GLOMERULONEPHRITIS

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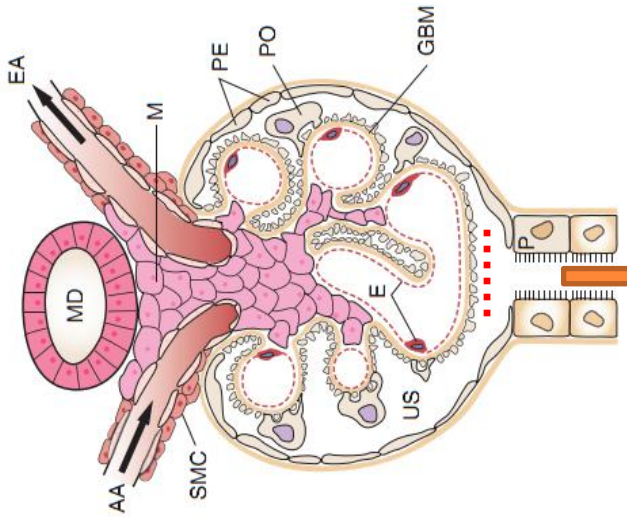
GLOMERULONEPHRITIS



Urine Change

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

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ACUTE GLOMERULONEPHRITIS

POSTSREPTOCOCCAL GLOMERULONEPHRITIS

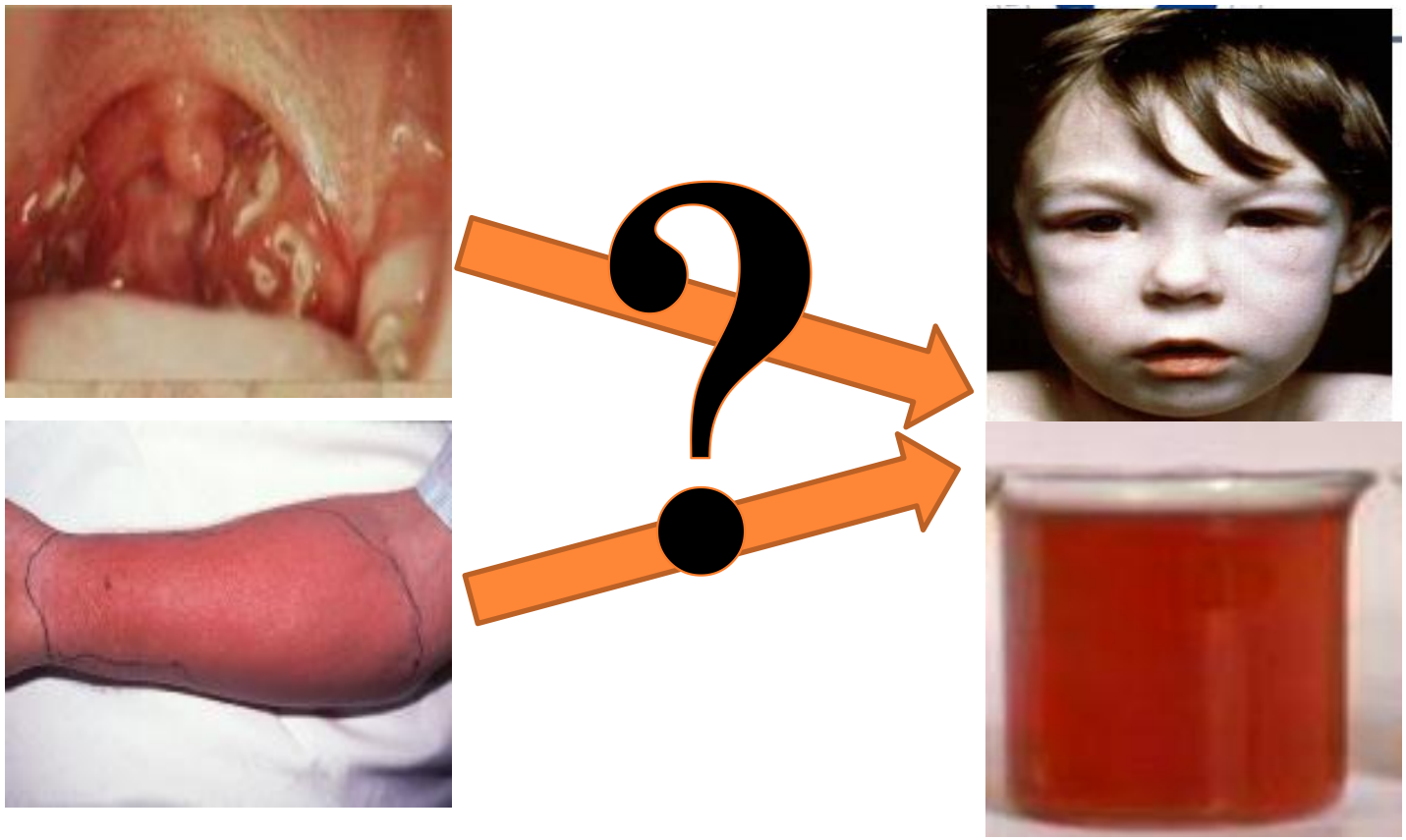
After

Infection

链球菌感染后肾小球肾炎

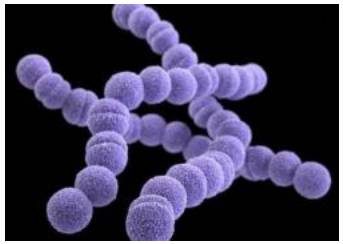
ACUTE GLOMERULONEPHRITIS

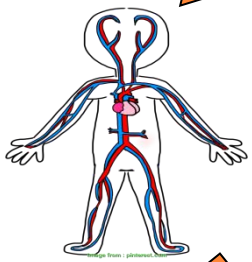
POSTSREPTOCOCCAL GLOMERULONEPHRITIS
链球菌感染后肾小球肾炎

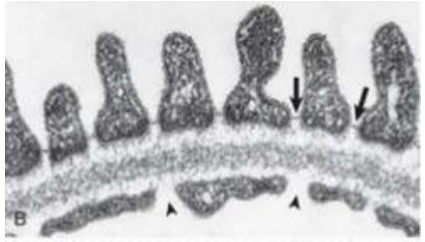


PATHOGENESIS

group A β-haemolytic streptococcus
(a nephritogenics type)



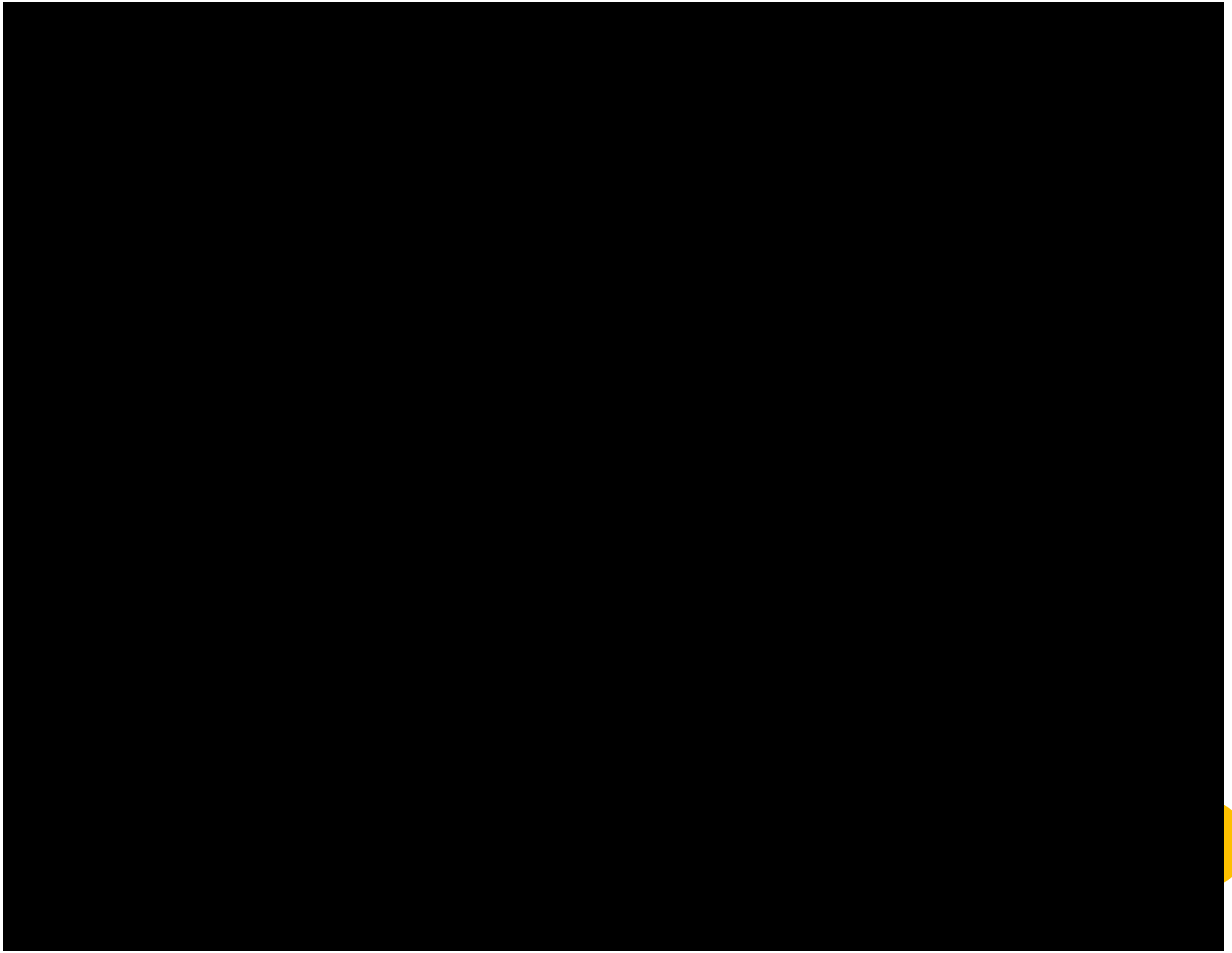


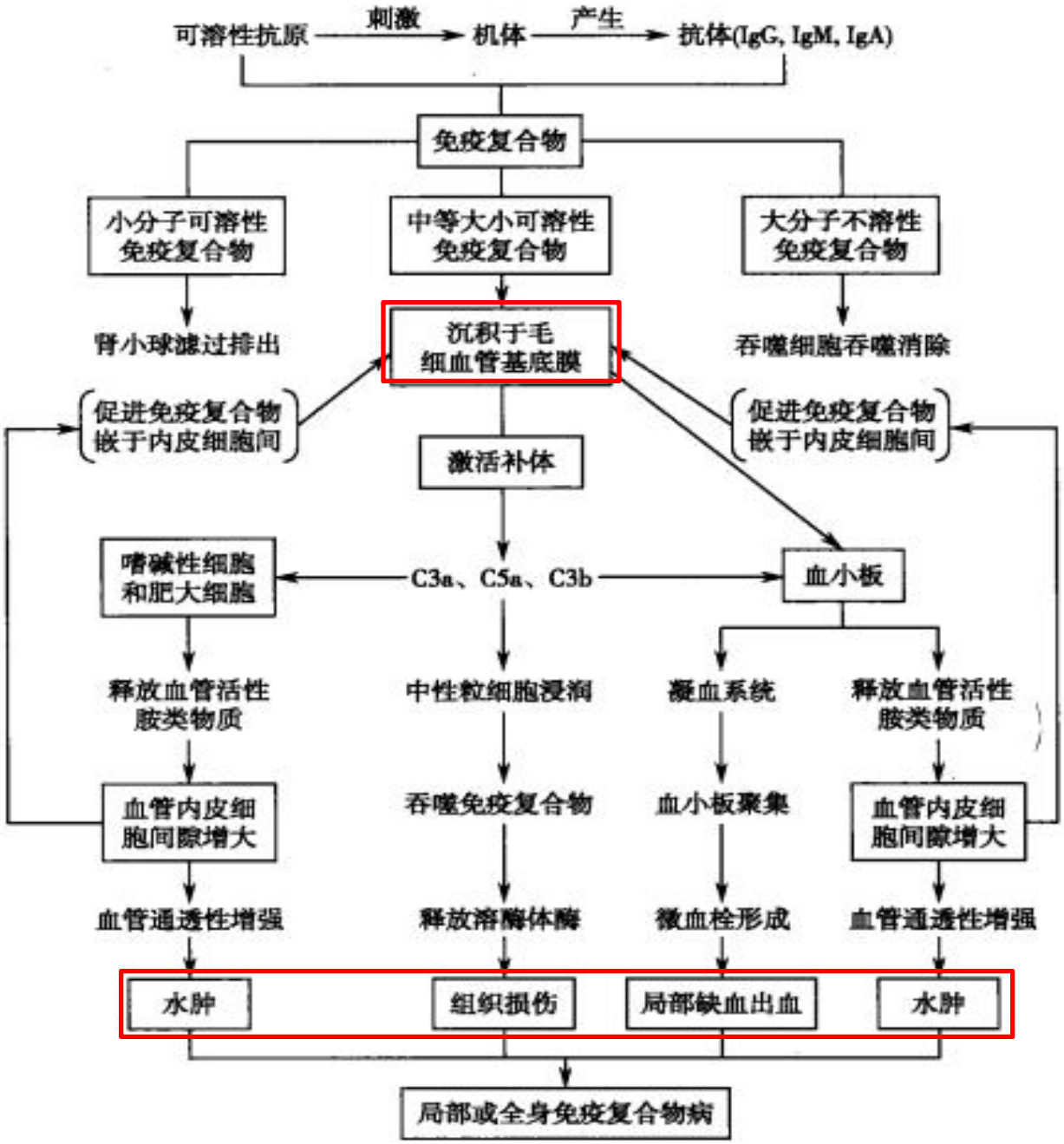


Immune response → **Latency period**

CIC **In situ IC**

Complement activation
Inflammation → **PSGN**




可溶性抗原
刺激
机体
产生
抗体(IgG, IgM, IgA)
免疫复合物
小分子可溶性免疫复合物
中等大小可溶性免疫复合物
大分子不溶性免疫复合物
肾小球滤过排出
沉积于毛细血管基底膜
吞噬细胞吞噬消除
促进免疫复合物嵌于内皮细胞间
促进免疫复合物嵌于内皮细胞间
激活补体
嗜碱性细胞和肥大细胞
C3a、C5a、C3b
血小板
释放血管活性胺类物质
中性粒细胞浸润
凝血系统
释放血管活性胺类物质
血管内皮细胞间隙增大
吞噬免疫复合物
血小板聚集
血管内皮细胞间隙增大
血管通透性增强
释放溶酶体酶
微血栓形成
血管通透性增强
水肿
组织损伤
局部缺血出血
水肿
局部或全身免疫复合物病

