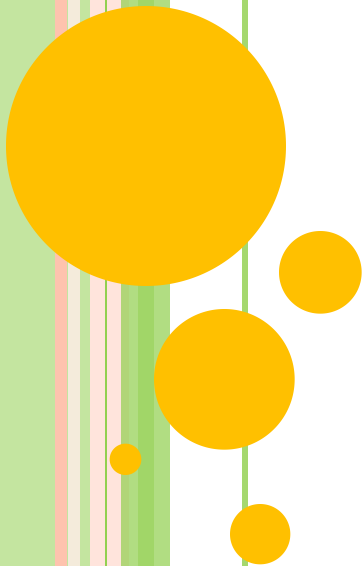


GLOMERULONEPHRITIS

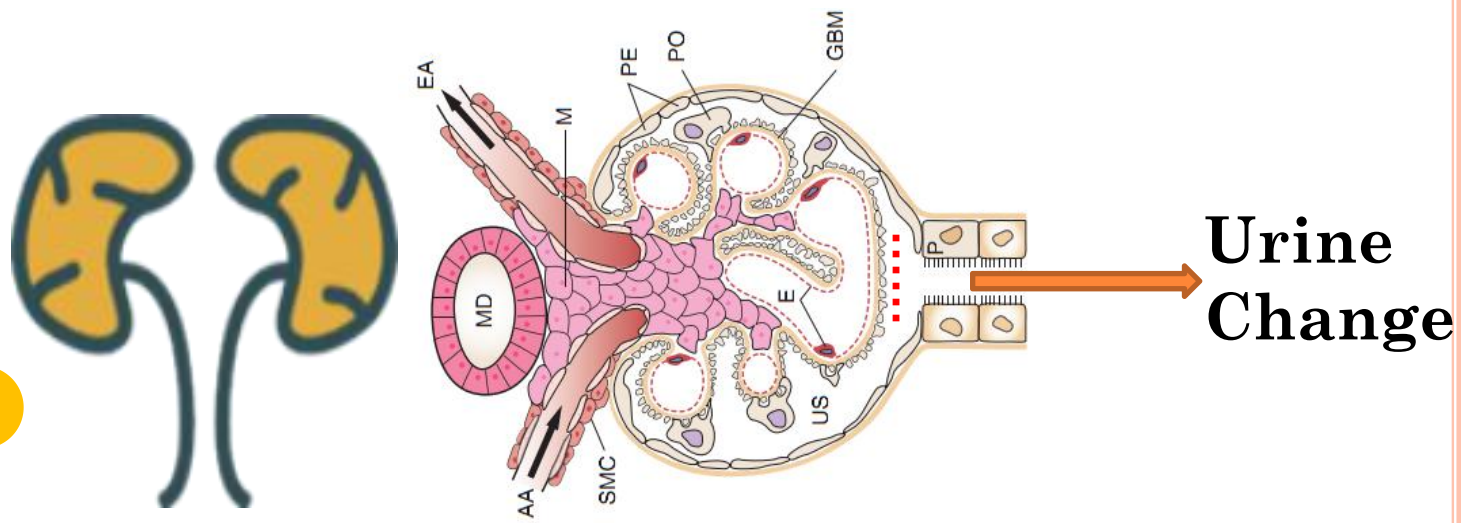
**The Second Clinic Medical College
Southern Medical University**

**彭芬芬 (Peng Fenfen)
doctorpff@163.com**





GLOMERULONEPHRITIS



CLINIC CLASSIFICATION

- Acute glomerulonephritis(AGN)

急性肾小球肾炎

- Rapidly progressive glomerulonephritis(RPGN)

急进性肾小球肾炎

- Chronic glomerulonephritis(CGN)

慢性肾小球肾炎

- Asymptomatic hematuria and/or proteinuria

无症状性血尿和或蛋白尿



CLINIC CLASSIFICATION

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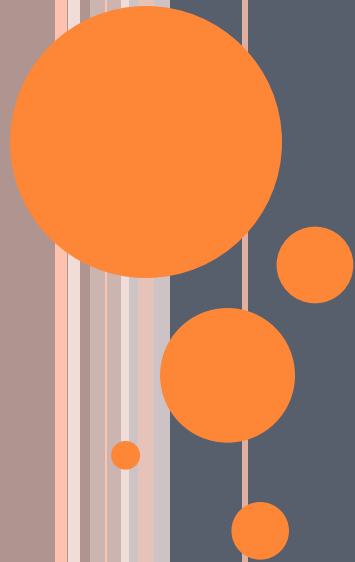
ACUTE GLOMERULONEPHRITIS

POSTSTREPTOCOCCAL GLOMERULONEPHRITIS

After

Infection

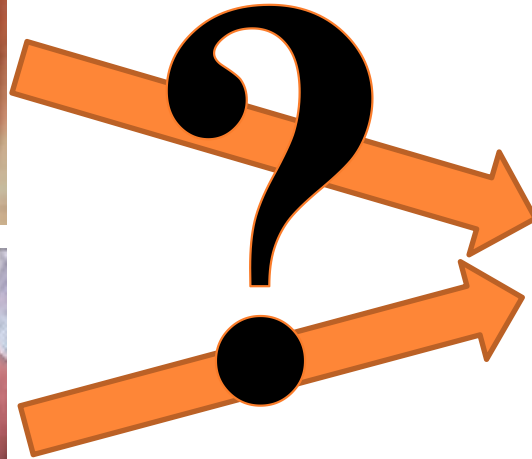
链球菌感染后肾小球肾炎



ACUTE GLOMERULONEPHRITIS

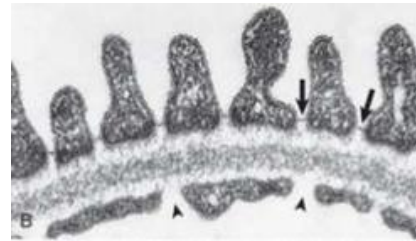
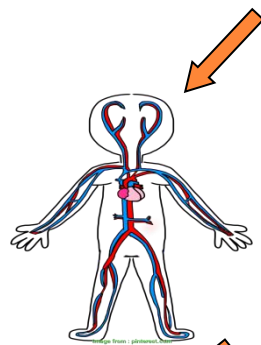
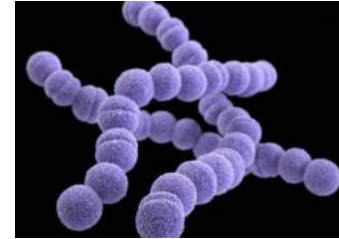
POSTSTREPTOCOCCAL GLOMERULONEPHRITIS

链球菌感染后肾小球肾炎



PATHOGENESIS

group A β -haemolytic streptococcus
(a nephritogenic type)



