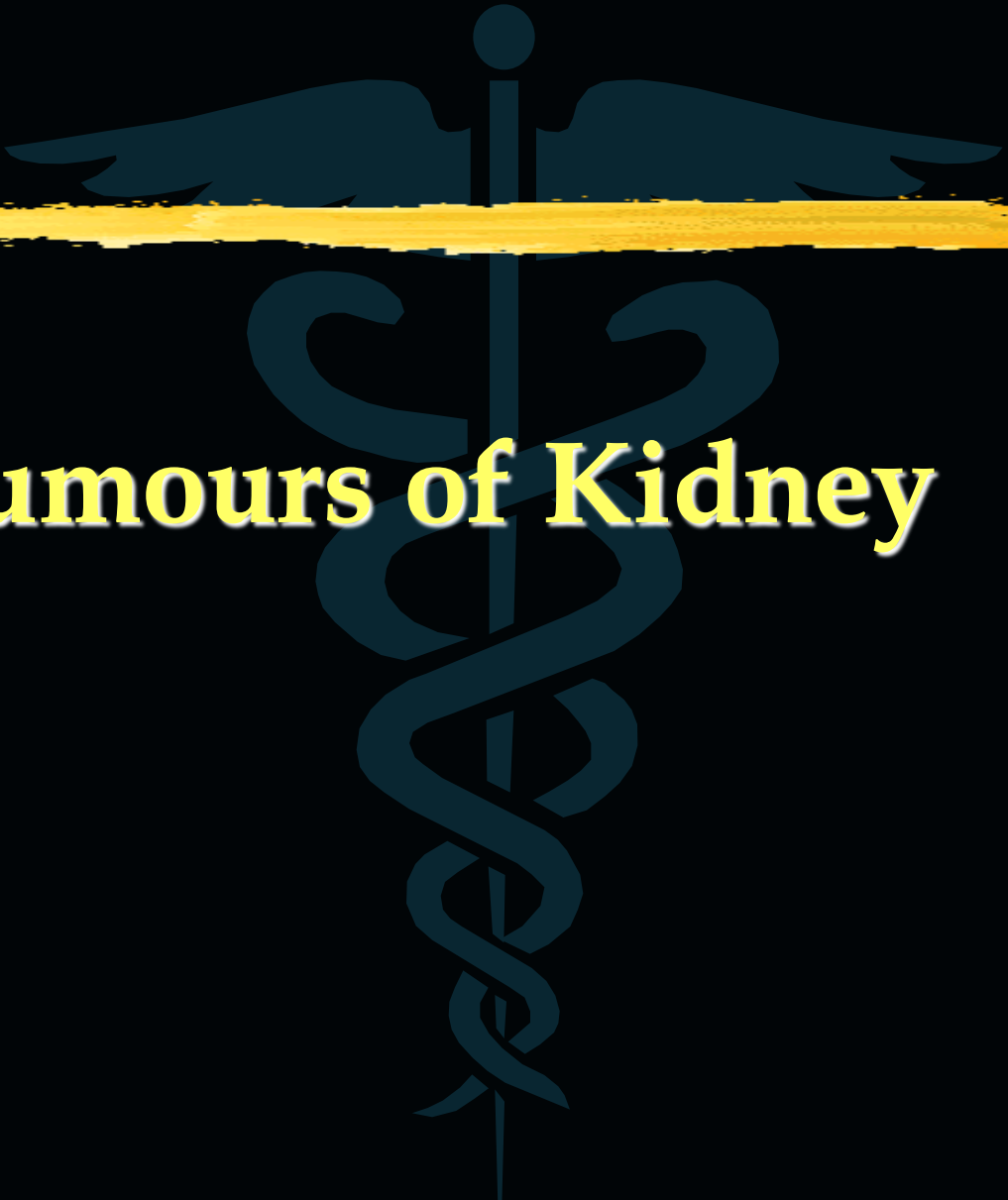




Tumours of Kidney



Persistent



Prof Dr. Arun Jamkar,
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Former Vice Chancellor,
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Distinguished Professor ;
Symbiosis International University,
Pune.
Director Academics,
Galaxy care hospitals, Pune

Renal Mass : Differential Diagnosis

- Metastasis
- Renal cell carcinoma - 80 - 85% of all primary neoplasm
- Transitional cell CA of renal pelvis(~8%)

Tumours of kidney

□ Renal Tumours of adult

I. Solid tumours from kidney parenchyma

- 1. Renal cell carcinoma Gravitz: tumour 2. Adenocarcinoma
- 3. Papillary Carcinoma 4. Sarcoma
- 5. Rare : Adenoma, Leiomyoma, fibroma.

II. Tumours of Renal pelvis

- Papilloma 2 Malignant Papilloma
- Squamous cell carcinoma
- Adenocarcinoma

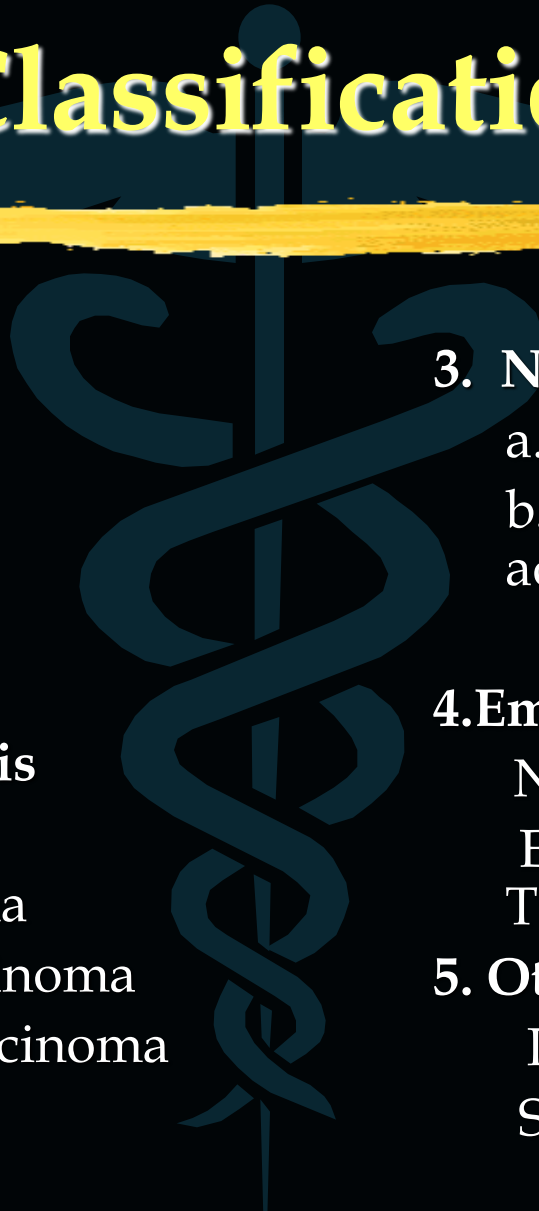
III. Tumours of capsule

- Lipoma 2 Fibroma 3 Sarcoma

□ Renal Tumour of Infancy & childhood

Wilm's Tumour

Glenn's Classification



1. Benign Tumours

- a. Capsule
- b. Renal parenchyma (Adenoma)
- c. Vascular Tumours

2. Tumours of Renal Pelvis

- a. Papilloma
- b. Malignant Papilloma
- c. Squamous cell carcinoma
- d. Transitional cell carcinoma

3. Nephrocarcinoma

- a. Renal cell carcinoma
- b. Papillary Cyst adenocarcinoma

4. Embryonic Tumours

Nephroblastoma,
Embryonic Mesothelial
Tumours, Sarcoma

5. Other Tumours

Primary Mesenchymal
Secondary Metastatic

Lymph Node Involvement

- Lymph of 1-2cm diameter may be caused by either metastasis or reactive hyperplasia
- Presence of lymph node enlargement upto 2cm doesn't preclude surgical management

Primary Renal Cancer

- Renal cell carcinoma
80-85% of malignant renal tumors
- Transitional cell Ca of renal pelvis
15-20% of renal Ca in adults
- Wilms tumor (Nephroblastoma) in
children (5-6%)

Nephrocarcinoma



- Also called as
 - Hypernephroma,
 - Gravitz Tumour,
 - Clear cell carcinoma,
 - Alveolar carcinoma
- Incidence : commonest Kidney Tumours 75% of GUT Tumours
- *In the United States, renal adenocarcinoma -- cancer of the kidney -- accounts for about 3% of all adult cancers. About 30,000 new cases are diagnosed annually. (1 per 771,76 per 100000)*
- Experimental :Methyl amine, Lead Acetate ,high oestrogen (Syri Golden hamster)

Renal Cell Cancer: History

- First described by Konig in 1826
- Robin in 1855 - Renal epithelium - most possible tissue of origin of the cancer
- Birch Hirschfeld in 1984 - Introduced the term Hypernephroid tumor (hypernephroma) - incorrect term
- Other Names
 - The Internist's tumor
 - The Radiologist's tumor

Renal Cell Carcinoma

- In USA, 27,600 new cases & 11,300 deaths from this cancer each year
- Incidence - 2-3% of all carcinoma
- 25-40% incidental renal mass
- 25-30% have metastases at presentation

Renal Cell Carcinoma

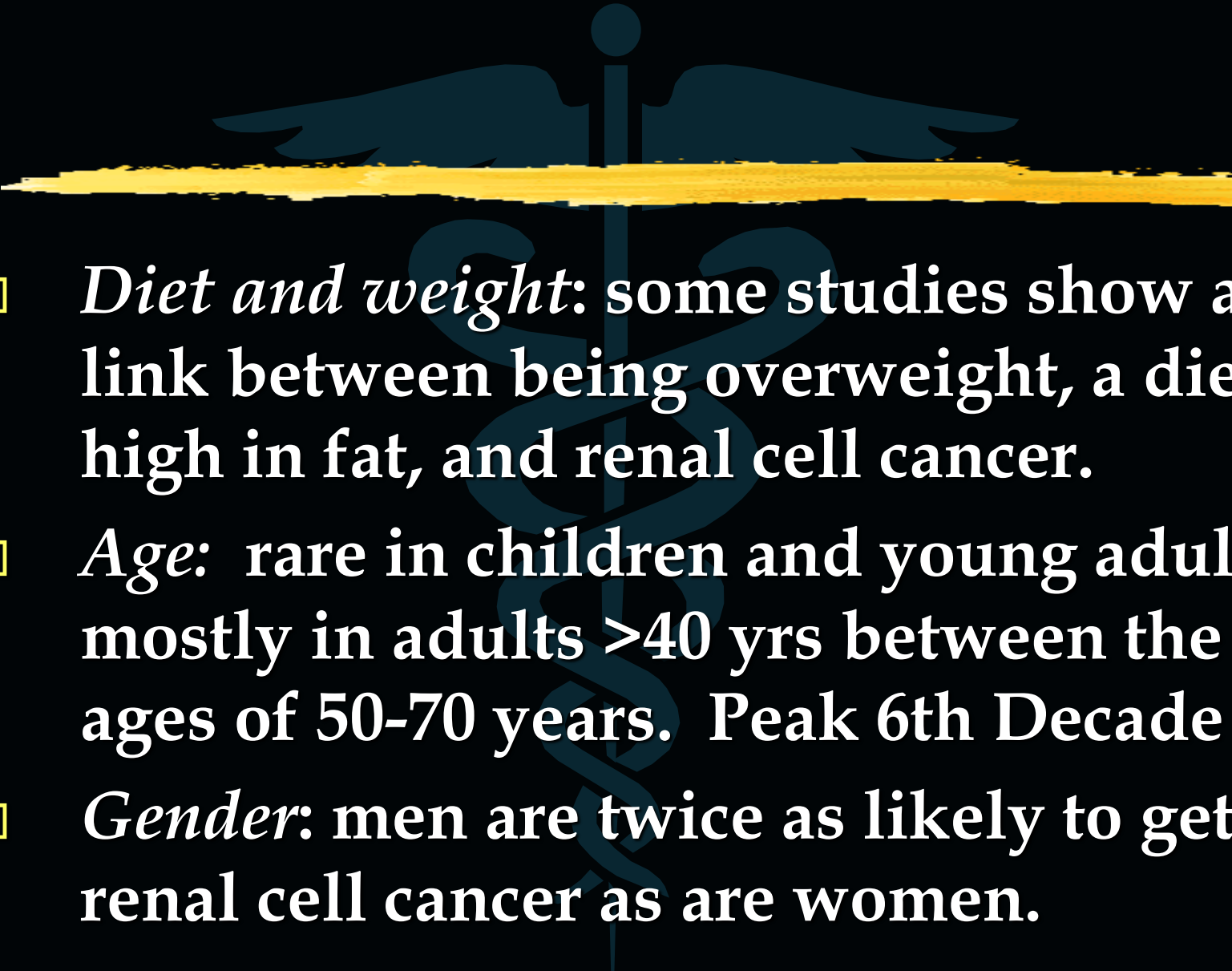
- Renal cell Carcinoma -
Originates in Renal Cortex (PCT)
- 1-3% bilateral
- Male : Female 2 : 1
- Predominantly 6th to 8th decade of Life

Pathology of Renal Cell Carcinoma

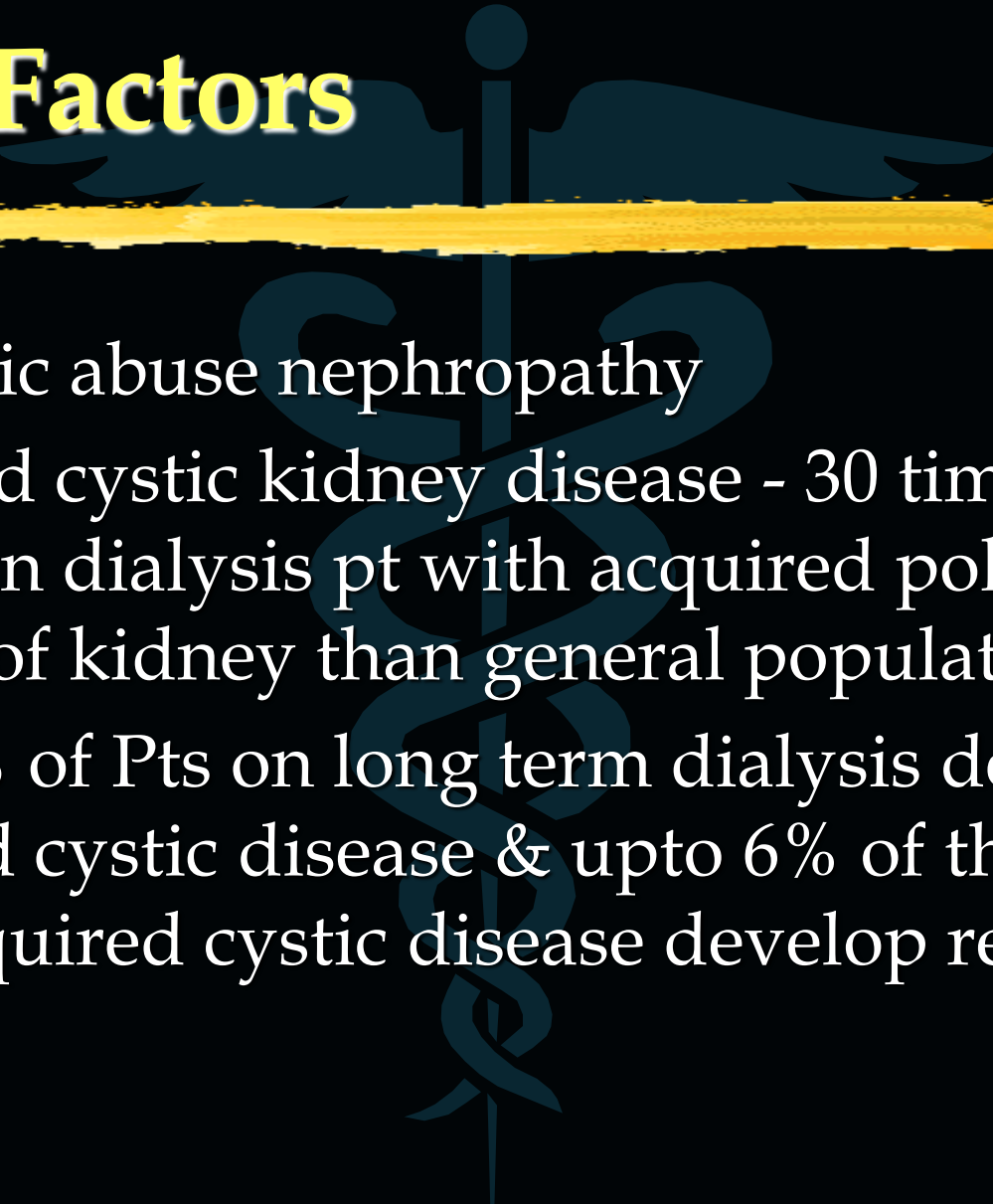
- RCC originates from Proximal renal Tubular Epithelium
- Equal Frequency on both the kidneys
- Usually at Poles: More common at upper
- Originates in Cortex and tends to grow in peri nephric tissue

Risk factors of RCC

- *Smoking*: smoking doubles the risk of getting kidney cancer. 30 % male and 24% Female RCC patients are related to smoking
- *Overuse of analgesics* Eg Phenacetin. , Analgesic nephropathy
- *Asbestosis*: some studies show a link between exposure to asbestos at work and kidney cancer.
- *Cadmium*: a link between cadmium exposure and kidney cancer.
- cadmium may increase the cancer-causing effect of smoking.

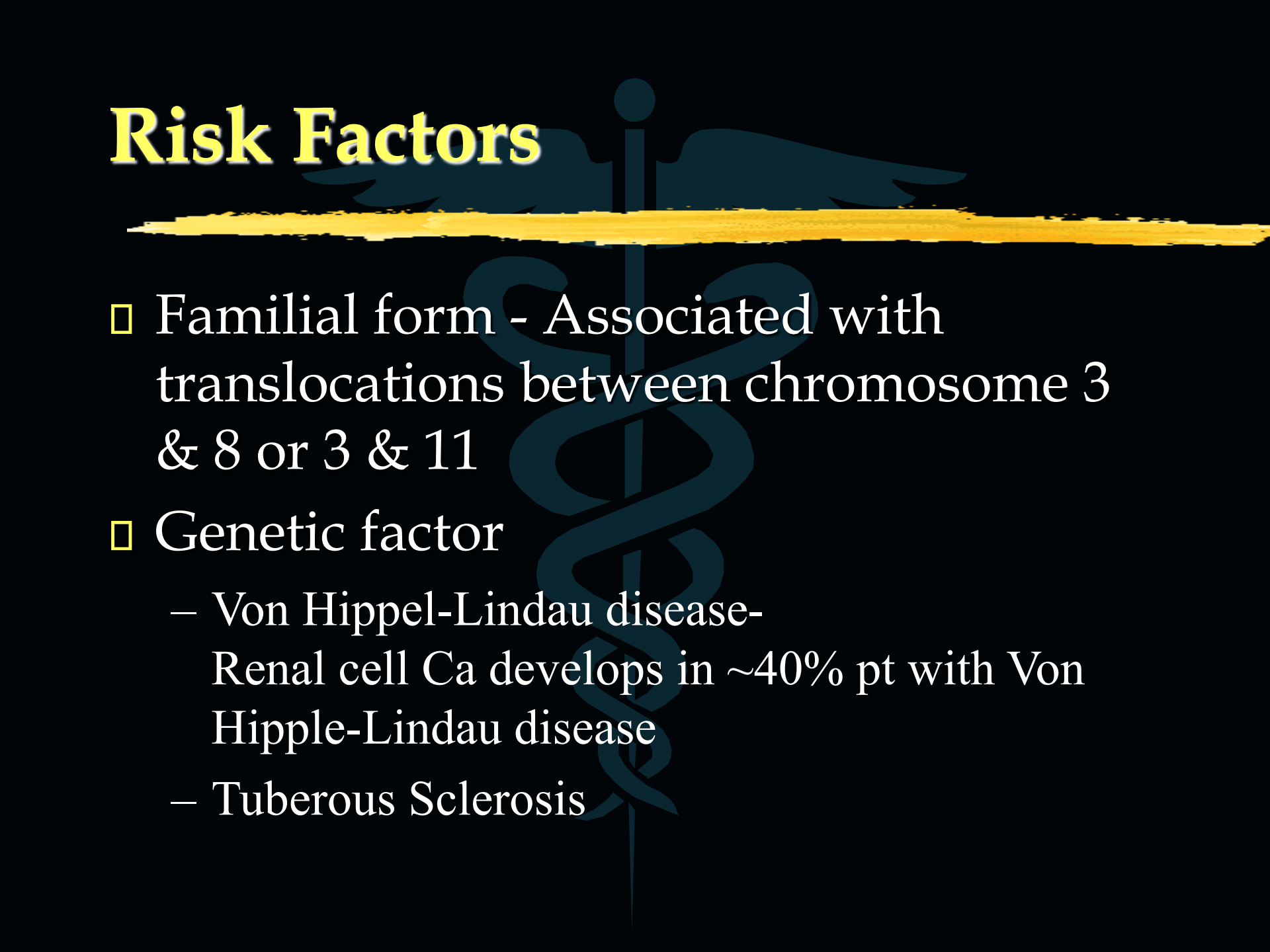
- 
- *Diet and weight:* some studies show a link between being overweight, a diet high in fat, and renal cell cancer.
 - *Age:* rare in children and young adults; mostly in adults >40 yrs between the ages of 50-70 years. Peak 6th Decade
 - *Gender:* men are twice as likely to get renal cell cancer as are women.

Risk Factors



- Analgesic abuse nephropathy
- Acquired cystic kidney disease - 30 times risk greater in dialysis pt with acquired polycystic disease of kidney than general population
- ~30-50% of Pts on long term dialysis develop acquired cystic disease & upto 6% of these Pt. with acquired cystic disease develop renal cancer

Risk Factors



- Familial form - Associated with translocations between chromosome 3 & 8 or 3 & 11
- Genetic factor
 - Von Hippel-Lindau disease- Renal cell Ca develops in ~40% pt with Von Hippel-Lindau disease
 - Tuberous Sclerosis

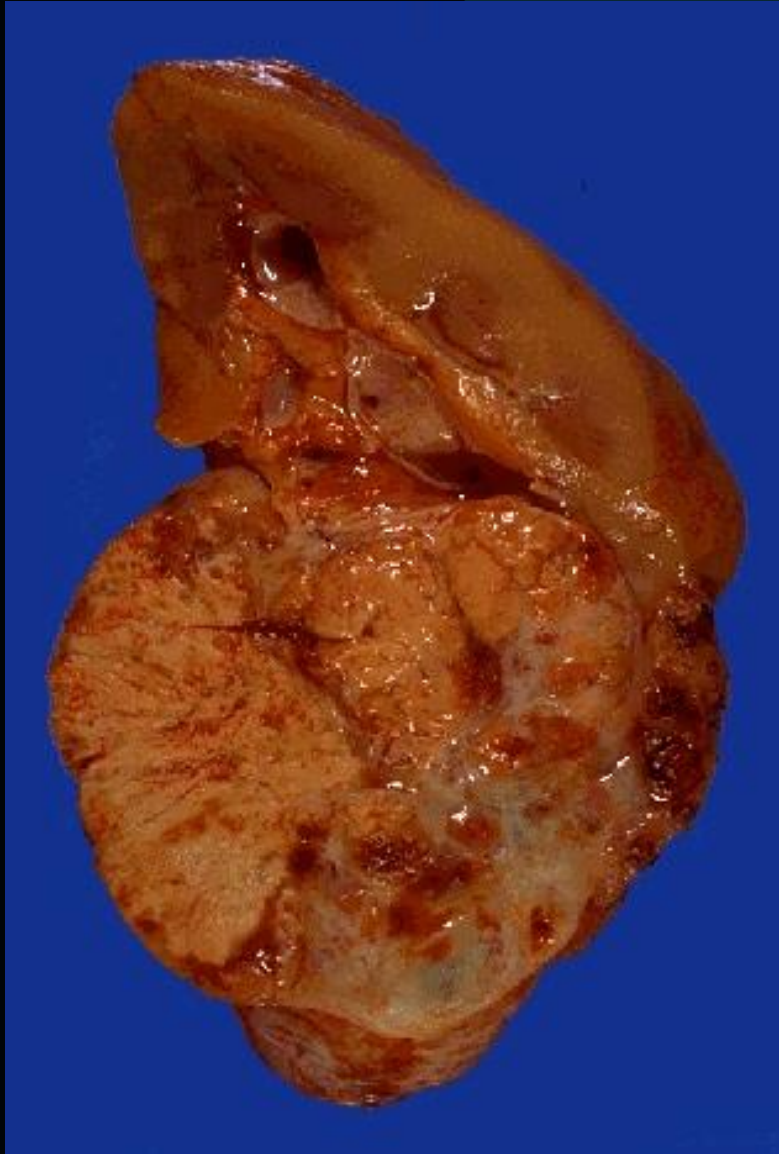
Pathology of Renal Cell Carcinoma

□ Macroscopy:

- Spherical in shape, on an average 7 to 8 cms but can grow in retro peritoneum.
- Golden yellow to orange in color, Dull white, semitransparent
- Central Hemorrhagic, Necrotic areas, cystic areas, Variegated appearance
- Firm capsulation: Pseudocapsule.