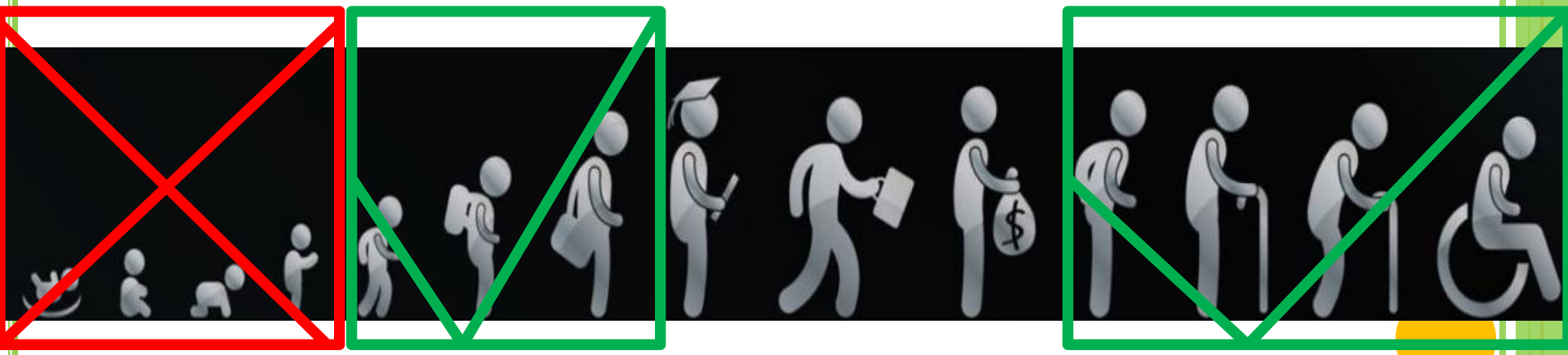
EPIDEMIOLOGY

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

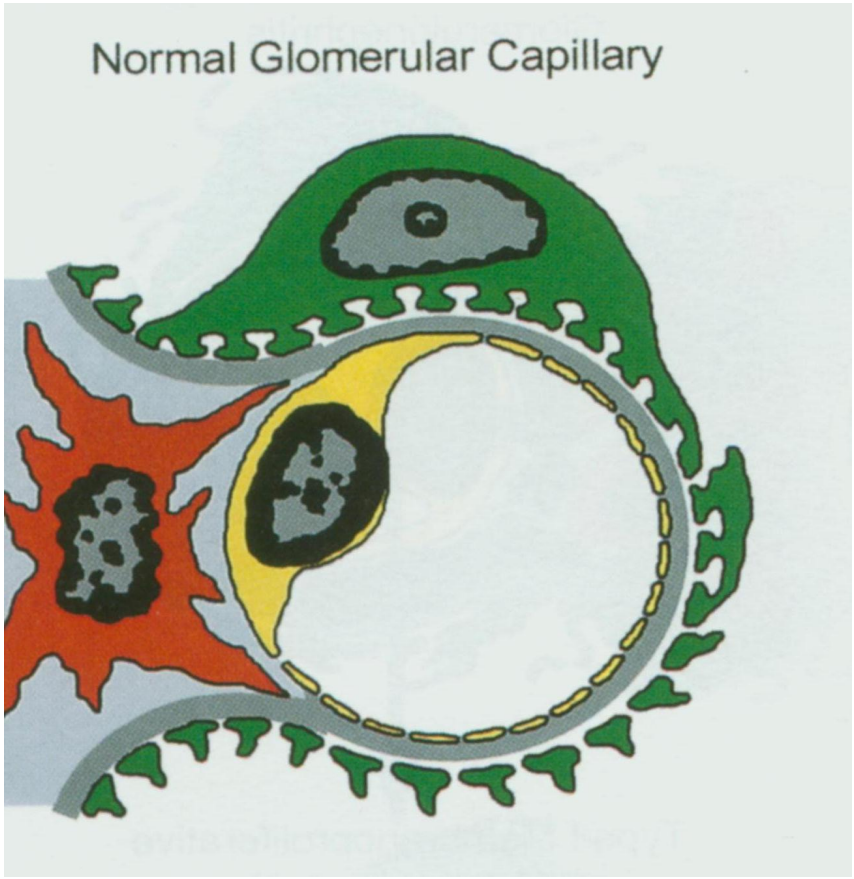


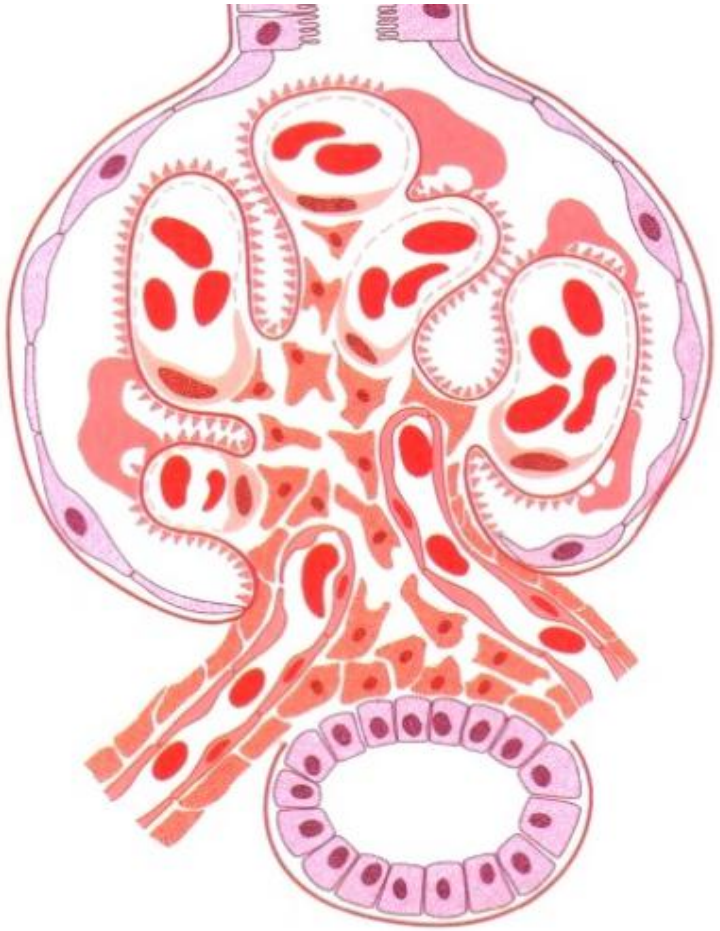
EPIDEMIOLOGY

- Group A streptococcal (GAS) infection

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

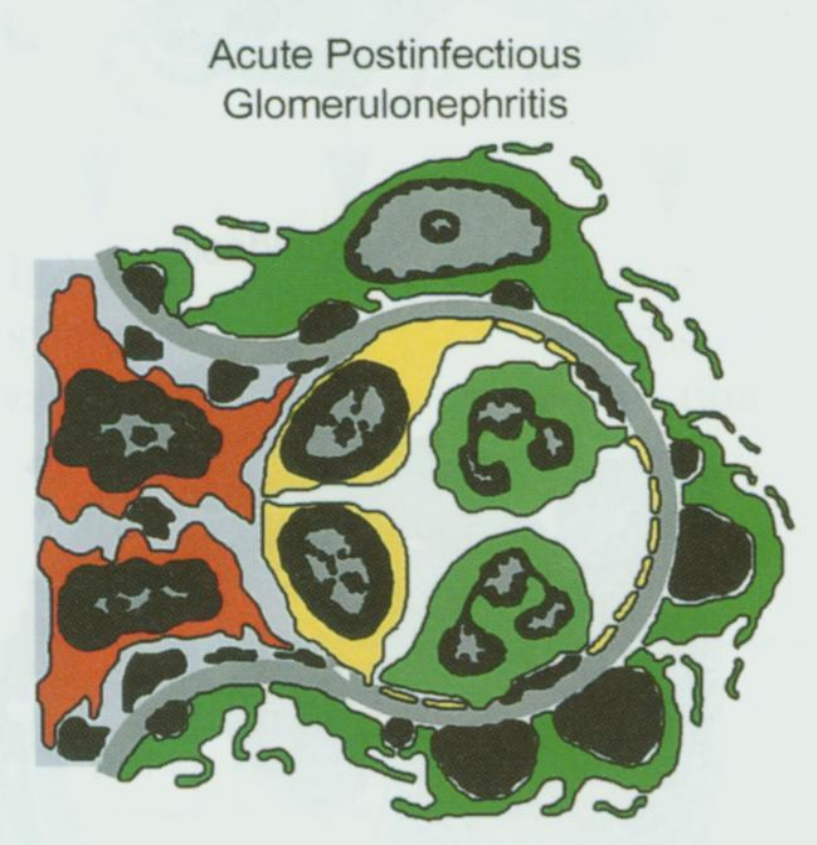
PATHOLOGY

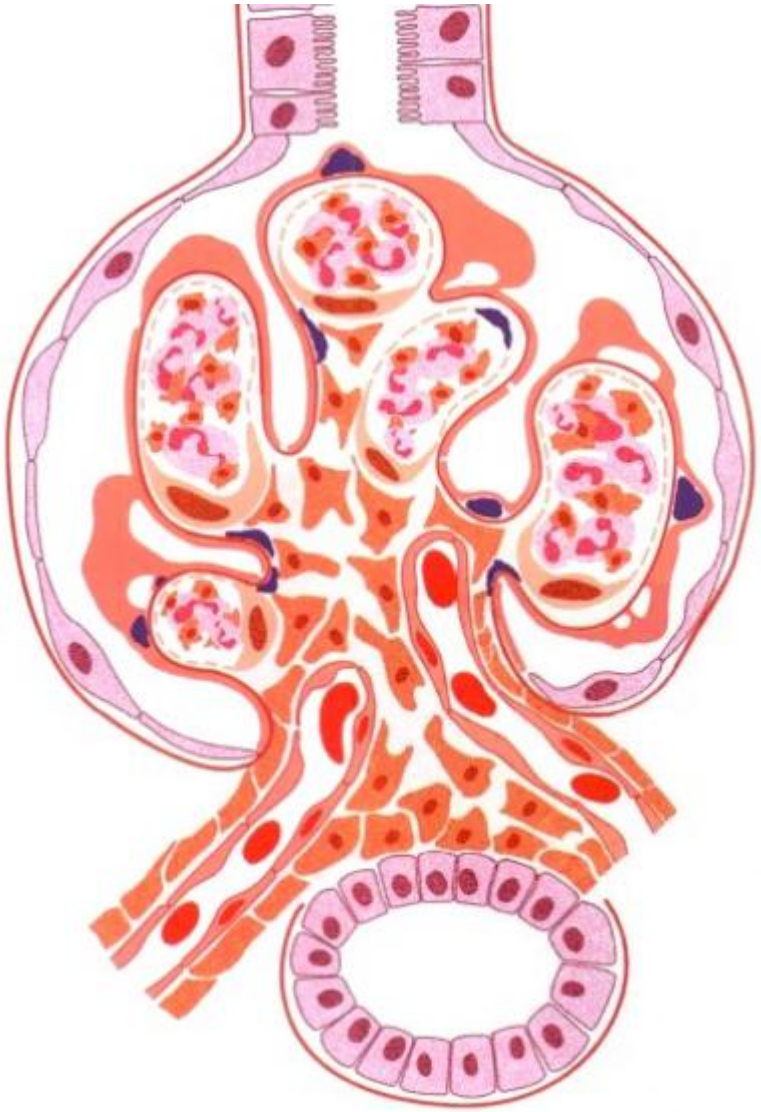


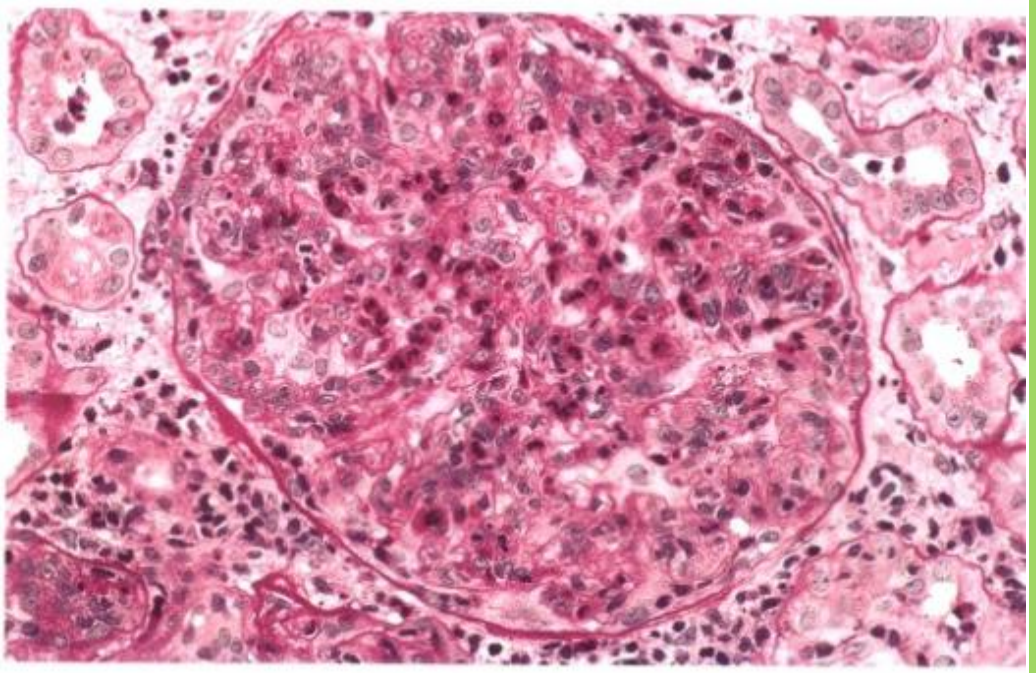


PATHOLOGY

endocapillary proliferative glomerulonephritis







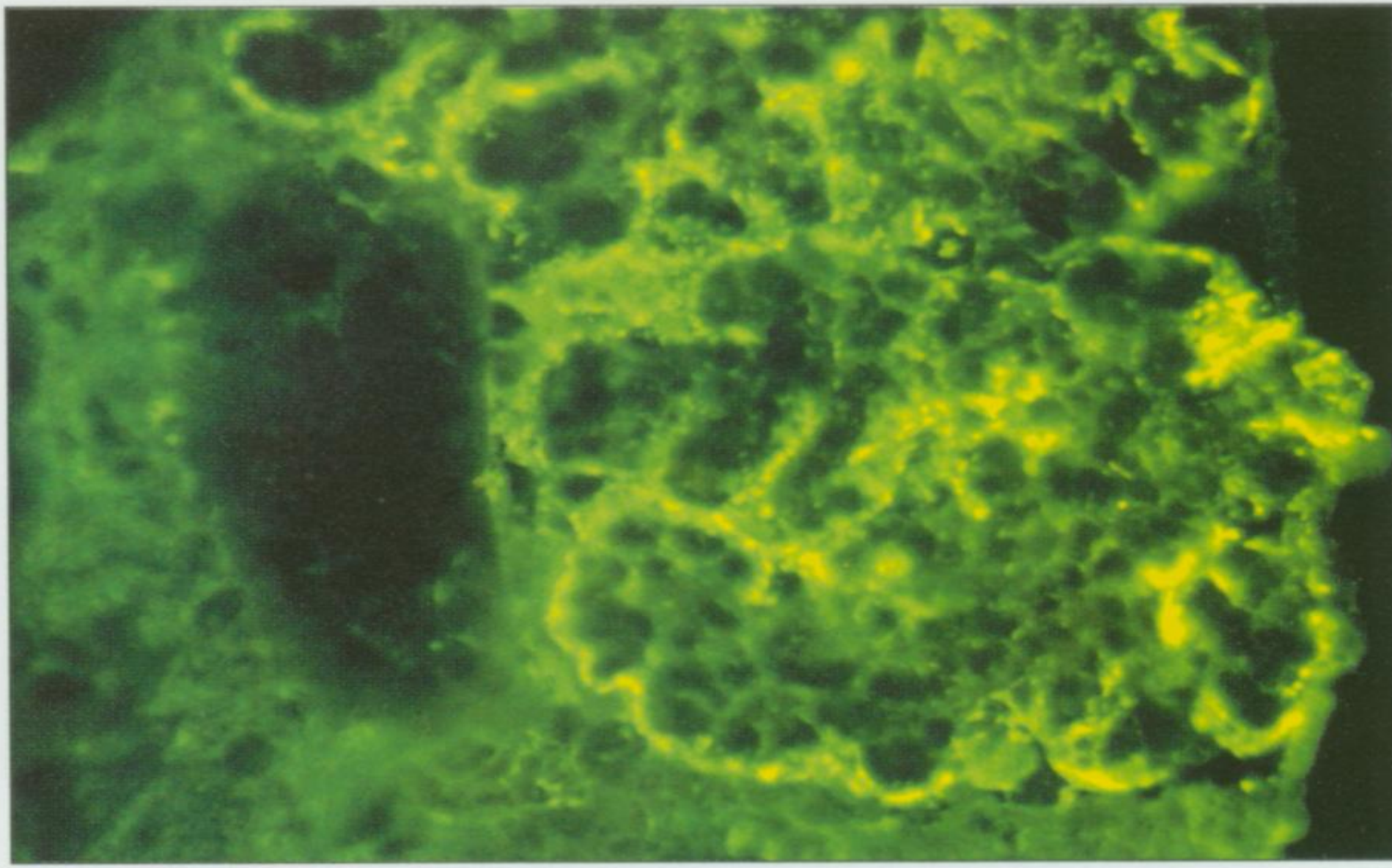
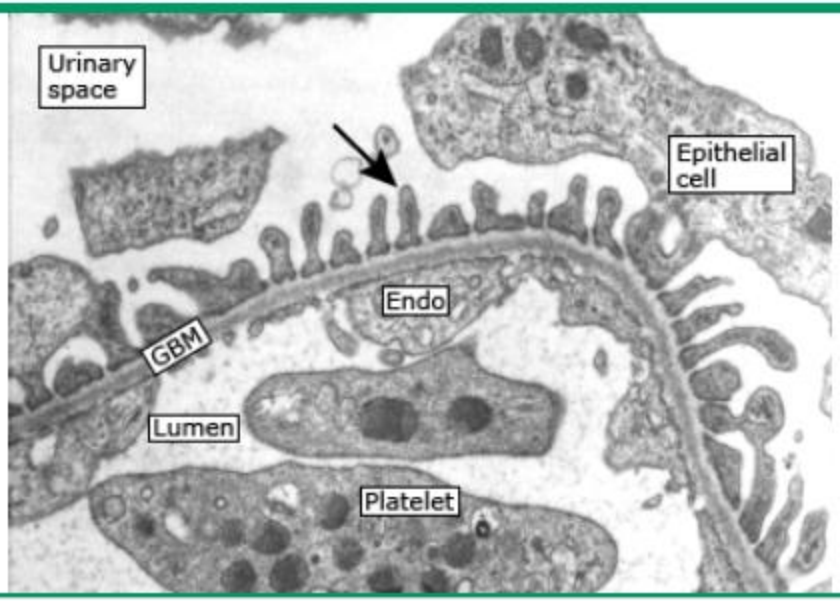