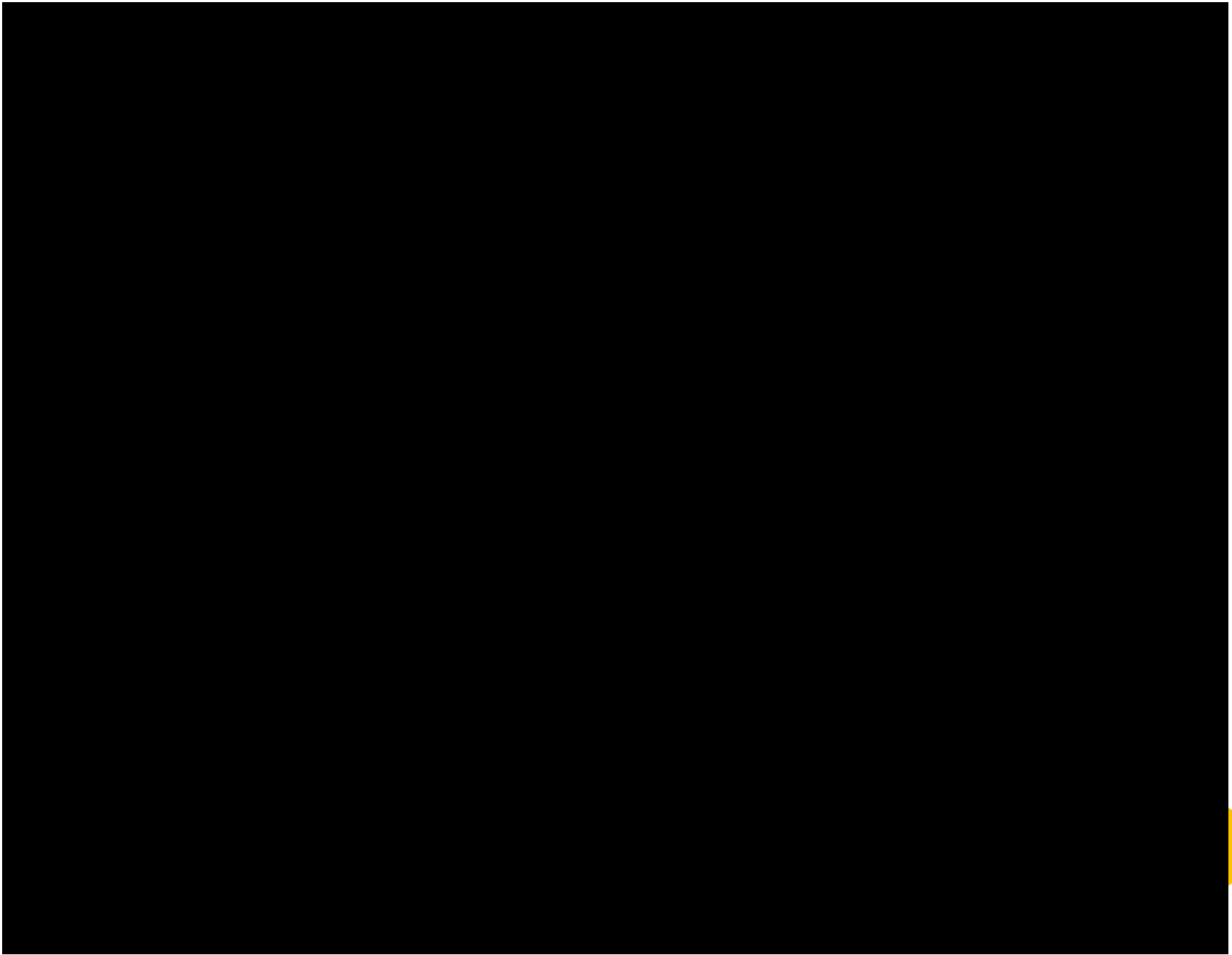
Immune response → Latency period

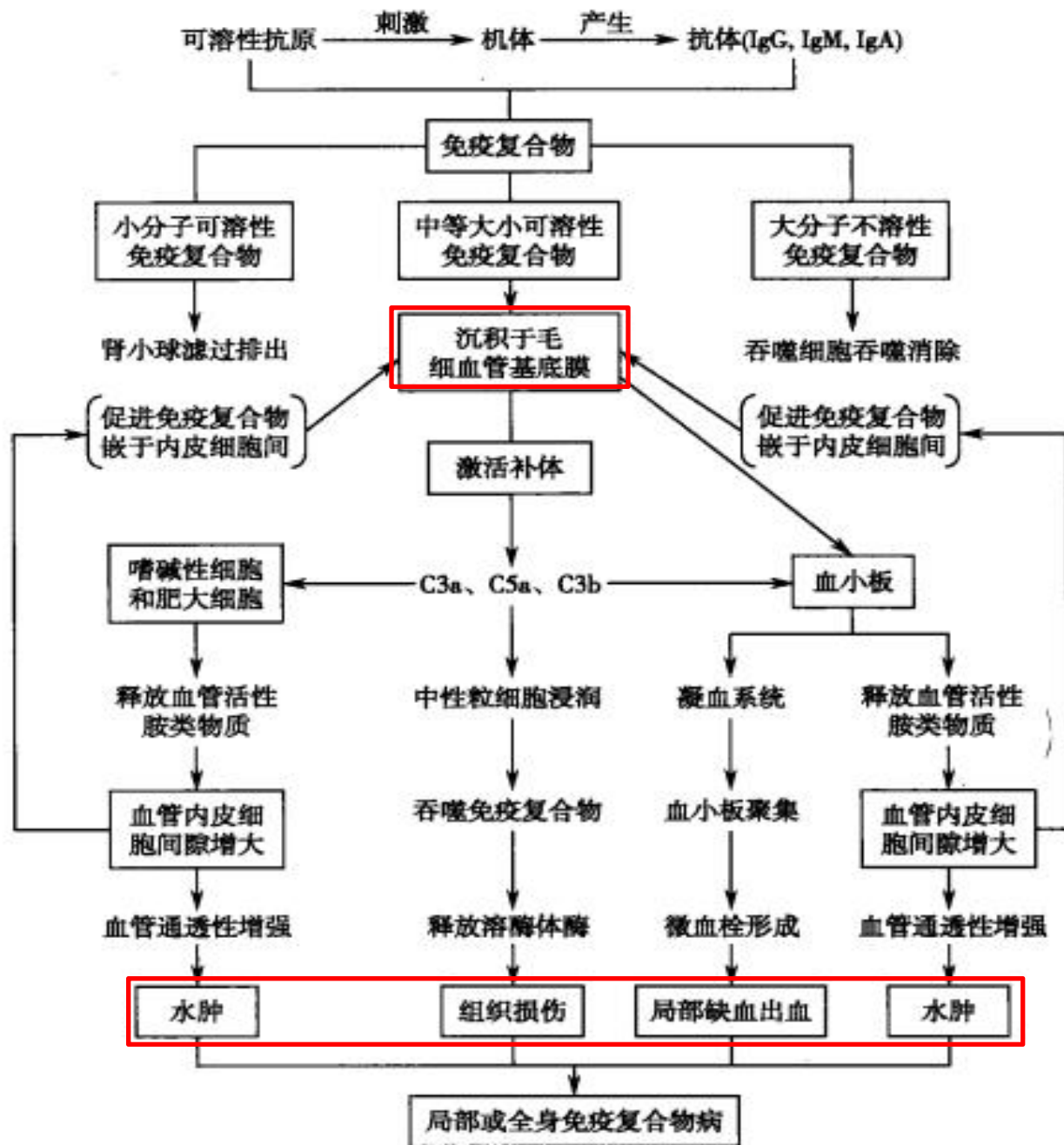
CIC

In situ IC

Complement activation
Inflammation → PSGN



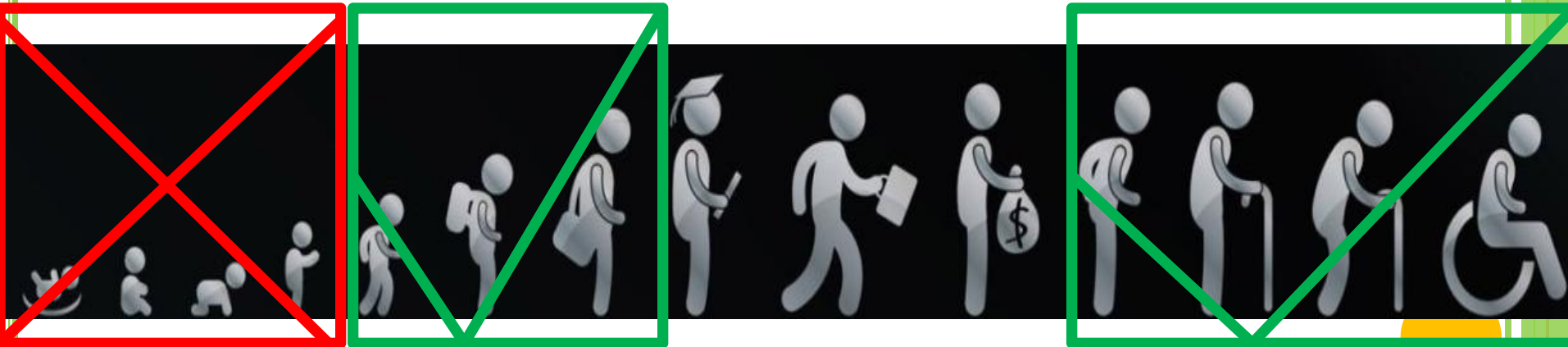




EPIDEMIOLOGY

uncommon in children less than three years of age
children between 5 and 12 years of age (**most cause**)
older patients (greater than 60 years of age)

twice as frequent in males as in females



EPIDEMIOLOGY

- Group A streptococcal (GAS) infection

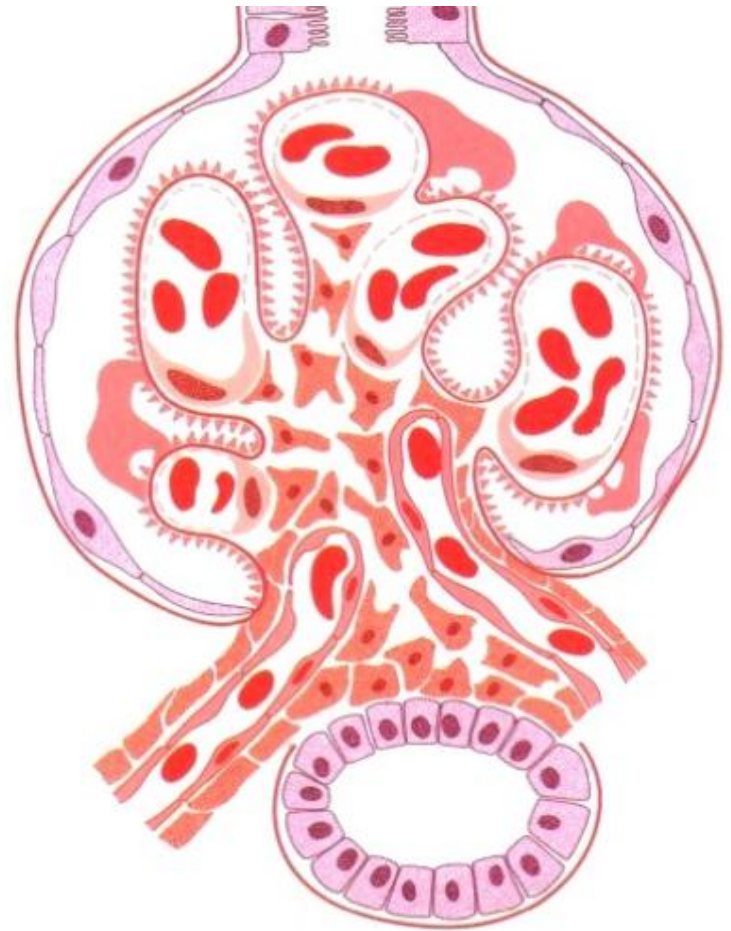
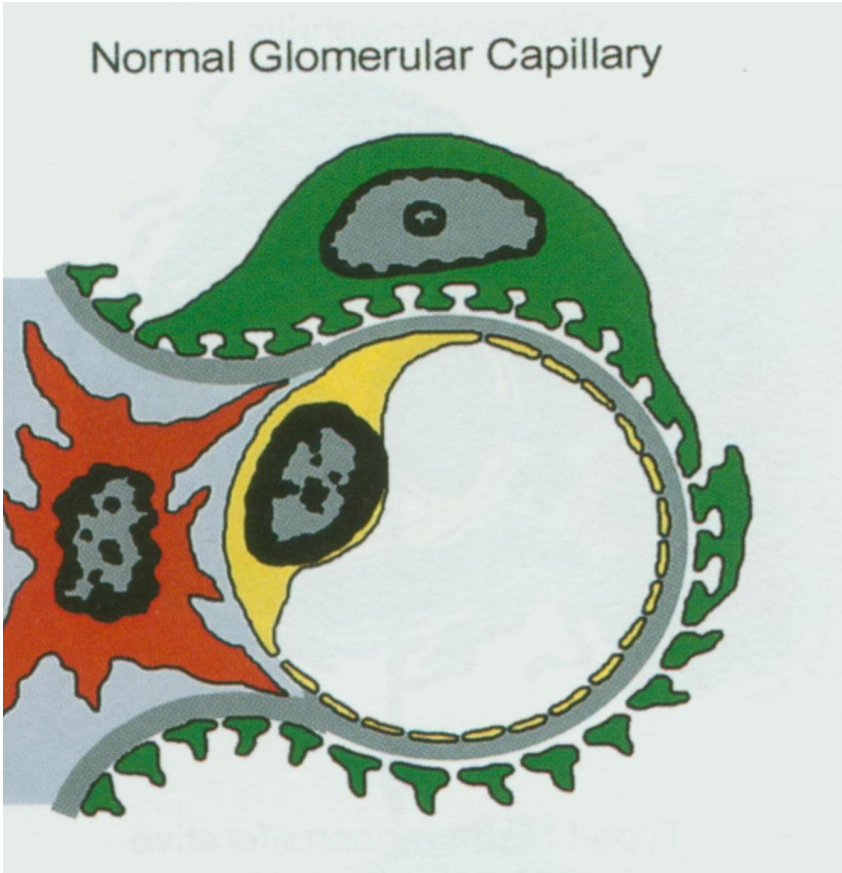
~~100%~~

(GAS epidemic) approximately 5 to 10 percent with pharyngitis and 25 percent with skin infections



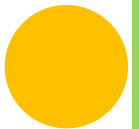
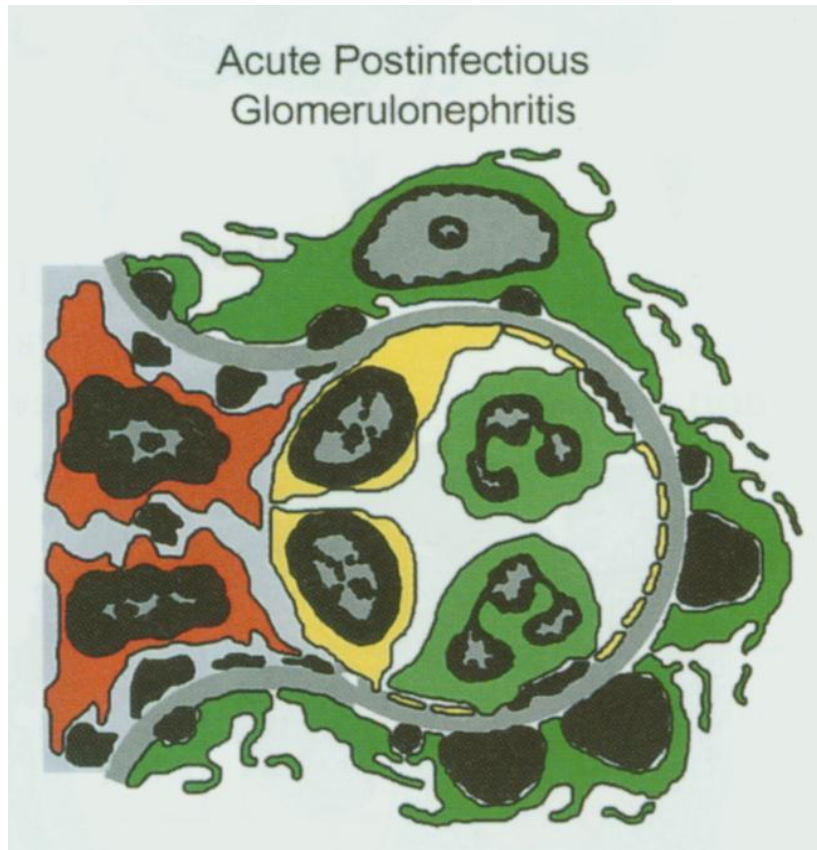
PATHOLOGY

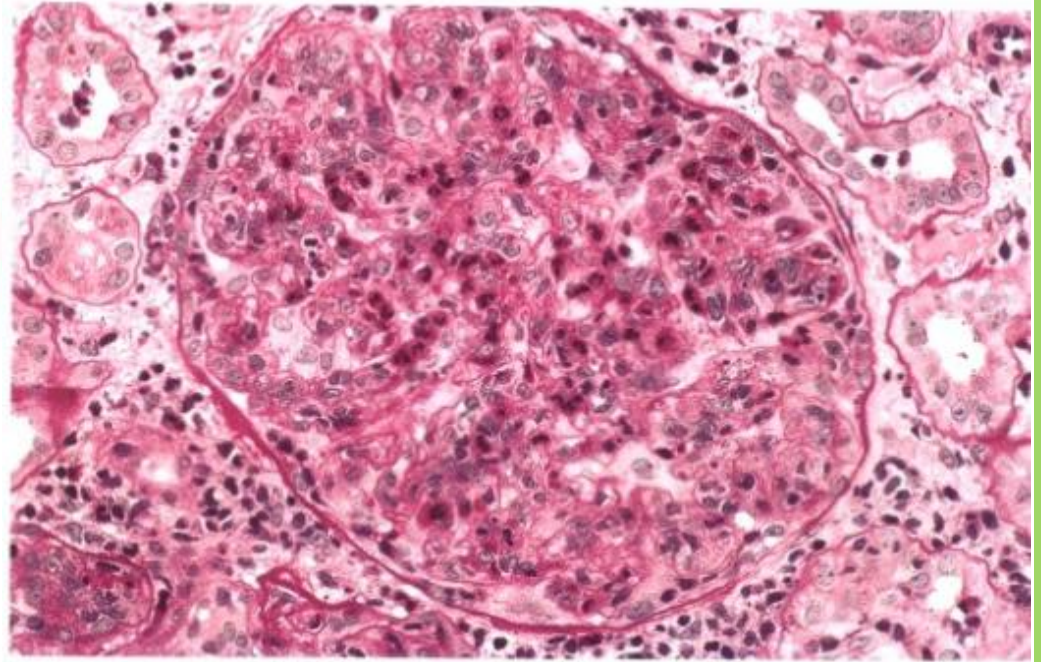
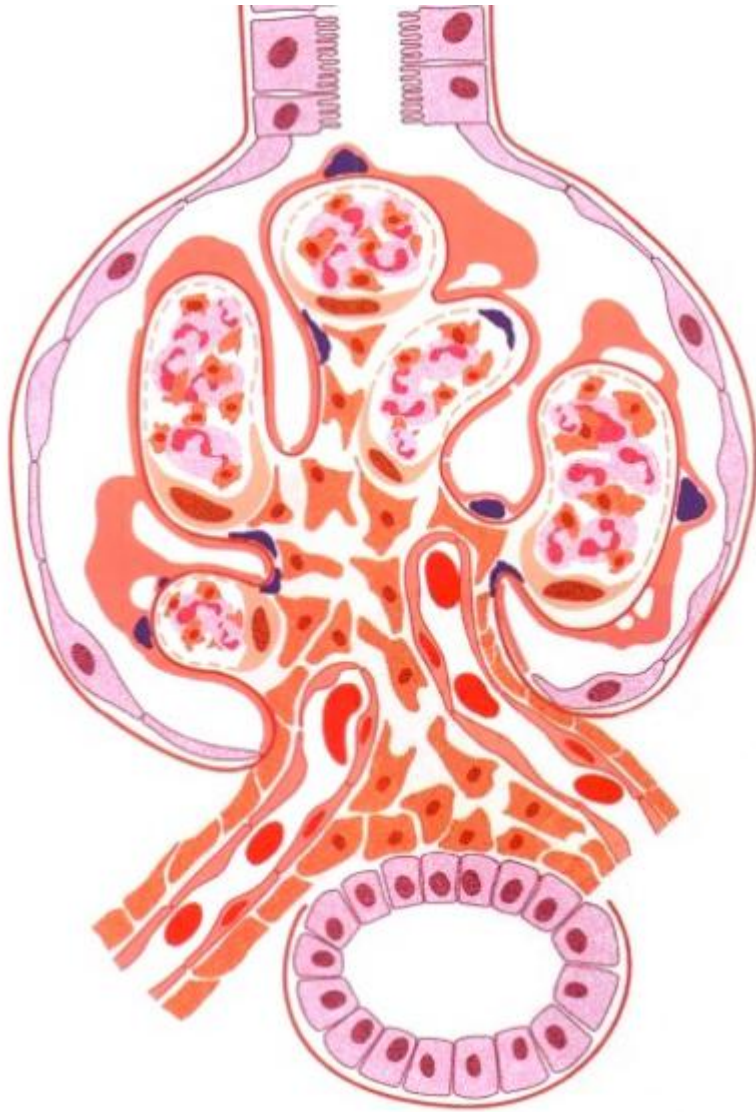
Normal Glomerular Capillary



