nephrotic syndrome

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Nephrotic syndrome

Nephrotic range proteinuria, (>40mg/m^2/hour), (> 50mg/kg/day), urine to protein creat ratio (>2mg/mg), +3-4 on dipstick

Hypoalbumenia (<3 g/dl)

Edema

Hyperlipidemia

M:F 2:1

Incidence 1-3/100,000.Prevelance 16/100,000

Age 2-7 y

ETIOLOGY

Primary or idiopathic(MCD,FSGS,Membranous,MPGN, Mesangial proliferation)

Congenital nephrotic syndrome (first 3months)

Secondary to infections (hepatitis B,C),systemic diseases (HSP,SLE),malignancy,drugs

Clinical presentation and LABS

History: periorbital swelling,ascitis,scrotal or sacral

edema,abdominal pain due hypovolemia,peritonitis

30-50%preceded by URTI

LABS: ,UA, spot protein/creatinine/ serum albumin,lipid profile

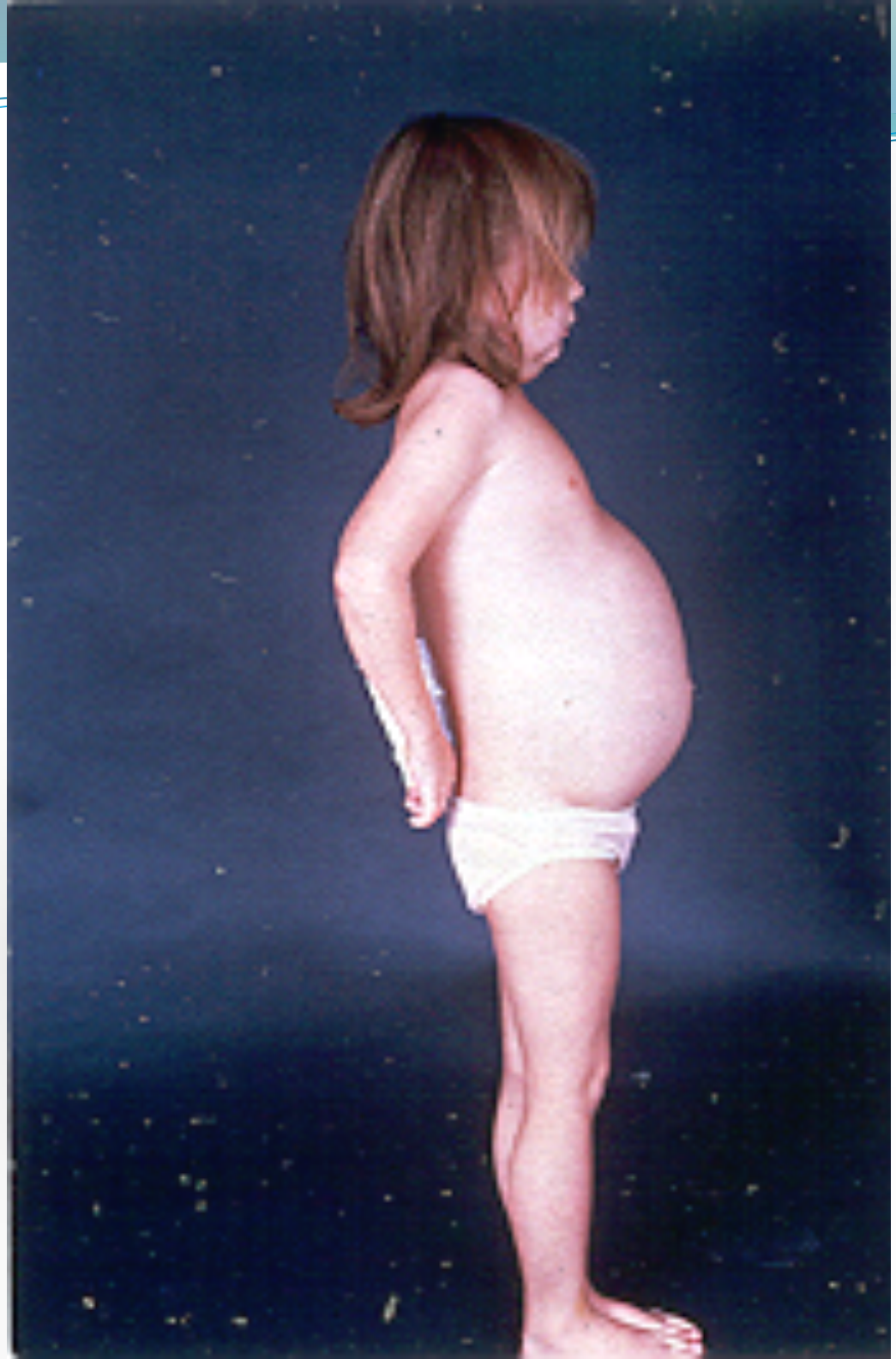
C3,C4,ANA,Hepatitis B,C

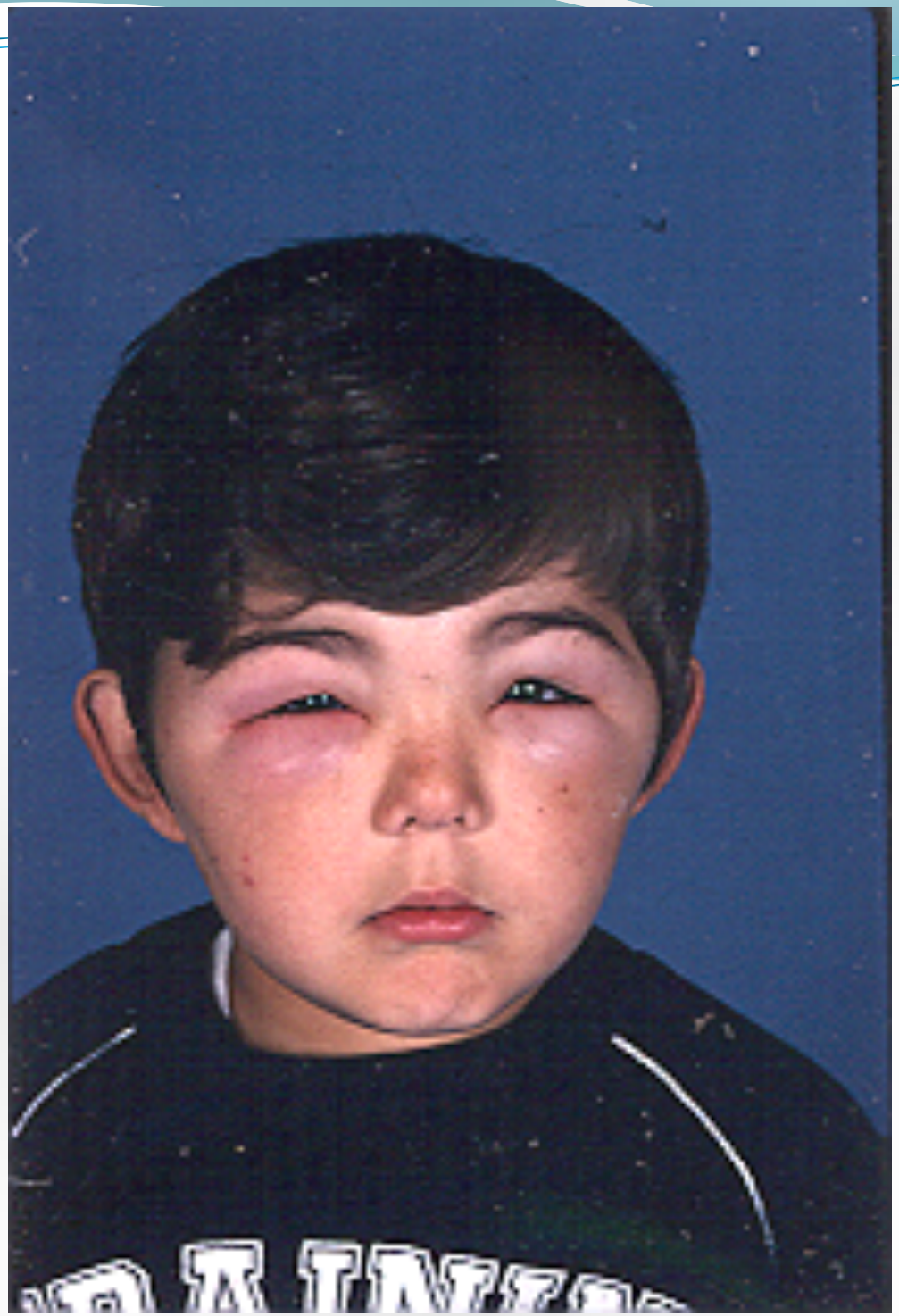
Urine Na <20 in underfill hypothesis

Microscopic hematuria

Hemoglobin high, plat high,Na low

Ca low with respect to albumin





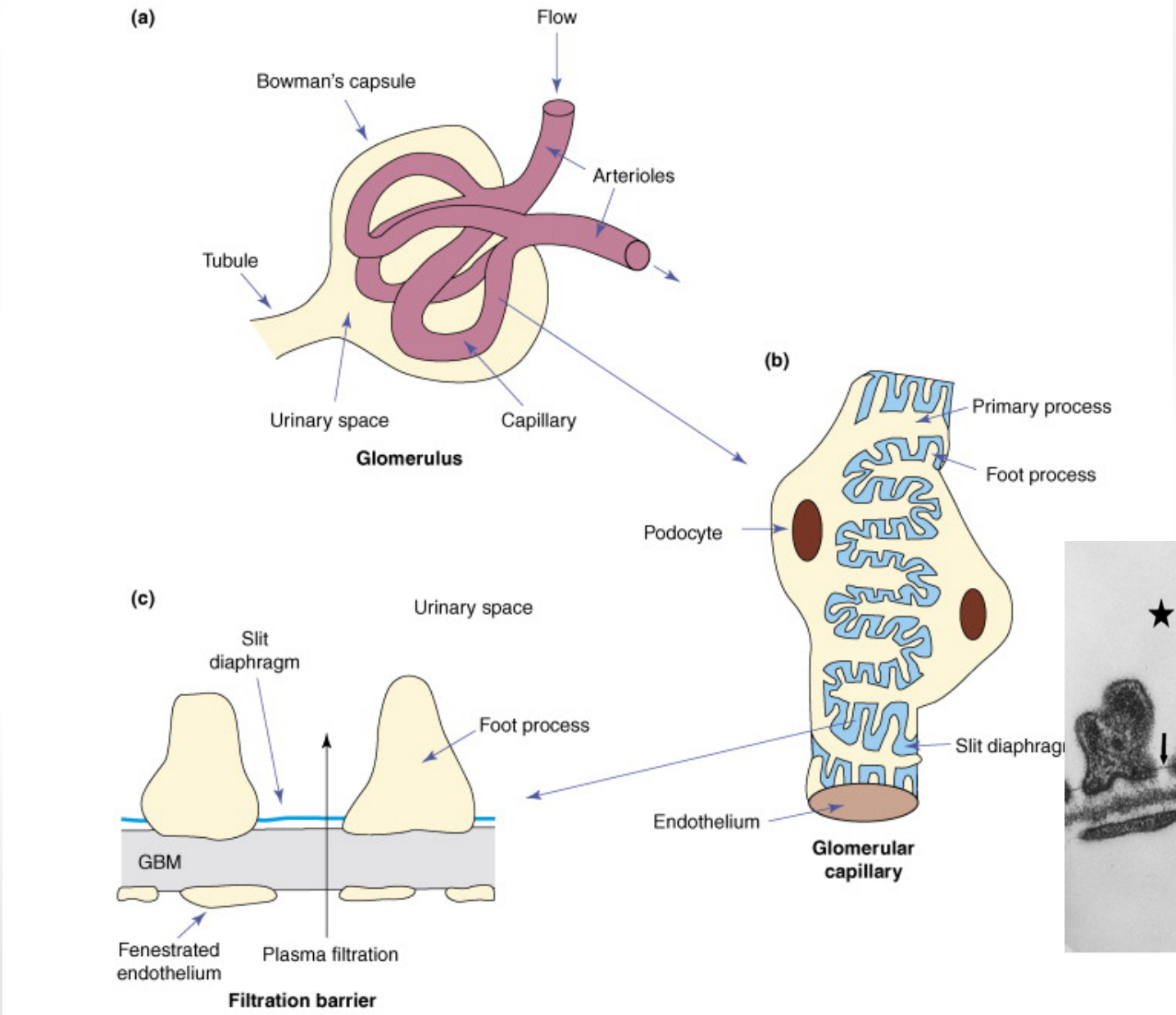
Pathogenesis

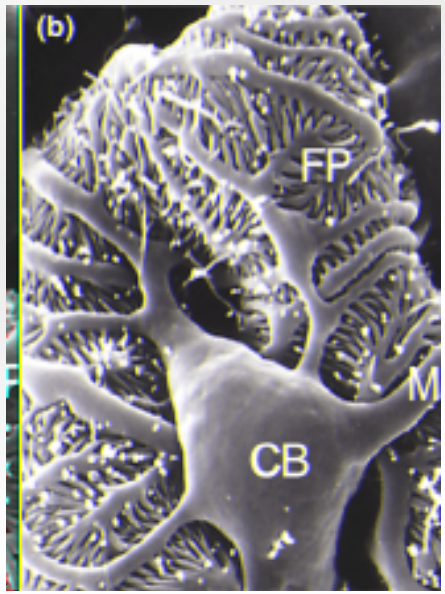
Defect in GBM,slit diaphram,genetic mutations in nephrin,podocin

