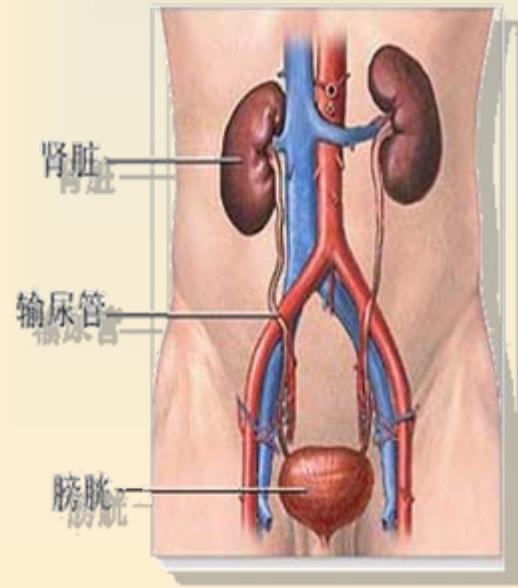




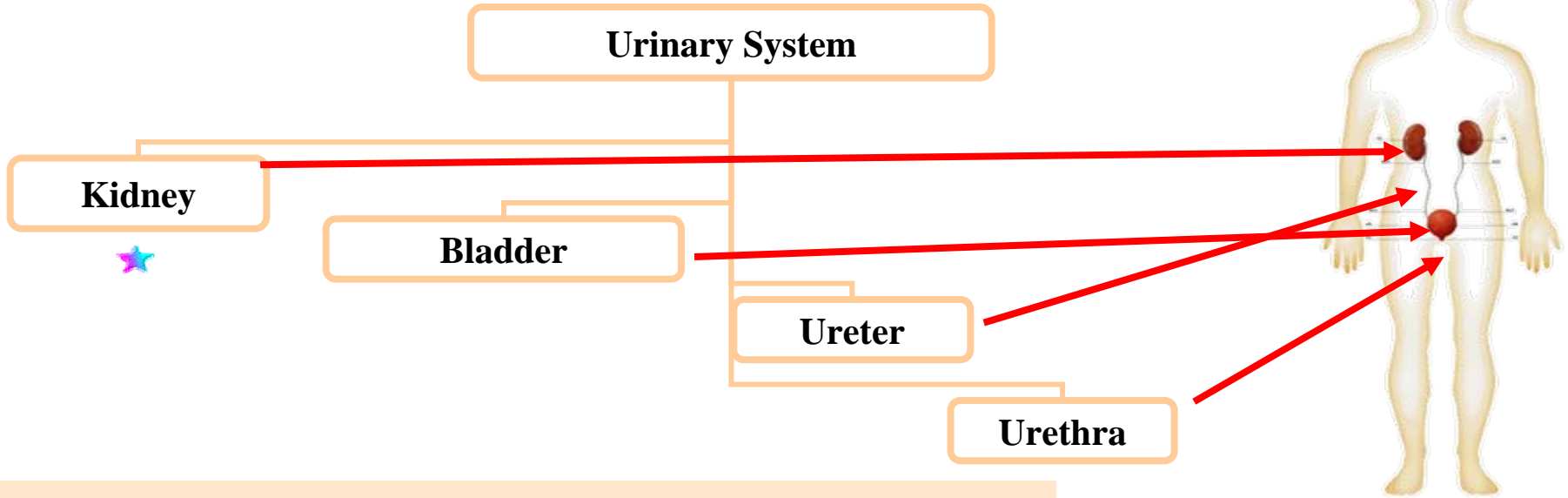
Diseases of the Urinary System



Wang Yishu
Department of Pathology
Basic Medical School

Introduction

Anatomy and Histology of Urinary System



Functions of kidney

Excretes the waste products of metabolism
Precisely regulates the body's concentration of water and salt
Maintains the appropriate acid-alkaline balance of plasma
Serves as an endocrine organ:
erythropoietin
renin
prostaglandin



World kidney day!




Take care your kidney
----Control Diabetes

ISN IFKF

关爱健康, 呵护肾脏
—— 及早诊断, 积极预防

“世界肾脏日”

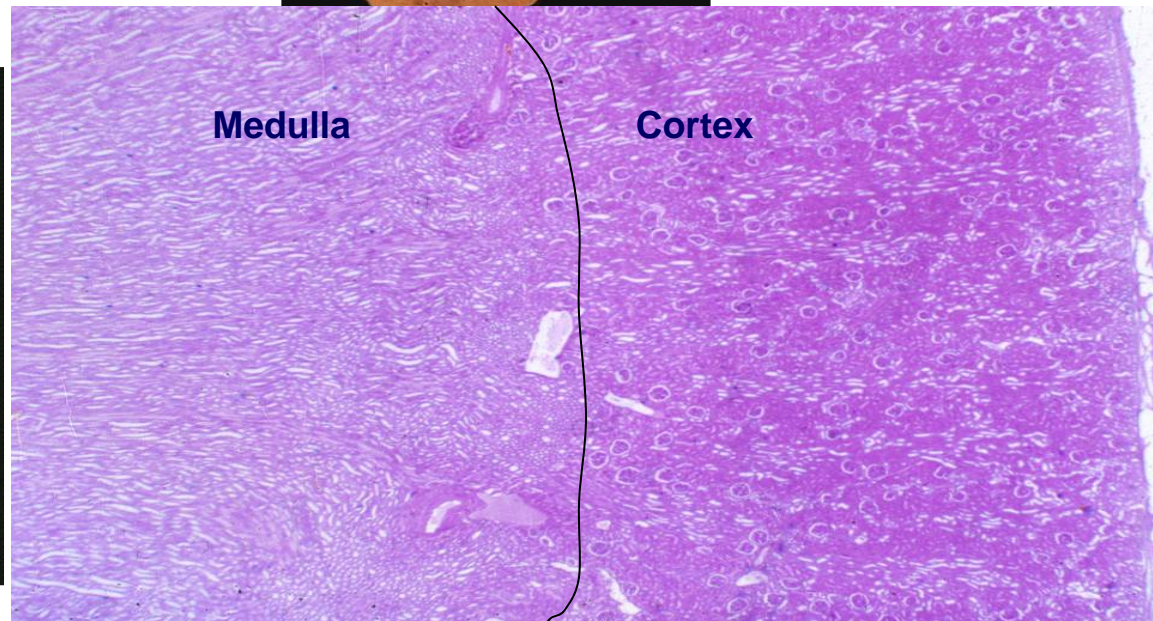
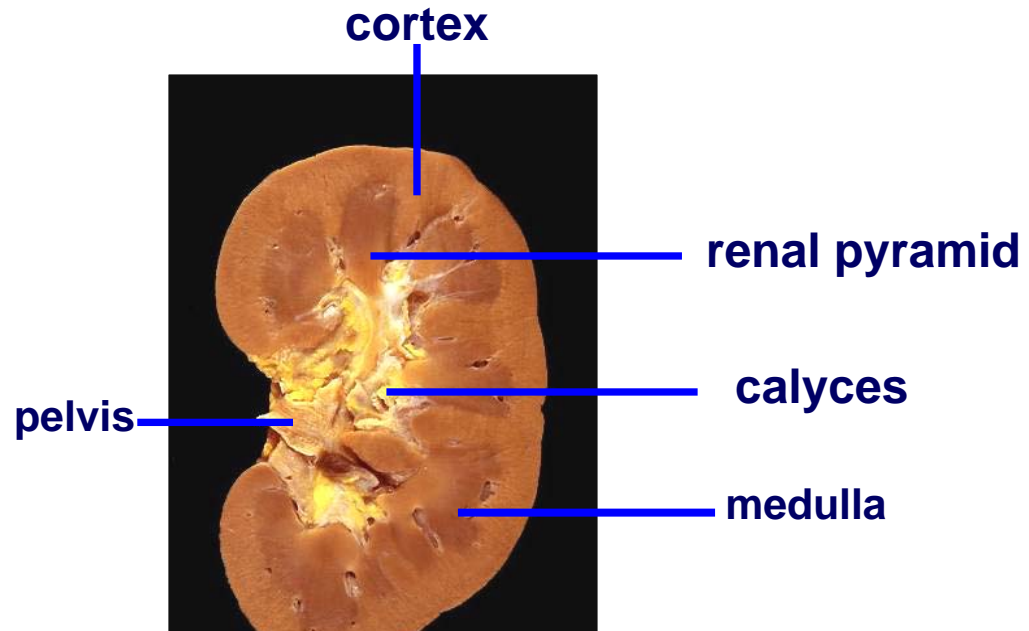
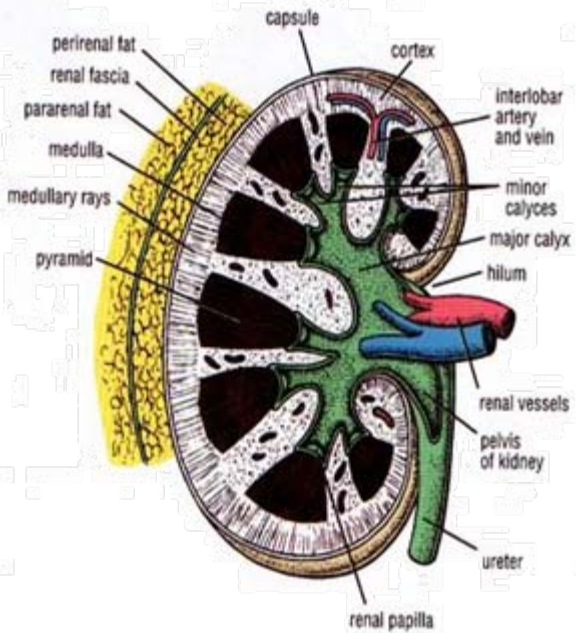
主办: 中华医学会肾脏病学分会 时间: 2006年3月9日



21世纪以来, 慢性肾脏病已成为危害全世界人民健康的公敌之一
国际肾脏病学会 (ISN) 和国际肾脏基金会 (IFKF) 联合提议设立“世界肾脏日”,
激励全世界各国人民共同为遏制慢性肾脏病做出努力。中华医学会肾脏病学分会 (CSN)
积极发挥学术引导作用, 与全国各相关单位通力协作, 推动中国肾脏病防治工作进展
及早诊断, 积极预防, 让我们从现在开始行动起来……

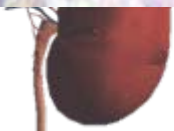
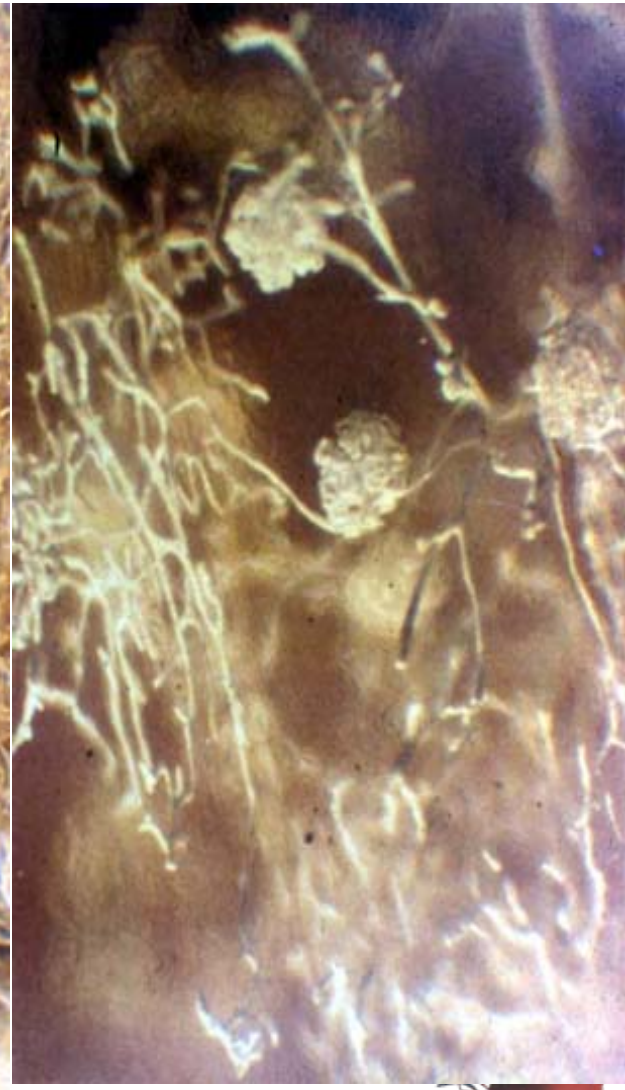
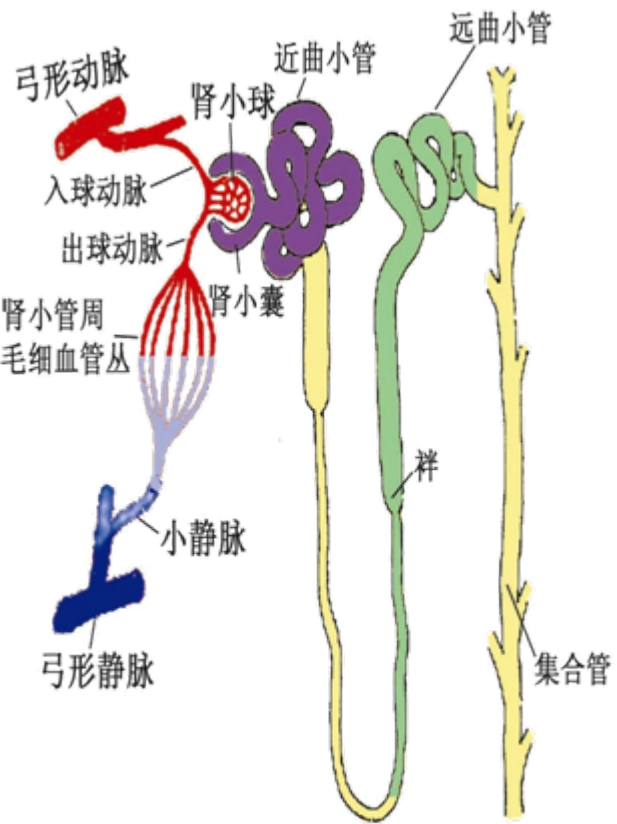


Still remember ?



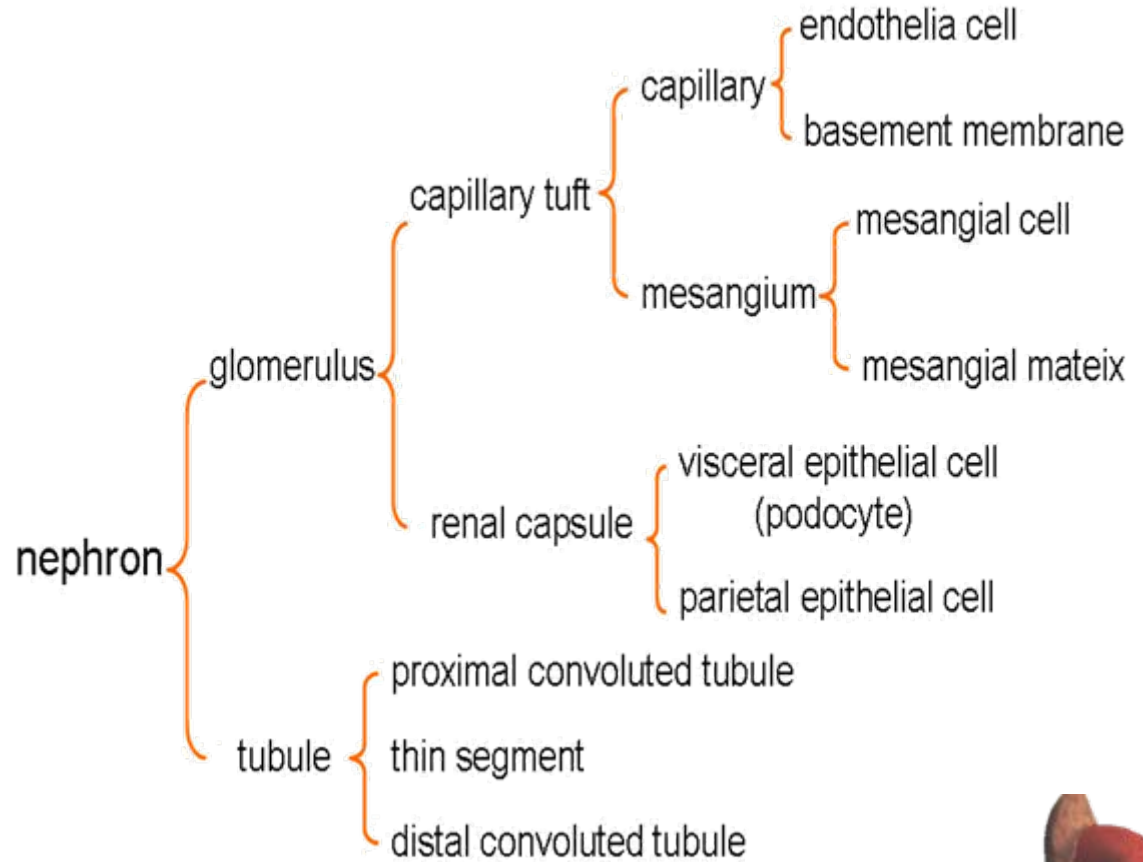
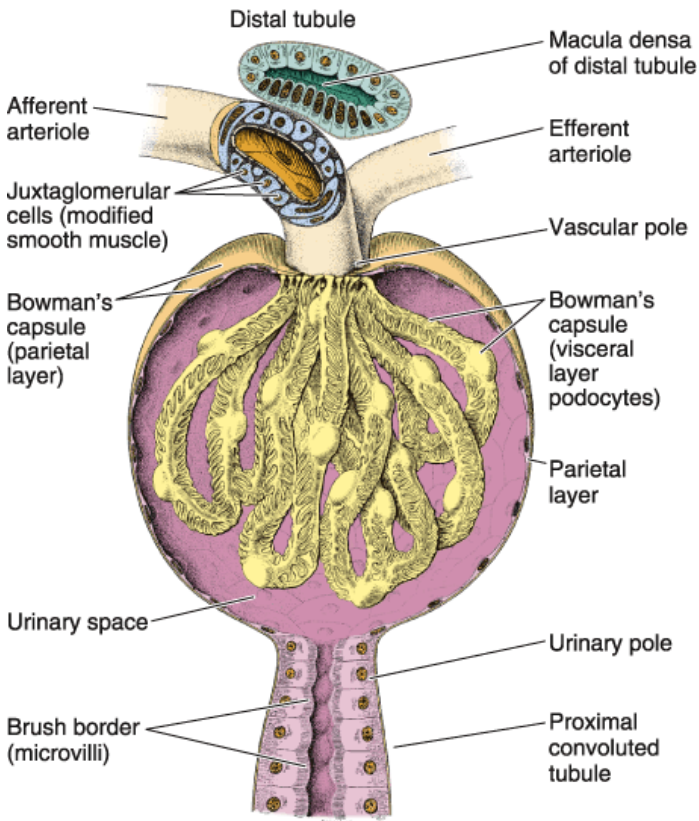


Still remember ?



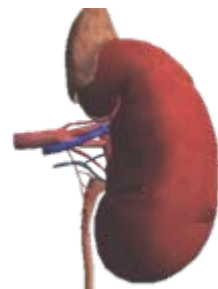
Still remember ?

Each kidney is composed of approximately 1-4 million nephrons.



Source: Junqueira LC, Carneiro J: *Basic Histology: Text and Atlas*, 11th Edition: <http://www.accessmedicine.com>

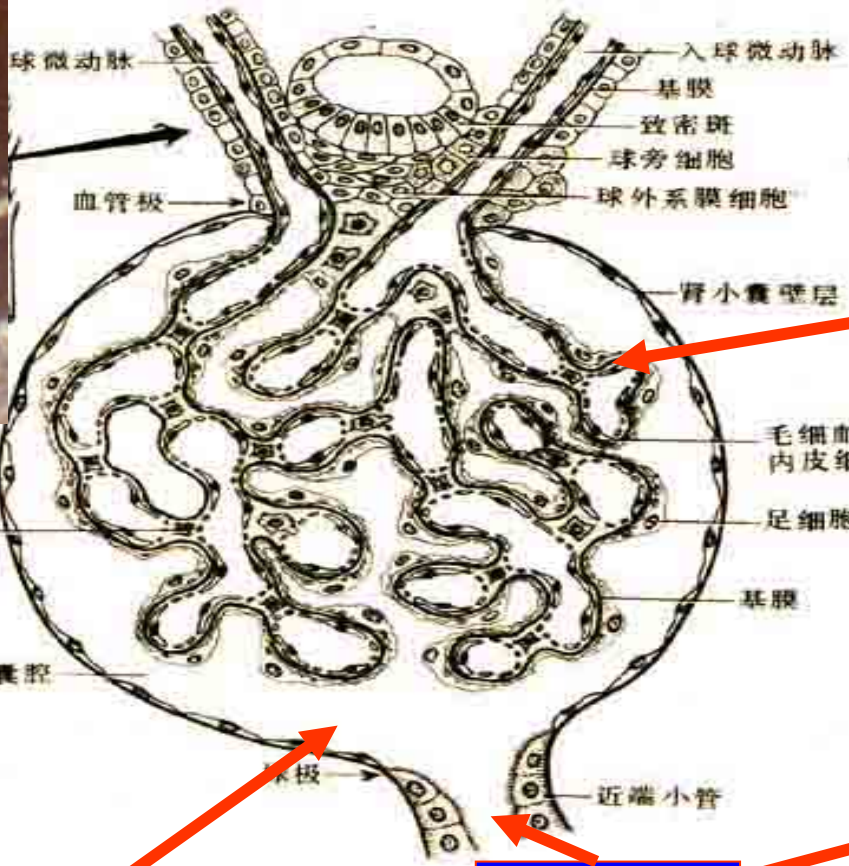
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nephron : glomerulus and renal tubule



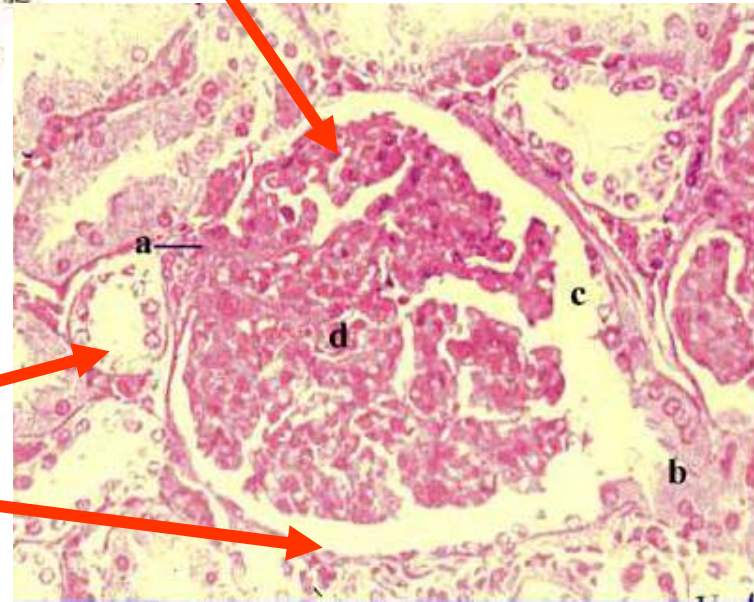
Still remember ?



glomus

Bowman's capsule

renal tubule

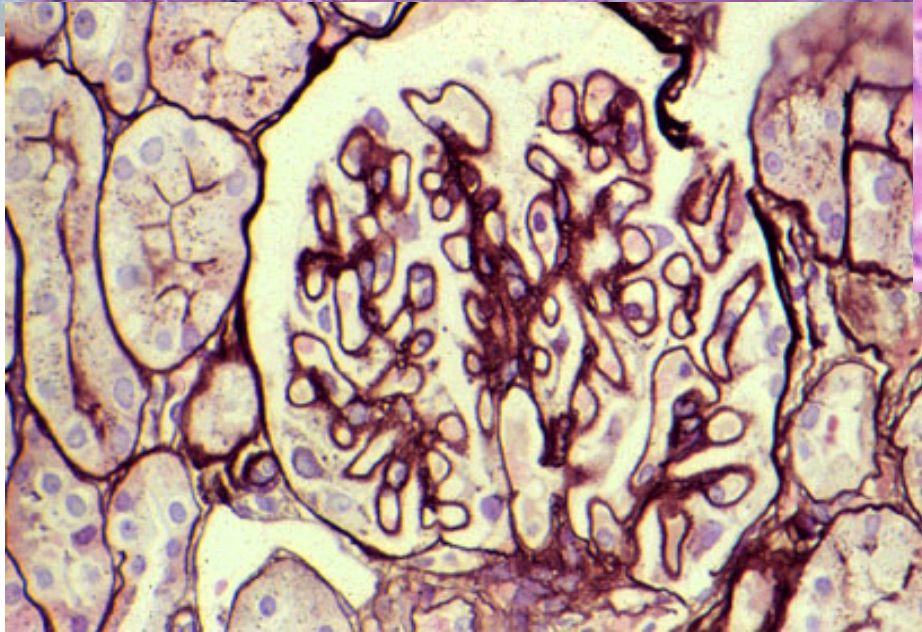
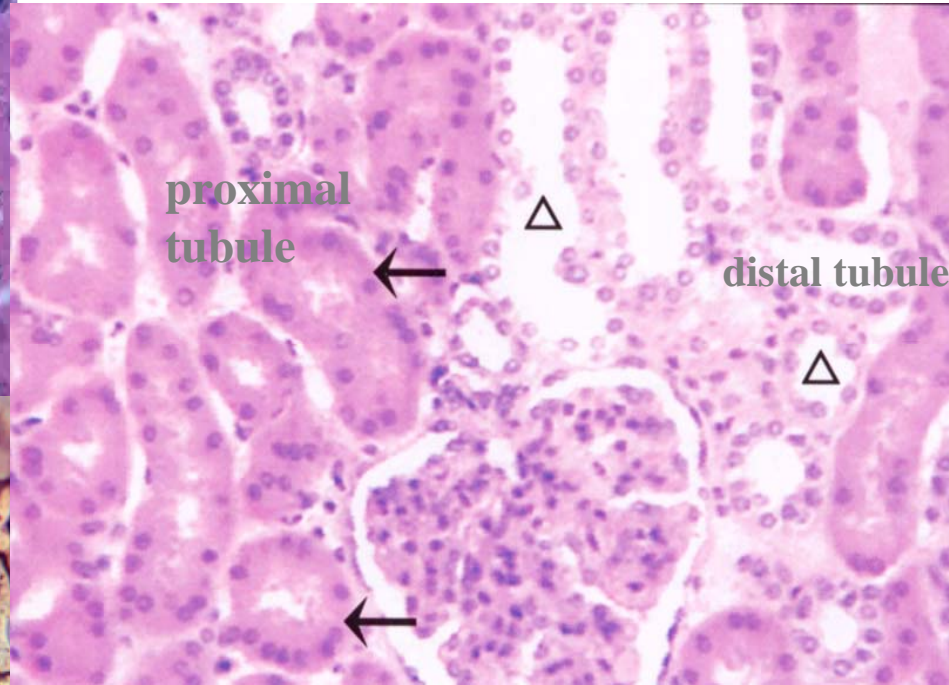
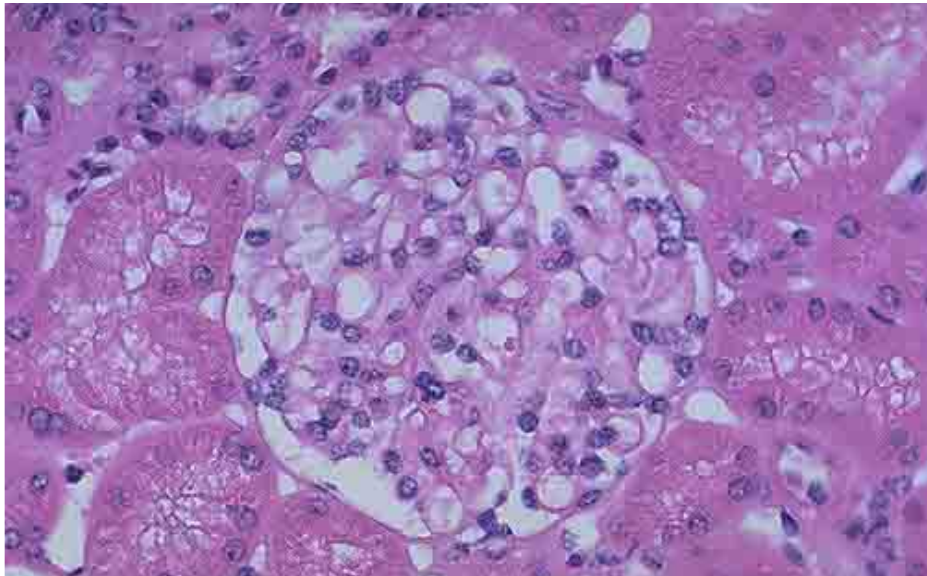


nephron : glomerulus and renal tubule





Still remember ?