PATHOLOGY

endocapillary proliferative glomerulonephritis





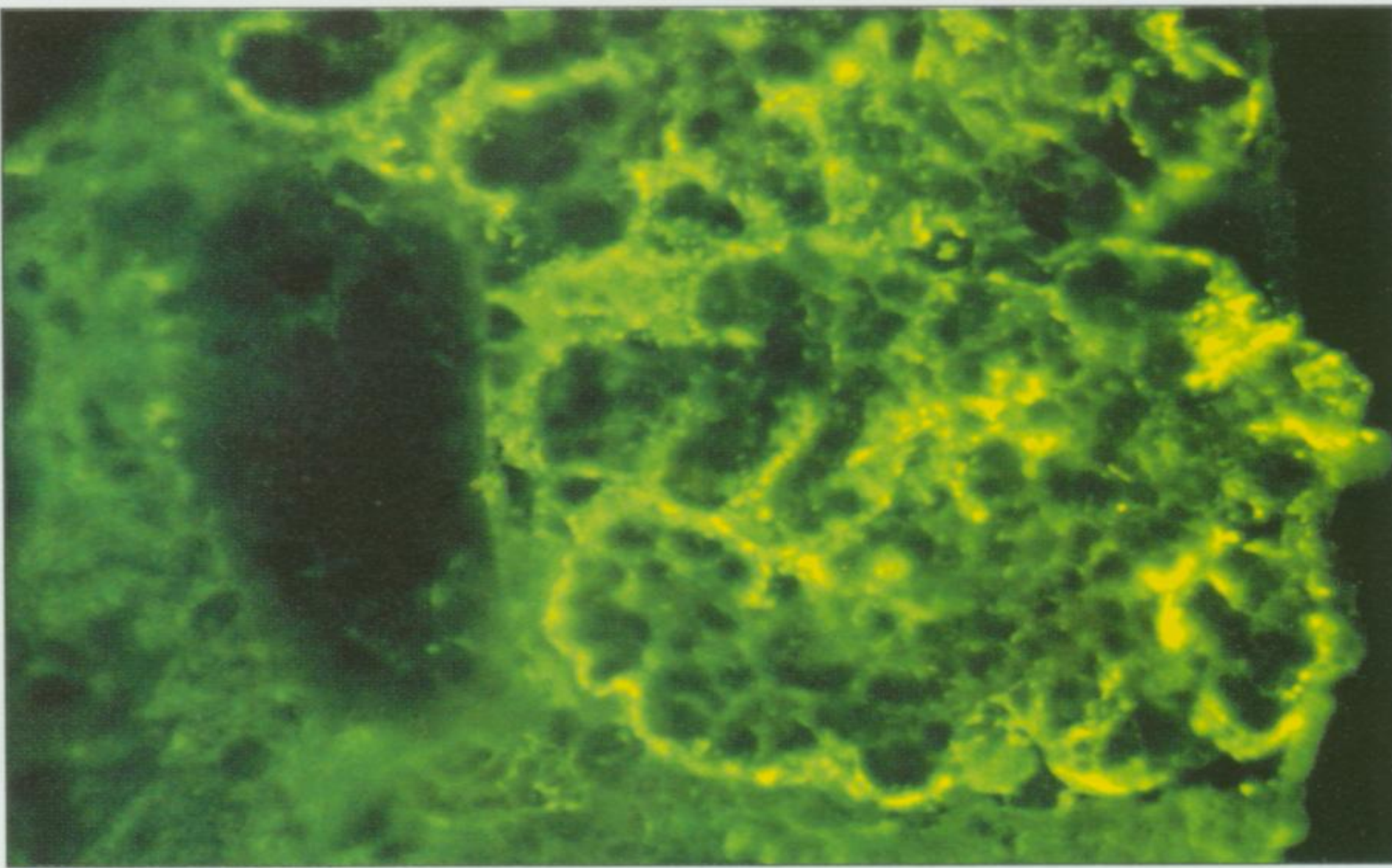
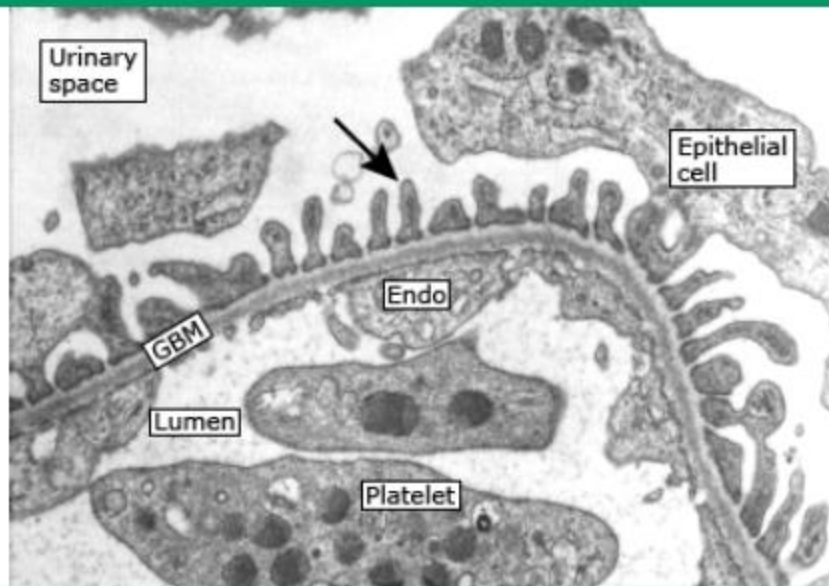


图 06 - 079 毛细血管内增生性肾小球肾炎, IgG
粗大颗粒状沿毛细血管壁沉积(荧光, $\times 400$)

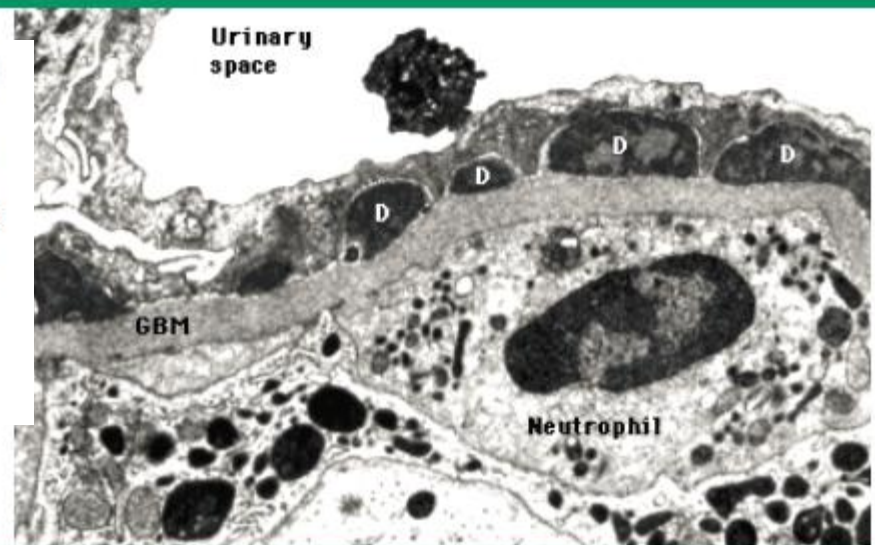
Electron micrograph of a normal glomerulus



Electron micrograph of a normal glomerular capillary loop showing the fenestrated endothelial cell (Endo), the glomerular basement membrane (GBM), and the epithelial cells with its interdigitating foot processes (arrow). The GBM is thin, and no electron-dense deposits are present. Two normal platelets are seen in the capillary lumen.

Electron micrograph of postinfectious glomerulonephritis

Electron micrograph shows subepithelial deposits (D) with a semilunar, hump-shaped appearance in postinfectious glomerulonephritis. The humps sit on top of the glomerular basement membrane (GBM). A neutrophil is attached to the denuded GBM, contributing to the glomerular inflammation. Neutrophil attraction requires the initial presence of subepithelial immune deposits so that complement chemoattractants have access to the systemic circulation.



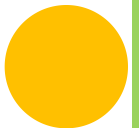
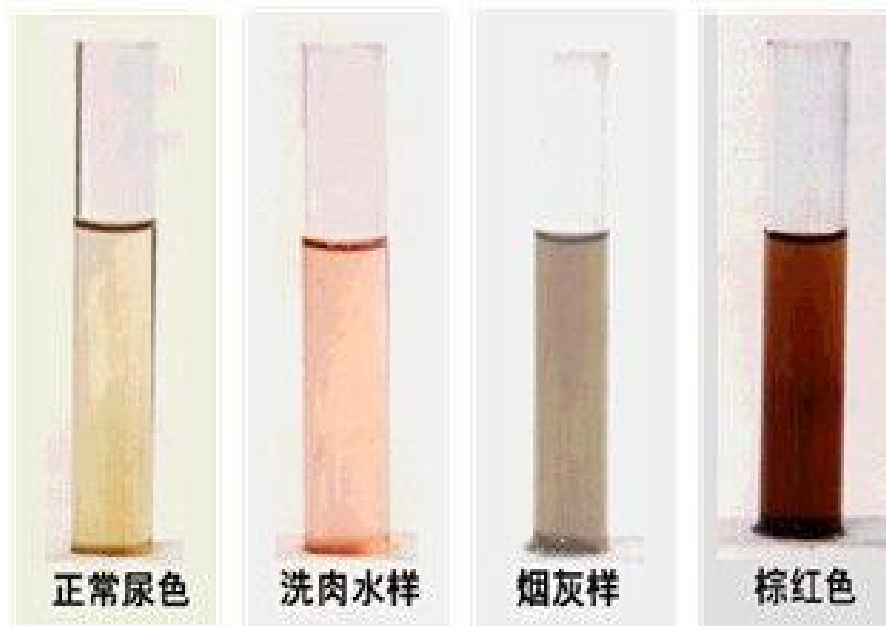
CLINICAL PRESENTATION

- Asymptomatic, microscopic hematuria
- An antecedent history of a GAS skin or throat infection
 - between 1-3 weeks following GAS pharyngitis
 - between 3-6 weeks following GAS skin infection
- Full-blown acute nephritic syndrome 急性肾炎综合征
 - Red to brown urine
 - Proteinuria (can reach the nephrotic range)
 - Edema
 - Hypertension
 - An elevation in serum creatinine



ACUTE NEPHRITIC SYNDROME

- Hematuria (30%-50% gross hematuria) 血尿
- Red to brown urine



ACUTE NEPHRITIC SYNDROME

- Proteinuria (can reach the nephrotic range) 蛋白尿



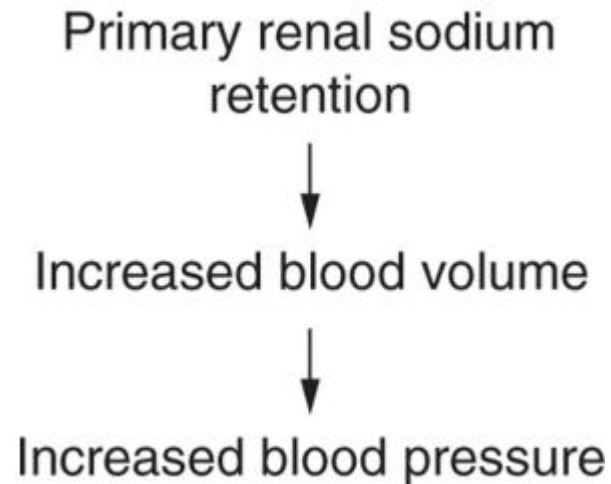
ACUTE NEPHRITIC SYNDROME

- Edema(80%, periorbital, leg or sacral)