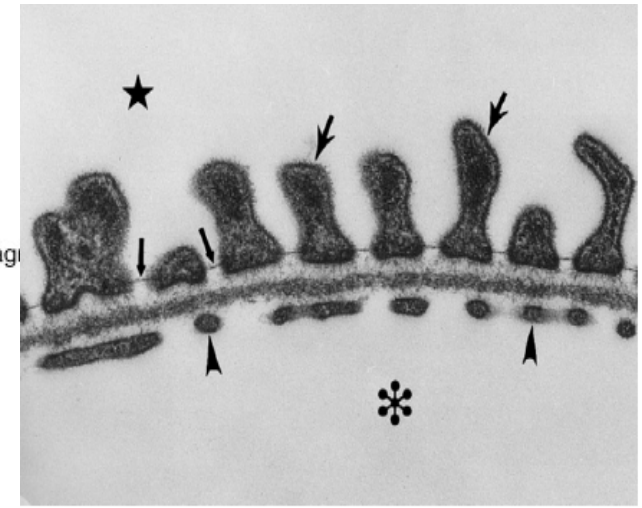
circulating factor,cytokine VPF explains early recurrence

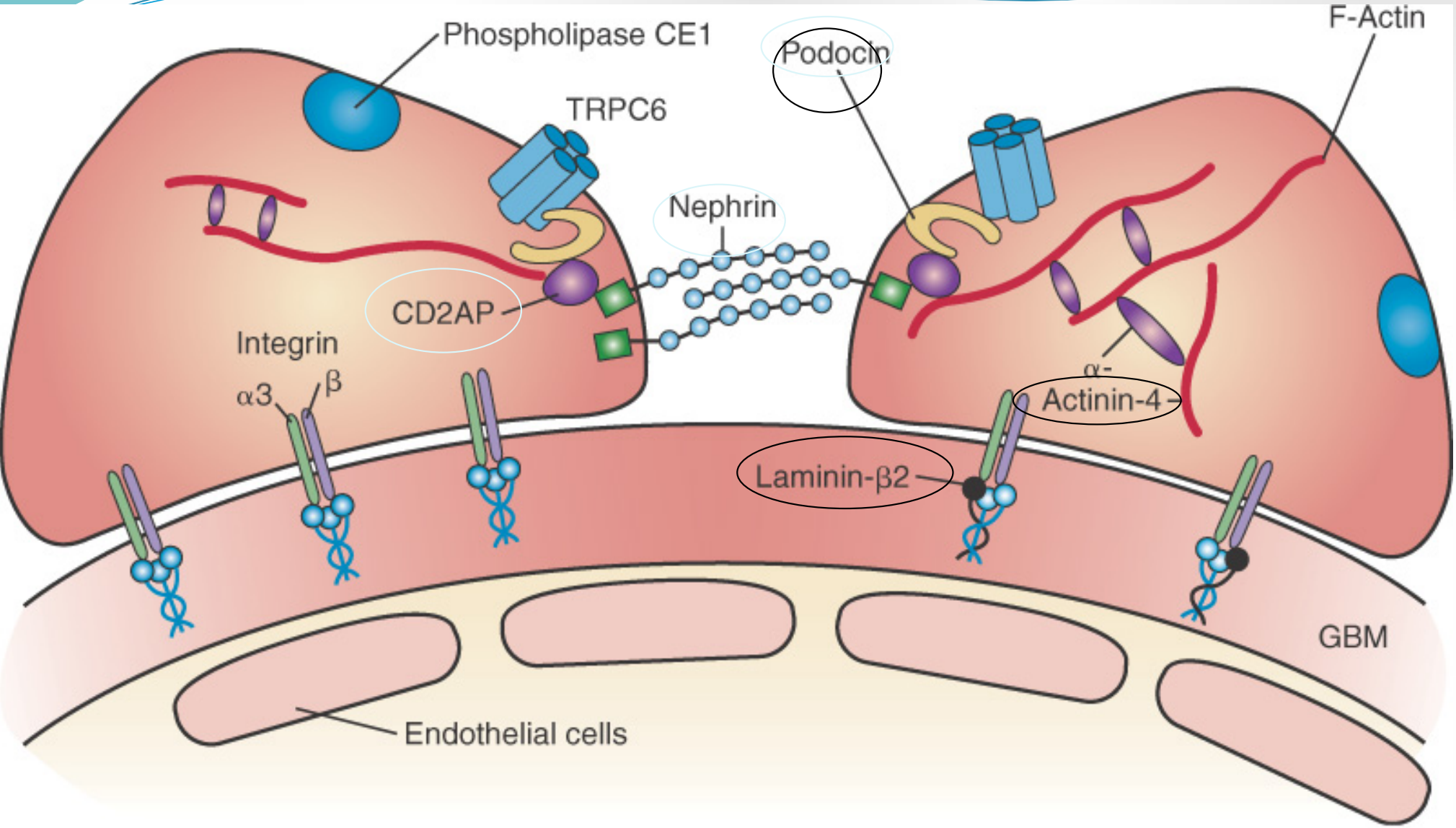
Immunological abnormality,T cell dysfunction,ass with Hodgkin lymphoma