图 06－079　毛细血管内增生性肾小球肾炎，IgG
粗大颗粒状沿毛细血管壁沉积(荧光，×400)

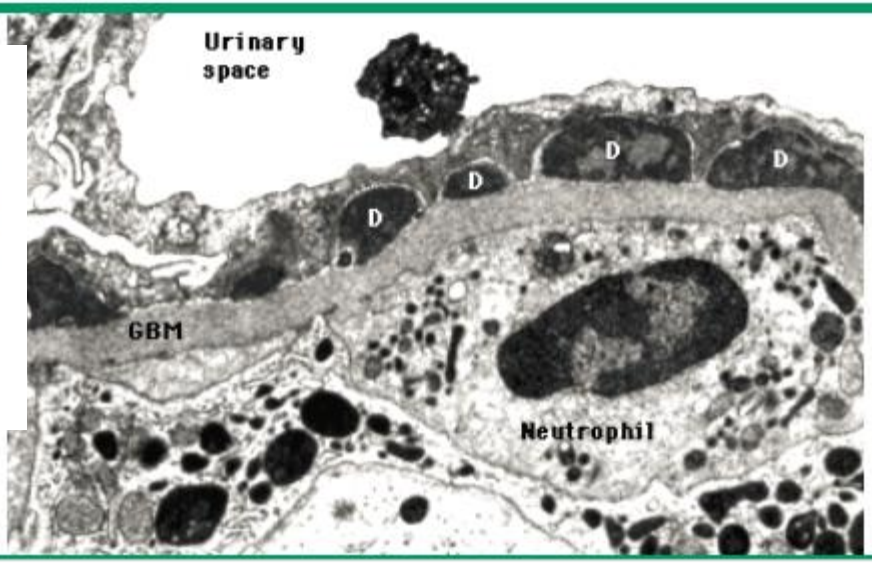
Electron micrograph of a normal glomerulus



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.

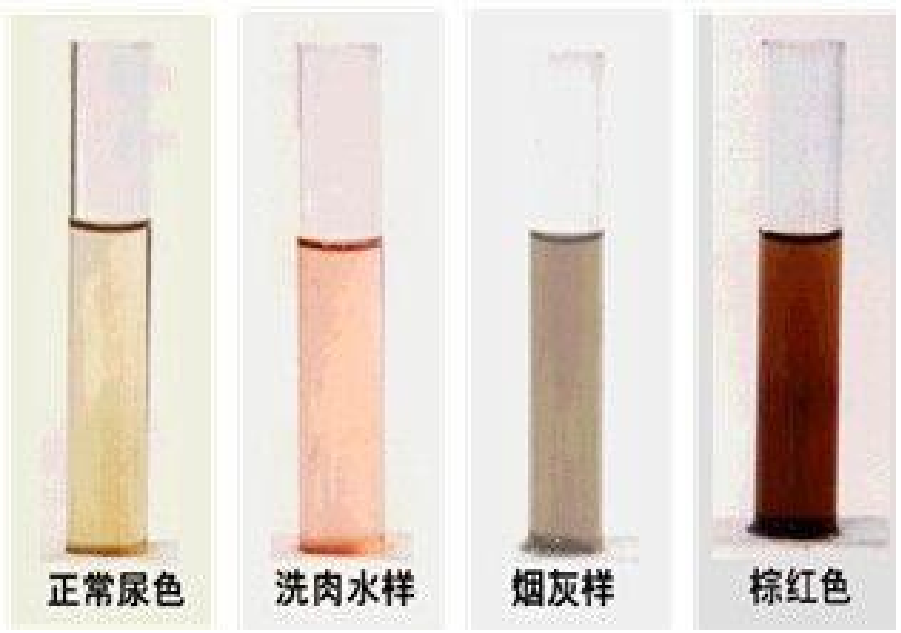


Clinical presentation

- 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

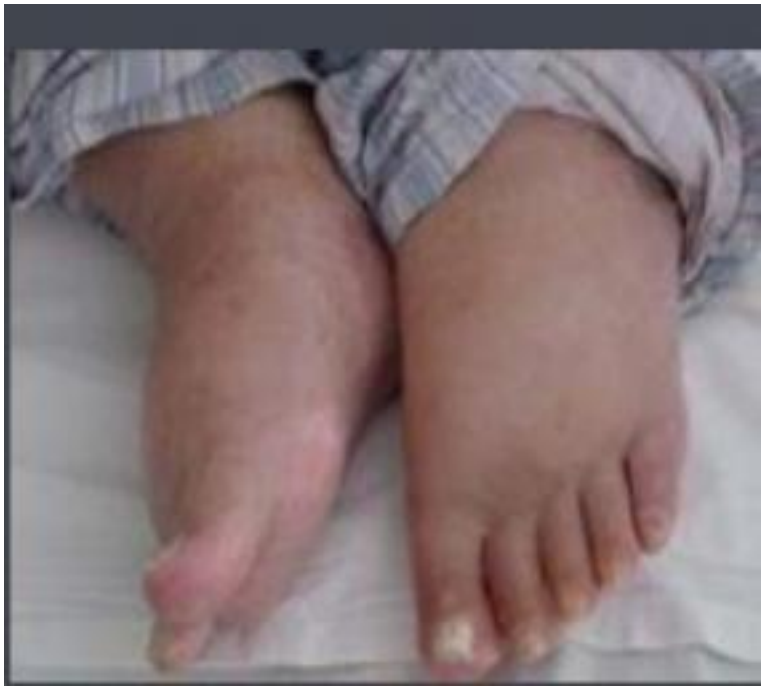


ACUTE NEPHRITIC SYNDROME

- Proteinuria (can reach the nephrotic range) 蛋白尿

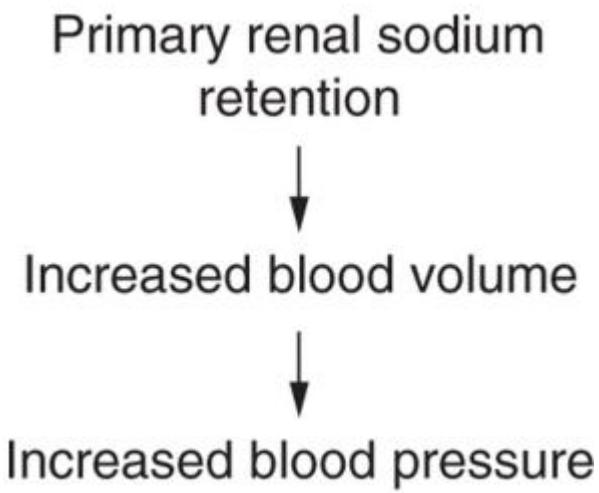
ACUTE NEPHRITIC SYNDROME

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



ACUTE NEPHRITIC SYNDROME

- Hypertension(50-90%)