ACUTE NEPHRITIC SYNDROME

- Hypertension(50-90%)



- An elevation in serum creatinine

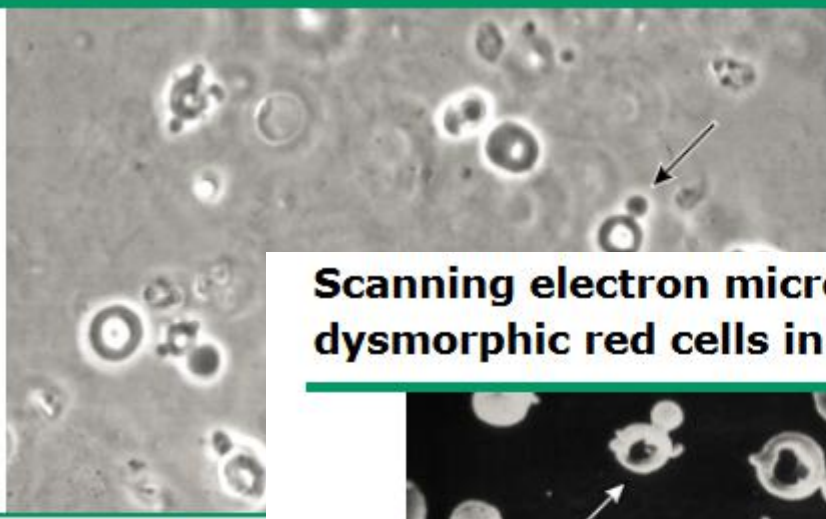


LABORATORY FINDINGS

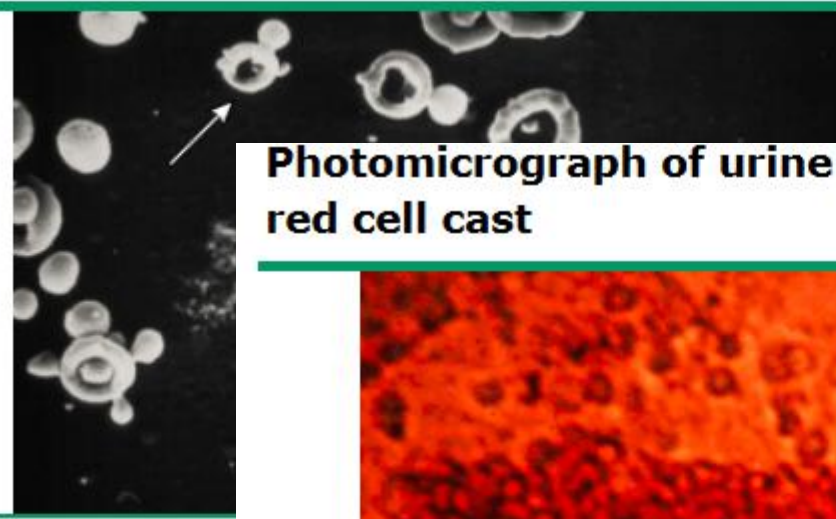
- Renal function---a rise in serum creatinine
- Urinalysis and urinary protein
 - Hematuria with or without red blood cell casts
 - varying degrees of proteinuria
 - often pyuria



Phase-contrast micrograph showing dysmorphic red cells in urine sediment

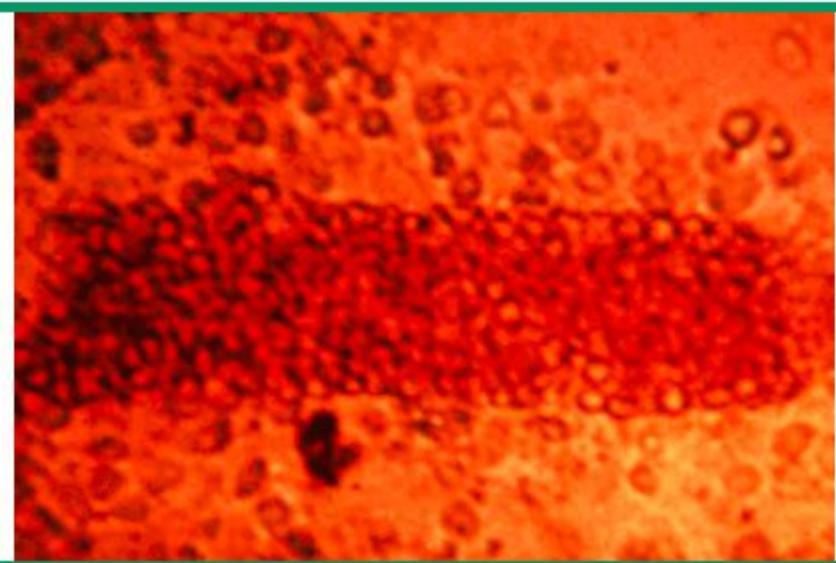


Scanning electron micrograph showing dysmorphic red cells in urine sediment

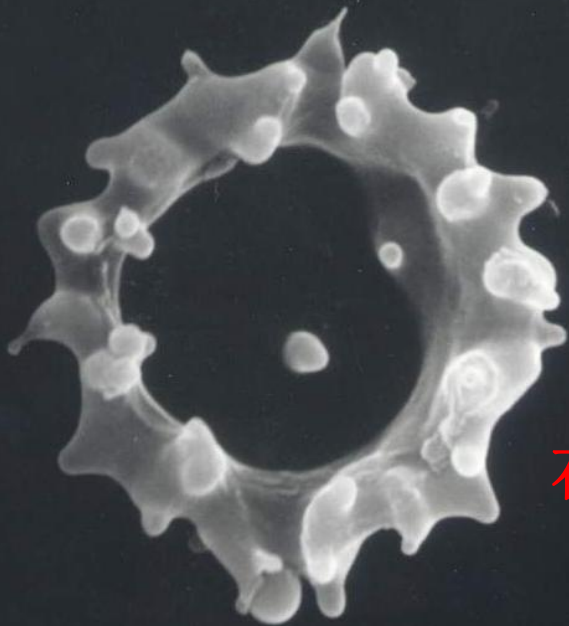


Phase-contrast microscop
patient with glomerular
recognized as ring form

Photomicrograph of urine sediment with a red cell cast

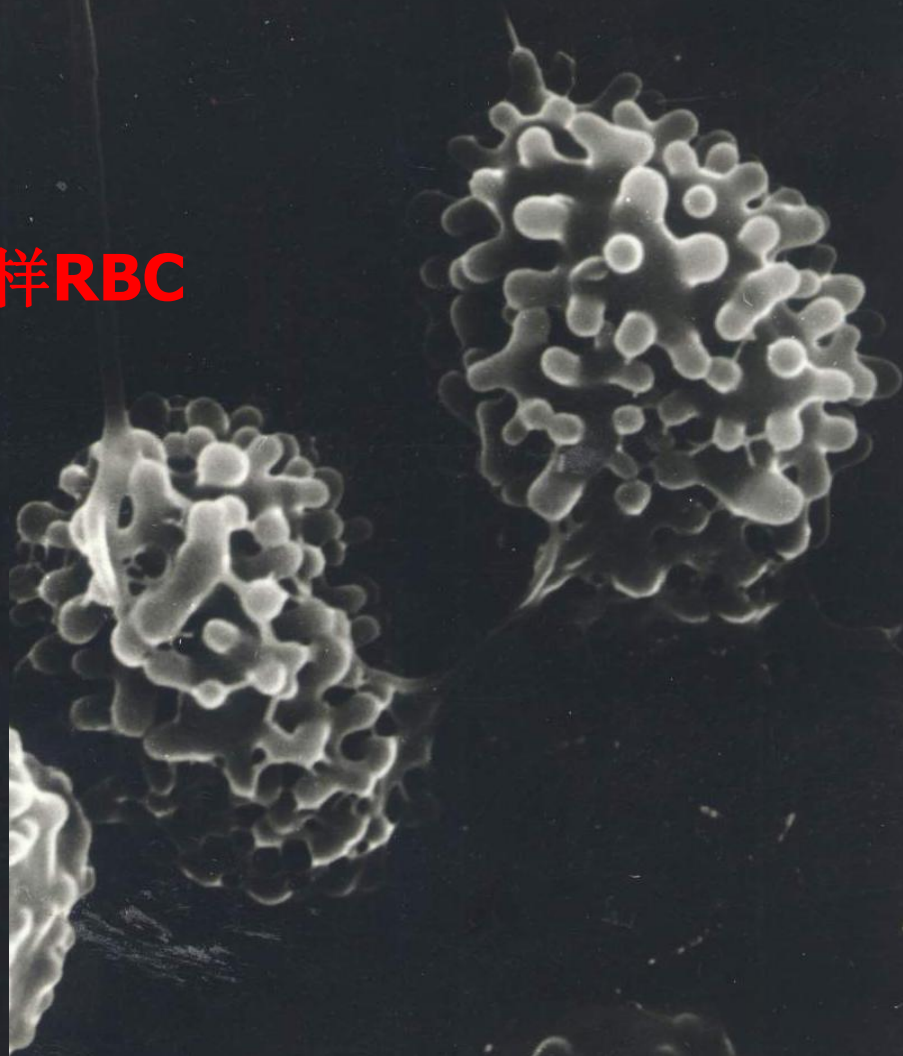


Scanning microscopy
with glomerular bleed
ring forms with vesic



花环样RBC

草莓状（桑葚样）RBC



虫蚀样RBC



840483 25KV 143*2NMC

LABORATORY FINDINGS

- Complement
 - C3 **depressed** 2 weeks → normal 8 weeks
- Culture ---25 percent%
- Serology---ASO



DIAGNOSIS

- Infection history
- Clinical manifestation
- Laboratory examination
- Renal biopsy is not performed in most patients to confirm the diagnosis of PSGN



WHEN NEED RENAL BIOPSY

- Oliguria exceed 1 week, or progressive renal damage
- The course of disease exceed 2 months and have no improvement
- Acute nephritic syndrome accompanied by nephrotic syndrome



DIFFERENTIAL DIAGNOSIS

➤ Membranoproliferative glomerulonephritis

膜增生性肾小球肾炎

- child
- persistent urinary abnormalities
- hypocomplementemia beyond four to six weeks
- possibly a further elevation in serum creatinine



DIFFERENTIAL DIAGNOSIS

- IgA nephropathy--- IgA肾病
 - a shorter time between the antecedent illness and hematuria
(less than 5d)
 - a history of prior episodes of gross hematuria



DIFFERENTIAL DIAGNOSIS

➤ Secondary causes of glomerulonephritis

- Lupus nephritis
 - Female
 - Arthralgias 关节痛
 - “butterfly” skin rash 蝴蝶斑
 - Serositis 浆膜炎
 - alopecia (hair loss) 脱发
 - central nervous system disease
 - C3 ↓



DIFFERENTIAL DIAGNOSIS

➤ Secondary causes of glomerulonephritis

- IgA vasculitis
 - 3-15 years old
 - Palpable purpura
 - Arthritis
 - Abdominal pain
 - C3 ↓



TREATMENT

- Supportive care
 - Antibiotic treatment for infection
 - control of hypertension, edema
- Dialysis: seldom needed
- Immunosuppressive therapy: not recommend
- Most patients, particularly children, have an excellent outcome



CASE

an 15-year-old boy

suffered from tonsillitis

after 10 days...

edema

hematuria



RBC 30-50/HP

Urine total protein 0.7g

Alb 37g/L

Creatine 73 $\mu\text{mol/L}$ (45-137)

C3 0.41(0.61-1.52)

ASO 47



One months later.....