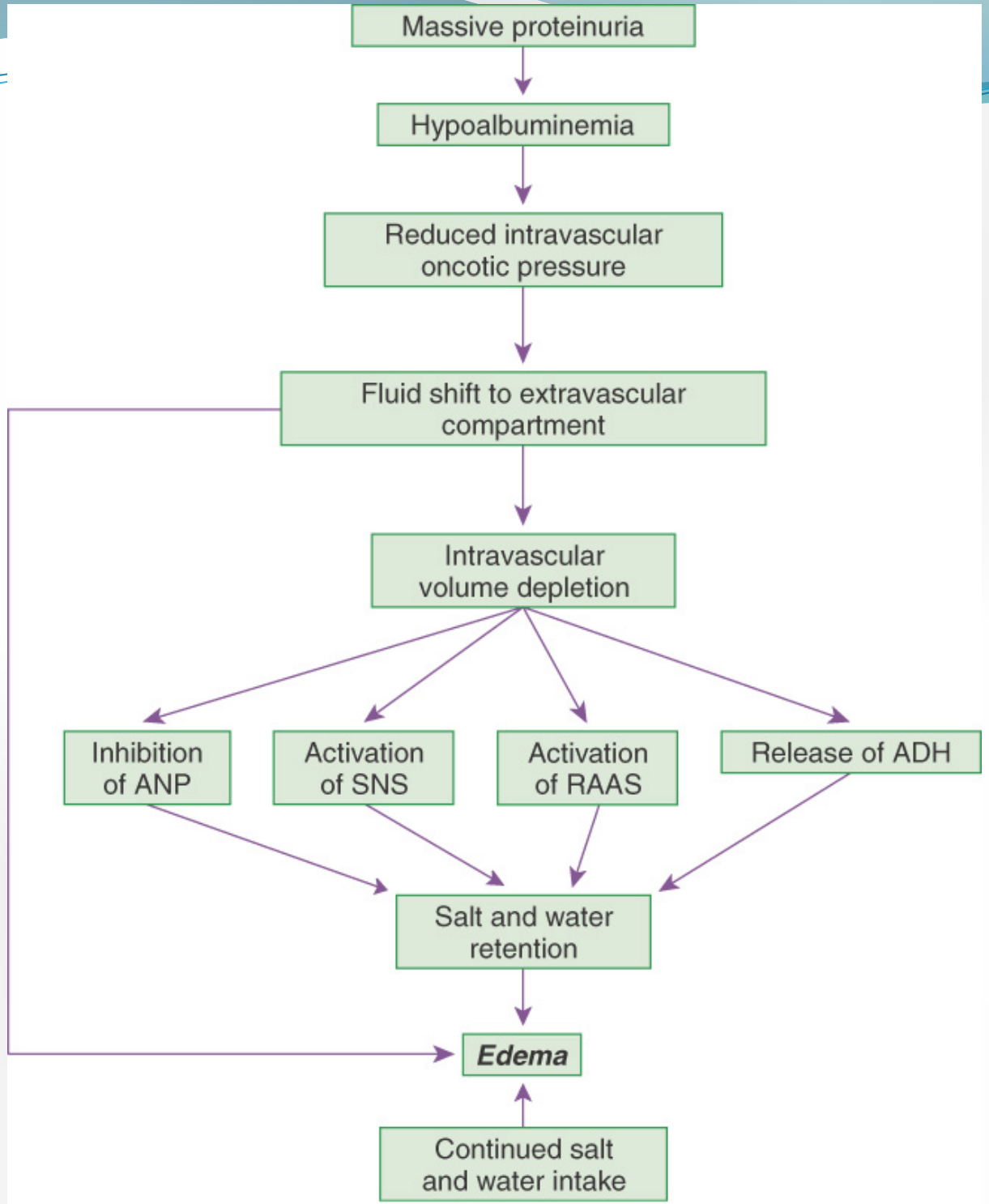
Podocytes and the slit diaphragm











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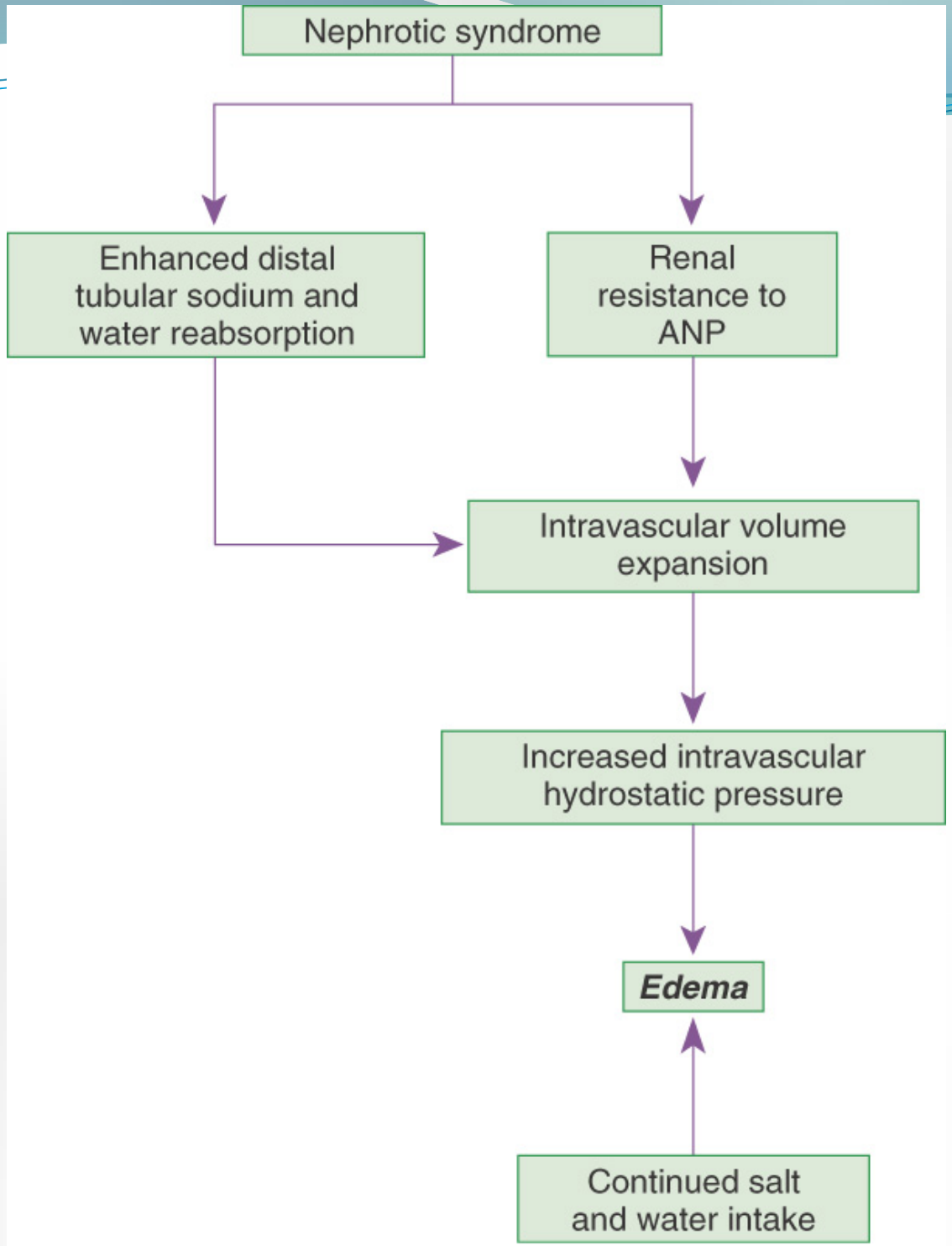