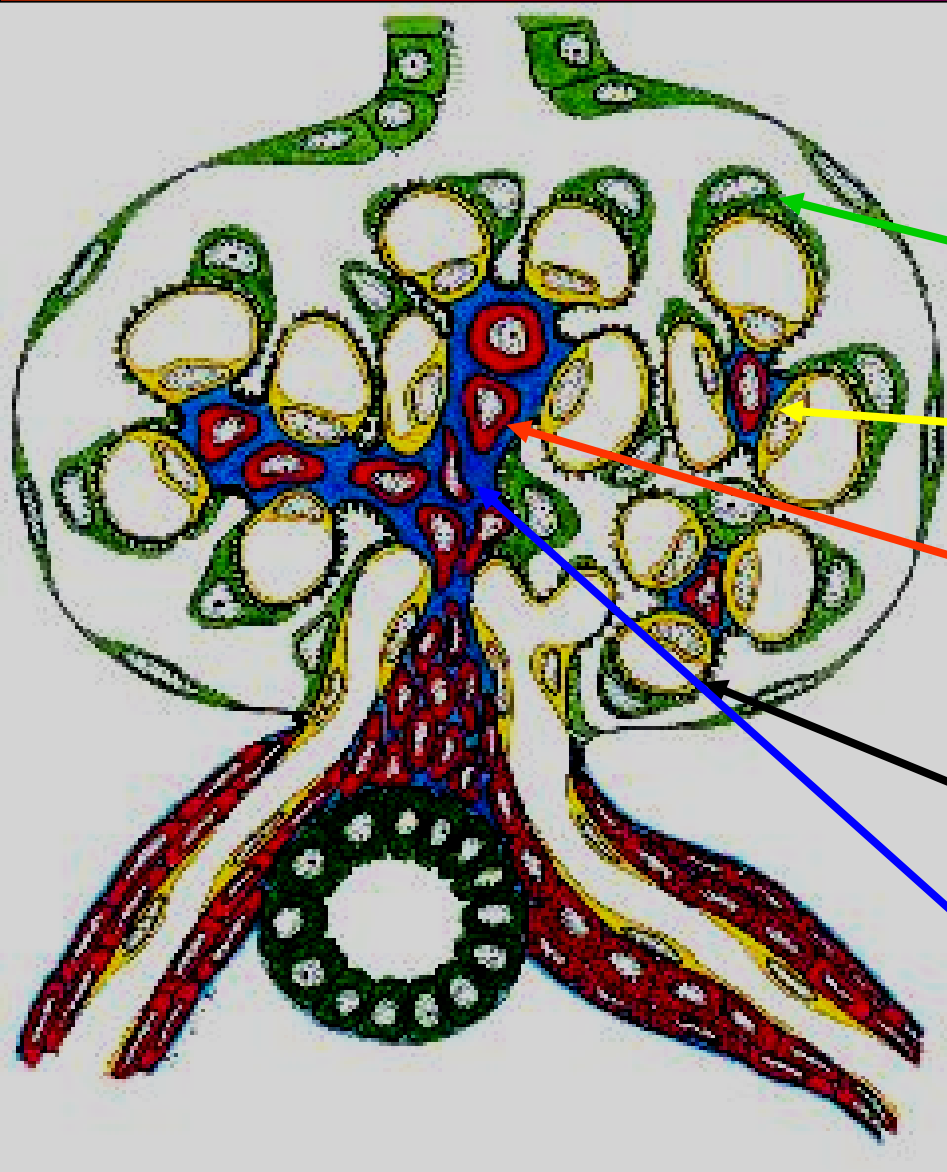


**nephron : glomerulus
and renal tubule**





Still remember ?



Cell types of glomerulus

epithelial cells

endothelial cells

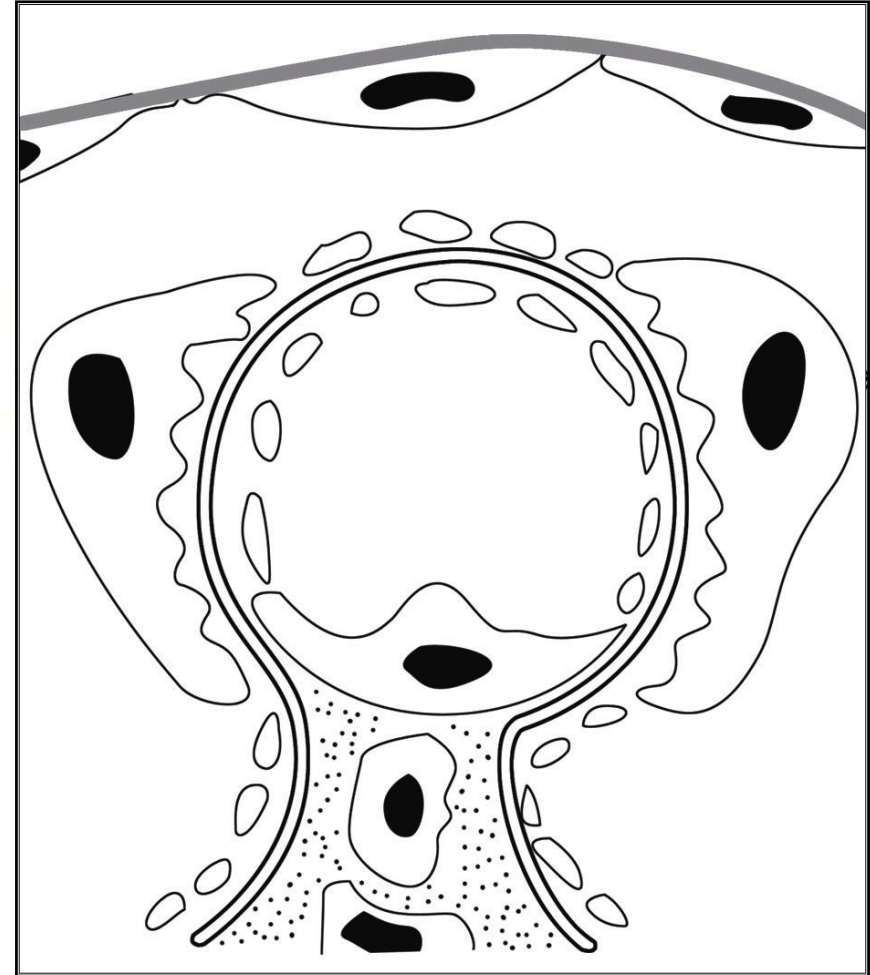
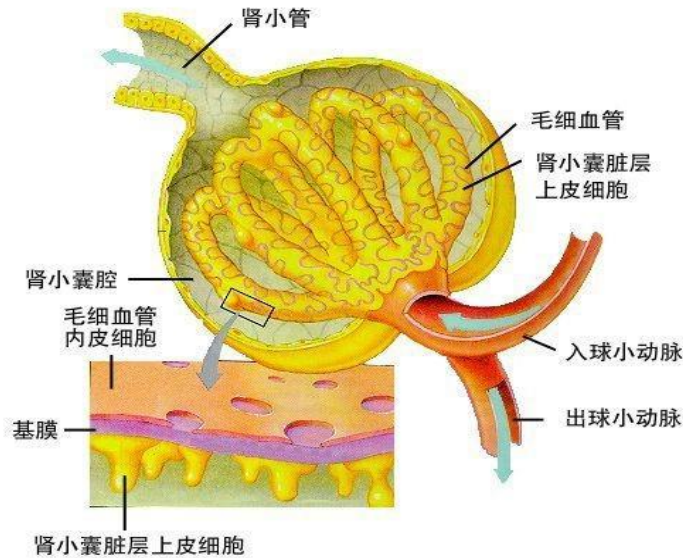
mesangial cells

**Glomerular basement
membrane (GBM)**

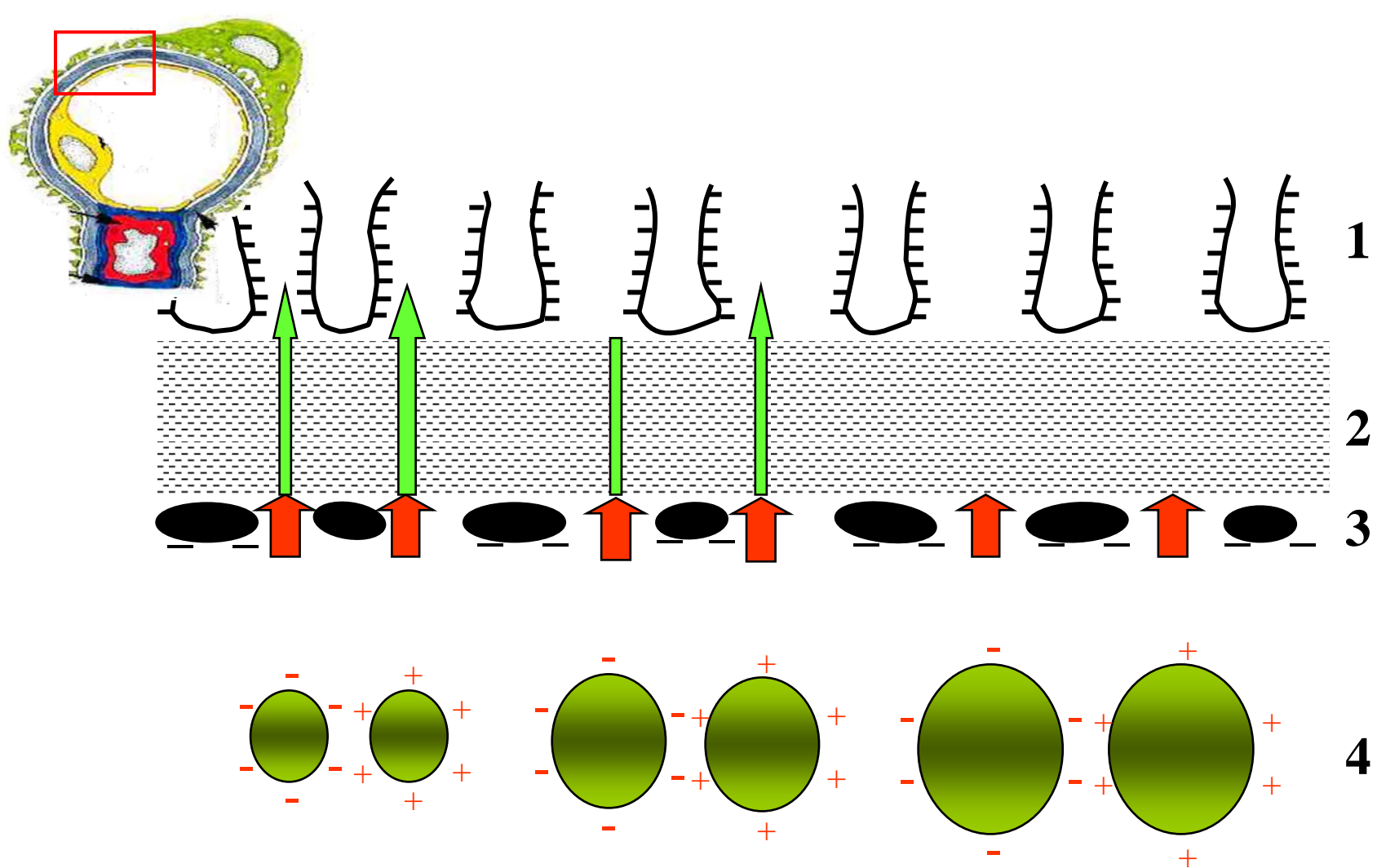
Mesangial Matrix



Still remember ?

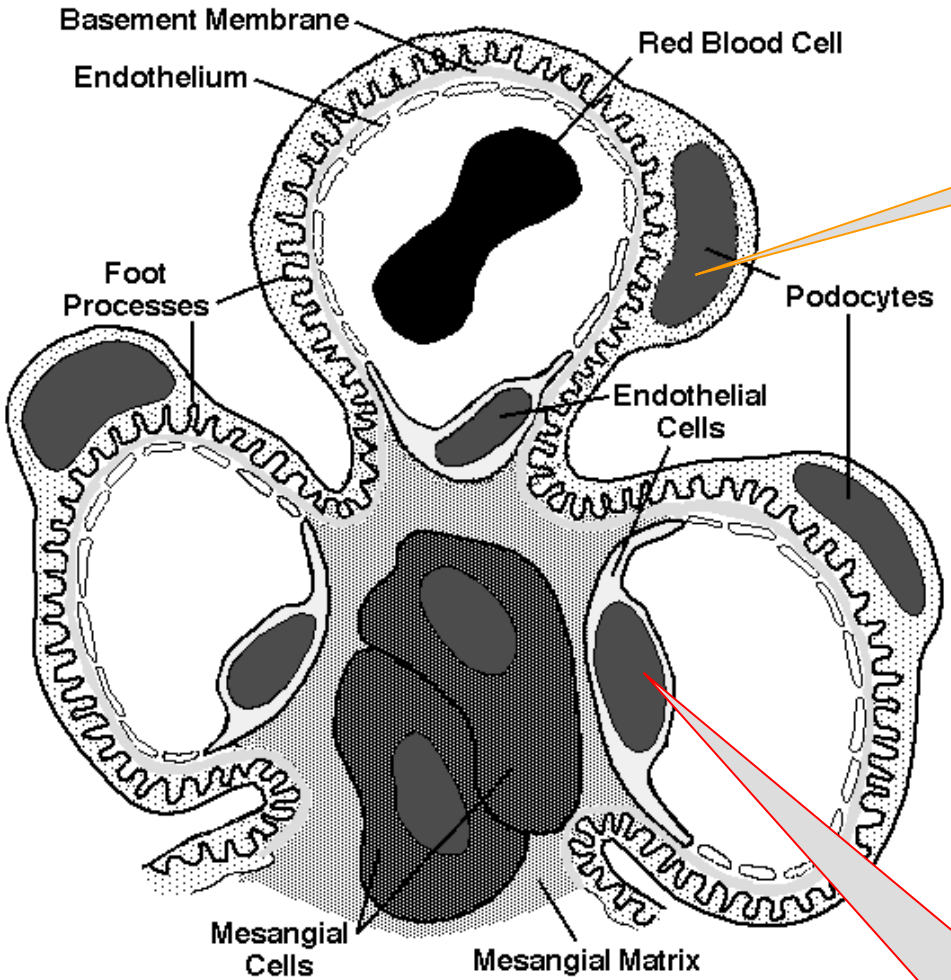


- **Filter membrane :**
 - ① **Endothelial cells (EC)**
 - ② **Glomerular basement membrane (GBM)**
 - ③ **Visceral epithelial cell (podocyte)**

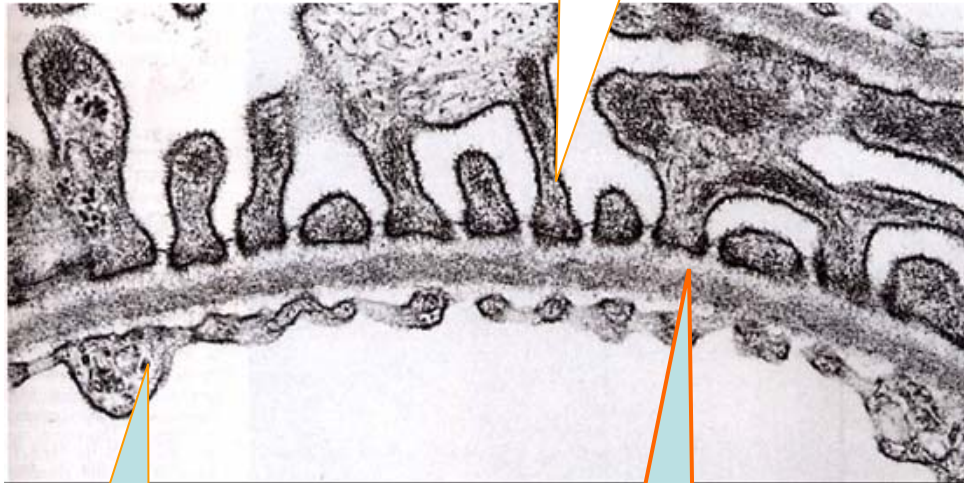


1. Endothelial cells 2. Glomerular basement membrane
3. Visceral epithelial cell (podocyte) 4. Filtrate material

① structure of filtering membrane ② charge of filtering membrane ③ Molecular size of filtrate material



**Podocyte
foot process**

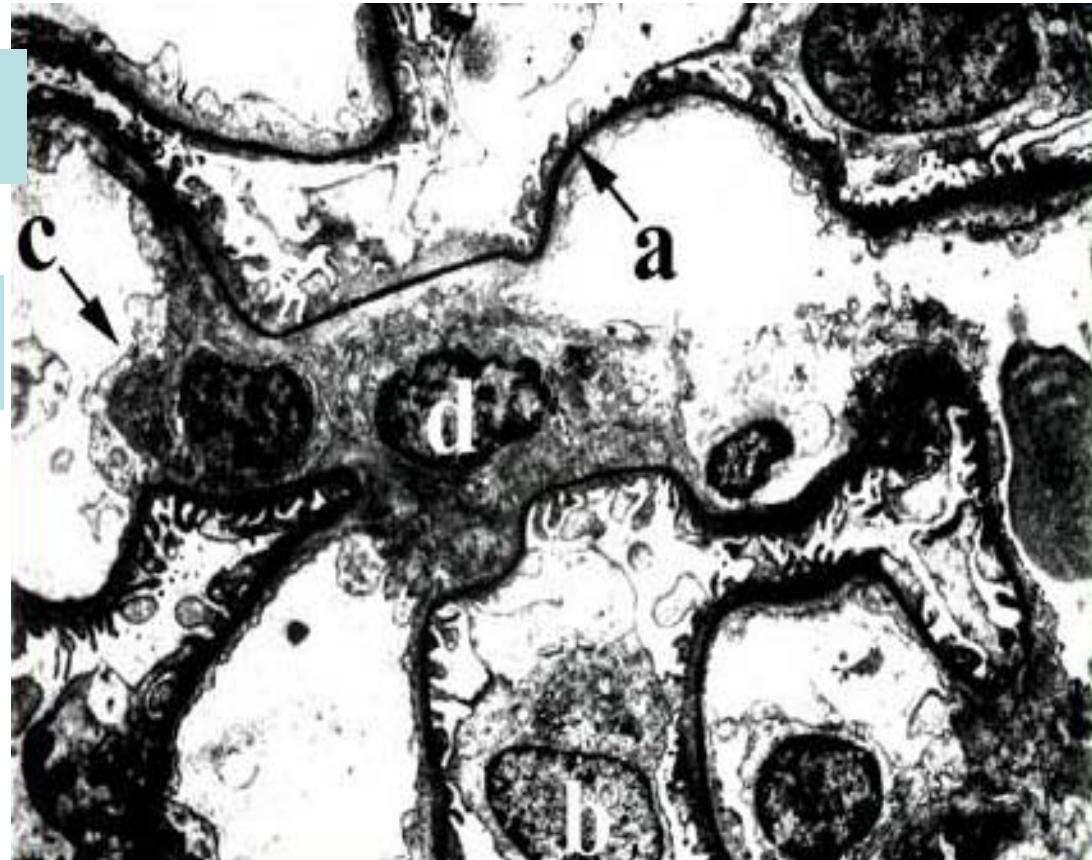
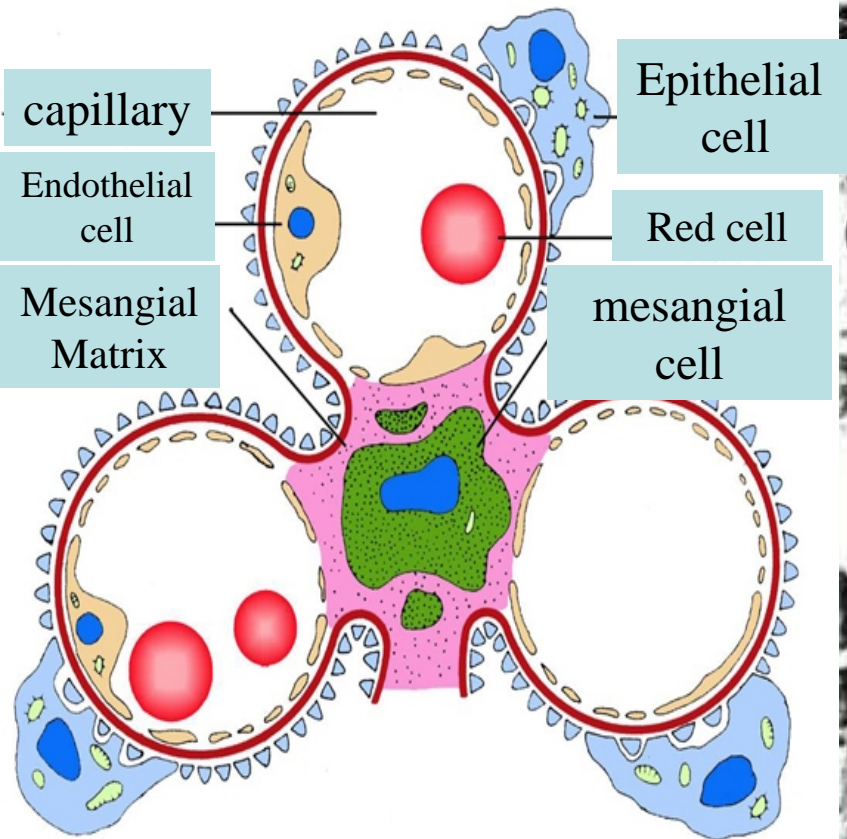


Endothelial cell

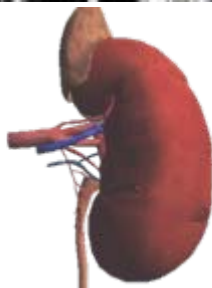
**Basement
Membrane**



Still remember ?



The relationship among epithelial cell, endothelial cell and mesangial cell
a. GBM b. visceral epithelial cell c. endothelial cell d. mesangial cell





Kidney Diseases

According pathogenesis:

- **Inflammation:** Glomerulonephritis, Pyelonephritis, Cystitis, Urethritis, Tuberculosis of Kidney, et al.
- **Tumor:** Renal cell carcinoma, transitional cell carcinoma, et al.
- **Metabolic Diseases:** Nephrosclerosis of Diabetes, et al.
- **Vascular Diseases:** Nephrosclerosis of Hypertension, et al.
- **Urinary tract obstruction:** urinary calculi, Nephredema, et al.
- **Toxic Diseases:** Acute tubularmerosis cause by Hydrargyrism, Sulfonamidas intoxication, et al.
- **Congenital Malformation:** Polycystic kidney, horseshoe kidney, et al.
- **Hereditary Diseases:** Alport syndrome.

According location:

- **Glomerular Diseases**
- **Renal tubular Diseases**
- **Interstitium Diseases**
- **Involve vascular Diseases**





- **Glomerulonephritis, GN** ★

- Etiology and pathogenesis
- Basic pathological changes
- Clinical appearance
- Pathological types of GN

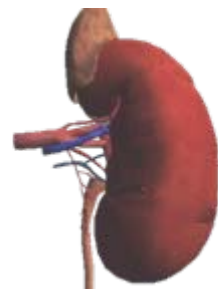
What we will learn?

- **Tubulointerstitial nephritis**

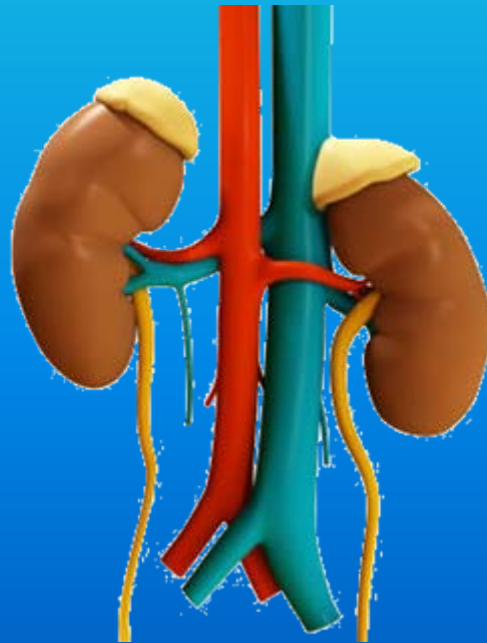
- nephropyelitis

- **Tumors of kidney and bladder**

- renal cell carcinoma
- nephroblastoma
- transitional cell carcinoma



Glomerulonephritis, GN





Introduction

肾小球肾炎(glomerulonephritis, GN), 简称肾炎, 是一组以肾小球损害为主的变态反应性炎症。

A group of allergy diseases mainly targeting glomerulus.

Types of glomerulonephritis:

原发性肾小球肾炎(primary glomerulonephritis)是原发于肾脏的独立性疾病, 肾为唯一或主要受累的脏器。肾小球病

(glomerulopathy) **Immune mechanisms**

继发性肾小球肾炎(secondary glomerular disease)的肾病变是由免疫性、血管性或代谢性全身疾病引起的肾小球病变, 如红斑狼疮性肾炎、过敏性紫癜性肾炎、血管病变(高血压)、代谢疾病(糖尿病)

遗传性疾病(hereditary nephritis): 一组以肾小球改变为主的遗传性家族性肾脏疾病。



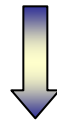


Etiology and pathogenesis

Pathogenetic factors (Antigen)



immune complex is located in the
glomerular---two patterns

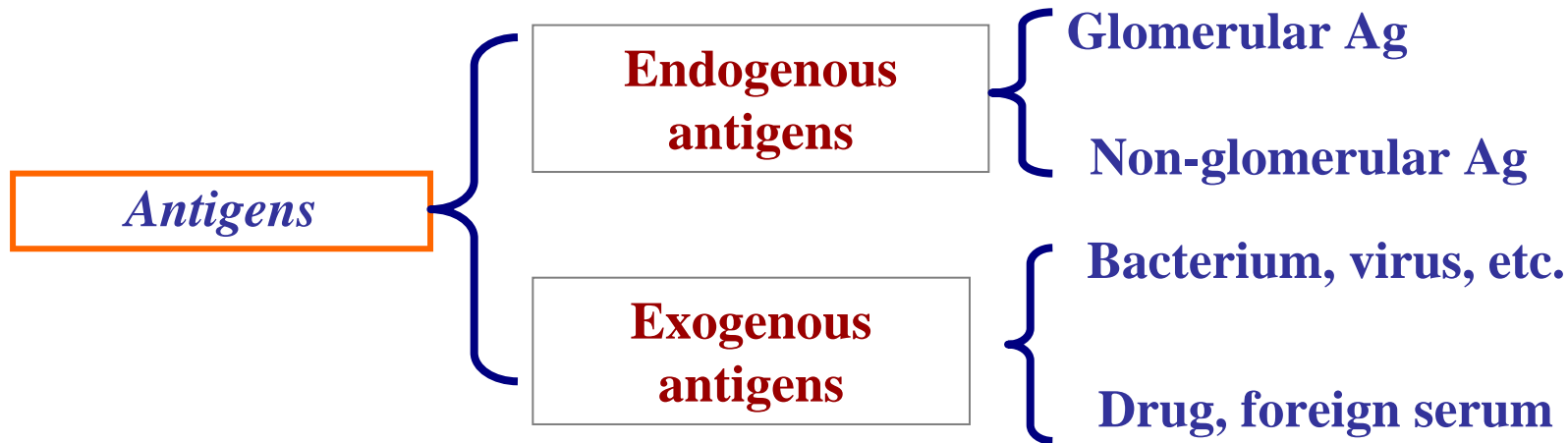


Glomerular injury--- mediators of
glomerular injury





Etiology and pathogenesis



Antibody: IgG、IgA、IgM

Antigen+Antibody=immune complex

Circulating immune complex nephritis

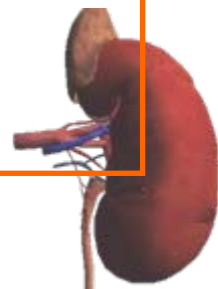
In situ immune complex deposition

Antibodies to glomerular cells

Cell-mediated immunity in glomerulonephritis

Activation of alternative complement pathway

.....





