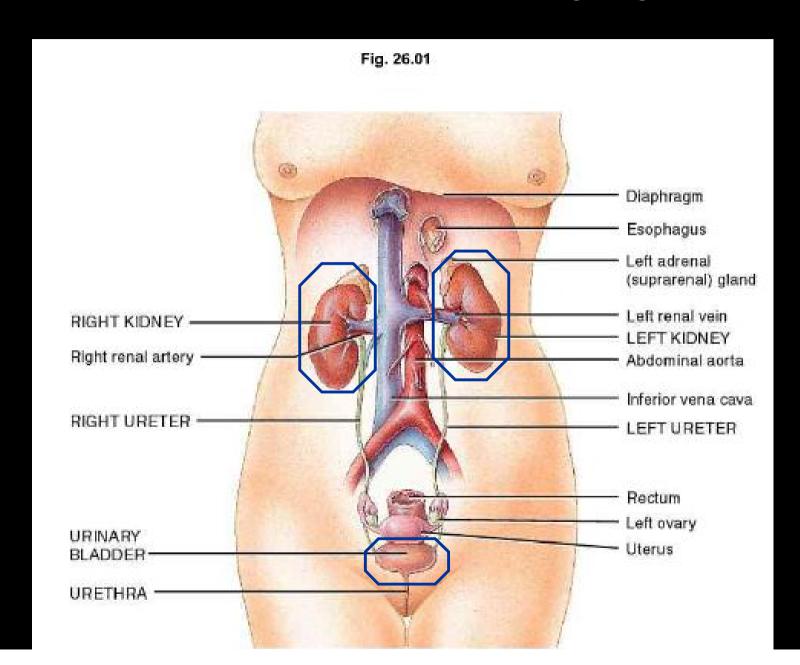
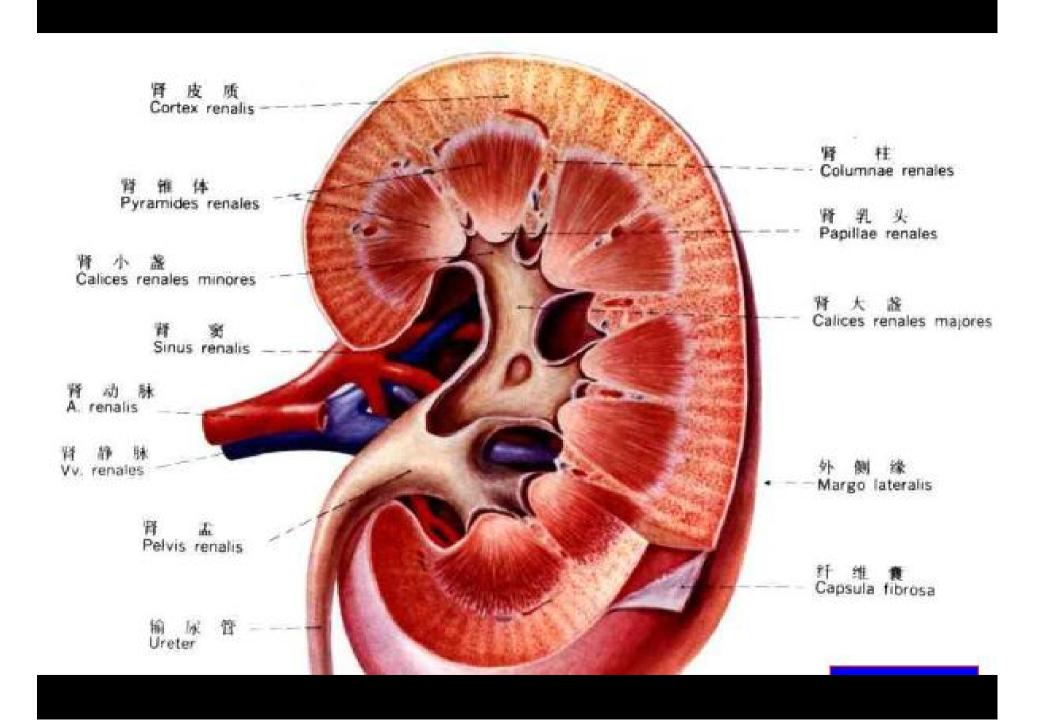
Diseases of the Urinary System

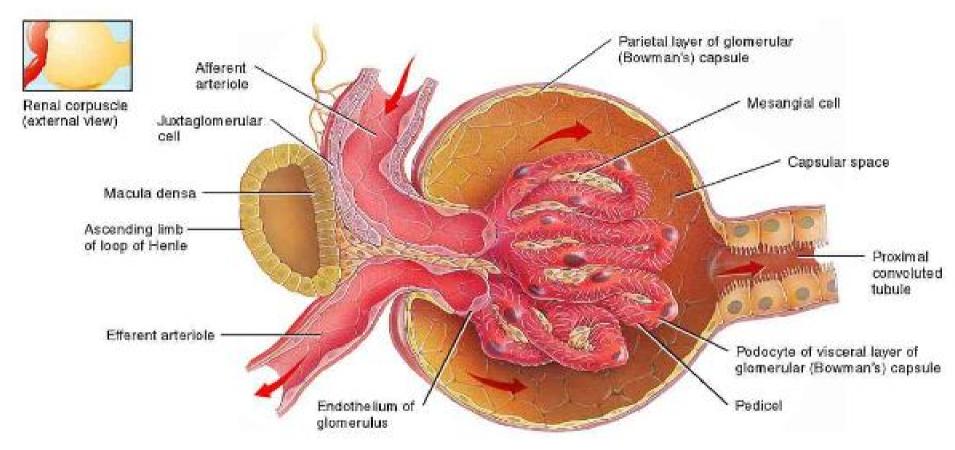
泌尿系统疾病

病理学教研室 王 莉

Components of the Urinary System







(a) Renal corpuscle (internal view)

Structure of Renal Glomerulus

- glomerulus
 - -afferent arteriol 入球小动脉
 - capillary loop 毛细血管袢
 - efferent arteriol 出球小动脉
- bowman capsule
 - parietal epithelial cells 壁层上皮细胞
 - visceral epithelial cells (podocytes) 脏层 -
 - -Bowman's space 肾小囊腔

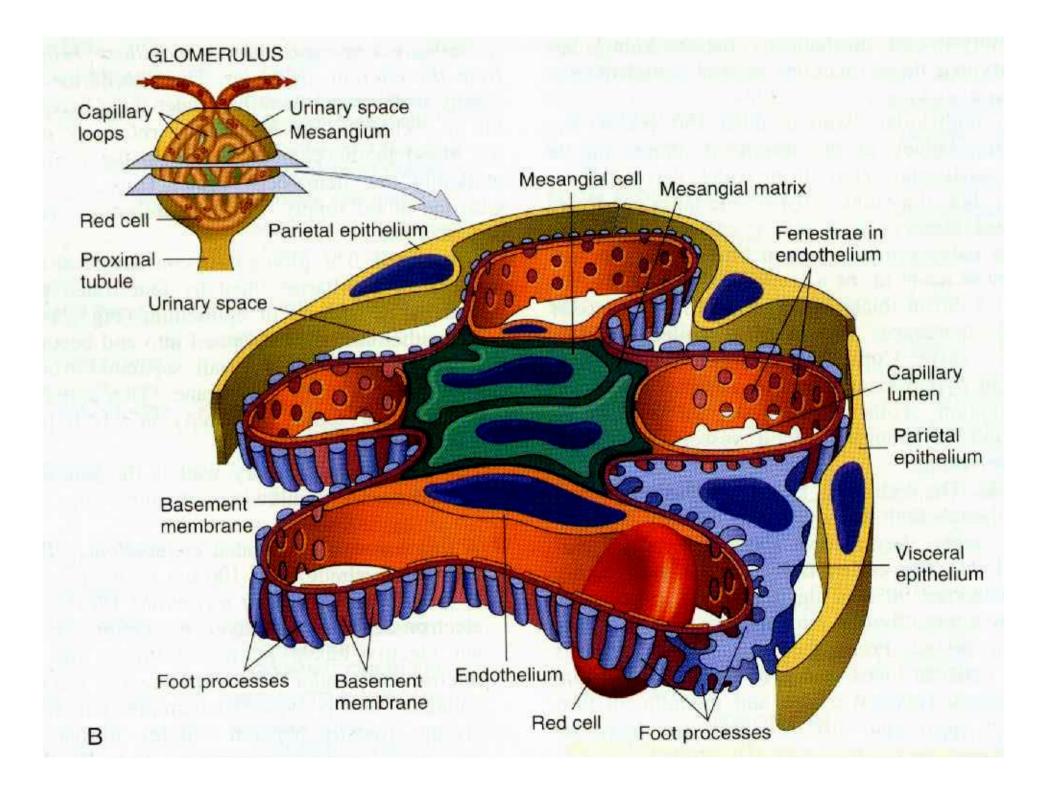
Structure of Renal Glomerulus

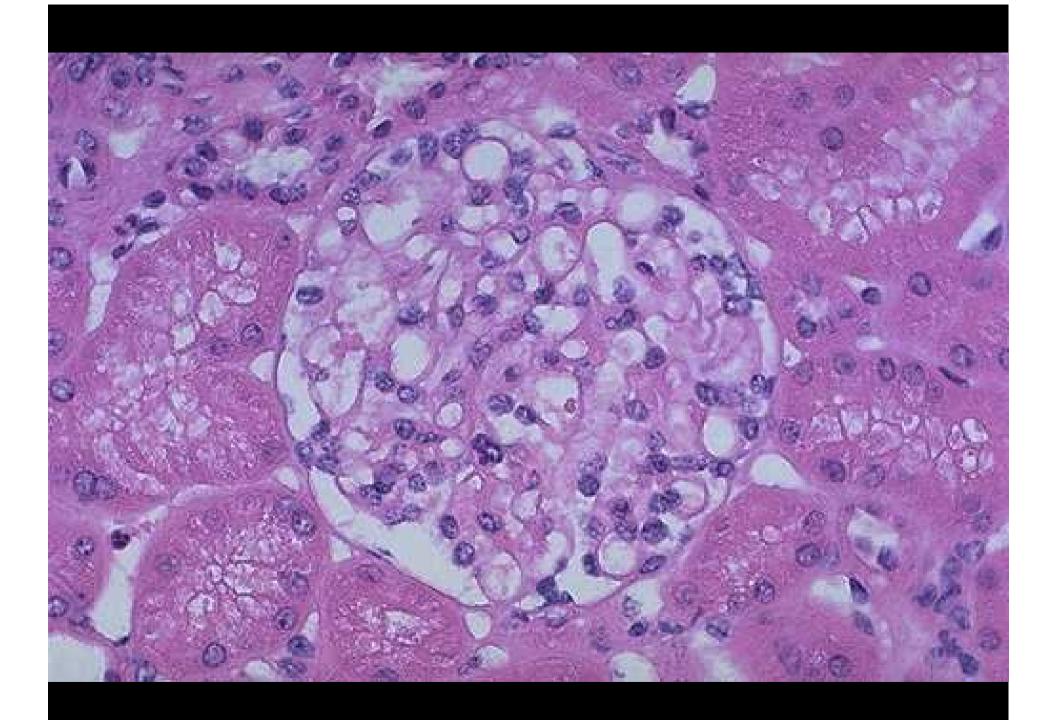
- Intraglomerular mesangium (球内系膜)
 - -mesangial cells 血管系膜细胞
 - -mesangial matrix 系膜基质

Structure of Filtering Barrier

肾小球滤过屏障

- Fenestrated endothelial cells 内皮细胞窗孔
- Glomerular basement membrane ,GBM 基底膜
- Visceral epithelial cells (podocytes) 脏层上皮细胞(足细胞)





Blood Supply of the Kidneys 血供特点

Efferent arterioles divide to form peritubular capillaries, which surround the renal tubule part of nephron

Types of Diseases of the Urinary System

- Glomerular diseases
 - *Primary glomerulonephritis
 - Secondary glomerular diseases
 - systemic diseases
 - vascular diseases
 - inherited diseases
- Tubulointerstitial nephritis
 - *Pyelonephritis
 - Toxin- and drug-induced tubulointerstitial nephritis
- *Tumors (kidney and bladder)

Primary Glomerulonephritis (GN)

原发性肾小球肾炎

Etiology and Pathogenesis 病因和发病机制

• Immune mechanisms underlie the majority of primary GN

• The most common mechanism is antibody-mediated injury

endogenous antigen

内源性抗原

- Components of glomerulus
 - -GBM
 - visceral epithelial cells
 - endothelial cells and mesangial cells
- Nonglomerular antigens
 - Tumour antigens, thyroid antigens
 - planted antigens:immunoglobulins, complement, DNA

exogenous antigen 外源性抗原

- infections
 - -Bacterial, viral, parasitic, etc
- drugs
 - -penicillamine

mechanisms

- Antibody-mediated injury
 - -In Situ Immune Complex Deposition 原位免疫复合物形成

- Circulating Immune Complex Nephritis 循环免疫复合物肾炎

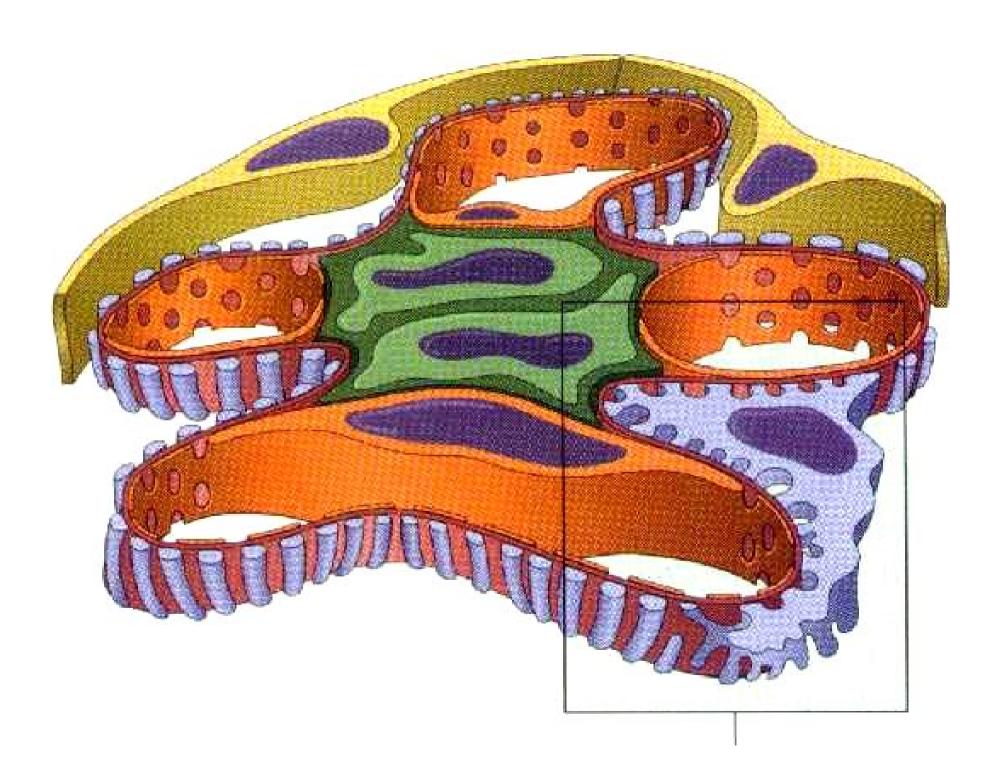
Cell-mediated immunity

In Situ Immune Complex Deposition

• Antigen-antibody immune complexes form within the kidney when antibodies react with intrinsic or planted antigens within the glomerulus

intrinsic antigens

Antiglomerular basement membrane disease is an example of reaction to intrinsic antigens.