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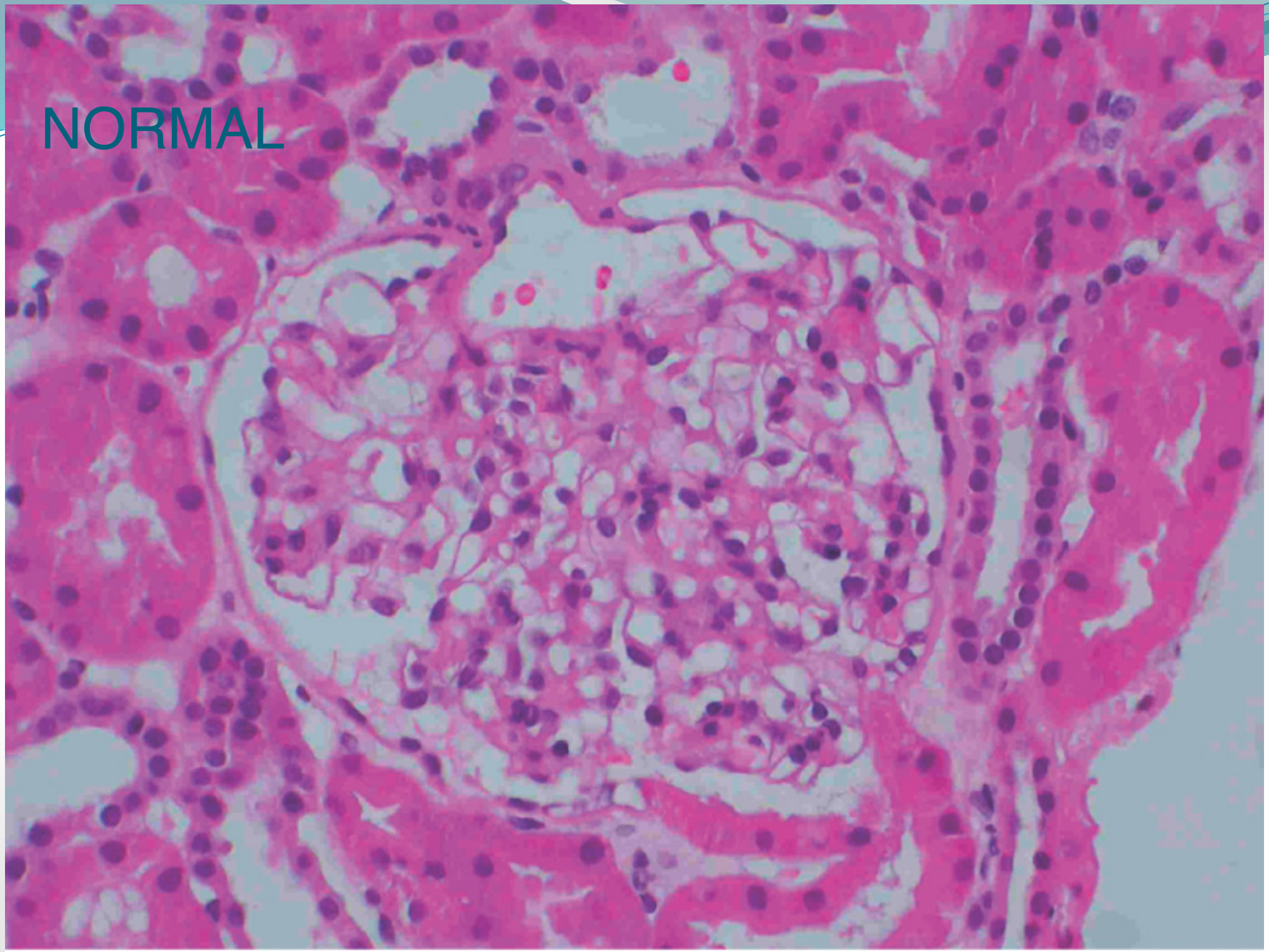
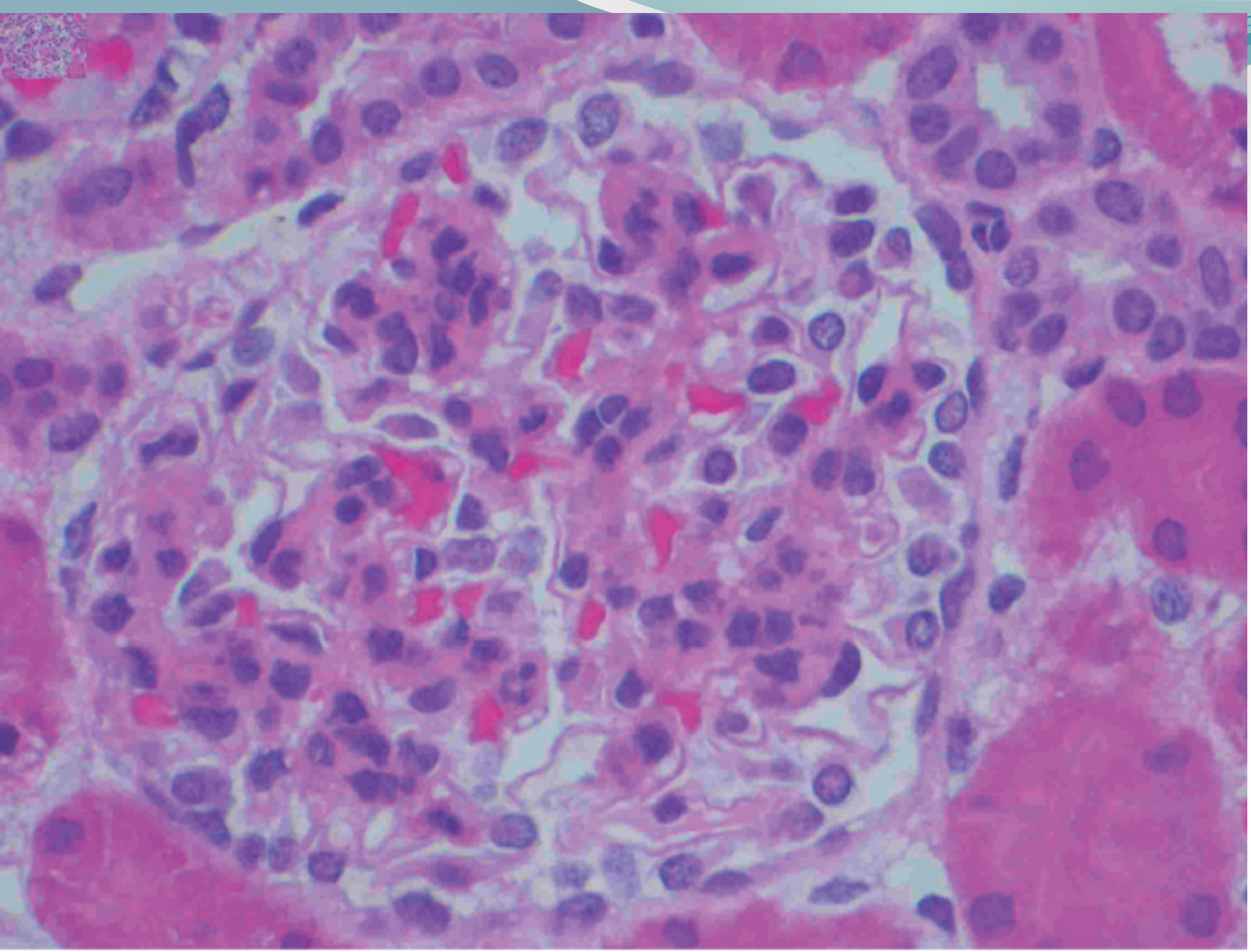
Histopathology