Etiology and pathogenesis

Circulating immune complex nephritis



Non-glomerular Ag

**Circulating
immune complex deposition**

**Cell of glomerulus
proliferation**

Neutrophil infiltration

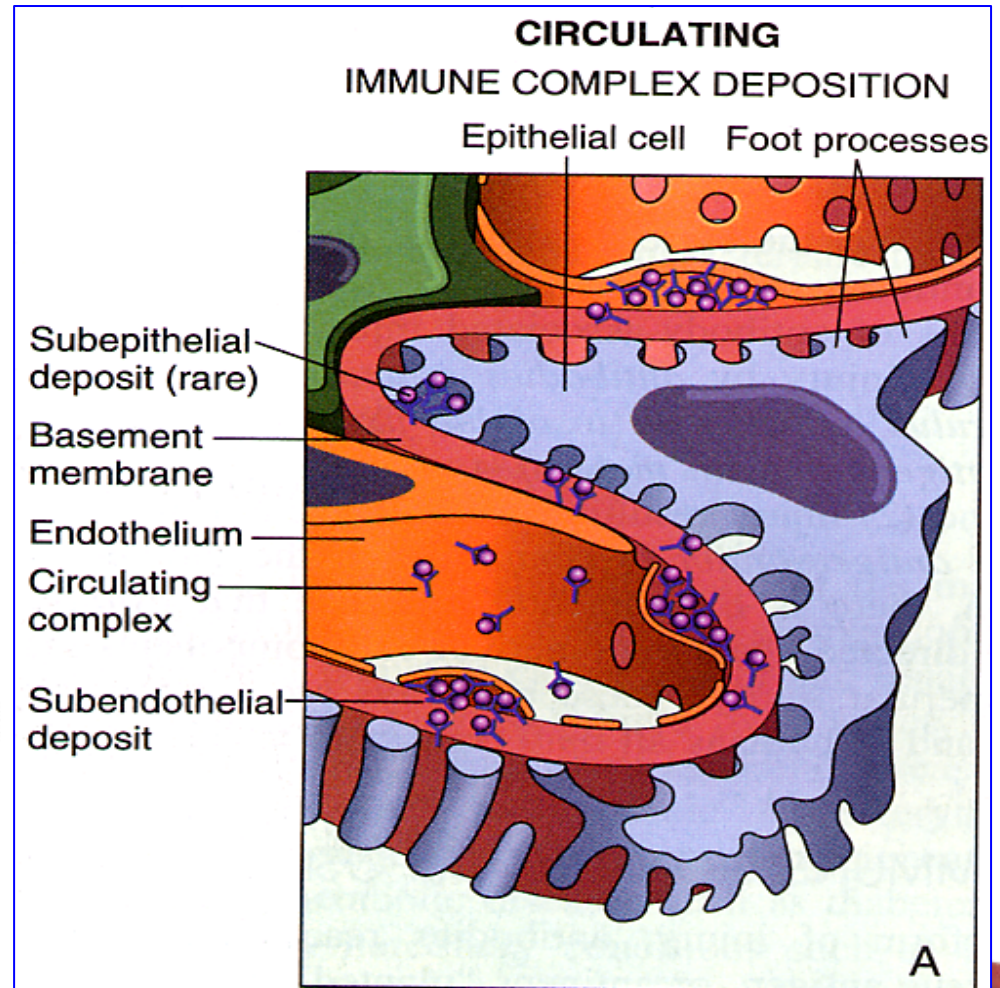
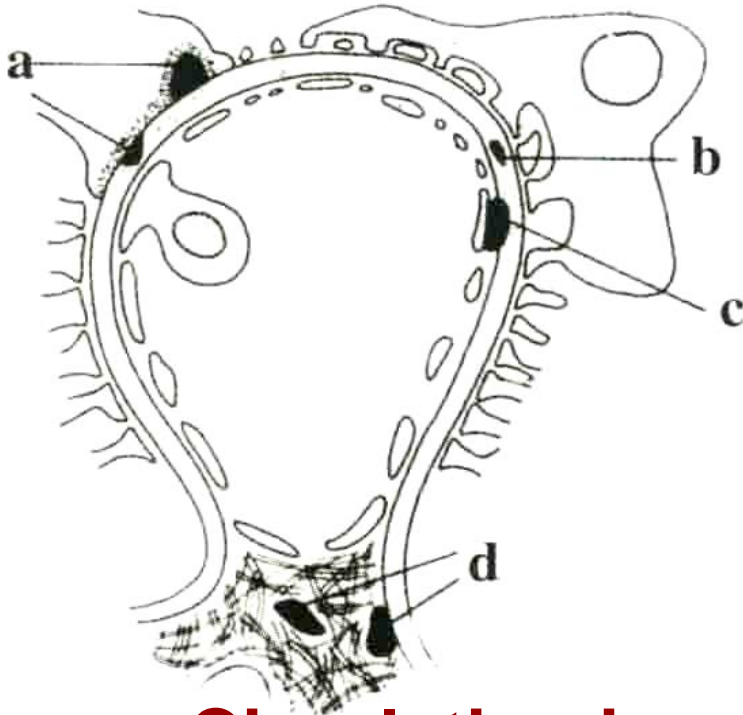




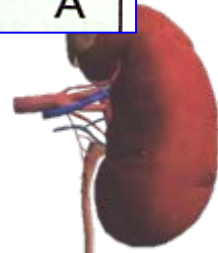
Etiology and pathogenesis

Deposits

- Subepithelial
- GBM
- Subendothelia
- Mesangium



Circulating immune complex nephritis





Etiology and pathogenesis

**In situ
immune complex deposition**

Glomerular Ag

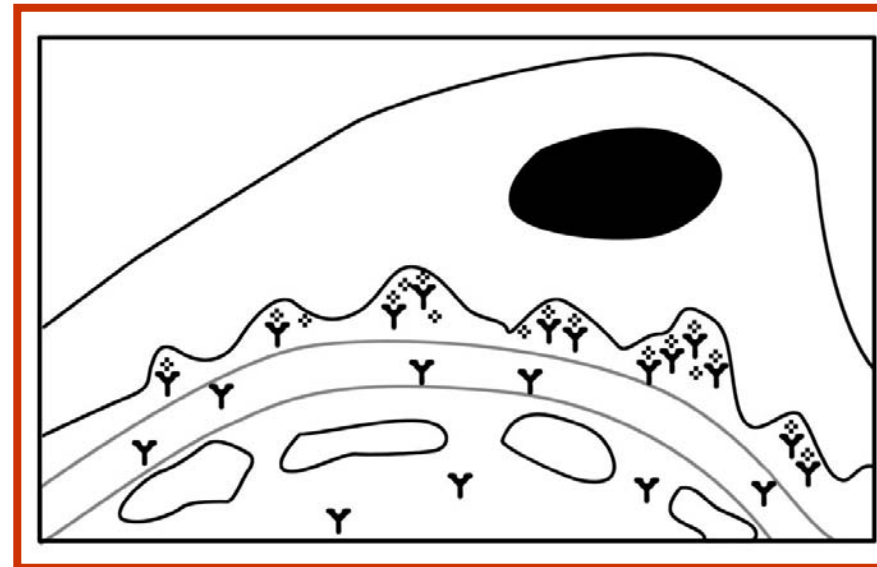
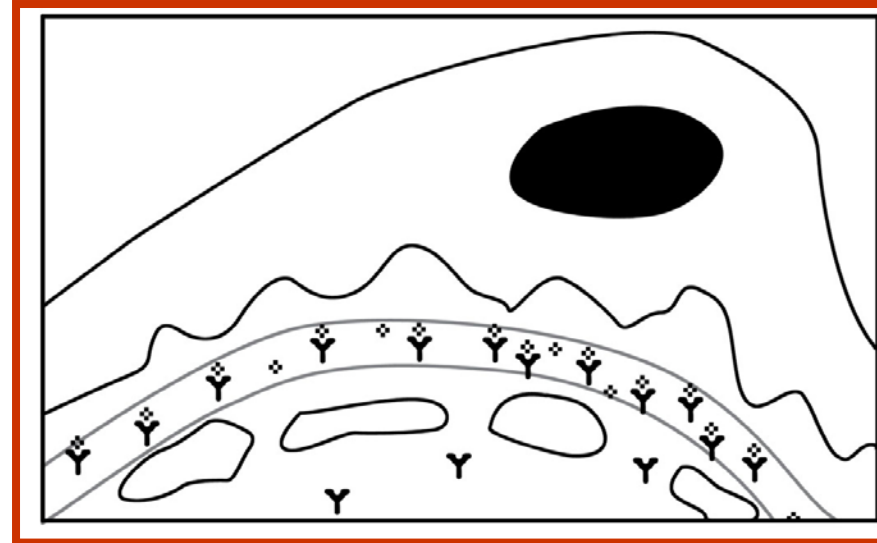
Planted Ag

GBM Ag

Heymann antigen

Autoantigen

Cross Ag





Etiology and pathogenesis

In situ immune complex deposition

--- Anti-GBM nephritis (Masugi's nephritis)

Rabbit



immunized with rat tissue



inject rat



**Ab direct against intrinsic fixed
Ag in the GBM**



nephritis

Immunofluorescence microscopy

Ab deposition in the GBM



continuous linear pattern fluorescence

Formation of GBM Ag

Structural changes of membrane

**Cross-reaction because of the
same Ag with organism**

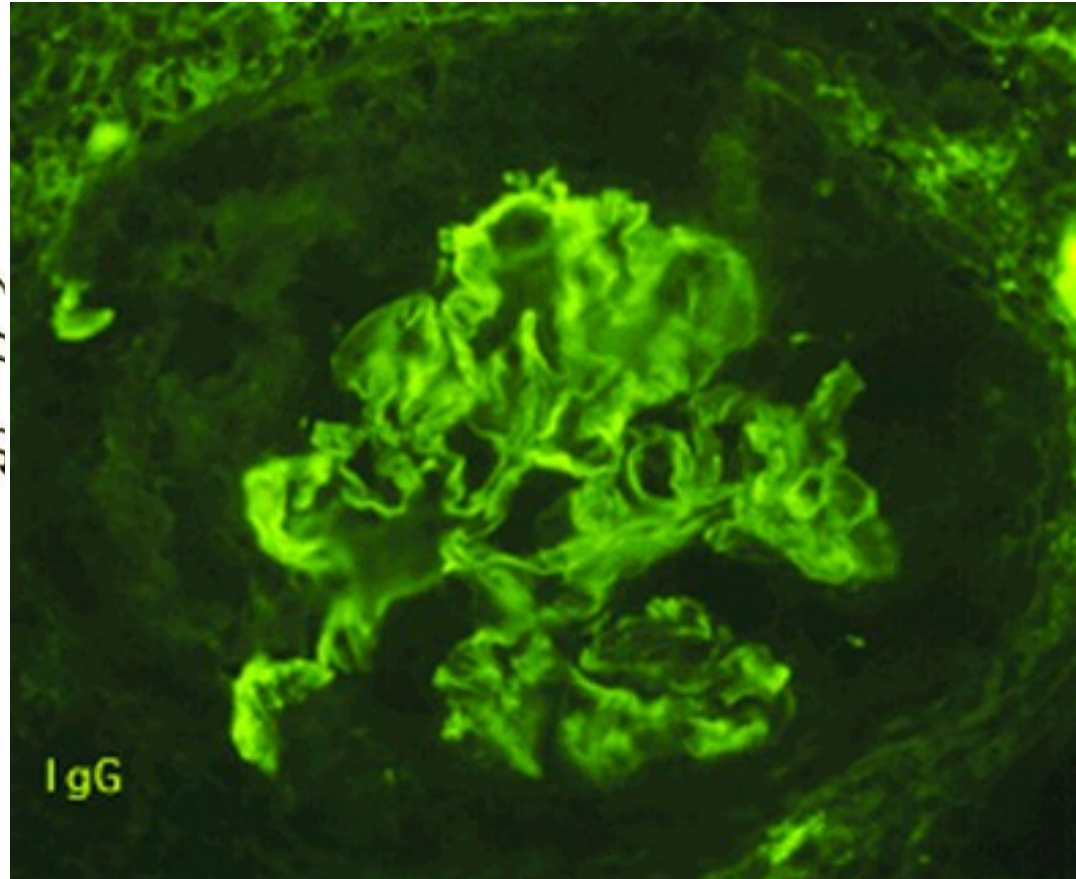
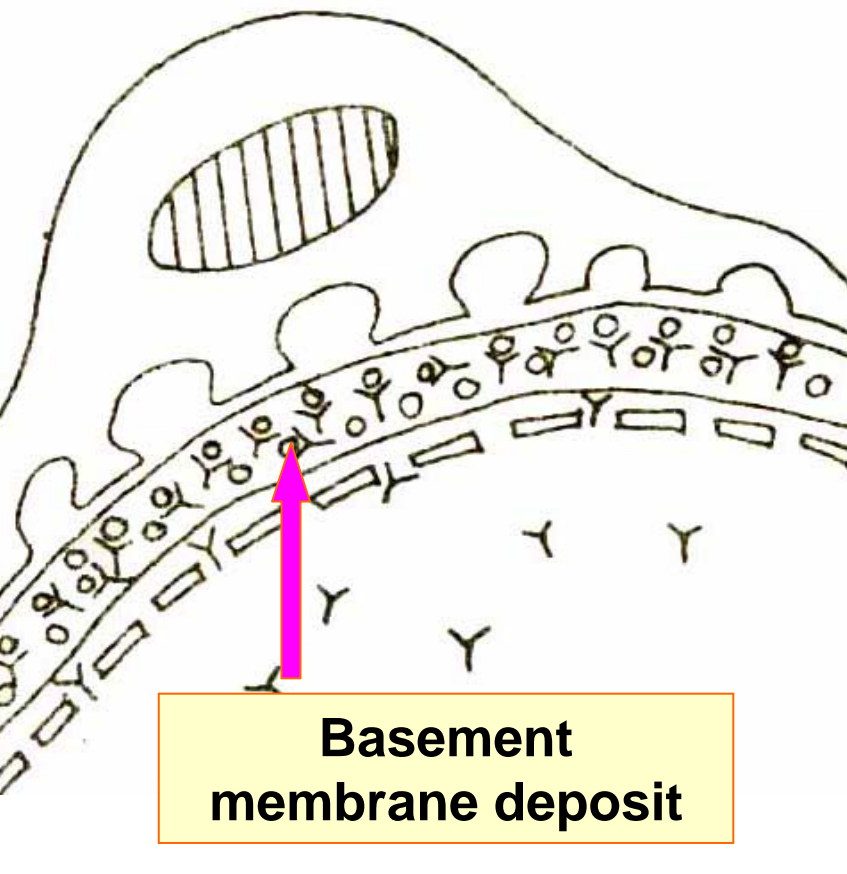




Etiology and pathogenesis

In situ immune complex deposition

Anti-GBM antibody---induced nephritis



direct IF shows linear staining of the glomerular capillary basement membranes for IgG



Etiology and pathogenesis

Heymann nephritis

Immunized rat with microvilli of tubular epithelial cell



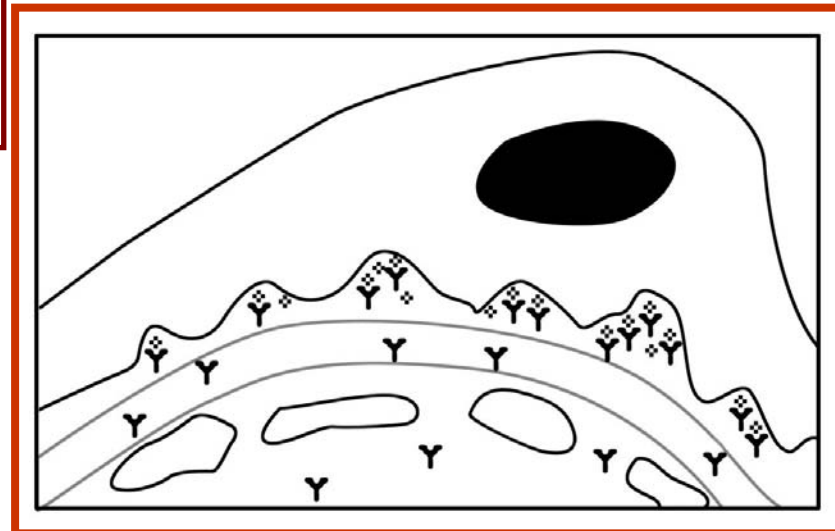
Ab to microvilli Ag



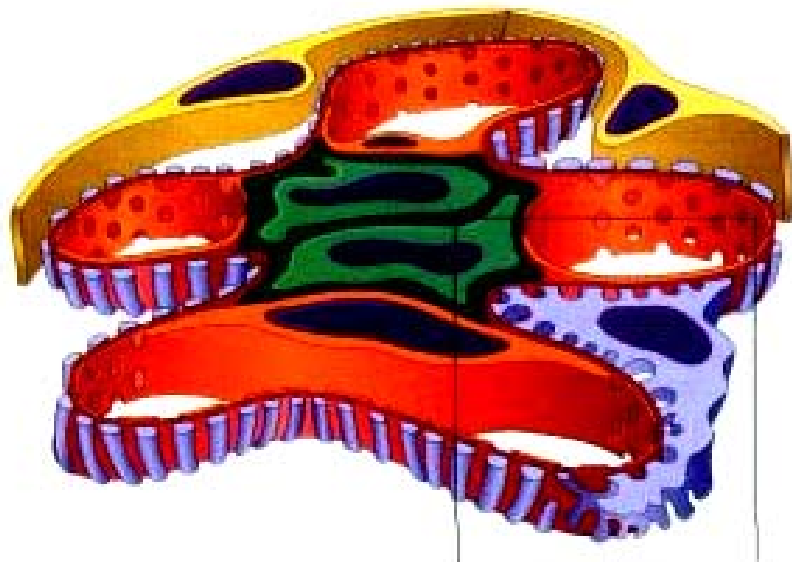
subepithelial deposits



Membranous GN

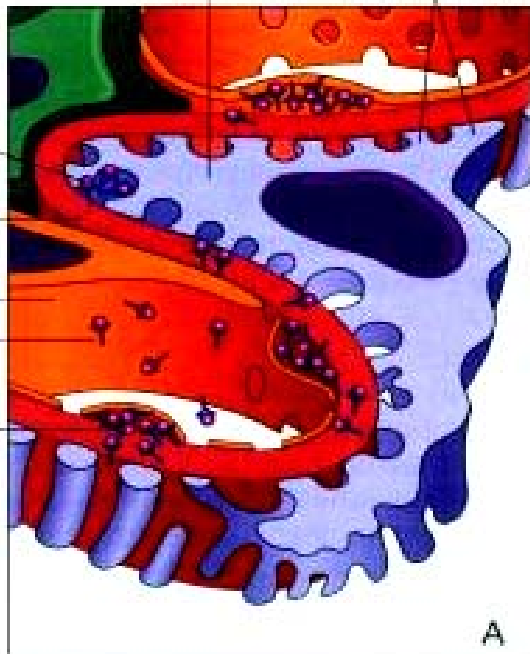


In situ immune complex deposition



**CIRCULATING
IMMUNE COMPLEX DEPOSITION**

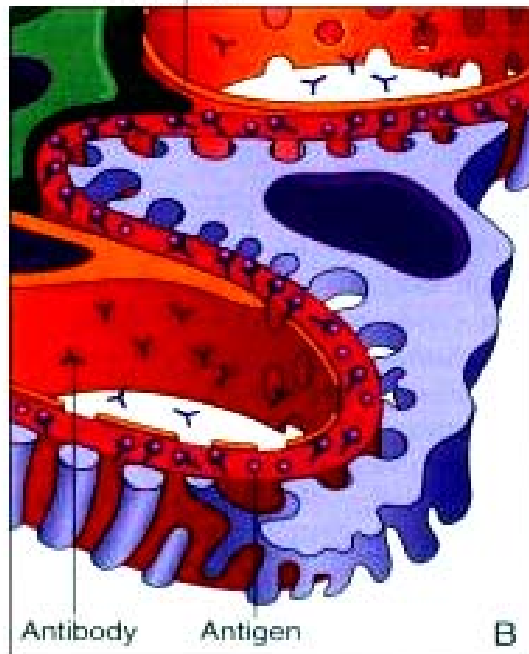
Epithelial cell Foot processes



A

ANTI-GBM

Endothelium



B

IN SITU

HEYMANN



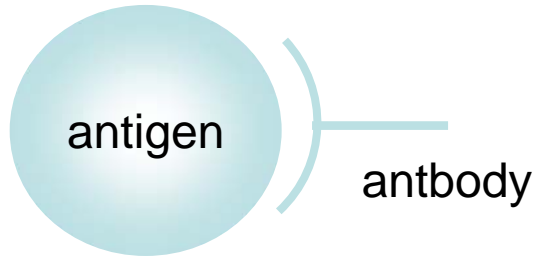
C



Etiology and pathogenesis

**Endogenous
antigens**

**Exogenous
antigens**



*Circulating immune complex
In situ immune complex*

**immune
complex**

**Mediators of
glomerular injury**

mediators of inflammation

glomerulus damage





Etiology and pathogenesis

Antibodies to glomerular cells

Cell-mediated immunity in glomerulonephritis

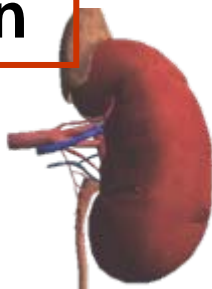
sensitized T cell



cause glomerular injury

Activation of alternative complement pathway

**cause membrane-proliferative GN
independently of immune-complex deposition**





Research method

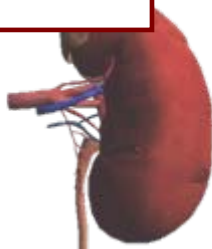
Material: Renal biopsy, Operation sample, Autopsy,
Animal experiment

Gross:

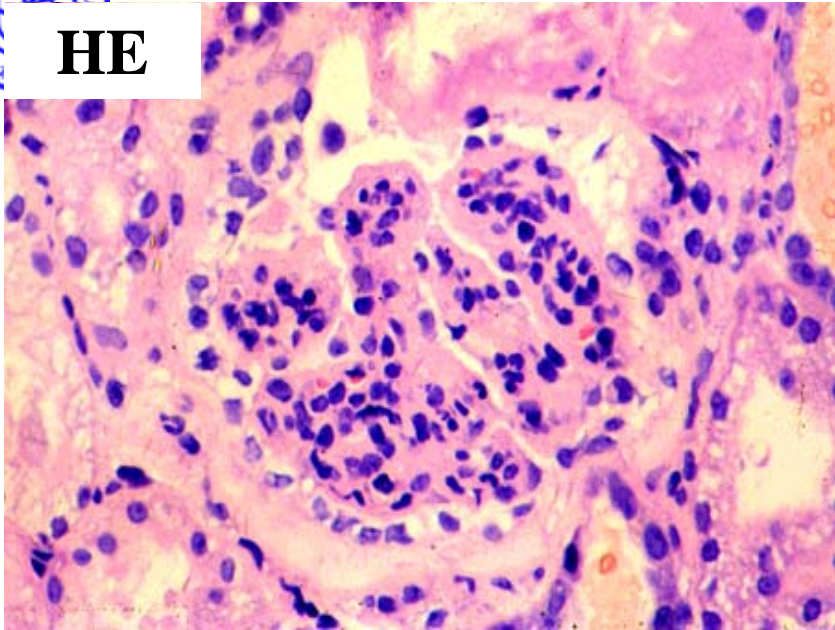
Light microscopy: HE, PAS, PASM, Masson

Immunofluorescence: IgG, IgM, IgA and C3

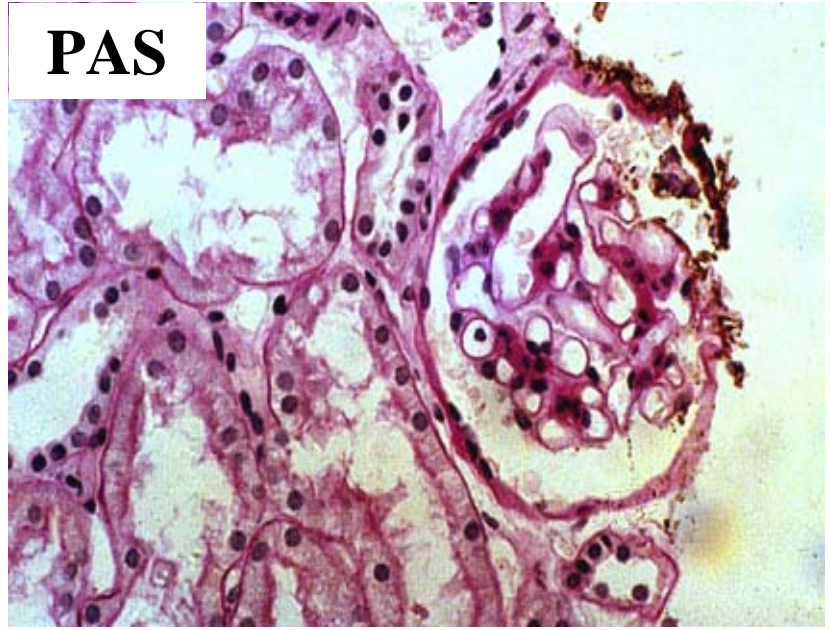
**Electron microscopy: structure and electron dense
deposition**