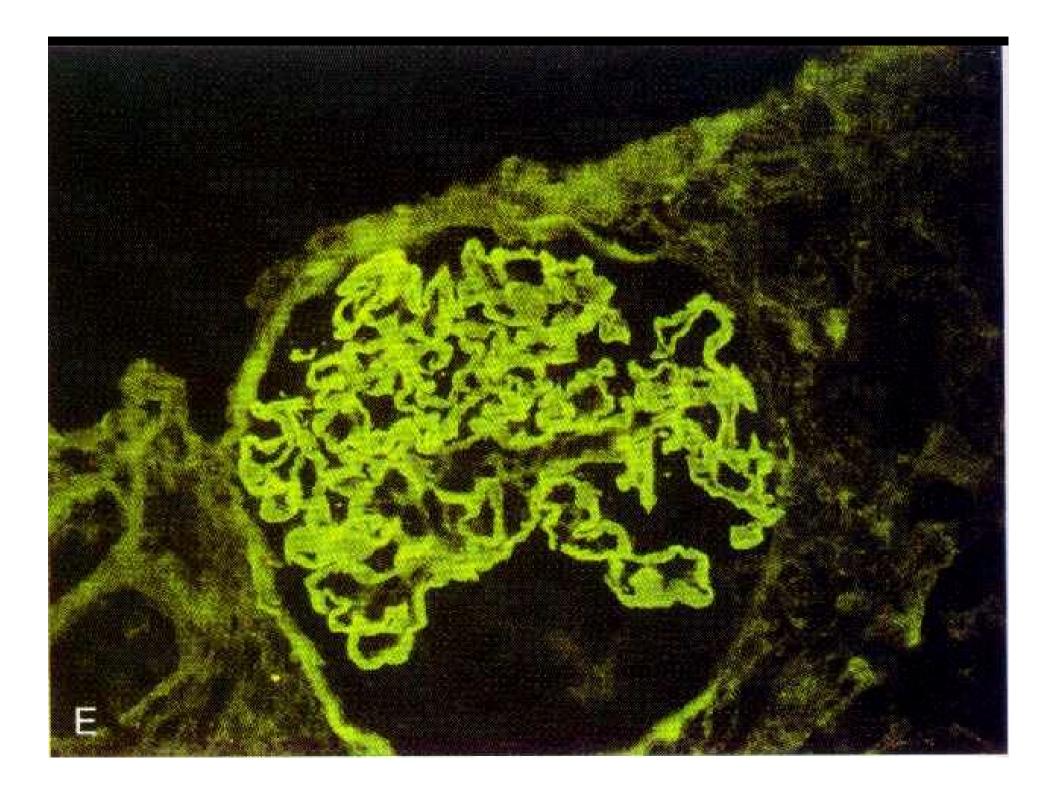


ANTI-GBM Endothelium

Antigen

В

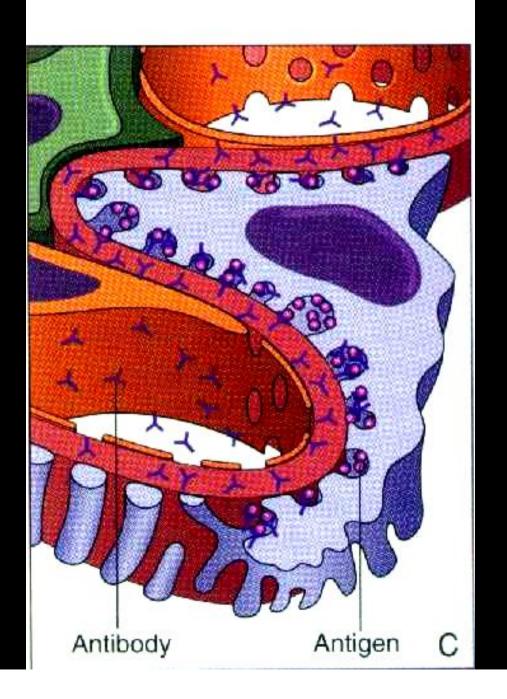
Antibody

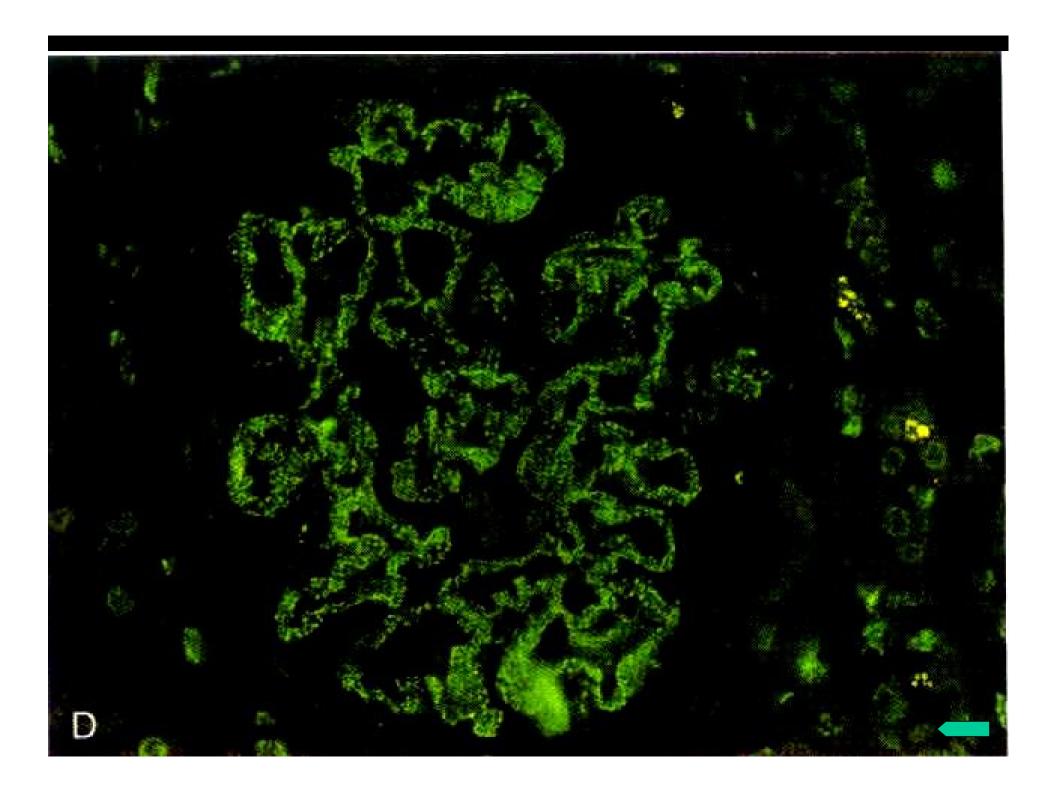


intrinsic antigens

Tubular brush border —>
 antibodies to brush border antigens
 / visceral epithelial cells —>
 Heymann nephritis / human
 membranous glomerulopathy

HEYMANN





planted antigens

Nonglomerular antigens +
 Components of glomerulus —>
 planted antigens

Nonglomerular antigens

- endogenous
 - -immunoglobulins + mesangium
 - -DNA + GBM
- exogenous
 - -Bacterial, viral, parasitic and drugs

Circulating Immune Complex Nephritis

• Immune complexes form outside the kidney and become trapped in the glomerulus after travelling to the kidney via the renal circulation

Circulating Immune Complex deposition

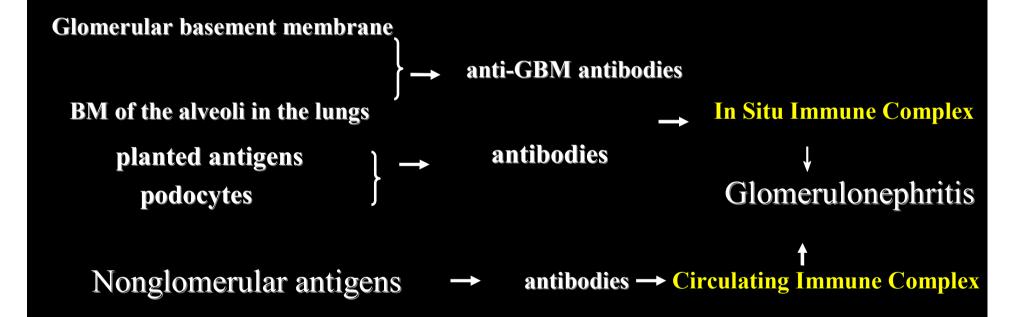
 large molecule and insoluble immune complexes -> subendothelial deposits or phagocytosed

 little molecule and soluble immune complexes-> subepithelial deposits or filtered out

Circulating Immune Complex deposition

 moderate immune complexes-> mesangium deposits

Pathogenesis of Glomerulonephritis



Cytotoxic antibodies

• This is uncommon

• Antibodies to glomerular cell antigens cause damage without the formation and deposition of immune complexes

Mediators of Glomerular Injury

• neutrophils:

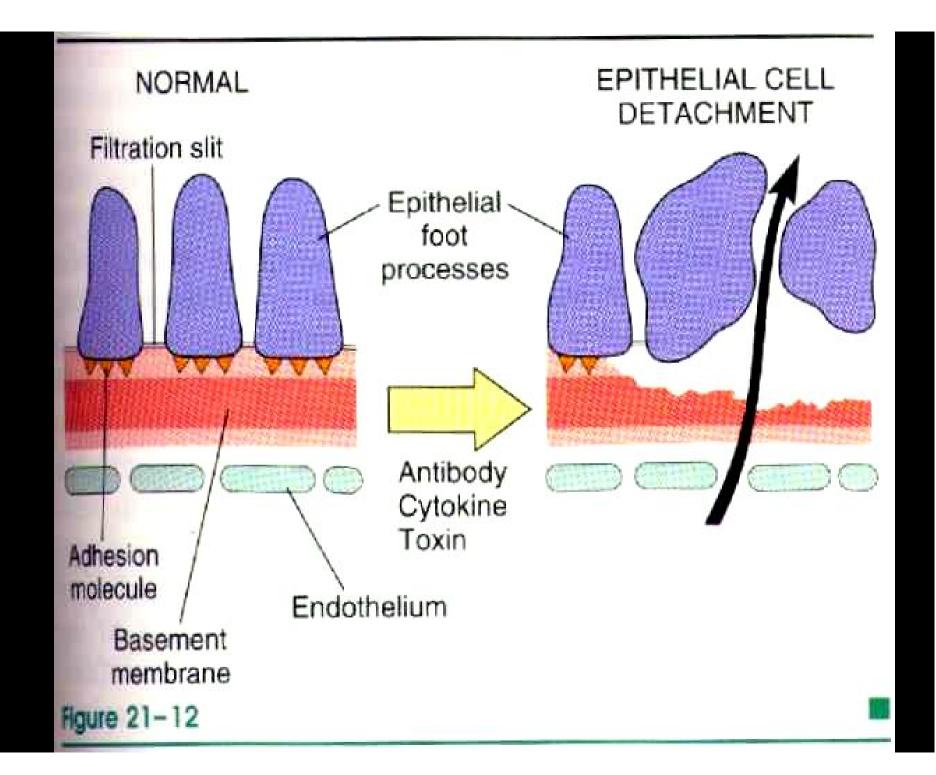
proteases, oxygen-derived free radicals, arachidonic acid metabolites 花生四烯酸代谢产物

• Monocytes and macrophages: biologically active molecules

Mediators of Glomerular Injury

platelets:
 prostaglandins and growth factors

• Epithelial, mesangial, and endothelial: cytokines (interleukin 1), growth factors, arachidonic acid metabolites, nitric oxide, endothelin

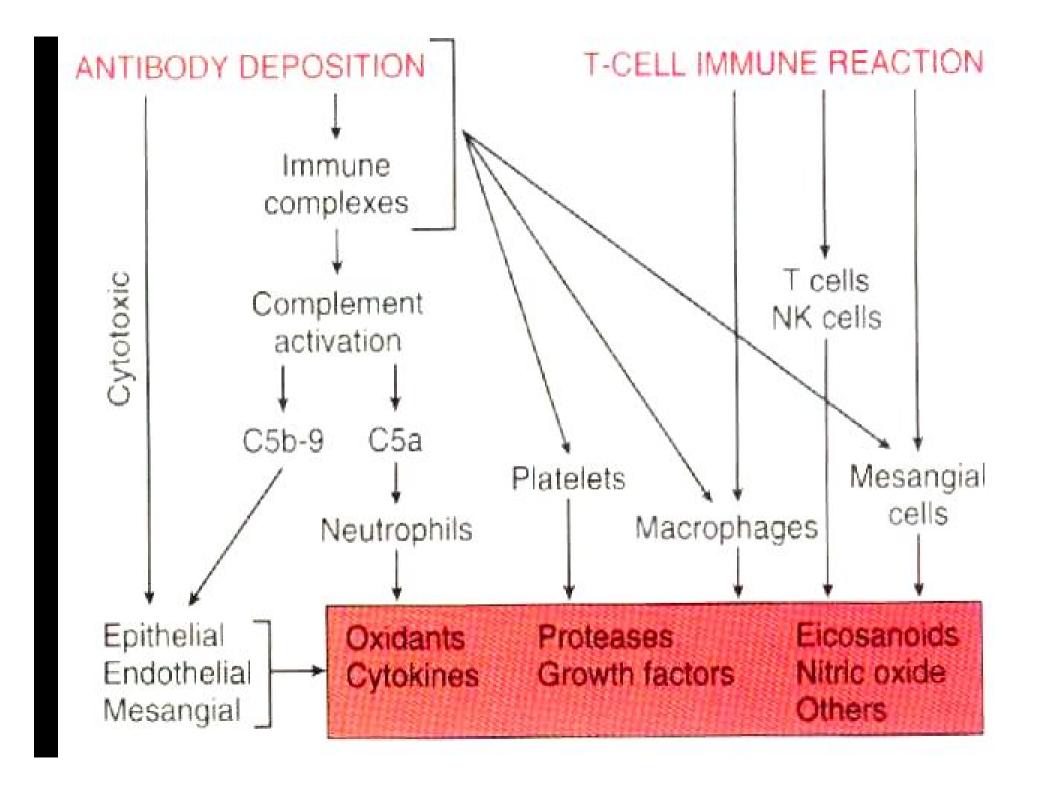


Cell-Mediated Immunity in GN

细胞免疫机制

 Sensitized T cells from cell-mediated immune reactions play a role in progression of GN

 Glomerular damage is thought to be mediated by macrophages and T lymphocytes



Histological Alterations

- changes of renal glomeluli
- renal tubule and interstitium
 - —Atrophy and degeneration of renal tubule
 - Dilation of renal tubule
 - Casts 管型 (granular 颗粒、cell and protein)
 - -infiltration of inflammatory cell, fibrosis

changes of renal glomeluli

- hypercellularity 细胞增多
 - —endothelial, mesangial, parietal epithelial cells and neutrophils

 uniform and diffuse loss of the foot processes of the podocytes

脏层上皮细胞足突融合、变平和消失

changes of renal glomeluli

• basement membrane (GBM) thickening

• fibrinoid necrosis of the capillary walls

proliferation of mesangium

changes of renal glomeluli

 degeneration and necrosis of the endothelial cells

• fibrin thrombi within the capillary lumina

neutrophilic and monocytic infiltration

Special Stains and Techniques Used in Renal Biopsies

- Periodic Acid-Schiff stain (PAS)
- Sliver impregnation stains or PASM
- Masson's trichrome stain
- Immunofluorescence
- Electron microscopy

Classification of Glomerulonephritis 原发性肾小球肾炎分类

- causes primary and secondary
- course of disease acute and chronic
- number of diseased glomeruli diffuse and focal
- degree of diseased glomerulus—
 global and segmental

Classification of Glomerulonephritis 原发性肾小球肾炎分类

• diffuse — affects all the glomeruli

• focal — affects only some glomeruli

• segmental — affects only part of the glomerulus

• global — affects the entire glomerulus

- Acute nephritic syndrome
 - Haematuria . 血尿
 - -Proteinuria 蛋白尿
 - Oliguria/anuria 少界 天界
 - Fluid retention seen as facial edema
 - Hypertension
 - -Uraemia 尿毒症

• Rapidly progressive nephritic syndrome

- -Hematuria
- -Oliguria 少尿
- -Hypertension
- -Renal failure

• Asymptomatic haematuria or proteinuria

- -recurrent or persistent
- -microscopic or macroscopic

- Nephrotic syndrome
 - Heavy proteinuria (>3.5g/24h)

大量蛋白尿

Hypoalbuminaemia

低蛋白血症

Severe edema

严重水肿

- Hyperlipidaemia and lipiduria

高脂血症和脂尿

- Chronic nephritic syndrome
 - —Polyuria 多尿 and nocturia 夜尽
 - -Hypertension 高血压
 - -Oedema 水肿
 - —Anaemia 资血
 - -Azotemia 氮质血症
 - -Uraemia 尽毒症

Pathological classification

- acute diffuse proliferative glomerulonephritis
- rapidly progressive(crescentic) GN
- membranous glomerulopathy
- membranoproliferative GN
- minimal change glomerulopathy

Pathological classification

- mesangioproliferative GN
- focal segmental glomerulosclerosis (FSGS)
- IgA nephropathy (Berger's disease)
- chronic glomerulonephritis