MCD: normal LM,neg IF,EM effacement of foot processes of podocytes

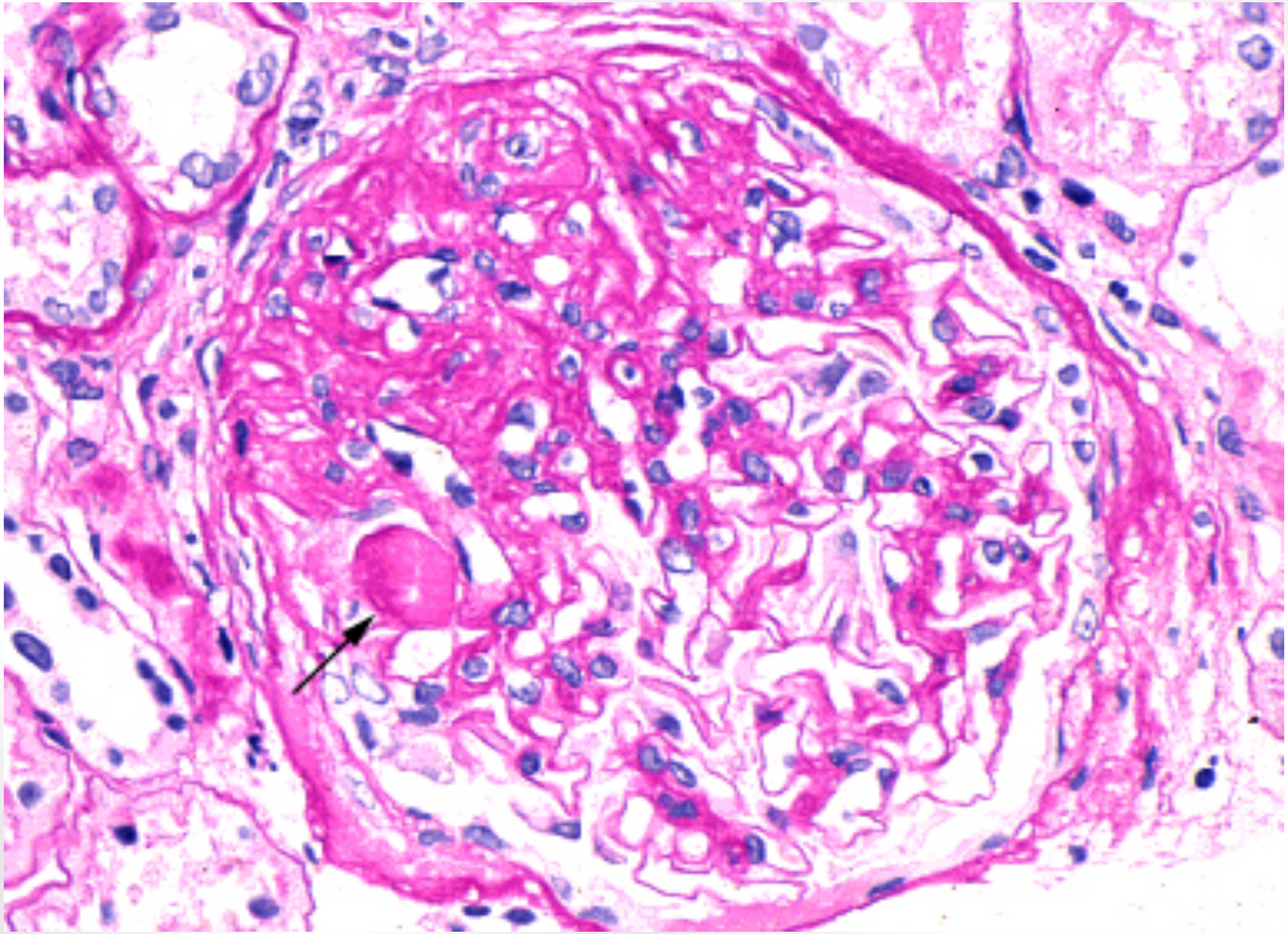
Mesangial proliferative,IgM nephropathy:positive IgM,C3 on IF