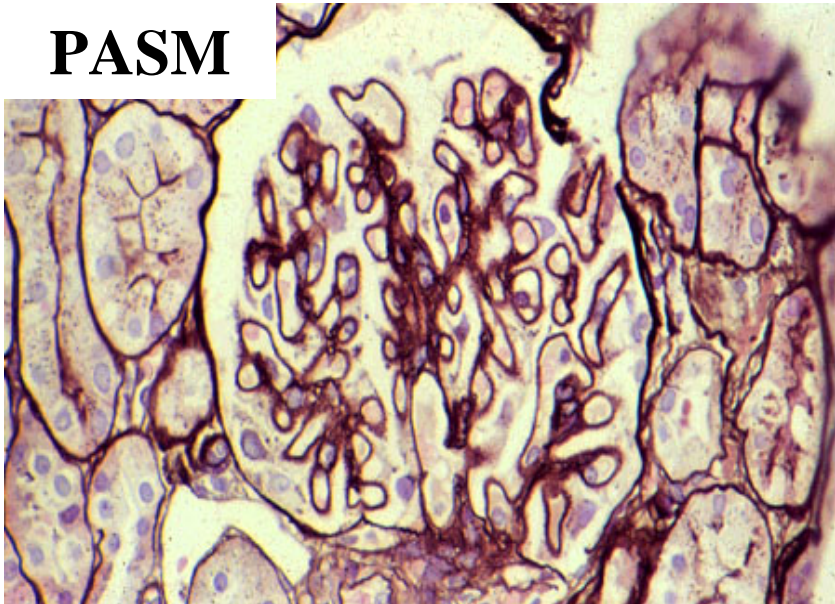
HE



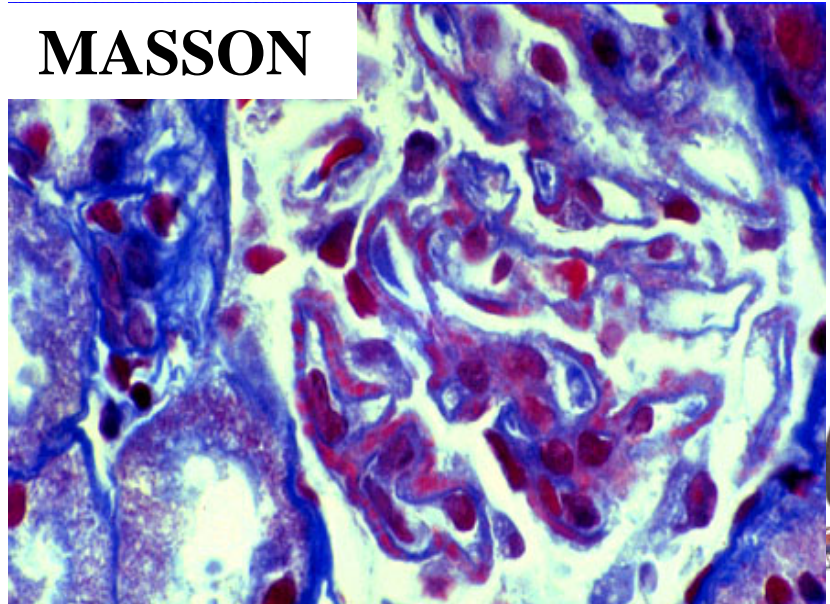
PAS

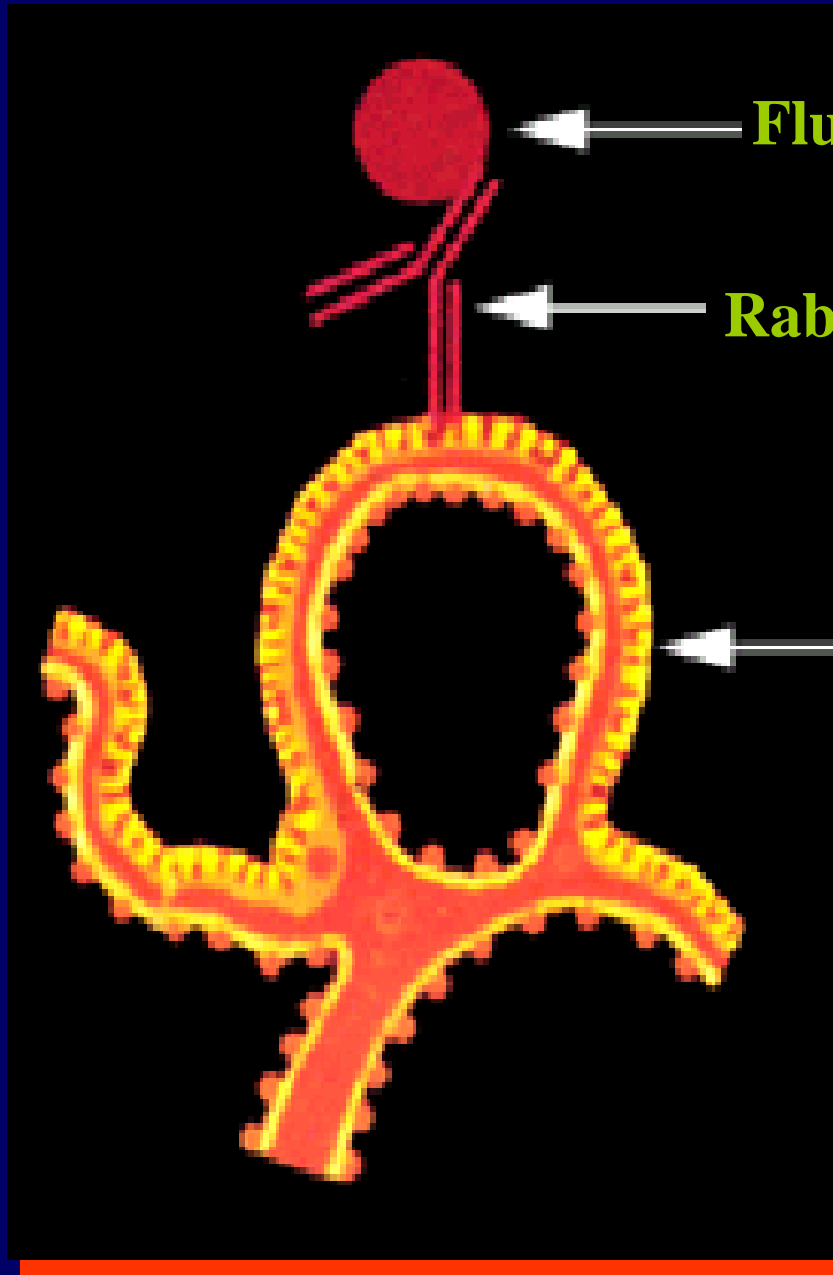


PASM



MASSON



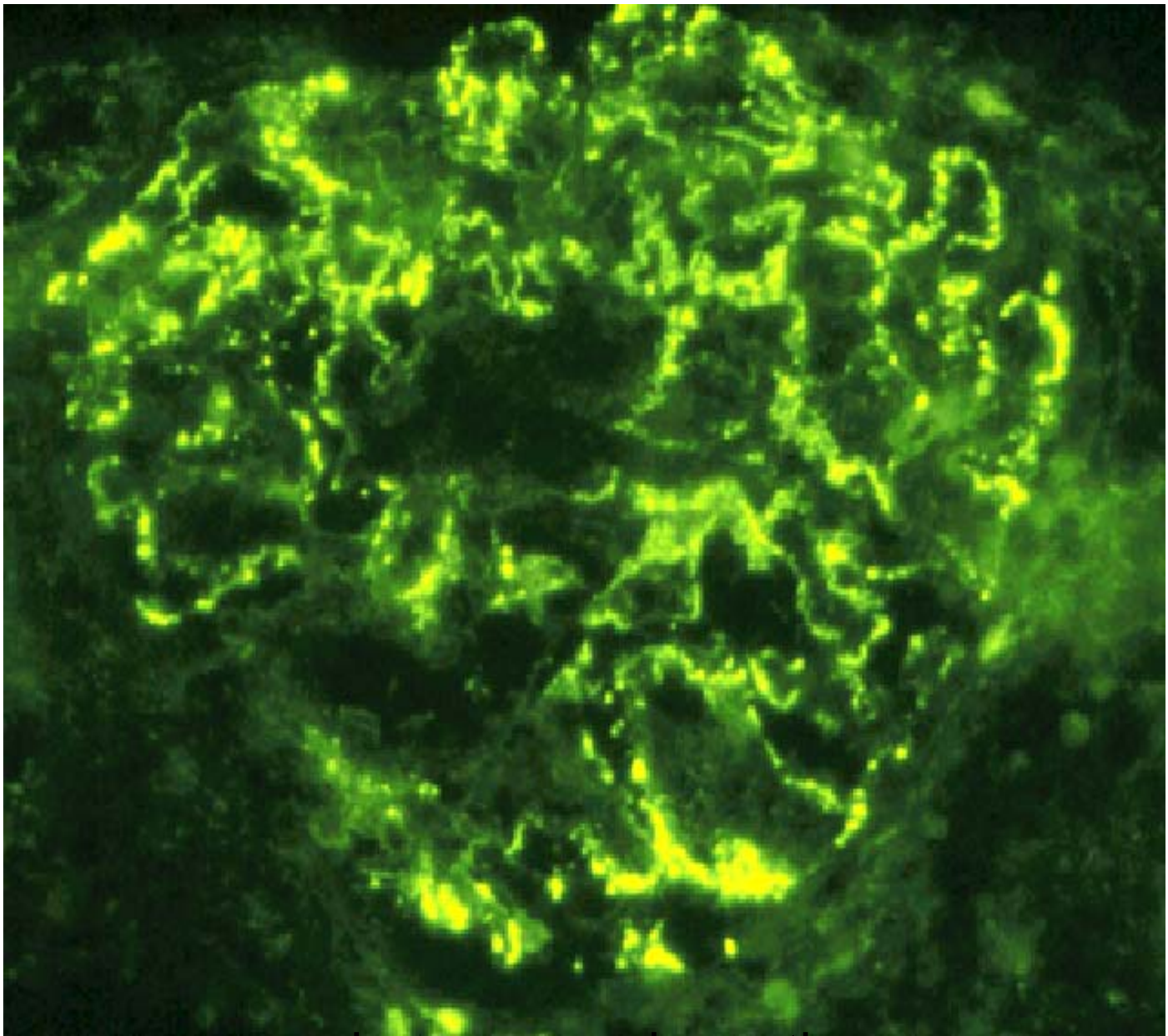


Fluorescein

Rabbit anti human IgG serum

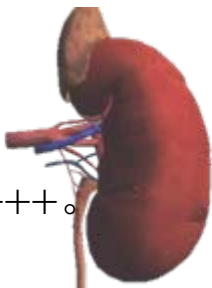
Immune complex include IgG

Direct immunofluorescence(DIF)
(Ideograph)



membranous nephropathy

Direct IF shows **granular pattern** staining of the glomerular capillary for IgG , +++。





Subepithelial

GBM

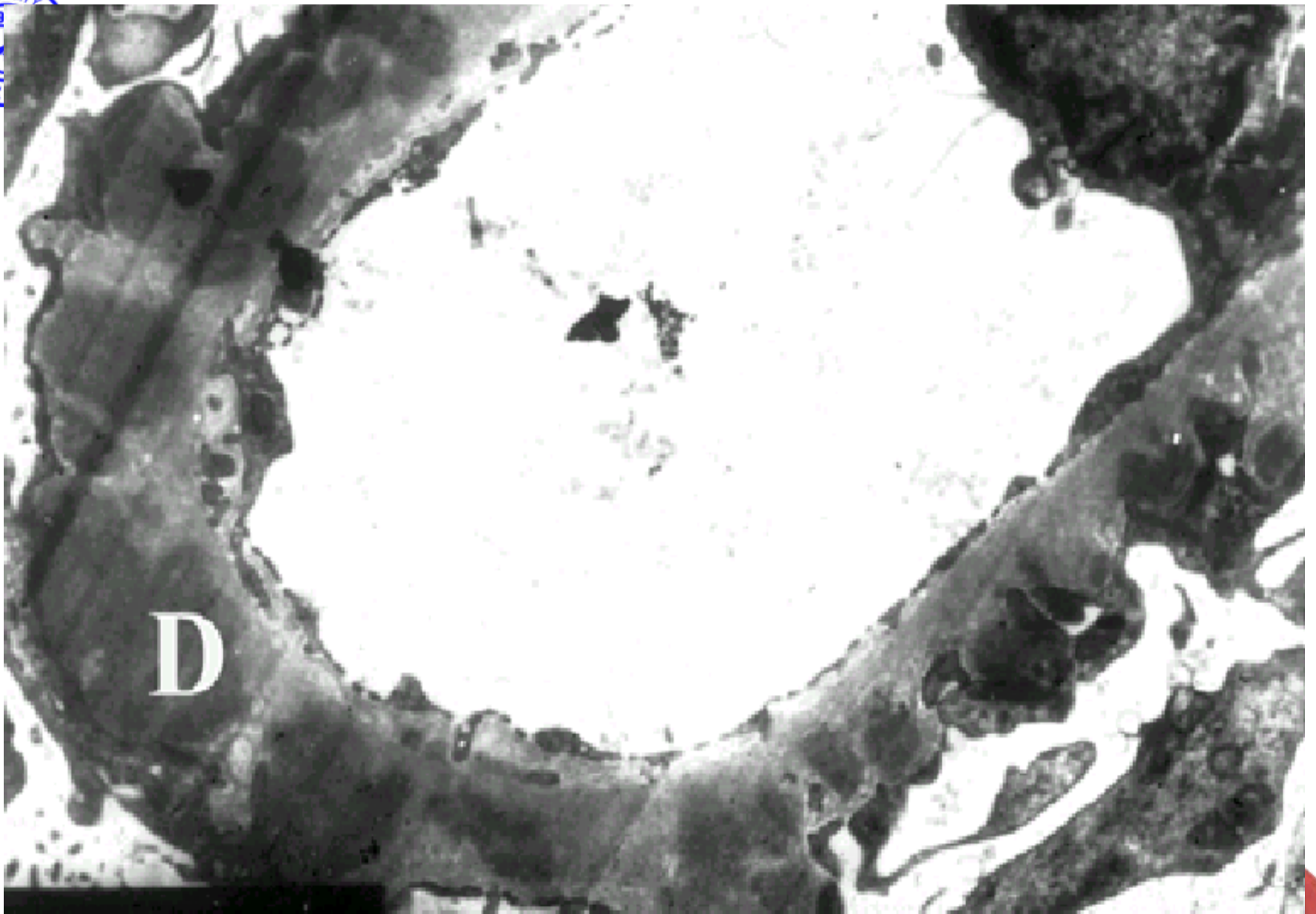
Subendothelial

Mesangium

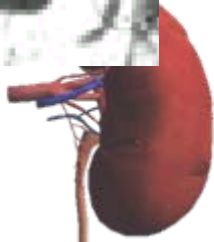
Location of electron dense deposits

(模式图)





Membranous nephropathy, Type II
Electron dense deposits in Subepithelial space (D)。





Basic pathological changes

Glomerulus

Proliferation: Parietal epithelial cells, Mesangial cells, Endothelia Cells

Infiltration: Neutrophils, LCs, Monocytes

increase

- **Hyaline change and Sclerosis**
- **Inflammatory exudation and necrosis**

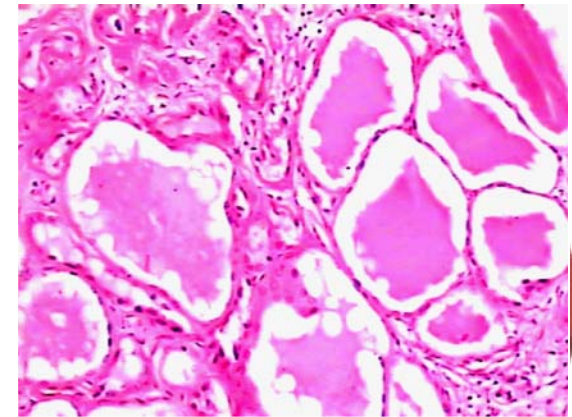
Tubules

Epithelial cell degeneration, Cast, Atrophy, Disappear

Renal interstitium

Hyperemia, Edema, Inflammatory cell infiltration, fibrosis

Blood vessel





Basic pathological changes

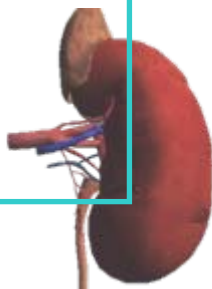
Inflammation

Proliferation: Epithelial cells, Mesangial cells, Endothelia Cells ;

GBM thickening and Mesangial matrix increase

Degeneration: Fibrinoid necrosis, Hyaline change and Sclerosis. Epithelial cell of tubules degeneration

Exsudation: Neutrophils, LCs , Monocytes





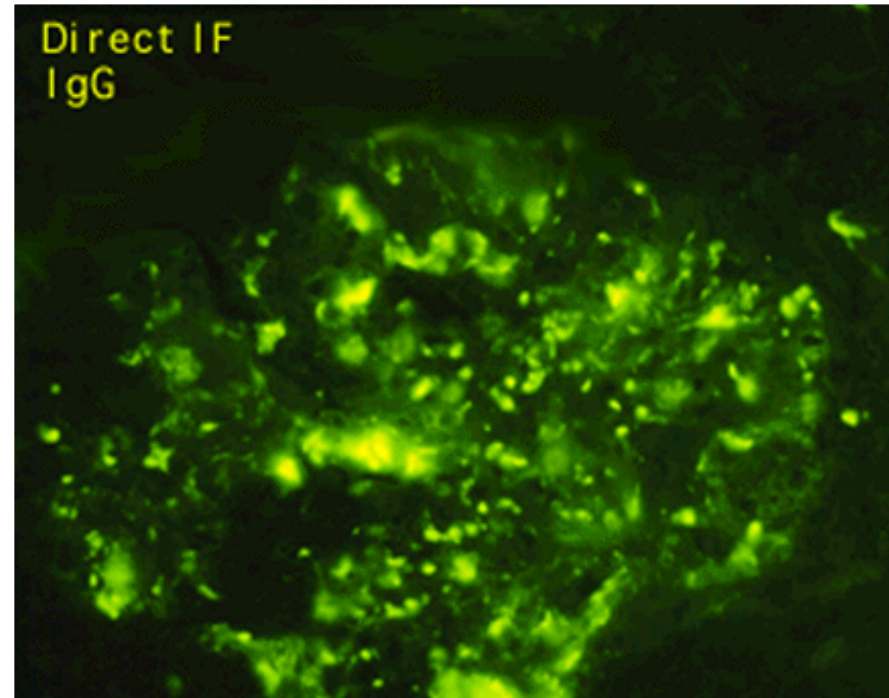
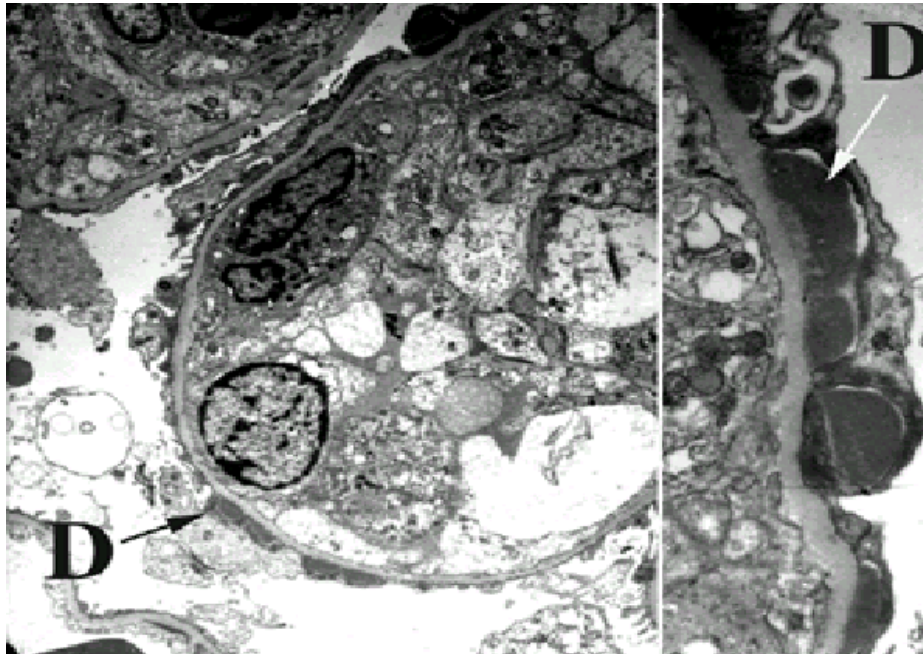
Basic pathological changes

Immunoreaction

Antigen+Antibody=immune complex

Circulating immune complex nephritis

In situ immune complex deposition

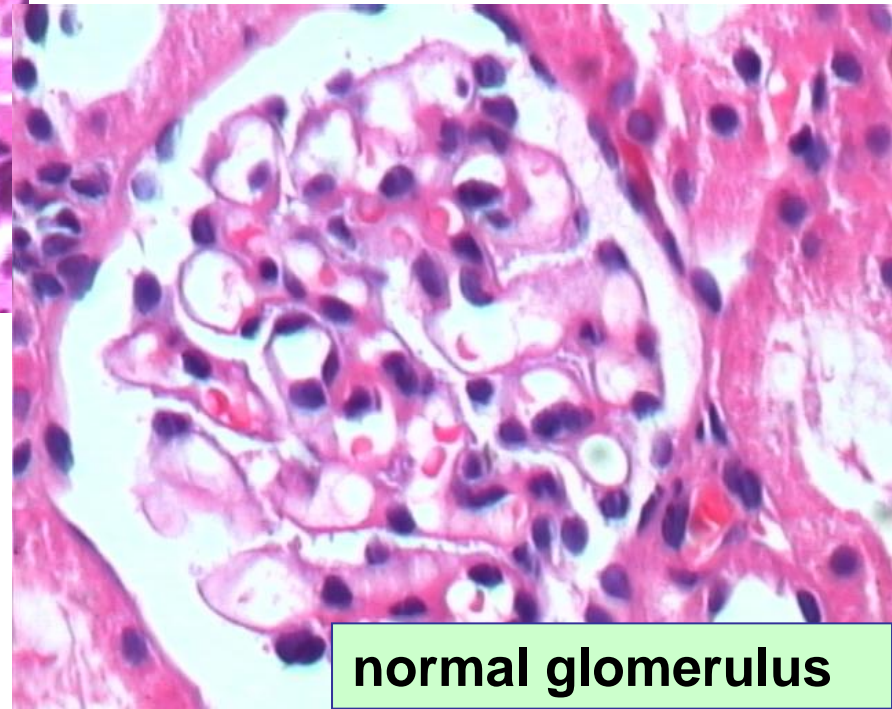




Basic pathological changes



hypercellularity

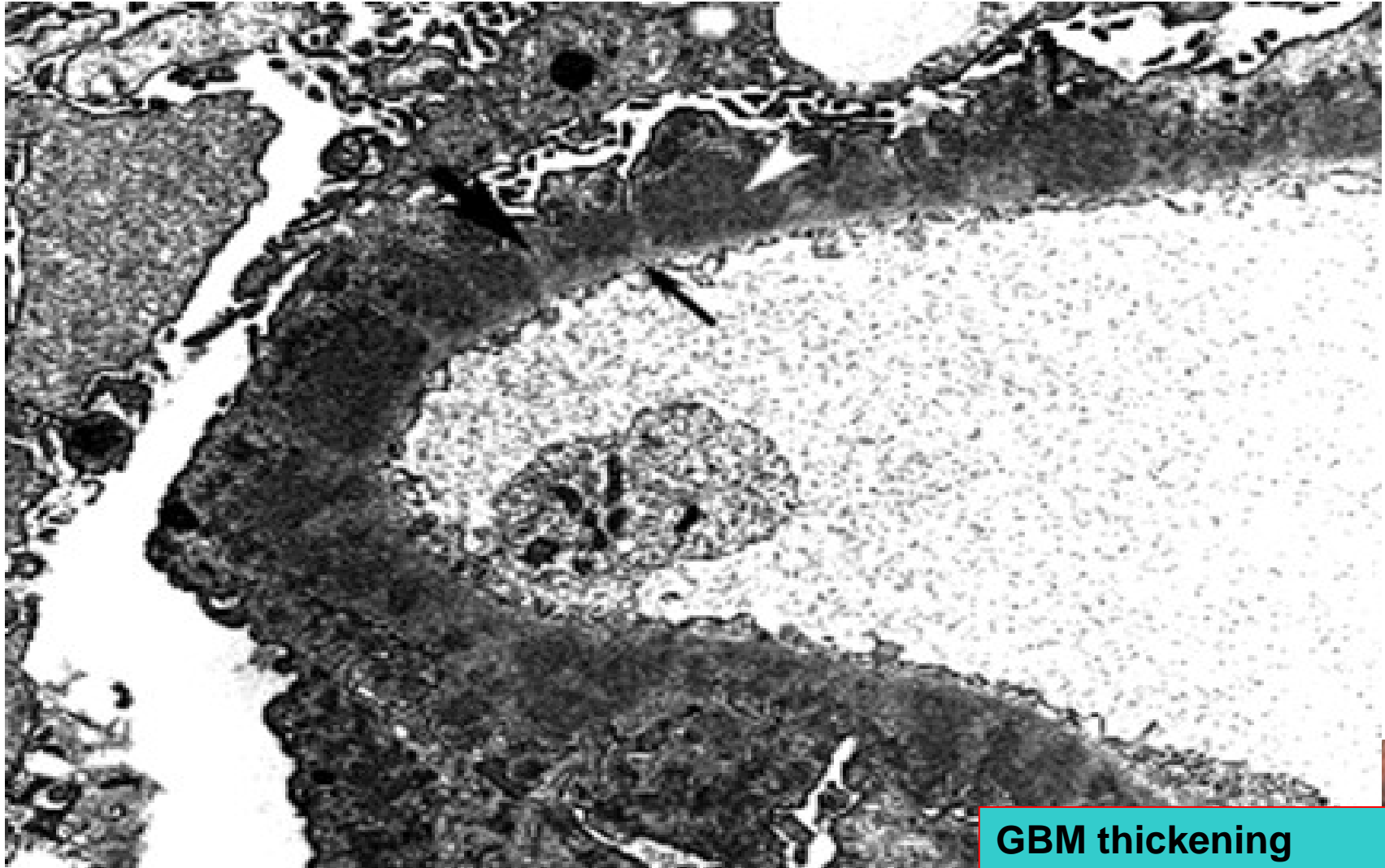


normal glomerulus

Hypercellularity



Basic pathological changes



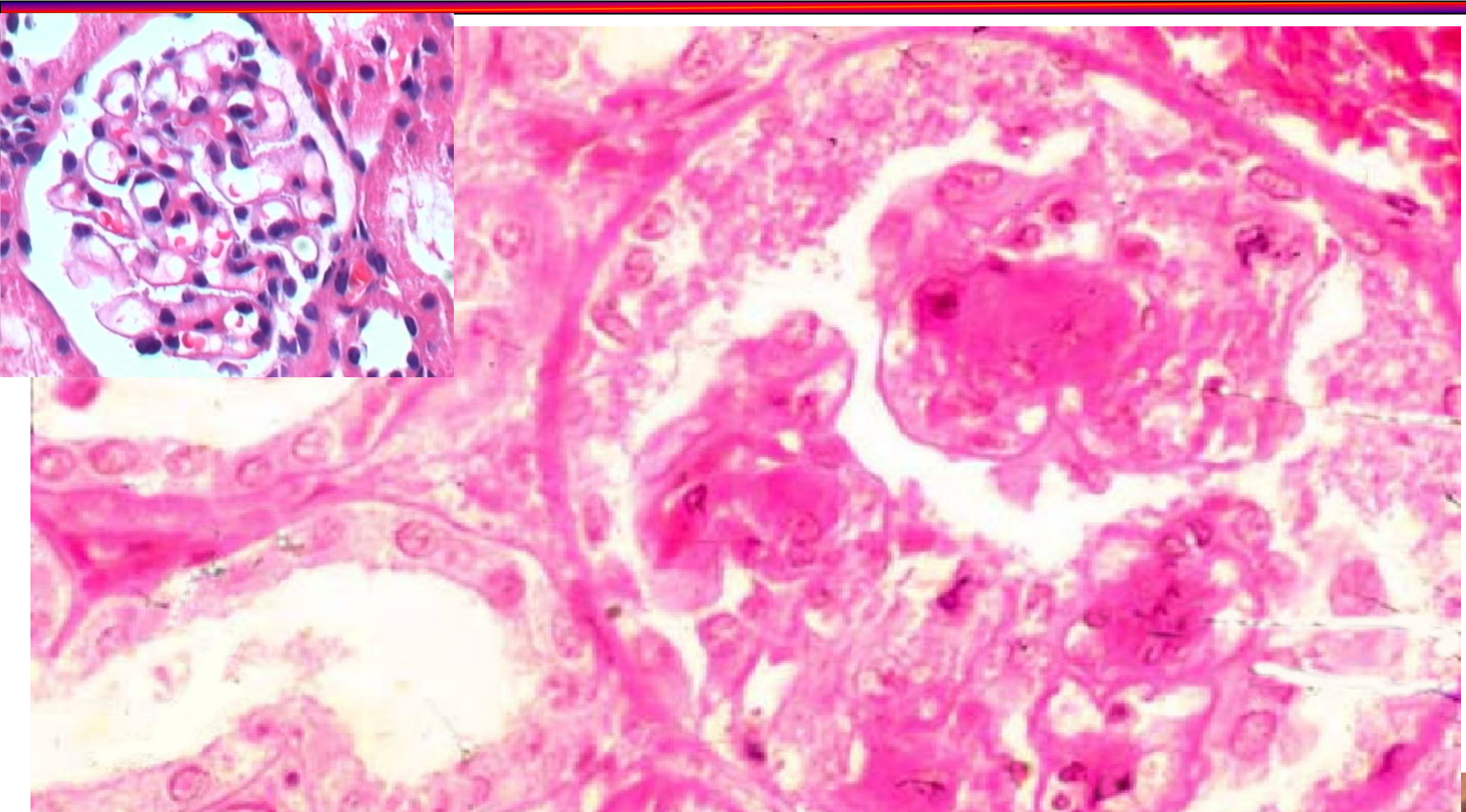
GBM thickening

Basement membrane thickening & mesangial matrix increasing





Basic pathological changes



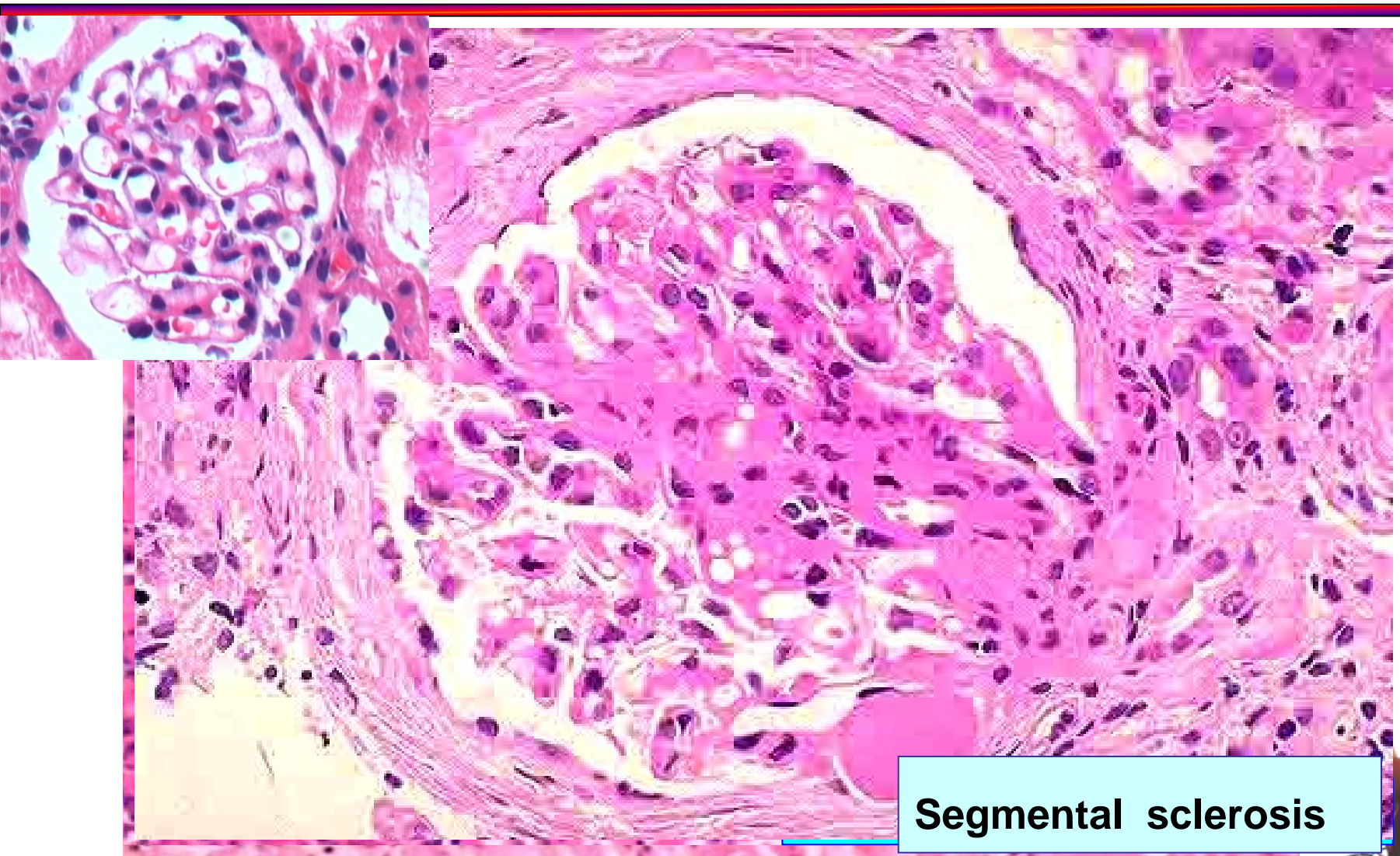
PAS staining: proliferation of mesangial matrix