Acute diffuse proliferative glomerulonephritis

急性弥漫增生性肾小球肾炎

- Postinfectious glomerulonephritis
 - poststreptococcal GN:

group A beta-hemolytic streptococcal

- Nonstreptococcal GN:

staphylococci, pneumococci, parasites, viruses

– pathological feature:

proliferation of mesangial and endothelial cells

· Immunofluorescence 免疫荧光

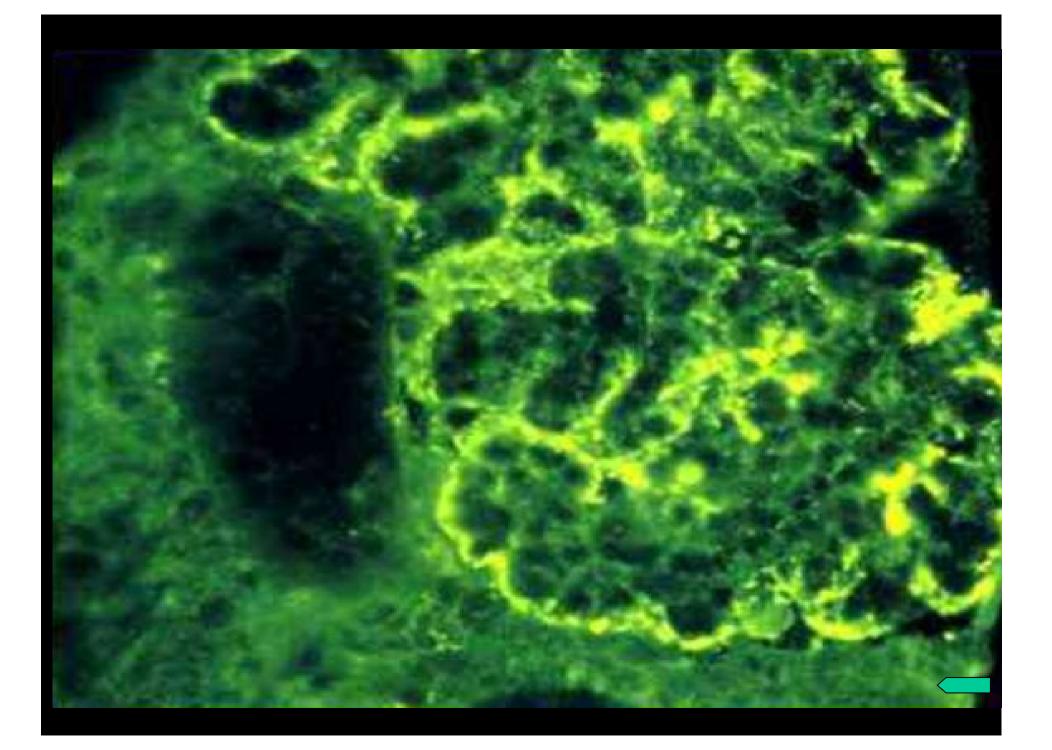
- IgG and complement within the granular deposits



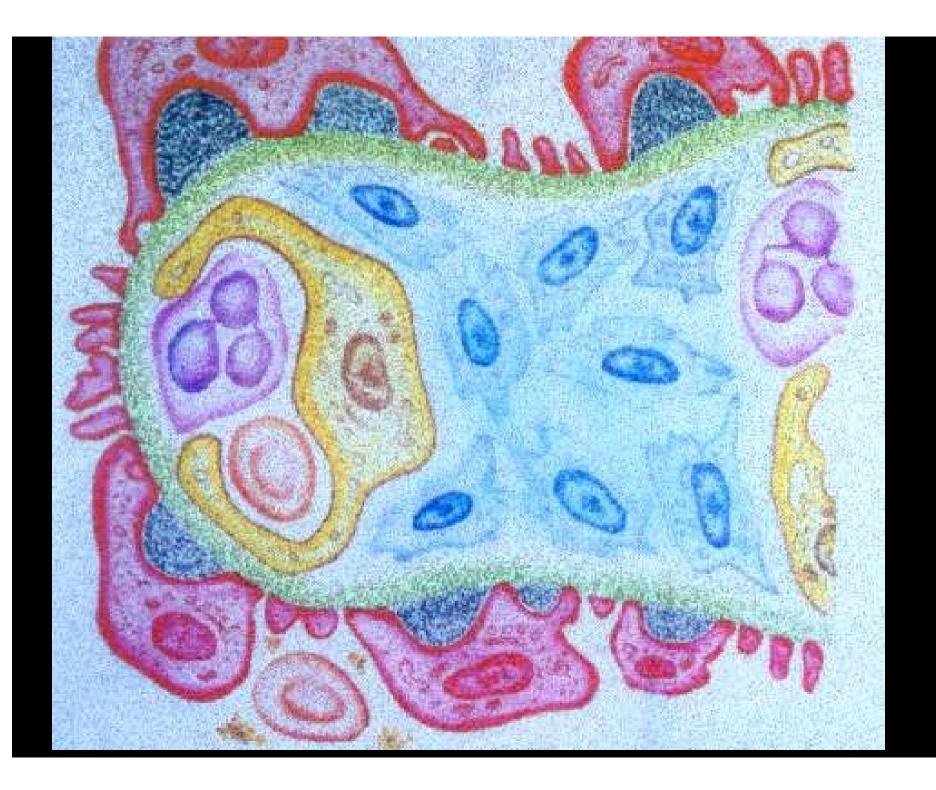
- Electron-dense subepithelial "hump" 驼峰 🕟
- Intramembranous and subendothelial deposits

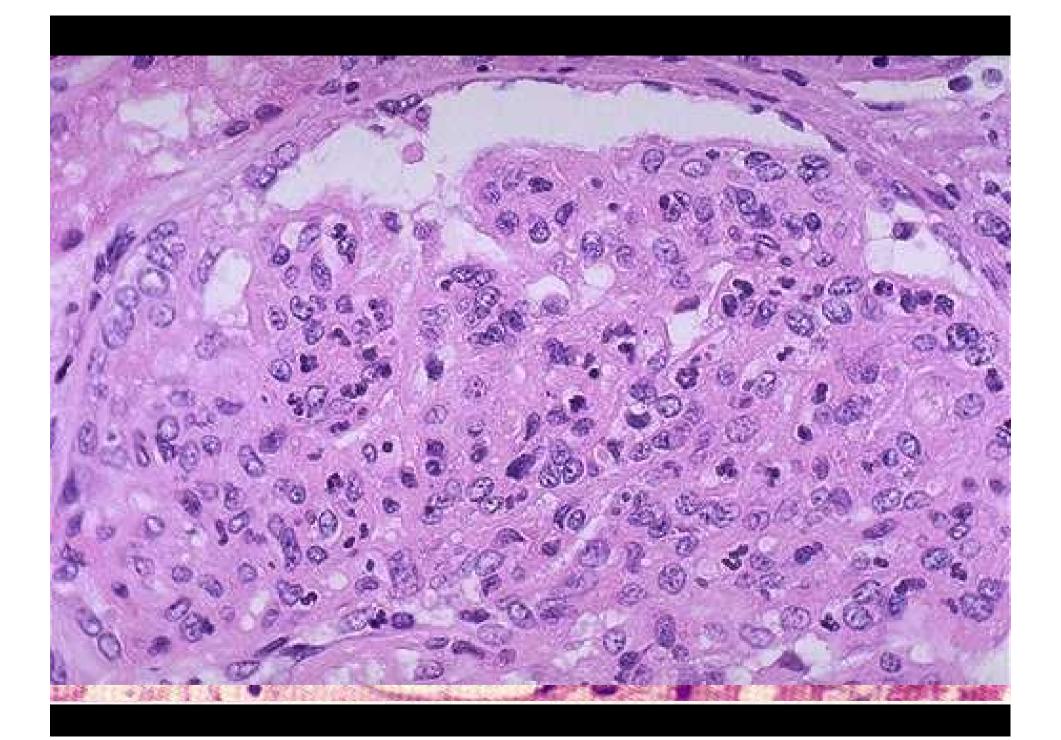
• Light Microscope, LM 光镜

- proliferation of mesangial and endothelial cells
- neutrophilic and monocytic infiltrate
 - glomerular hypercellularity
- fibrinoid necrosis of the capillary walls fibrin thrombi within the capillary lumina
- fibrin and neutrophilic exudate in Bowman's capsule
- degeneration of renal tubule and forming casts









Gross appearance 肉眼

 The kidneys are enlarged and red, often with petechial hemorrhages on the cortical surfaces

Clinical Course

Acute nephritic syndrome

· Sequela 结局

- Recovery occurs in most children
- rapidly progressive GN or chronic renal disease
- End-stage renal disease



肾小球毛细血管壁通透性 1 —>血尿、蛋白尿或管型尿

变态反应—>全身毛细血管壁通透性 1 —>水肿

少尿无尿

细胞数↑—>管腔狭小和阻塞—> 肾小球滤过率↓ 肾小管重吸收正常

水钠潴留—>血量↑

高血压

Rapidly Progressive (Crescentic) Glomerulonephritis (RPGN)

快速进行性肾小球肾炎

Crescentic glomerulonephritis, CrGN

新月体性肾小球肾炎

pathological feature:
 proliferation of parietal epithelial cells
 Formation of distinctive crescents

壁层上皮细胞增生,形成新月体

• Immunofluorescence 免疫荧光

- Postinfectious cases exhibit granular immune deposits
- Godpasture syndrome cases show linear fluorescence
- Idiopathic cases may have granular, linear, or little deposition (pauci-immune)

• EM 电镜

- Electron-dense subepithelial , intramembranous and subendouthelial deposits
- Ruptures of GBM

Classification of RPGN

- Type I RPGN (Anti-GBM disease)
 - Idiopathic 原发性
 - Goodpasture syndrome

(Pulmonary hemorrhage and Crescentic GN)

- Type II RPGN (Immune complex-mediated disease)
 - Idiopathic
 - Postinfectious
 - Systemic lupus erythematosus
 - Henoch-Schonlein purpura (IgA)
 - Others
- Type III RPGN (Pauci-immune type)
 - Idiopathic
 - Wegener granulomatosis
 - Microscopic polyarteritis nodosa 显微型结节性多动脉炎

• LM 光镜

- -Glomerular injury results in leakage of fibrin, which stimulates parietal epithelial cells and macrophages within the Bowman' capsule to proliferate and form crescent-shape masses
- Neutrophils and lymphocytes may be present
- Fibrin strands are prominent between the cellular layers in crescents
- The crescents obliterate Bowman space and compress the glomerular tuft

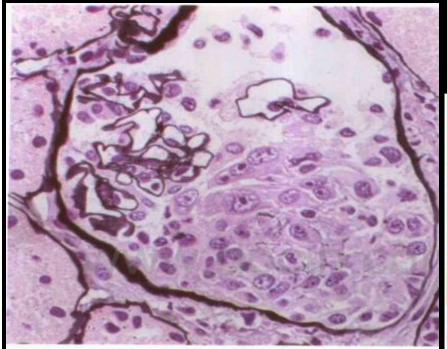


图 11-4 细胞性新月体。PASM 染色

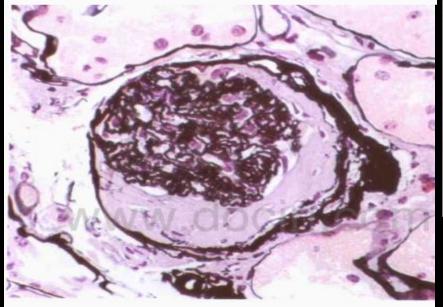


图 11_6 纤维性新日休 PΔ QM 込色



图 11-5 纤维细胞性新月体。PASM 染色

• Gross appearance 肉眼

- The kidneys are enlarged and pale

• Clinical Course

Rapidly progressive nephritic syndrome ►

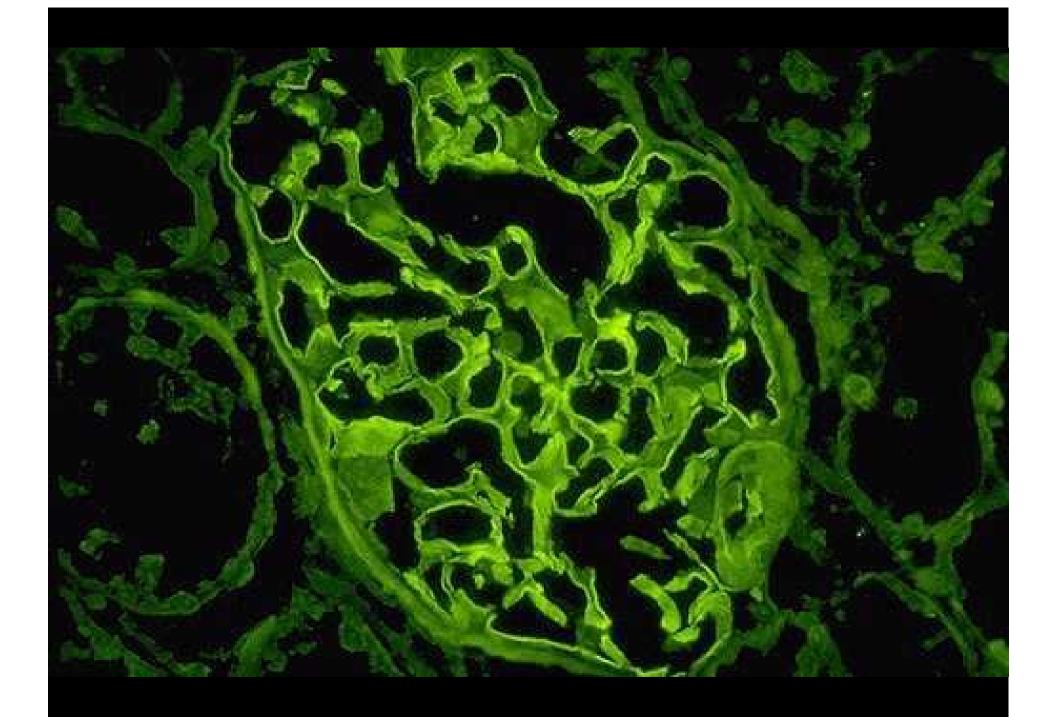
· Sequela 结局

 The disease progresses very rapidly and there is a loss of renal function within days to weeks 毛细血管壁纤维素样坏死 —> 血尿明显 基底膜缺损 蛋白尿轻