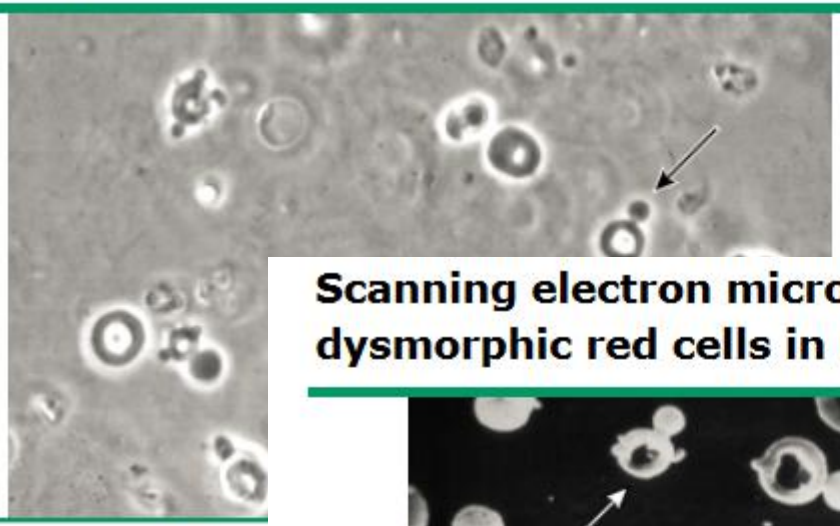


- An elevation in serum creatinine

LABORATORY FINDINGS

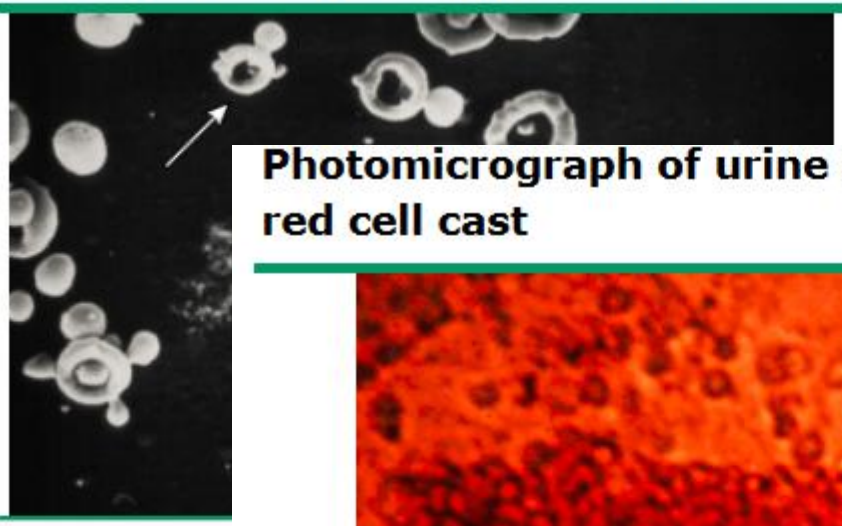
- Renal function---a rise in serum creatinine
- Urinalysis and urinary protein
  - Hematuria with or without red blood cell casts
  - varying degrees of proteinuria
  - often pyuria

Phase-contrast micrograph showing dysmorphic red cells in urine sediment



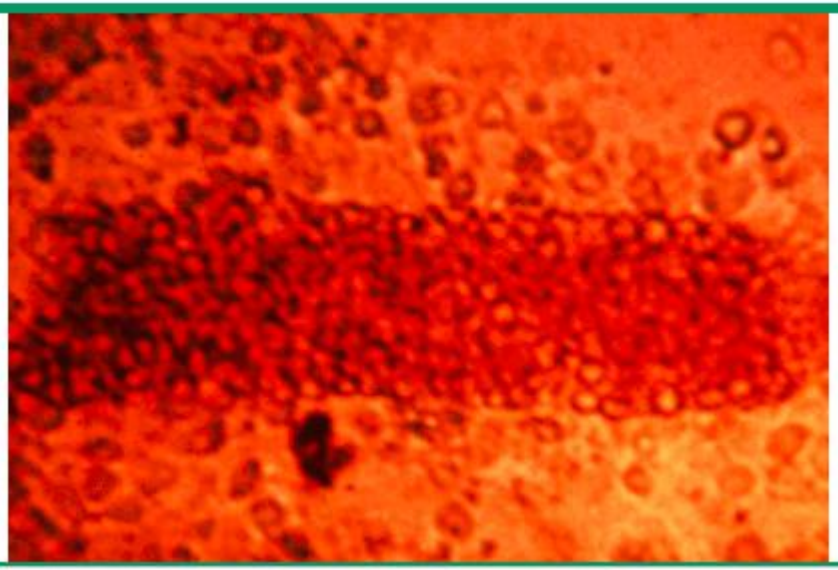
Phase-contrast microsc
patient with glomerula
recognized as ring forn

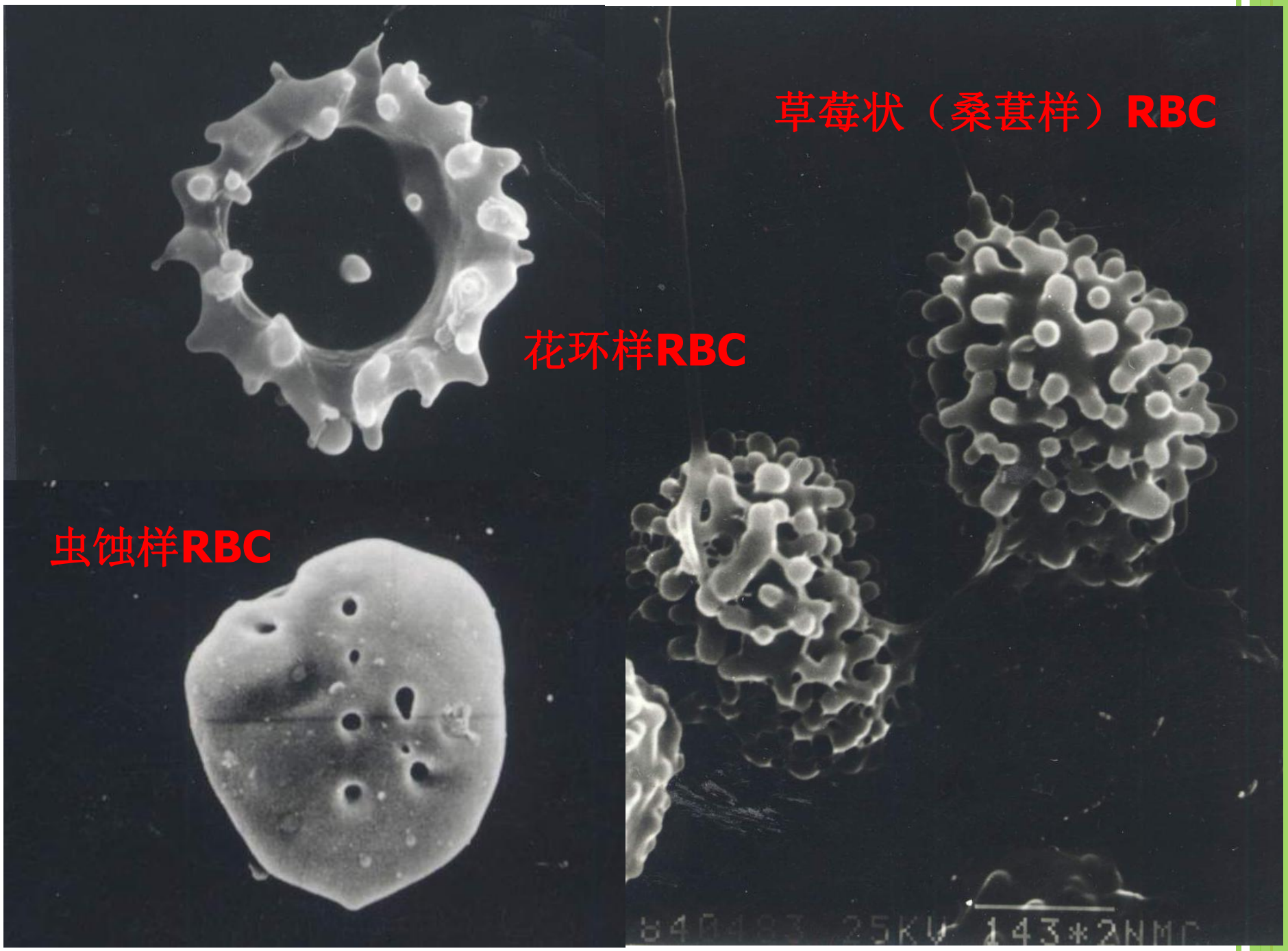
Scanning electron micrograph showing dysmorphic red cells in urine sediment



Scanning microscopy
with glomerular blee
ring forms with vesic

Photomicrograph of urine sediment with a red cell cast




草莓状（桑葚样）RBC
花环样RBC
虫蚀样RBC
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

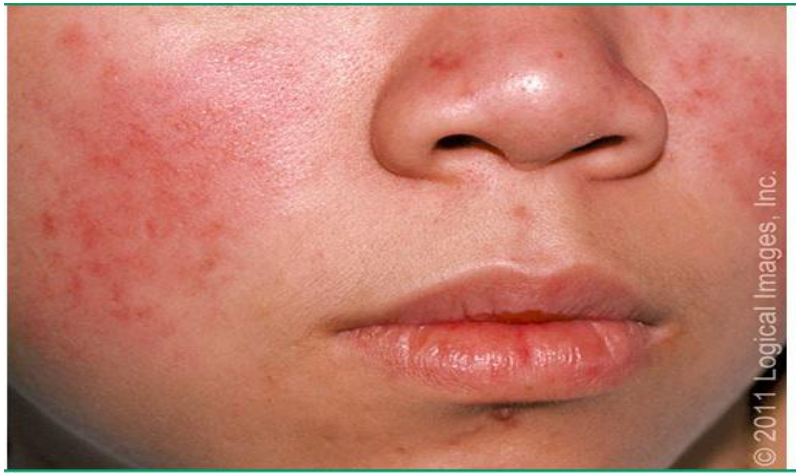
  - child
  - persistent urinary abnormalities
  - hypocomplementemia beyond four to six weeks
  - possibly a further elevation in serum creatinine

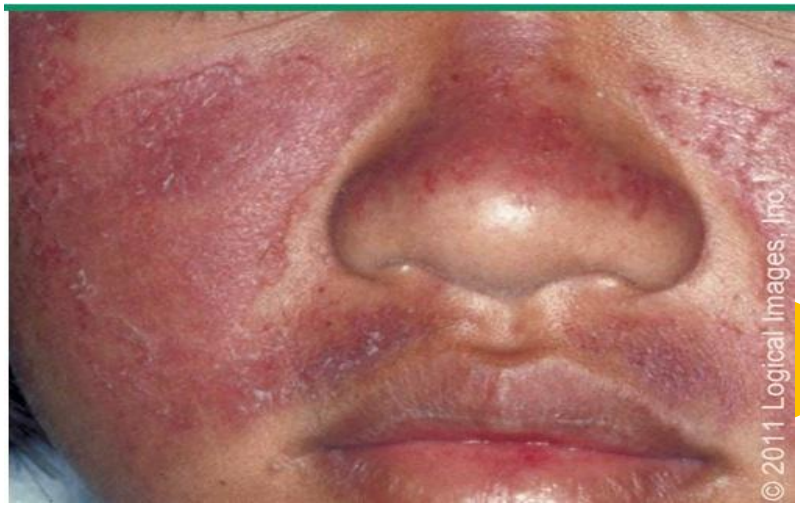
DIFFERENTIAL DIAGNOSIS

- 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

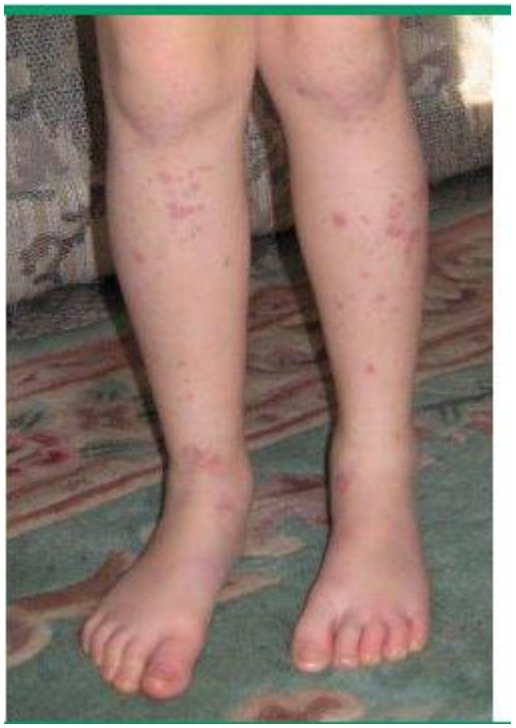
- Secondary causes of glomerulonephritis
  - Lupus nephritis
    - Female
    - Arthralgias 关节痛
    - “butterfly” skin rash 蝴蝶斑
    - Serositis 浆膜炎
    - alopecia (hair loss) 脱发
    - central nervous system disease
    - C3↓

