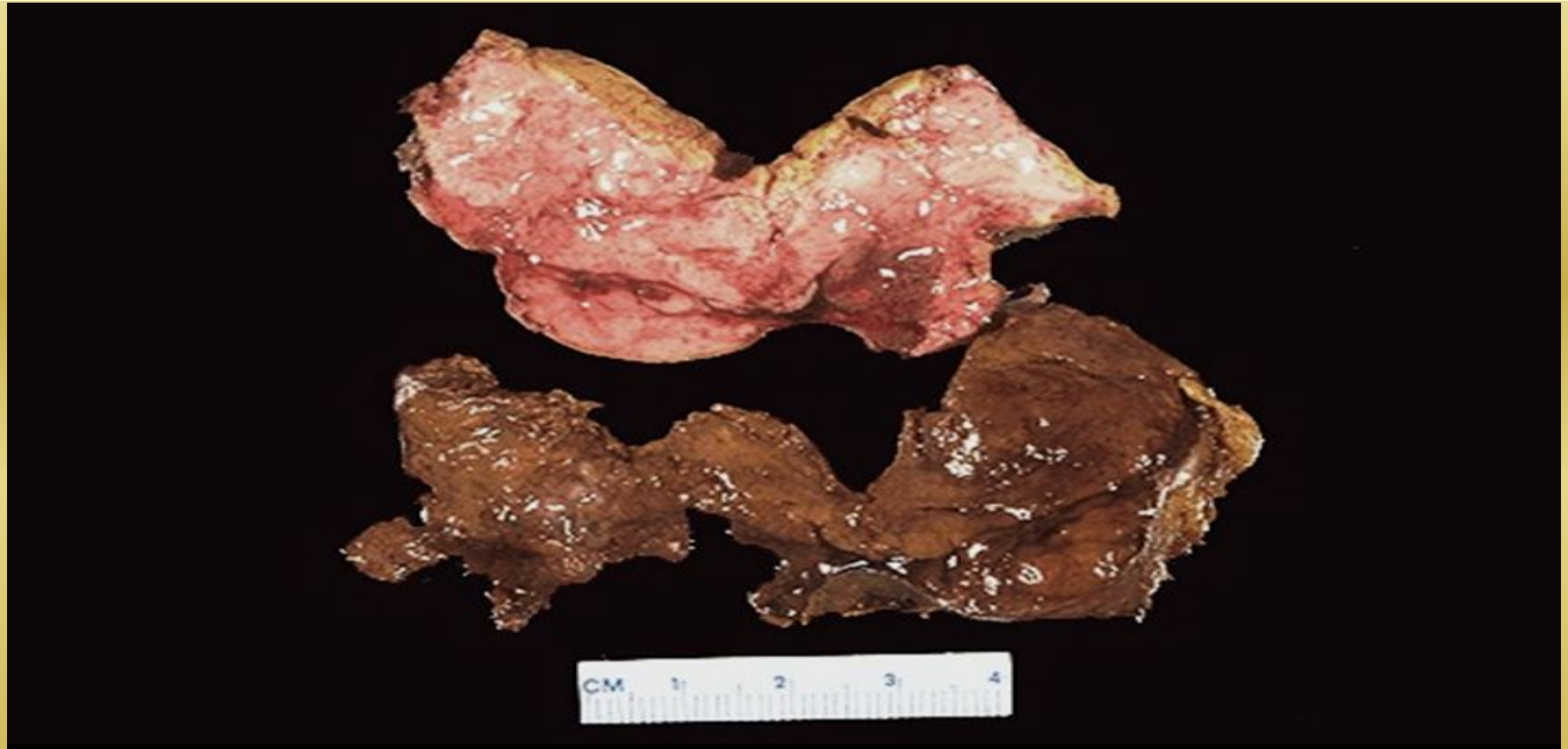
Pheochromocytoma

Gross: The yellow-tan tumor is enclosed within an attenuated yellowish cortex and demonstrates areas of hemorrhage.

(The residual adrenal is seen below.)