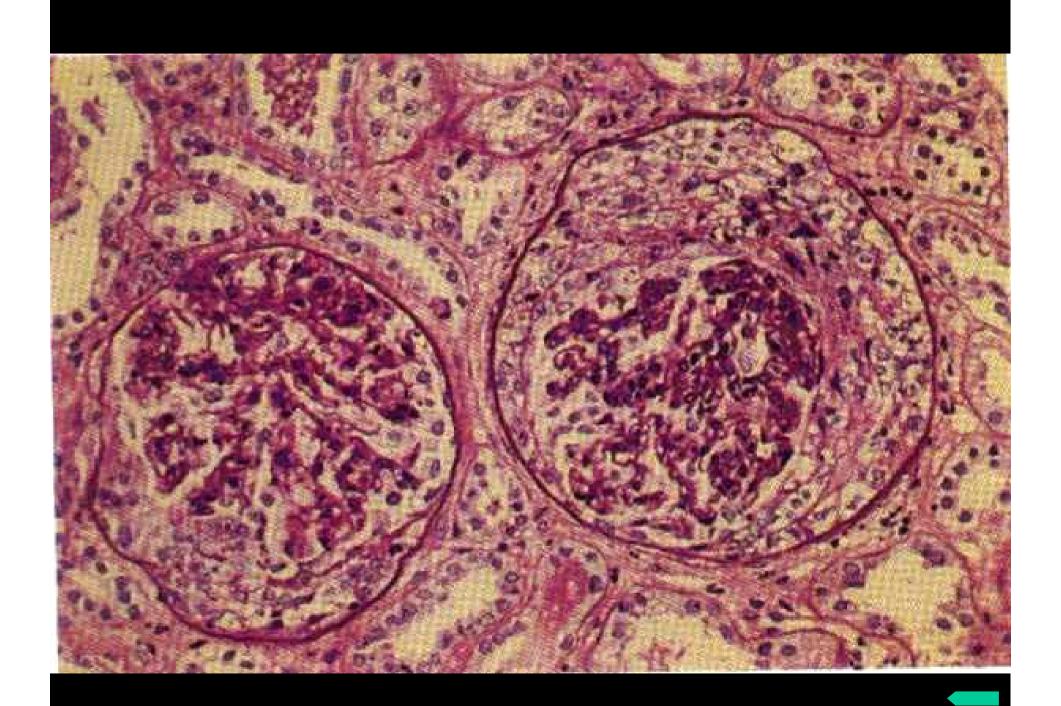
新月体阻塞肾球囊腔—>血浆滤过障碍—>少尿 无尿

球囊内压 ↑ —>肾缺血—>高血压<—血容量 ↑

代谢物不能排出——>氮质血症,尿毒症







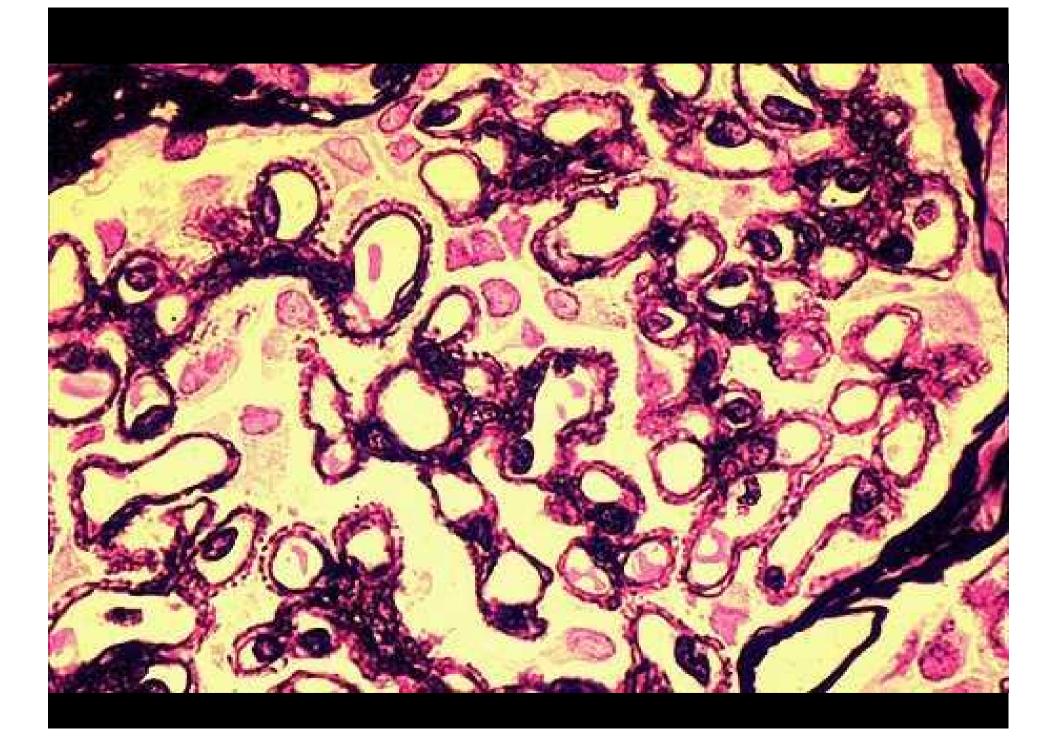
membranous glomerulopathy 膜性肾小球病

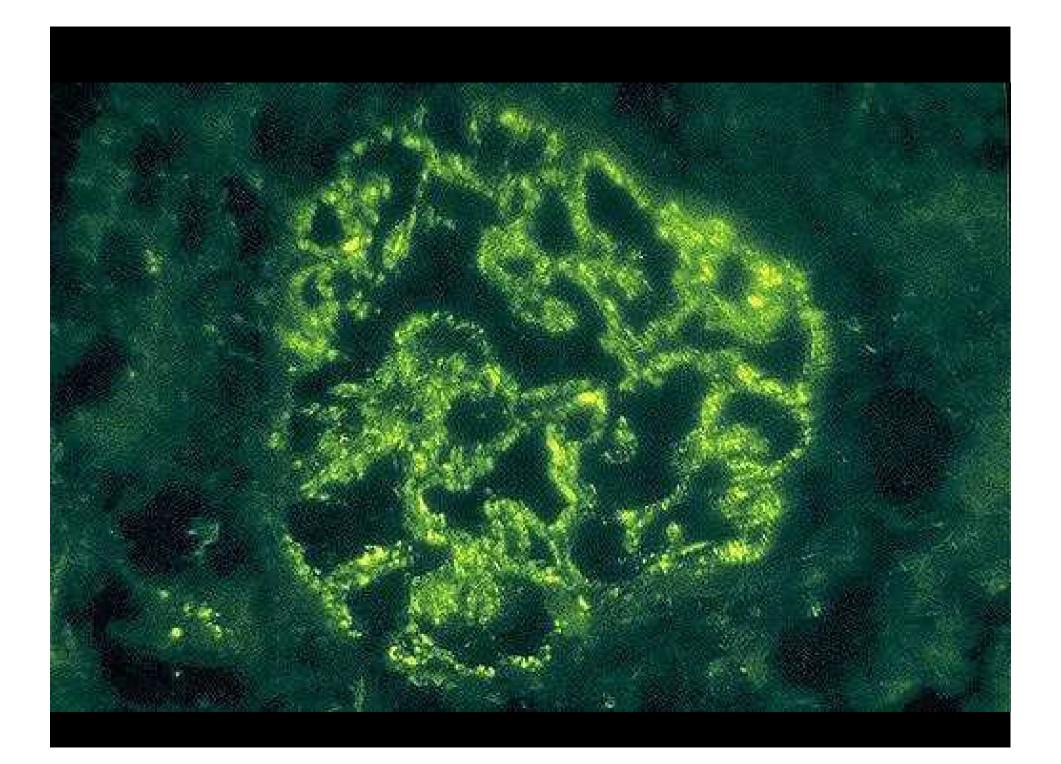
- Membranous Nephropathy 膜性肾病
- most common cause of the nephrotic syndrome in adults 成人肾病综合征的主要原因
 - pathological feature: diffuse thickening of the GBM
- · Immunofluorescence 免疫荧光
 - Granular deposits contain both IgG and C3
- EM 电镜
 - Irregular dense deposits between the basement membrane and the overlying epithelial cells
 - The podocytes lose their foot processes
 - Basement membrane material is laid down between these deposits, appearing as irregular spikes protruding(钉状突起)from the GBM.
 - The membrane thickening progressively encroaches on the capillary lumens

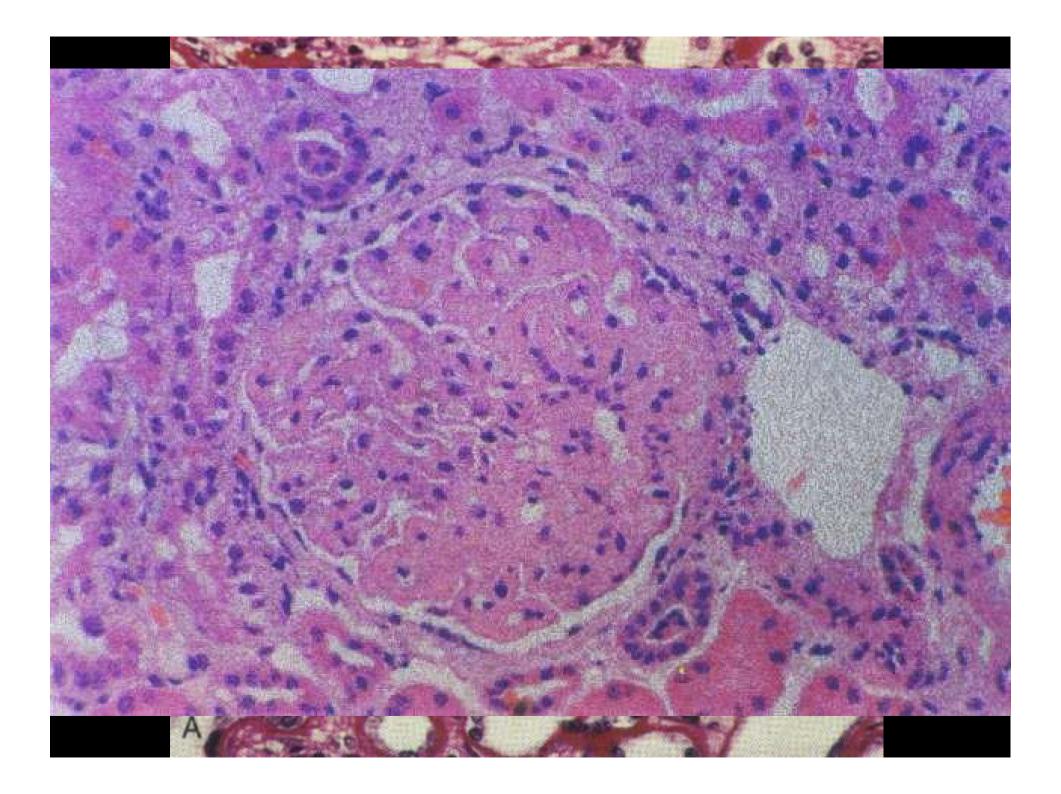
基底膜外致密物沉积->基底膜与钉突形成梳齿->基底膜呈虫蚀状->基底膜明显增厚

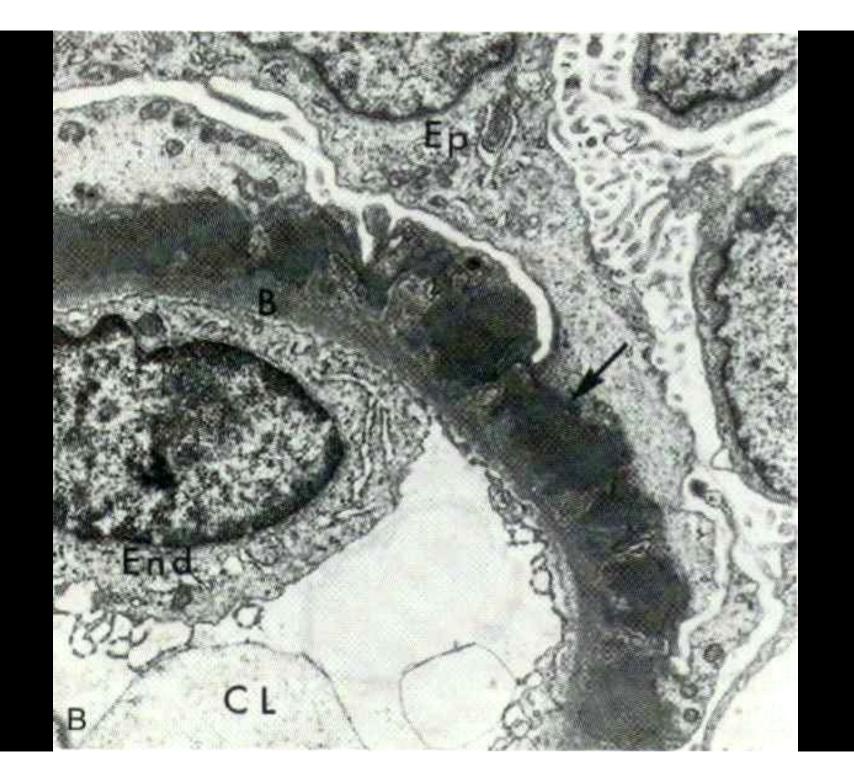
· LM 光镜

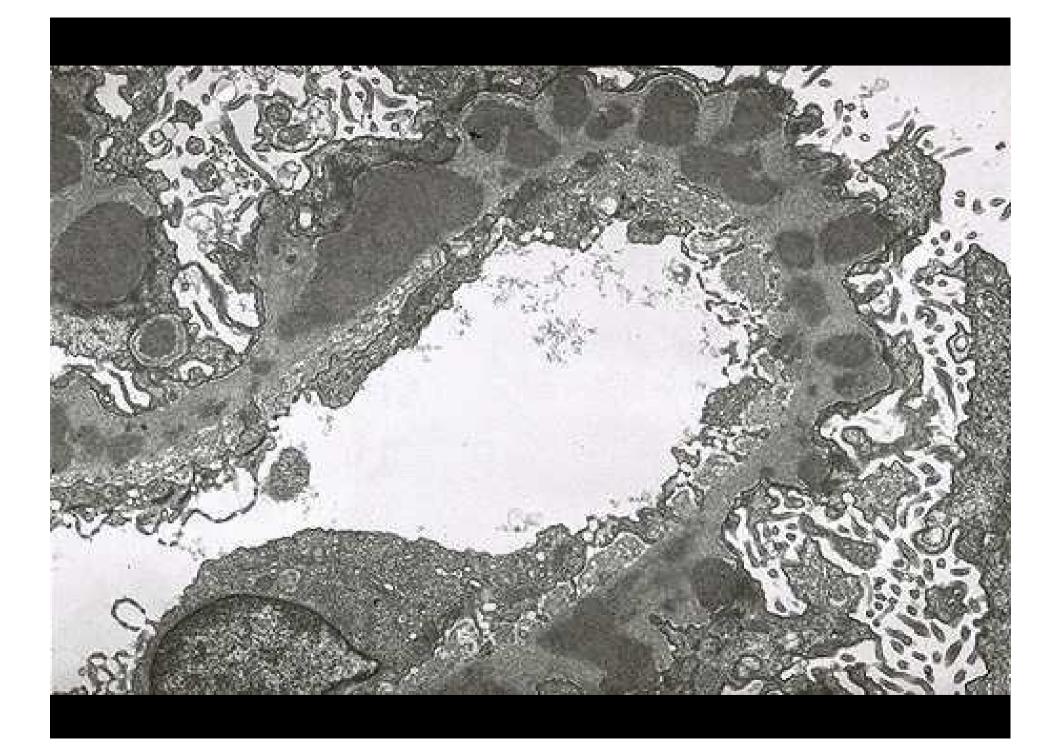
- -diffuse thickening of the glomerular capillary wall
- These spikes are seen by silver stains











• Gross appearance 肉眼

- The kidneys are enlarged and pale 大白肾

Clinical Course

- Nephrotic syndrome

· Sequela 结局

- Proteinuria persists in over 60% of patients
- Progressive disease terminating in renal failure in about 40% of patients
- 10% to 30% have a more benign course with partial or complete remission of proteinuria ▶



基底膜严重损伤—>严重蛋白尿(非选择性)—>低蛋白血症—>血浆胶体渗透压降低—>水肿

高脂血症原因不明

minimal change glomerulopathy

微小病变性肾小球病

- Minimal change glomerulonephritis 微小病变性肾小球肾炎
- Minimal change nephrosis 微小病变性肾病
- · Lipoid nephrosis 脂性肾病
 - —most frequent cause of the nephrotic syndrome in children
 - -minimal change disease results from a disorder of T cells

• pathological feature:

glomeruli that have a normal appearance under the light microscope

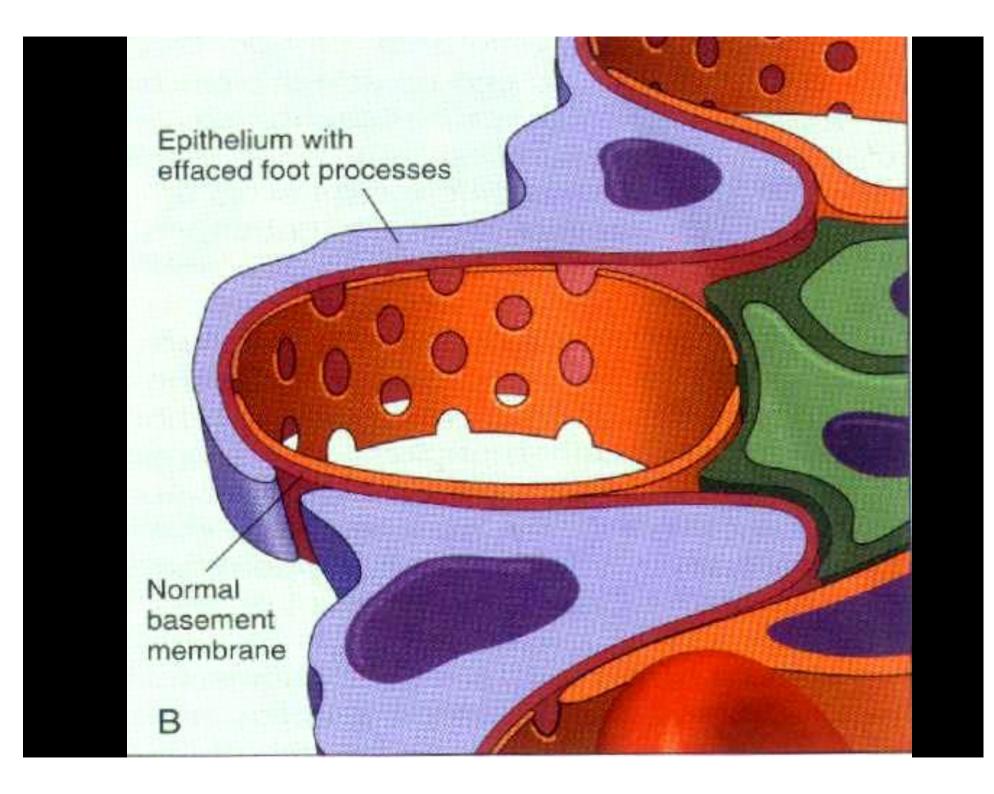
diffuse loss of visceral epithelial foot processes with the electron microscope

• EM 电镜

- Fusion and loss of the processes of the podocytes

· Immunofluorescence 免疫荧光

- No immunoglobulin or complement deposits



- Gross appearance 肉眼
 - The kidneys are enlarged and pale. Section show yellow streak

- LM 光镜
 - Glomeruli appear nearly normal
 - The cells of the proximal convoluted tubules are often heavily laden with lipid
- Clinical Course
 - Nephrotic syndrome
- Sequela 结局
 - Long-term prognosis is excellent