Basement membrane thickening & mesangial matrix increasing





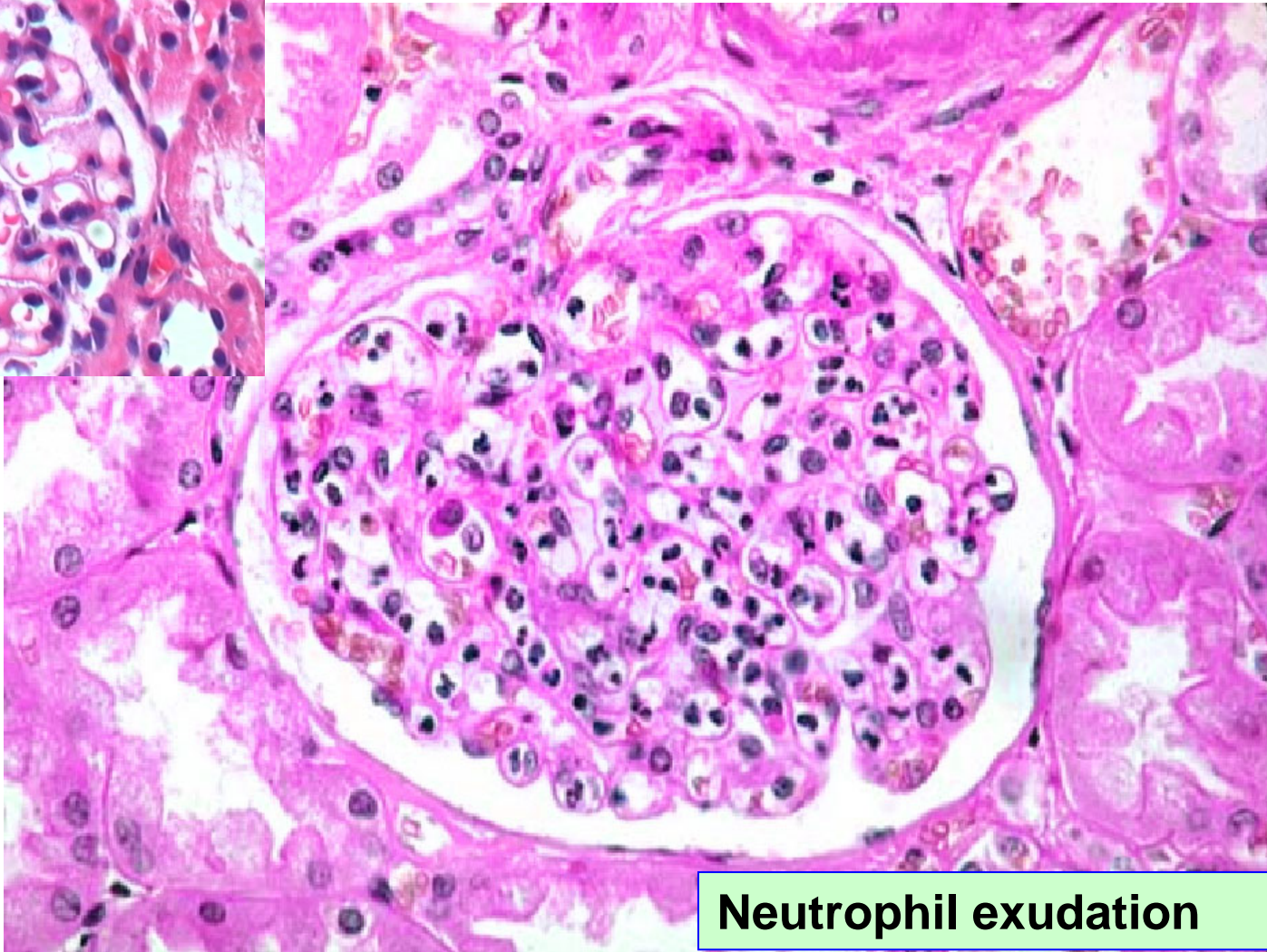
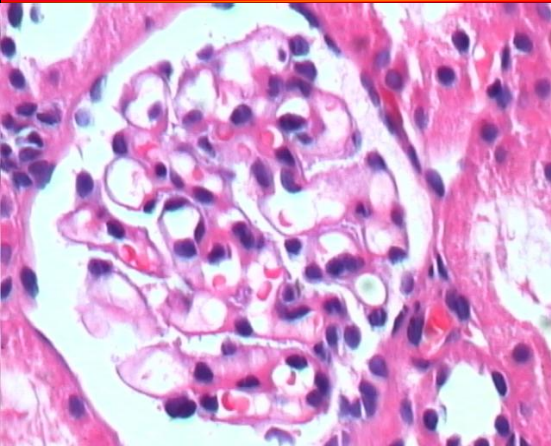
Basic pathological changes



Hyalinization and sclerosis



Basic pathological changes

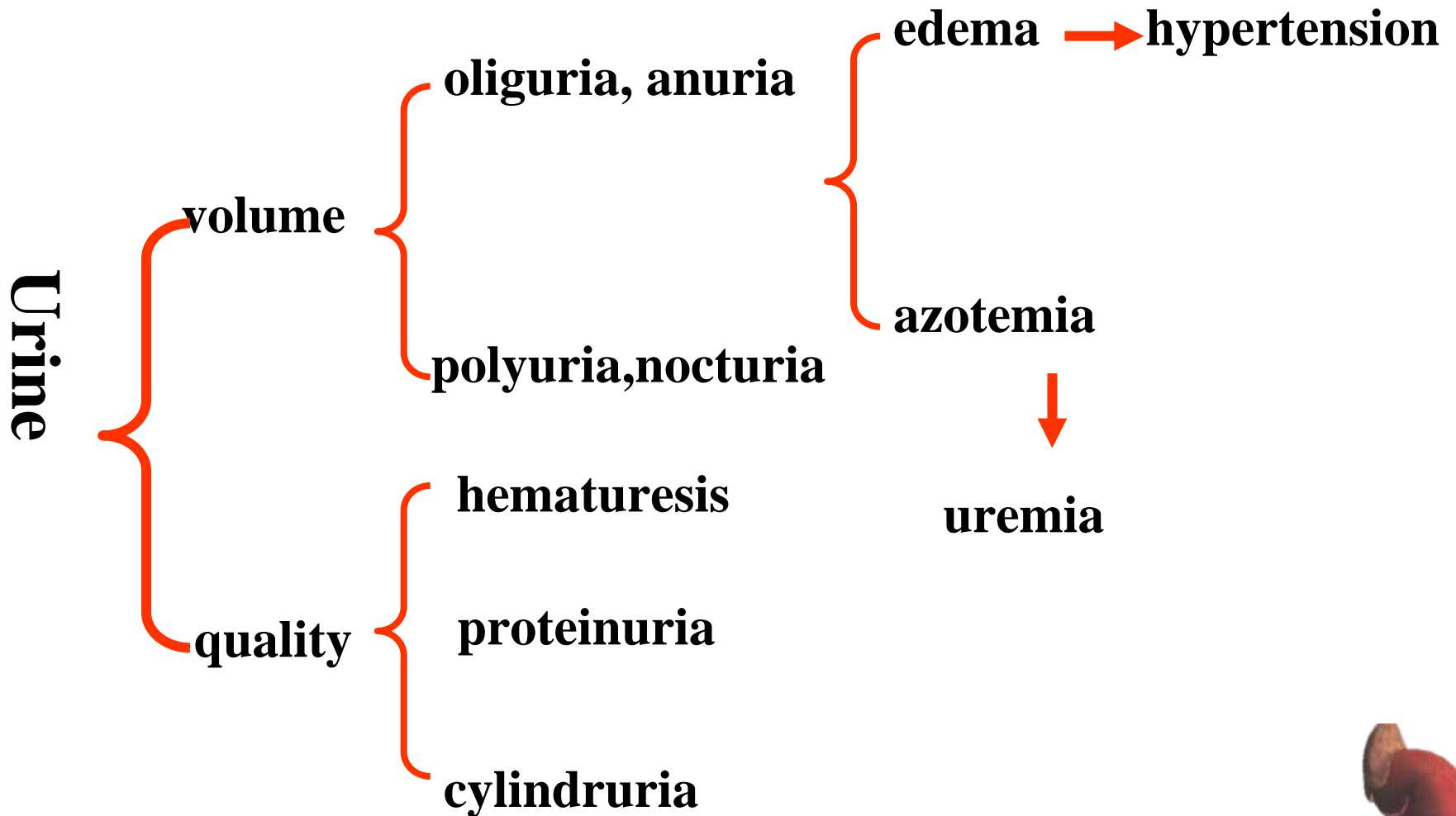


➤ **Inflammatory exudate and necrosis**





Clinical manifestation





Clinical manifestation

- **Acute nephritic syndrome**
 - Hematuria, proteinuria, Edema, Hypertension, Severe → azotemia
- **Rapidly progressive nephritic syndrome**
 - Hematuria, Proteinuria, Oliguria or Anuria, Edema, Azotemia → acute renal failure
- **Nephrotic syndrome**
 - ① Heavy proteinuria ($\geq 3.5\text{g}$) ② Severe edema ③ Hypoalbuminemia ($< 30\text{g/L}$) ④ Hyperlipidemia and lipiduria.
- **Asymptomatic hematuria or proteinuria**
 - Continuous or recurrent hematuria (macroscopic or microscopic), Mild proteinuria
- **Chronic nephritic syndrome**
 - Polyuria, nocturia, low specific gravity urine, Hypertension, Azotemia and uremia, Anemia





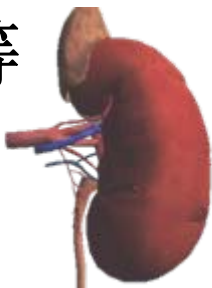
Clinical manifestation

azotemia

肾小球病变可使肾小球滤过率下降，引起血尿素氮（BUN）和血浆肌酐水平增高。此类生化改变称氮质血症

uremia

发生于病变晚期，除氮质血症的表现外，还具有一系列自体中毒的症状和体征。如尿毒症性胃肠炎、周围神经病变、纤维素性心外膜炎等





Pathological type

Acute diffuse proliferative glomerulonephritis (GN)

Rapidly progressive GN (RPRN)

Crescentic glomerulonephritis (CrGN)

Membranous GN (membranous nephropathy)

Membranoproliferative GN (MPGN)

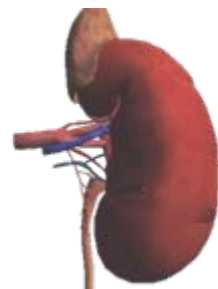
Mesangial proliferative GN

Minimal change GN (lipoid nephrosis)

Focal segmental glomerulosclerosis (FSG)

IgA nephropathy

Chronic GN





Nomenclature of glomerular injury

- **Diffuse** : involving all or majority of glomeruli (>50%)
- **Focal** : involving a certain proportion of glomeruli (<50%)
- **Global**: involving the entire glomerulus or large part of each glomerulus (>50%)
- **Segmental**: affecting a part of each glomerulus (<50%)





Case

患儿男性，7岁。因眼睑浮肿、尿少3天入院。10天前在外玩耍时，右膝关节皮肤严重擦伤，2天后局部皮肤化脓，随后进行局部消炎处理，10天后出现上述症状。

体格检查：血压130/90mmHg，眼睑浮肿，双下肢浮肿。实验室检查：尿常规示，红细胞（+），尿蛋白（++），红细胞管型0~2/HP；24小时尿量400ml；尿素氮11.2mmol/L，（正常值<9mmol/L）；肌酐192 μ mol/L（<178 μ mol/L），均高于正常。

B超检查示：双肾对称增大。遂住院治疗，经对症支持治疗一个月病情基本好转，上述症状消失。

- 1、诊断是什么？与皮肤感染有无联系？为什么？
- 2、为何出现高血压、水肿、少尿、血尿、蛋白尿？





Acute diffuse proliferative GN





Introduction

- **Etiology and pathogenesis**

- **Main factors:**

- **most common:**

- Group A β -hemolytic streptococci 90% → type 12. 4. 1

- **others: pneumococci, staphylococci, HBV**

Postinfectious GN

- **Immune mediated disease**

- **Immune complex depositing**

- **Anti-o Ab ↑**

- **Serum complement level ↓**

- **Clinical manifestation**

Acute nephritic syndrome

- **Features**

- **Mesangial Cell and EC → proliferation**

- **Neutrophil and Macrophage → infiltration**

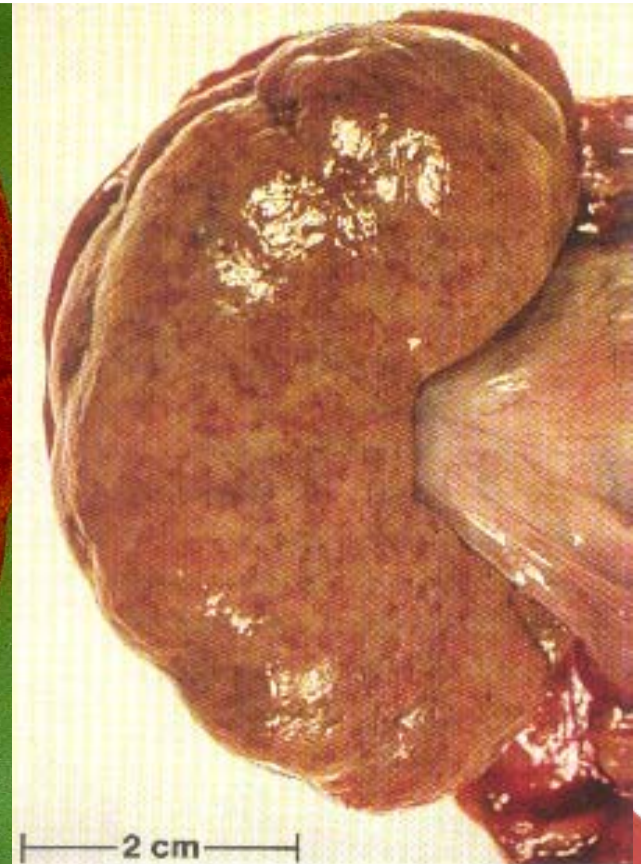
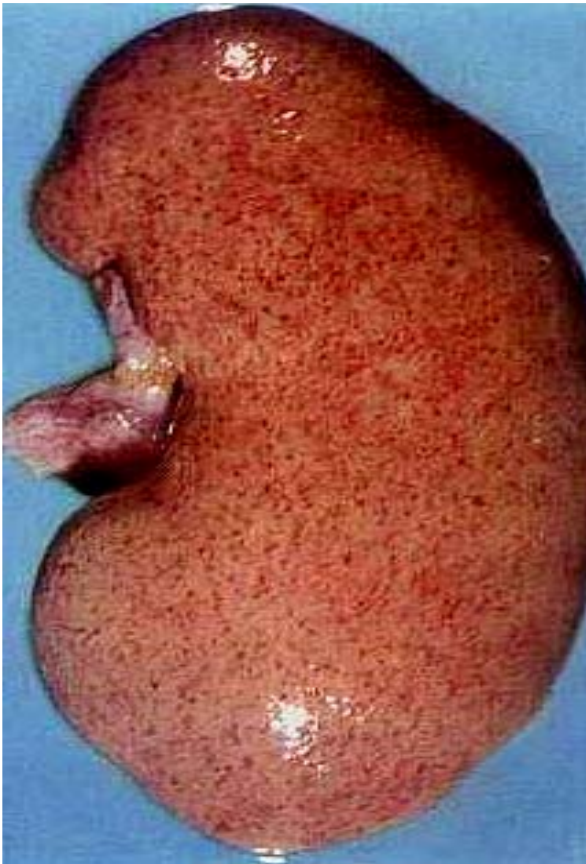
Endocapillary proliferative glomerulonephritis





Pathological changes

- **Gross: “red large kidney”, “flea-biting kidney”**

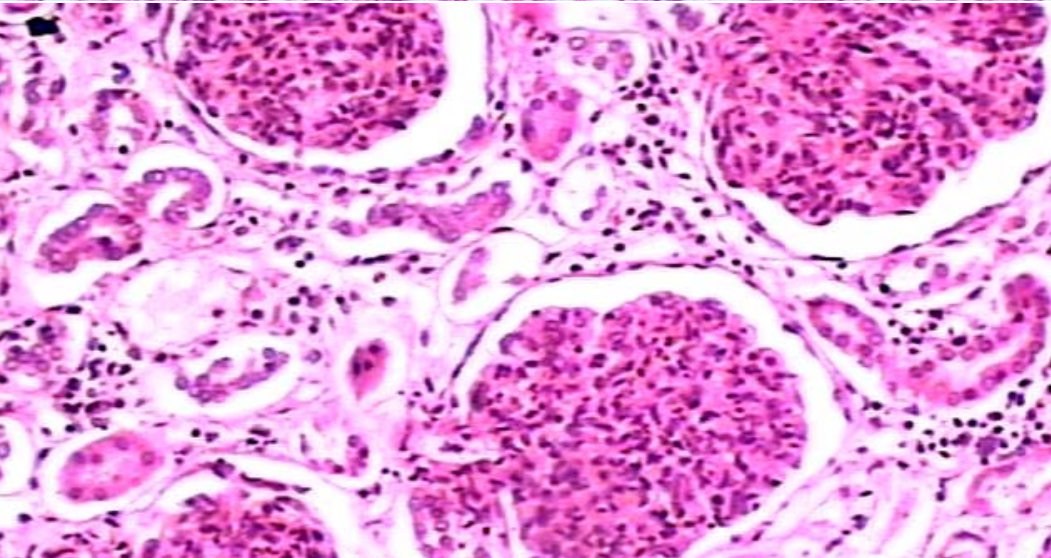
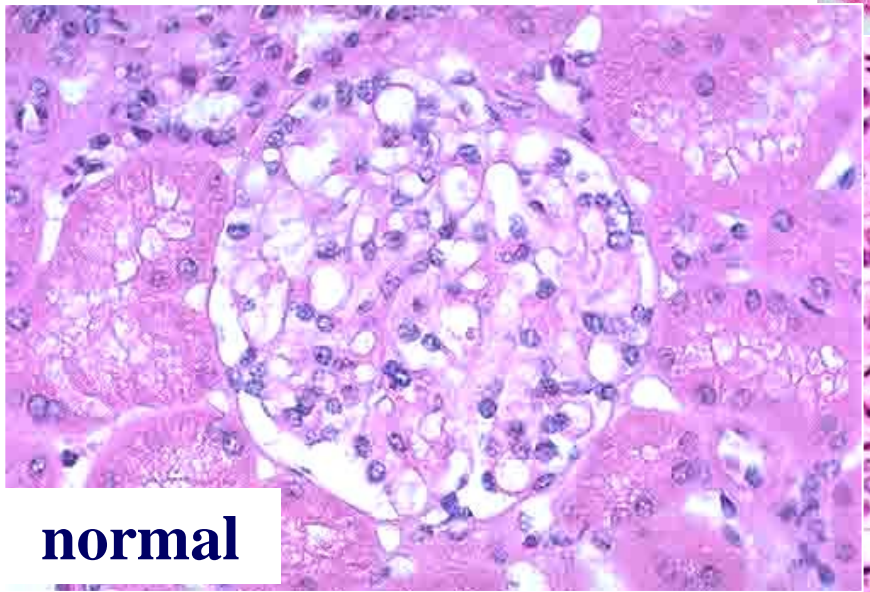
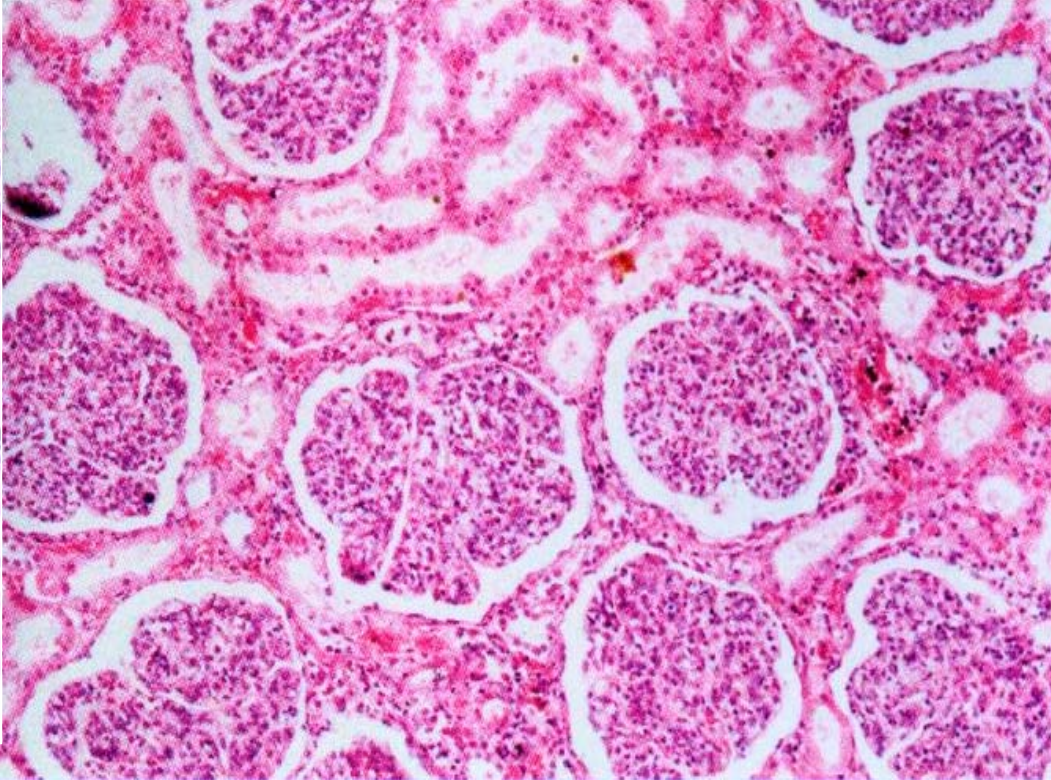
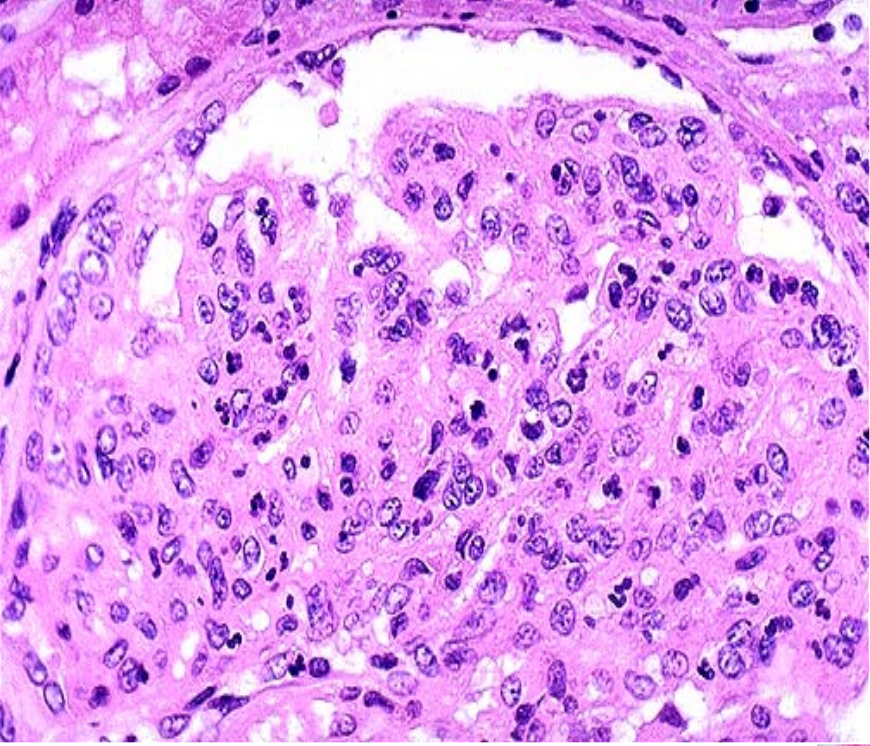




Pathological changes

- **LM: ---enlarged and hypercellular glomeruli**
 - i **Proliferative cell**
 - { Endothelial cell
 - { Mesangial cell
 - ii **Infiltrative cell**
 - { Neutrophil
 - { Macrophage



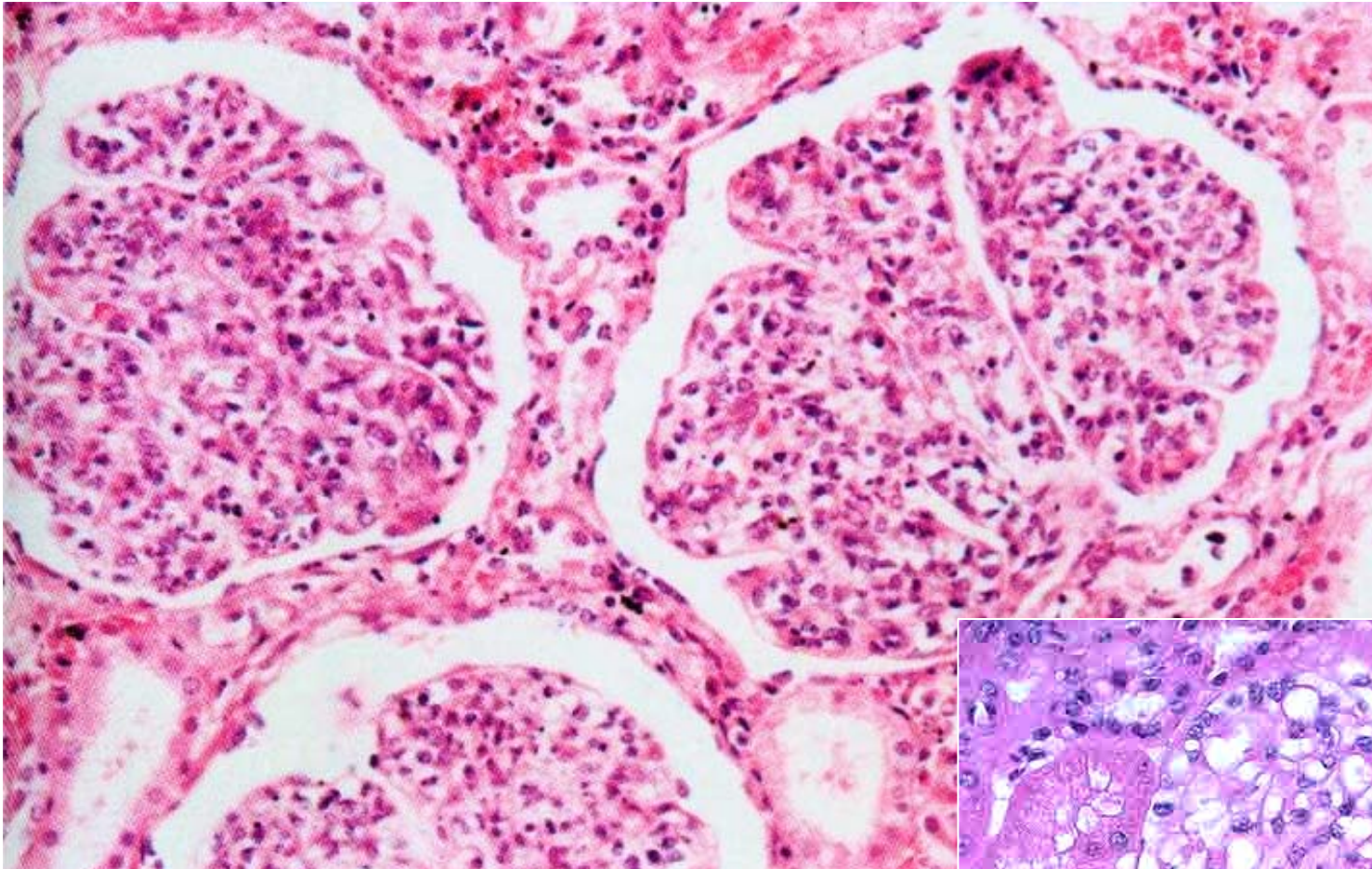


normal

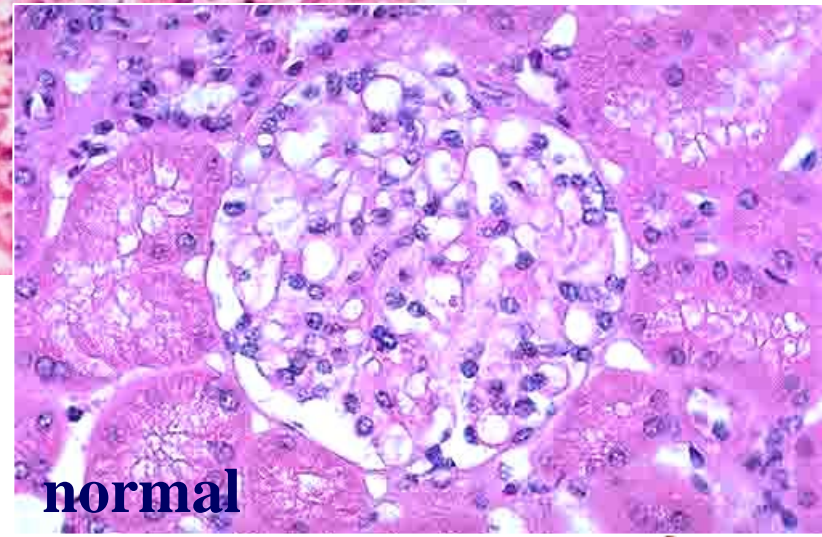
The glomerulus shows marked, diffuse hypercellularity.