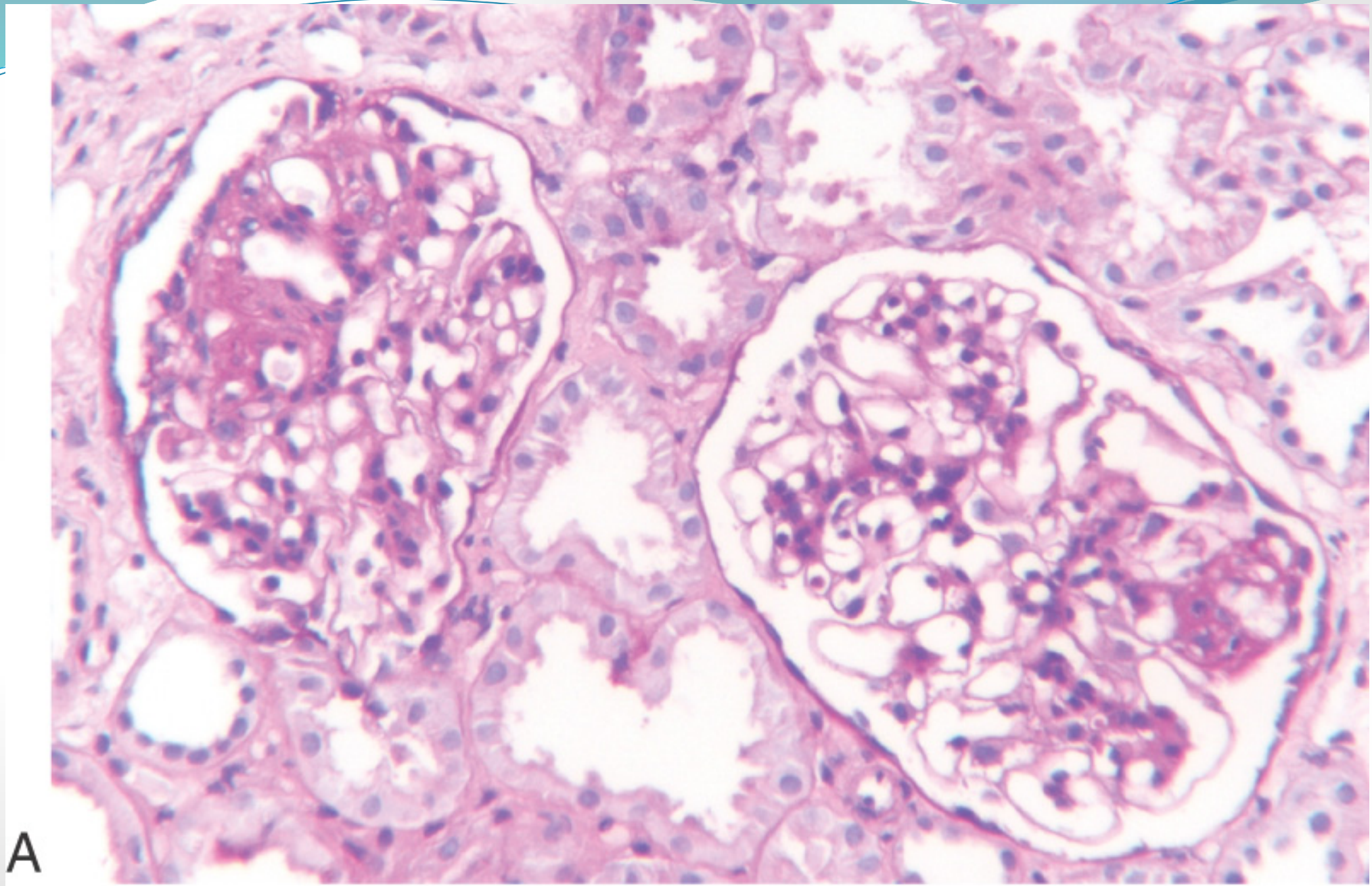
FSGS:juxtamedullary glomeruli





Moderate FSGS





Course

30% single episode

80-90% have one or more relapse

50% frequent relapses

80% complete remission by 8 y, 15-25% progress to adulthood

Risk of ESRD,CKD in SRNS is 50% within 5 ys.

66% of SRNS in first y have underlying genetic defect

80% respond to steriods

- 93% MCD
- 25-50% of FSGS,MPGN

CLASSIFICATION	DEFINTION
REMISSION	Urine prot <4mg/m^2/hour,urine prot/creat <.2mg/mg, 0 on dipstick for 3 days
STERIOD RESISTANCE	Failure to respond after initial 4-6 weeks of steroids
RELAPSE	Urine prot >40mg/m^2/hour,urine prot/creat >2mg/mg,+3 prot on dipstick for 3 days or edema
INFREQUENT RELAPSE	1 relapse in 6 months,1 to 3 in 12 months
FREQUENT RELAPSE	2 or more relapse in 6 months,4 or more in 12 months
STERIOD DEPENDANT	Two consecutive relapses during steroid therapy or within 14 days of ceasing therapy

When a renal biobsy is done ??

Indication for kidney biopsy*	• Children presenting with nephrotic syndrome ≥ 12 years of age • Steroid-resistant nephrotic syndrome or subsequent failure to respond to glucocorticoids in steroid-sensitive nephrotic syndrome (secondary steroid-sensitive nephrotic syndrome) • A high index of suspicion for a different underlying pathology (macroscopic hematuria, systemic symptoms of vasculitis, hypocomplementemia, etc.) • At onset, kidney failure not related to hypovolemia. Subsequently, decreasing kidney function in children receiving calcineurin inhibitors or prolonged exposure to calcineurin inhibitors (2 to 3 years)
Genetic testing	• Steroid-resistant nephrotic syndrome • Congenital and infantile forms of nephrotic syndrome (<1 year of age) • Nephrotic syndrome associated with syndromic features • Family history of steroid-resistant nephrotic syndrome or focal segmental glomerulosclerosis

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Complications

Infections

Hypertension,hyperlipidemia

Hypovolumeia

Acute renal failure

Thrombosis

Decrease bone density

COMPLICATIONS

1-Infections:losses of IgG in urine,abn T cell function,low factor B (C3 proactivator),steriod use,impaired opsonization

Encapsulated bact streptococcus pneumonia,staph,Ecoli

Primary bacterial peritonitis

Immunization against pneumococcus,varicella

complications

2-Thromboembolism:increased clotting factors,fibrinogen,low Antithrombin 3,platlelet aggregation,hyperviscosioty

Venous,RVT,sagital sinus,veins of legs

3.ARF due to acute tubular necrosis from hypovolumeia

Table 28-3

Infections in nephrotic syndrome

Clinical syndrome	Risk factors
Pneumococcal peritonitis	Low IgG
Haemophilus infection	Low factor B
Gram negative sepsis	Edematous tissue
Staphylococcus cellulitis	Impaired lymphocyte function
	Corticosteroids
	Immunosuppressive drugs

Table 28-4

Thrombosis in nephrotic syndrome

Clinical syndrome	Risk factor
Pulmonary emboli	Hypovolemia
Pulmonary artery thrombosis	Hyperviscosity
Cerebral venous thrombosis	Low anti-thrombin III
Renal vein thrombosis	High fibrinogen
Peripheral venous	Platelet hyperaggregability
Artery thrombosis	Hyperlipemia

Supportive Treatment

Fluid restriction if hyponatremia

Salt restriction

Albumin and furosemide in hypovolumeia, Scrotal swelling,anasarca,oliguria

Vitamin D,calcium

Vaccination for varicella,pneumococcal vaccine,influenza

KDIGO Clinical Practice Guideline

for Glomerulonephritis

4.3.1 Initial treatment of NS in children

Recommendation 4.3.1.1: We recommend that oral glucocorticoids be given for 8 weeks (4 weeks of daily glucocorticoids followed by 4 weeks of alternate-day glucocorticoids) or 12 weeks (6 weeks of daily glucocorticoids followed by 6 weeks of alternate-day glucocorticoids) *(1B)*.