大量蛋白尿 (选择性)—>低蛋白血症—>血浆胶体渗透压↓—>明显 水肿 水肿 肝脏合成脂蛋白↑—>高脂血症

Membranoproliferative glomerulonephritis 膜增生性肾小球肾炎

- Mesangiocapillary glomerulonephritis 系膜毛细血管性肾小球肾炎,
- Hypocomplemetemia glomerulonephritis 低补体血症性肾小球肾炎

• pathological feature:

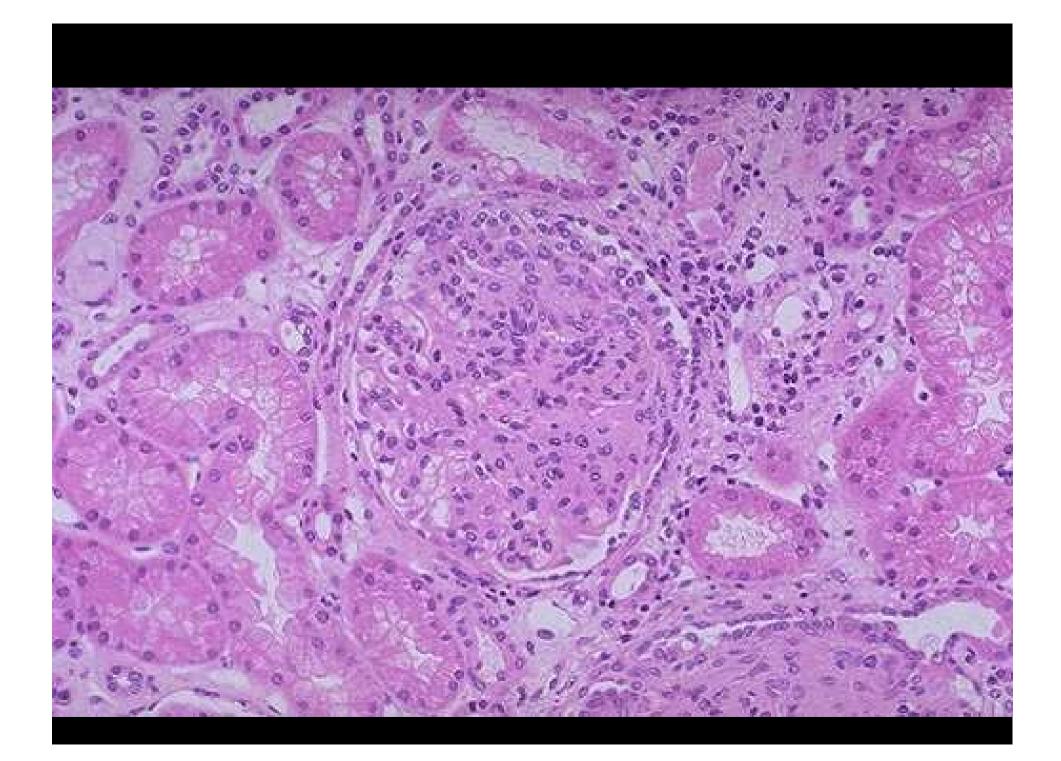
alterations in the basement membrane proliferation of gomerular cells (mesangium), and leukocyte infiltration

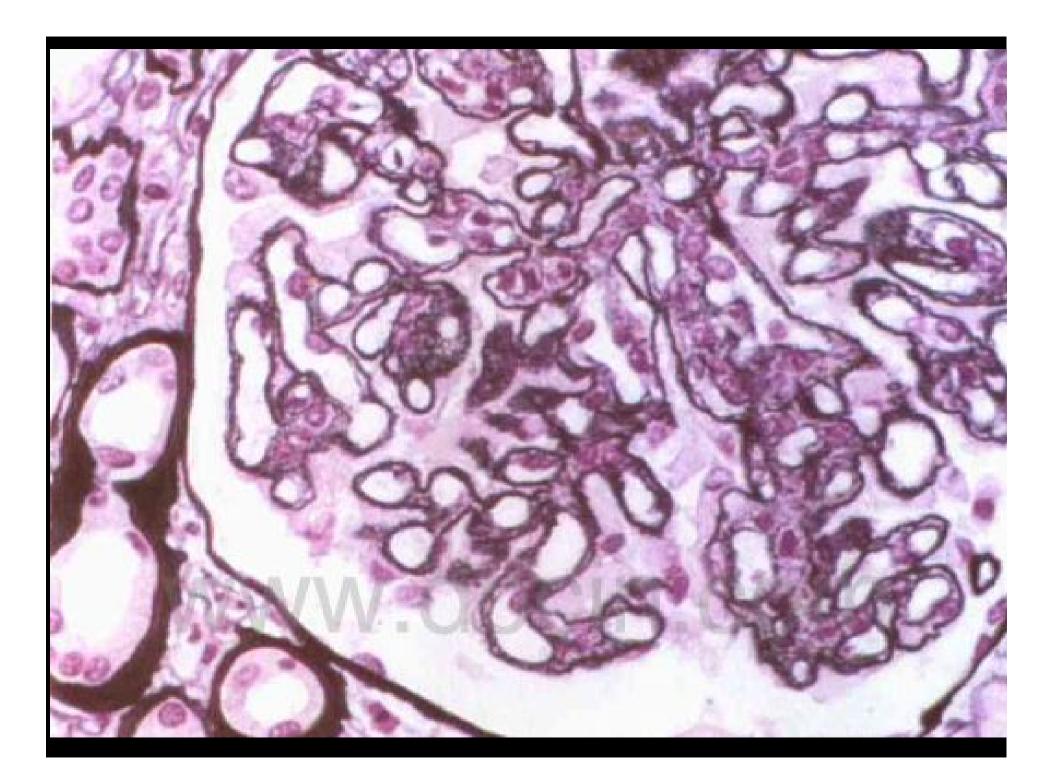
• LM

-The glomeruli are large and hypercellular (proliferation of mesangial cells) -> lobular appearance

-The GBM is thickened

-Silver or PAS stains: the glomerular capillary wall shows a "double-contour" of "tram-track" appearance

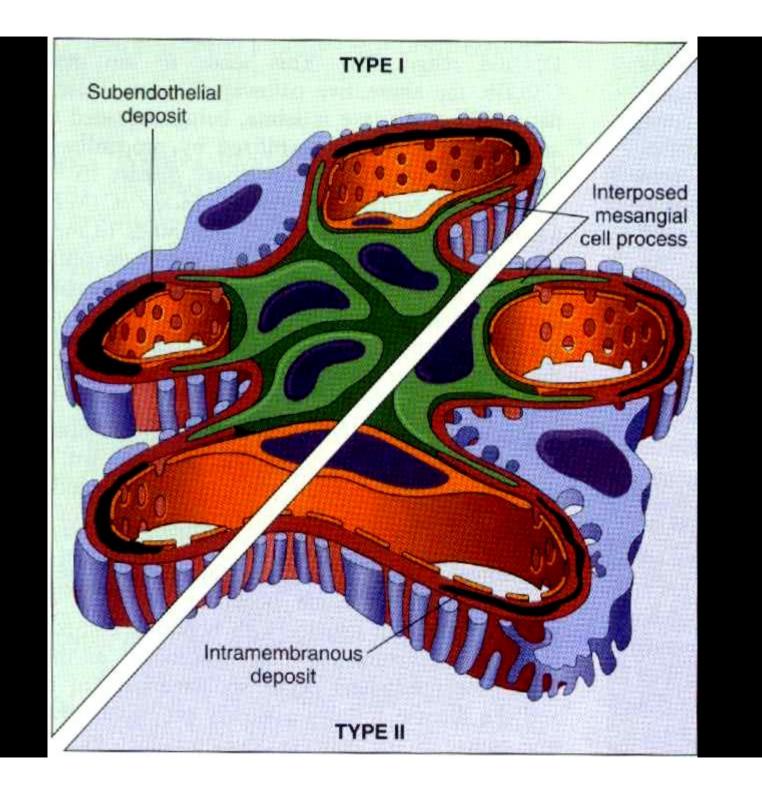




Immunofluorescence and EM

Type I: subendothelial electron-dense deposits. C3 is present in a granular patter, and IgG and early complement components (C1q and C4) are present.

- Type II (dense deposit disease): C3 is present in irregular granular-linear foci in the basement membranes. IgG and the early-acting complement components(C1q and C4) are absent.



Clinical Course

- Nephrotic syndrome
- Hematuria or proteinuria

· Sequela 结局

- Chronic renal failure
- Crescentic glomerulonephritis

mesangioproliferative glomerulonephritis 系膜增生性肾小球肾炎

• LM:

 proliferation of mesangial cells and matrix —> sclerosis of mesangium

• EM

-IgM or IgG and C3 deposited in mesangium of the glomeruli

• Immunofluorescence

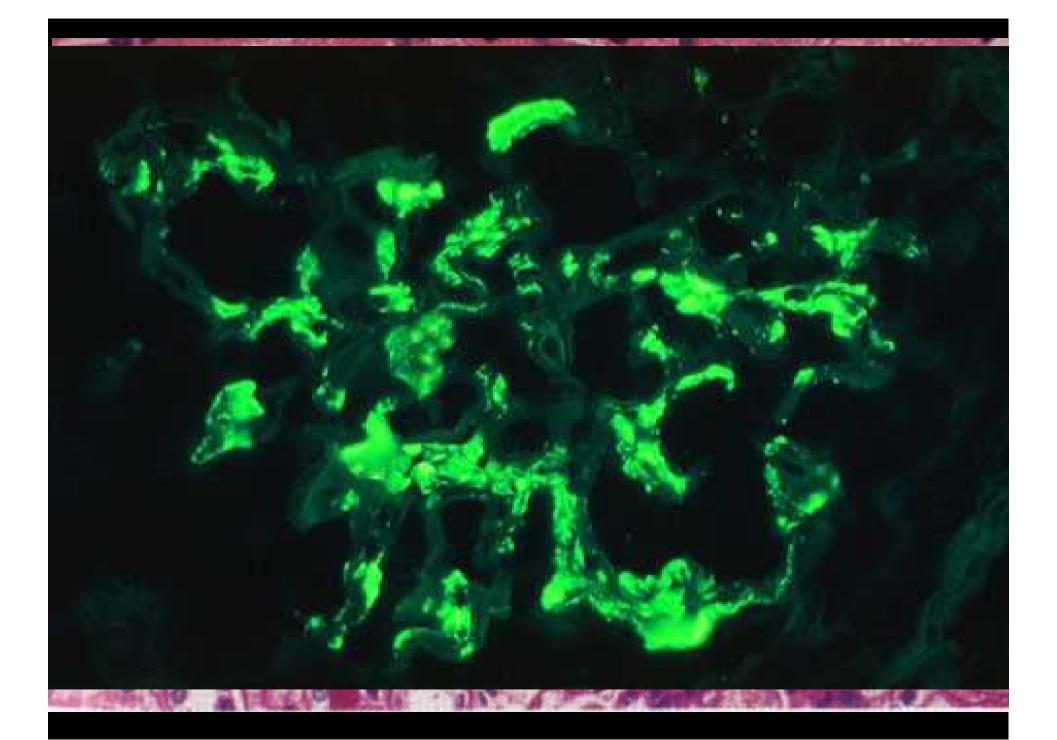
-dense deposits in the mesangium

Clinical Course:

- -Asymptomatic haematuria or proteinuria
- -Nephrotic syndrome or chronic nephritic syndrome

• Sequela:

- -good prognosis
- -some patients develop sclerosing GN



focal segmental glomerulosclerosis 局灶性节段性肾小球硬化

pathological feature:

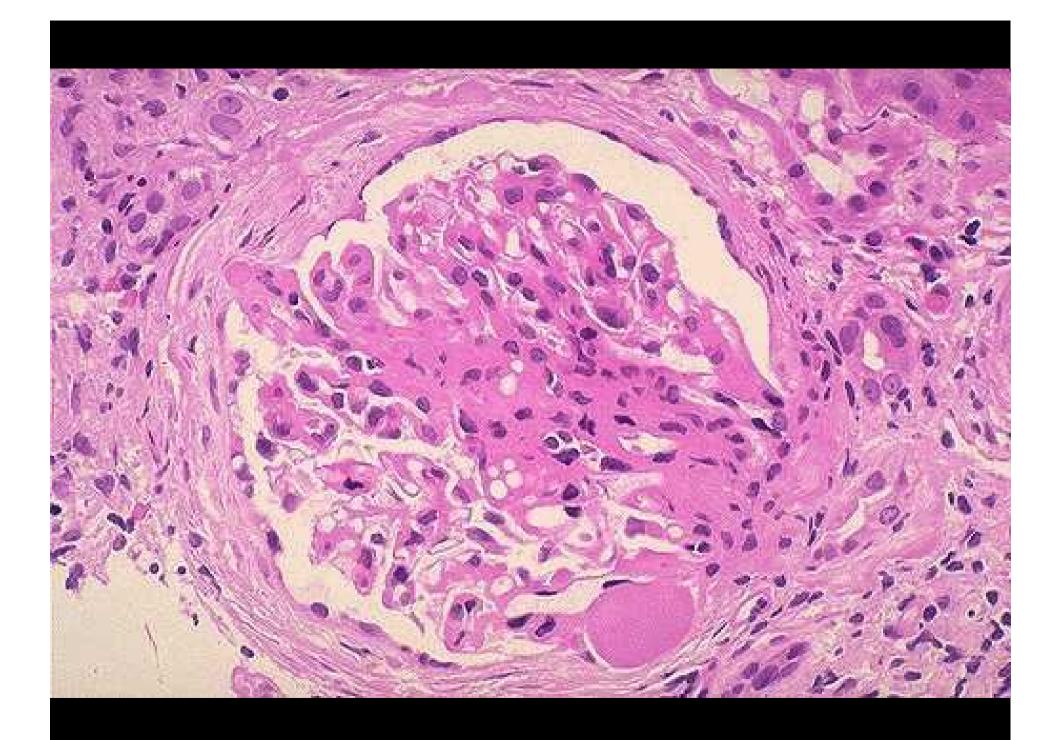
- sclerosis of some, but not all glomeruli. In the affected glomeruli, only a portion of the capillary tuft is involved.
- focal collapse and sclerosis, with hyaline deposits in glomerular segments

· Immunofluorescence 免疫荧光

-IgM and C3 are present within the hyaline masses in the sclerotic areas

• EM 电镜

 Both sclerotic and nonsclerotic areas show the diffuse loss of foot processes



Features differ from minimal change disease:

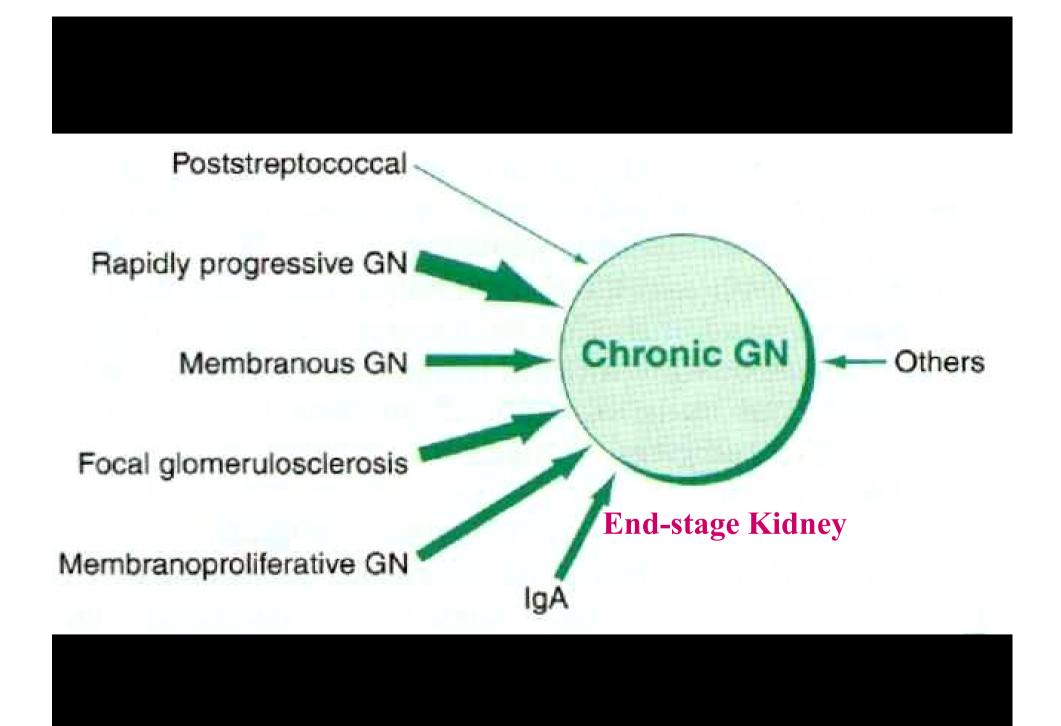
- High incidence of hematuria, reduced GFR, and hypertension;
- Proteinuria, more often nonselective;
- respond poorly to corticosteroid therapy;
- Immunofluorescence microscopy showing deposition of IgM and C3 in the sclerotic segment
- poor prognosis, at least 50% develop endstage renal disease within 10 years