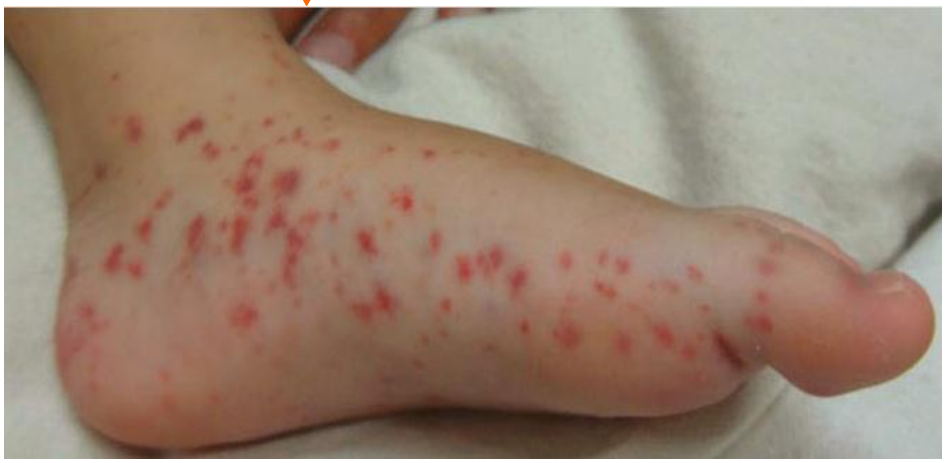




DIFFERENTIAL DIAGNOSIS

- 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 μmol/L (45-137)

C3 0.41(0.61-1.52)

ASO 47

One months later……

Oliguria

Creatine 73 → 3[illegible]4 μ[illegible]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 syndro idly
  developin 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 polyan (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–mediate
  3. Type III—with few or no immune deposits of Ig ("pauci-immune"
  4. Antineutrophil cytoplasmic antibody–induced, forme 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(typeI)**

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

  Goodpasture's syndrome

- **Granular immunofluorescent pattern(immune complex-mediated RPGN) (typeII)**

  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

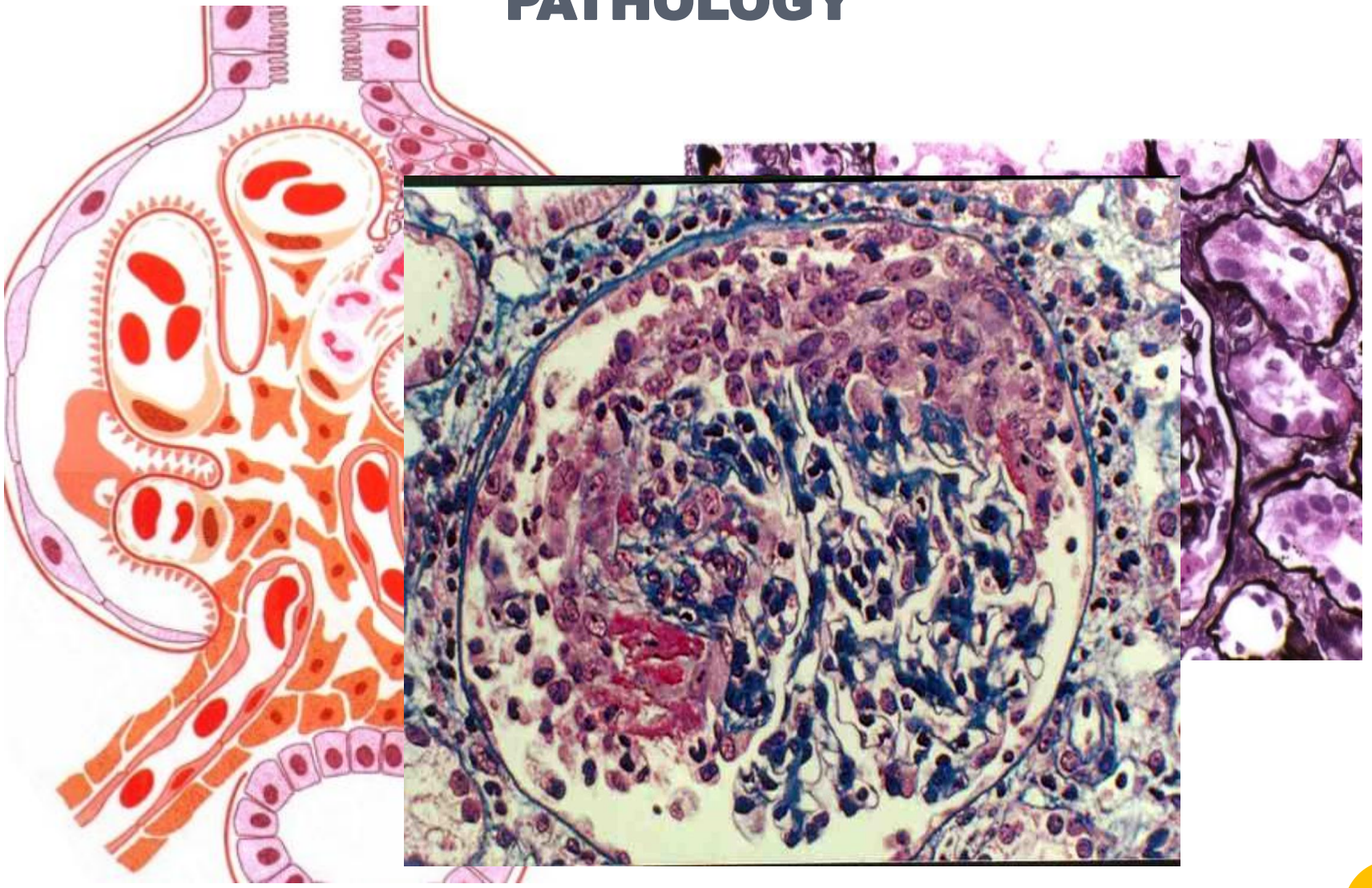
PATHOLOGY

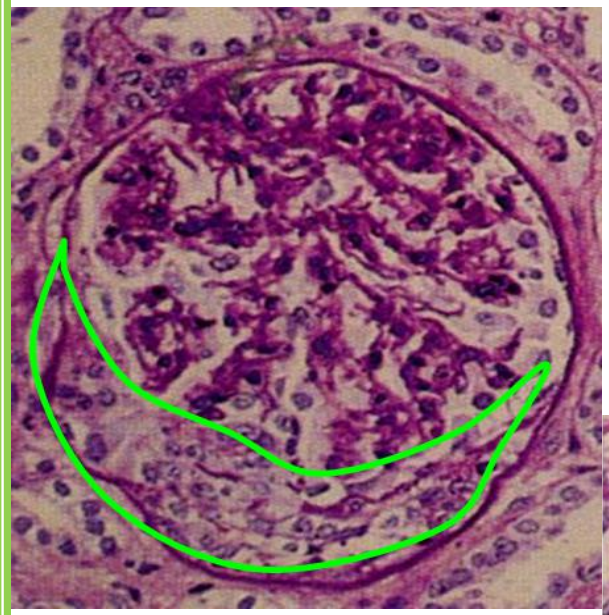
大量新月体形成

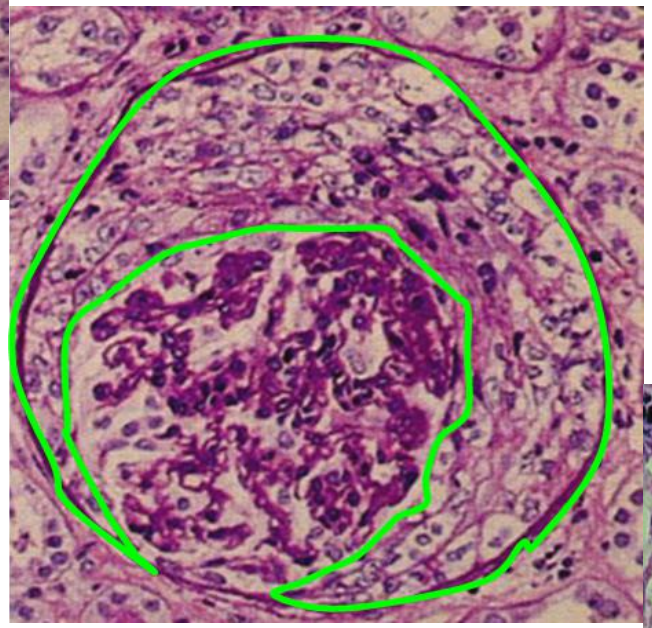
- **新月体(crescents)**：肾小球囊内细胞增生、纤维蛋白沉积，病理切片上似新月状。

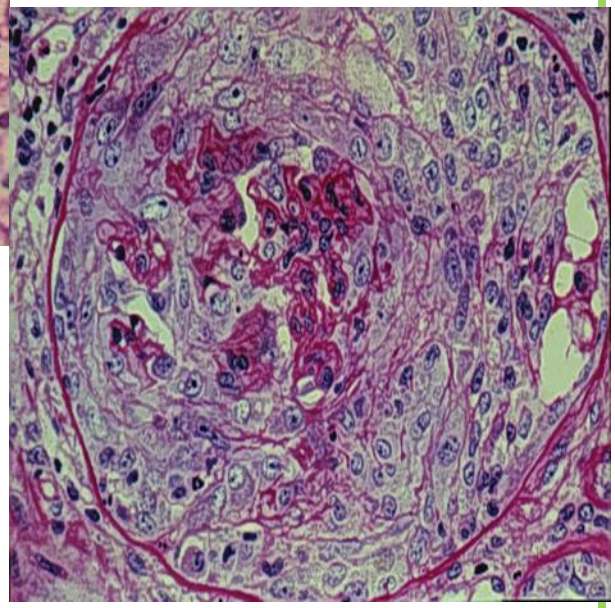
- **新月体肾炎(crescentic GN)**：新月体面积>肾小囊50%、受累肾小球数量>50%。

PATHOLOGY









cresents：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

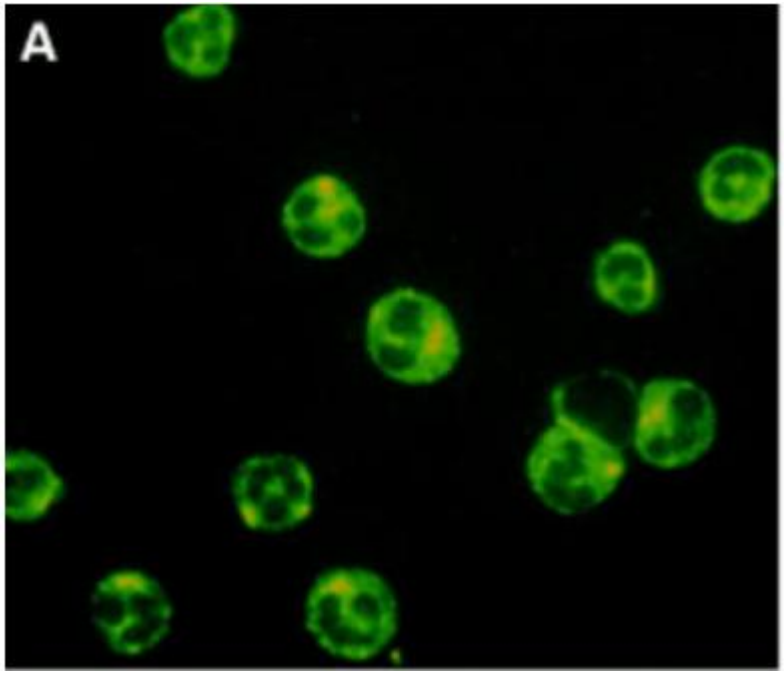
Anti-glomerular basement membrane antibody disease
抗肾小球基底膜病

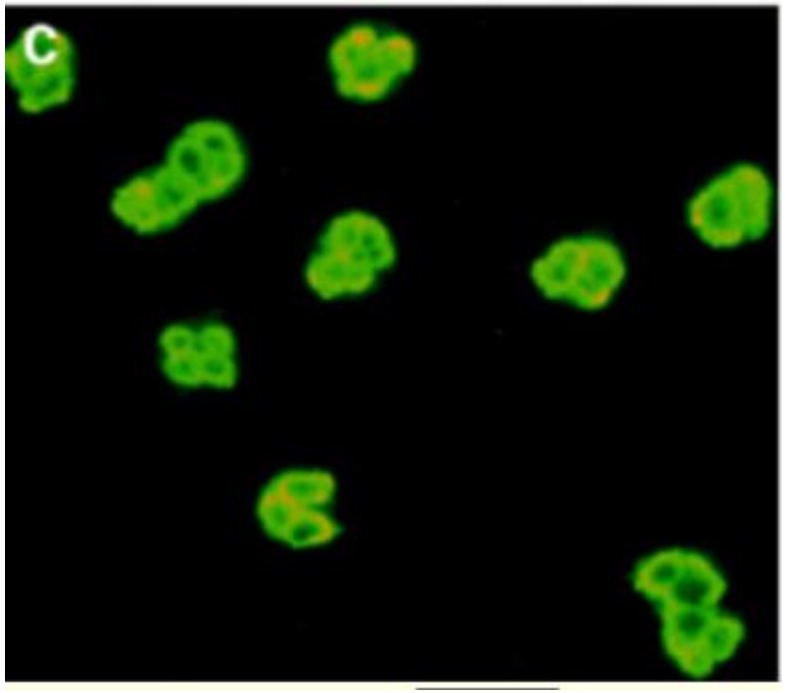
- caused by circulating antibodies that are directed against the noncollagenous domain of the α3 chain of type IV collagen and that damage the GBM.
- If the anti-GBM antibodies cross-react with and damage the basement membrane of pulmonarycapillaries, the patient develops pulmonary hemorrhage and hemoptysis, 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	LM	EM	IF	Serology
I	Crescent >50% GBM breakage	ED (-)	IgG、C3 linear deposition	Anti-GBM(+)
II	Crescent >50% proliferation	ED (+)	IgG、C3 granular deposition	CIC(+)、C3↓
III	Crescent >50% necrosis	ED (-)	(-)	ANCA (+)