Oliguria

Creatine 73 → 324 μ ol/L (45-137)

C3 0.41 → 0.12(0.61-1.52)

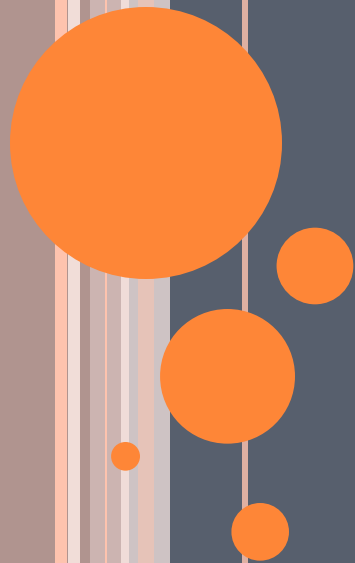
serious edema

RBC 30-50 → 200-300 /HP



RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

急进性肾小球肾炎



RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

急进性肾小球肾炎

- A syndrome characterized by rapidly developing renal insufficiency over a period of weeks to months



CAUSES OF RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

I. Infectious diseases

- A. Poststreptococcal glomerulonephritis^a
- B. Infective endocarditis
- C. Occult visceral sepsis
- D. Hepatitis B infection (with vasculitis and/or cryoglobulinemia)
- E. HIV infection
- F. Hepatitis C infection (with cryoglobulinemia, membranoproliferative glomerulonephritis)

II. Multisystem diseases

- A. Systemic lupus erythematosus
- B. Henoch-Schönlein purpura
- C. Systemic necrotizing vasculitis [including granulomatosis with polyangiitis (Wegener's)]
- D. Goodpasture's syndrome
- E. Essential mixed (IgG/IgM) cryoglobulinemia
- F. Malignancy
- G. Relapsing polychondritis
- H. Rheumatoid arthritis (with vasculitis)

III. Drugs

- A. Penicillamine
- B. Hydralazine
- C. Allopurinol (with vasculitis)
- D. Rifampin

IV. Idiopathic or primary glomerular disease

- A. Idiopathic crescentic glomerulonephritis
 1. Type I—with linear deposits of Ig (anti-GBM antibody-mediated)
 2. Type II—with granular deposits of Ig (immune complex-mediated)
 3. Type III—with few or no immune deposits of Ig ("pauci-immune")
 4. Antineutrophil cytoplasmic antibody-induced, forms fruste of vasculitis
 5. Immunotactoid glomerulonephritis
 6. Fibrillary glomerulonephritis
- B. Superimposed on another primary glomerular disease
 1. Mesangiocapillary (membranoproliferative) glomerulonephritis (especially type II)
 2. Membranous glomerulonephritis
 3. Berger's disease (IgA nephropathy)

CLASSIFIED BY IMMUNOPATHOGENESIS

- **Linear immunofluorescent pattern(type I)**

Idiopathic anti- glomerular basement membrane antibody(GBM)-mediated
RPGN

Goodpasture's syndrome

- **Granular immunofluorescent pattern(immune complex-mediated
RPGN) (type II)**

IgAN

Idiopathic immune complex-mediated RPGN

- **Negative immunofluorescent pattern(pauci-immune RPGN) (type III)**

Anti-Neutrophil Cytoplasmic Antibodies(ANCA)-associated systemic
vasculitides

PATHOGENESIS

Type I (抗肾小球基底膜抗体型)

- 血液循环：游离抗肾小球基底膜抗体 (IgG)

+

- 肾小球：

肾小球基底膜抗原



原位免疫复合物

+

活化补体 (C3)



急进性肾炎



PATHOGENESIS

Type II (免疫复合物型)

- 血液循环：循环免疫复合物（抗体+抗原）



- 肾小球：系膜区或内皮下沉积



活化补体 (C3)



急进性肾炎



PATHOGENESIS

Type III（非免疫复合物型）

- 血液循环：抗中性粒细胞胞浆抗体（ANCA）

+

- 肾小球：毛细血管内皮细胞表面抗原



超氧化物、蛋白酶



急进性肾炎



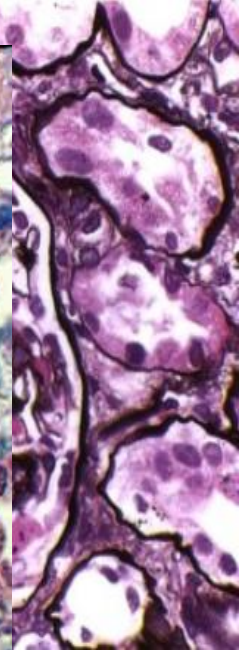
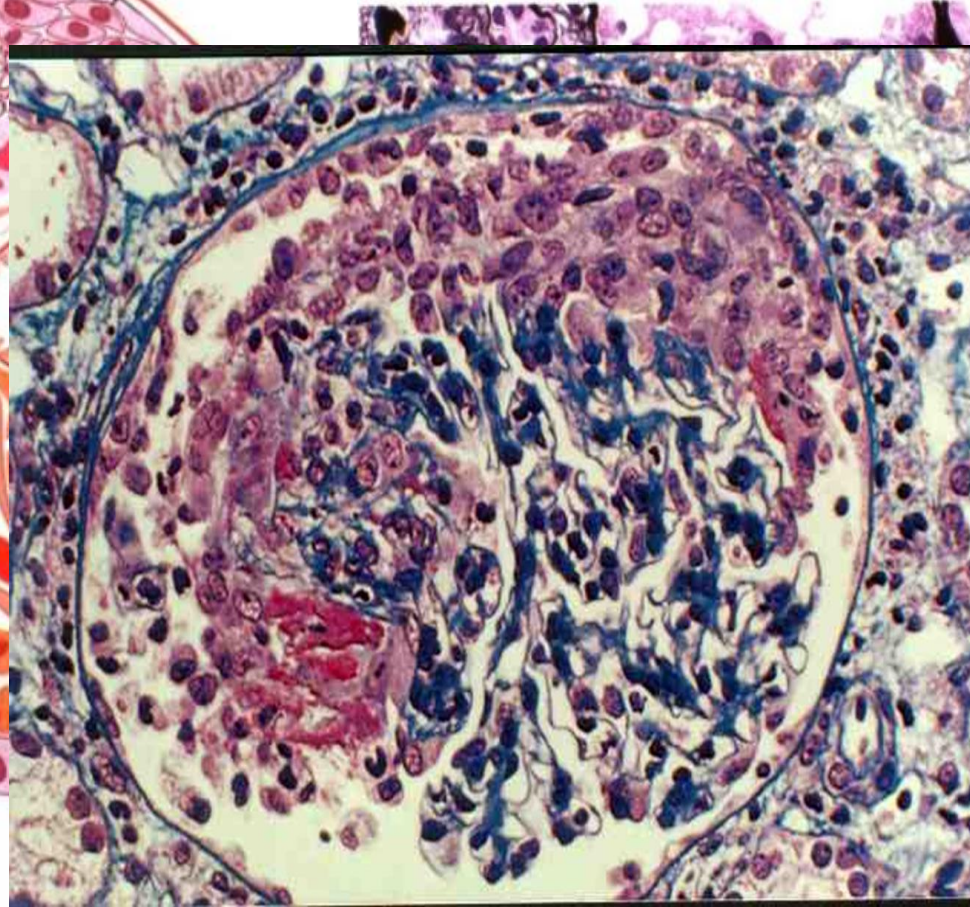
PATHOLOGY

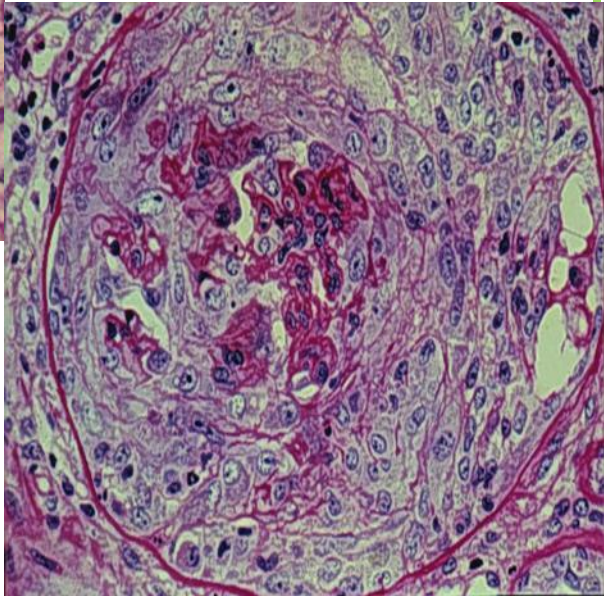
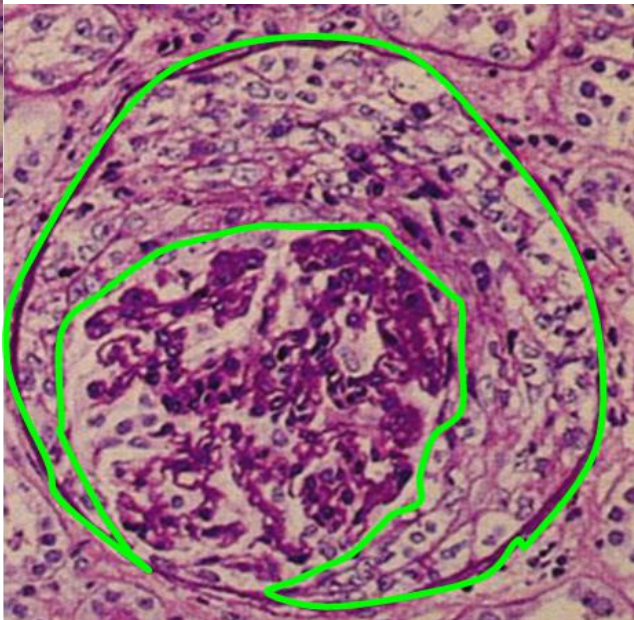
大量新月体形成

- **新月体(crescents)**: 肾小球囊内细胞增生、纤维蛋白沉积，病理切片上似新月状。
- **新月体肾炎(crescentic GN)**: 新月体面积>肾小囊50%、受累肾小球数量>50%。



PATHOLOGY





crests: 细胞性 → 细胞纤维性 → 纤维性

TABLE 123-5 CLASSIFICATION OF RAPIDLY PROGRESSIVE
("CRESCENTIC") GLOMERULONEPHRITIS

PRIMARY

Type I: Anti-glomerular basement membrane antibody disease, Goodpasture's syndrome (with pulmonary disease)

Type II: Immune complex mediated

Type III: Pauci-immune (usually antineutrophil cytoplasmic antibody-positive)

SECONDARY

Membranoproliferative glomerulonephritis

Immunoglobulin A nephropathy, Henoch-Schönlein purpura

Post-streptococcal glomerulonephritis

Systemic lupus erythematosus

Polyarteritis nodosa, hypersensitivity angiitis



ANTI-GLOMERULAR BASEMENT MEMBRANE ANTIBODY DISEASE

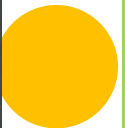
抗肾小球基底膜病

- Two peaks of occurrence 发病高峰

in the third decade of life in men



in women after 60 years of age



ANTI-GLOMERULAR BASEMENT MEMBRANE ANTIBODY DISEASE

抗肾小球基底膜病

- caused by circulating antibodies that are directed against the noncollagenous domain of the $\alpha 3$ chain of type IV collagen and that damage the GBM.
- If the anti-GBM antibodies cross-react with and damage the basement membrane of pulmonary capillaries, the patient develops pulmonary hemorrhage and hemoptysis, an association called Goodpasture's syndrome.



IMMUNE COMPLEX RPGN

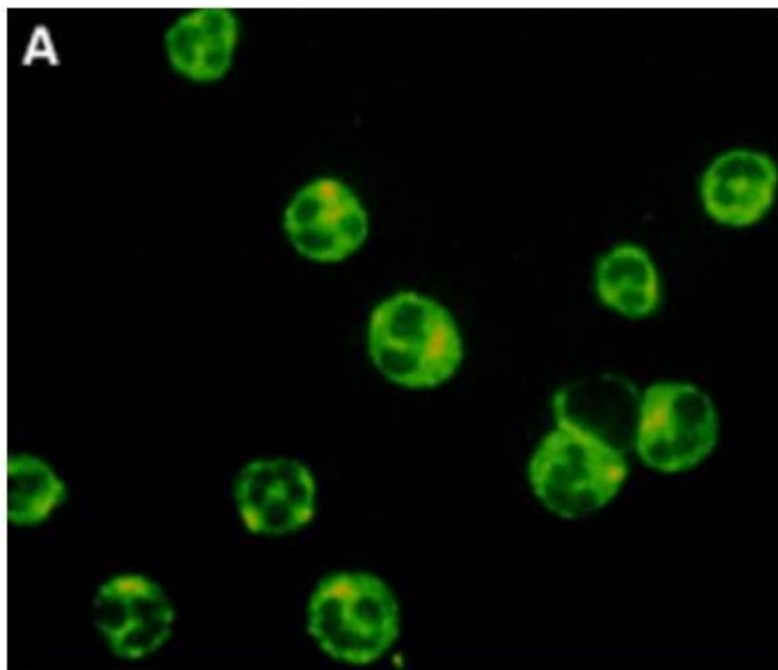
免疫复合物介导的急进性肾炎

- IgA nephropathy
- MPGN
- Postinfectious glomerulonephritis
- SLE（系统性红斑狼疮）



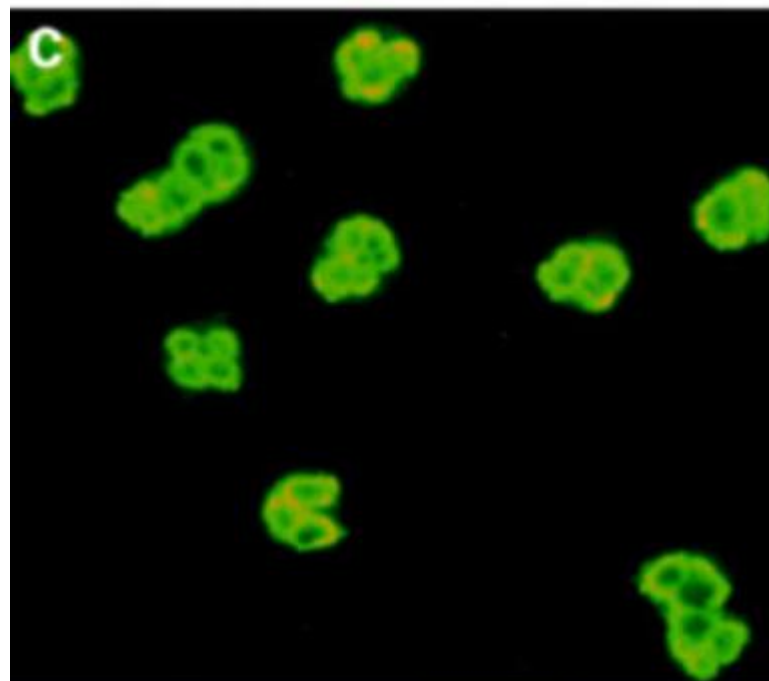
PAUCI-IMMUNE RPGN

寡免疫复合物型急进性肾炎



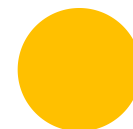
cytoplasmic -ANCA (胞浆型)

directed against granulocyte
serine proteinase, anti-PR3
丝氨酸酶



perinuclear-ANCA (核周型)

directed against granulocyte
myeloperoxidase 髓过氧化物酶



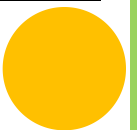
ANCA-ASSOCIATED, PAUCI-IMMUNE RPGN

- A prodromal, “flulike” syndrome
 - myalgias, fever, arthralgias, anorexia, and weight loss.
 - 肌痛，发热，关节痛，厌食症 及体重下降
- complications of associated systemic vasculitis
- Hemoptysis 咳血 pulmonary hemorrhage 肺出血