IgA nephropathy IgA 肾病

(Berger's Disease)

- common in France, Australia and Singapore
- young men affected after an upper respiratory tract infection
- a major cause of recurrent glomerular hematuria
- IgA and C3 deposits seen in mesangium of all the glomeruli, with some mesangial proliferation-> sclerosis of the damaged segment
- presentation with microscopic hematuria and proteinuria and renal impairment, also with hypertension and higher plasma IgA
- worse prognosis -> end-stage renal failure

Chronic (sclerosing) glomerulonephritis 慢性肾小球肾炎

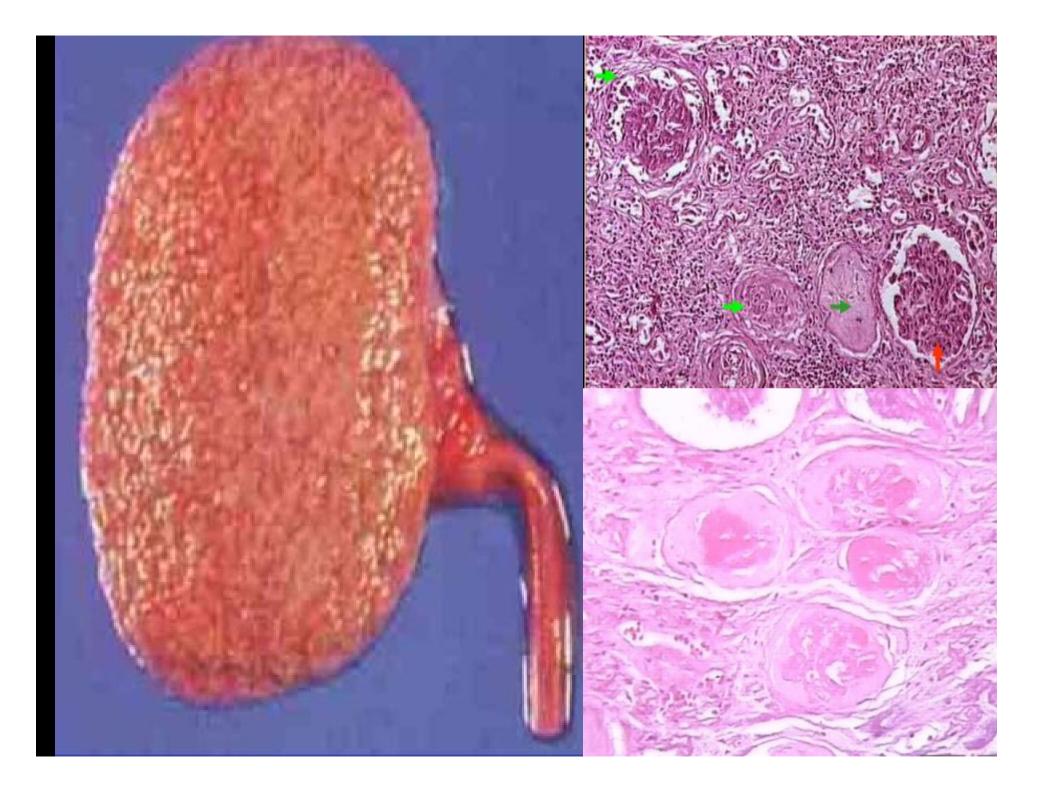


Gross appearance

The kidneys are small and shrinks, with cortical thinning and granular scarring

• LM

- Glomeruli hyalinization
- -tubular atrophy
- -interstitial fibrosis
- glomeruli and tubular compensatory enlargement
- dilated tubules containing protein casts



- Clinical Course
 - -Chronic nephritic syndrome

- Sequela
 - -treatment is dialysis透析 and renal transplantation

-death of uremia, heart failure and hemorrhage of brain or infection

	毛细血管内 增生性 GN	系膜增生 性 GN	膜性增生 性 GN	膜性 GN	新月体性 GN	轻微病变性 GN	硬化性 GN
光镜	内皮细胞、 系膜细胞肿 胀增生	系膜细胞 和基质明 显增生	毛细血管 壁增厚, 系膜增生	毛细血管 壁均匀增 厚	壁层上皮细胞增生,新月体,环状小体	肾小管上皮 细胞玻璃样 或脂肪变性	
电镜	上皮细胞下 驼峰状沉积	系膜内有 致密物沉 积		基底膜外侧钉状突起			
免 疫 荧光	颗粒荧光, IgG,C3	系 膜 内 IgM IgG C3 沉 积,	底膜内 C3	•	颗粒性或线性 荧光或免疫球 蛋白及补体均 阴性	及补体均阴	
大体	对 称 性 肿 大,大红肾, 蚤咬肾		无明显变 化	双侧肾肿大,大白肾		增大	对称性颗粒 固缩肾
临床	急性肾炎	隐匿性、肾 病综合征、 慢性肾炎	蛋白尿、肾 病综合征、 慢性肾炎	肾病 综合 征	急进型肾炎	肾病综合征	慢性肾炎

pyelonephritis 肾盂肾炎

bacterial infection of kidney

• purulent inflammation and damage to the tubules, interstitium, renal calyces and pelvis

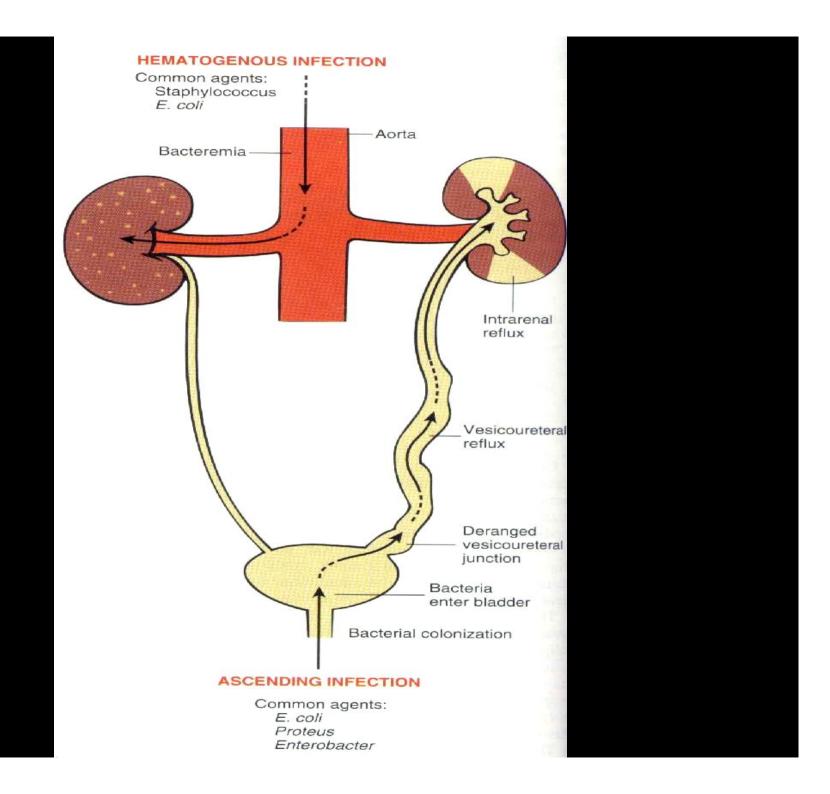
Etiology and Pathogenesis

- infectious routes:
 - -Ascending infection:

bacteria from the gut -> lower urinary tract -> kidney

-hematogenous(descending) infection:

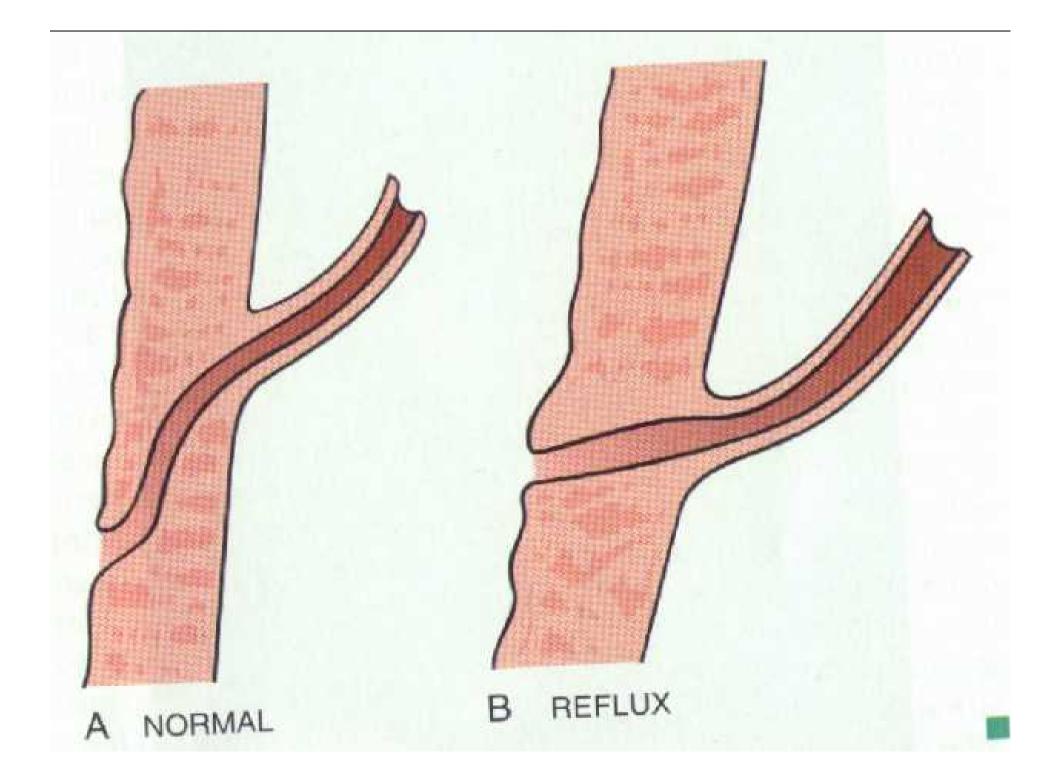
patients with septicemia of infective endocarditis pathogens include bacteria (staphylococci), fungi and viruses



Etiology and Pathogenesis

predisposing factors:

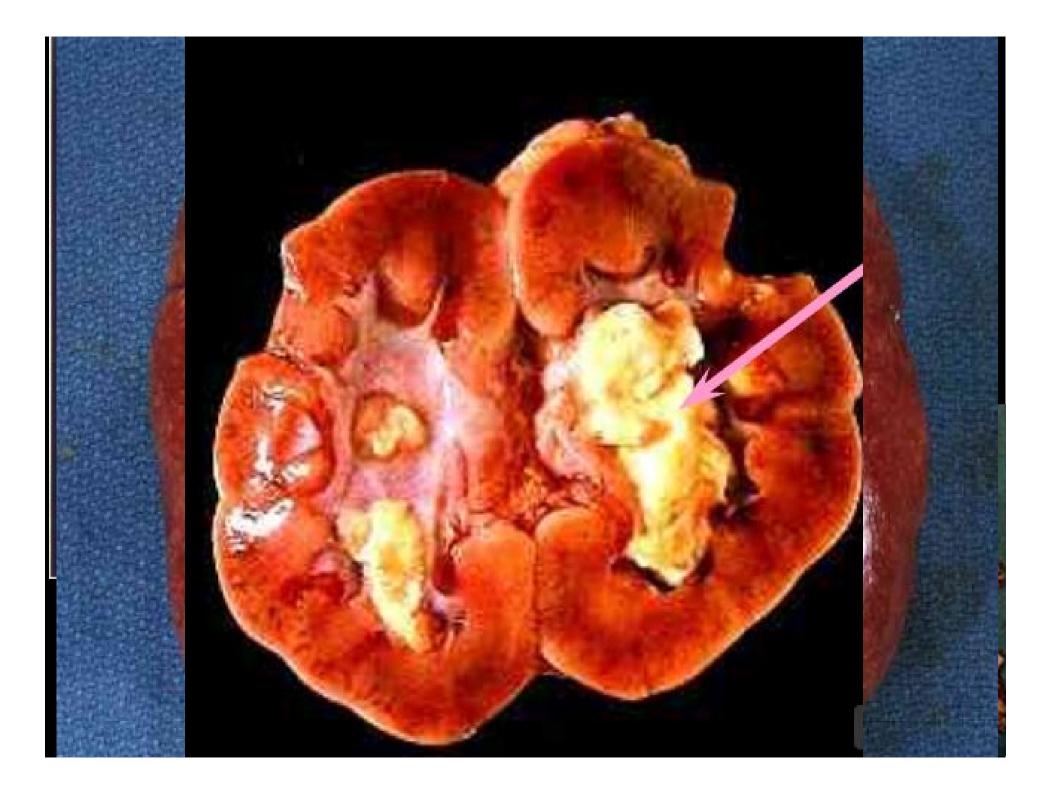
- urinary tract obstruction (stones, tumours or congenital abnormalities)
- -vesicoureteric reflux (VUR) 膀胱输尿管逆流 and intrarenal reflux 肾内反流
- instrumentation of the urinary tract
- Sexual intercourse
- diabetes mellitus
- -Immunosuppression (HIV, lymphoma and transplants)

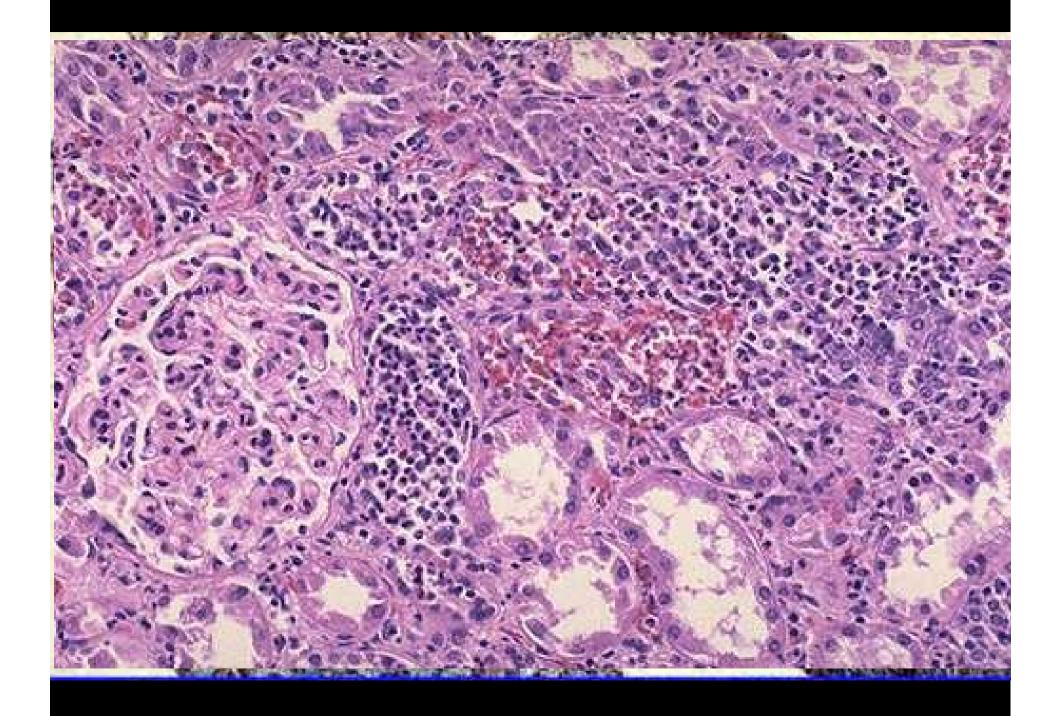


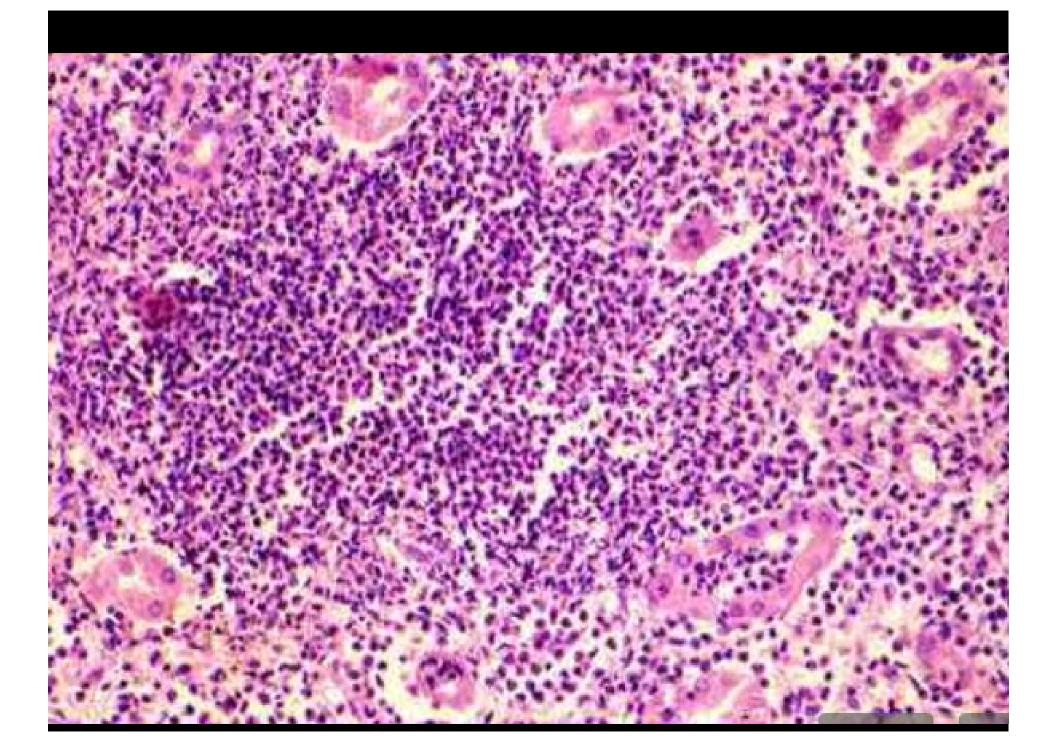
Acute pyelonephritis

- Gross appearance
 - infection spreads into the renal pelvis and papillae and causes abscess formation throughout the cortex and medulla