Pathology



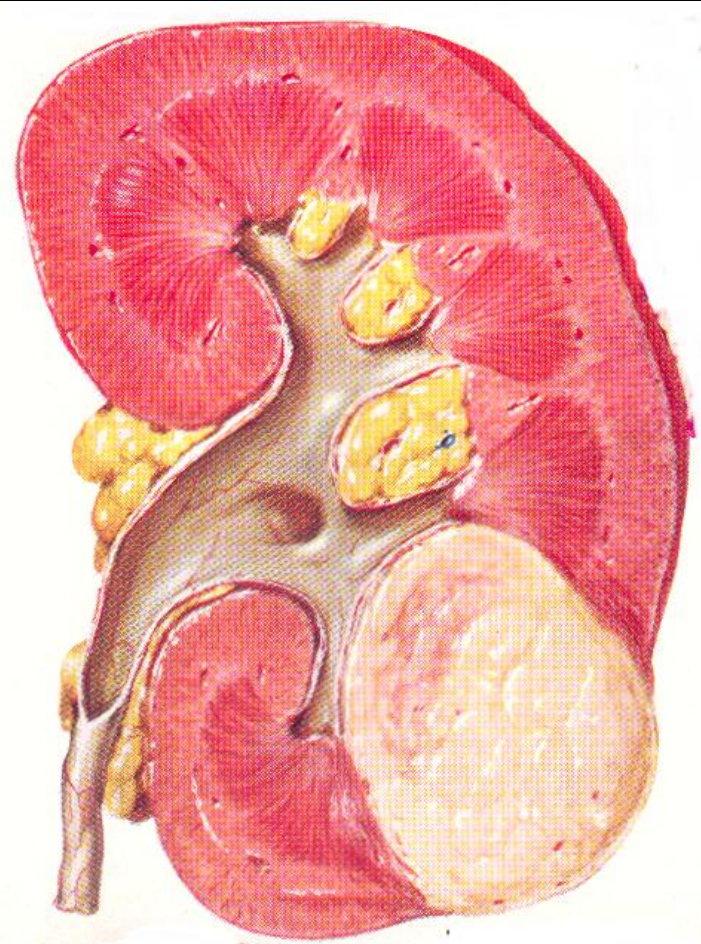
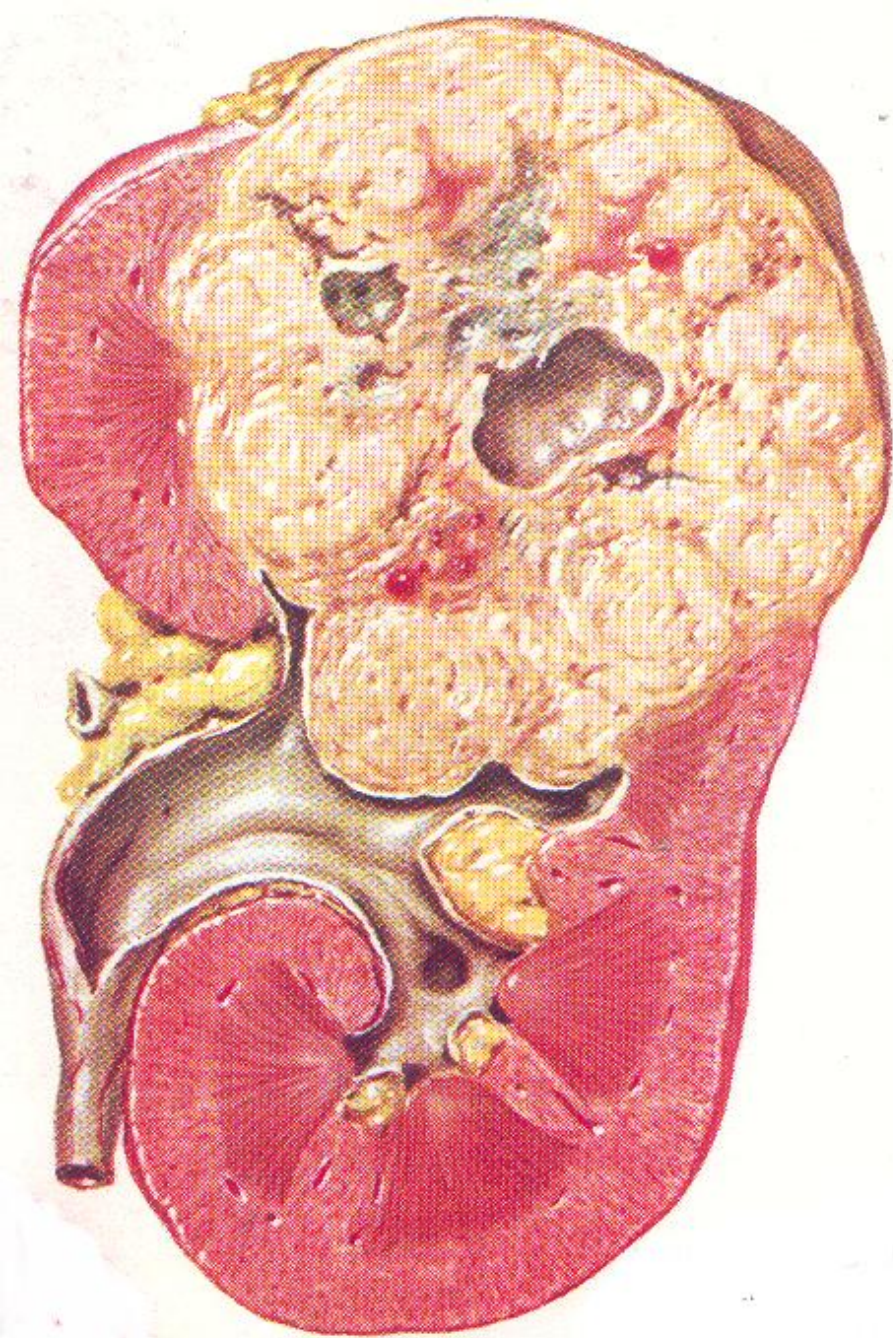
- Arising from lower pole, round to ovoid
- It is fairly circumscribed, pseudocapsule
- The cut surface - a variegated appearance with yellowish areas, white areas, brown areas, and hemorrhagic red areas

On sectioning - mainly cystic with extensive hemorrhage. Sometimes large simple renal cysts may develop hemorrhage and mimic this appearance





RCC and Adenoma of Kidney



Pathology of Renal Cell Carcinoma

Spread of RCC:

- Vascular Tumor:

- Local Spread:

Through renal capsule

Peri nephric space, Fat Adjacent Viscera

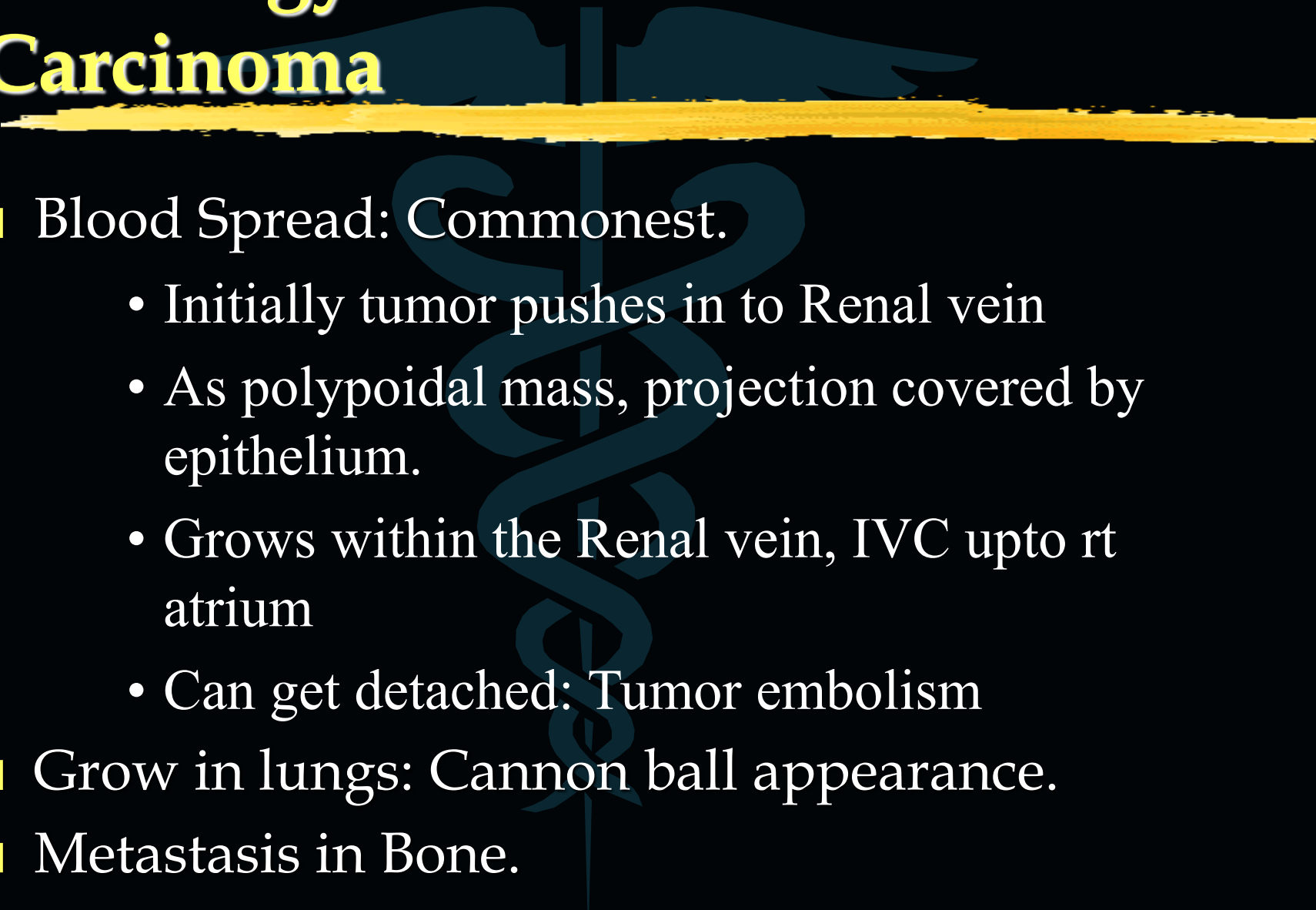
- Lymphatic Spread:

Usually after local spread Into peri-Renal Tissue

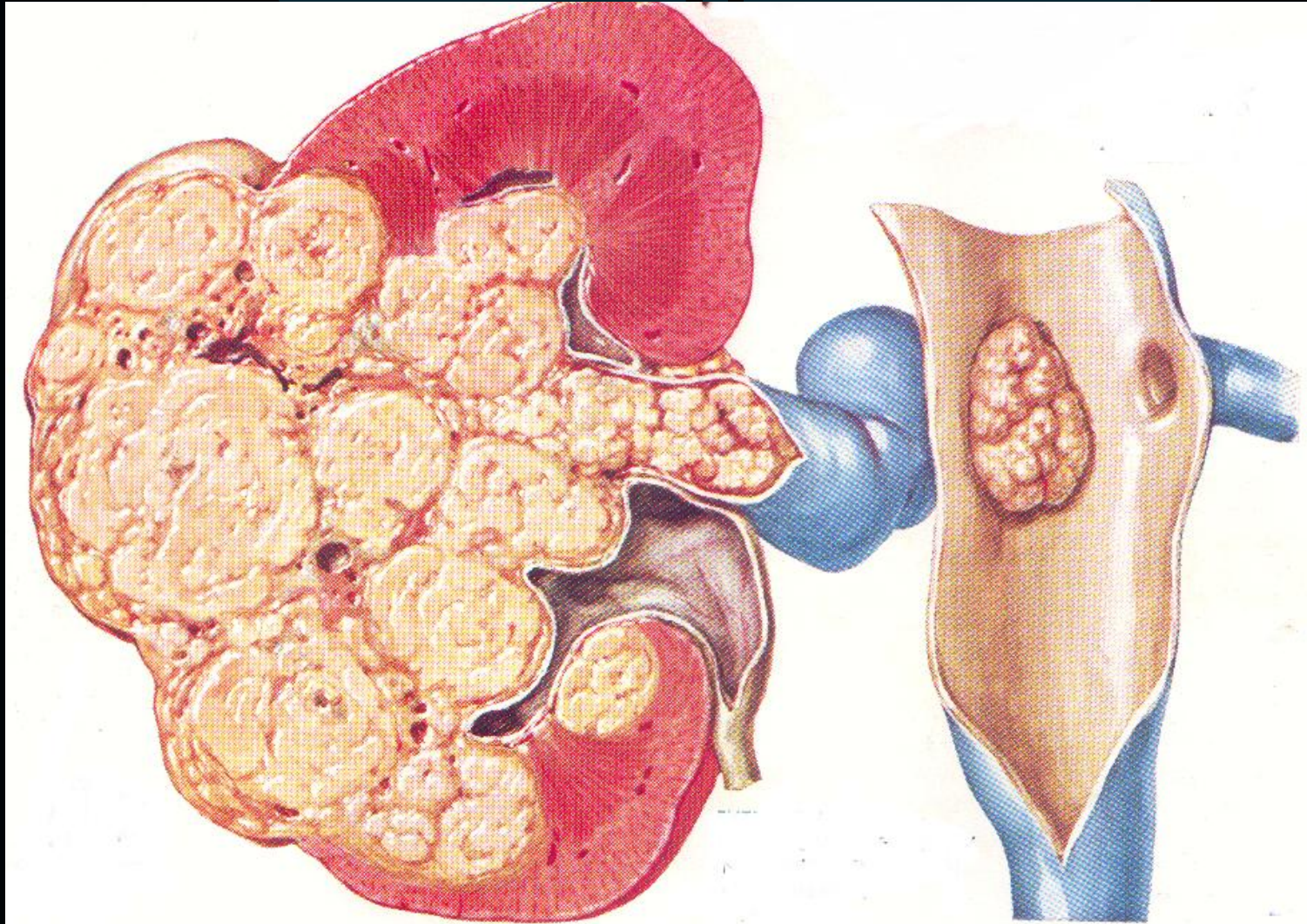
Para nephric node, Para Caval Nodes

Pre-aortic Node, Para aortic node

Pathology of Renal Cell Carcinoma



- Blood Spread: Commonest.
 - Initially tumor pushes in to Renal vein
 - As polypoidal mass, projection covered by epithelium.
 - Grows within the Renal vein, IVC upto rt atrium
 - Can get detached: Tumor embolism
- Grow in lungs: Cannon ball appearance.
- Metastasis in Bone.



Pathology of Renal Cell Carcinoma

Microscopy:

- Clear cell type: 25%: Most common, with above features. High glycogen content.
- Granular cell type
- Larger cells, large nuclei, stain darker
- Mixed cell type
- Sarcomatoid type

Histological type

- ❑ Clear cell - 75-85%, (loss of heterozygosity of chromosome 3p in ~ 90%)
- ❑ Chromophilic (papillary) - 14%, ~low stage at presentation, better prognosis than clear cell type
- ❑ Chromophobic - 4% (excellent prognosis)
- ❑ Oncocytic - rare
- ❑ Collecting duct (Bellini's duct) - extremely rare

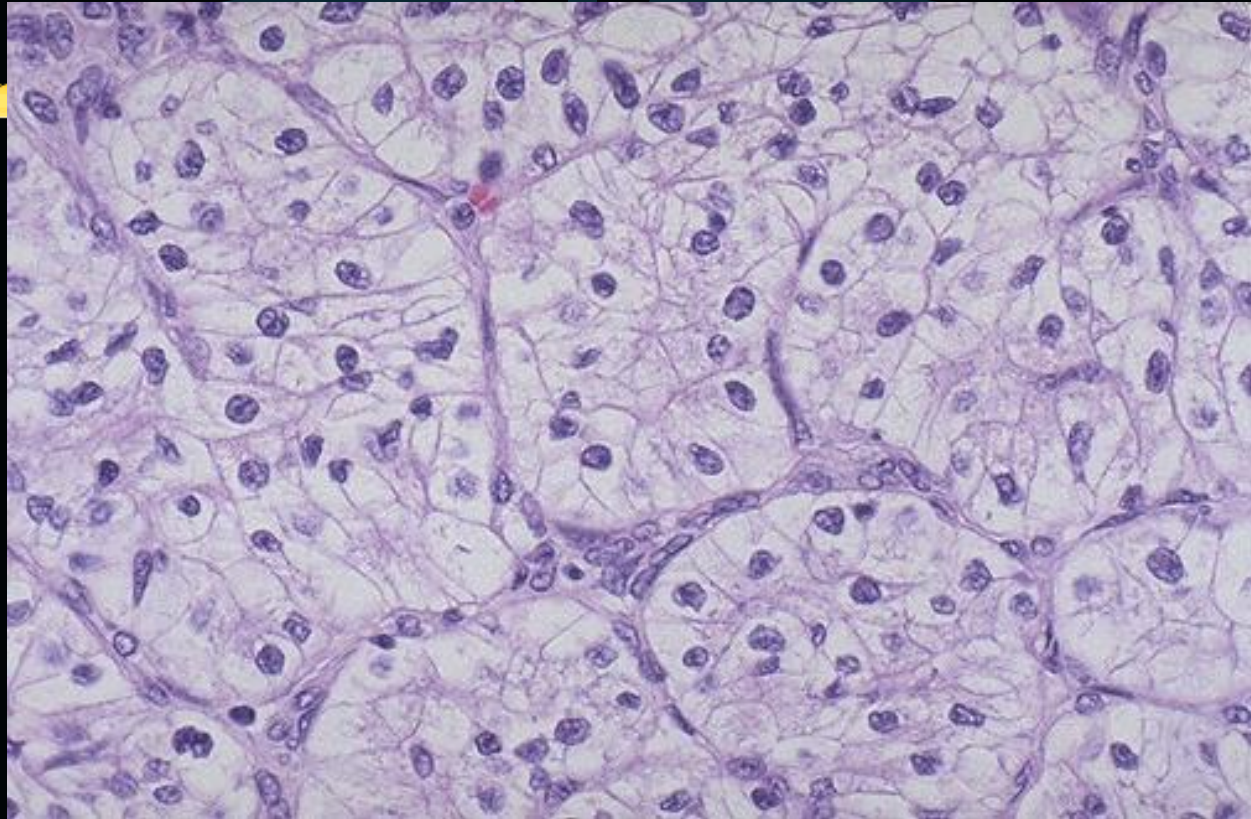
Histological types of RCC

Adenocarcinomas derived from renal tubular epithelial cells

- Clear cell – PCT
- Papillary
- Chromophobic
- Collecting duct
- Medullary cell

From
distal
tubules

1) Clear cell – 70 to 80%



The neoplastic cells have clear cytoplasm and are arranged in nests with intervening blood vessels

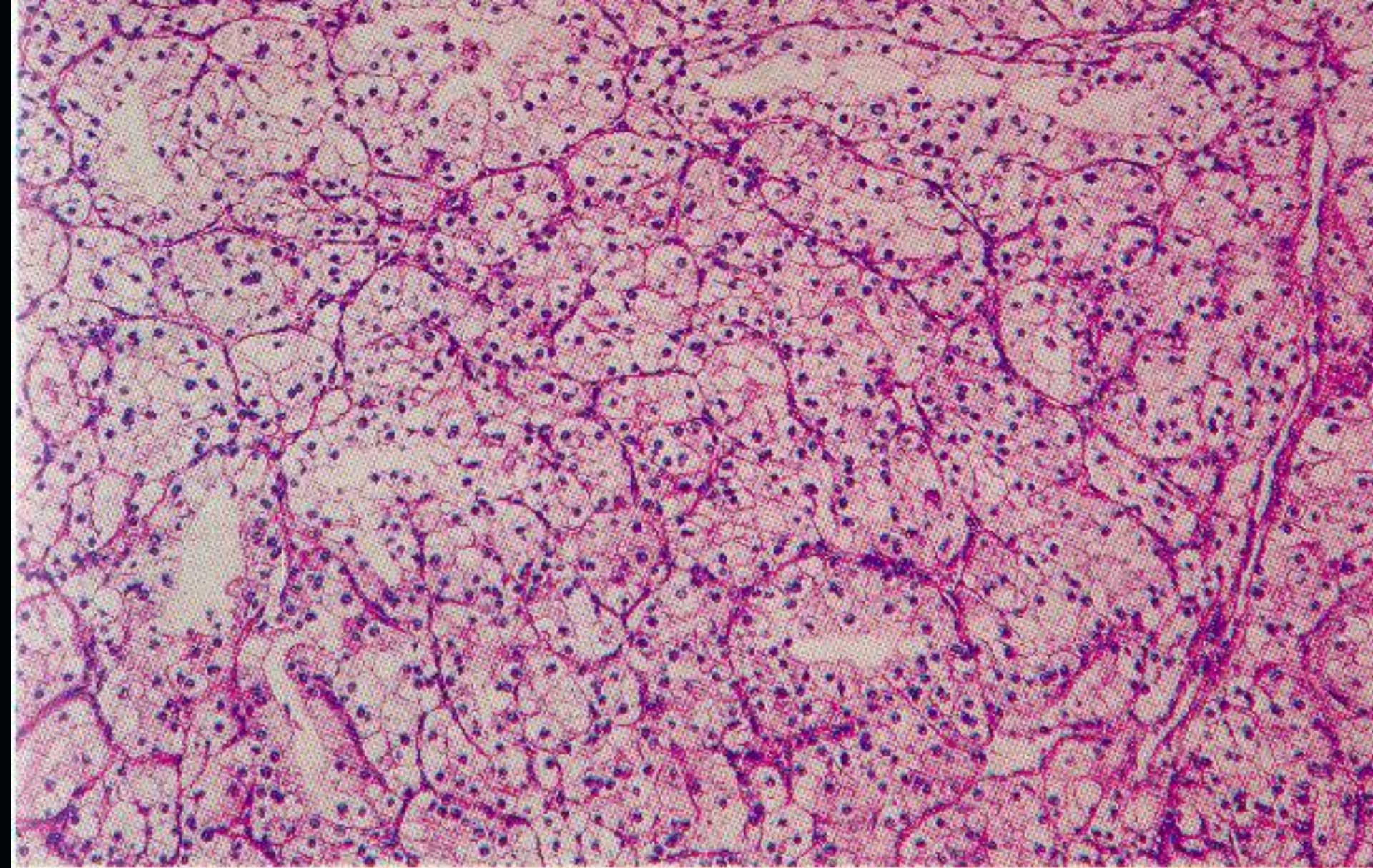
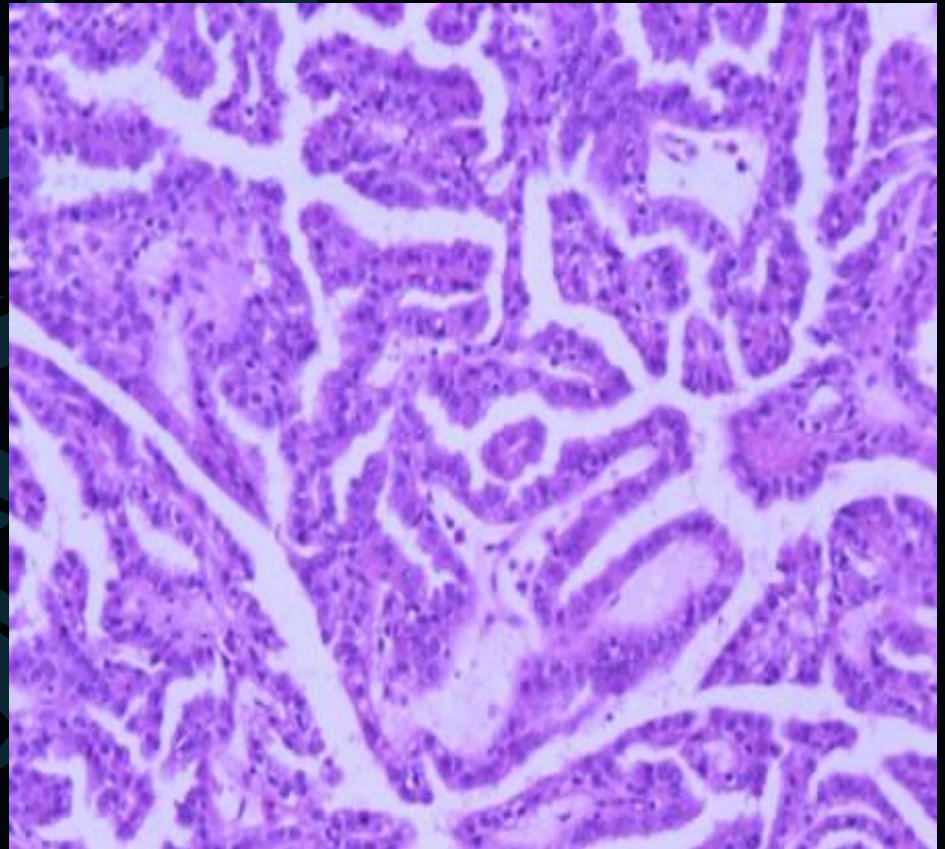


Fig. 9. Renal cell carcinoma

Clear cells in acinar, tubular and solid arrangements. $\times 100$.

2) Papillary/Tubulopapillary Carcinoma – 10 – 15%

- Seen more in in patients with end stage renal failure and acquired renal cystic disease



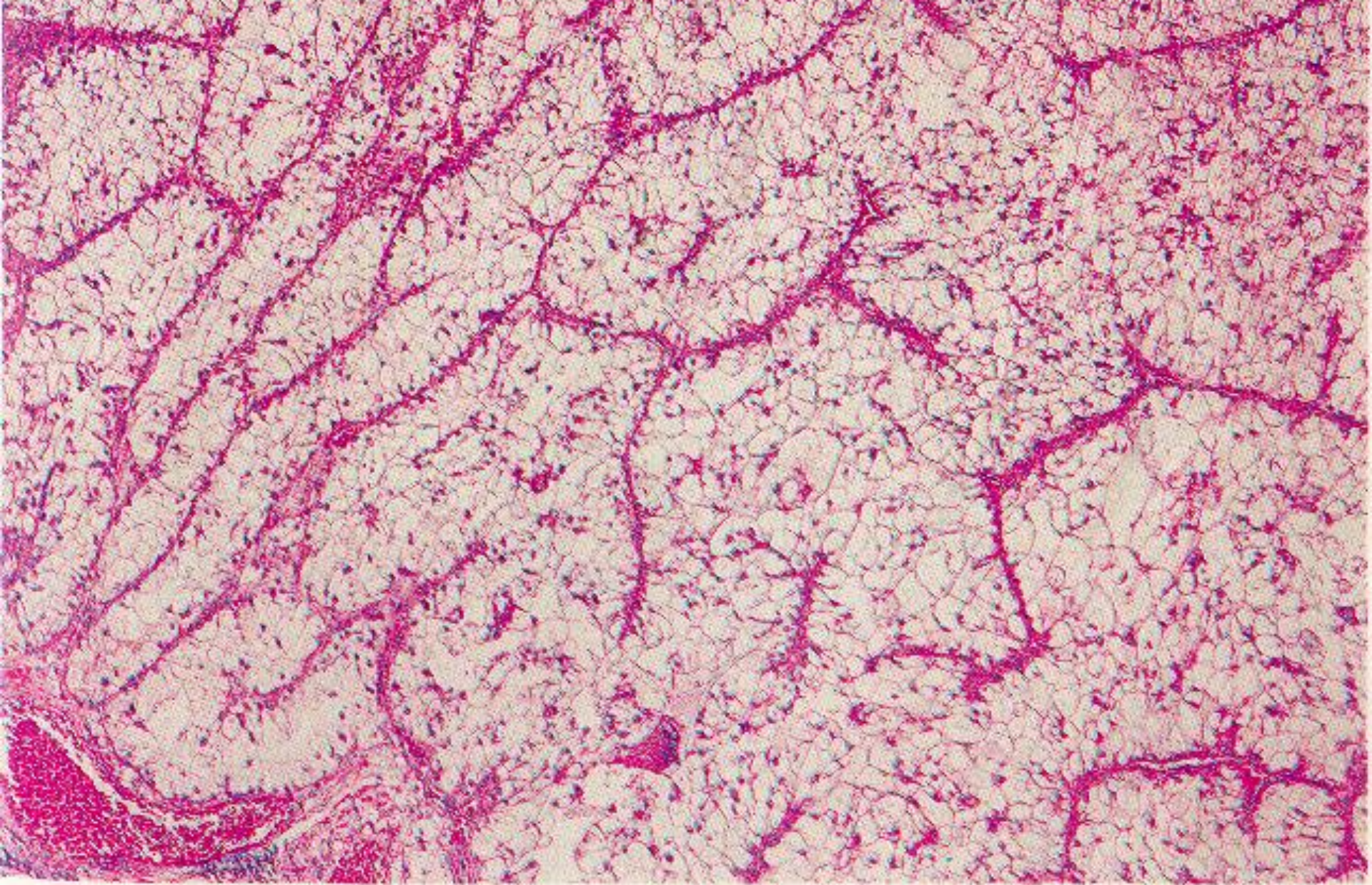
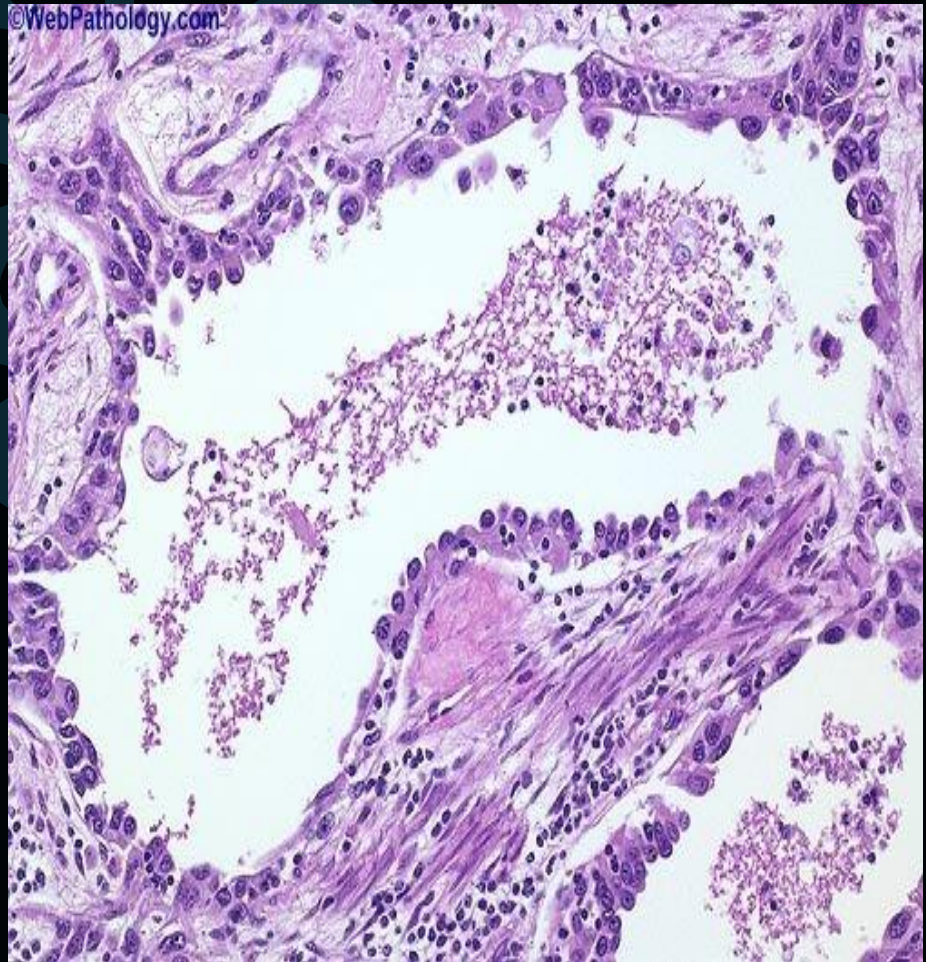


Fig. 10. Renal cell carcinoma

Large clear cells in solid and tubular patterns. $\times 60$.