Pathological changes

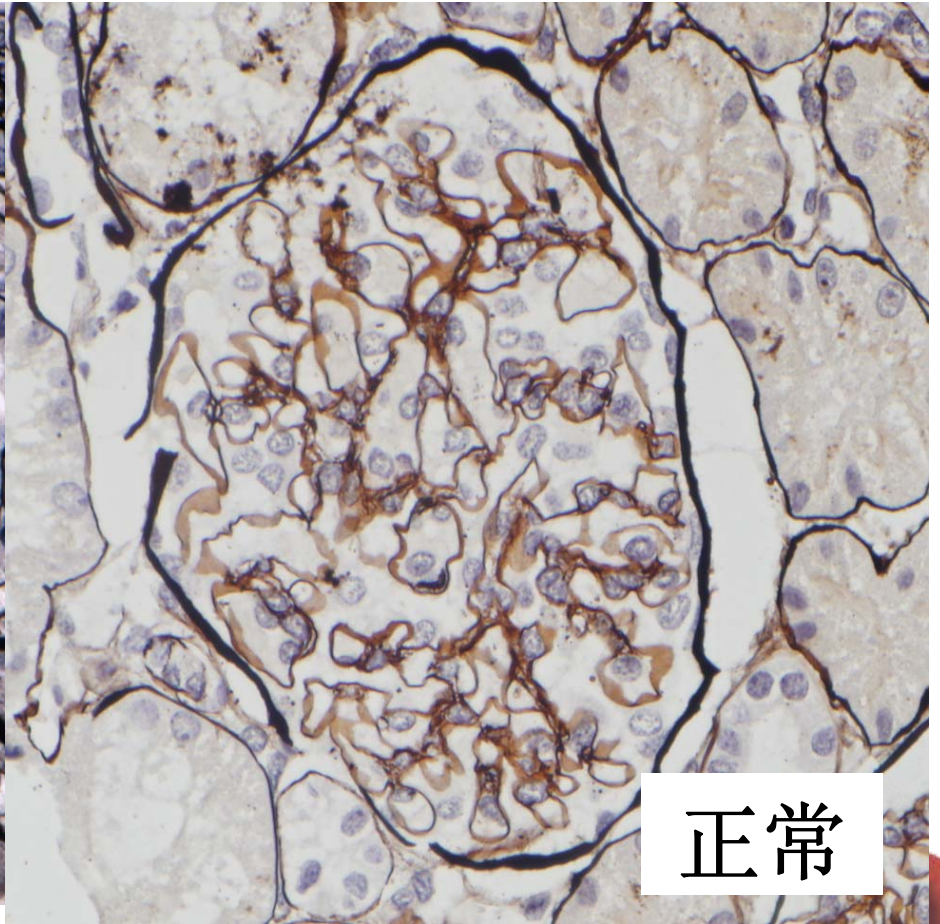
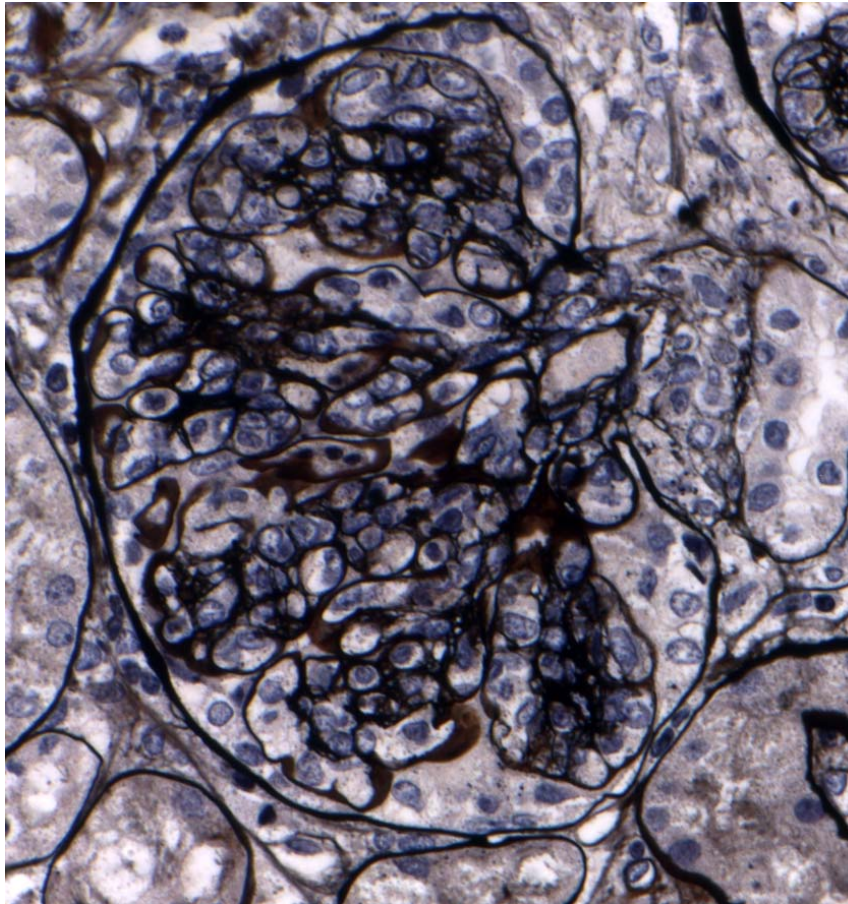


The glomerulus are hypercellular and capillary loops are poorly defined.

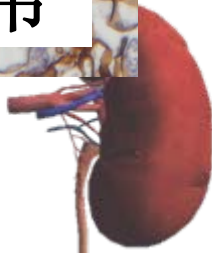




Pathological changes

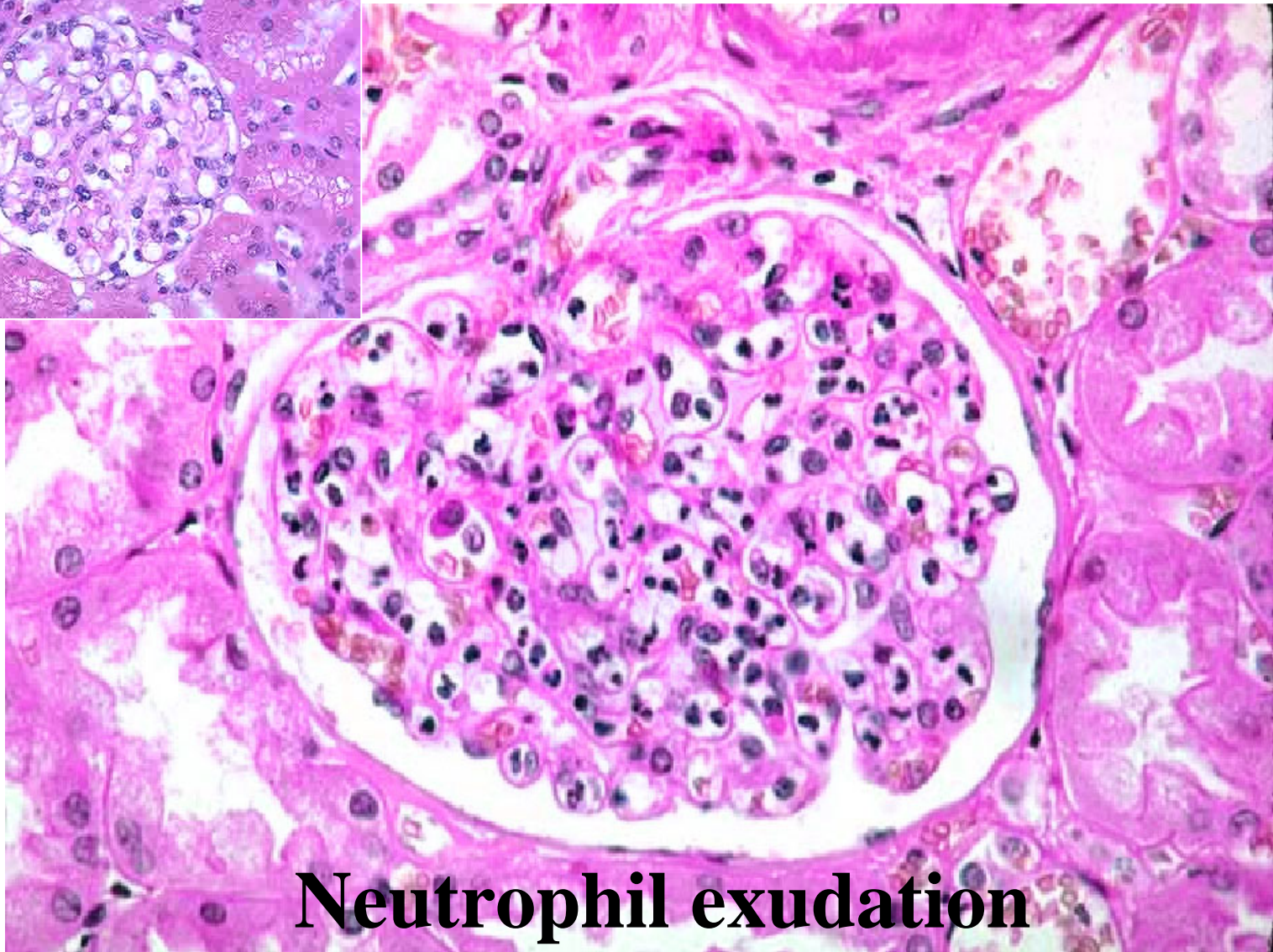
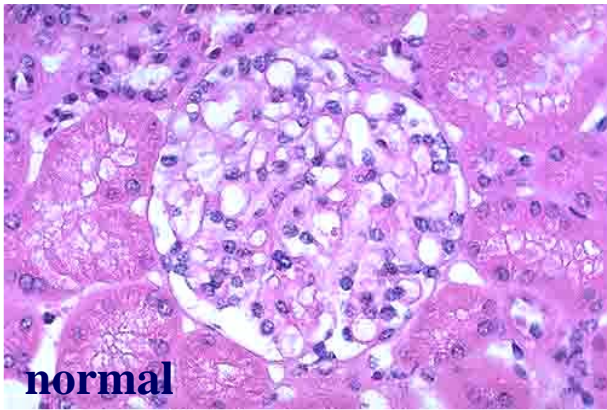


正常



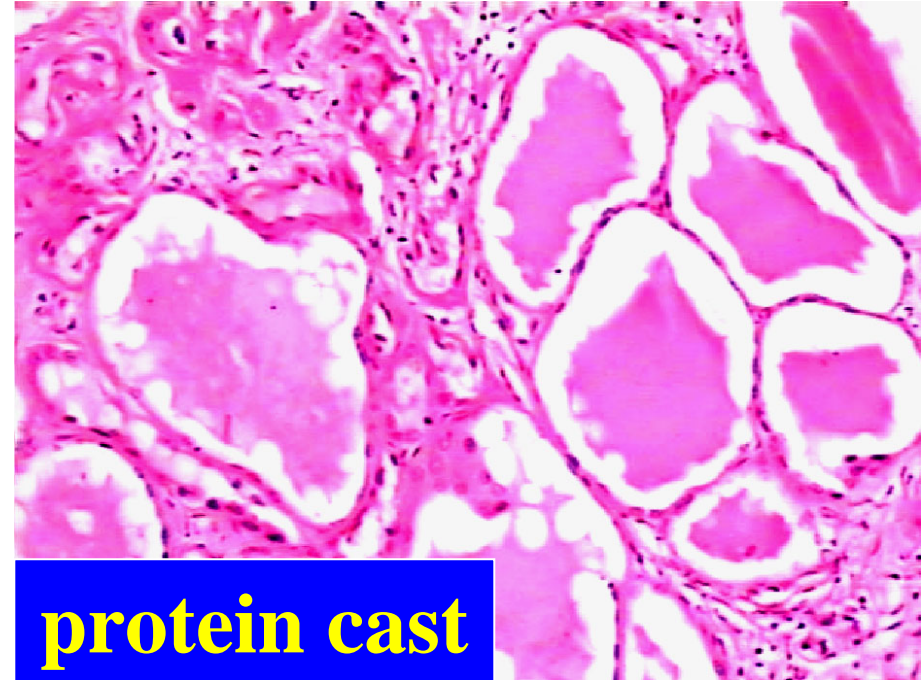
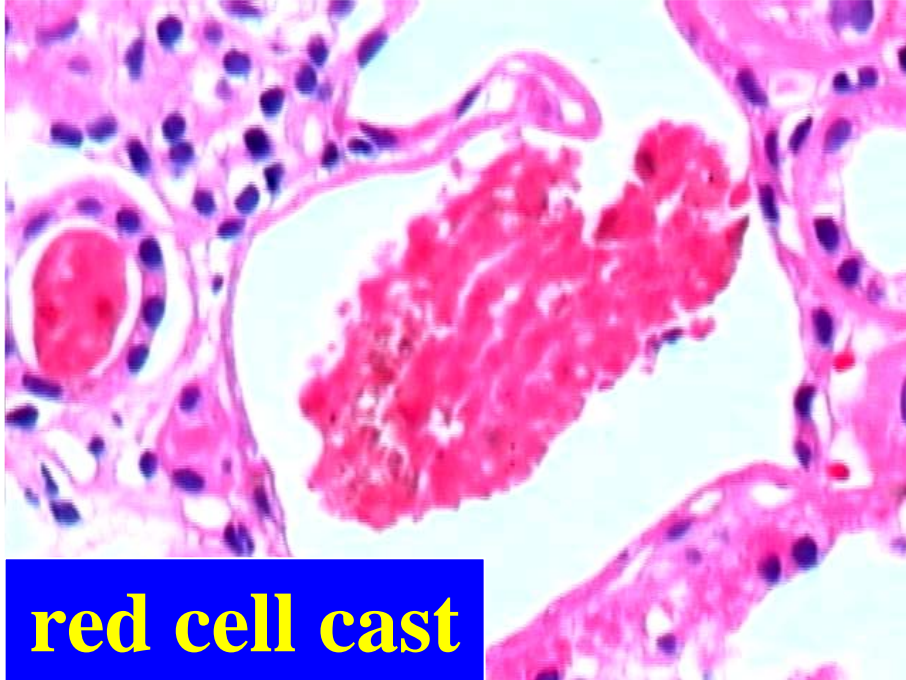


Pathological changes





Pathological changes

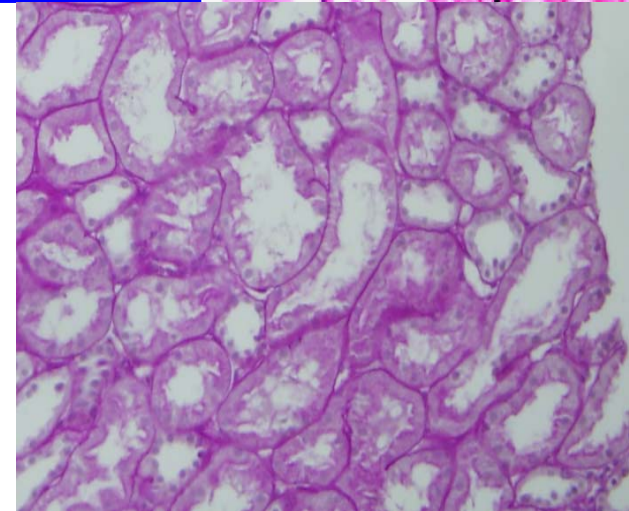


Tubule: degeneration

cast (protein, RBC, WBC, granular)

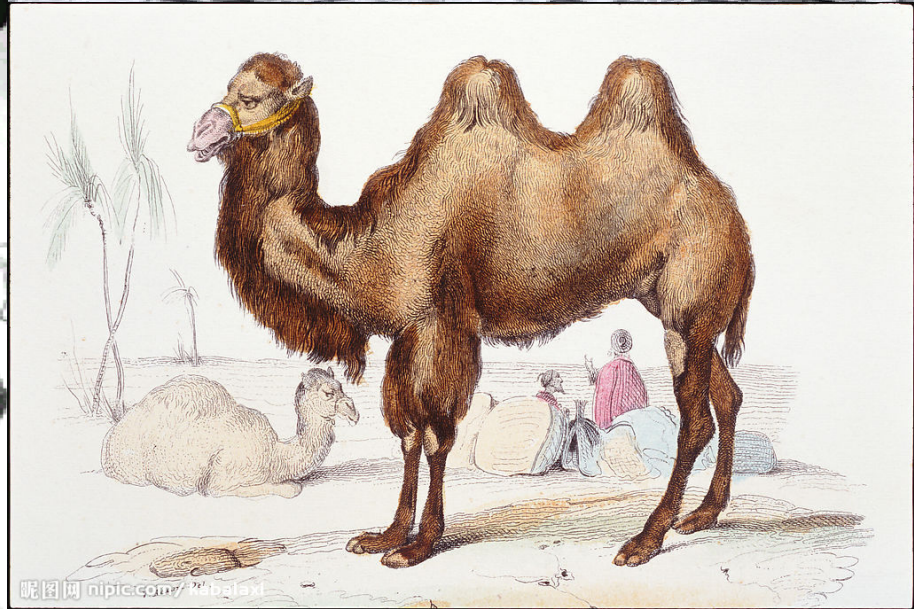
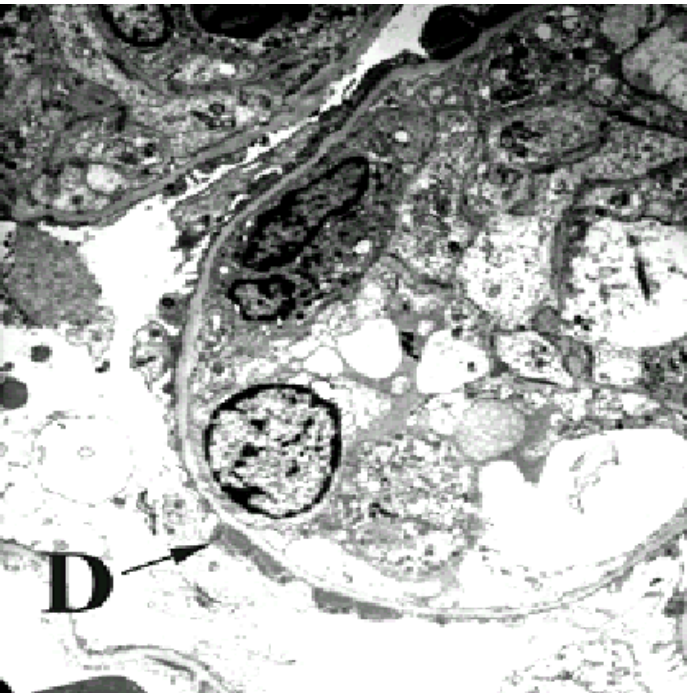
Interstitium: hyperemia, edema

infiltration of inflammatory cells



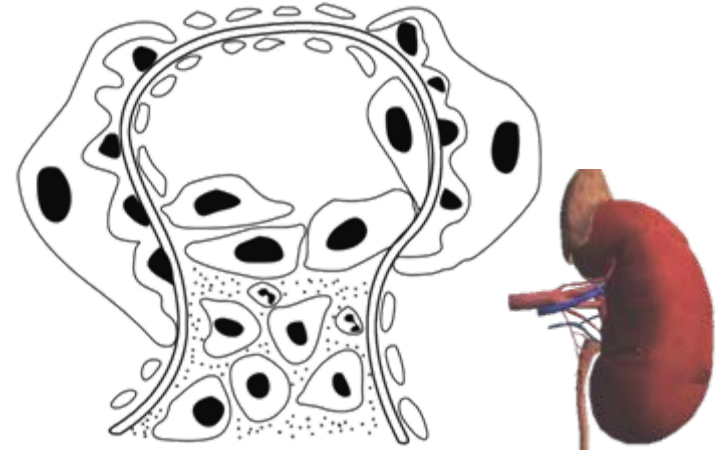


Pathological changes



EM:

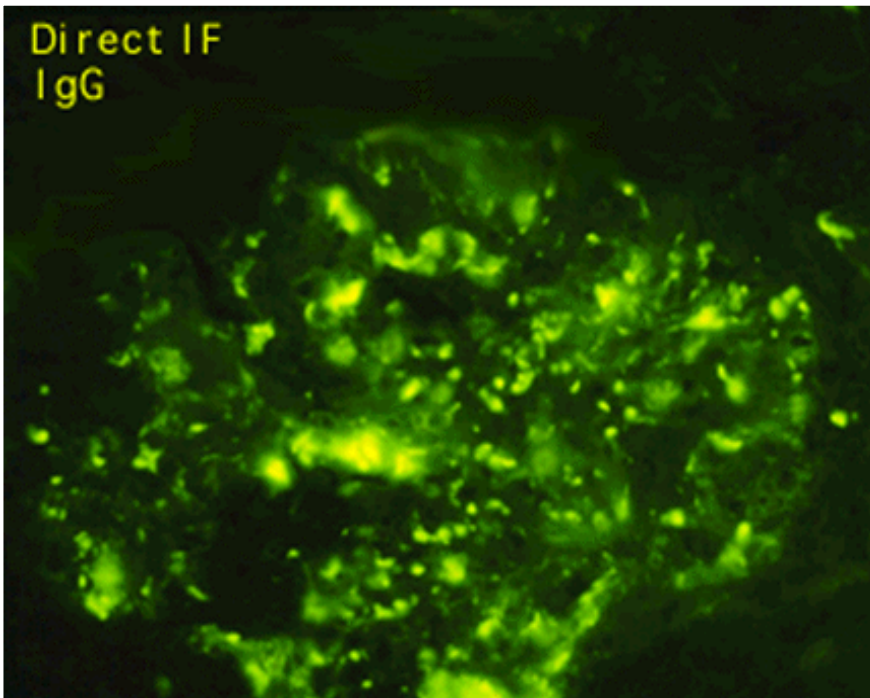
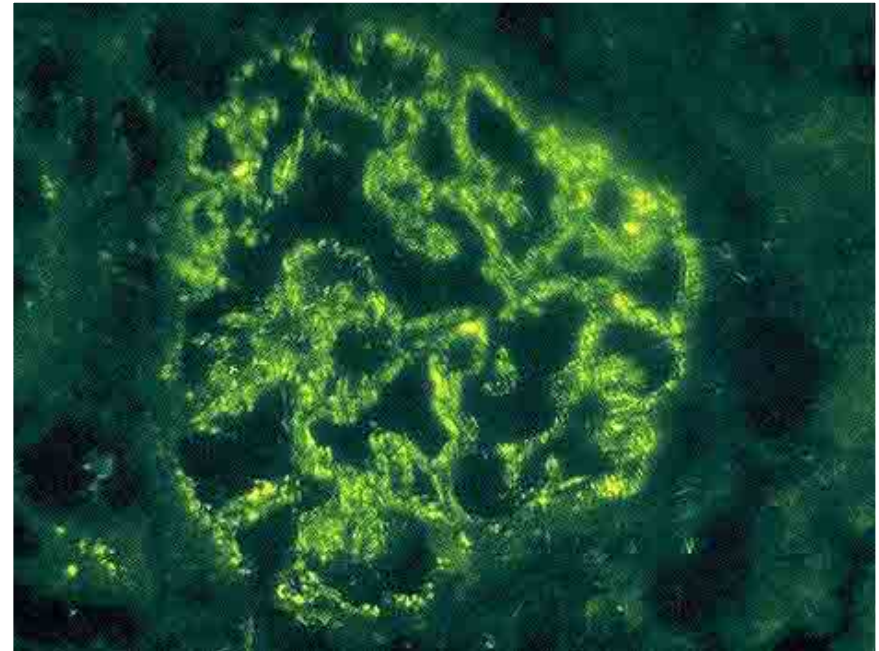
“humps” electron-dense deposits:
subepithelial cells (commonly)
subendothelial cells
intramembrane





Pathological changes

- **IF:** Immune deposits are distributed in the capillary loops in a **granular**, bumpy pattern which are positive for **IgG, IgM and C3**.



Circulating immune complex-mediated proliferative GN





Clinical features

**Most cases are in the pediatric age group
(Most patients are in childhood.)**

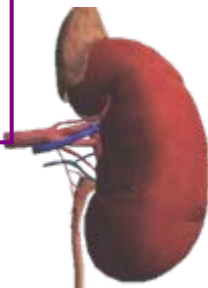
Appears 1-4 weeks after a streptococcal infection

Acute nephritic syndrome

- ◆ hematuria, proteinuria, urine casts, Oliguria or Anuria
- ◆ edema
- ◆ hypertension
- ◆ Serum levels of antistreptolysin O is often elevated.

Prognosis

Most children have excellent prognosis but a small number of patients rapidly progress to renal failure.