- —polymorphic infiltration of the tubules
- interstitial edema
- focal inflammation







Acute pyelonephritis

complications:

- renal papillary necrosis
- perinephric abscesses 肾周脓肿
- pyonephrosis 肾盂积脓
- chronic pyelonephritis
- fibrosis and scarring

clinical course:

 malaise, fever, loin pain, tenderness and rigors with or without symptoms of lower urinary tract infections

Chronic pyelonephritis

- Type:
 - -chronic obstructive:

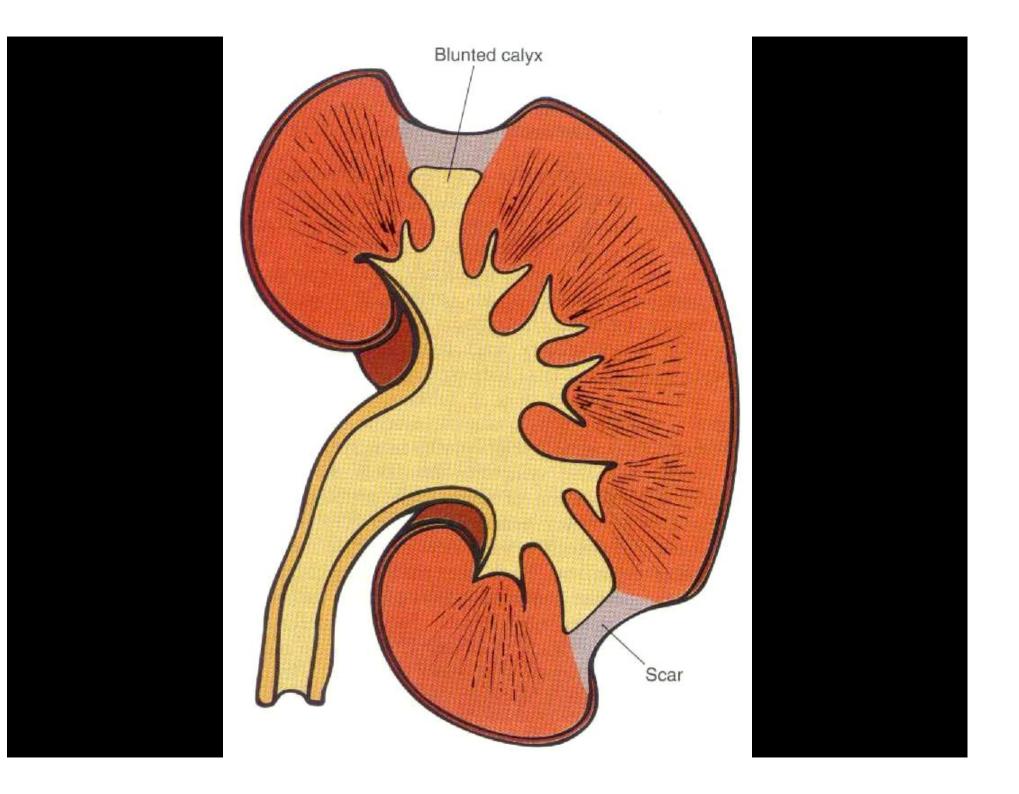
-reflux nephropathy: 返流性肾病

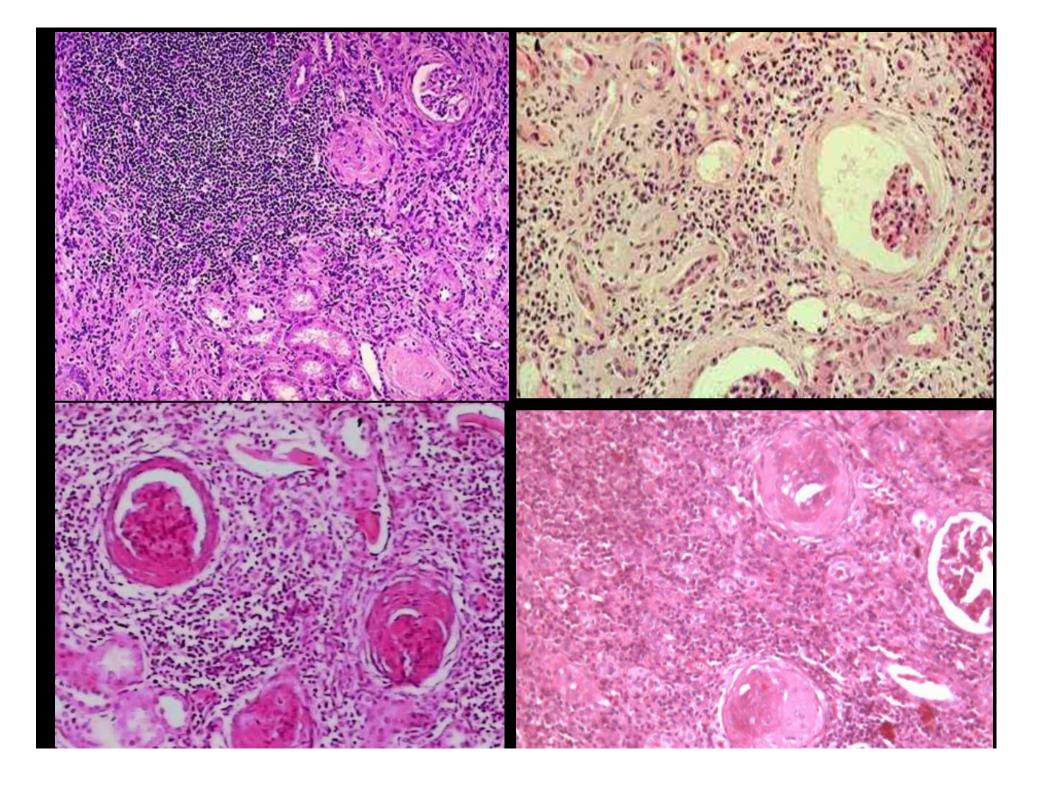
reflux results from the abnormal angle at which the ureter enters the bladder wall

Chronic pyelonephritis

- Gross appearance
 - -deep irregular scars on cortical surface

- -chronic inflammation of tubules, interstitium, renal calyces and pelvis
- interstitial fibrosis and dilated tubules containing eosinophilic casts





Tumours of the Urinary System

Renal cell carcinoma 肾细胞癌

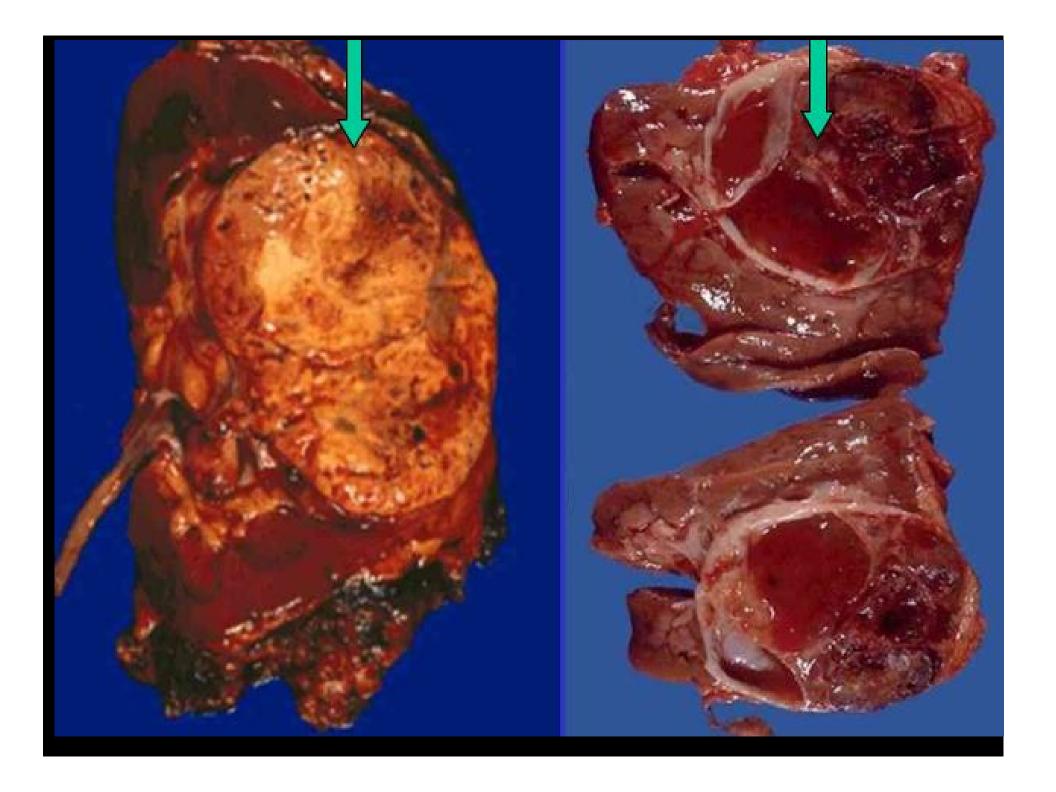
nephroblastoma 肾母细胞瘤

Transitional Cell Carcinoma of the Bladder 膀胱移行细胞癌

Renal cell carcinoma 肾细胞癌

- Clinical course
 - -pain, mass and hematuria

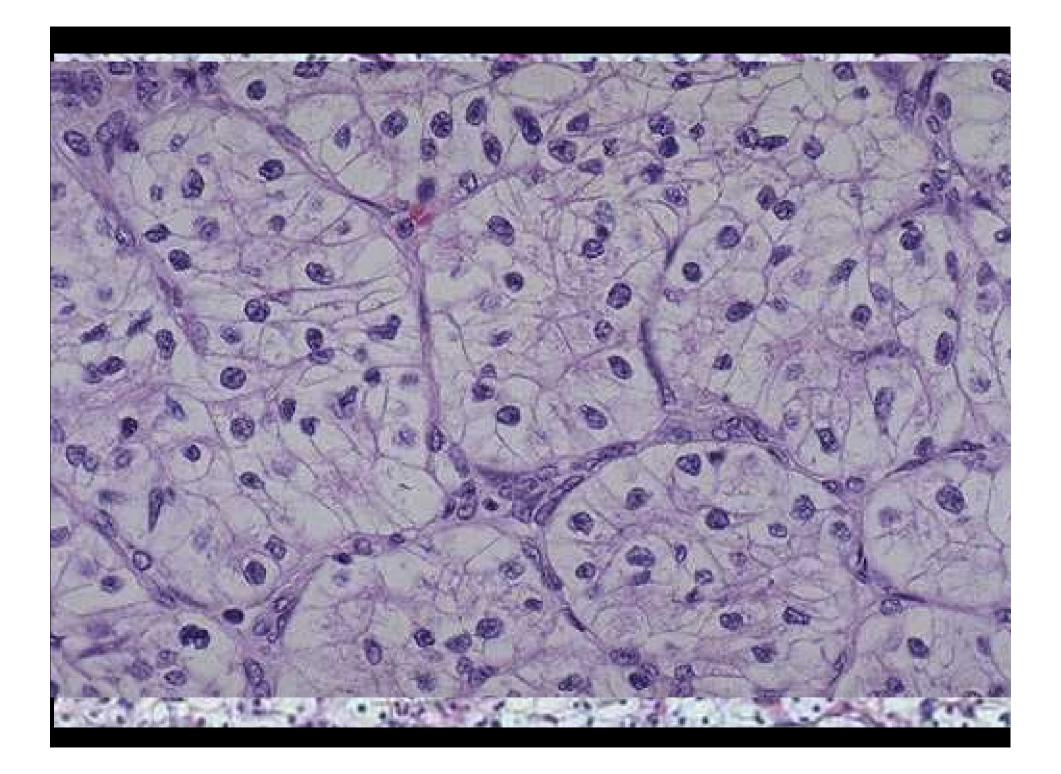
- •Gross appearance
 - -sites: at the upper pole of the kidney and in the renal cortex
 - yellow-brown, well-demarcated mass, diameter of 3-15cm
 - with hemorrhage, necrosis and cyst formation

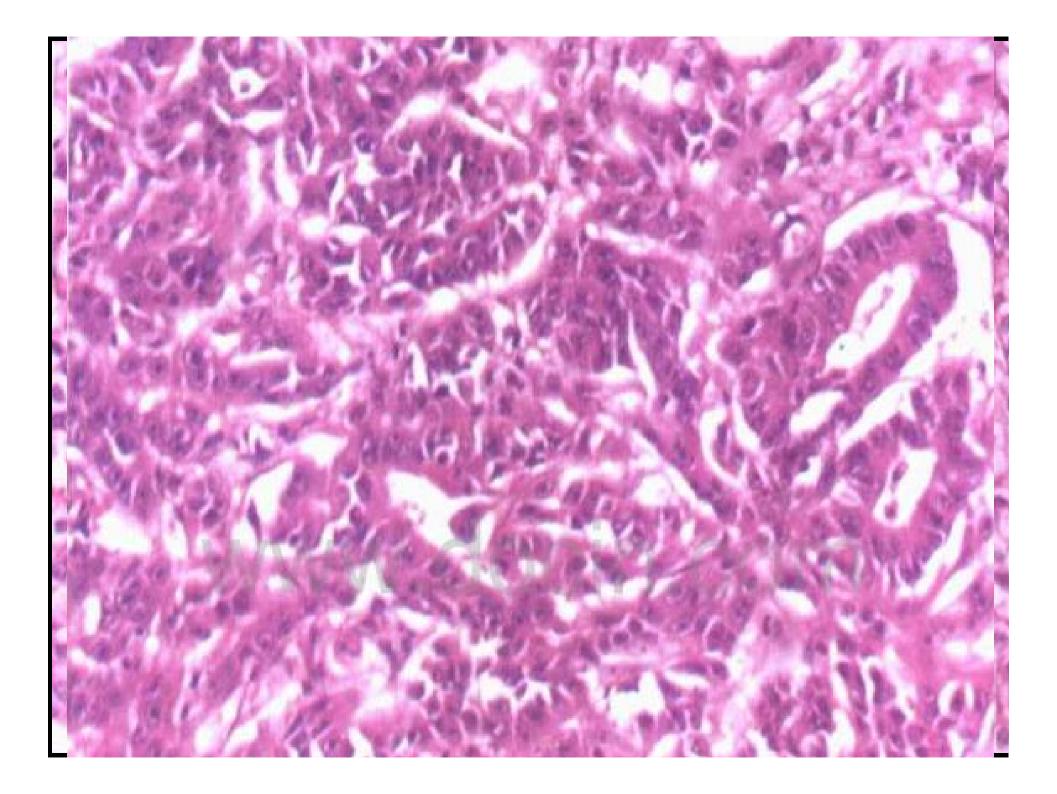


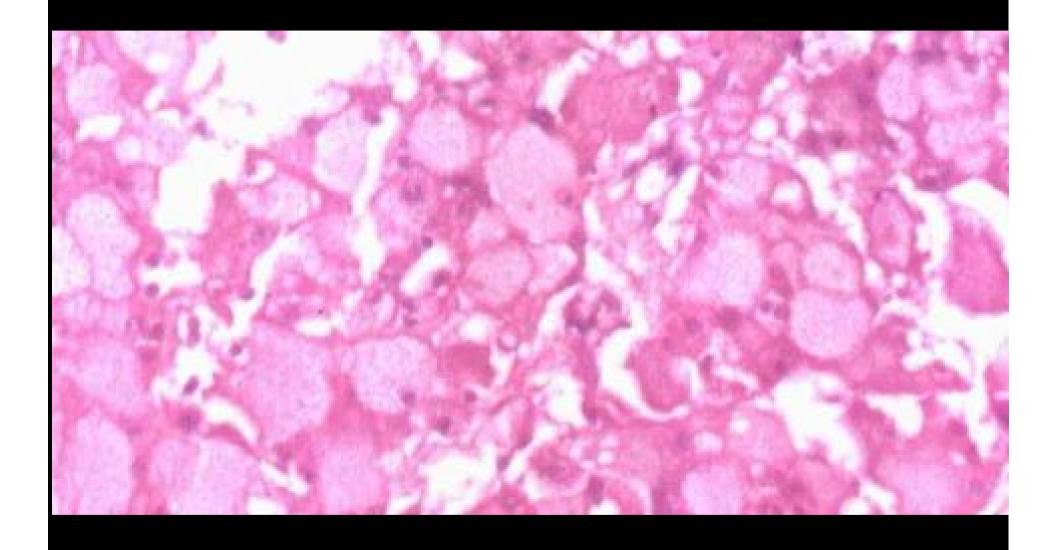
Renal cell carcinoma 肾细胞癌

•LM

- -clear cell carcinomas 透明细胞癌
- -papillary renal cell carcinomas 乳头状癌
- -chromophobe renal carcinomas 嫌色细胞癌