4)Collecting duct carcinoma - <1%

- Dilated tubules and papillary structures lined by a single layer of cuboidal cells – Cobblestone appearance, Hobnail appearance



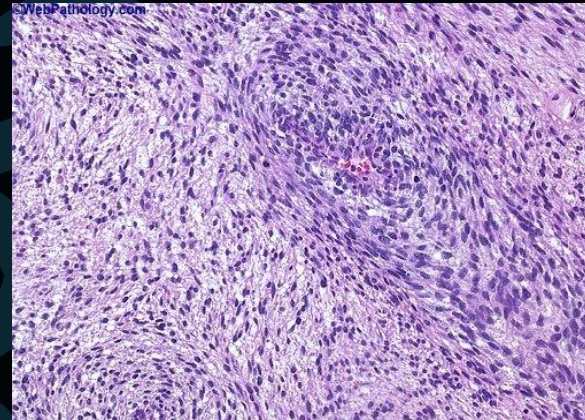
5) Medullary carcinoma – new histological subtype



- Association with sickle cell trait
- In young African – Americans
- 3rd decade of life
- Arise from calyceal epithelium near renal papillae
- Hypoxic environment – tumorigenesis
- Histology – like collecting duct carcinoma

6) Sarcomatoid change

- ❑ In 5% of RCC
- ❑ Spindle cell histology
- ❑ Positive staining for vimentin
- ❑ Infiltrative growth pattern, aggressive local and metastatic behavior
- ❑ Poor prognosis



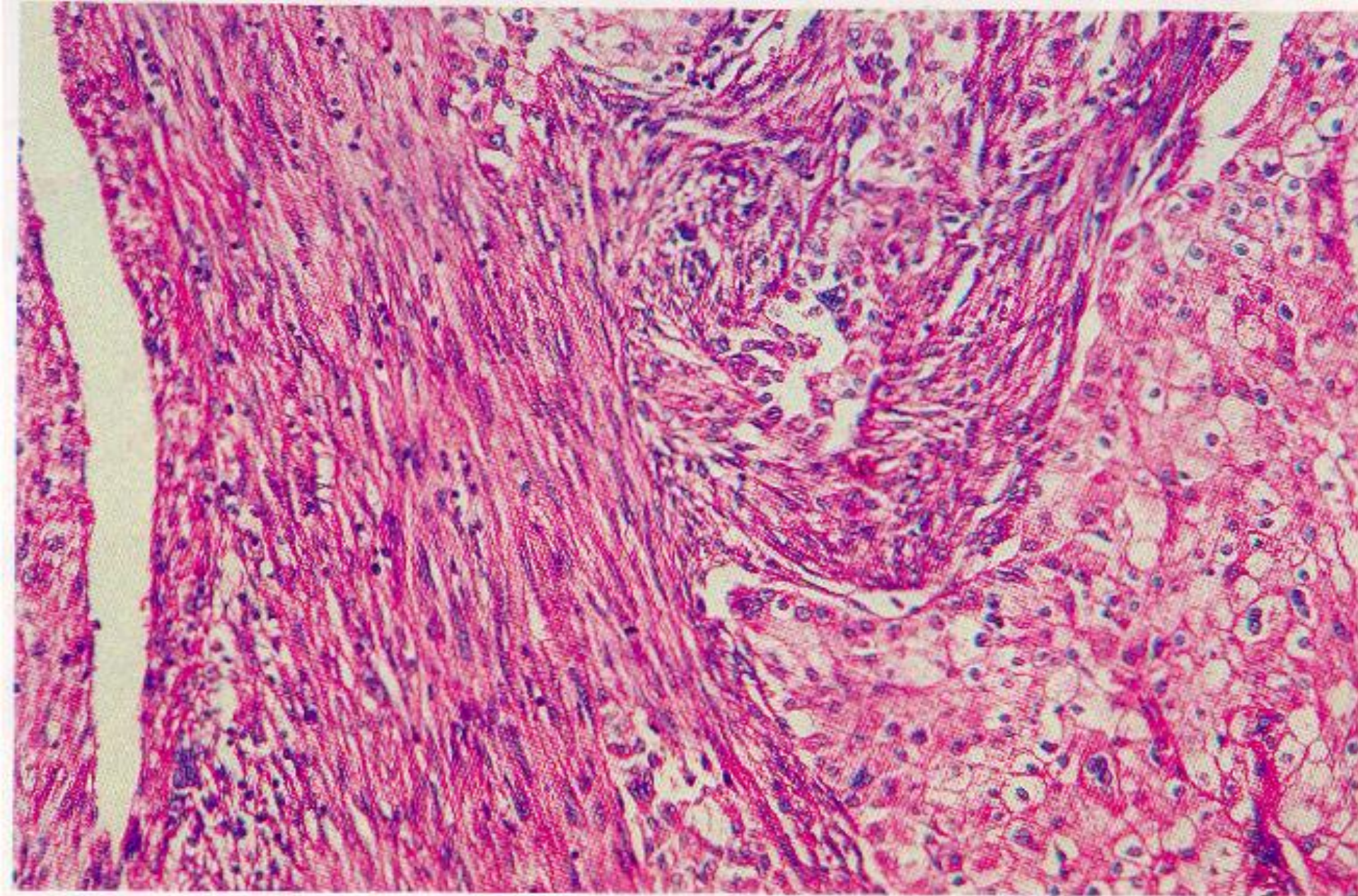
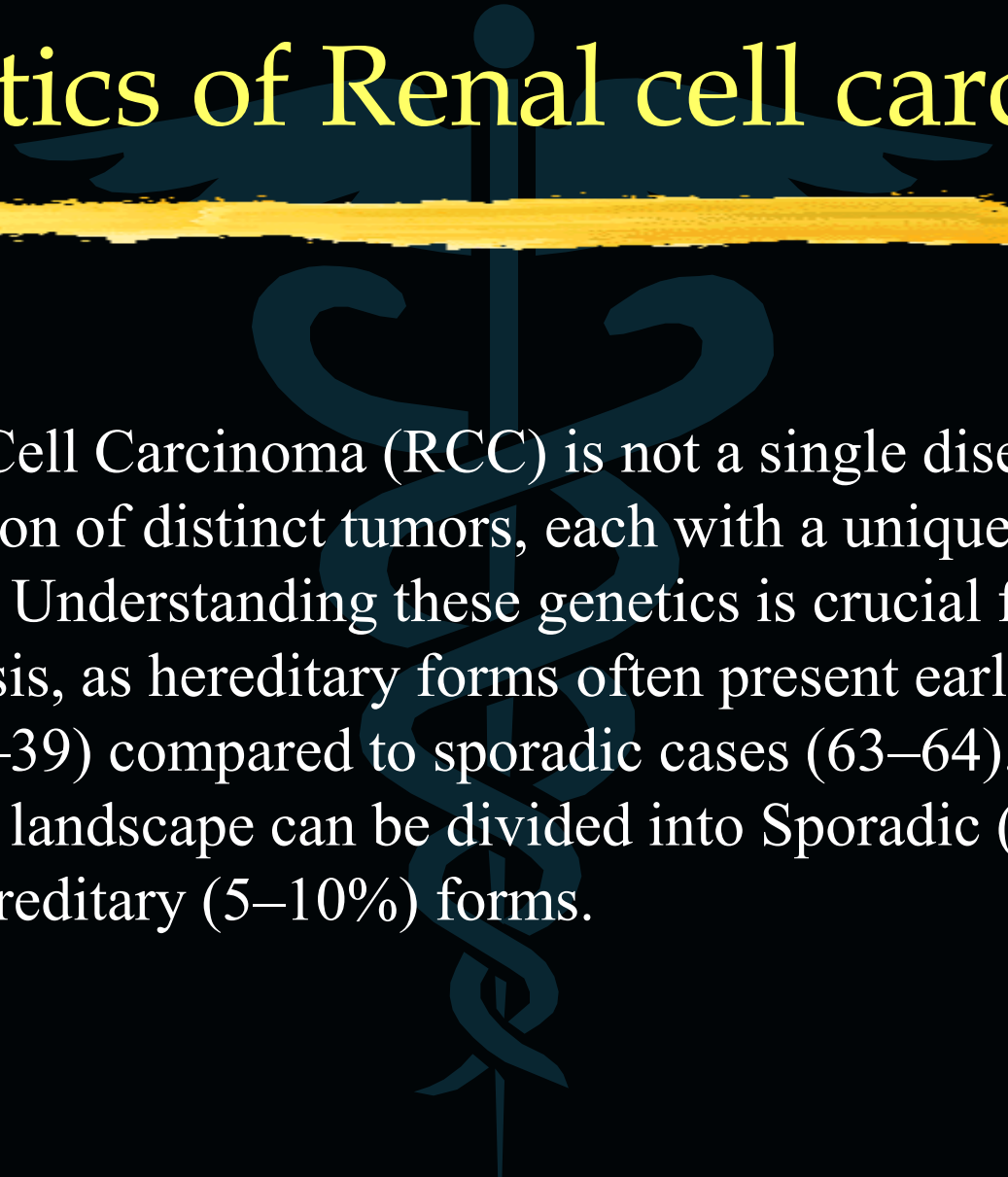


Fig. 27. Renal cell carcinoma
Solid and spindle cell areas. $\times 160$.

Pathological classification of Renal cell carcinoma

CARCINOMA TYPE	GROWTH PATTERN	CELL OF ORIGIN	CYTOGENIC CHARACTERISTICS		INCIDENCE (%)
			MAJOR	MINOR	
Clear cell	Acinar or sarcomatoid	Proximal tubule	-3p	+5,+7,+12,-6q,-8p,-9,-14q,-Y	75-85
Chromophilic	Papillary or sarcomatoid	Proximal tubule	+7,+17,-Y	+12,+16,+20,-14	12-14
Chromophobic	Solid, tubular, or sarcomatoid	Intercalated cell of cortical collecting duct	Hypodiploid	—	4-6
Oncocytic	Typied by tumor nests	Intercalated cell of cortical collecting duct	Undetermined	—	2-4
Collecting duct	Papillary or sarcomatoid	Medullary collecting duct	Undetermined	—	1

Genetics of Renal cell carcinoma



Renal Cell Carcinoma (RCC) is not a single disease but a collection of distinct tumors, each with a unique genetic profile. Understanding these genetics is crucial for diagnosis, as hereditary forms often present earlier (mean age 37–39) compared to sporadic cases (63–64).⁺¹ The genetic landscape can be divided into Sporadic (90–95%) and Hereditary (5–10%) forms.

1. Clear Cell RCC (ccRCC)

This is the most common subtype (75%), characterized by metabolic shifts and the "pseudohypoxia" pathway.

- VHL Gene (3p25): The hallmark of ccRCC. Inactivation of the VHL tumor suppressor gene occurs in over 90% of sporadic cases.
 - o Mechanism: Loss of VHL leads to the accumulation of HIF (Hypoxia-Inducible Factor), which triggers the transcription of VEGF (angiogenesis) and GLUT1 (glucose transport), even when oxygen is plenty.
- Chromosome 3p Deletions: Often involves the loss of an entire arm of chromosome 3, which houses other key driver genes:
 - o PBRM1: A chromatin-remodeling gene (mutated in ~40%).
 - o BAP1: Associated with a more aggressive phenotype and poorer prognosis.
 - o SETD2: A histone methyltransferase; its loss is linked to tumor progression.
- mTOR Pathway: Mutations in MTOR, TSC1/2, or PTEN occur in about 20% of cases, providing a target for mTOR inhibitors.

Papillary RCC (pRCC)

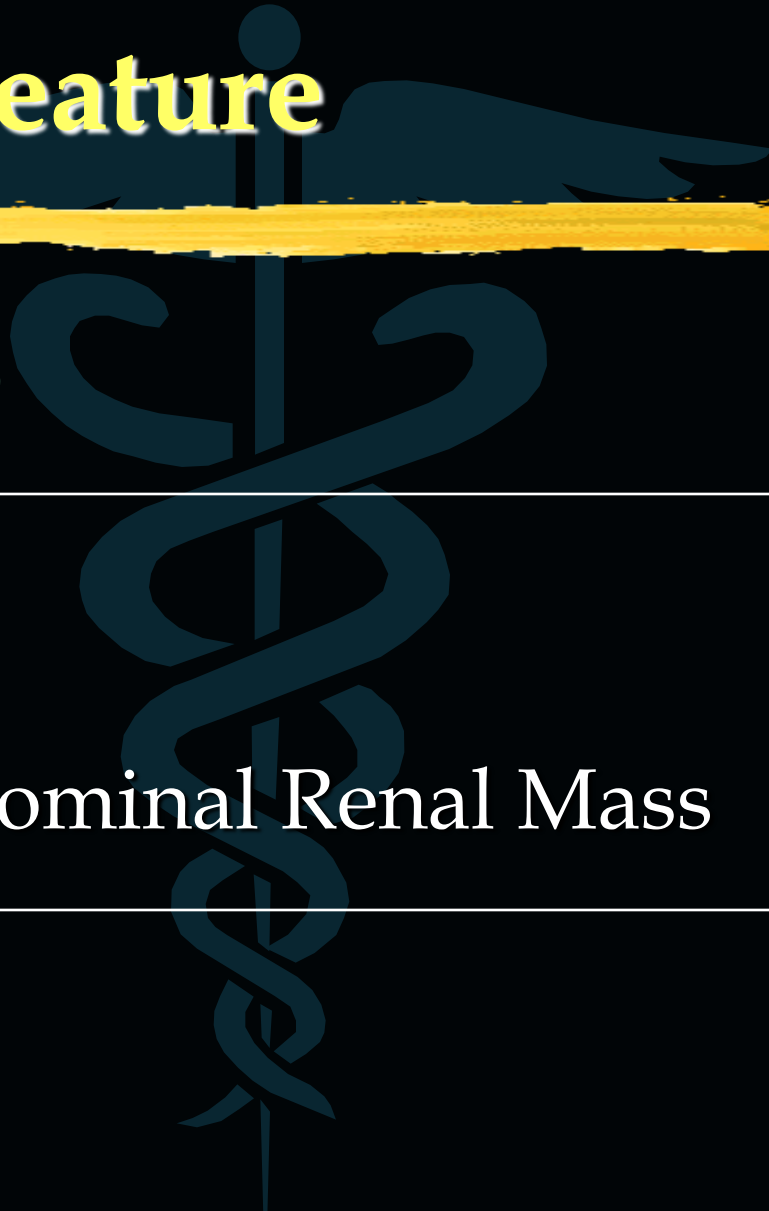
- **MET Proto-oncogene (7q31):** The primary driver for **Type 1 Papillary RCC**.
 - **Hereditary Papillary Renal Cancer (HPRC):** Caused by germline activating mutations in *MET*.
 - **Sporadic pRCC:** Often shows gain of chromosome 7 (where *MET* resides) and chromosome 17.
- **Type 2 Papillary RCC:** More heterogeneous; involves alterations in *NF2*, *SETD2*, and *CDKN2A*.

3. Chromophobe RCC (chRCC)

- **Chromosomal Loss:** Unlike ccRCC, chRCC is characterized by a "low mutation rate" but massive **monosomy** (loss of entire copies) of chromosomes 1, 2, 6, 10, 13, 17, and 21.
- **TP53 and PTEN:** Mutations in these genes are often seen in the more aggressive sarcomatoid variants of chRCC.

Syndrome	Gene	Histology	Extra-renal Features
VHL Disease	<i>VHL</i>	Clear Cell	Hemangioblastomas (CNS/Retina), Pheochromocytomas .
HLRCC (Reed's)	<i>FH</i>	Papillary (Type 2)	Cutaneous/Uterine leiomyomas; Very aggressive.
Birt-Hogg-Dubé	<i>FLCN</i>	Chromophobe / Hybrid	Lung cysts, Spontaneous pneumothorax, Skin bumps.
HPRC	<i>MET</i>	Papillary (Type 1)	Multiple/Bilateral kidney tumors; usually limited to kidney.
Tuberous Sclerosis	<i>TSC1/2</i>	Any (rarely)	Angiomyolipomas (AMLs), Facial angiofibromas, Seizures.

Clinical Feature



Classical TRIAD

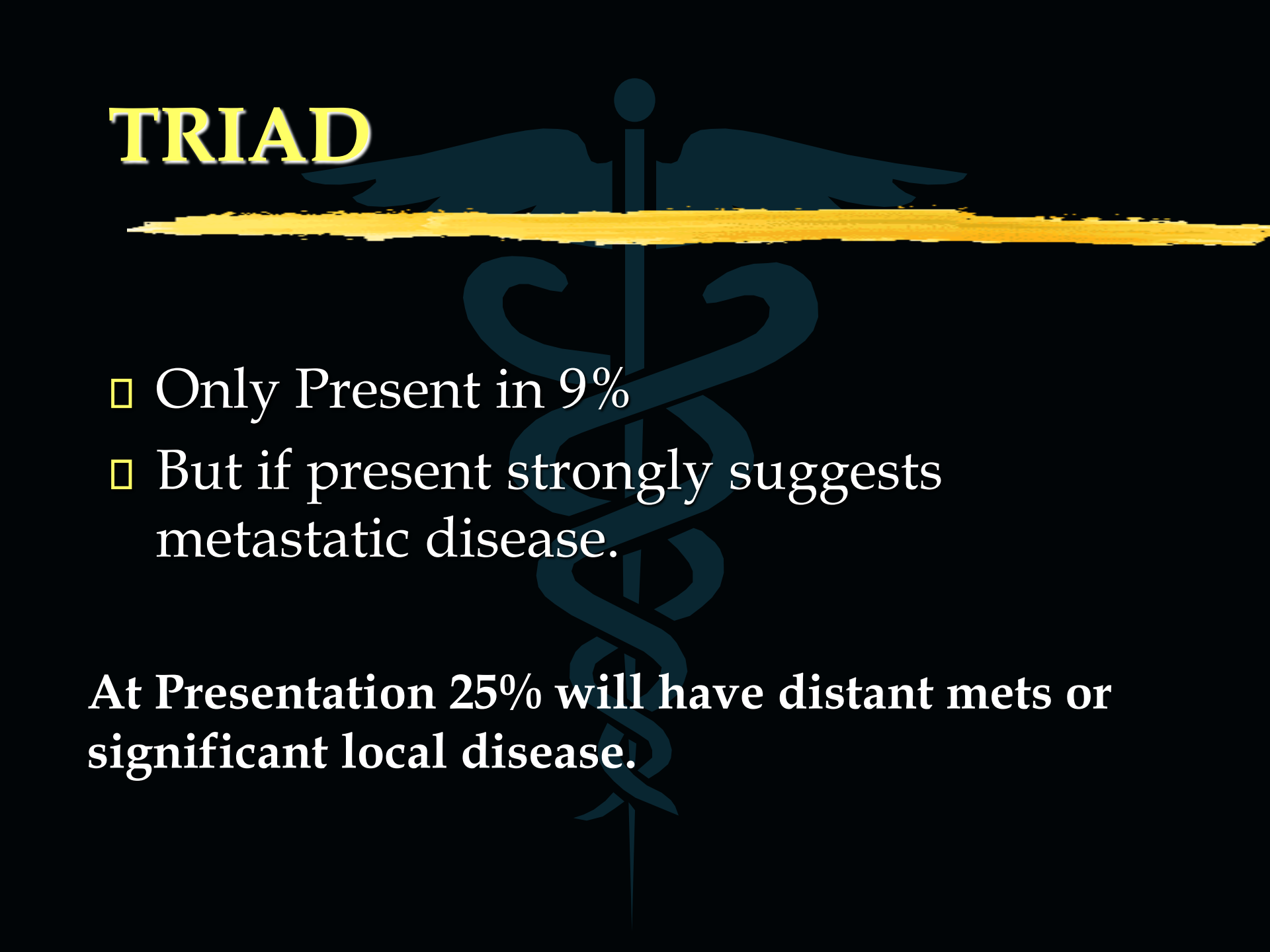
- Flank pain
- Hematuria
- Palpable Abdominal Renal Mass

Signs and Symptoms Of RCC

□ Classical Triad

- Hematuria ; Microscopic or gross 59%
 - First sign, Intermittent followed CLOT COLIC
- Pain in the flank or lower back not associated with an injury; 45%
 - Dull , constant Pain , followed by clot colic
- An abdominal mass or lump in lumbar region 49%
 - Enlarged Kidney, Globular, Smooth Nontender

TRIAD



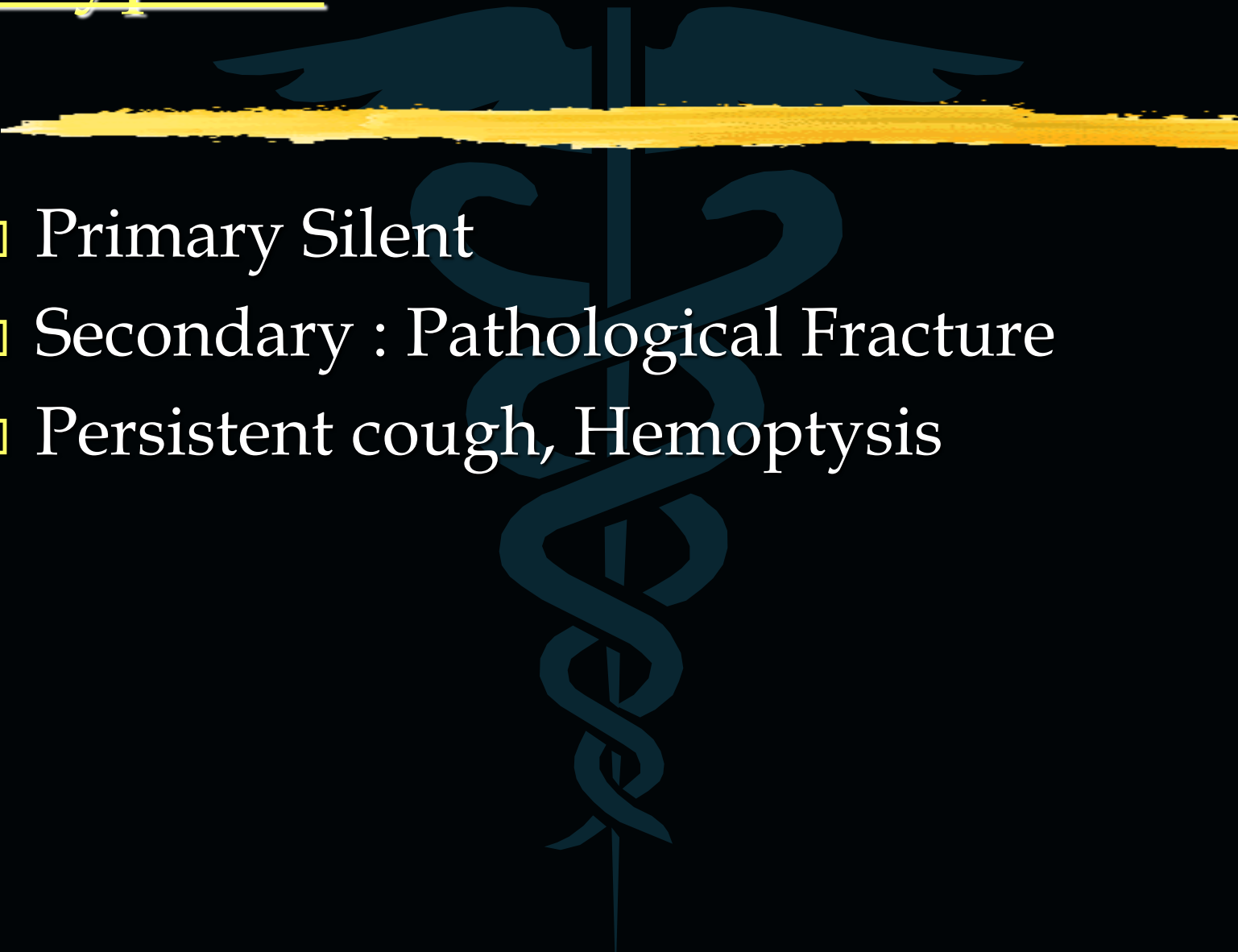
- Only Present in 9%
- But if present strongly suggests metastatic disease.

At Presentation 25% will have distant mets or significant local disease.