Acute diffuse proliferative GN

- ✓ **Gross: “red large kidney”**
- ✓ **LM: enlarged and hypercellular glomeruli**
- ✓ **EM: hump-like electron dense deposits on the subepithelial cells**
- ✓ **IF: granular fluorescence for IgG, IgM and C3**





Case

患儿男性，7岁。因眼睑浮肿、尿少3天入院。10天前在外玩耍时，右膝关节皮肤严重擦伤，2天后局部皮肤化脓，随后进行局部消炎处理，10天后出现上述症状。

体格检查：血压130/90mmHg，眼睑浮肿，双下肢浮肿。实验室检查：尿常规示，红细胞（+），尿蛋白（++），红细胞管型0~2/HP；24小时尿量400ml；尿素氮11.2mmol/L，（正常值<9mmol/L）；肌酐192 μ mol/L（<178 μ mol/L），均高于正常。

B超检查示：双肾对称增大。遂住院治疗，经对症支持治疗一个月病情基本好转，上述症状消失。

- 1、诊断是什么？与皮肤感染有无联系？为什么？
- 2、为何出现高血压、水肿、少尿、血尿、蛋白尿？





Case

患者，男性，26岁。因浮肿、血尿、少尿20天，恶心、呕吐3天入院。

体格检查：血压164/100mmHg，面色苍白，颜面部及双下肢浮肿。

实验室检查：24小时尿量150ml，尿色洗肉水样，尿蛋白（++），红细胞（+++），红细胞管型1~3个/HP；肌酐 $426\ \mu\text{mol/L}$ （ $< 178\ \mu\text{mol/L}$ ）。B超检查示：双肾增大。

诊断：快速进行性肾小球肾炎





Rapidly progressive GN, RPGN

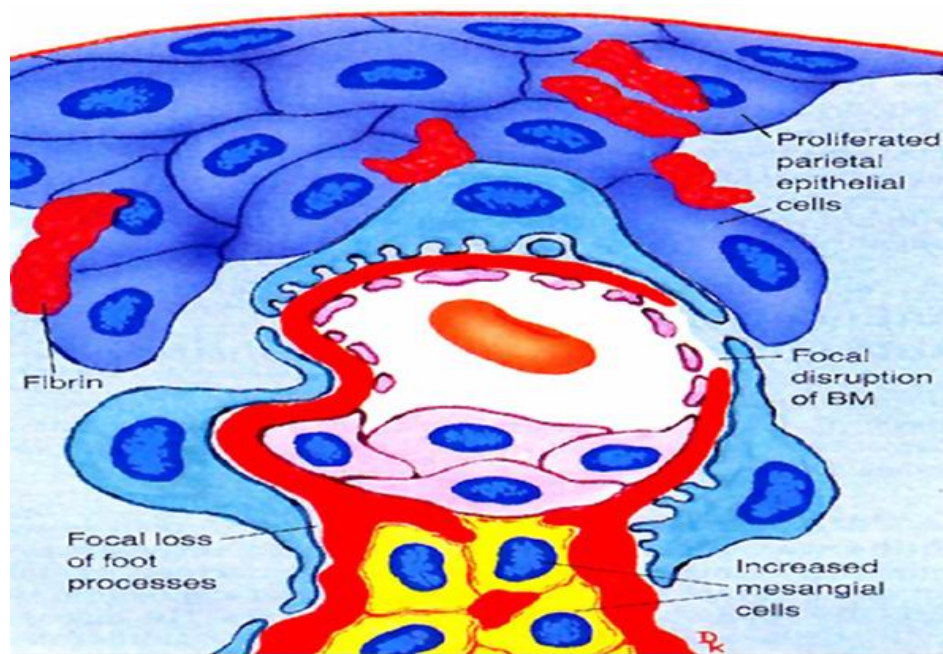




Introduction

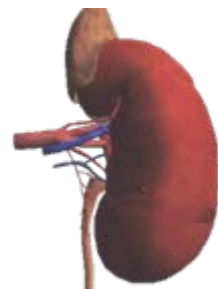
Pathological character

- Hyperplasia of **parietal epithelial cells** → formation of **crescent**
- **Crescentic glomerulonephritis, CrGN**



Clinical manifestation

Rapidly progressive nephritic syndrome





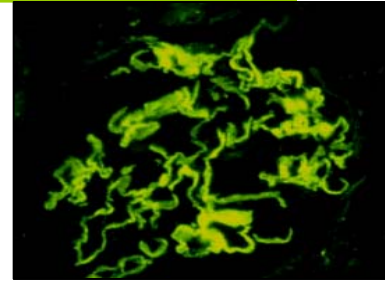
Classification and pathogenesis

Type I RPGN (anti-GBM antibody)

anti-GBM nephritis

linear immunofluorescence

linear deposits of IgG, C3
→ glomerular and
alveolar BM



Type II RPGN (Immune complex)

electron-dense deposits
BM and mesangium

granular immunofluorescence

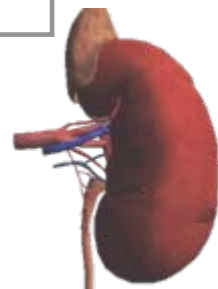
granular (BM, mesangium)



Type III RPGN (pauci-Immune)

There are minimal immune
deposits or none

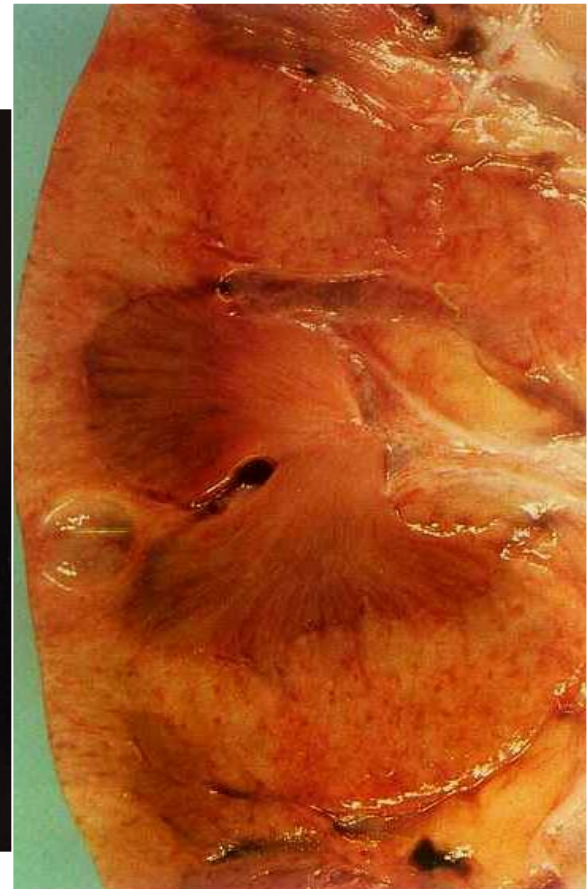
immunofluorescence (-)





Pathological changes

- ✓ **Gross: large pale kidney , the cortex is pale and swollen**





Pathological changes

LM: Crescent formation (>70%)

Crescents: glomeruli(>50%)

proliferation of parietal epithelial cells in Bowman's space
infiltration of monocytes, macrophages and fibrin

Process:

cellular crescent



fibrous-cellular crescent



fibrous crescent

EM: crescents, focal defect or disruption of BM

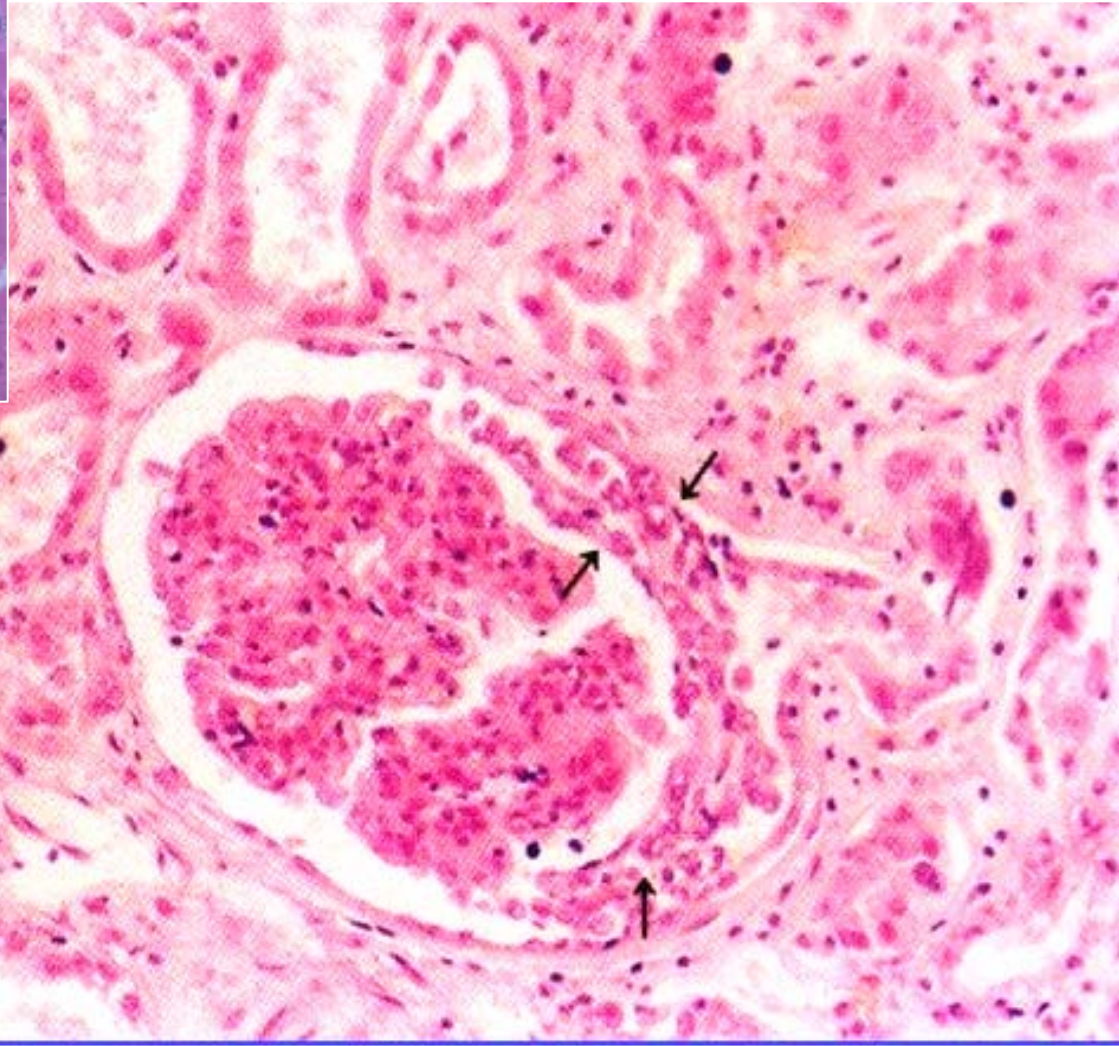
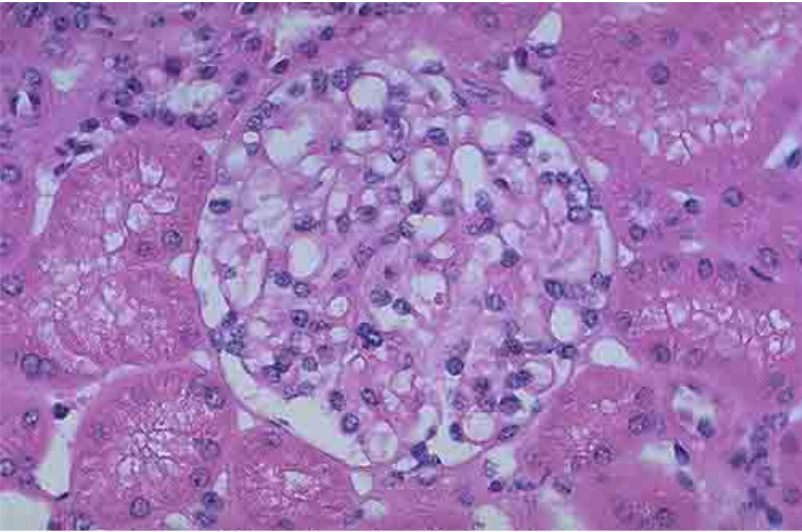
IF: Type I (linear immunofluorescence), Type II (granular fluorescence)

Type III (no fluorescence)



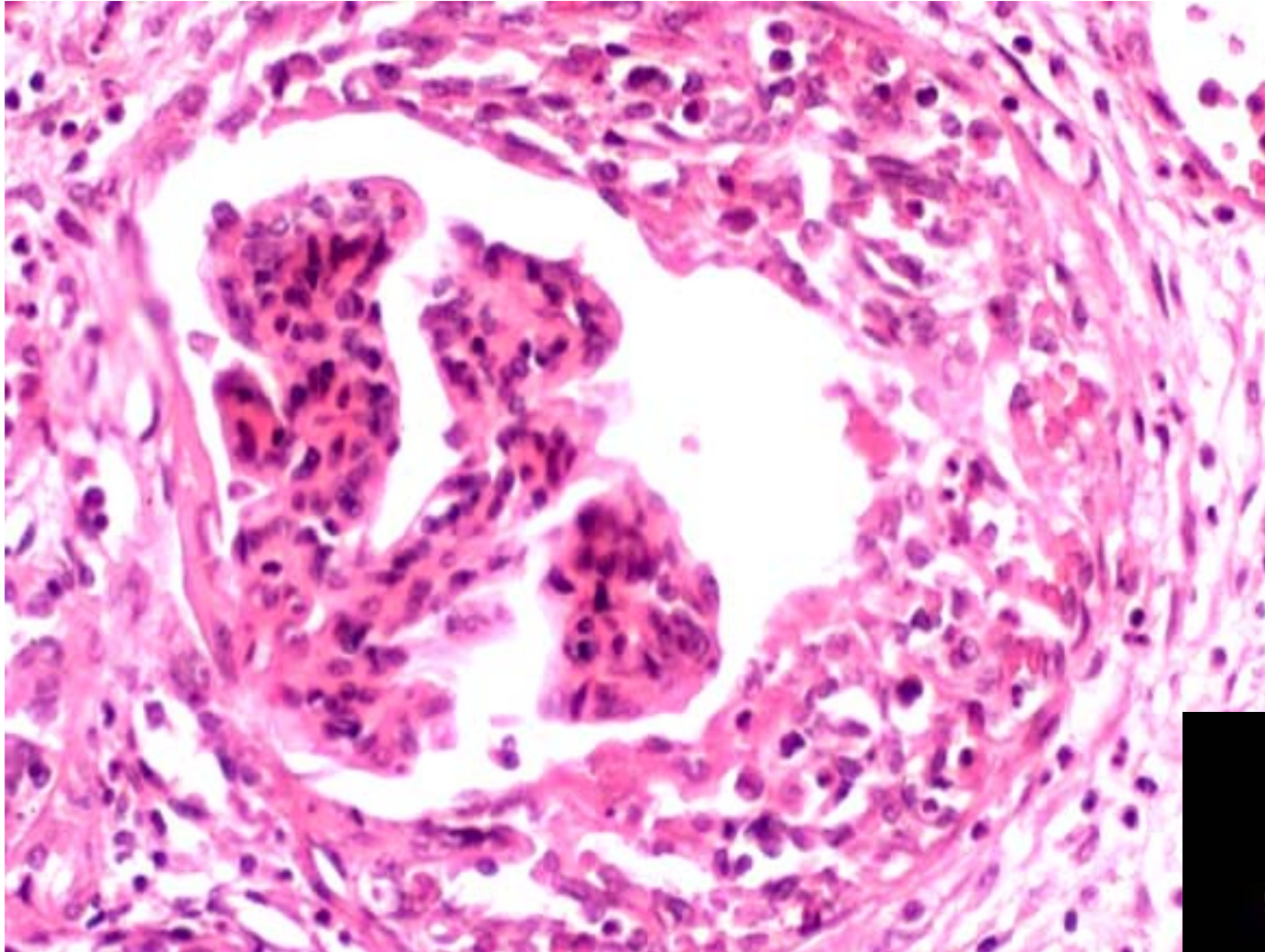


Pathological changes

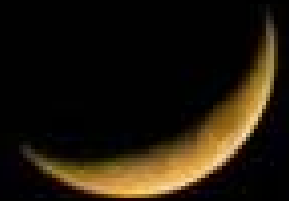




Pathological changes

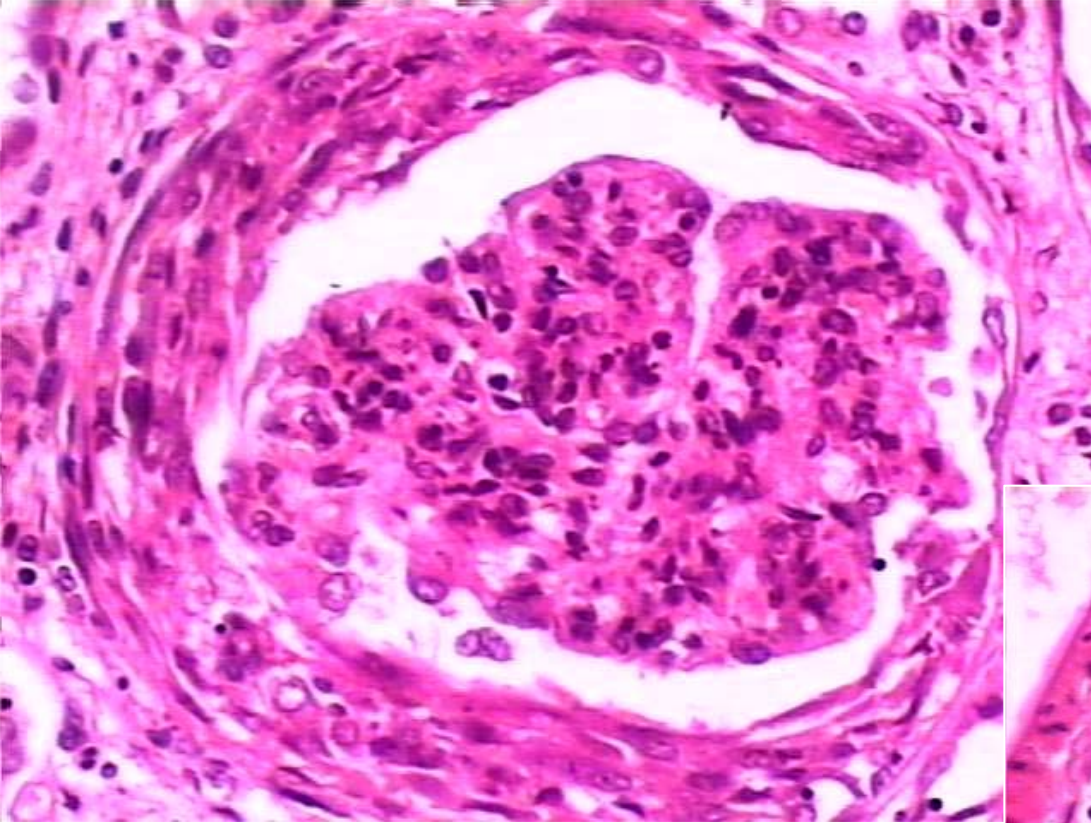


cellular crescent



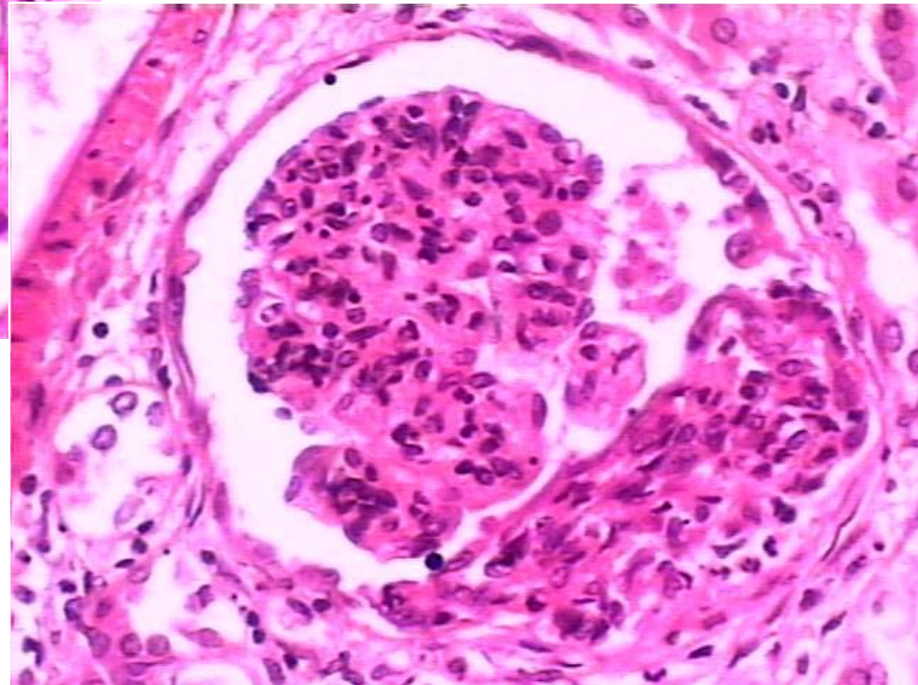


Pathological changes



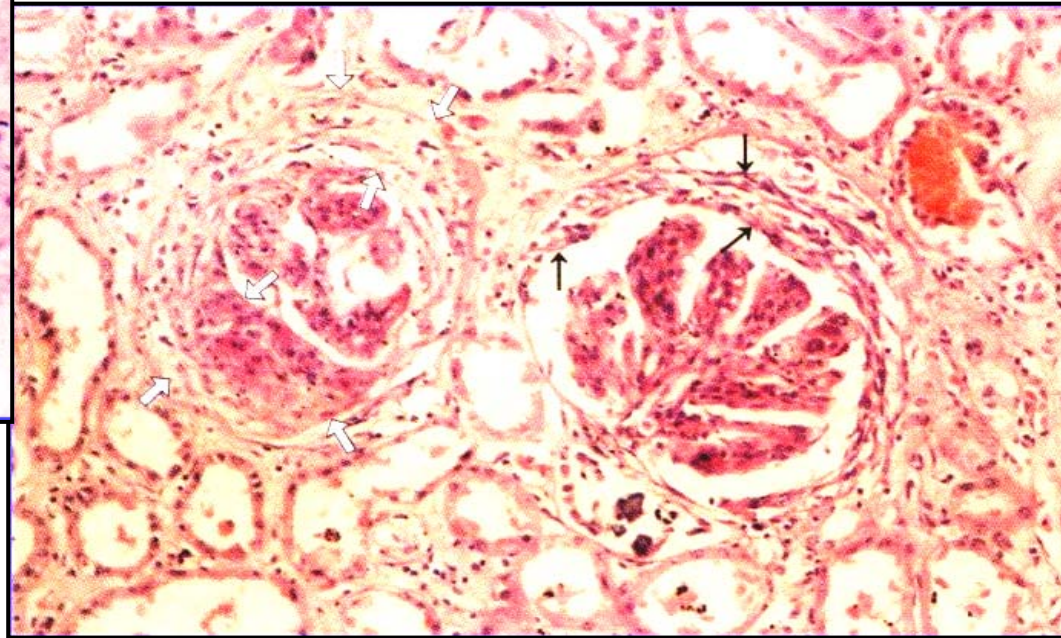
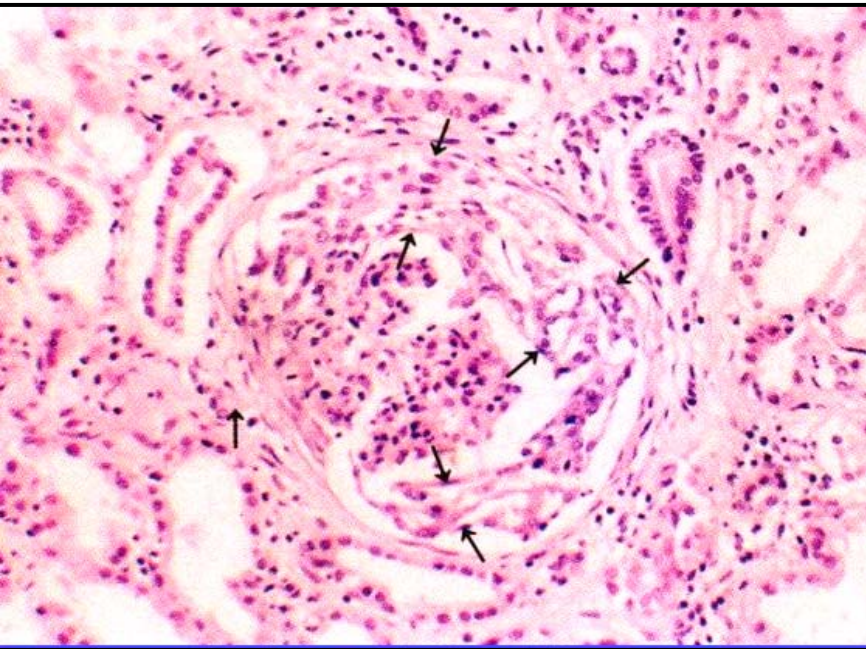
fibrous-crescent