Renal cell carcinoma 肾细胞癌

- Spread
 - -direct invasion

pelvis肾盂, calyces肾盏 and ureter输尿管 adrenal glands, perinephric soft tissue

- -metastases via lymph tract lymphonodi of renal hilus 肾门 and aorta
- -matastases via blood lung,bone,opposite kidney and adrenal glands

Nephroblastoma, Wilms tumor 肾母细胞瘤

• a malignant tumour common among kids of 1-4 years old

• an embryonic tumour derived from the primitive metanephros

 common symptoms are abdominal mass and occadionally hematuria, abdominal pain and hypertension

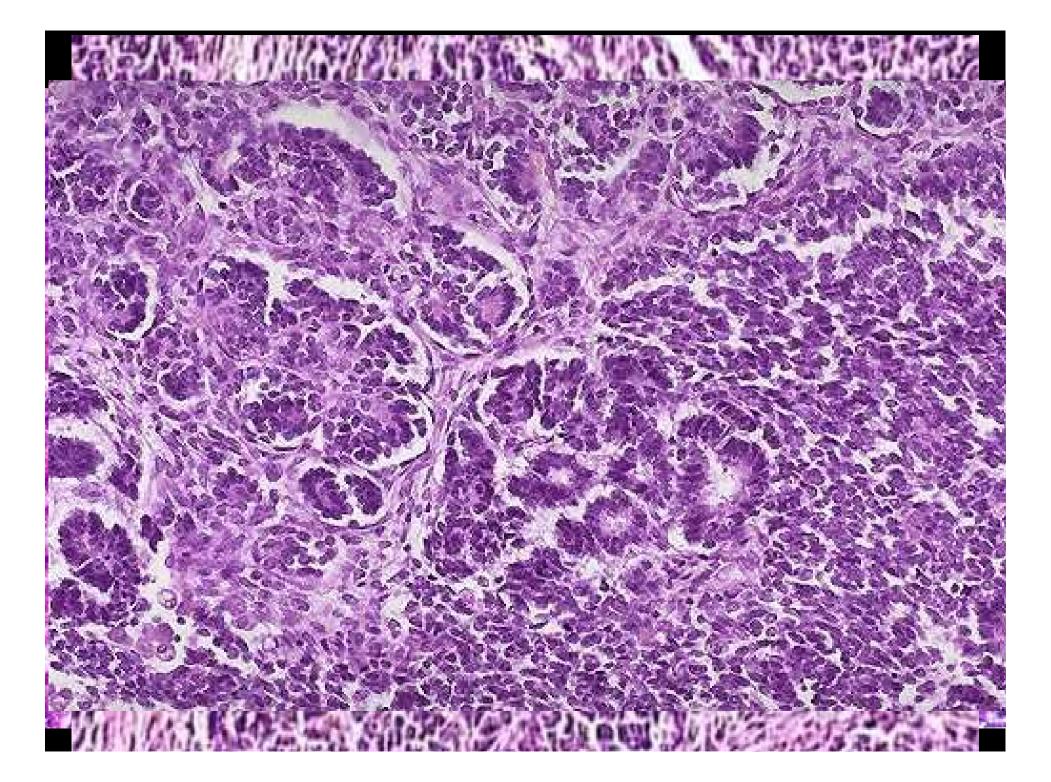
Nephroblastoma, Wilms tumor 肾母细胞瘤

- Gross appearance
 - —large solid masses of firm white tissue with areas of necrosis and hemorrhage

• LM

—spindle cells or primitive blastema cells with epithelial and mesenchymal 阿叶 tissues, cartilage, bone and muscle





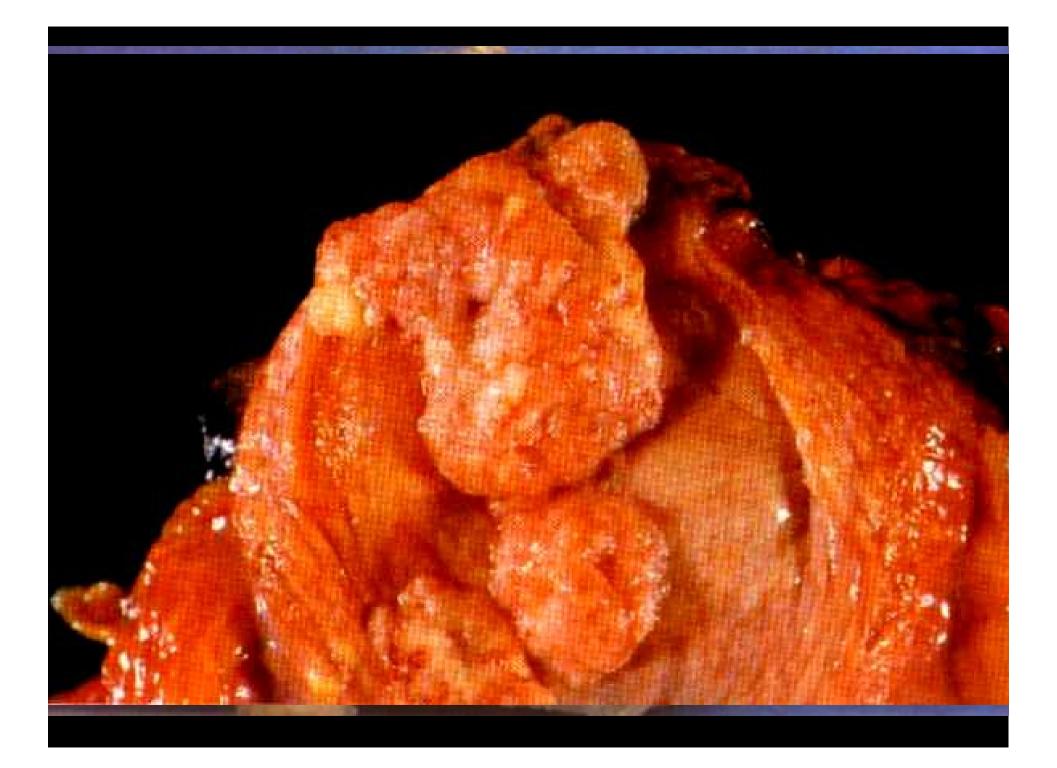
Urethelial carcinoma

tumour sites:

•bladder(90%);

(transitional cell carcinoma)

- •kidney calyces and pelvis (10%);
- •ureters (<1%)



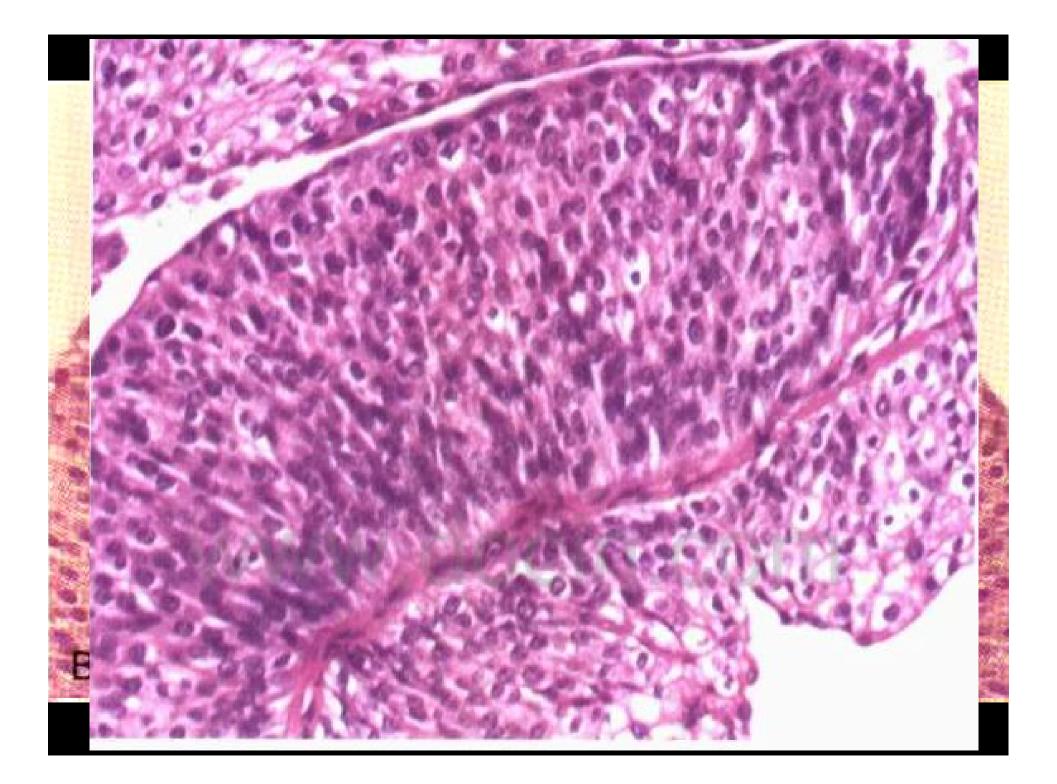
Grade I

•gross appearance

•similar to that of papilloma

Grade I

- cytologic and architectural atypia, but well differentiated and closely resembling normal transitional cells
- Mitoses are rare
- a significant increase in the number of layers of cells but only slight loss of polarity



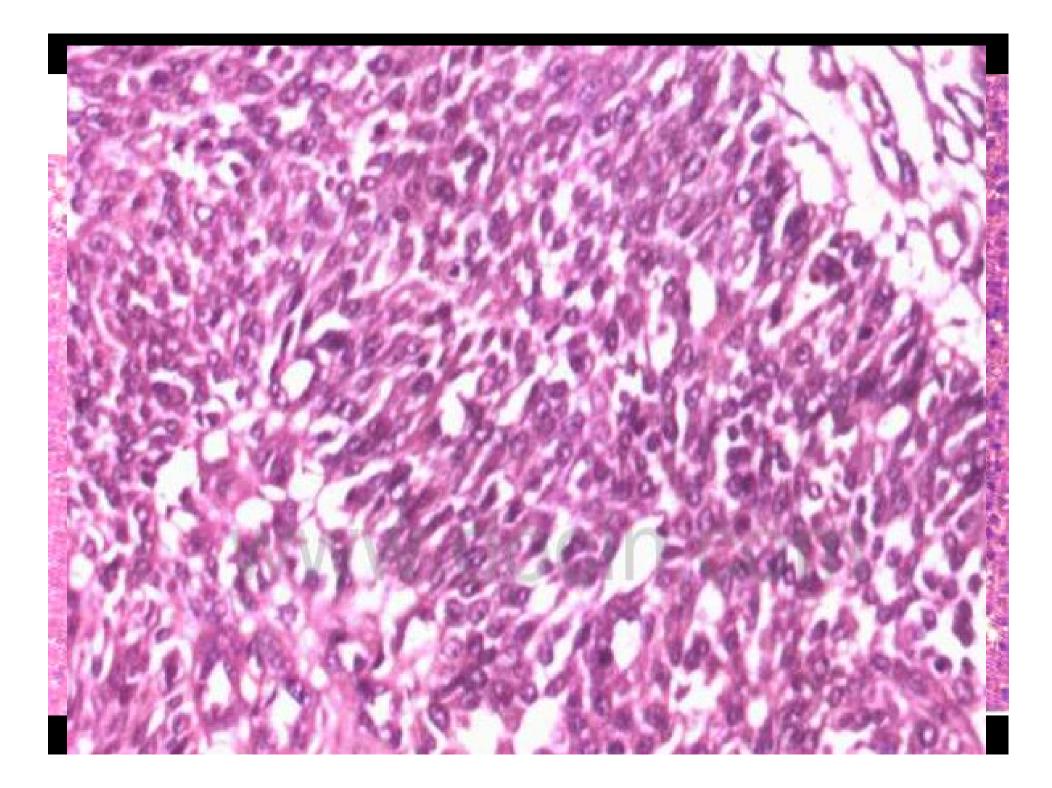
Grade II

• gross appearance

• papillary, but have contiguous flat regions

Grade II

- recognizable as of transitional origin
- layers of cells increased
- greater loss of polarity
- more variable in cell size, shape, and chromaticity

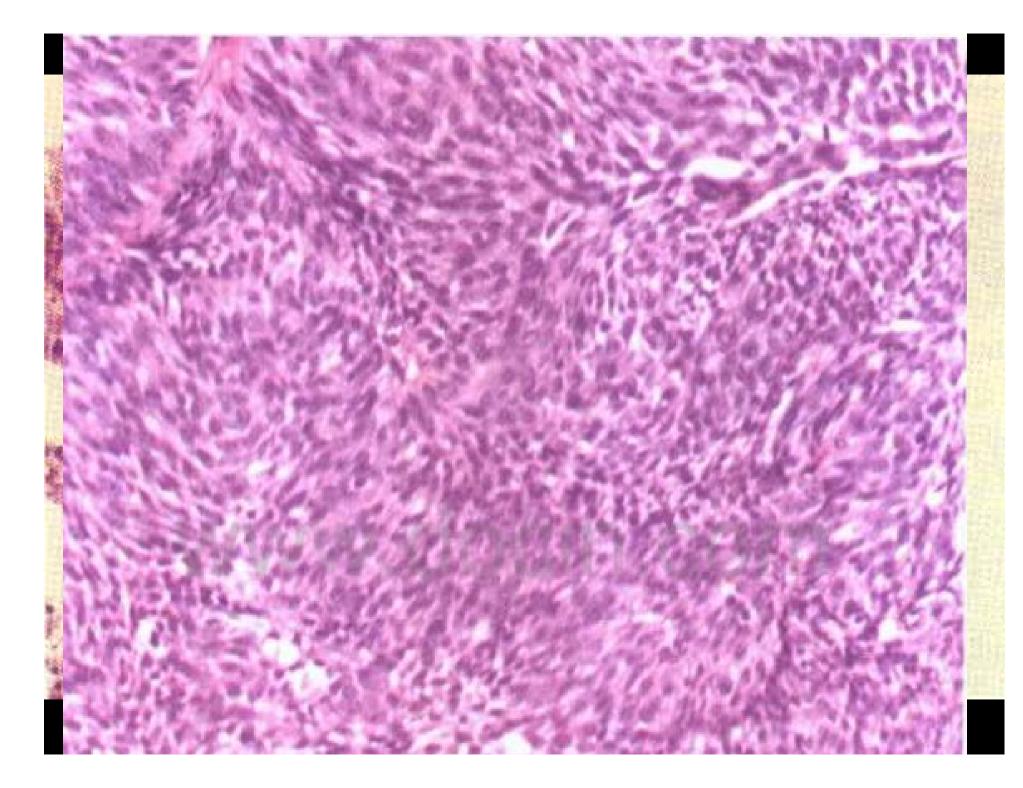


Grade III

- gross appearance
 - papillary, flat, or both
 - tend to be larger, to be more extensive, and to show a high preponderance for invasion of the muscularis.

Grade III

- tumor cells show anaplastic changes
- there is evident disarray of cells with loosening and framentation of the superficial layers of cells.



transitional cell carcinoma of Bladder

- produce painless hematuria
- Frequency, urgency, and dysuria 排尿困难 occasionally accompany the hematuria
- When the ureteral 输尿管 orifice is involved, pyelonephritis or hydronephrosis 肾盂积水 may follow.