Pheochromocytoma Chromaffin reaction

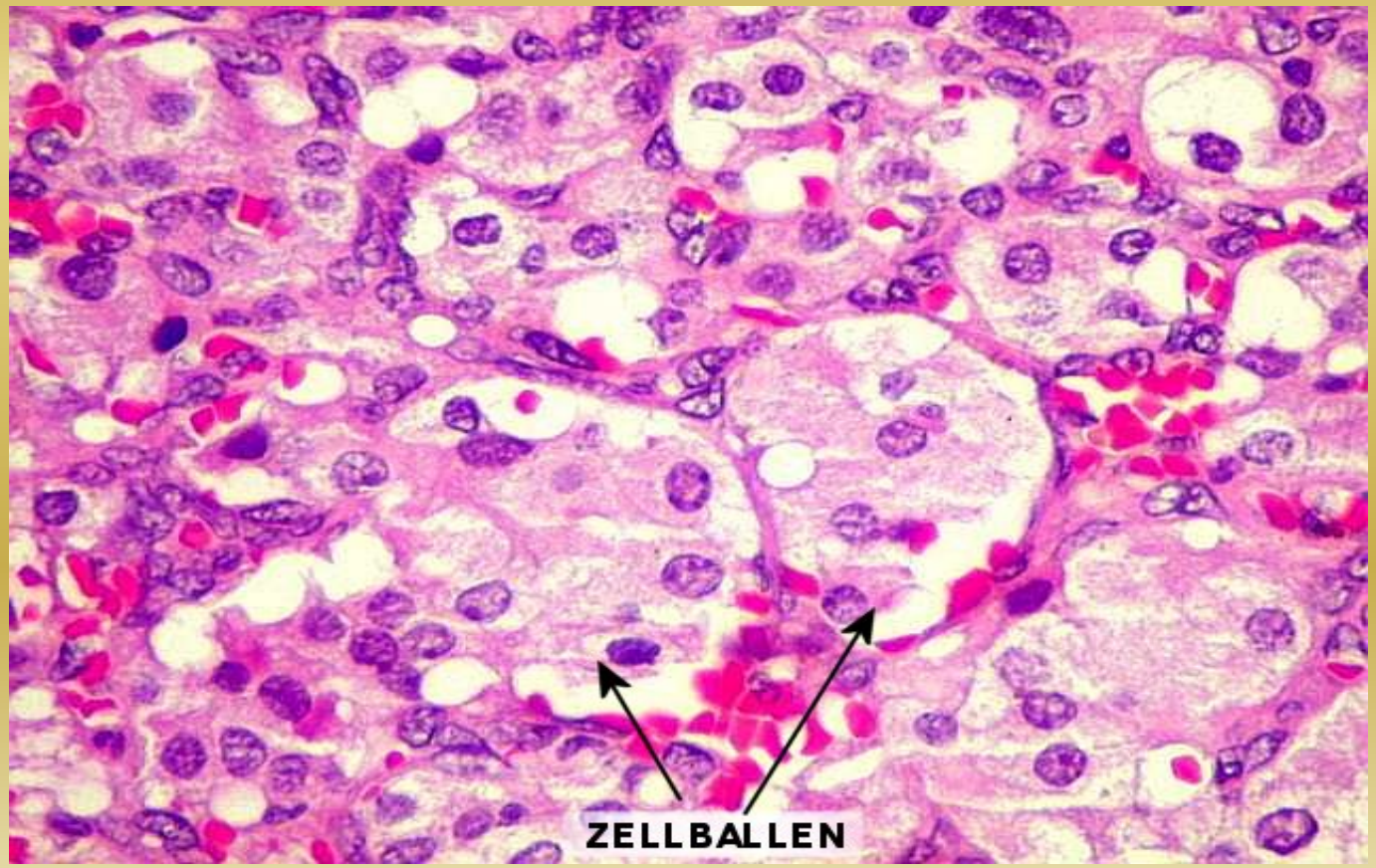


The section of tumor at the bottom has been placed into a dichromate fixative which turns the tissue brown as the catecholamines are oxidized.
a positive chromaffin reaction.
Compare to the section of pink to yellow tumor at the top which has not been placed in dichromate fixative*.