Clinical manifestation

- Hematuria(macroscopic or microscopic)

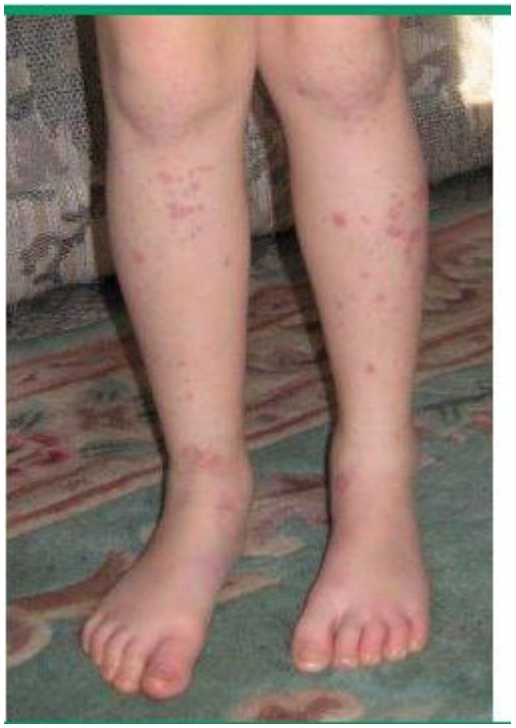
  red-cell casts are typically seen on urine microscopy

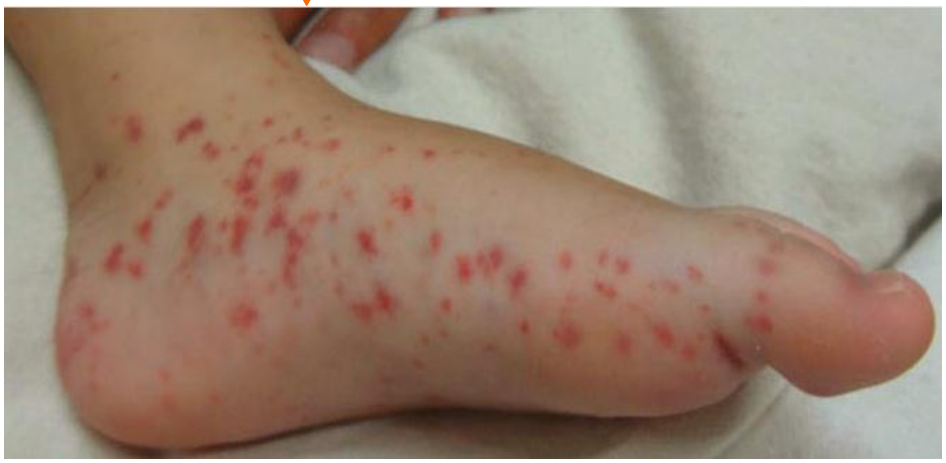
- Proteinuria
- progressive oliguria and renal function failure

- Systemic symptoms: fever, arthrodynia

DIFFERENTIAL DIAGNOSIS

- Secondary causes of glomerulonephritis
  - IgA vasculitis
    - 3-15 years old
    - Palpable purpura
    - Arthritis
    - Abdominal pain
    - C3↓





Clinical manifestation

- TypeI: 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 ↓

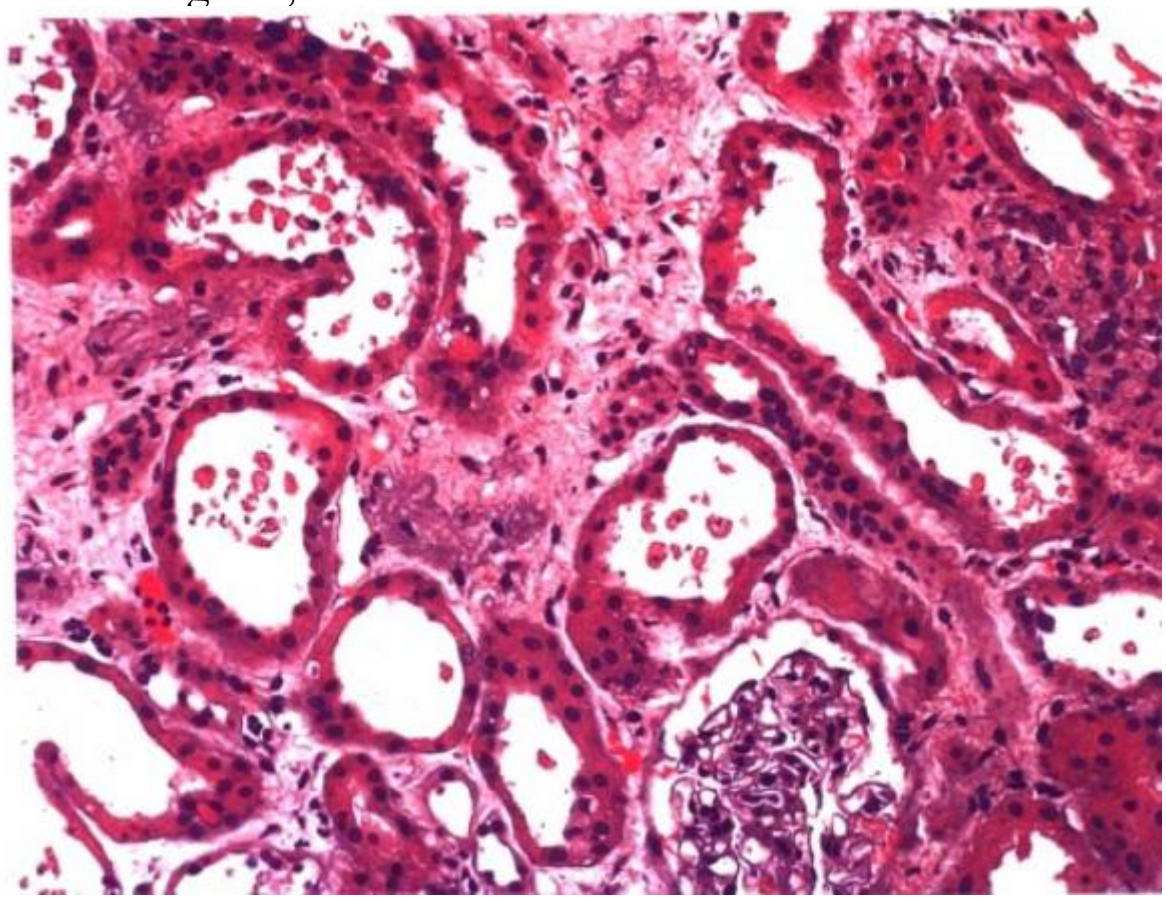
Type III : ANCA(+)

Ultrasound: kidneys enlargment

- Pathological characters

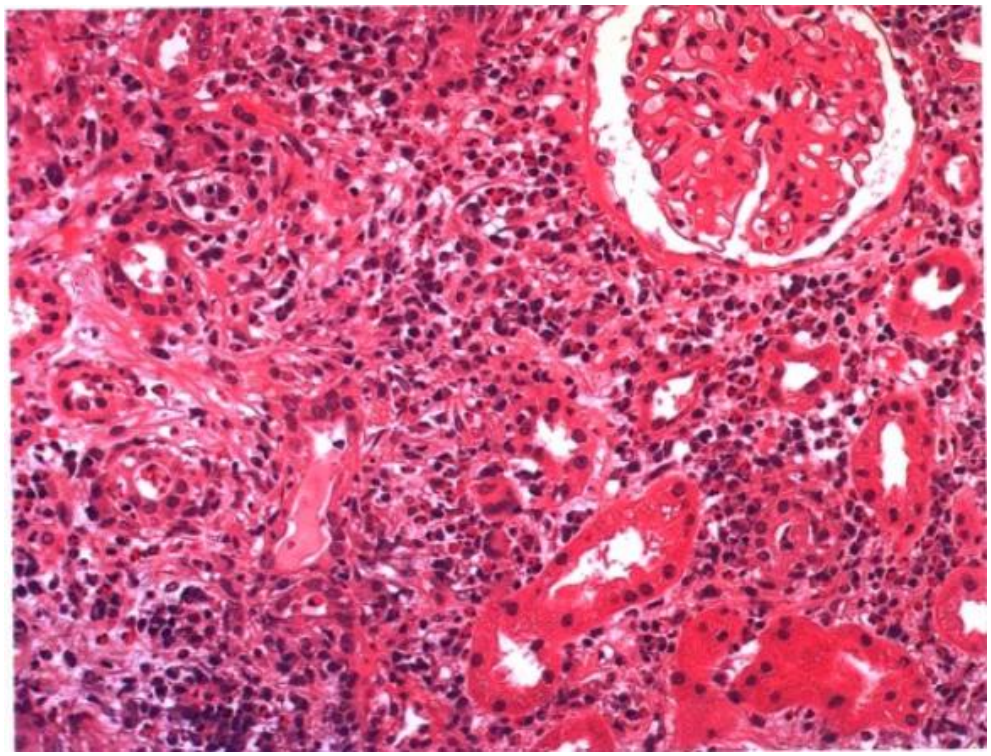
DIFFERENTIAL DIAGNOSIS

- 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, hemauria, an increased in Scr, esoinophilia