PATHOLOGY

Type	<u>LM</u>	EM	IF	Serology
I	Crescent >50% GBM breakage	ED (-)	IgG、C3 <u>linear deposition</u>	Anti-GBM(+)
II	Crescent >50% proliferation	ED (+)	IgG、C3 <u>granular deposition</u>	CIC(+), C3↓
III	Crescent >50% necrosis	ED (-)	(-)	ANCA (+)



CLINICAL MANIFESTATION

- Hematuria(macroscopic or microscopic)
red-cell casts are typically seen on urine microscopy
- Proteinuria
- progressive oliguria and renal function failure
- Systemic symptoms: fever, arthrodynia



DIFFERENTIAL DIAGNOSIS

➤ Secondary causes of glomerulonephritis

- IgA vasculitis
 - 3-15 years old
 - Palpable purpura
 - Arthritis
 - Abdominal pain
 - C3 ↓



CLINICAL MANIFESTATION

- Type I: about 2/3 patients have goodpasture's syndrome with associated lung haemorrhage
- Type III: lung haemorrhage, dermis purpuric rash or vasculitic ulceration



DIAGNOSIS

- Clinical manifestation
- Laboratory examination:

Type I : anti-GBM(+)

Type II : CIC(+), C3 ↓

Type III : ANCA(+)

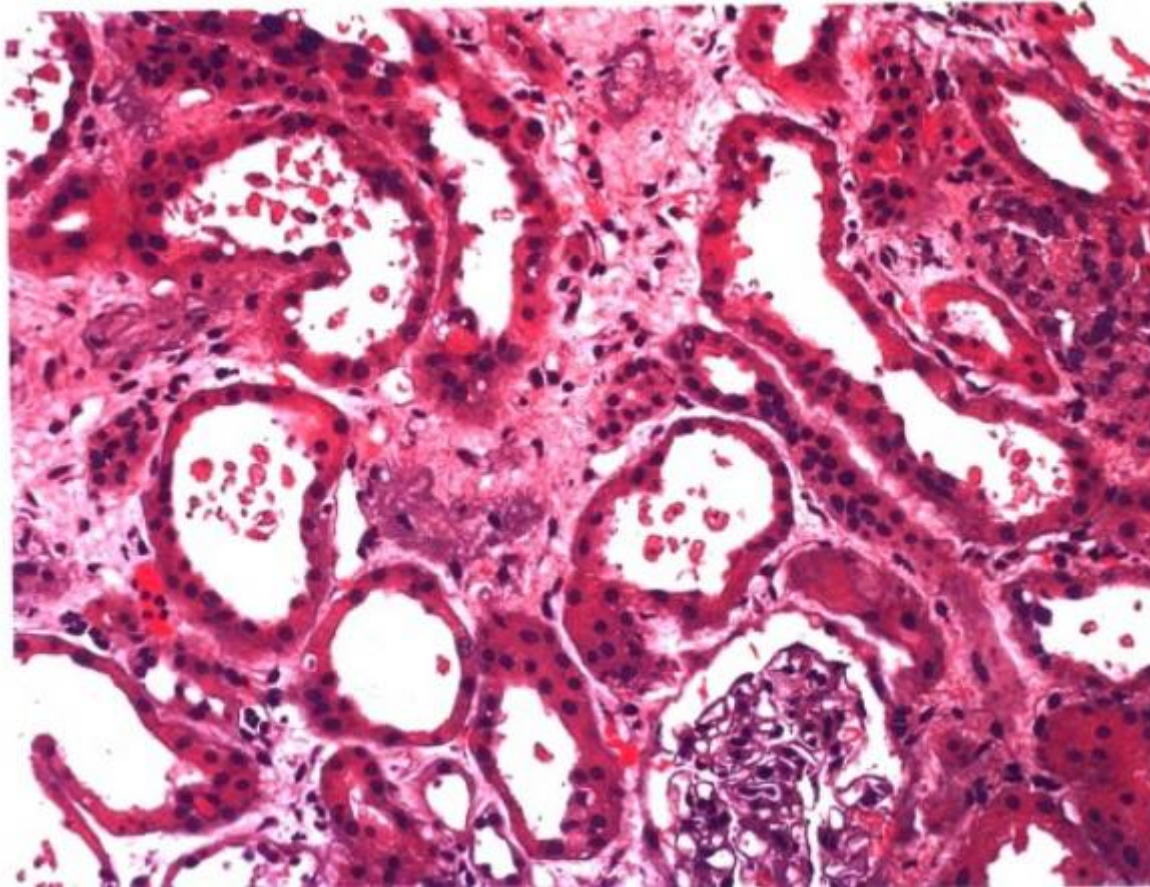
Ultrasound: kidneys enlargement

- Pathological characters



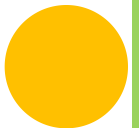
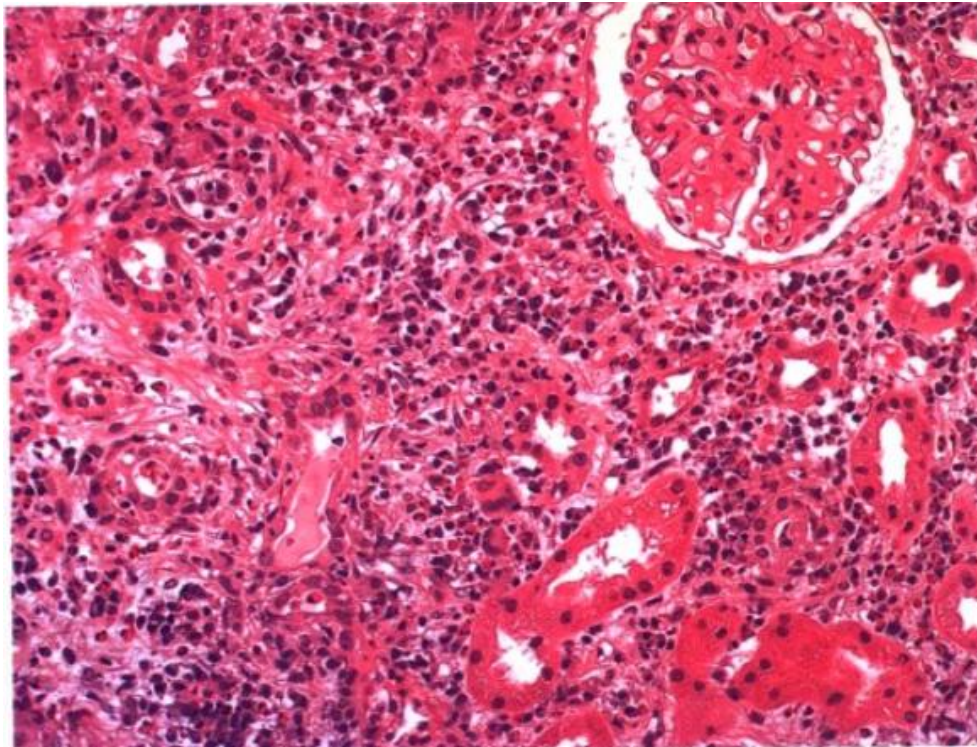
DIFFERENTIAL DIAGNOSIS

- Acute renal tubular necrosis 急性肾小管坏死
 - Oliguria, acute renal failure



DIFFERENTIAL DIAGNOSIS

- Acute drug-induced tubulointerstitial nephritis 急性药物性间质性肾炎
 - Fever, hematuria, an increased in Scr, esoinophilia



DIFFERENTIAL DIAGNOSIS

- Obstructive nephropathy 梗阻性肾病
 - Oliguria
 - ultrasound



DIFFERENTIAL DIAGNOSIS

➤ Secondary causes of glomerulonephritis

- Lupus nephritis
 - Female
 - Arthralgias 关节痛
 - “butterfly” skin rash 蝴蝶斑
 - Serositis 浆膜炎
 - alopecia (hair loss) 脱发
 - central nervous system disease
 - C3 ↓



TREATMENT

- **Corticosteroids and cyclophosphamide**

- ① methylprednisolone pulse(1g/d for 3 consecutive days) + cyclophosphamide intravenous pulse

- ② oral prednisolone(maximum 80mg/d, reducing over time to 15mg/d by 3 months) and cyclophosphamide(2mg/kg.d)

- **Adjuvant plasma exchanges(7 × 3 – 4L over 14d)**

- **RRT**



PROGNOSIS

- Type III > II > I
- Scr < 600 μmol/L
- Older



3 days later.....

Oliguria

Creatine 324 → 517 $\mu\text{mol/L}$ (45-137)

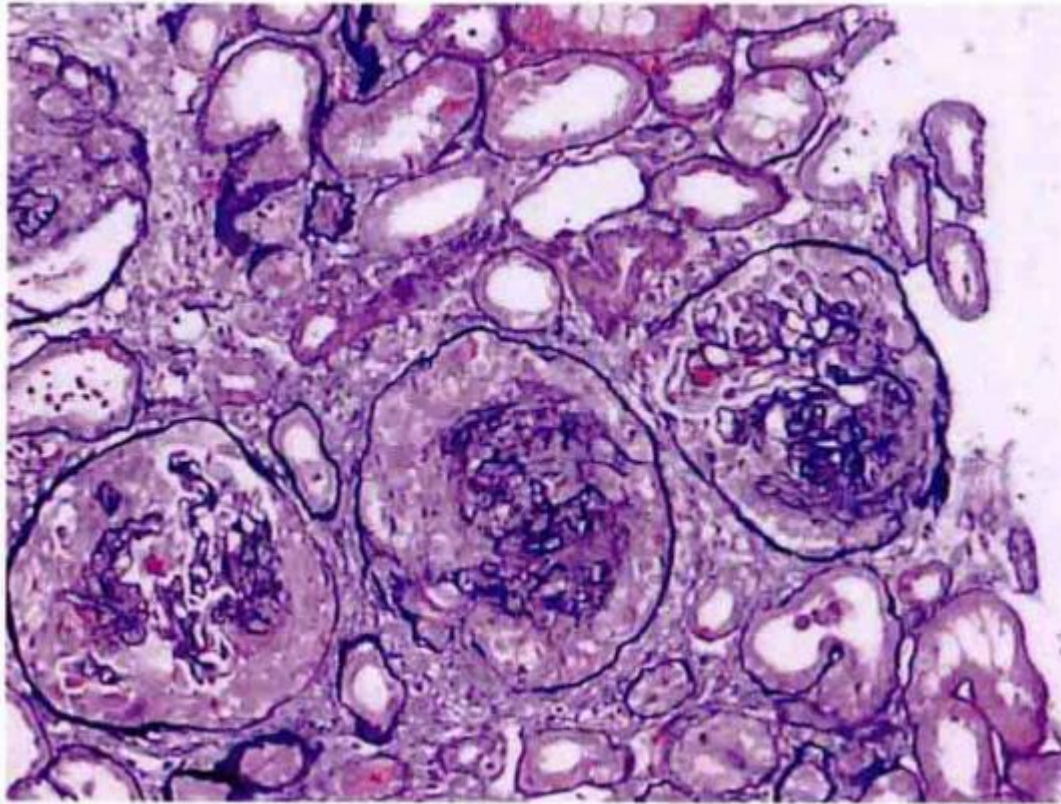
Anti-GBM(-)

ANCA(-)

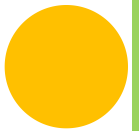
MP冲击

Renal biopsy





II型新月体肾炎



MP冲击3次，口服30mg

Urine volume 700ml/d

Creatine 517 → 218 μ mol/L (45-137)

RBC → 10-20/HP



Prognosis ???