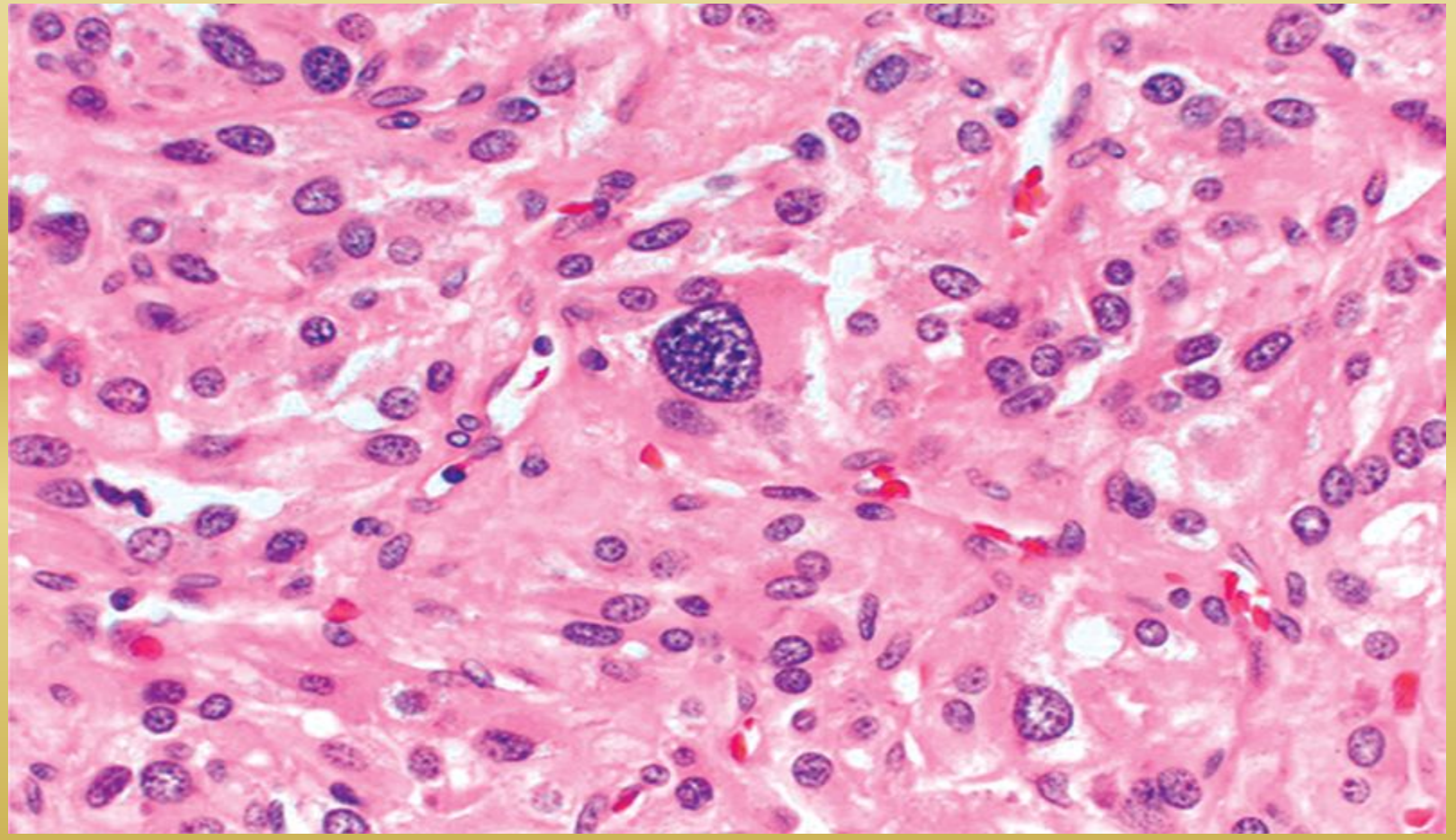
Tumors are composed of clusters (“zellballen”) of polygonal to spindle-shaped chief cells (exhibiting neuroendocrine markers) admixed with sustentacular cells , all delimited by a rich vascular network.
Cellular and nuclear pleomorphism is common.

Zellballen

Small nests
Separated by
Sinusoidal
network



Pheochromocytoma



The section demonstrates characteristic nesting of cells ("Zellballen") with abundant pinkish cytoplasm.

Metastasis is the sole criterion of malignancy.

Multiple Endocrine Neoplasia Syndromes (MEN)

Multiple endocrine neoplasia (MEN) is a group of heritable diseases resulting in proliferative lesions (e.g., hyperplasia, adenomas, and carcinomas) of multiple endocrine organs .

Tumors associated with MEN:-

- Occur at a younger age
- Arise in multiple organs, either synchronously (at the same time) or sequentially
- Are often multifocal
- Are usually preceded by asymptomatic endocrine hyperplasia alone or involving the cell of origin (e.g., C-cell hyperplasia adjacent to medullary thyroid cancers)
- Are usually more aggressive and recur in a higher proportion of cases

MEN-1, Wermer Syndrome

MEN-1 is caused by germline mutations in the MEN1 tumor suppressor gene, encoding the protein menin—a component of several different transcription factor complexes

(3 P's)

- HYPER PARATHYROIDISM, chiefly hyperplasia
- Pancreatic endocrine tumors
- Pituitary adenoma, usually prolactinoma

MEN-2

- MEN-2A : Pheochromocytoma, Medullary CA., Parathyroid hyperplasia
- MEN-2B: NO hyperparathyroidism, but neuromas present, familial Medullary Thyroid CA in addition to pheochromocytoma

MEN-1 genetic screening has questionable long-term value,
Screening of at-risk family members in the MEN-2 syndromes can be life-saving since early thyroidectomy can potentially mitigate the fatal complications of medullary thyroid carcinoma.

Thank you for your attention!