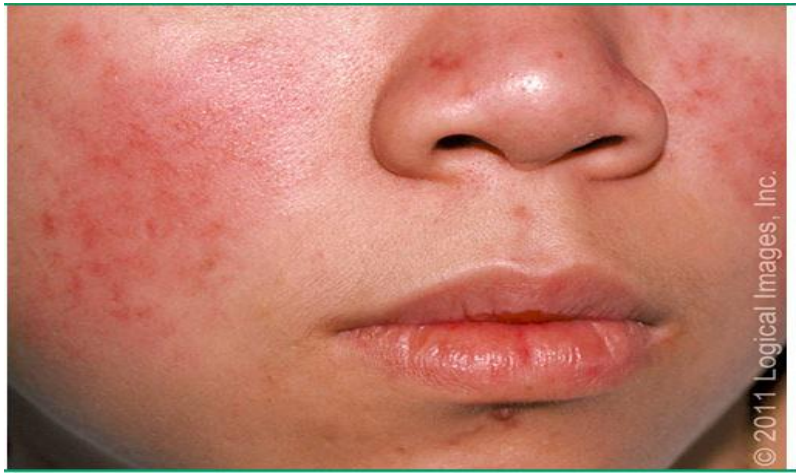


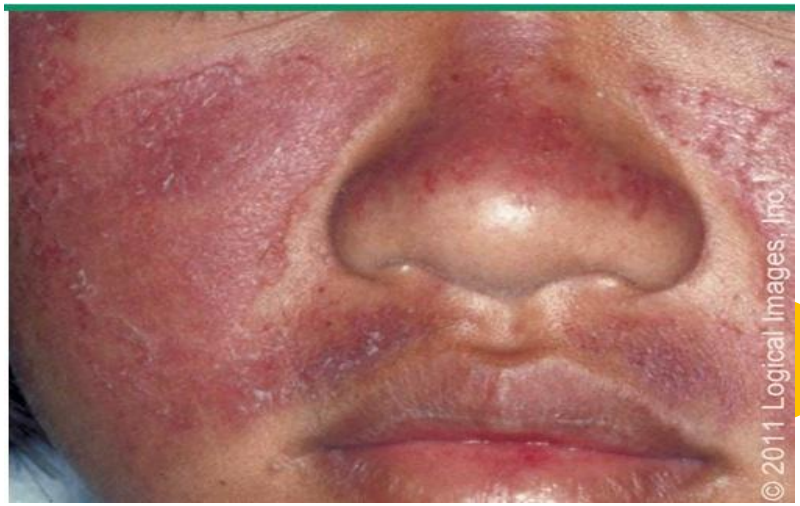
DIFFERENTIAL DIAGNOSIS

- 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**

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

②oral 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 <600μmol/L
- Older

3 days later……

Oliguria

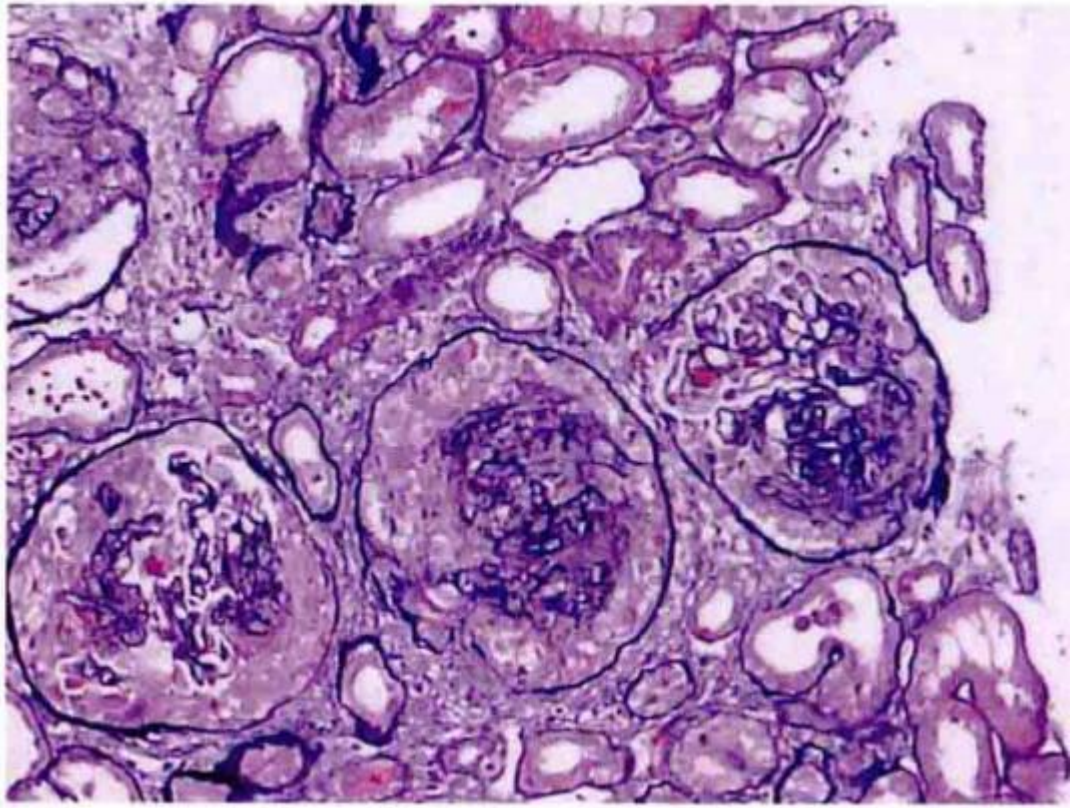
Creatine 324→517 μmol/L (45-137)

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→218μmol/L (45-137)

RBC → 10-20/HP

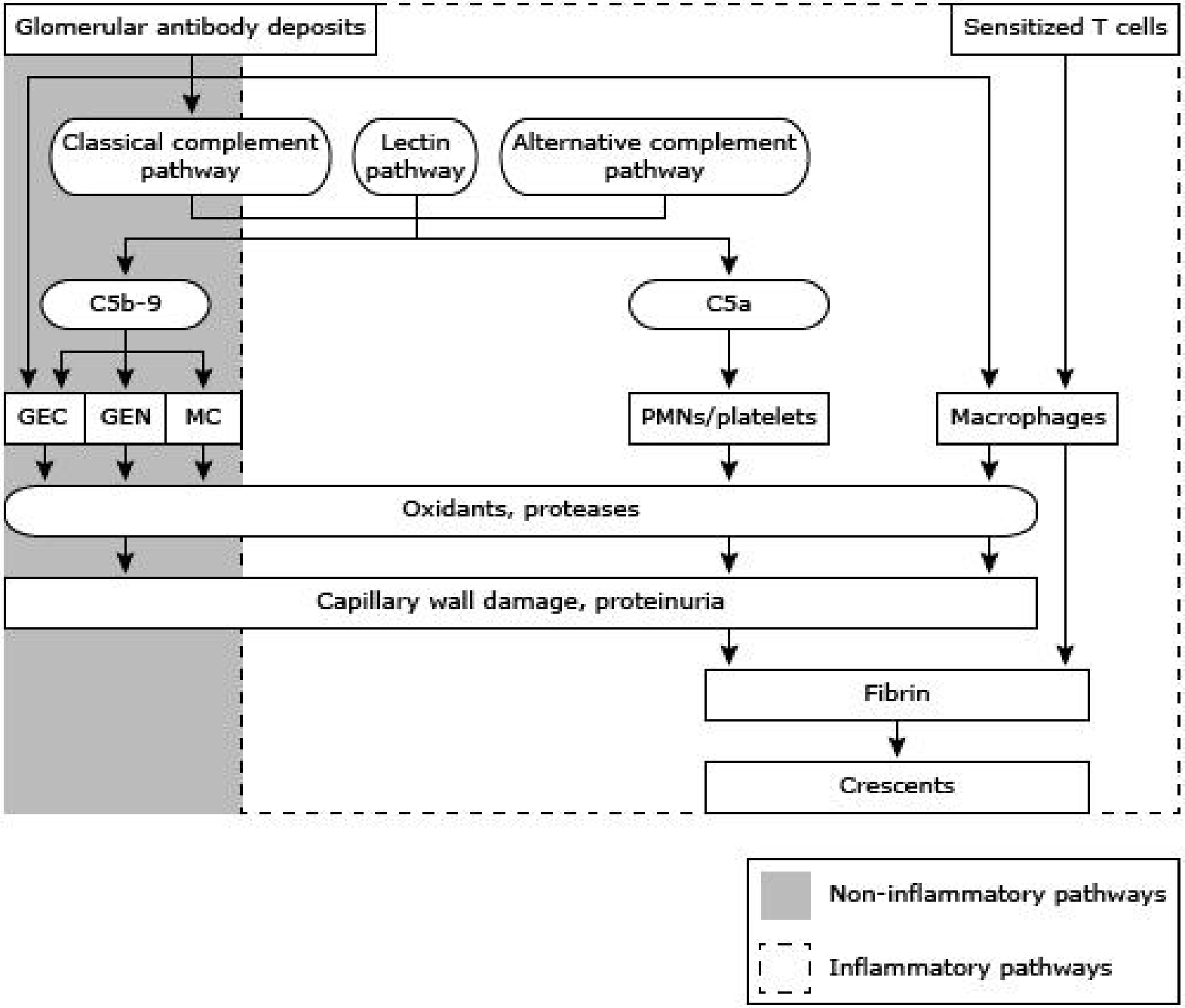
Prognosis ???

Chronic Glomerulonephritis

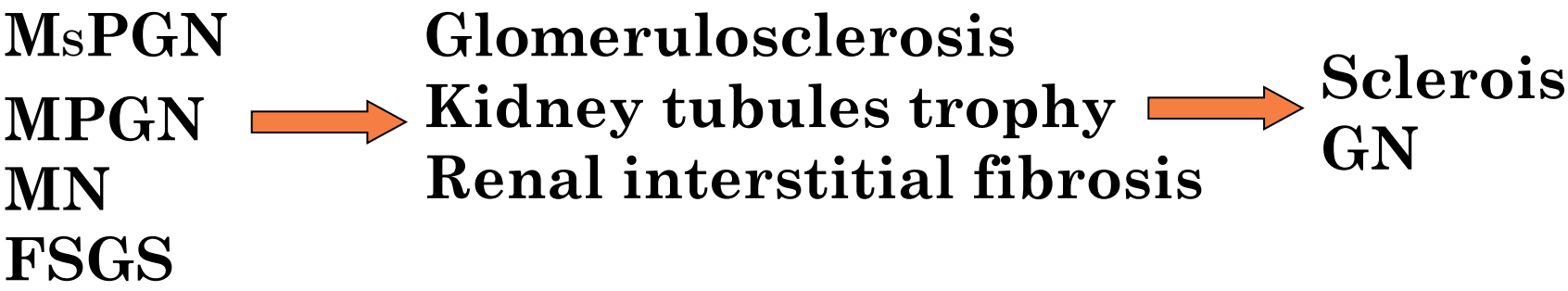
慢性肾小球肾炎

Chronic Glomerulonephritis

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


Glomerular antibody deposits
Sensitized T cells
Classical complement pathway
Lectin pathway
Alternative complement pathway
C5b-9
C5a
GEC
GEN
MC
PMNs/platelets
Macrophages
Oxidants, proteases
Capillary wall damage, proteinuria
Fibrin
Crescents
Non-inflammatory pathways
Inflammatory pathways

PATHOLOGY


MsPGN
MPGN
MN
FSGS
Glomerulosclerosis
Kidney tubules trophy
Renal interstitial fibrosis
Sclerois
GN

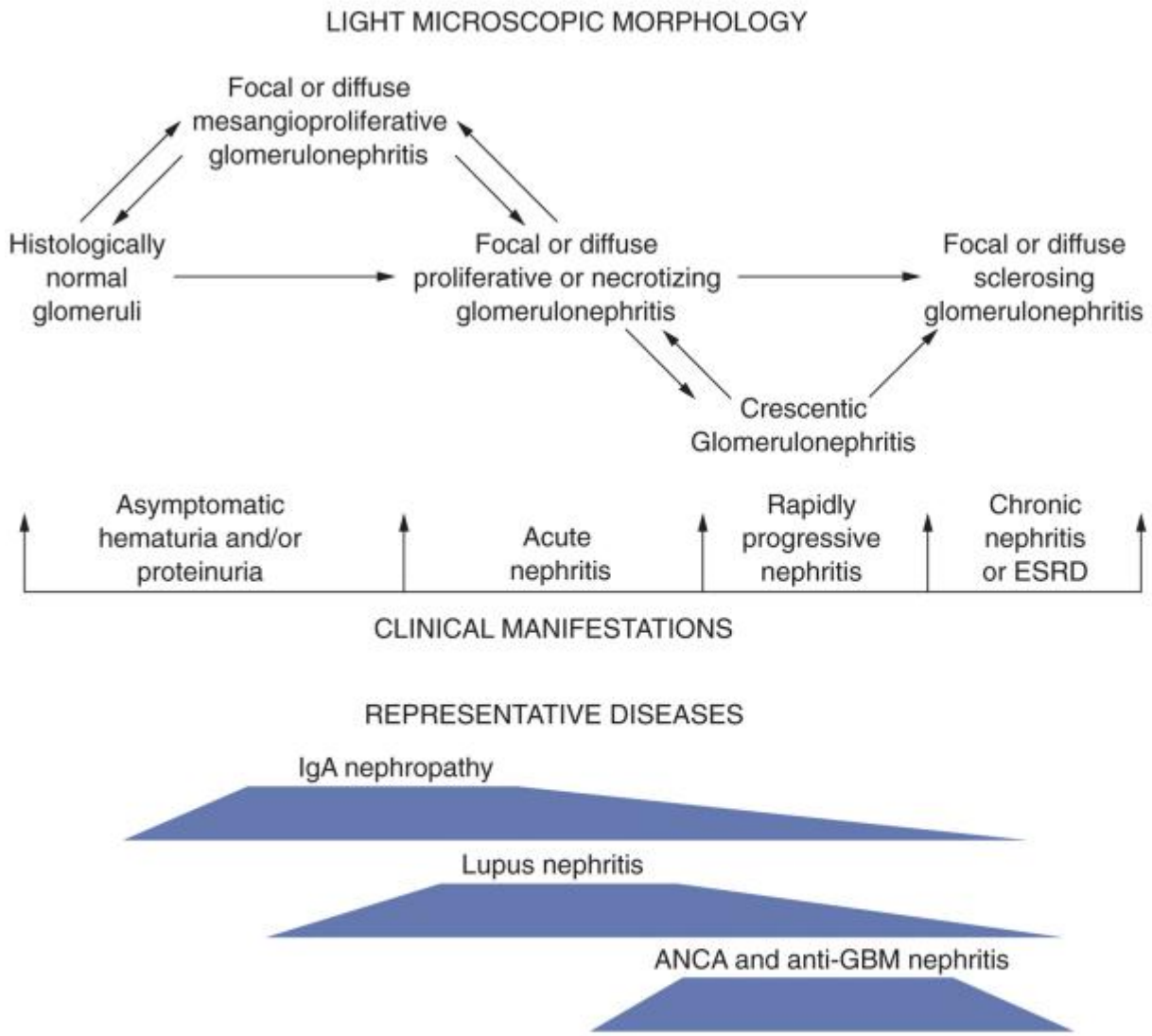


FIGURE 30-18 Diagram depicting the continuum of structural changes that can be caused by glomerular inflammation (top), the usual clinical syndromes that are caused by each expression of glomerular injury (middle), and the portion of the continuum that is most often attained by several specific categories 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≤1g/d; Bp＜ 130/80 mmHg
  - UTP≥1g/d; Bp＜ 125/75 mmHg
- Drugs
  - Diuretic
  - ACEI / ARB
  - CCB
  - β-Blocker
  - α-Blocker