Others symptoms

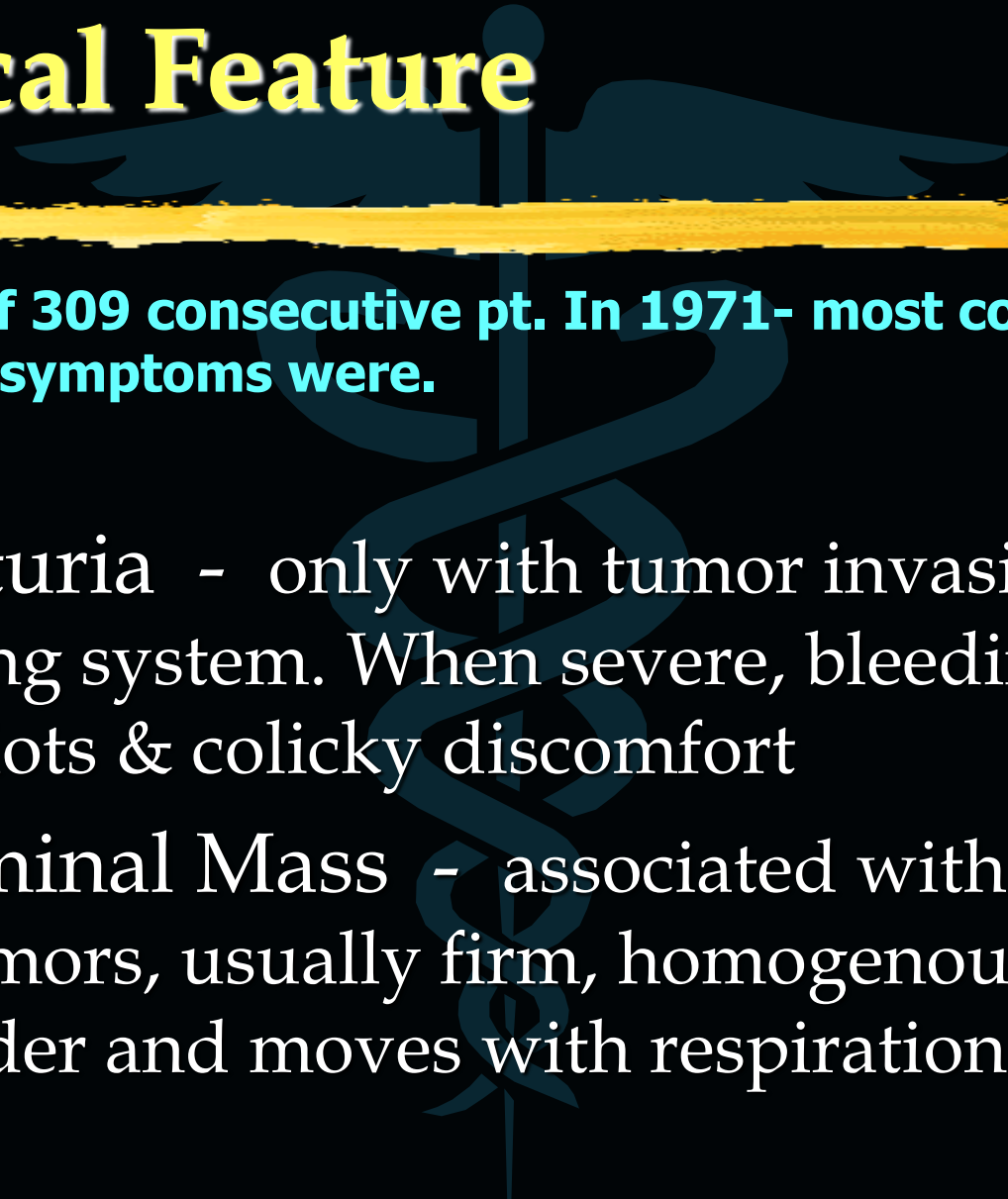
- Anaemia disproportionate to hematuria 20%
 - Normocytic normochromic, or Microcytic hypochromic
 - A persistent feeling of fatigue; weakness, lassitude
- Fever not caused any infection
 - Necrotic material from tumour, Endogenous pyrogen
 - Nephrectomy comes Back with Mets
- Rapid, unexplained weight loss;
- Oedema of leg
- Nausea, vomiting, constipation,
- Hypertension 10 –25%:
 - AV shunting. Pressure substance Production
 - Goldblatt effect of vascular Compression at Hilum

Atypical Presentation : 25%



- Primary Silent
- Secondary : Pathological Fracture
- Persistent cough, Hemoptysis

Clinical Feature



In a review of 309 consecutive pt. In 1971- most common presenting symptoms were.

- Hematuria - only with tumor invasion of the collecting system. When severe, bleeding may cause clots & colicky discomfort
- Abdominal Mass - associated with lower pole tumors, usually firm, homogenous, nontender and moves with respiration

Clinical Feature



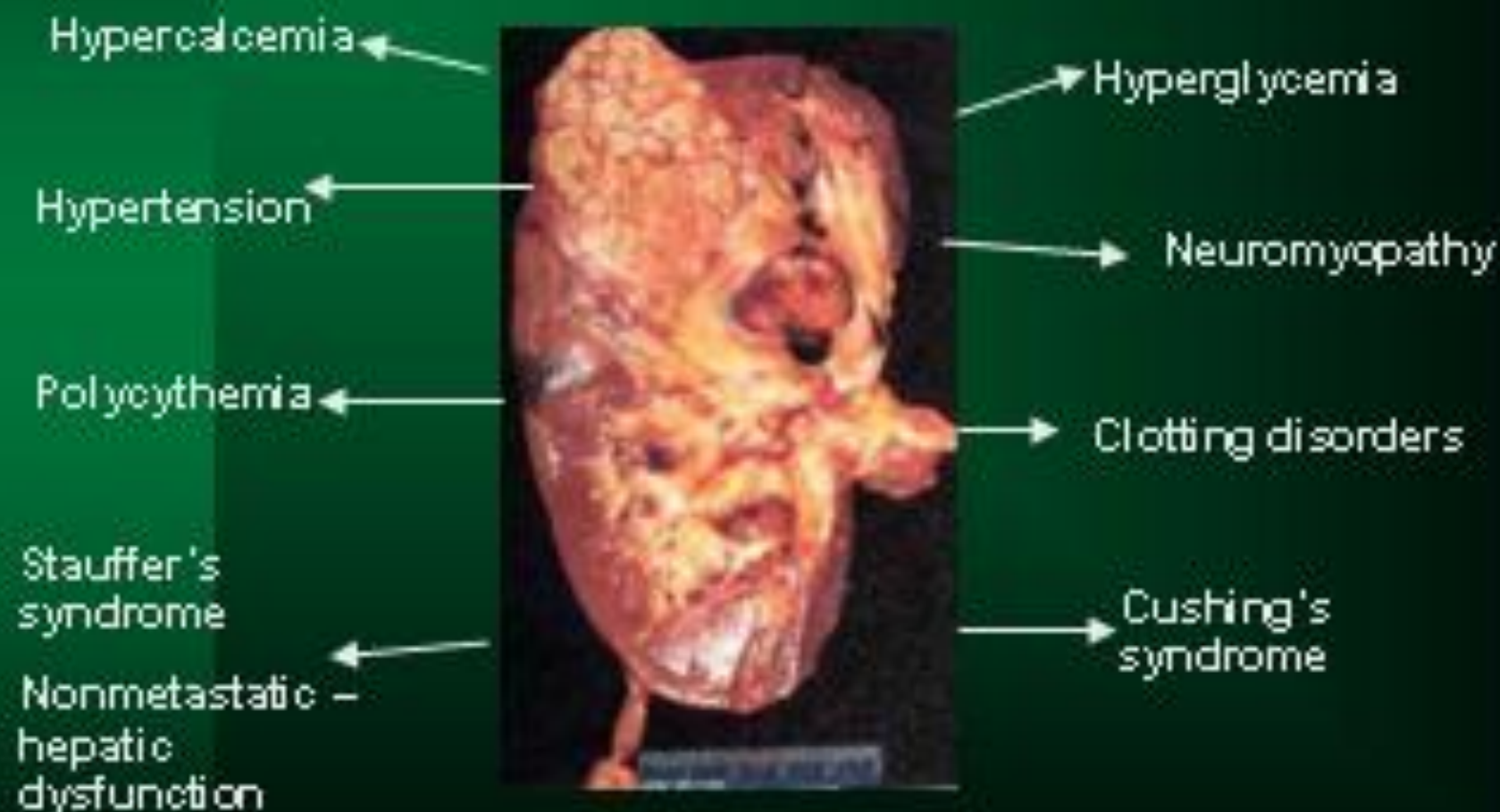
- Fever ~ 15%
- Night sweats
- Weight Loss
- Inferior vena caval involvement - ~ 5% - Most often occurs with Rt.. Sided renal tumor and is usually associated with metastasis in nearly 50% of patients

Clinical Feature

- Less frequent but suggestive features
- **Acute onset of either**
 - Lower extremity edema
 - Scrotal Varicocele (~11%) left sided, typically fail to empty when pt is recumbent (due to obstruction of the testicular vein where it enters the renal vein)



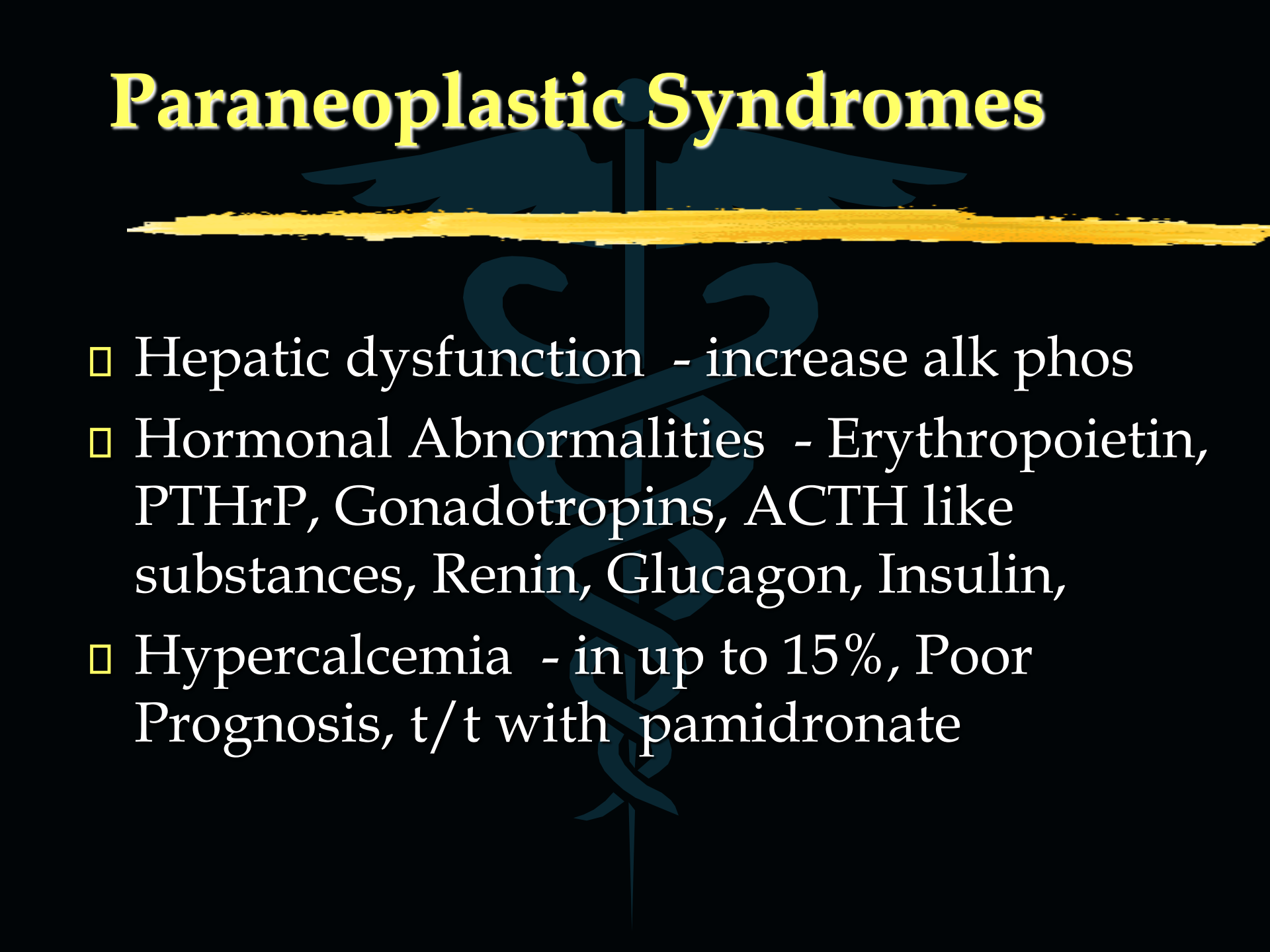
Paraneoplastic syndromes- in 20% of RCC



Extranephric Non Metastatic Paraneoplastic Syndromes

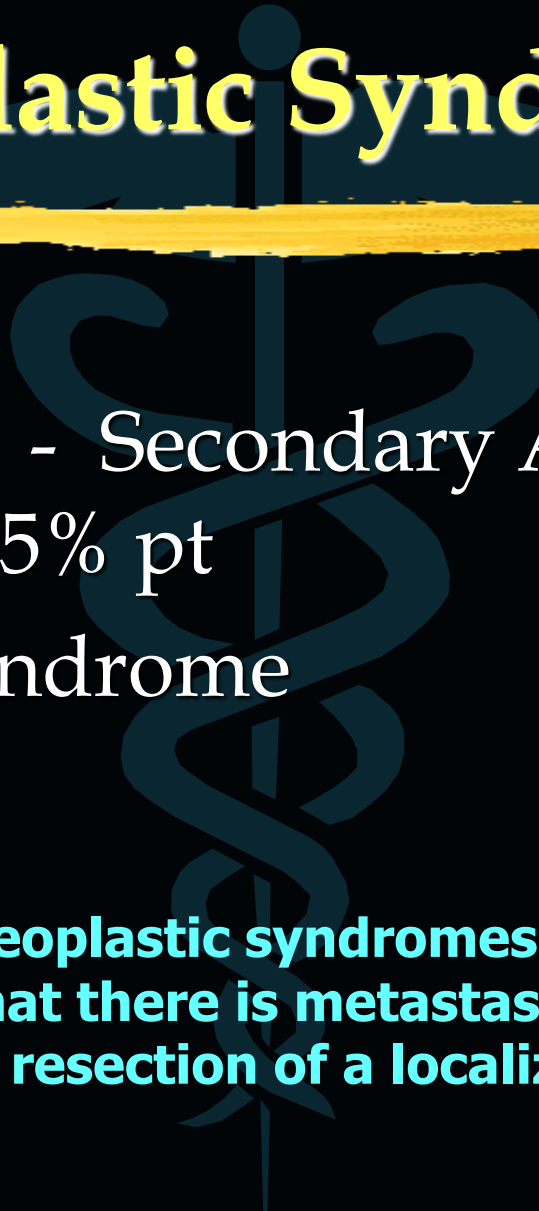
- Fever - In upto 20% pt. ,
 - Intermittent with night sweats
- Anemia - (29- 88%)
 - Can be either normocytic or microcytic
- Erythrocytosis - 1-5%
- Cachexia

Paraneoplastic Syndromes



- Hepatic dysfunction - increase alk phos
- Hormonal Abnormalities - Erythropoietin, PTHrP, Gonadotropins, ACTH like substances, Renin, Glucagon, Insulin,
- Hypercalcemia - in up to 15%, Poor Prognosis, t/t with pamidronate

Paraneoplastic Syndromes



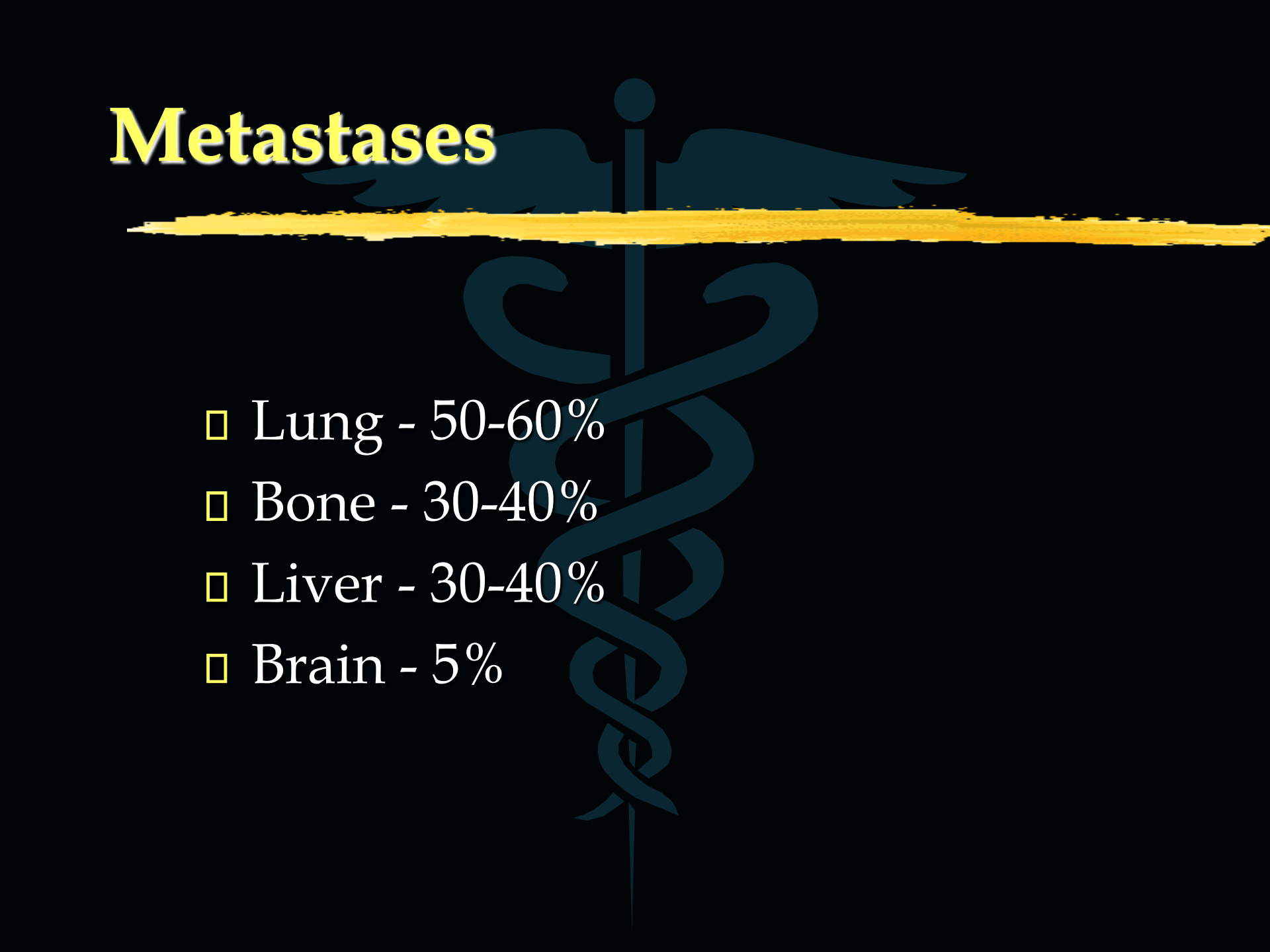
- Amylodosis - Secondary Amylodosis, present in 3-5% pt
- Stauffer's syndrome

Presence of Paraneoplastic syndromes does not necessary imply that there is metastasis disease or contraindicate the resection of a localized tumor.

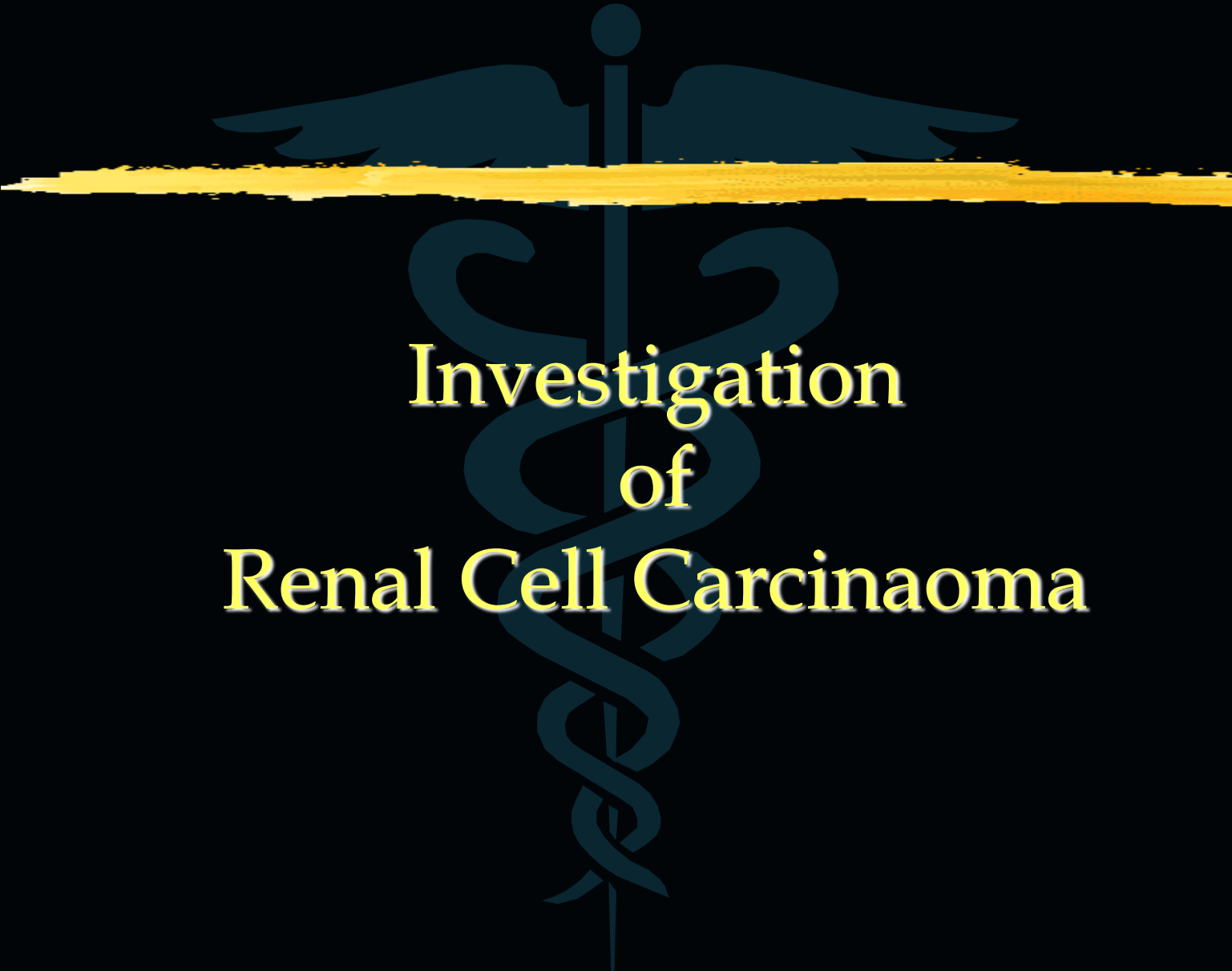
Clinical Presentation

- Localized disease, 45%
- Locally advanced disease 25%
- Metastasis 30%
 - Lung - 50-60%
 - Bone - 30-40%
 - Liver - 30-40%
 - Brain - 5%
 - Soft Tissue 36%,
 - Skin 8%

Metastases



- Lung - 50-60%
- Bone - 30-40%
- Liver - 30-40%
- Brain - 5%



Investigation of Renal Cell Carcinoma

Evaluation for distant Mets.

(If renal neoplasm suspected)

- CBCD
- Chemistry
- Chest X ray
- Bone Scan
- LFT
- CT scan of head (not if no neurological symptoms)

Evaluation of Renal Masses

□ Ultrasound

□ IVP

□ CT

□ MRI

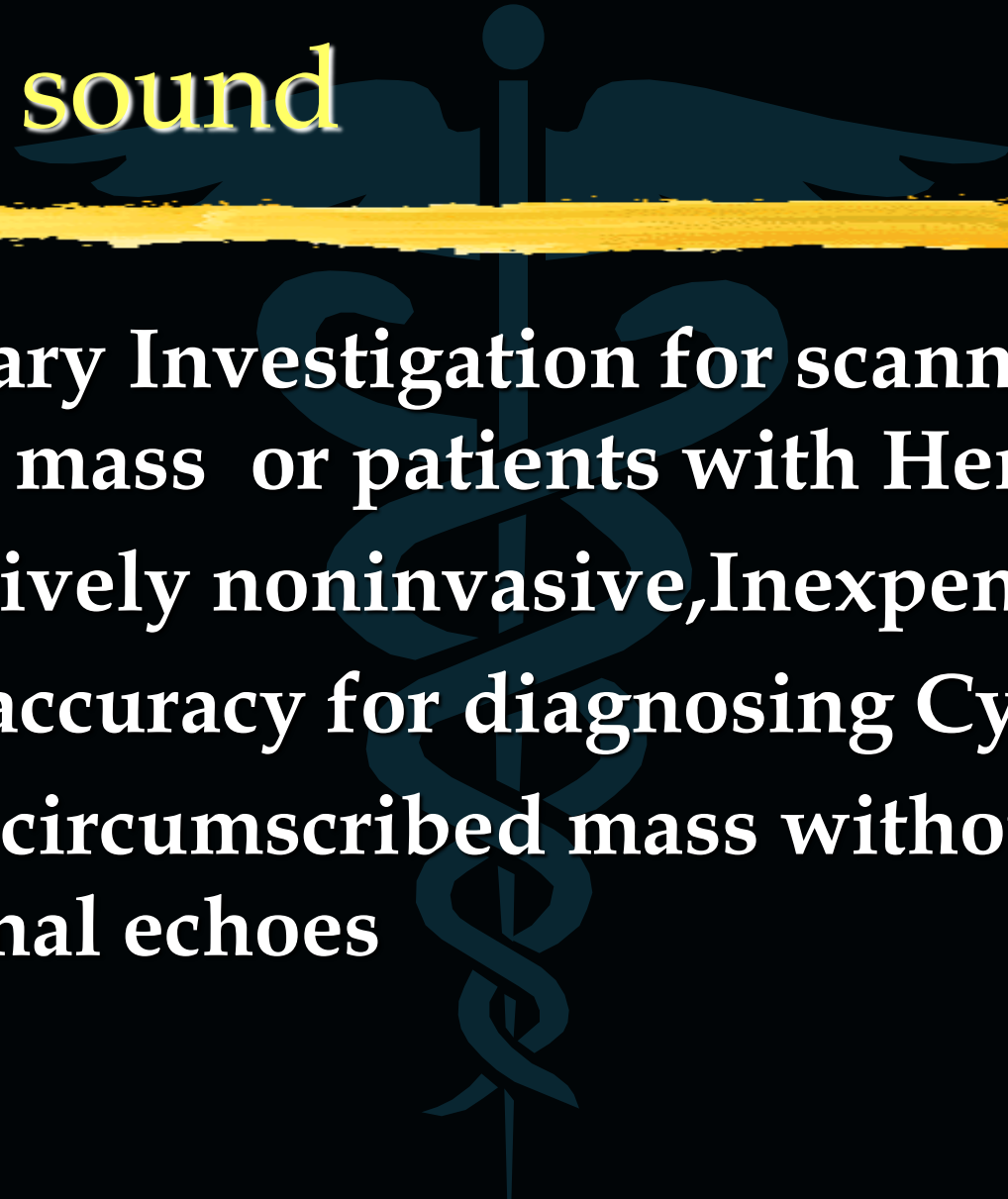
For Tumors < 3 cm in dia. Sensitivities of