For relapsing SSNS Corticosteriods

Practice Point 4.3.2.1: The initial approach to relapse should include oral prednisone/prednisolone as a single daily dose of 60 mg/m^2/d or 2 mg/kg/d (maximum 60 mg/d) until the child remits completely for ≥3 days.

Practice Point 4.3.2.2: After achieving complete remission, reduce oral prednisone/prednisolone to 40 mg/m^2 or 1.5 mg/kg (maximum 50 mg) on alternate days for ≥4 weeks.

Practice Point 4.3.2.4: For children with frequently relapsing nephrotic syndrome without serious glucocorticoid-related adverse effects, low-dose alternate-day oral prednisone/prednisolone (optimally ≤0.5 mg/kg/d) can be prescribed to prevent relapse.

Recommendation 4.3.2.2: For children with frequently relapsing nephrotic syndrome who develop serious glucocorticoid-related adverse effects and for all children with steroid-dependent nephrotic syndrome, we recommend that glucocorticoid-sparing agents be prescribed, rather than no treatment or continuation with glucocorticoid treatment alone *(1B)*.

Practice Point 4.3.2.5: Patients should ideally be in remission with glucocorticoids prior to the initiation of glucocorticoid-sparing agents such as oral cyclophosphamide, levamisole, mycophenolate mofetil (MMF), rituximab, or calcineurin inhibitors (CNIs). Coadministration of glucocorticoids is recommended for ≥2 weeks following initiation of glucocorticoid-sparing treatment.

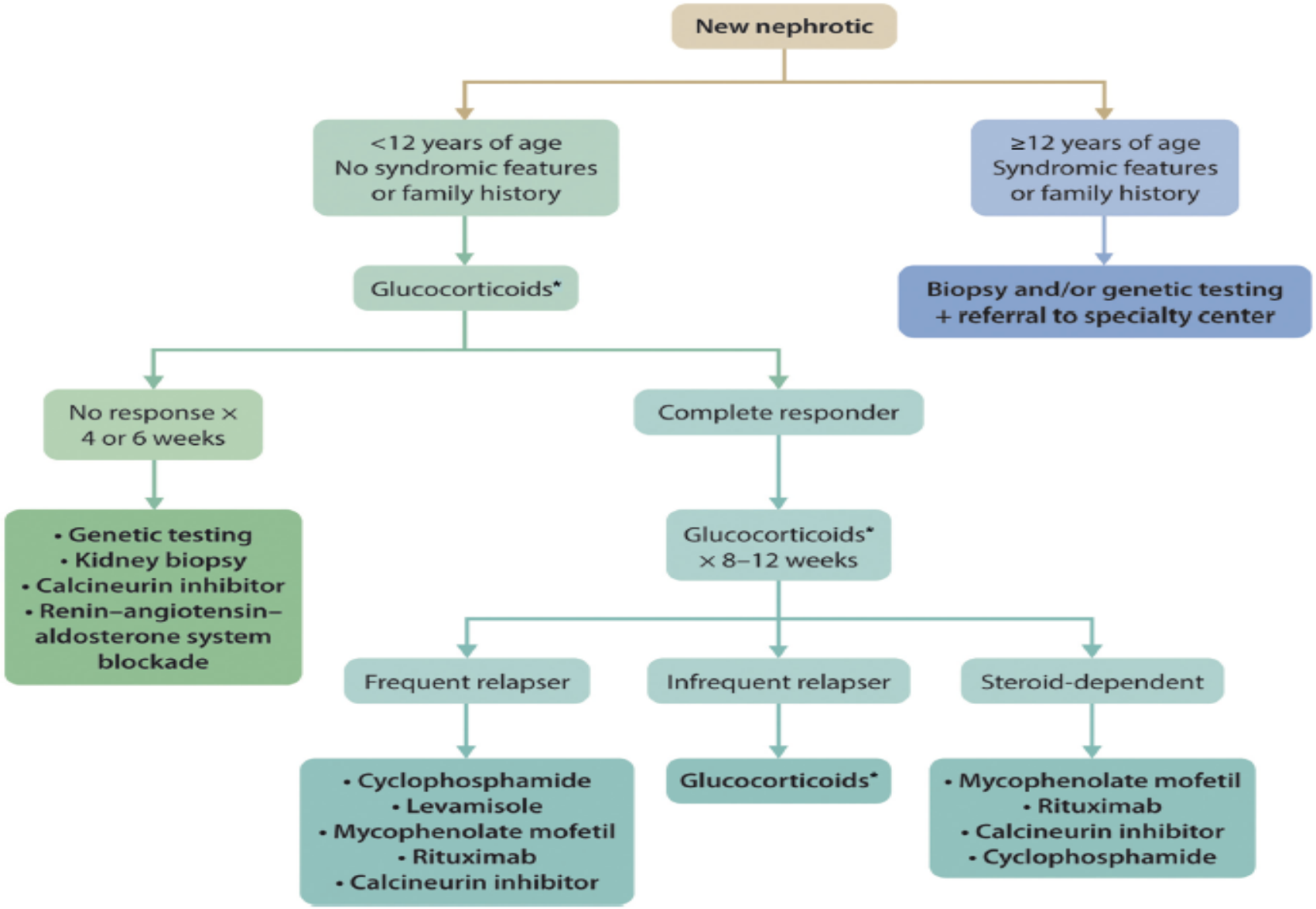

Figure 8 | Treatment algorithm for NS in a newly nephrotic child. Therapeutic approach to NS in children from onset. Refer to clinical trial where appropriate. *Glucocorticoids: p.o. prednisone or prednisolone. NS, nephrotic syndrome.

Growth ,bone density,catarcts,avascular necrosis	steriods
Hemorrhagic cystitis,leukopenia,oligospermia	Alkylating agents
Renal impairment,Gingival hyperplasia,hirsuitism,hyperkalemia	CNI
abdominal pain,Diarrhea,leukopenia	MMF

Treatment of CNS

No role for steriods

Albumin infusions

Nutrition:130kcal/kg,4g/kg protein

Hypothyroidism

ACEI

Indomethacin

diuertics

Anticoagulants,prophylactic pencillin

Nephrectomy,dialysis,tranplantation

SRNS

Mostly FSGS,genetic forms,immune mediated recur after Tx

ACEI,diuertic to control edema.

Calcinurin inhibitors are first line of treatment


THANK YOU