CHRONIC GLOMERULONEPHRITIS

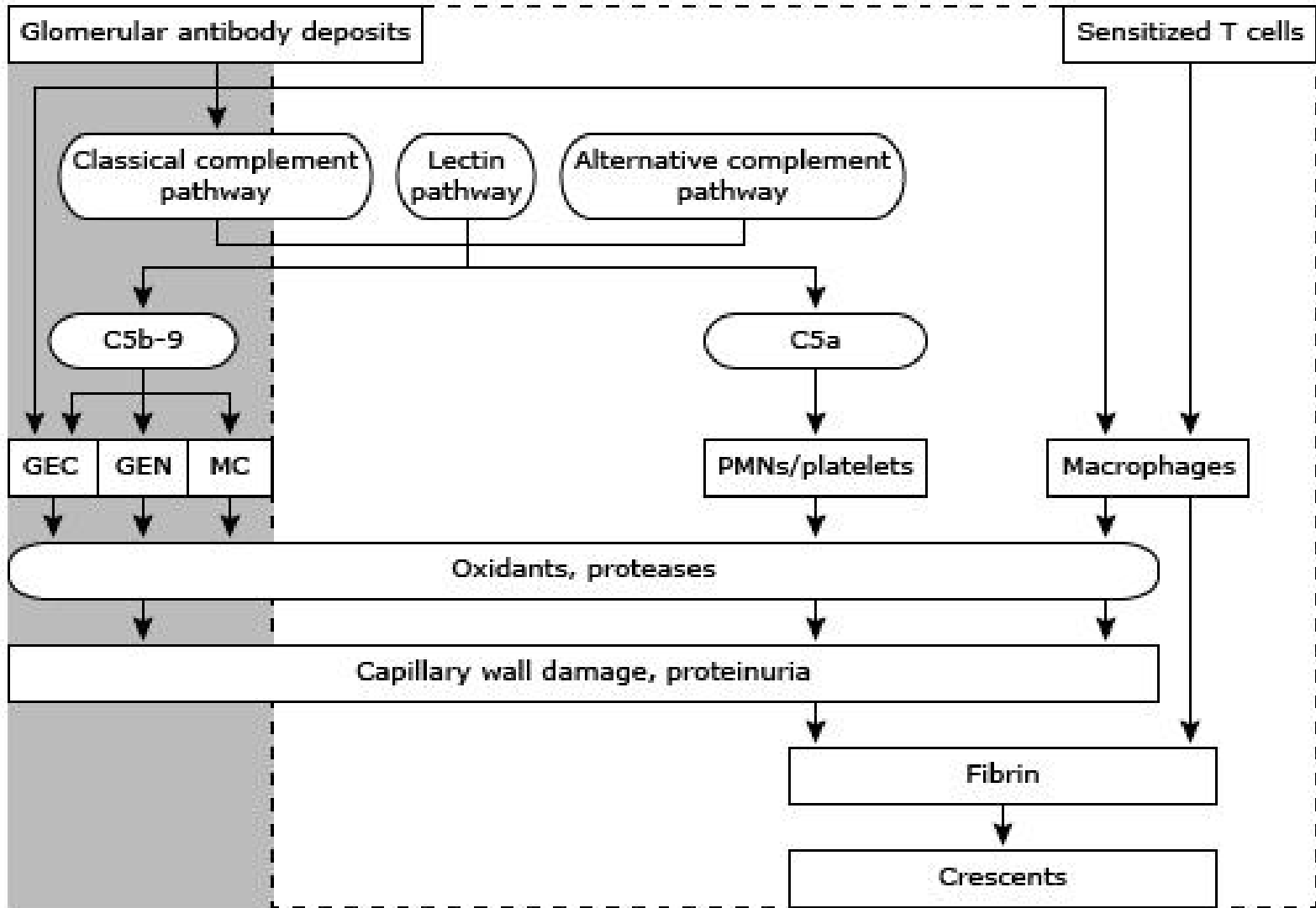


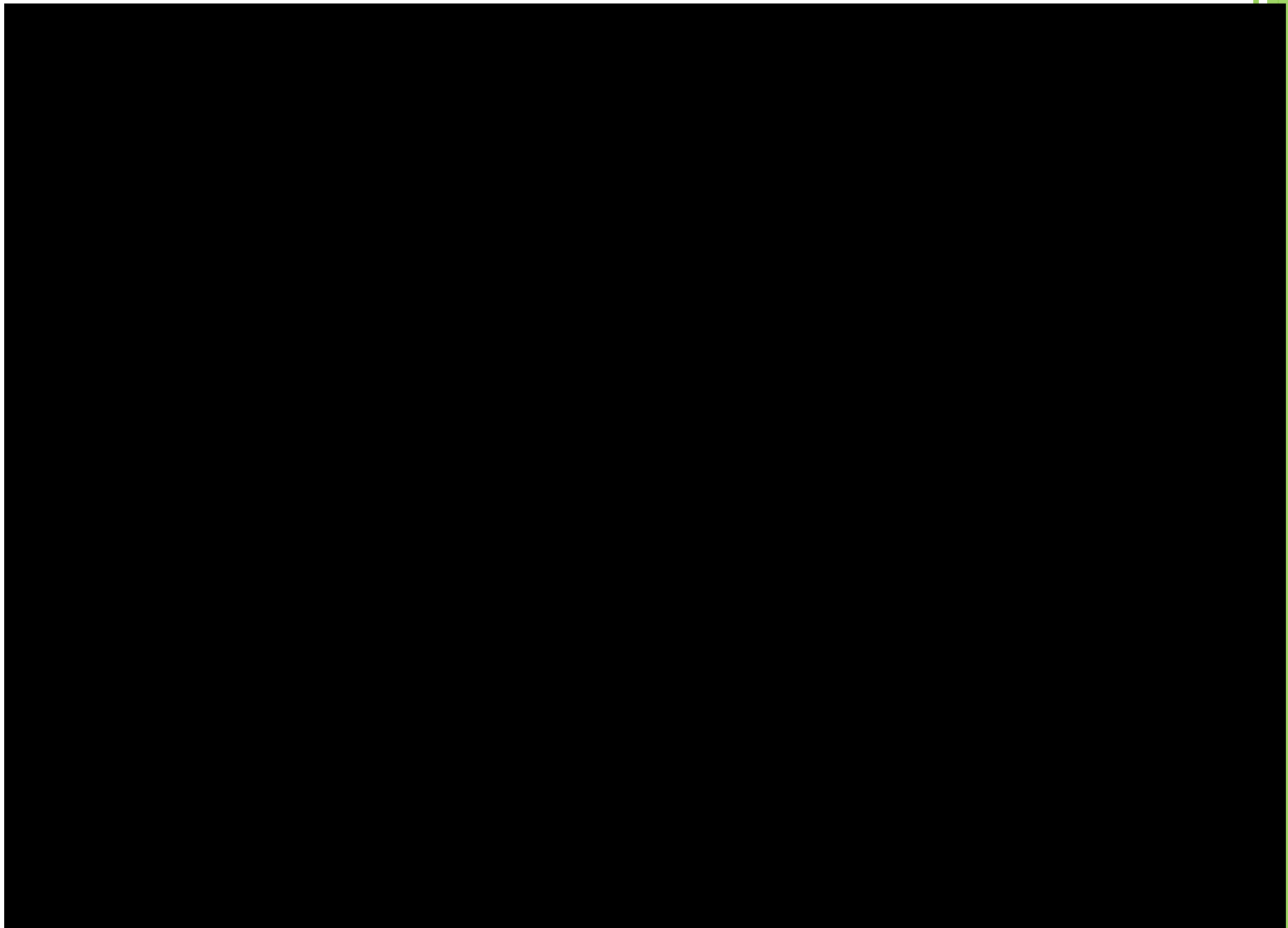
慢性肾小球肾炎

CHRONIC GLOMERULONEPHRITIS

- A group of primary glomerulopathies
- Nephritic syndrome
- Inevitable, chronic renal failure







PATHOLOGY

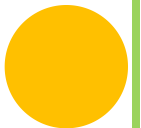
MsPGN
MPGN
MN
FSGS



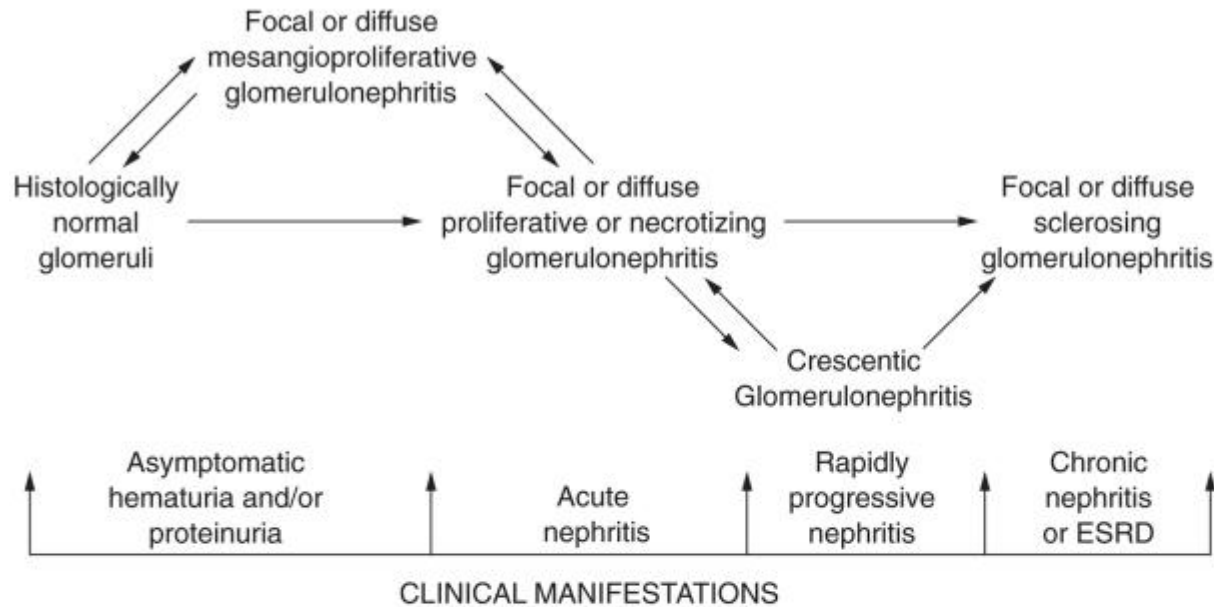
Glomerulosclerosis
Kidney tubules trophy
Renal interstitial fibrosis



**Sclerois
GN**



LIGHT MICROSCOPIC MORPHOLOGY



REPRESENTATIVE DISEASES

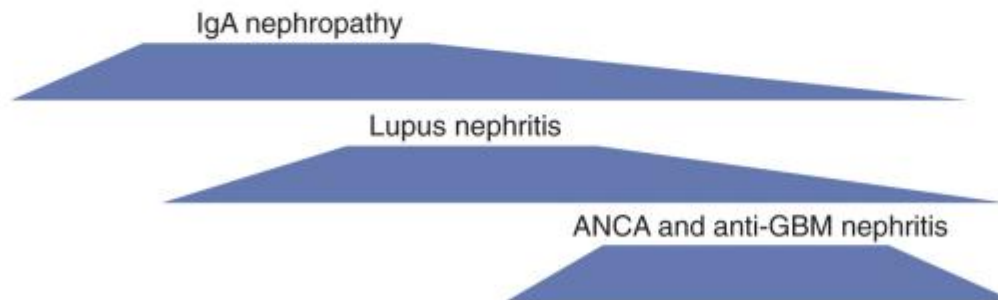


FIGURE 30-18 Diagram depicting the continuum of structural changes that can be caused by glomerular inflammation (top), the usual clinical syndromes that are caused by each expression of glomerular injury (middle), and the portion of the continuum that is most often attained by several specific categories of glomerular disease (bottom). (From Ferrario F, Kourilsky O, Morel-Maroger L: *Acute endocapillary glomerulonephritis in adults: A histologic and clinical comparison between patients with and without initial acute renal failure. Clin Nephrol* 19:17-23, 1983, with permission.)