Urography - 67%

Ultrasound - 79%

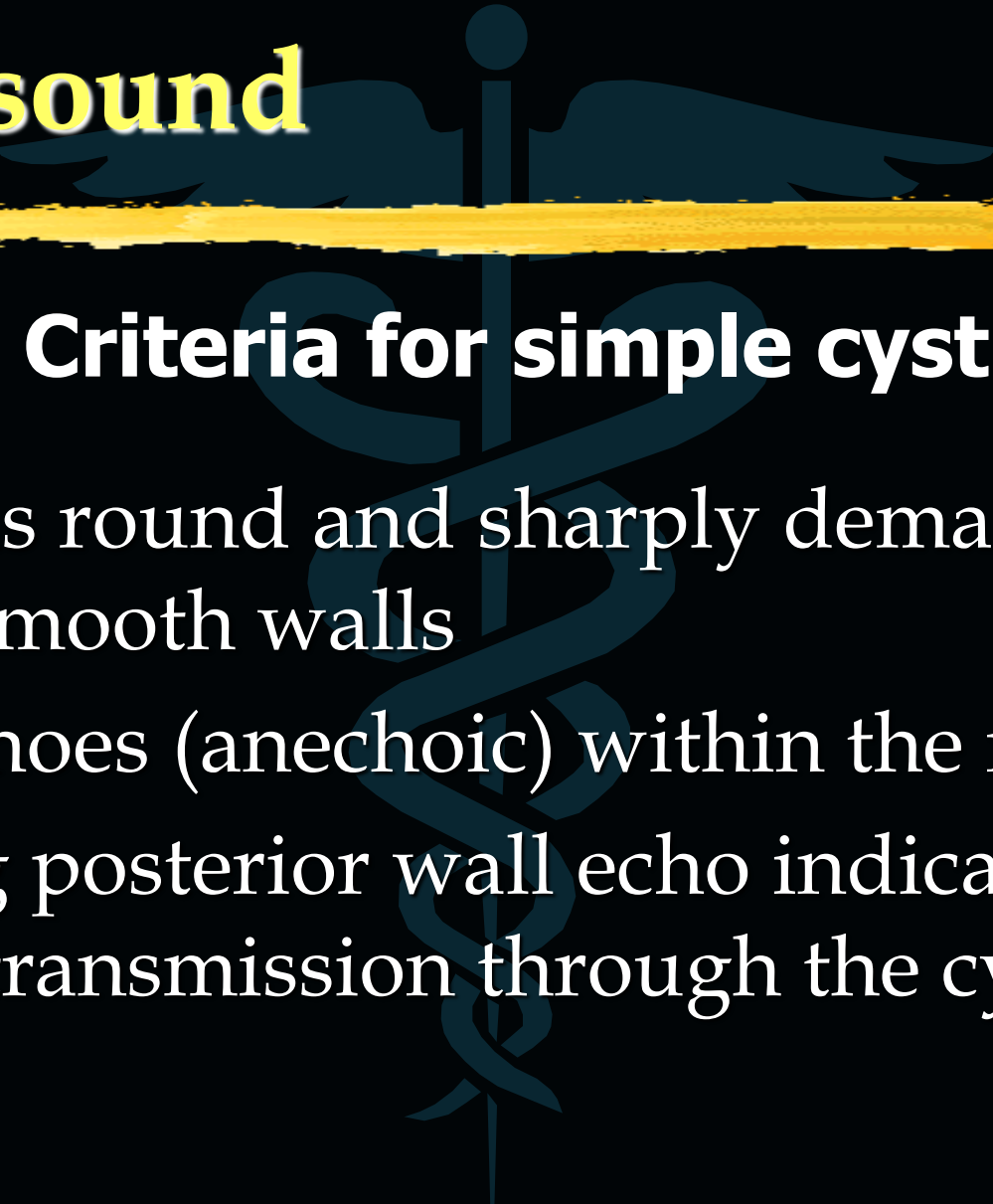
CT Scan - 94%

Ultra sound



- Primary Investigation for scanning the renal mass or patients with Hematuria
- Relatively noninvasive, Inexpensive
- 98% accuracy for diagnosing Cysts
- Well circumscribed mass without internal echoes

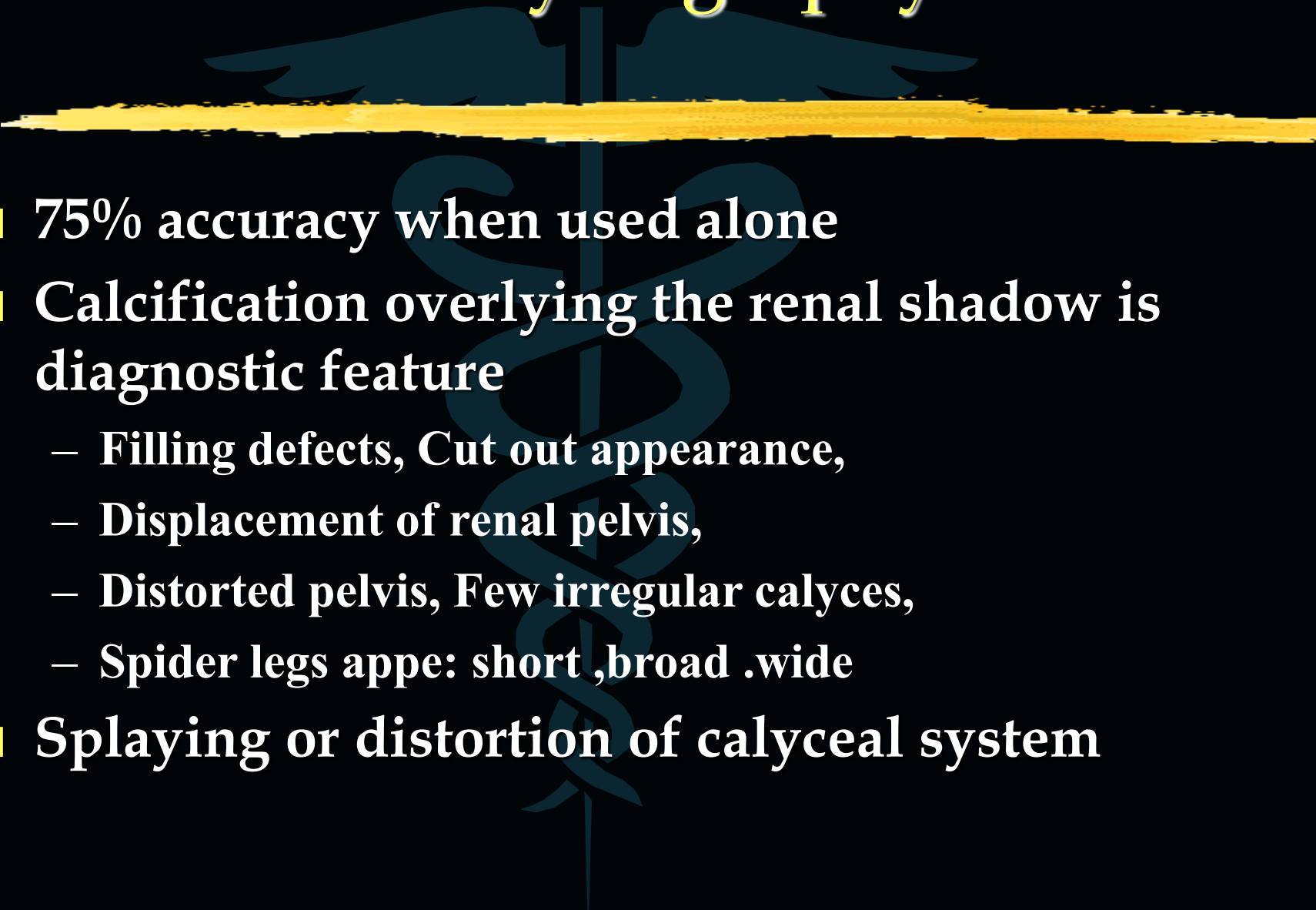
Ultrasound



3 Major Criteria for simple cyst

- Mass is round and sharply demarcated with smooth walls
- No echoes (anechoic) within the mass
- Strong posterior wall echo indicating good transmission through the cyst

Intra-Venous Pyelography



- 75% accuracy when used alone
- Calcification overlying the renal shadow is diagnostic feature
 - Filling defects, Cut out appearance,
 - Displacement of renal pelvis,
 - Distorted pelvis, Few irregular calyces,
 - Spider legs appe: short ,broad .wide
- Splaying or distortion of calyceal system



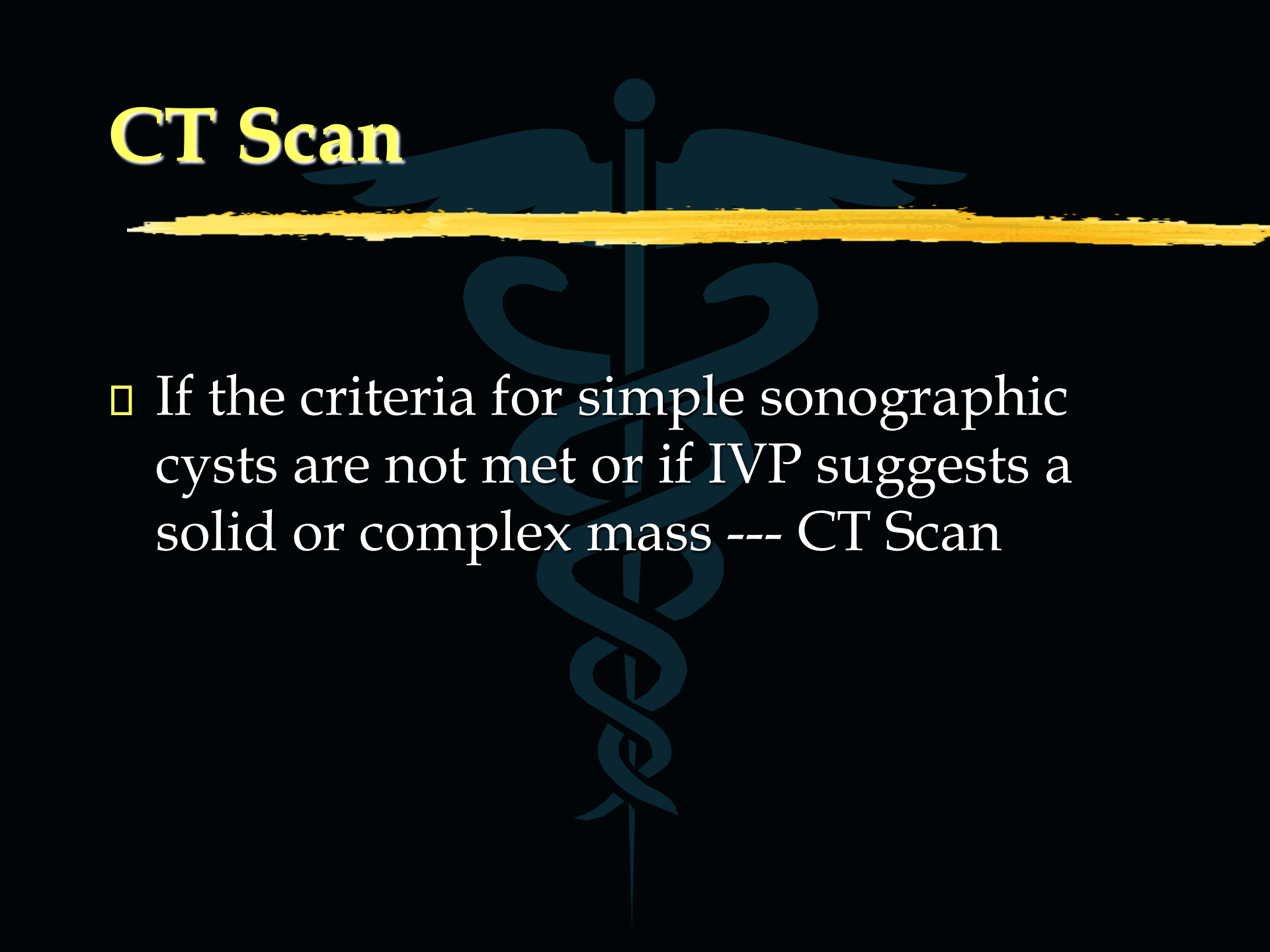
IVP in Polycystic Kidney Disease

- IVP: Spider Leg Appearance
Thin, long, Regular,
No cut out,
Bilateral,
Both Poles involved
Elongation,
Broadening,
Bending of Calyces



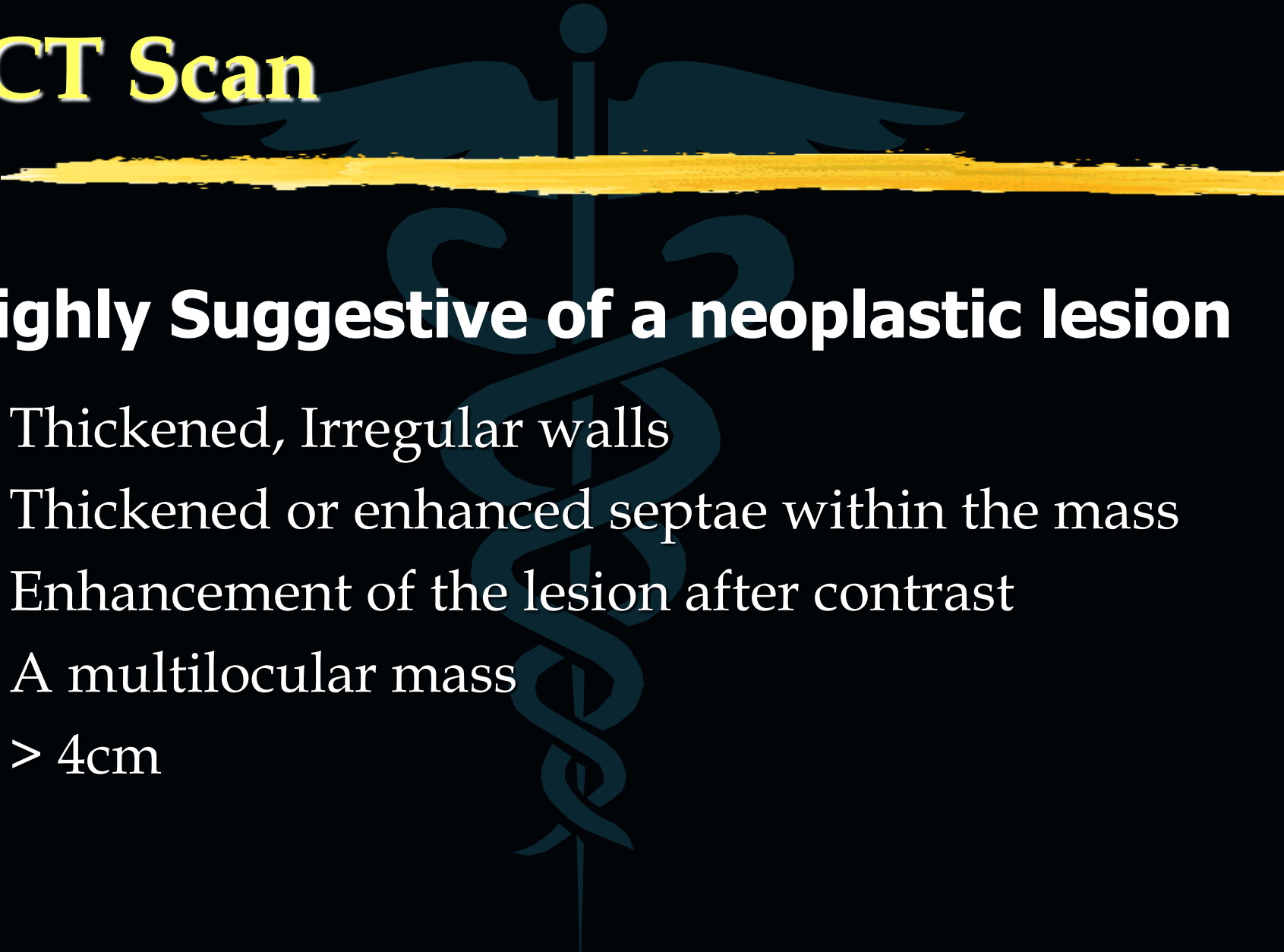
INTRAVENOUS PYELOGRAM: BILATERAL
POLYCYSTIC DISEASE

CT Scan



- If the criteria for simple sonographic cysts are not met or if IVP suggests a solid or complex mass --- CT Scan

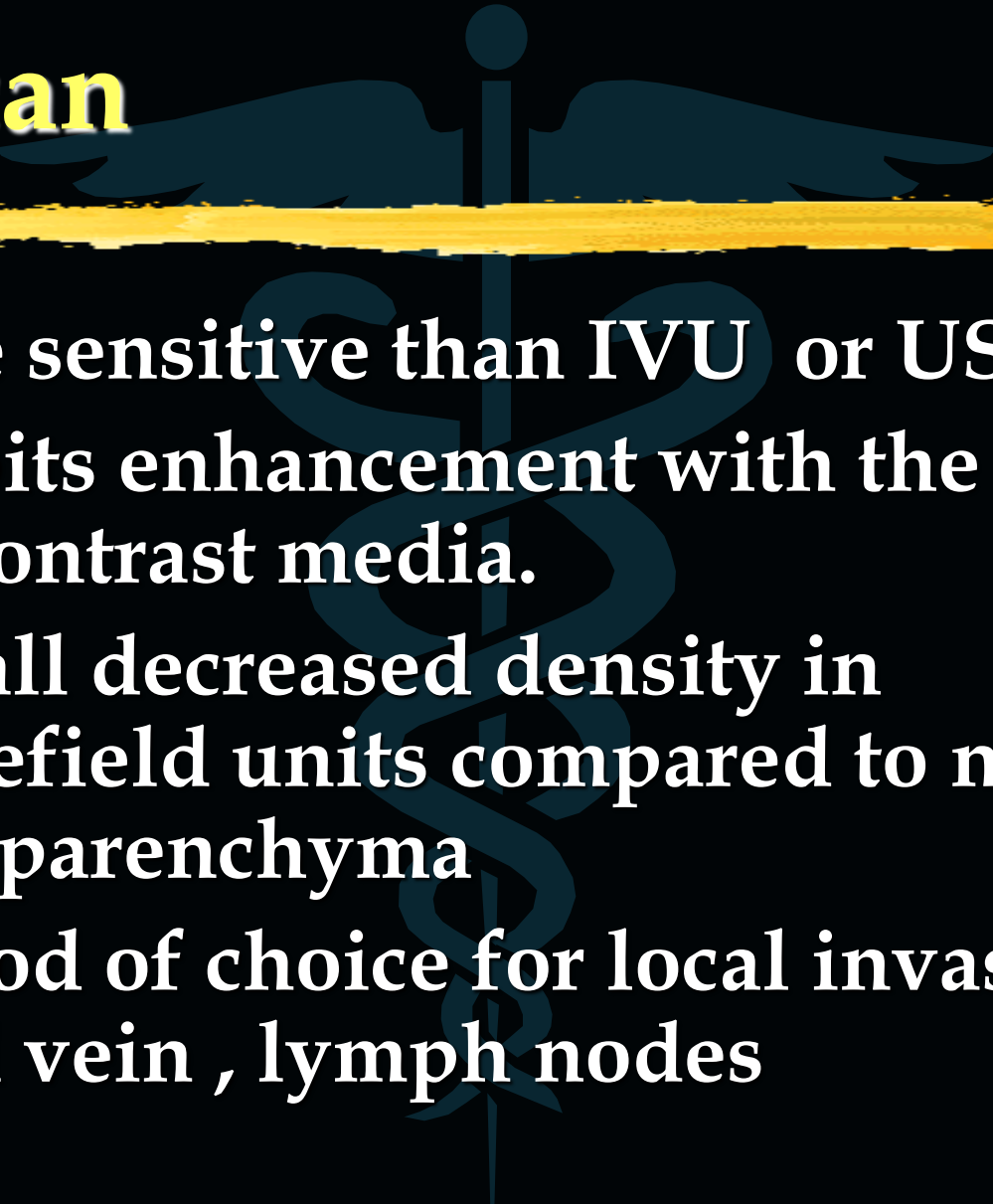
CT Scan



Highly Suggestive of a neoplastic lesion

- Thickened, Irregular walls
- Thickened or enhanced septae within the mass
- Enhancement of the lesion after contrast
- A multilocular mass
- > 4cm

CT scan



- More sensitive than IVU or USG
- Exhibits enhancement with the use of IVP contrast media.
- Overall decreased density in Housefield units compared to normal renal parenchyma
- Method of choice for local invasion , Renal vein , lymph nodes

OV 40.0cm
ND/P



Medscape ©

<http://www.medscape.com>

00
D/P



Medscape ©

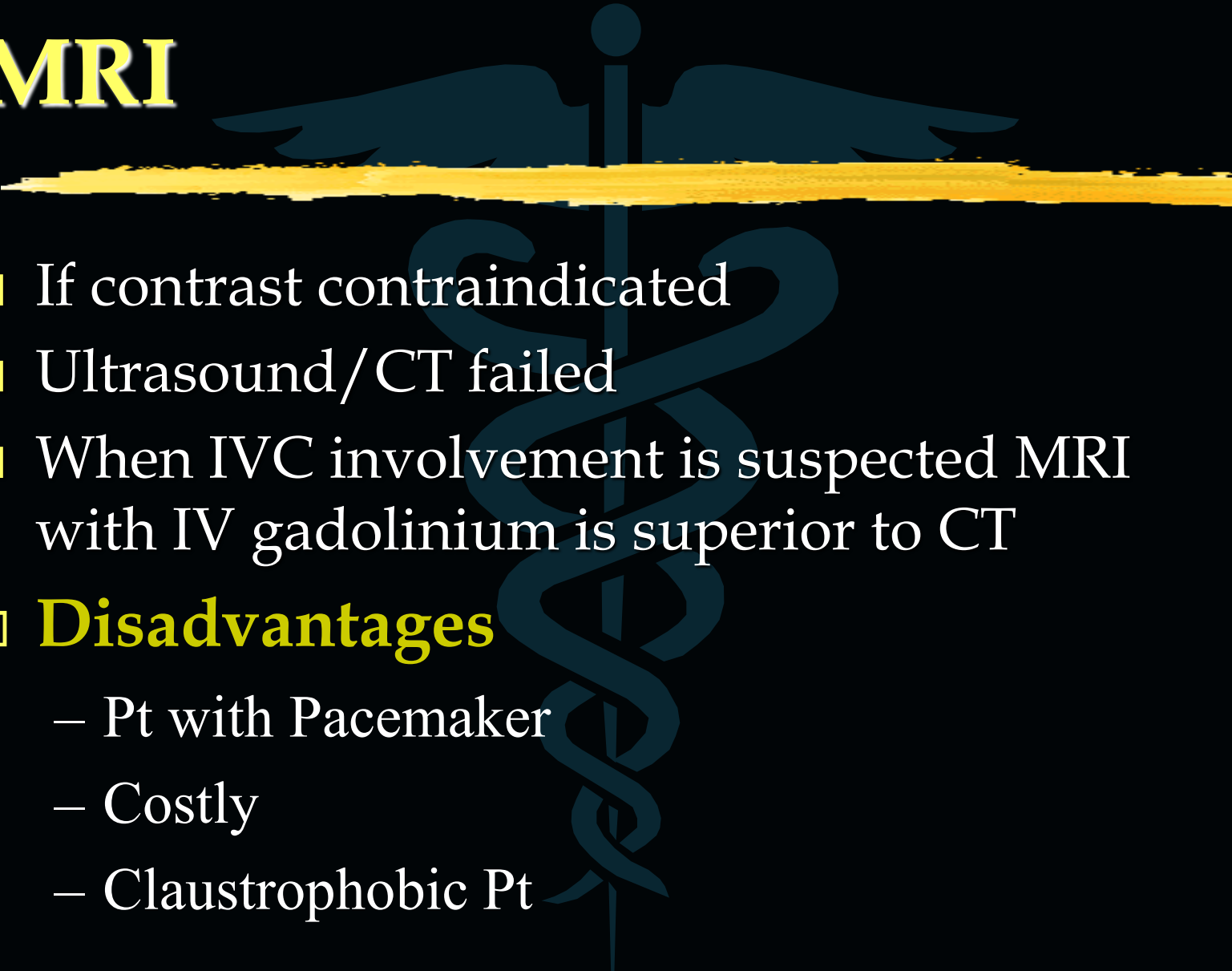
<http://www.medscape.com>

Case history RCC

- This 50 year old man presented with left loin pain and macroscopic haematuria. This film is from an intravenous contrast enhanced abdominal CT scan. It shows a large partially necrotic mass replacing much of the left kidney. The features are those of a renal cell carcinoma. In renal cell carcinoma, contrasted enhanced CT allows assessment of metastatic spread and tumour invasion of the renal vein and inferior vena cava