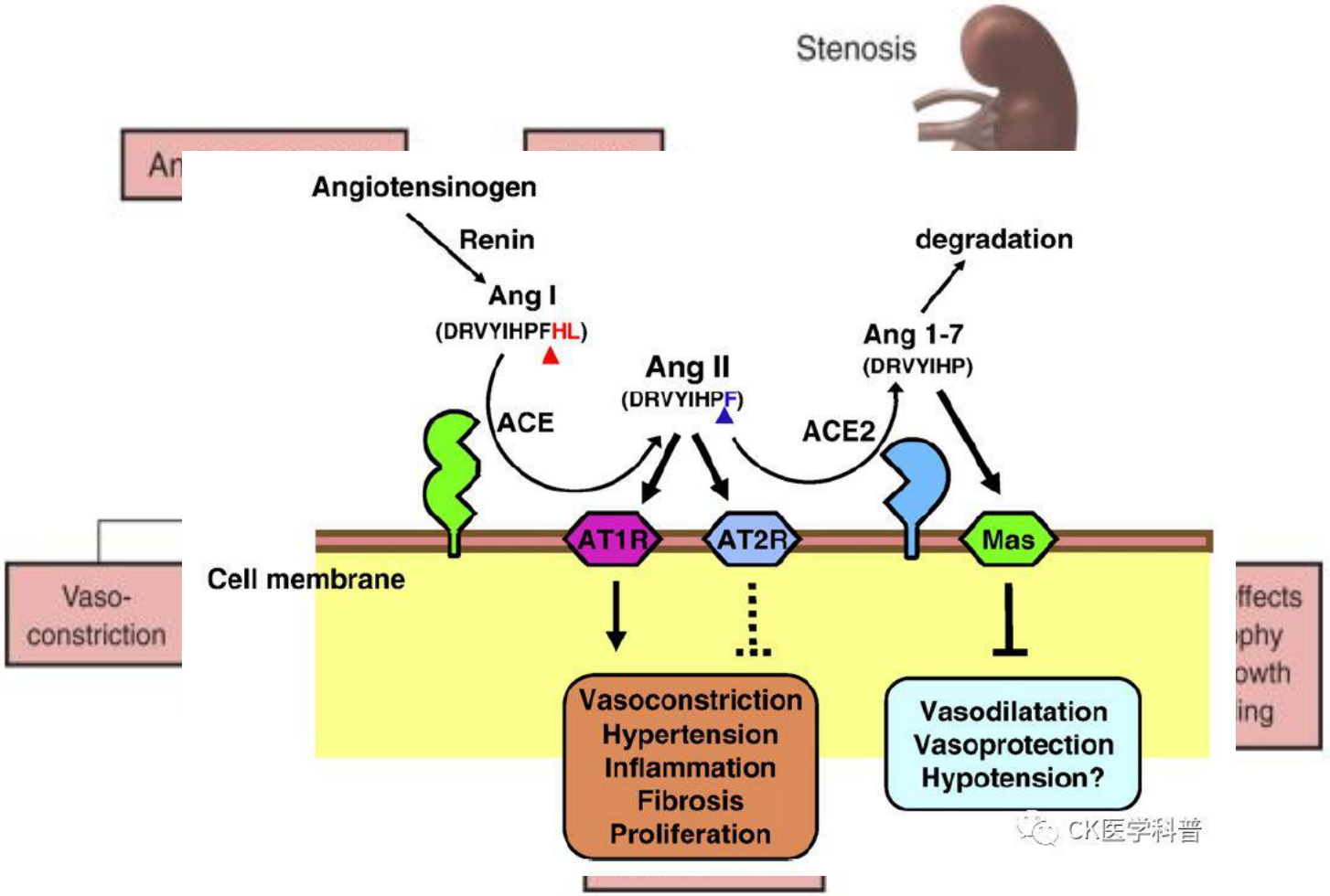

Stenosis
Angiotensinogen
Renin
Ang I
(DRVYIHPFHL)
ACE
Ang II
(DRVYIHPF)
ACE2
degradation
Ang 1-7
(DRVYIHP)
AT1R
AT2R
Mas
Cell membrane
Vaso-
constriction
Vasoconstriction
Hypertension
Inflammation
Fibrosis
Proliferation
Vasodilatation
Vasoprotection
Hypotension?
CK医学科普

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

↓

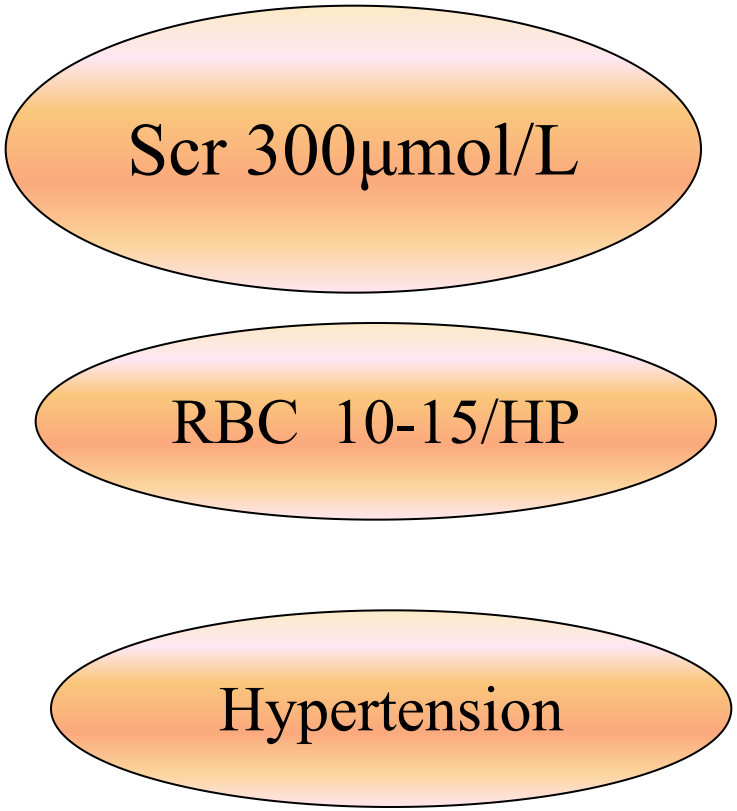
减缓肾间质纤维化

↓

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 300μmol/L
RBC 10-15/HP
Hypertension

Asymptomatic hematuria and/or proteinuria

- Latent glomerulonephitis
- UTP<1g/d
- Glomerular microhematuria
- Without edema, hypertension and have an 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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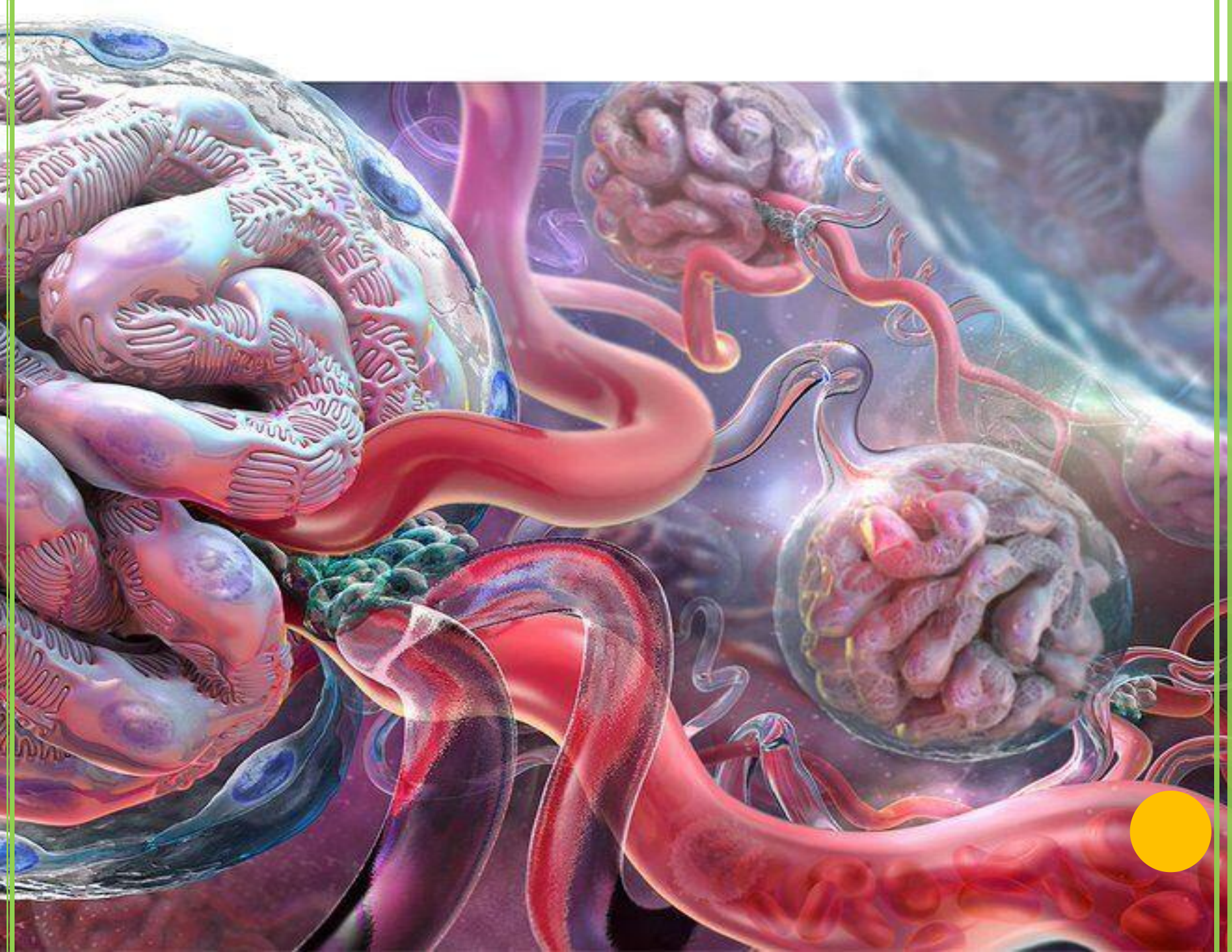
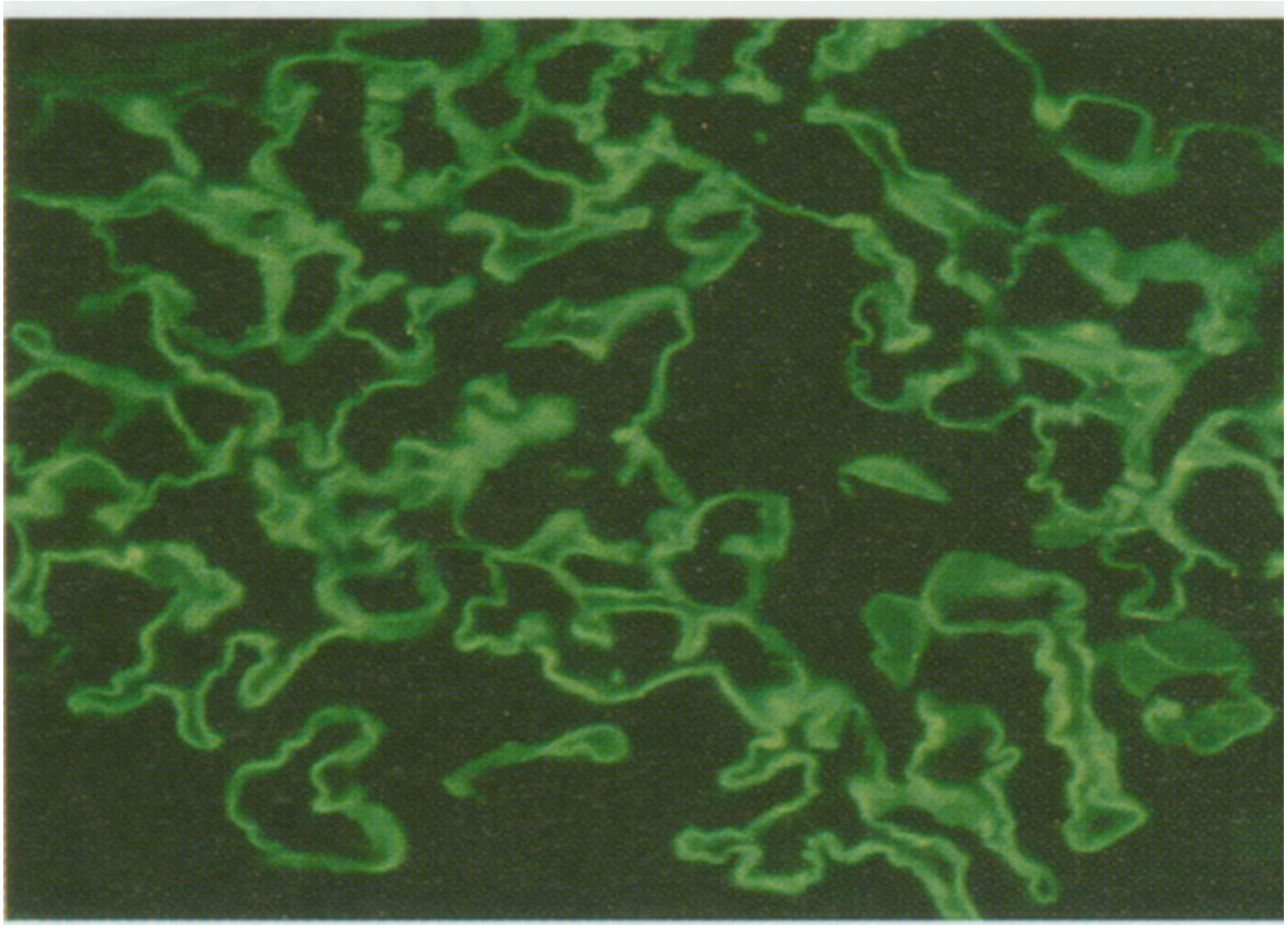



Thank you



Anti-GBM GN (IgG)