CLINICAL MANIFESTATION

➤ Chronic Nephritis syndrome

- Edema
- Hemauria
- Proteinuria
- Hypertension
- An increase in Scr

➤ Acute on Chronic

➤ Chronic renal failure



DIAGNOSIS

- History >3months
- Clinical manifestation
- eGFR normal or decline
- Exclude secondary GN
 - SLE
 - HT,etc



TREATMENT--DIET

- Low salt diet (<6g/d)
- Low protein diet (0.6-0.8g/kg/d)
- Low phosphorus diet (<600~800mg/d)



TREATMENT—BLOOD PRESSURE

- Target
 - $UTP \leq 1 \text{ g/d}$; $Bp < 130/80 \text{ mmHg}$
 - $UTP \geq 1 \text{ g/d}$; $Bp < 125/75 \text{ mmHg}$
- Drugs
 - Diuretic
 - ACEI / ARB
 - CCB
 - β -Blocker
 - α -Blocker



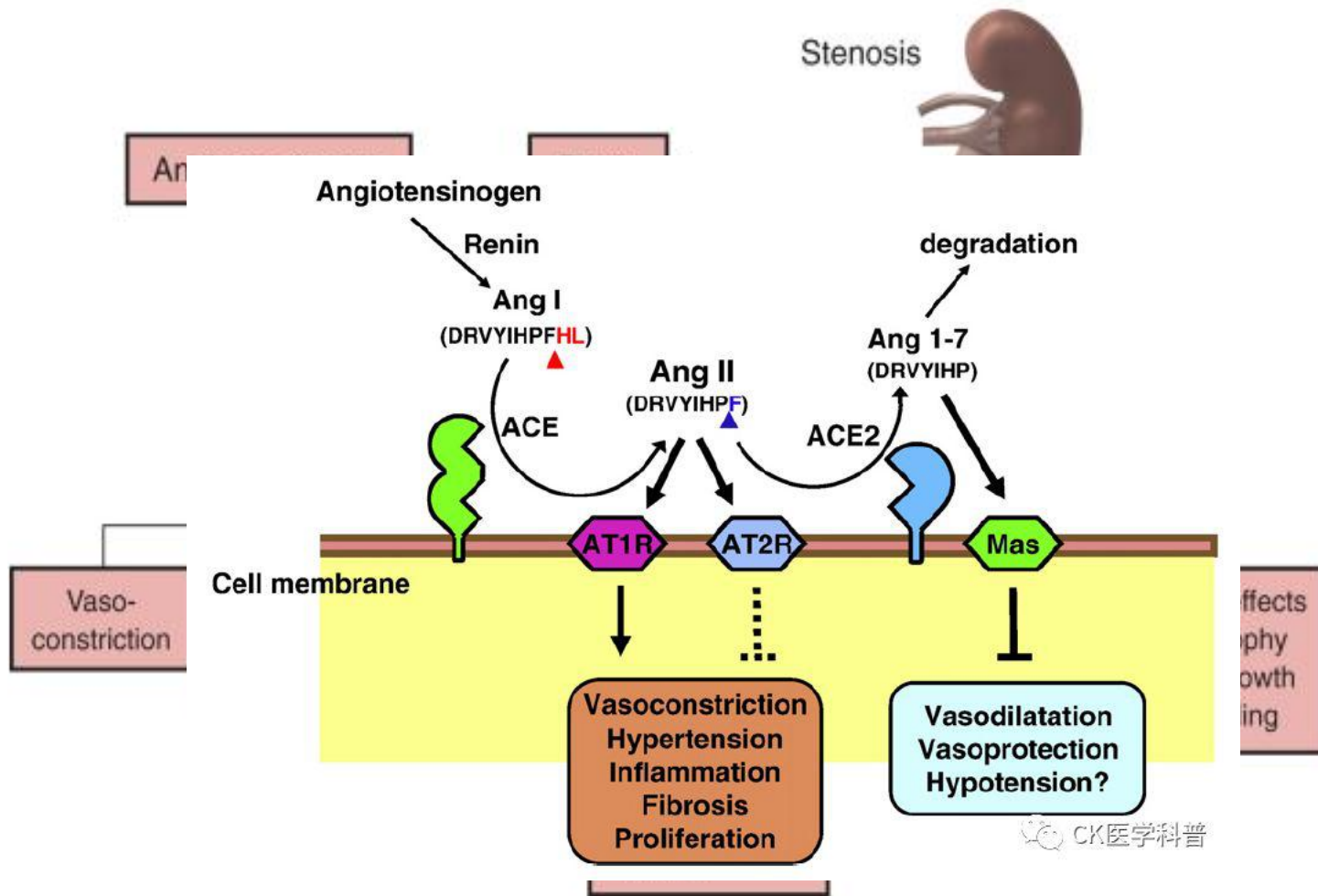


TABLE 45-2 -- Antihypertensive Mechanism of Action of Angiotensin-Converting Enzyme Inhibitors

↓ Peripheral vascular resistance
↓ Vasodilatory bradykinins
Enhance vasodilatory prostaglandin synthesis
Improve nitric oxide-mediated endothelial function
Reverse vascular hypertrophy
↓ Aldosterone secretion
Induce natriuresis
Augment renal blood flow
Blunt SNS activity and pressor responses
Inhibit NE and AVP release
Inhibit baroreceptor reflexes
↓ Endothelin-1 levels
Inhibit thirst
Inhibit oxidation of cholesterol
Inhibit collagen deposition in target organs

AVP, arginine vasopressin; NE, norepinephrine; SNS, sympathetic nervous system.



ACEI/ARB的肾脏保护作用

降低系统高血压
优先扩张出球小动脉



降低肾小球Cap压
降低肾小球灌注压
降低肾小球滤过压



改善GBM的通透性



抑制细胞因子
减少细胞外基质



减缓肾小球硬化



减缓肾间质纤维化



降低肾小球内压、减少蛋白尿、延缓肾功能恶化。



TABLE 45-5 -- Potential Renoprotective Effects of Angiotensin-Converting Enzyme Inhibitors

Restore pressure-natriuresis relationship to normal
Inhibit tubule sodium resorption
Decrease arterial pressure
Decrease aldosterone production
Decrease proteinuria
Improve altered lipid profiles
Decrease renal blood flow
Decrease filtration fraction
Decrease renal vascular resistance
Reduce scarring and fibrosis
Attenuate oxidative stress and free radicals



Scr 300 μ mol/L

RBC 10-15/HP

Hypertension



ASYMPTOMATIC HEMATURIA AND/OR PROTEINURIA

- Latent glomerulonephritis
- UTP < 1g/d
- Glomerular microhematuria
- Without edema, hypertension and have a normal eGFR.
- Followed closely.



随堂测验



- 水肿 edema
- 少尿 oliguria
- 血尿 hematuria
- 高血压 hypertension
- 肾小球肾炎 glomerulonephritis
- 蛋白尿 proteinuria





致敬英雄
欢迎回家

南方医科大学珠江医院
Southern Medical University
Zhujiang Hospital

战疫英雄
返来啦

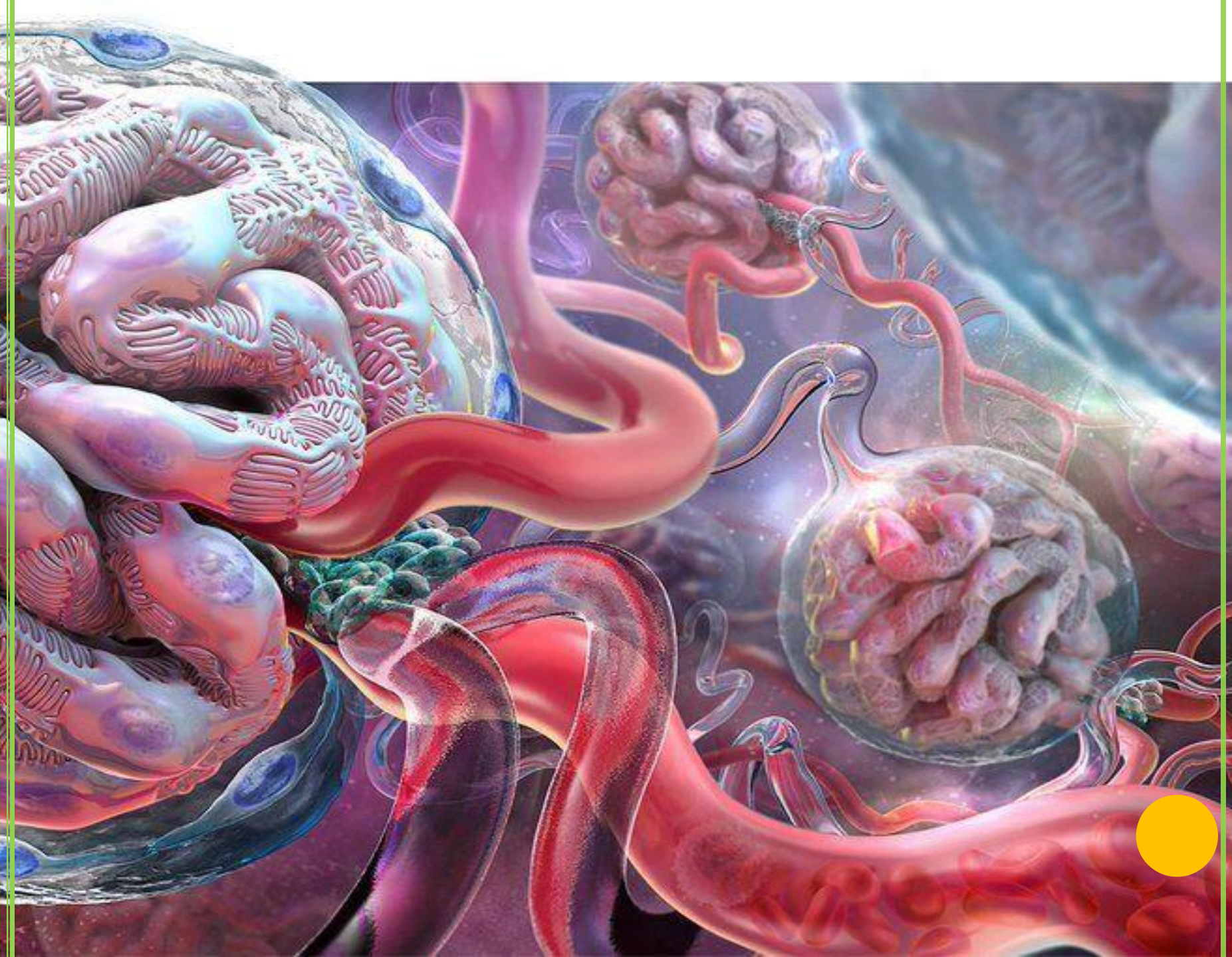
战疫英雄
返来啦

致敬英雄 欢迎回家

珠江汉江携手抗疫
精医报国英雄归来

南方医科大学珠江医院
Zhujiang Hospital of Southern Medical University

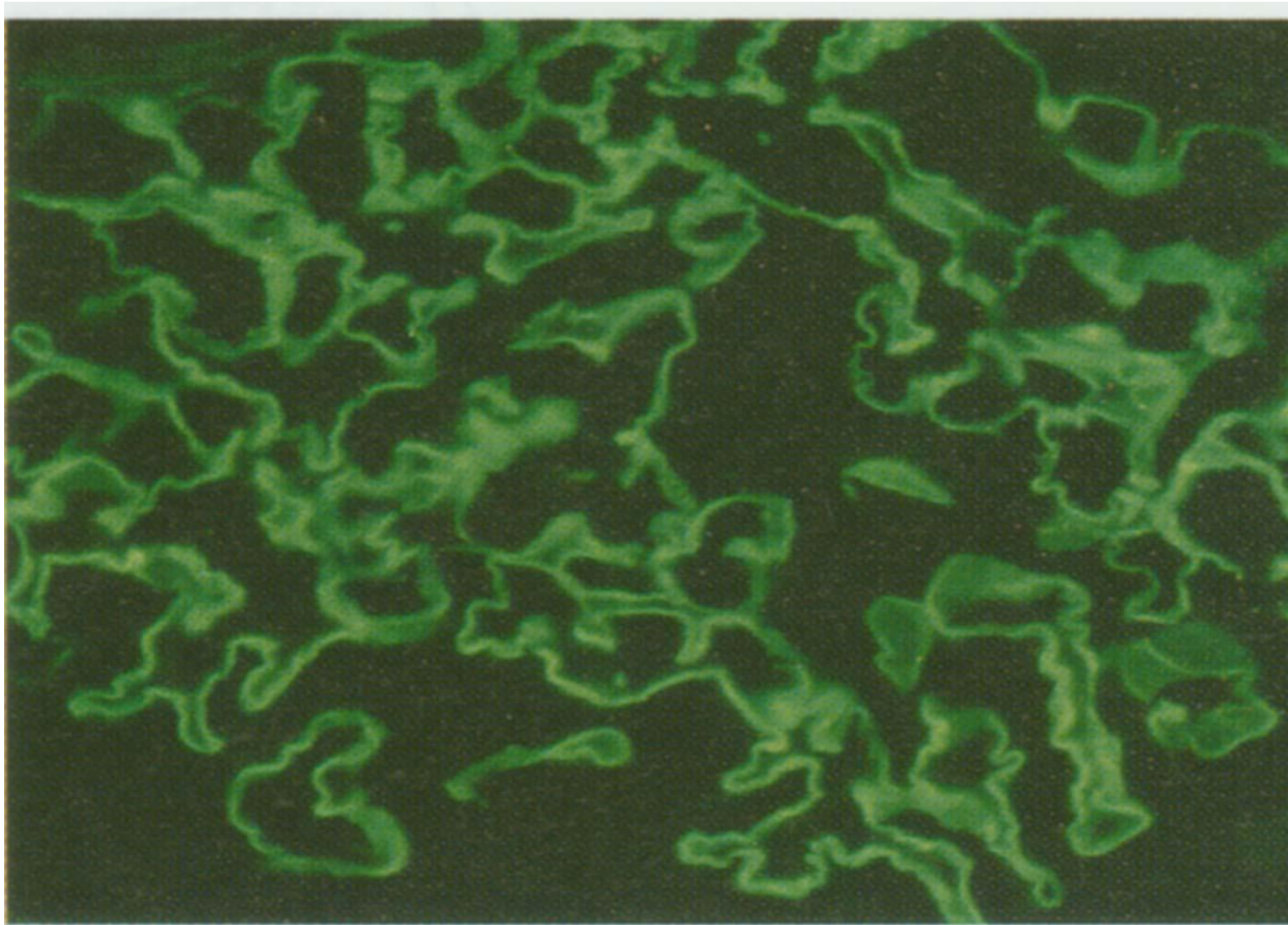
珠江汉江携手抗疫
精医报国英雄归来





Thank you





Anti-GBM GN (IgG)