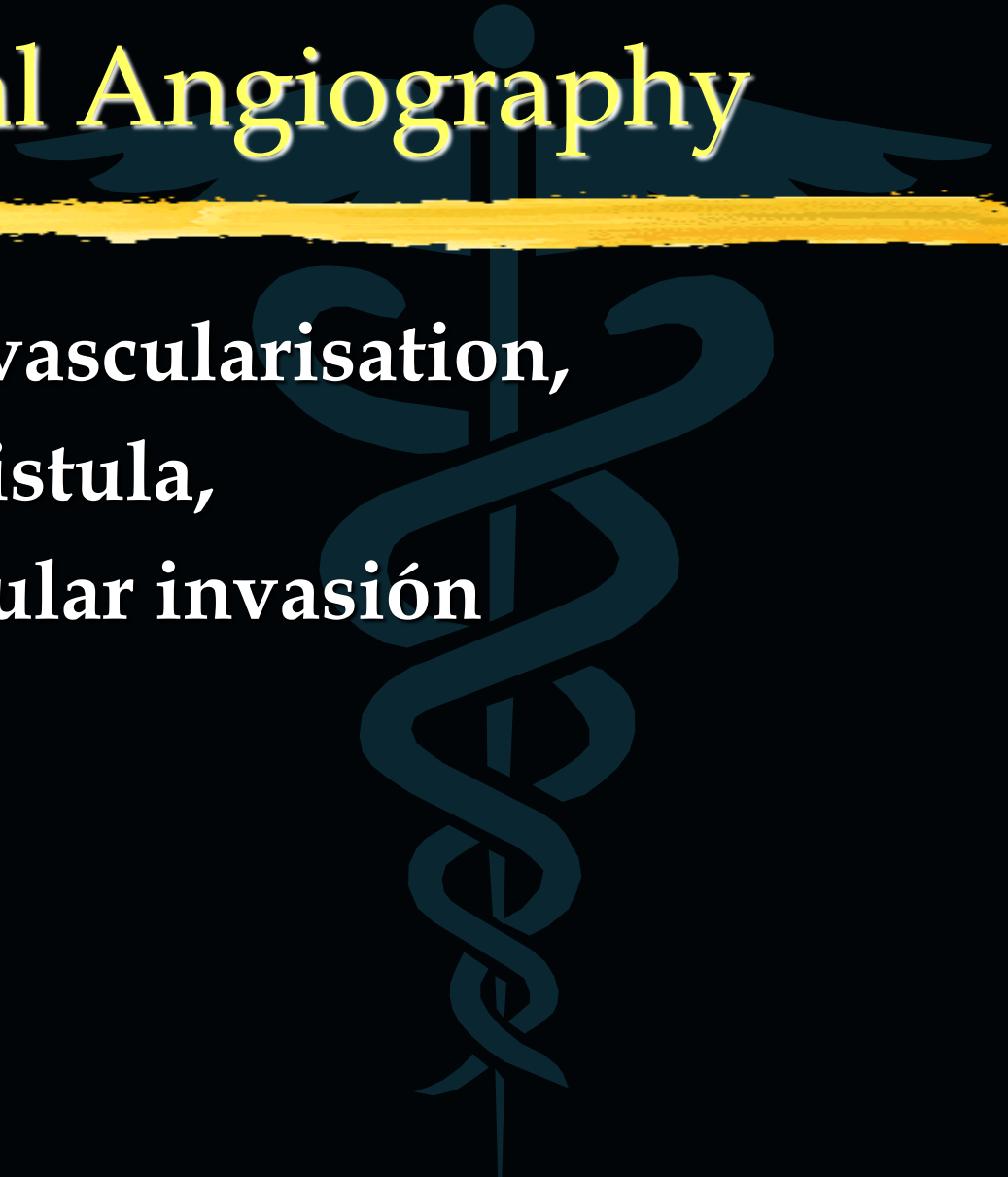


MRI

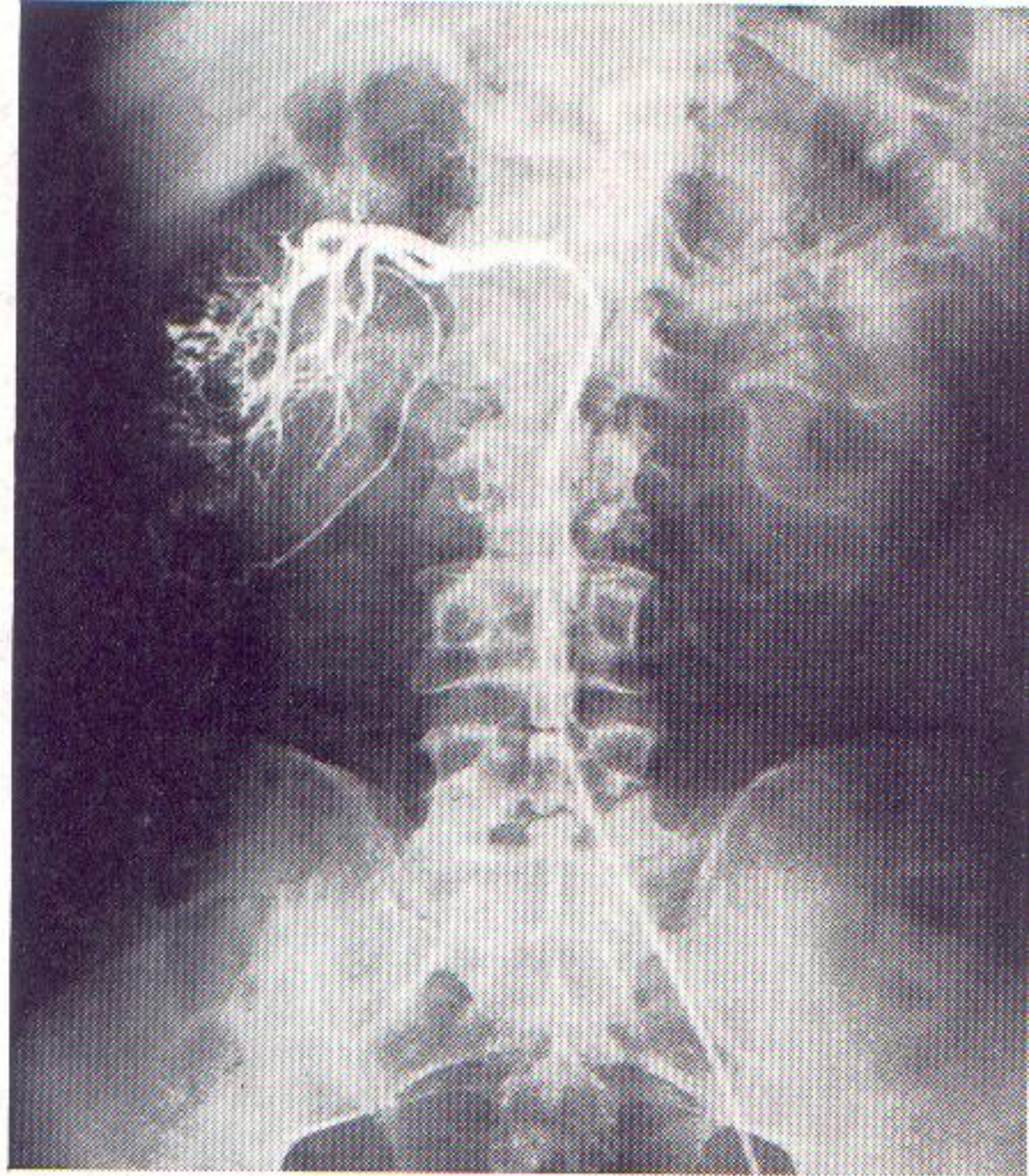


- If contrast contraindicated
- Ultrasound/CT failed
- When IVC involvement is suspected MRI with IV gadolinium is superior to CT
- **Disadvantages**
 - Pt with Pacemaker
 - Costly
 - Claustrophobic Pt

.Renal Angiography



- Neo vascularisation,
- AV fistula,
- vascular invasión



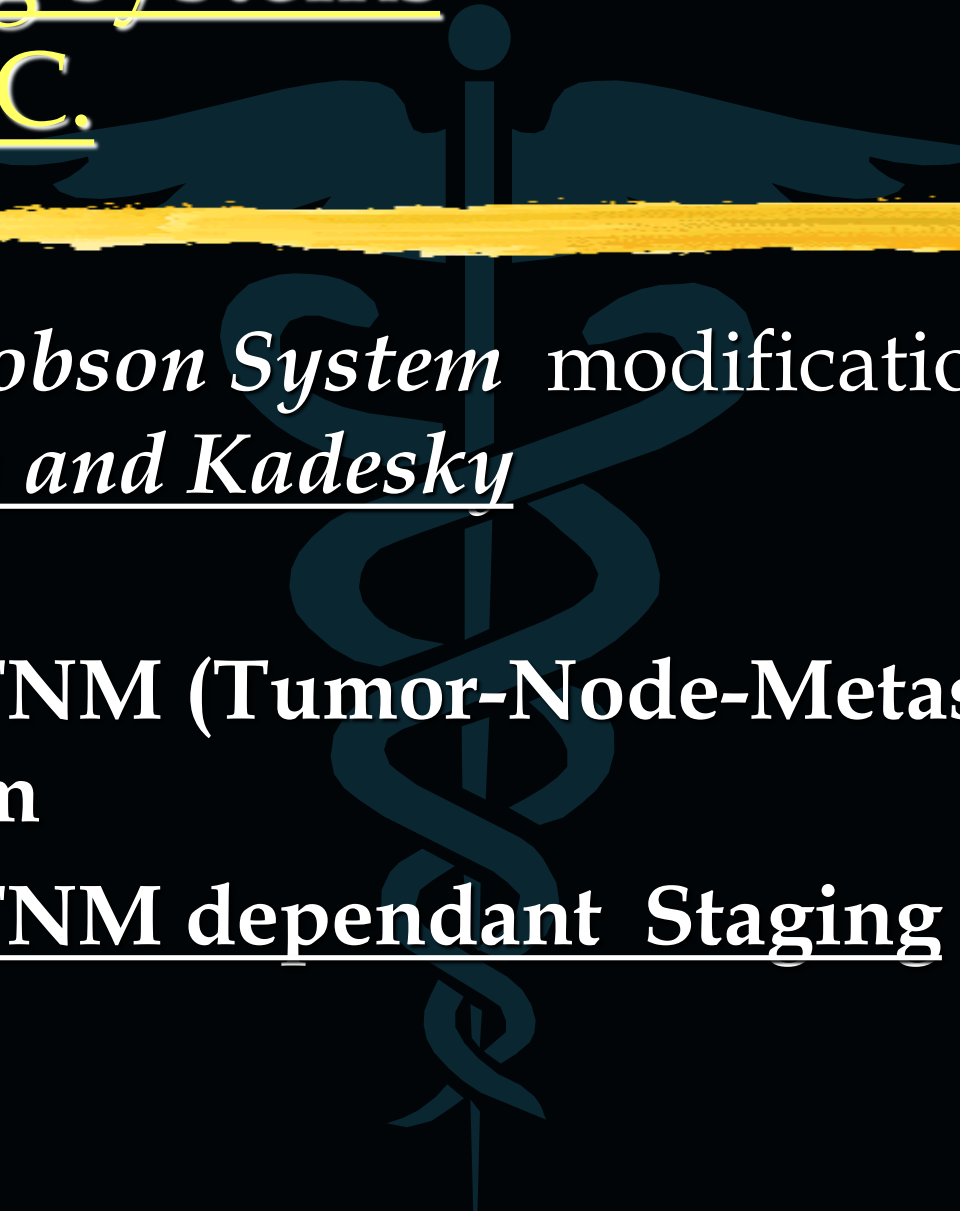
SELECTIVE RIGHT RENAL ARTERIOGRAM SHOWING TYPICAL TUMOR VESSEL PATTERN CHARACTERISTIC OF ADENOCARCINOMA (HYPERNEPHROMA)

X-ray chest

Cannon ball due to metastasis



Staging systems for RCC.



- The *Robson System* modification of *Flocks and Kadesky*
- The TNM (Tumor-Node-Metastases) System
- The TNM dependant Staging

The Robson System modification of Flocks and Kadesky

- **Stage 1** -- The tumor is confined to the kidney, but does not involve the capsule of tissue that surrounds the kidney.
- **Stage 2** -- The tumor extends through the capsule of the kidney. But confined to Gerota's fascia
- **Stage 3**
 - **A.** : Extends into the renal vein or inferior vena cava
 - **B.** : The tumor shows evidence of lymph node involvement,
 - **C.** : Both Lymphatics and Vascular
- **Stage 4** :
 - **A.** The tumor has invaded organs adjacent to the kidney like the pancreas or bowel,
 - **B.** shows evidence of distant Metastasis to organs such as the lungs.

Renal cell Carcinoma

TNM Staging

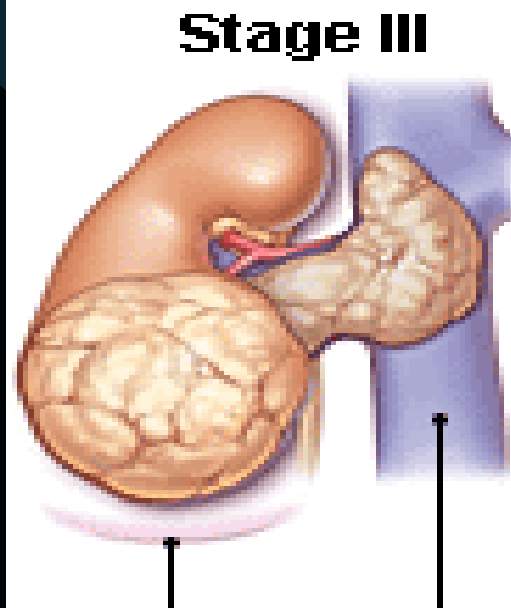
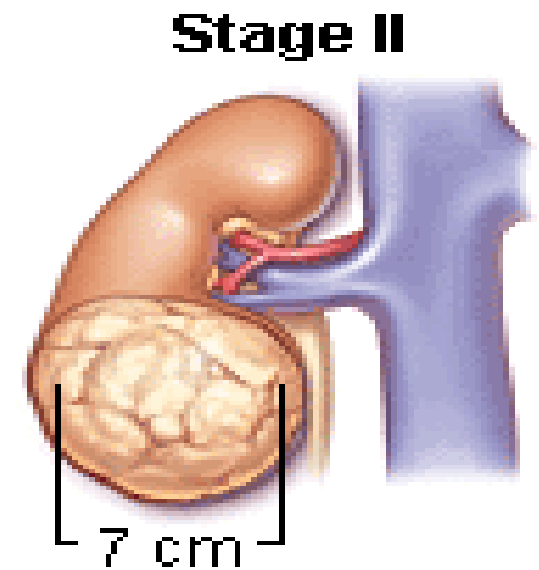
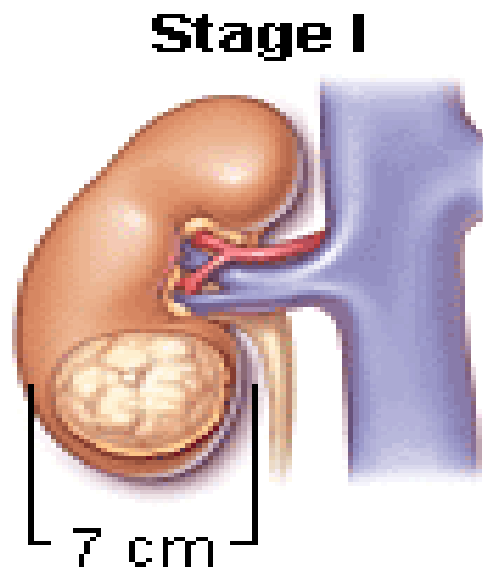
- T1- < 7.0 cm; Limited to kidney , T1a < 4cm , T1b 4-7cm
- T2- > 7.0 cm; Limited to kidney
- T3- Into major veins, adrenal or perinephric invasion.
 - T3a- Adrenal or Perinephric fat
 - T3b- Venacava below diaphragm
 - T3c- Venacava above diaphragm
- T4- Invades beyond Gerota fascia
- N1- Single regional node
- N2- More than one regional node

KIDNEY CANCER

TNM-Staging 8th Ed.

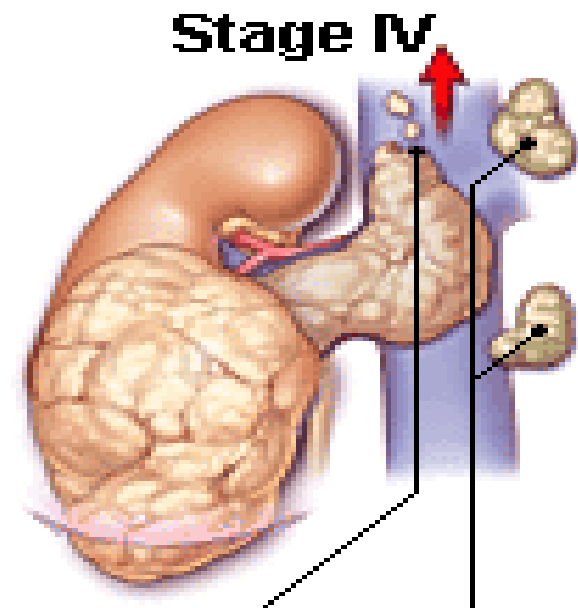
T1a	≤4 cm
T1b	4.1–7 cm
T2a	7.1–10 cm
T2b	>10 cm
T3a	Invades perinephric or sinus fat and/or the renal vein
T3b	Invades the IVC below the diaphragm
T3c	Invades the IVC above the diaphragm
T4	Invades beyond Gerota's fascia
N1	Involves regional lymph nodes
M1	Distant spread

T1a < 4cm
T1b 4-7cm



Gerota's
fascia

Vena
Cava



to other
organs

lymph
nodes

T3a- Adrenal
Perinephric fat
T3b- Venacava
< diaphragm
T3c- Venacava
> diaphragm

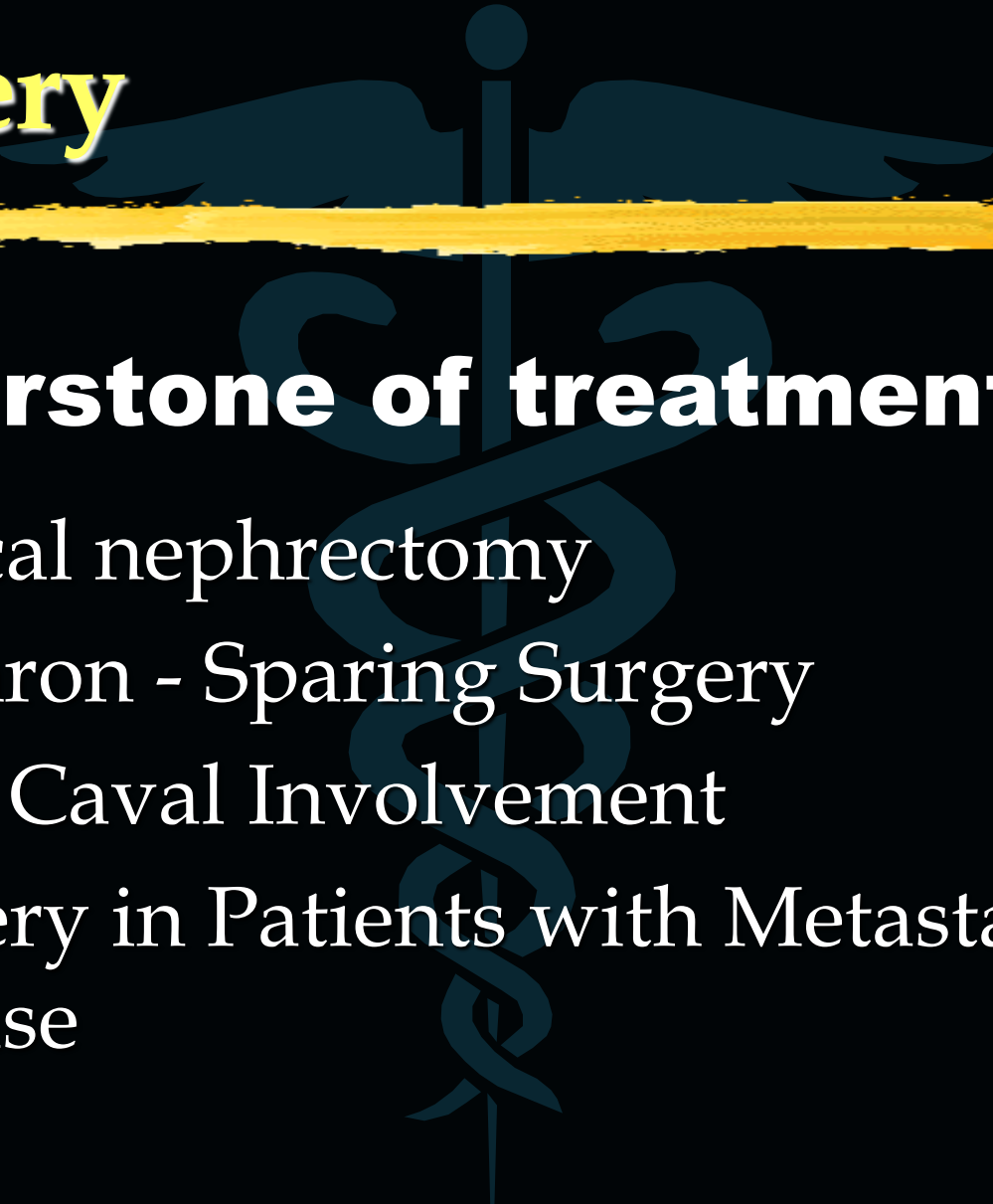
The TNM dependant Staging

- *Stage 1:* Small tumors (less than 1 inch) that don't show evidence of local invasion; no lymph node involvement and absence of distant disease. (T1N0M0)
- *Stage 2:* Tumors larger than 1 inch that don't show evidence of local invasion; no lymph node involvement and absence of distant disease. (T 2 N0 M0)
- *Stage 3:* Tumors of any size that involve one lymph node (less than 1 inch in size), tumors that invade the adrenal gland or surrounding renal tissues, or tumors that invade the renal vein or the inferior vena cava. (T1, T2 N1 M0, T3a N0/N1 M0, T3b N0/N1 M0)
- *Stage 4:* A mixed group including tumors that invade adjacent structures; any tumor that has evidence of distant spread; or any tumor in which more than one lymph node is involved (T4 any N M0, Any T N2/N3 M0, Any T any N ,M1)

Comparison of Modified Robson and TNM Staging systems for Renal Adenocarcinoma

Modified Robson Stage	T	N	M
I – Confined by renal capsule	T1 (small) T2 (large)	N0	M0
II – Through renal capsule confined by Gerota's fascia	T3a	N0	M0
IIIA – Renal vein involvement	T3b	N0	M0
IIIB – Lymphatic involvement	T1-3b	N1-4	M0
IV – Contiguous organ involvement or Metastatic spread	T1-3b T1-3b	N0-4 N0-4	M0 M0

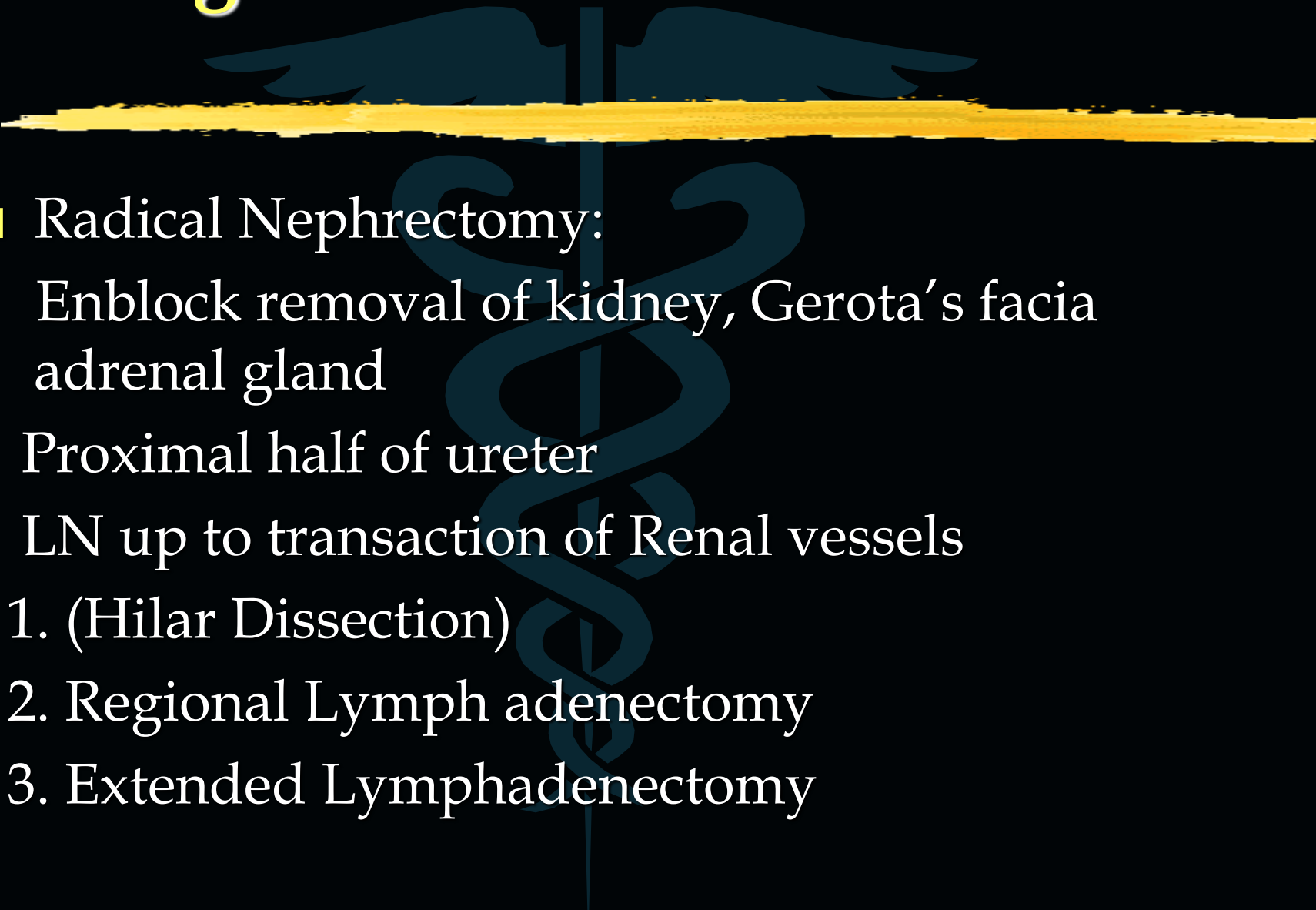
Surgery



Cornerstone of treatment

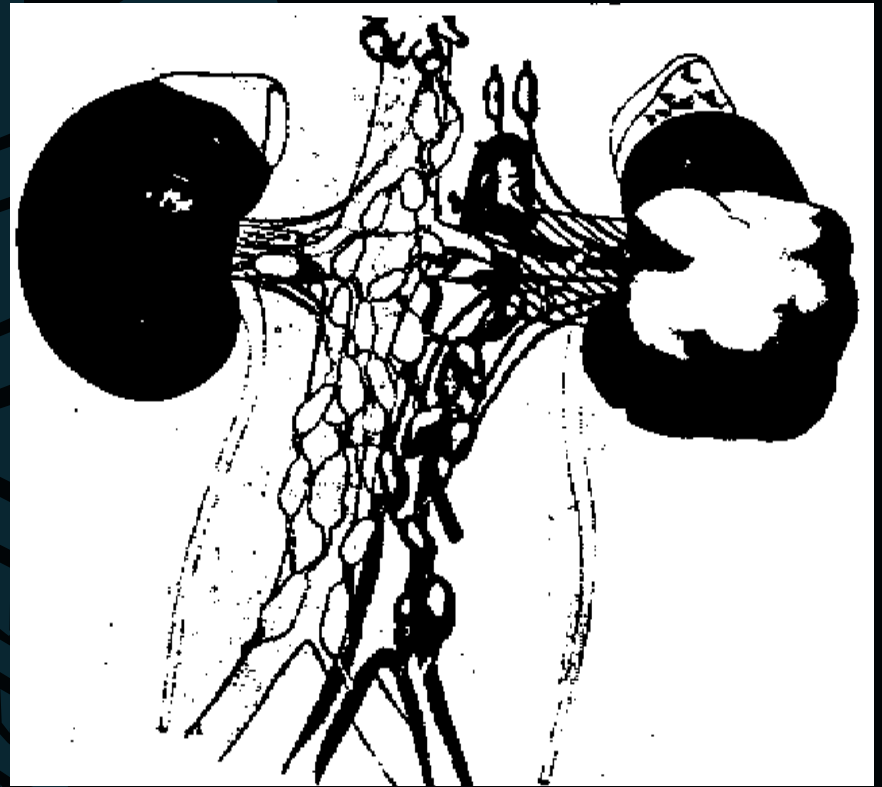
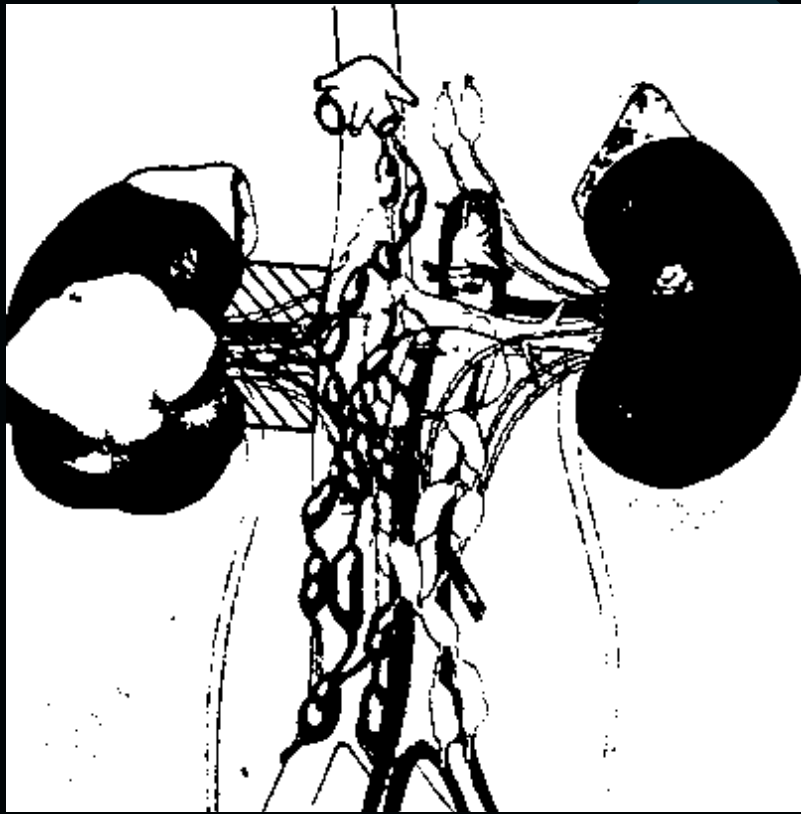
- Radical nephrectomy
- Nephron - Sparing Surgery
- Vena Caval Involvement
- Surgery in Patients with Metastatic Disease