fibrous-cellular crescent





Pathological changes

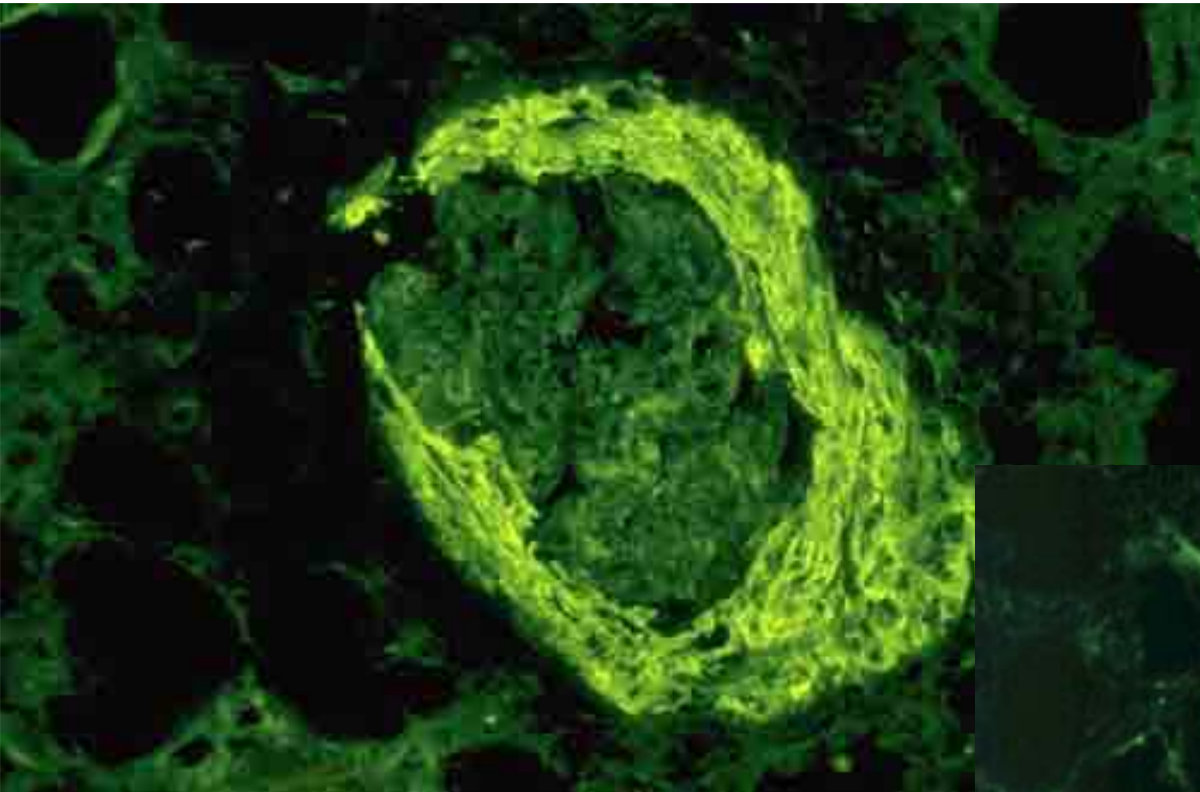


fibrous-crescent

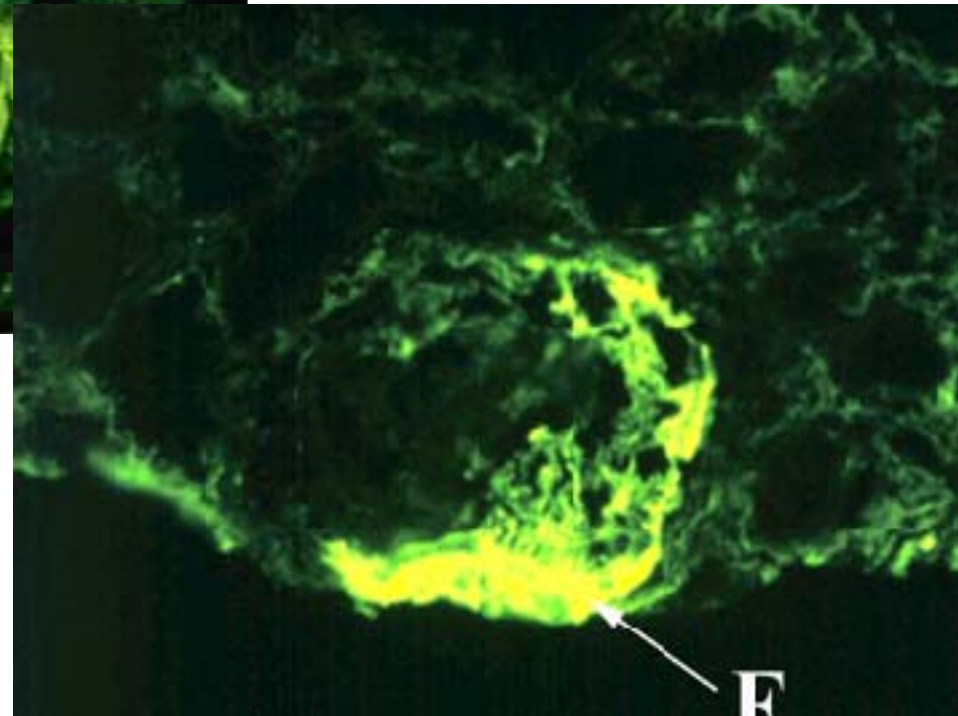




Pathological changes

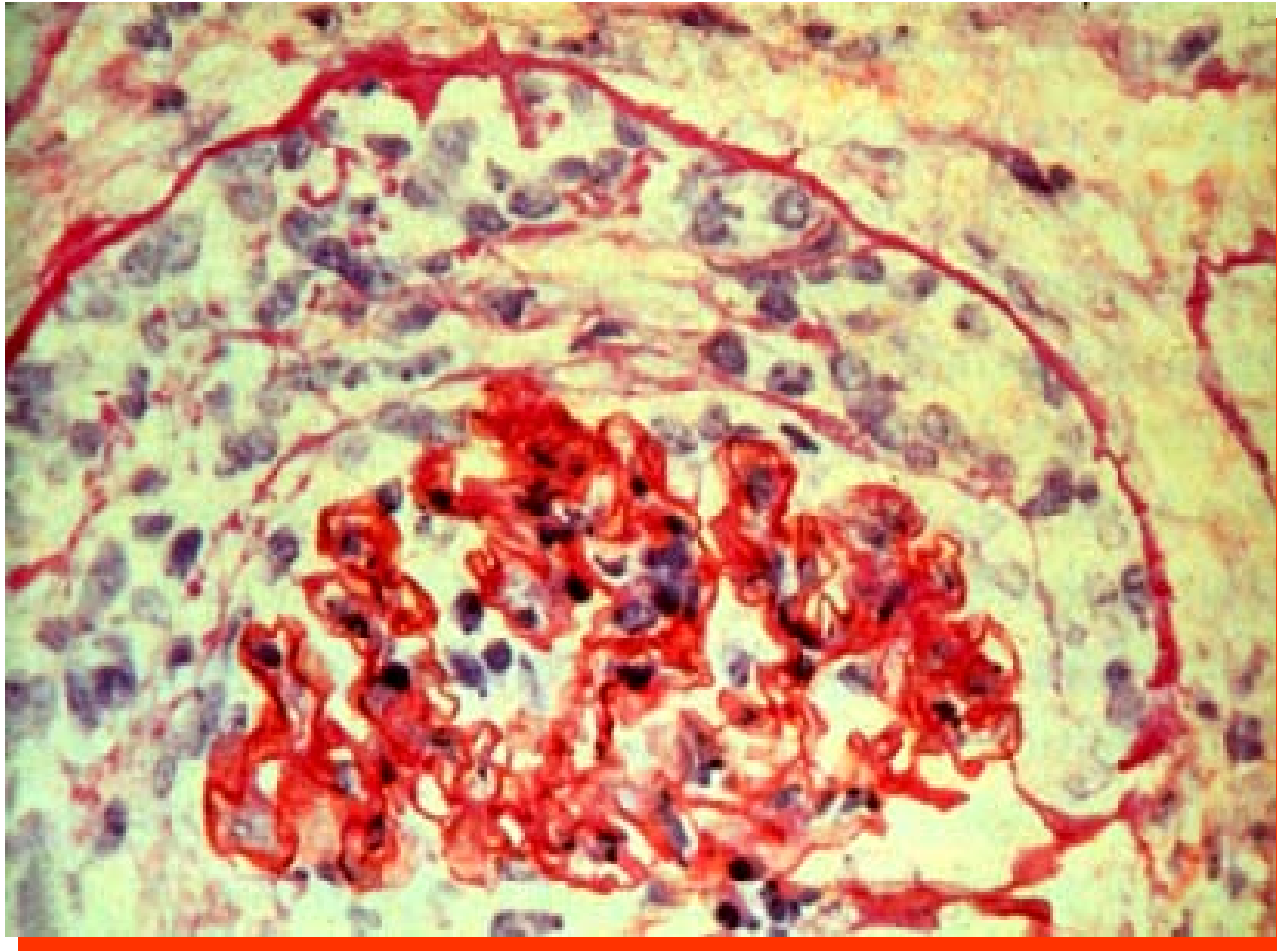


This IF micrograph of a glomerulus demonstrates positivity with antibody to fibrinogen.





Pathological changes

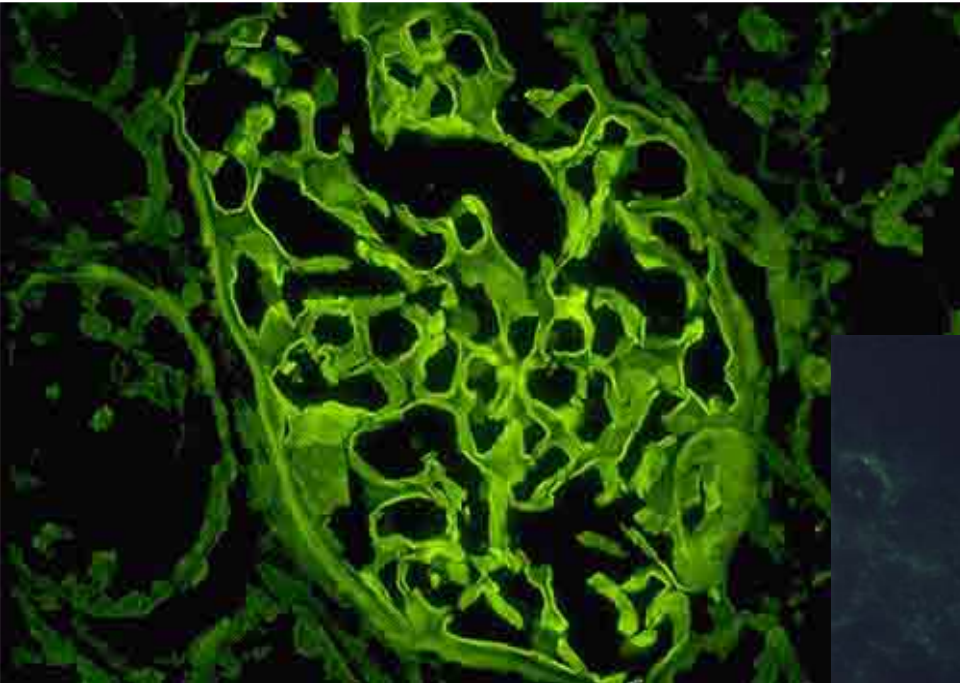


Type I, linear immunofluorescence of IgG

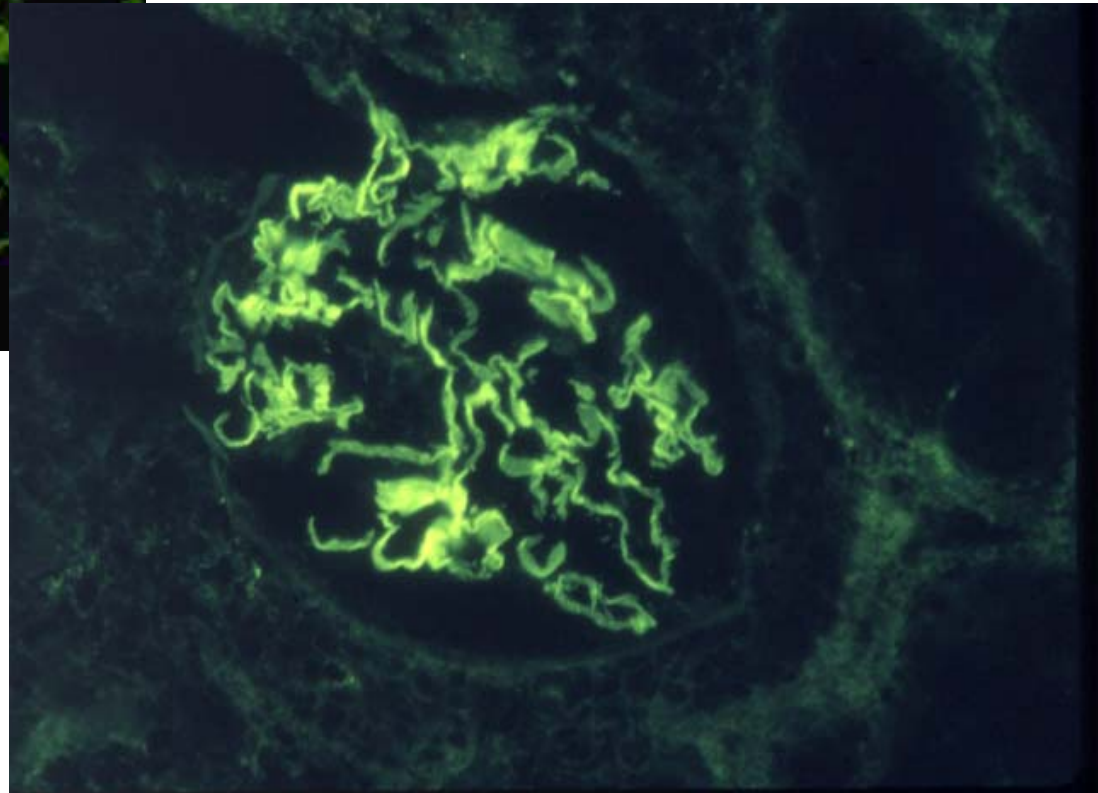




Pathological changes

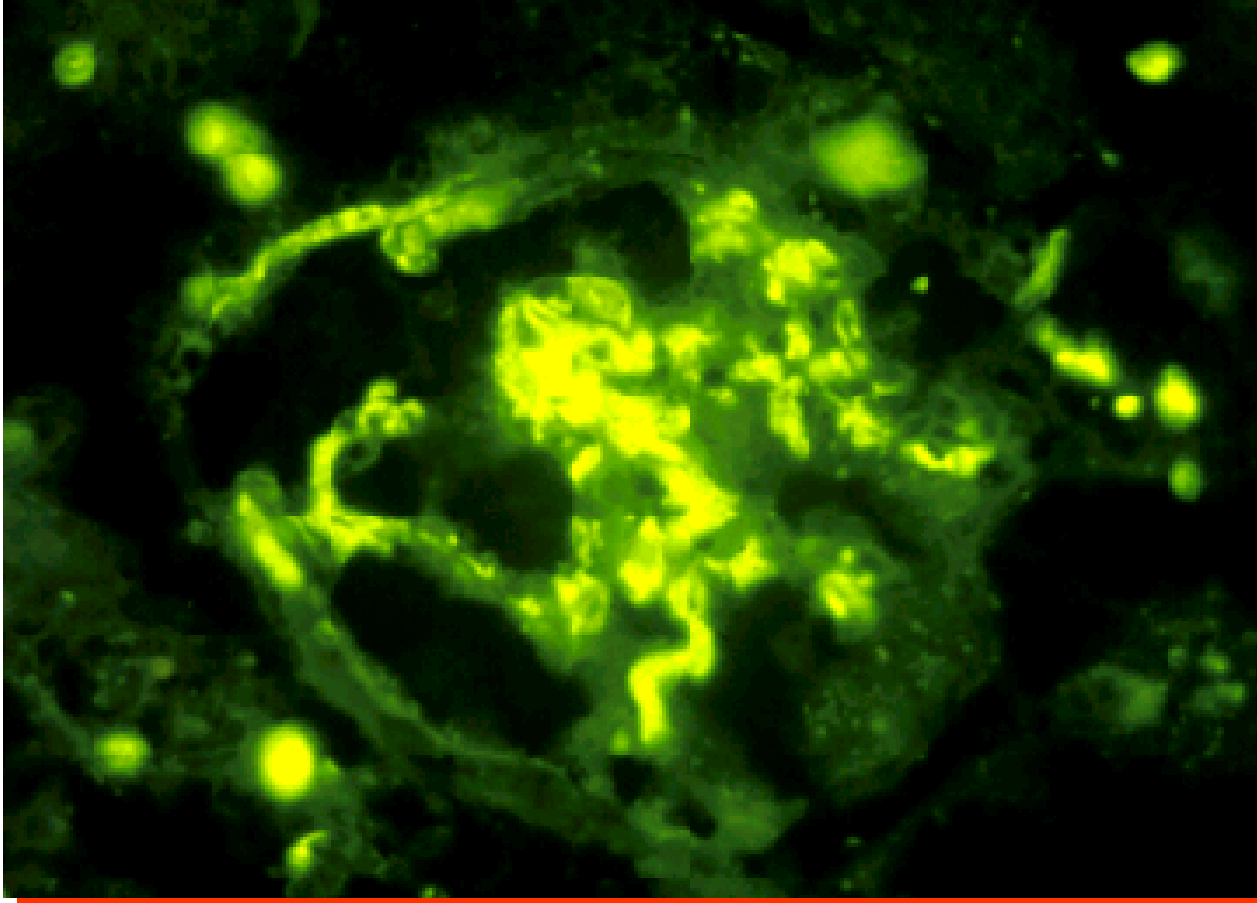


fluorescence in a smooth,
diffuse, linear pattern



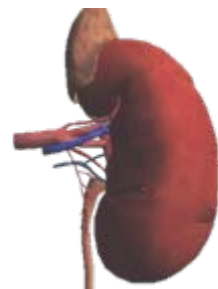


Pathological changes



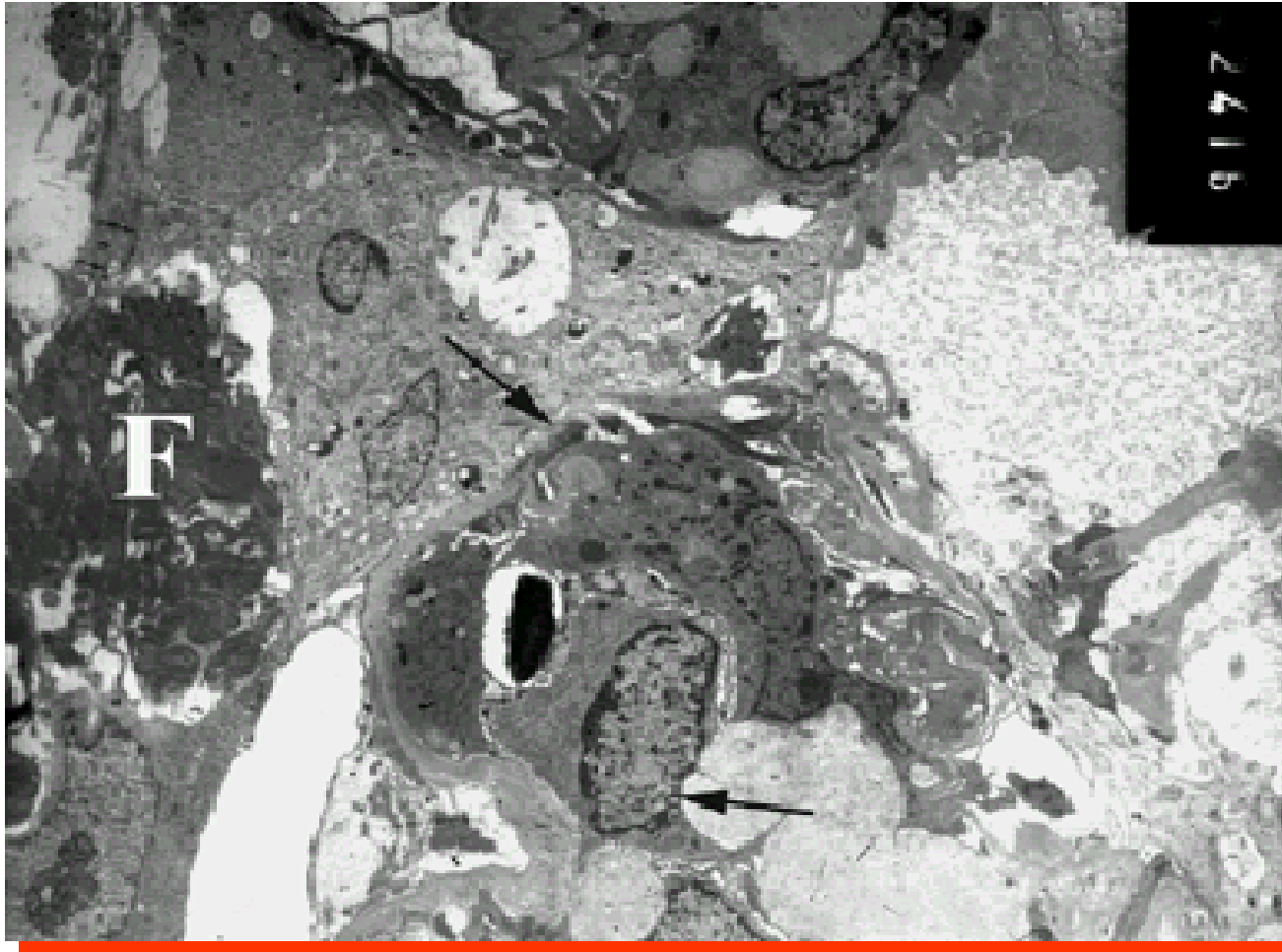
Crescentic glomerulonephritis, Type II

Direct IF shows **mass and granular pattern** staining of the glomerular capillary and Mesangium for IgA.

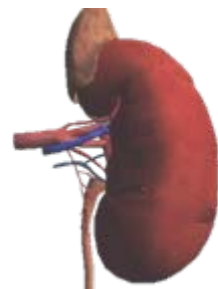




Pathological changes



GBM break(↑), Fibrin deposition (F)。





Pathological changes

Renal tubules : hyaline change

Intracellular hyaline



hyaline droplets

Atrophy

Interstitium

{ edema

{ inflammatory infiltration





Clinical features

- Characterized clinically by **rapid and progressive loss of renal function** associated with **severe oliguria** and death from renal failure within weeks to months.
- **Rapidly progressive nephritic syndrome**

Hematuria, Proteinuria, Oliguria or Anuria, Edema, Azotemia → acute renal failure





Rapidly progressive GN (Crescentic GN)

Pathological changes

- ✓ **Gross: large pale kidney**
- ✓ **LM: formation of crescents**
- ✓ **EM: crescents, focal defect or disruption of BM**
- ✓ **IF: Type I (linear immunofluorescence), Type II (granular fluorescence)
Type III (no fluorescence)**





summary

Antigens

Endogenous antigens

Exogenous antigens

Antibody: IgG、IgA、IgM

Antigen+Antibody=immune complex

Circulating immune complex nephritis

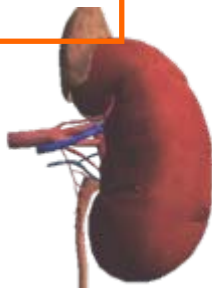
In situ immune complex deposition

Antibodies to glomerular cells

Cell-mediated immunity in glomerulonephritis

Activation of alternative complement pathway

.....





Basic pathological changes

Inflammation

Proliferation: Epithelial cells, Mesangial cells, Endothelia Cells ;

GBM thickening and Mesangial matrix increase

Degeneration: Fibrinoid necrosis, Hyaline change and Sclerosis. Epithelial cell of tubules degeneration

Exsudation: Neutrophils, LCs , Monocytes

Immunoreaction

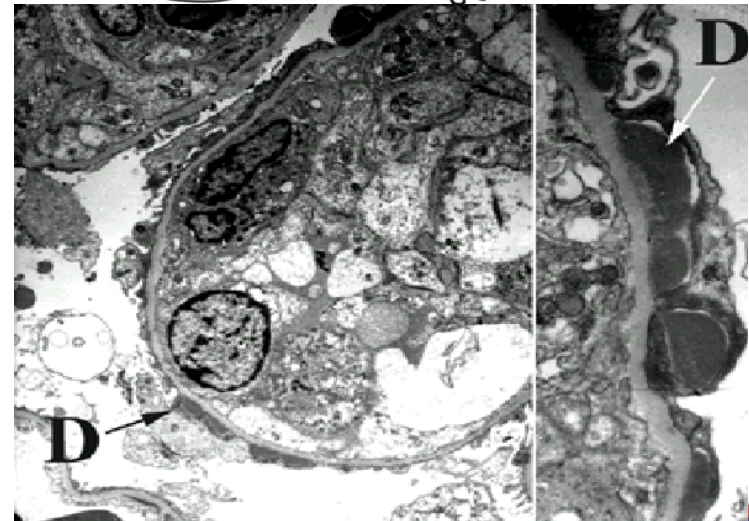
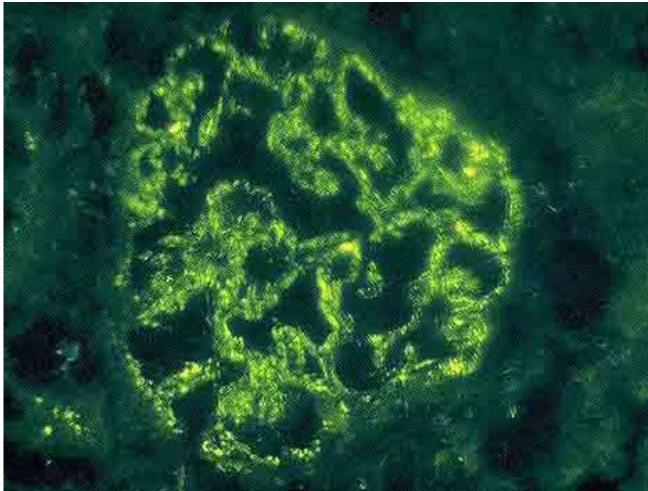
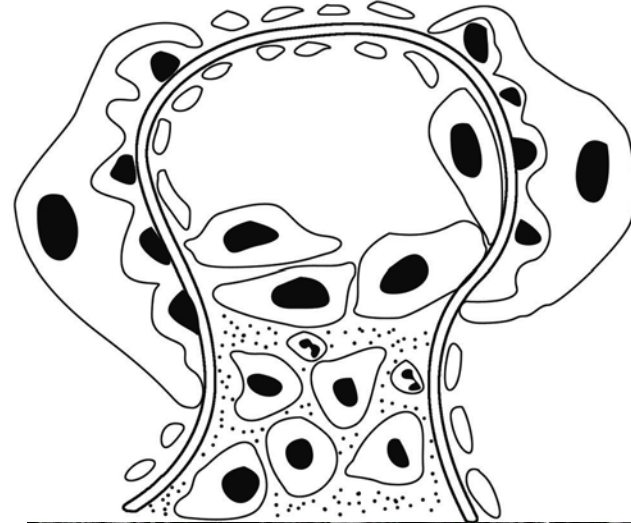
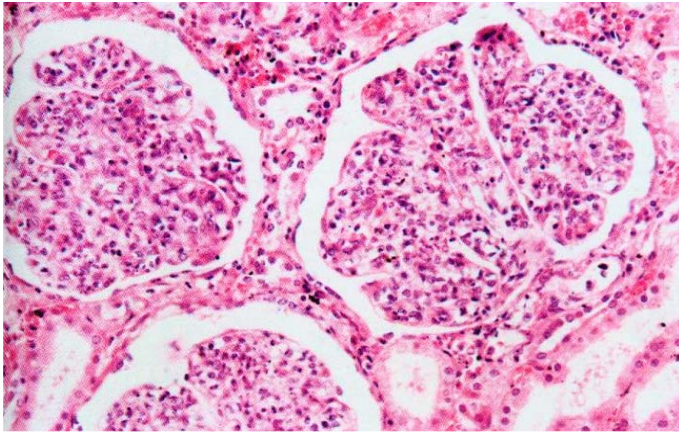
Antigen+Antibody=immune complex
Circulating immune complex nephritis
In situ immune complex deposition





summary

Acute diffuse proliferative glomerulonephritis, Post-infectious GN



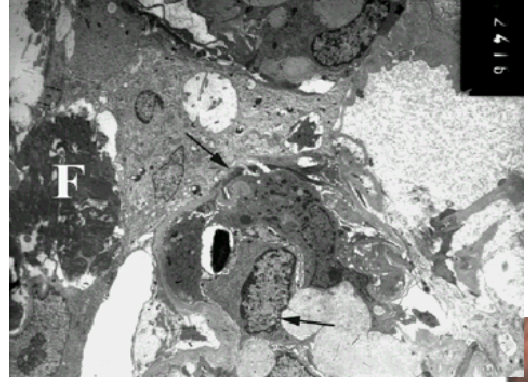
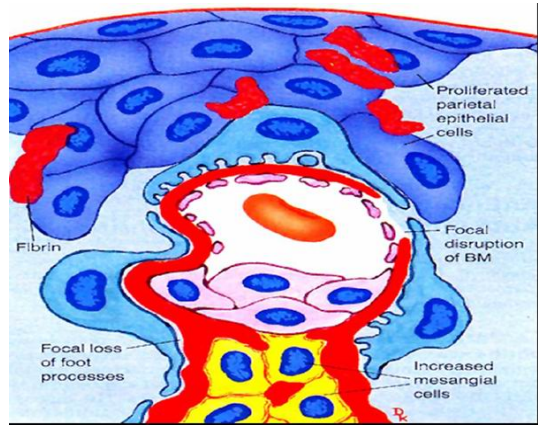
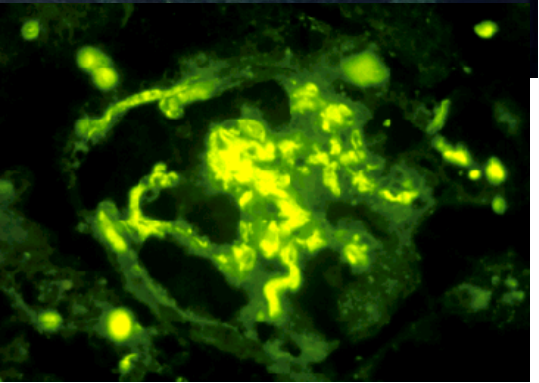
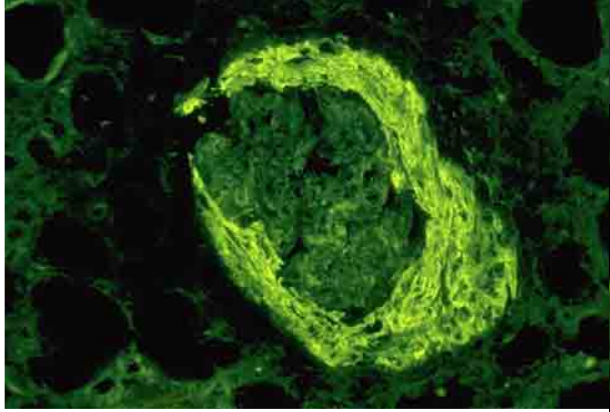
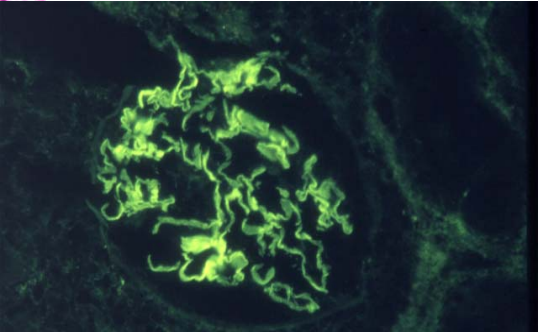
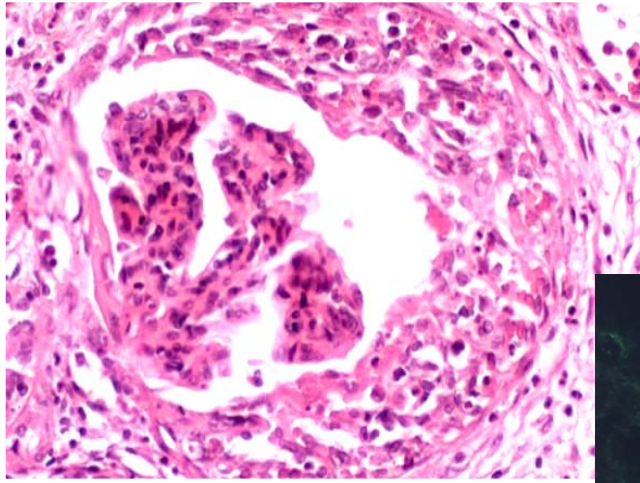
acute nephritic syndrome





summary

rapidly progressive glomerulonephritis, RPGN



rapidly progressive nephritic syndrome