Management of RCC



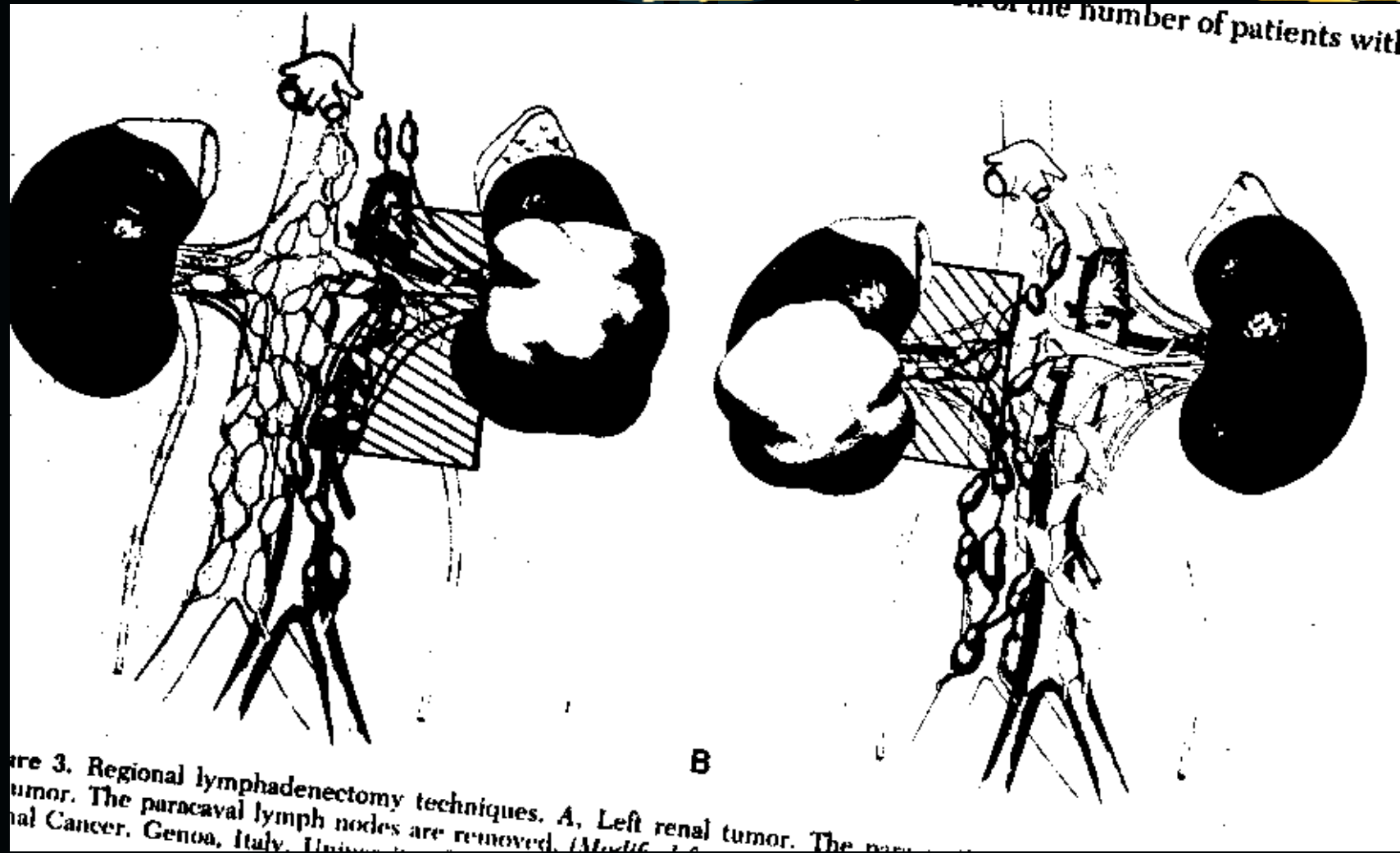
- Radical Nephrectomy:
 - Enblock removal of kidney, Gerota's fascia
 - adrenal gland
 - Proximal half of ureter
 - LN up to transaction of Renal vessels
 - 1. (Hilar Dissection)
 - 2. Regional Lymph adenectomy
 - 3. Extended Lymphadenectomy

Hilar Dissection of Lymphadenectomy for A: Left Kidney B; Rt. Kidney



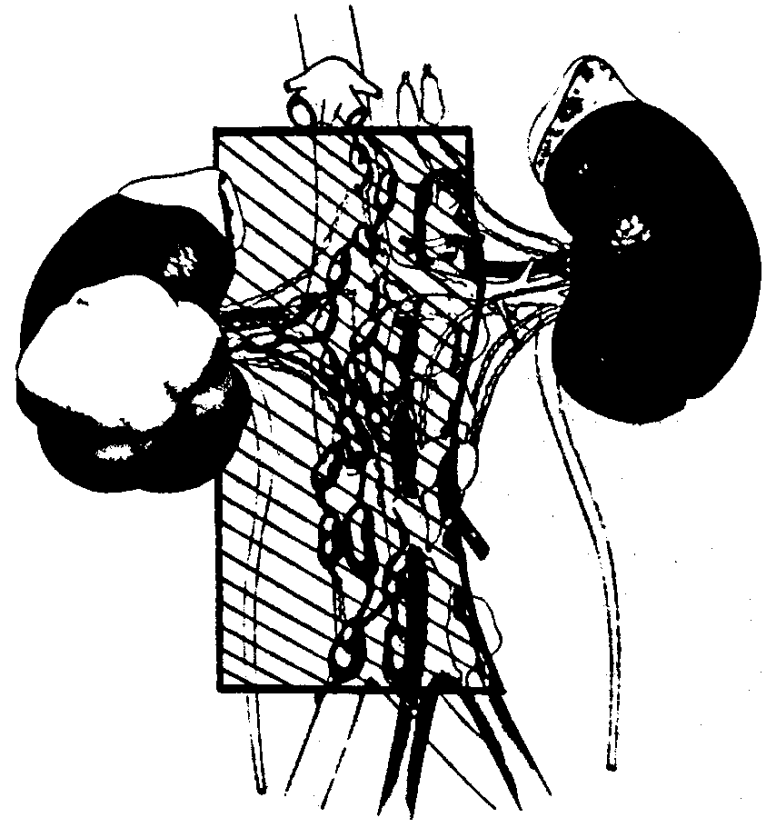
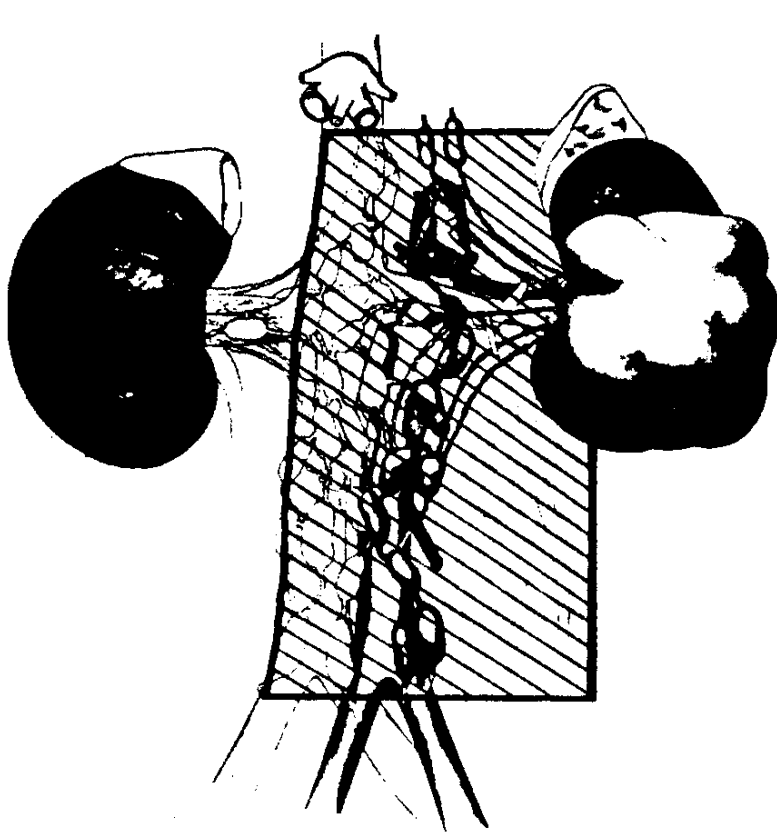
Regional Lymphadenectomy

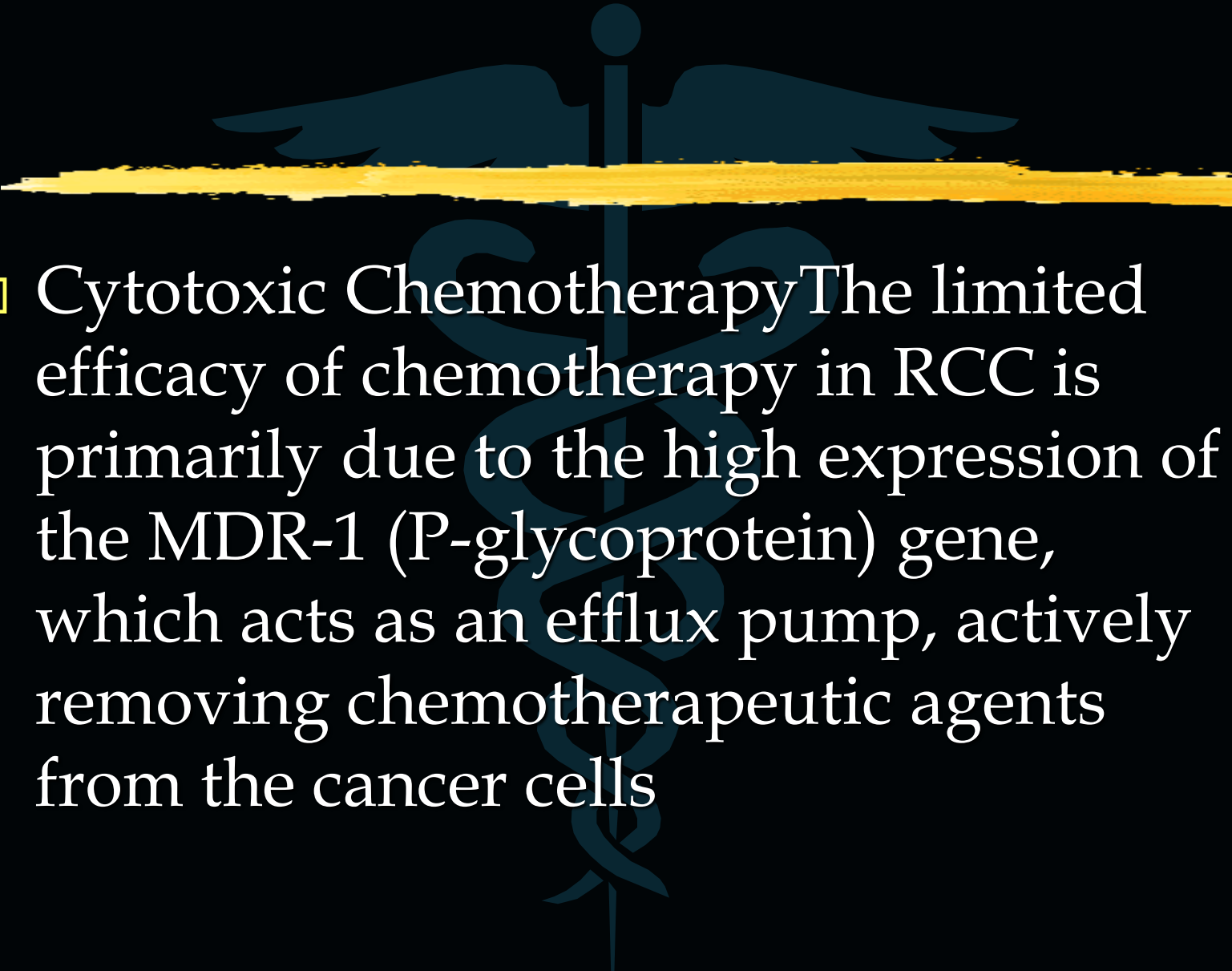
A; Left Kidney B: Rt Kidney



Extended Lymphdenectomy

A; Left Kidney B: Rt Kidney



- 
- Cytotoxic ChemotherapyThe limited efficacy of chemotherapy in RCC is primarily due to the high expression of the MDR-1 (P-glycoprotein) gene, which acts as an efflux pump, actively removing chemotherapeutic agents from the cancer cells

- 
- .Clear Cell RCC (ccRCC): * Status: Conventional chemotherapy (e.g., Vinblastine, 5-FU) is not recommended in any frontline or standard salvage setting.
 - Outcome: Response rates are historically <10\ %, with no proven survival benefit over modern IO/TKI combinations.

- ❑ Collecting Duct Carcinoma (CDC) & Renal Medullary Carcinoma (RMC): These are highly aggressive, rare variants that behave more like urothelial or aggressive adenocarcinomas than typical RCC.
- ❑ Regimen: Platinum-based doublets (e.g., Cisplatin + Gemcitabine or Carboplatin + Paclitaxel) are the standard of care.¹
- ❑ Outcome: These tumors are chemosensitive but prone to early relapse. Recent data suggest adding Bevacizumab to chemotherapy may improve Progression-Free Survival (PFS) in CDC.

Renal Cell Carcinoma of Kidney

- ✦ Localised RCC
- ✦ Locally Advanced RCC
- ✦ Metastatic RCC

Localized Cancer Kidney

- Radical Nephrectomy
- Nephron Sparing Surgery
- Close Observation

Radical Nephrectomy

- Excision of Gerota's fascia and its contents, including the kidney and the adrenal gland



Radical Nephrectomy - Concepts

- ✦ Early ligation of Renal Artery and Vein
- ✦ Removal of Kidney outside Gerota's Fascia
- ✦ Removal of ipsilateral adrenal gland
- ✦ Complete Lymphadenectomy

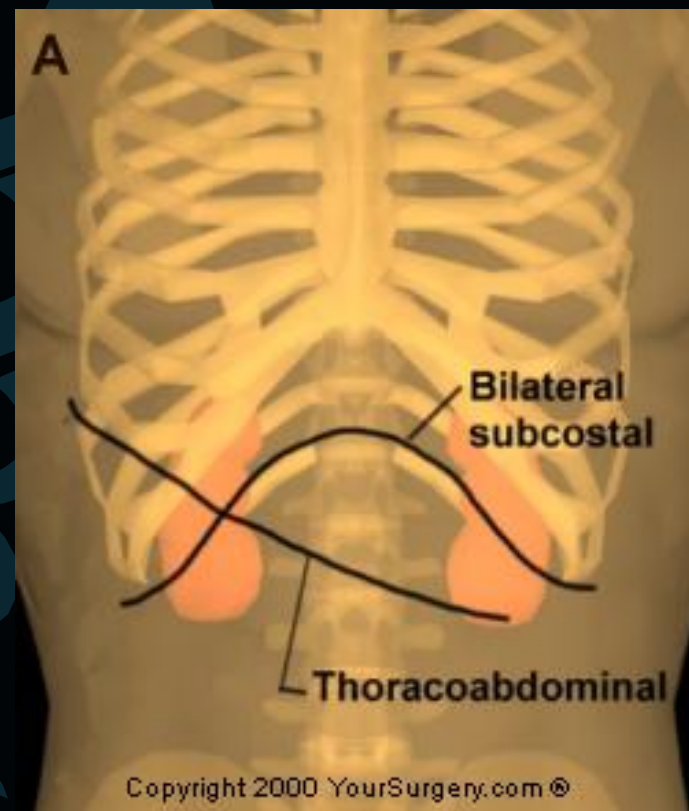
Radical Nephrectomy

Surgical Approach

- Size/Location of the tumor
 - Patient's body habitus
 - Unilateral/ Bilateral / IVC Thrombus
 - Concurrent extra renal pathology
- OPEN
 - Transperitoneal
 - Thoraco-abdominal
 - LAPAROSCOPIC
 - Conventional
 - Hand assisted

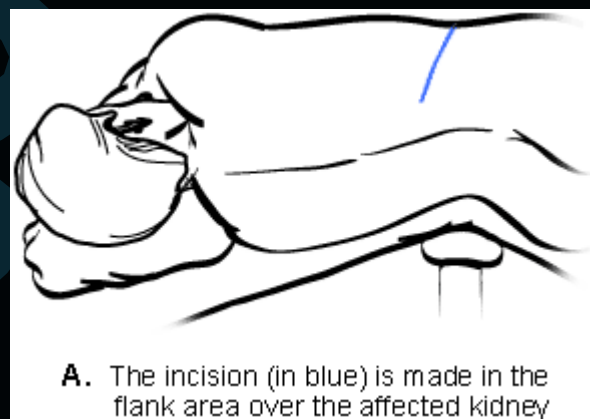
Thoracoabdominal Approach

- ❑ Optimal Exposure of Suprarenal area
- ❑ Large Upper Polar Tumors
- ❑ Pulmonary Morbidity & Postop Pain
- ❑ Occasionally, Infrahepatic IVC Thrombus



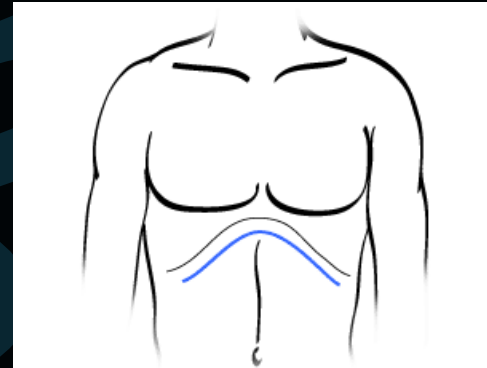
Lateral Flank Approach

- 11/12 Rib Bed
Extrapleural
Extraperitoneal
- Obese Patients –
Panniculus falls
forward
- Suboptimal Exposure of
Renal Pedicle
- Unsuitable in scoliosis
or cardiorespiratory
problems

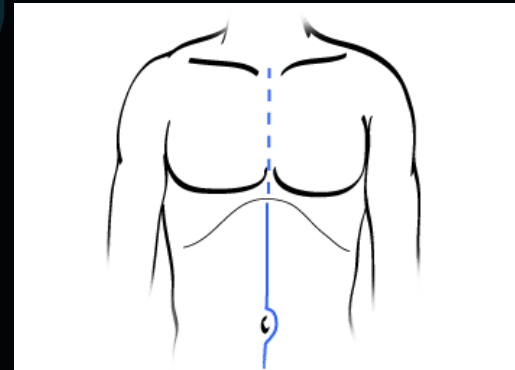


Anterior Trans peritoneal Approach

- ❑ Renal Pedicle- Excellent exposure
- ❑ Intrabdominal viscera explored thoroughly
- ❑ Bilateral tumors or concomitant extrarenal pathology
- ❑ Longer ileus and increased(?) adhesions
- ❑ Subcostal/ vertical incision



C. The incision (in blue) is under the ribcage on both sides of the body, in an upside-down V

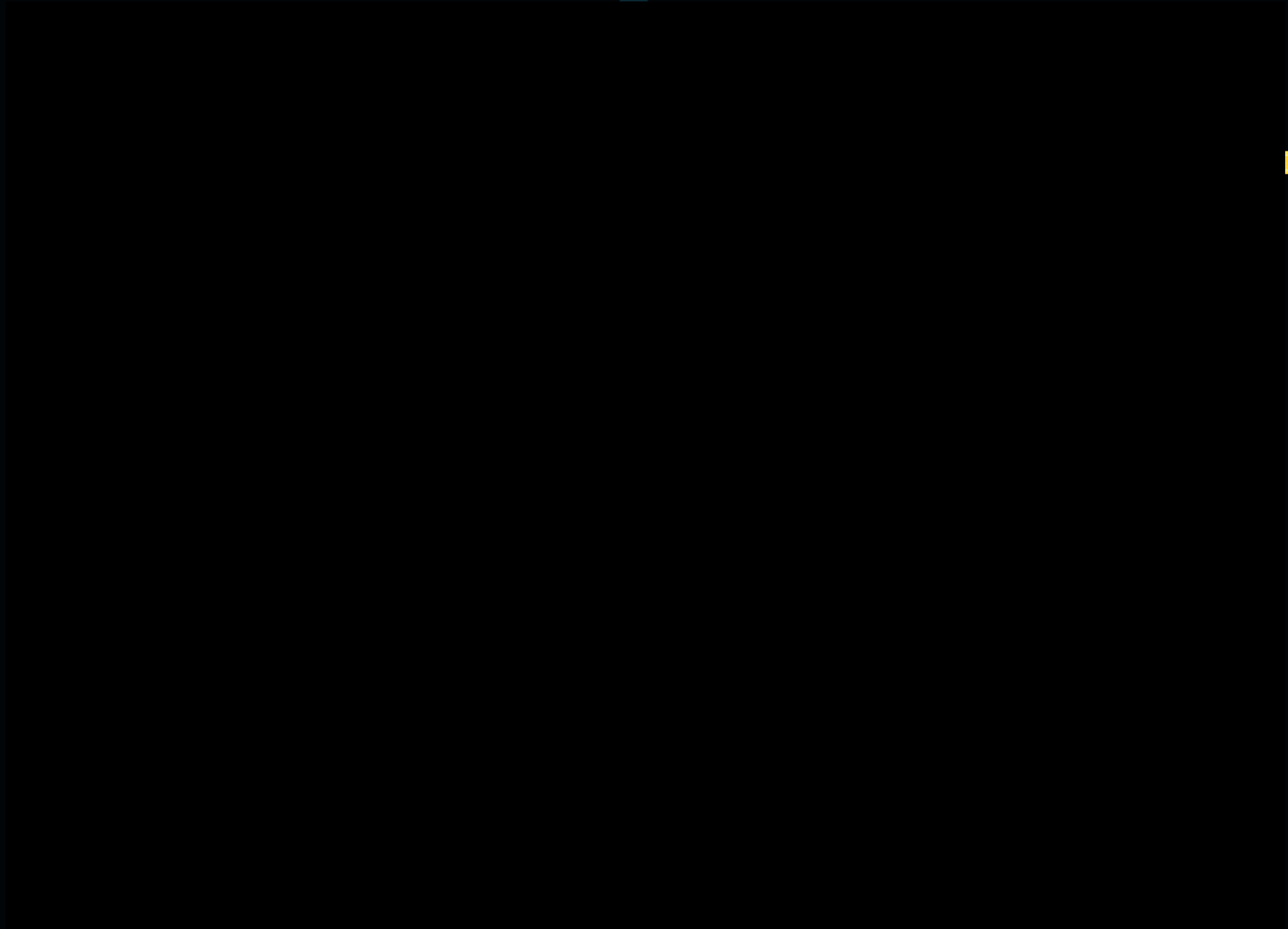


D. The incision (in blue) is in the center of the abdomen, extending from the breastbone to below the navel

LAPAROSCOPIC RADICAL NEPHRECTOMY

- Alternative to open Surgery
- Low volume < 8 cm, no local invasion
- No renal vein involvement or lymphadenopathy
- Early results comparable, but long term data for validation of Cancer efficacy awaited
- Hand Assisted Laparoscopy (HAL)

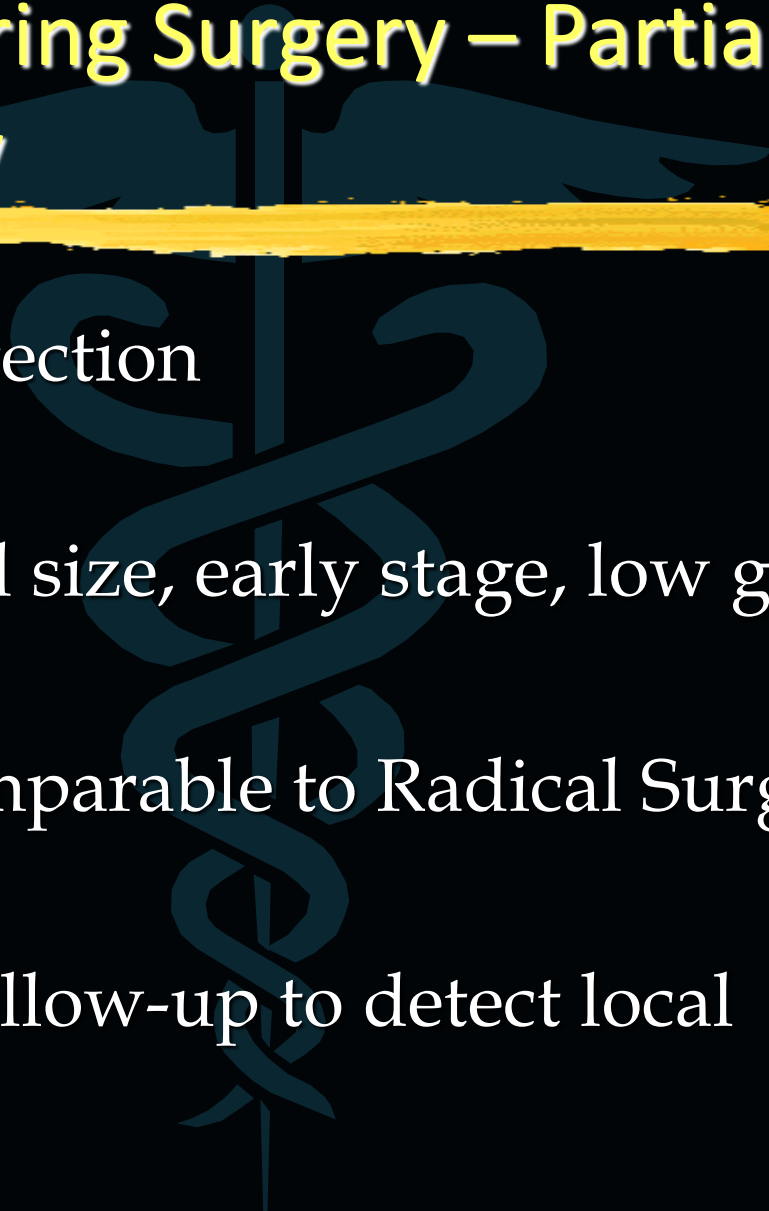
Radical Nephrectomy



Radical Nephrectomy - Results

Stage	5 -year survival - %
I	65 - 93
II	41 - 77
III	34 - 51
IV	2-10

Nephron Sparing Surgery – Partial Nephrectomy



- Incidental detection
- Tumor - small size, early stage, low grade
- Survival - comparable to Radical Surgery
- Meticulous follow-up to detect local recurrence

Indications- Partial Nephrectomy

Absolute:

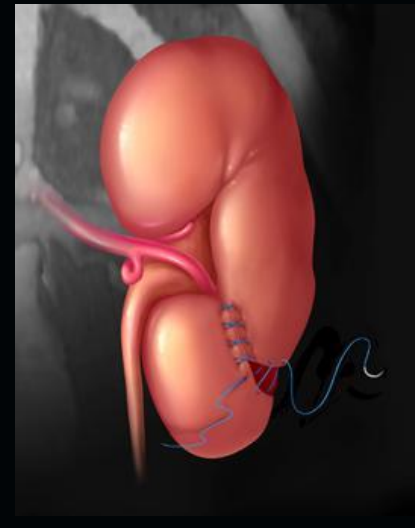
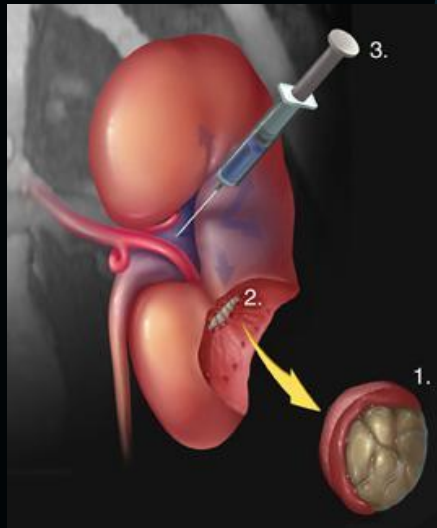
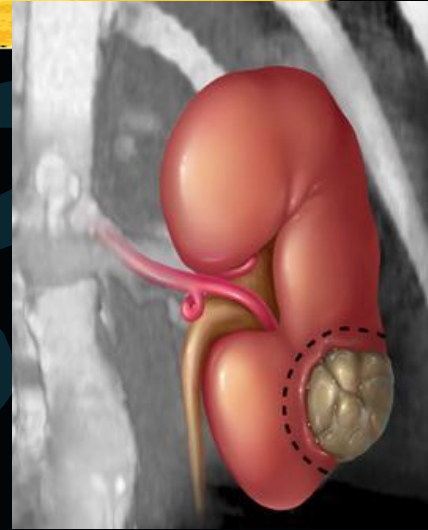
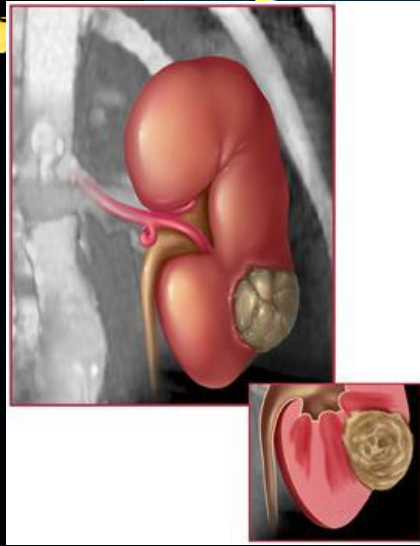
- Bilateral Renal Cancer
- Tumor in solitary functioning kidney
- Familial- VHL, AML in Tuberous Sclerosis

Elective:

- Normal opposite kidney
- Conditions threaten future function

<4cm tumor in a peripheral location

Surgical Technique- Partial Nephrectomy

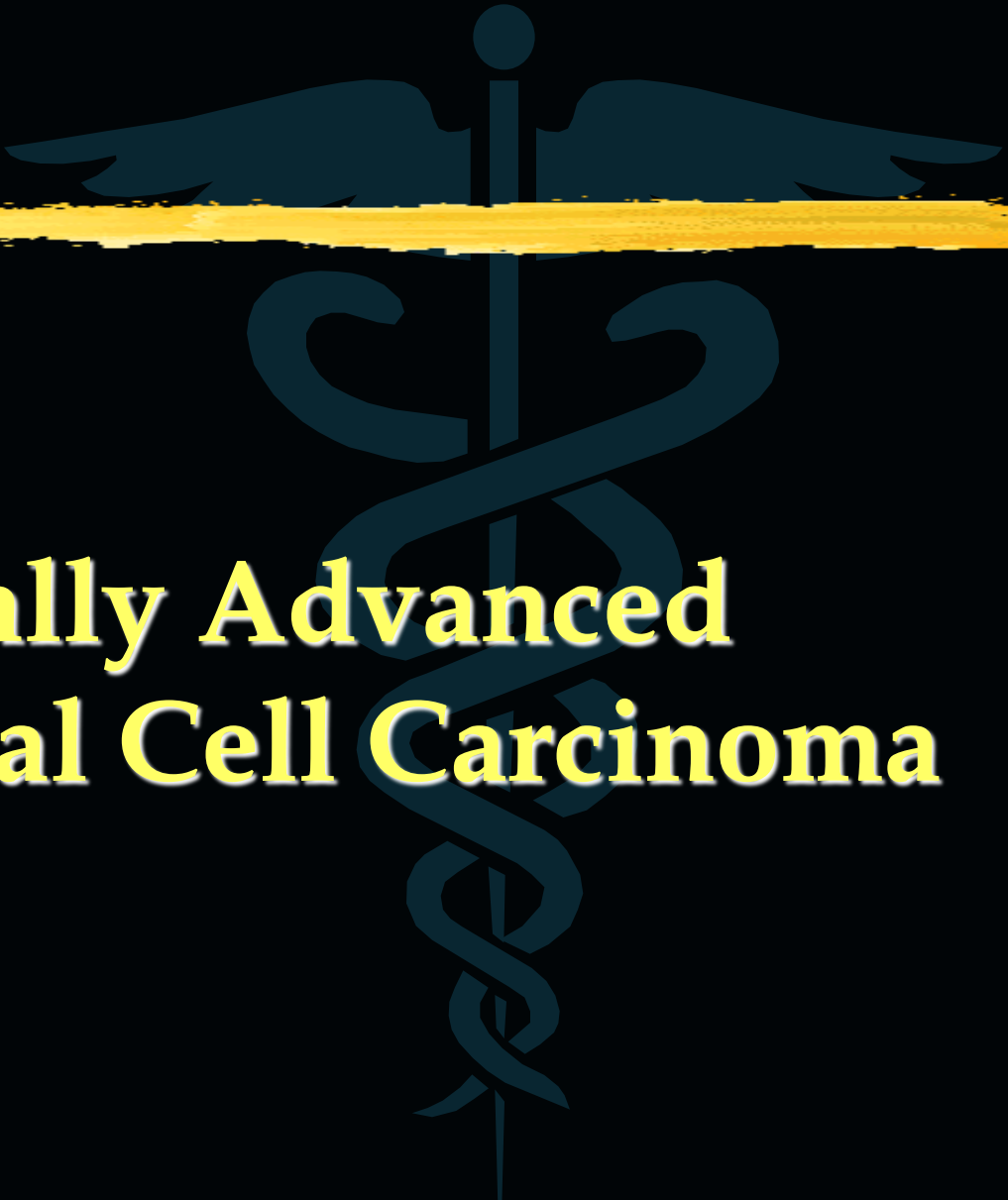




Partial Nephrectomy (PN):

- Indication:
- Gold standard for clinical T1a tumors (≤ 4 cm) and preferred for T1b (4–7 cm) when technically feasible.
- Outcomes: Equivalent oncologic control to radical nephrectomy (RN) but with superior preservation of the estimated Glomerular Filtration Rate (eGFR), reducing long-term cardiovascular morbidity

- .Radical Nephrectomy (RN):Indication: Reserved for T2–T4 tumors or complex T1 masses not amenable to PN.Technique: Laparoscopic or robotic-assisted approaches are preferred for their reduced morbidity and faster recovery compared to open surgery.



Locally Advanced Renal Cell Carcinoma

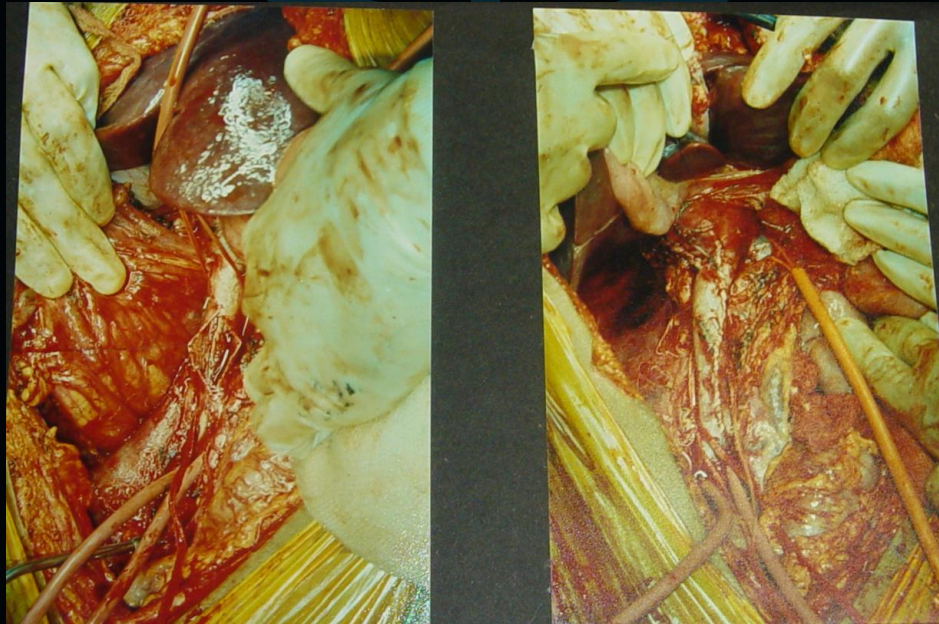
Locally Advanced RCC

- Venacaval Involvement
- Locally Invasive Tumors
- Local Tumor Recurrence – RN/PN

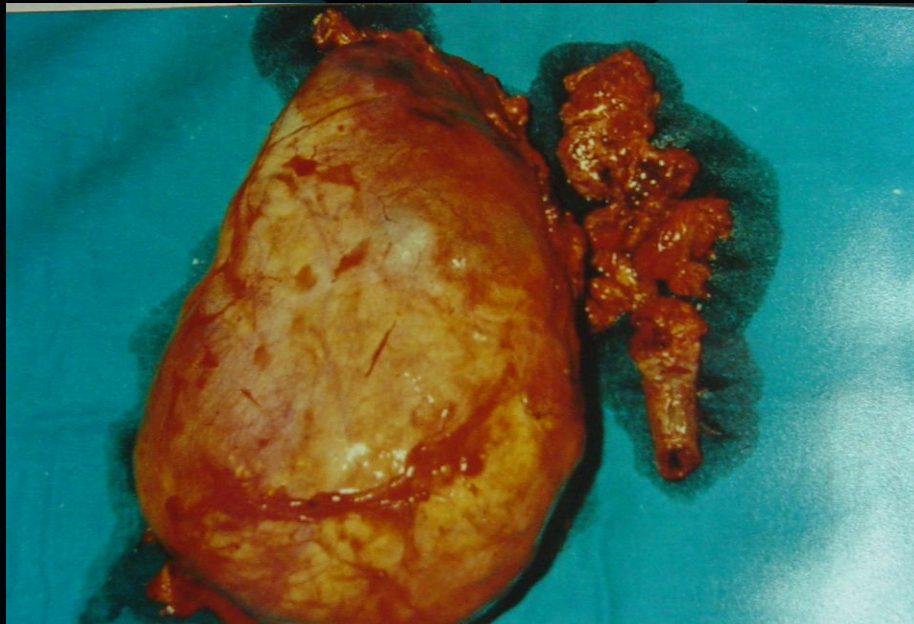
IVC Thrombus

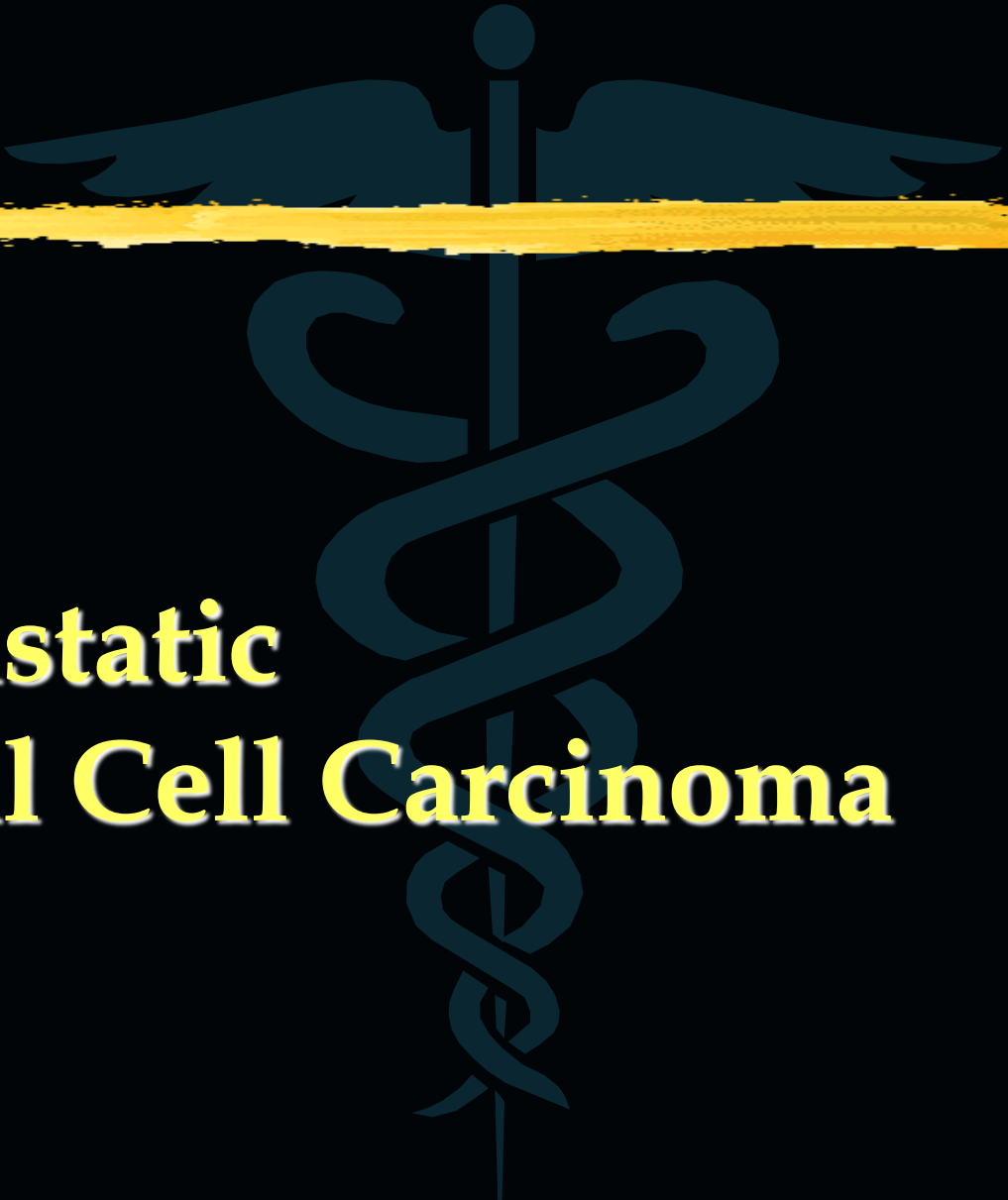


RCC – IVC Thrombus



RCC -IVC Thrombus





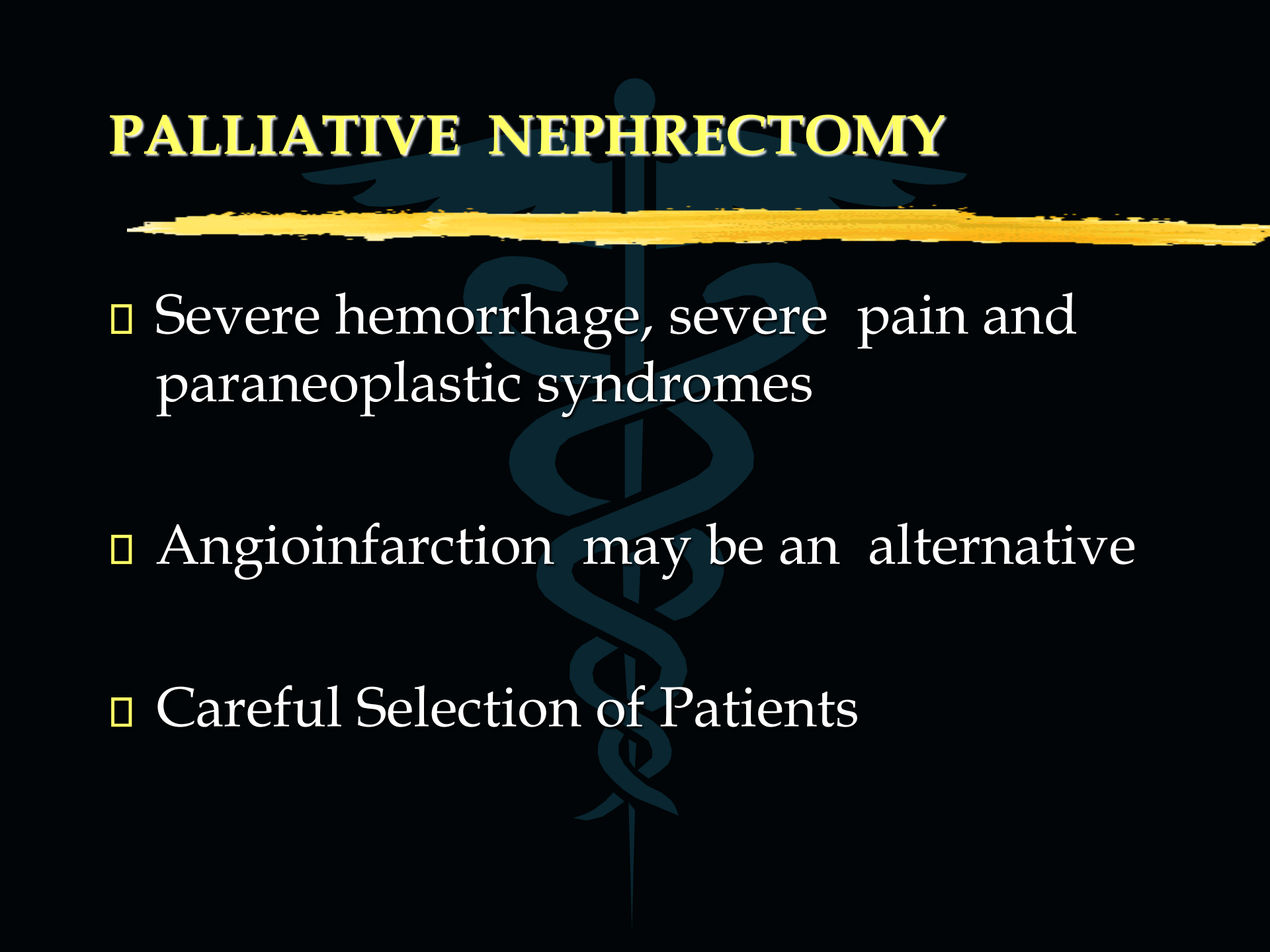
Metastatic Renal Cell Carcinoma

Metastatic Cancer Kidney



- Nephrectomy
- Immunobiologic Therapy
- Hormonal Therapy
- Chemotherapy
- Radiotherapy

PALLIATIVE NEPHRECTOMY

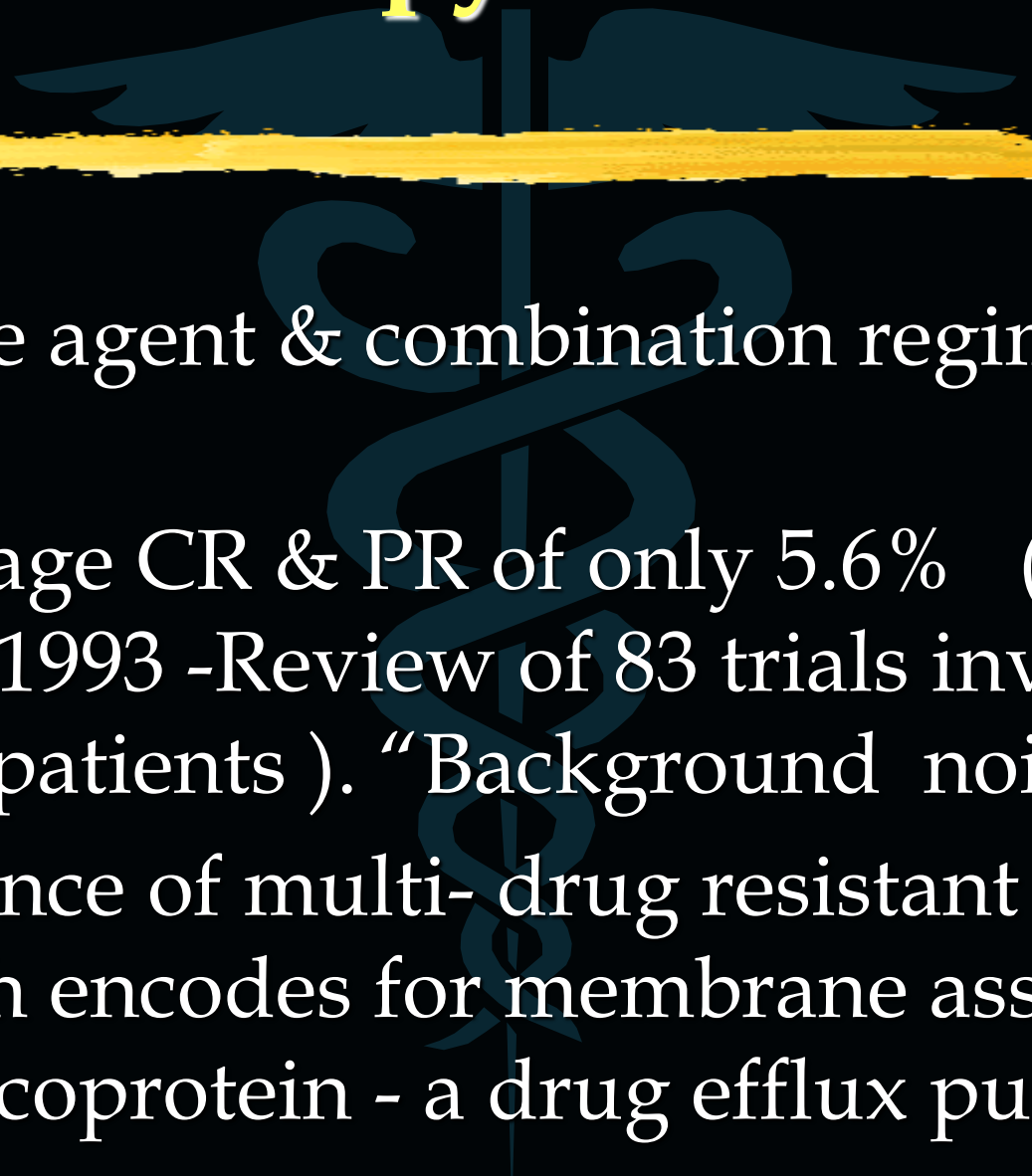


- Severe hemorrhage, severe pain and paraneoplastic syndromes
- Angioinfarction may be an alternative
- Careful Selection of Patients

ADJUNCTIVE NEPHRECTOMY

- Nephrectomy in presence of metastases for ? prolonging survival or causing spontaneous regression of metastases
- Spontaneous regression rate – anecdotal
- Adjunctive to immunobiologic therapy

Chemotherapy in Metastatic RCC



- Single agent & combination regimens tried .
- Average CR & PR of only 5.6% (Yagoda et al ;1993 -Review of 83 trials involving 4093 patients). “Background noise “
- Presence of multi- drug resistant gene which encodes for membrane associated P-glycoprotein - a drug efflux pump

Medical & Targeted Therapy (TKI)

- The medical management of RCC revolves around inhibiting the Vascular Endothelial Growth Factor (VEGF) pathway, which is nearly always upregulated in clear cell RCC (ccRCC) due to VHL gene mutations.
- **Tyrosine Kinase Inhibitors (TKIs):**
 - **Agents:** Axitinib, Cabozantinib, Lenvatinib, and Sunitinib.
 - **Mechanism:** Competitive inhibition of ATP-binding sites on VEGFR, PDGFR, and c-KIT.
 - **Outcomes:** Cabozantinib is particularly effective in patients with bone metastases and those who have failed prior VEGF therapy. TKIs offer high Objective Response Rates (ORR) but rarely achieve durable complete remissions as monotherapy.
- **HIF-2 α Inhibition:**
 - **Belzutifan:** Represents a new class of therapy, specifically targeting the Hypoxia-Inducible Factor 2- α . Primarily used in VHL-associated RCC and increasingly in the refractory metastatic setting.

Five Year Survival

Robson Stage

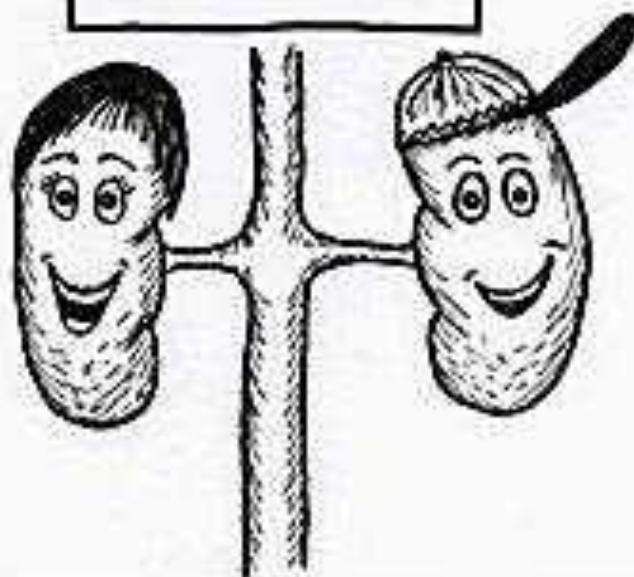
□ Stage I	-	65-85%
□ Stage II	-	45-80%
□ Stage III	-	15-35%
□ Stage IV	-	0-10%

- 20-30% of pt with localized tumors relapse after Radical Nephrectomy
- The median time of relapse after nephrectomy - 15-18 months
- 85% of relapses occur within 3 years

Comparison of Therapeutic Modalities (Academic Summary)

Modality	Primary Mechanism	Clinical Utility	Expected Result
Surgical	Physical cytoreduction	Localized disease (T1-T3)	Curative in 60-90% of cases
Medical (TKI)	VEGFR / HIF-2 α inhibition	Metastatic / Cytoreduction	High ORR; Disease stabilization
Immunotherapy	T-cell disinhibition	Frontline metastatic / Adjuvant	Potential for "Durable Remission"
Chemotherapy	DNA damage / Microtubule disruption	Only CDC, RMC, or Sarcomatoid	Palliative; High toxicity

KIDNEYS.



ADULTNEYS.



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