Interactive case

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Presentation of patient

- 33-year-old man
- He complained of pain in the right side of his chest
- Started 5 days earlier and continued to worsen until the time of presentation
- It did not worsen with movement of arm and shoulder
- Pain exacerbated with deep inspiration and when he was lying down
- Patient also had noted mild swelling of the shins and ankles in both legs during the preceding several weeks
- He reported NO dyspnea, cough, hemoptysis, sore throat, fever, chills, nausea, vomit, rashes, pruritus, abdominal pain, diarrhea, leg pain, chest trauma, or recent travel, including air travel

Medical history

- Patient underwent colonoscopy with biopsy 4 years ago because of chronic diarrhea and unexplained iron-deficiency anemia
- A biopsy specimen revealed chronic active colitis with no granulomas
- He was treated with mesalamine for 3 months
- The diarrhea resolved, and he decided to discontinue treatment
- He did not follow up with medical care thereafter and had no recurrent diarrhea or abdominal pain until the current presentation

Social history

- Is married, with 2 children under 10 years of age
- Works as a health care administrator
- He denied smoking, alcohol intake, using of illicit drugs

Family history

- Mother suffered from systemic lupus erythematosus without renal involvement
- Father and brother are well, without known medical problems
- No family history of venous thromboses, miscarriages, inflammatory bowel disease, or known cancer

Physical examination

- Temperature - 36.9˚C
- Pulse - 110 beats per minute and regular
- Blood pressure - 141/82 mm Hg
- Respiratory rate - 16 breaths per minute
- Oxygen saturation - 98%
- Alert and oriented to time and place, able to answer questions

Symptom-oriented examination?

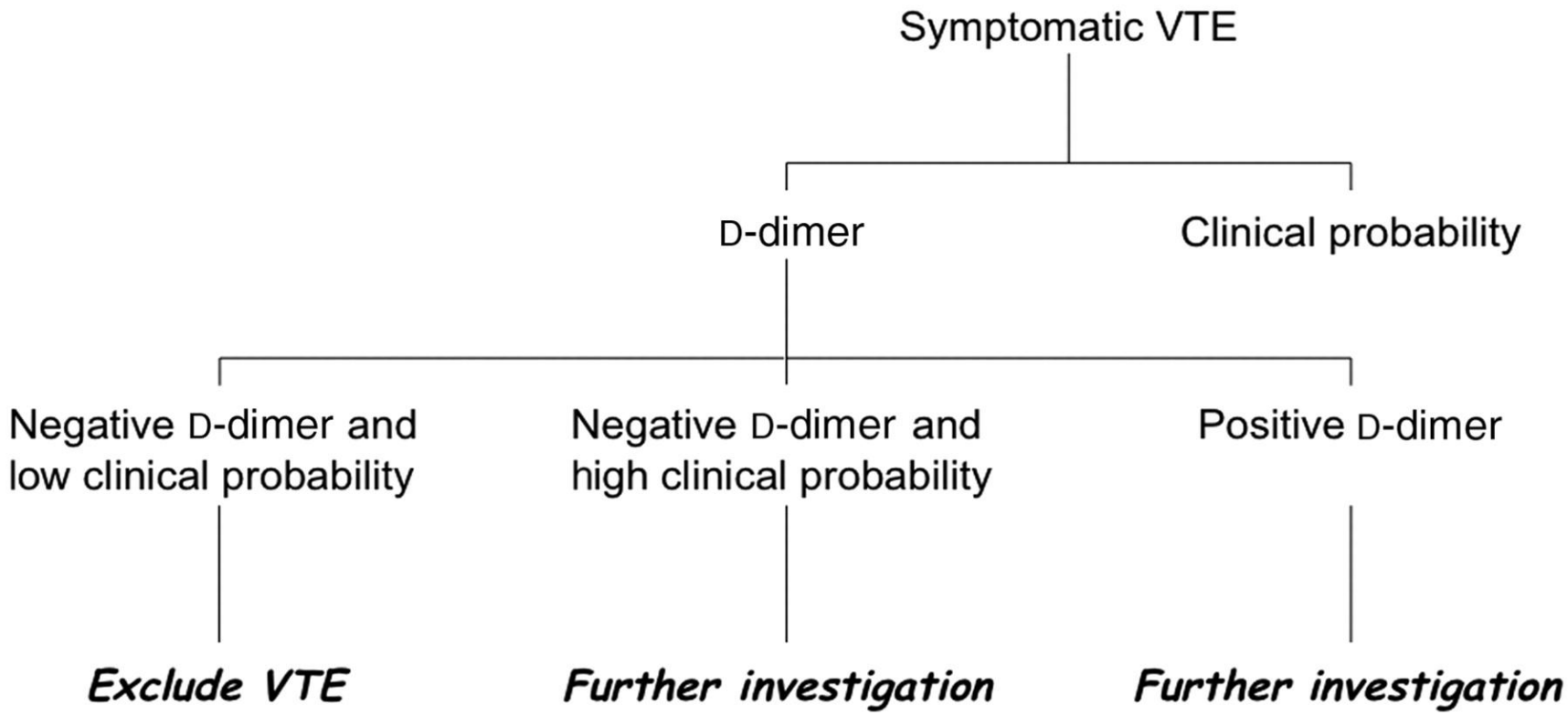
- Chest
- Heart
- Lungs
- Abdomen
- Lower extremities
- Skin
- Joints
- Lymph nodes

Which of the following tests are indicated to evaluate the patient's symptoms? (3)

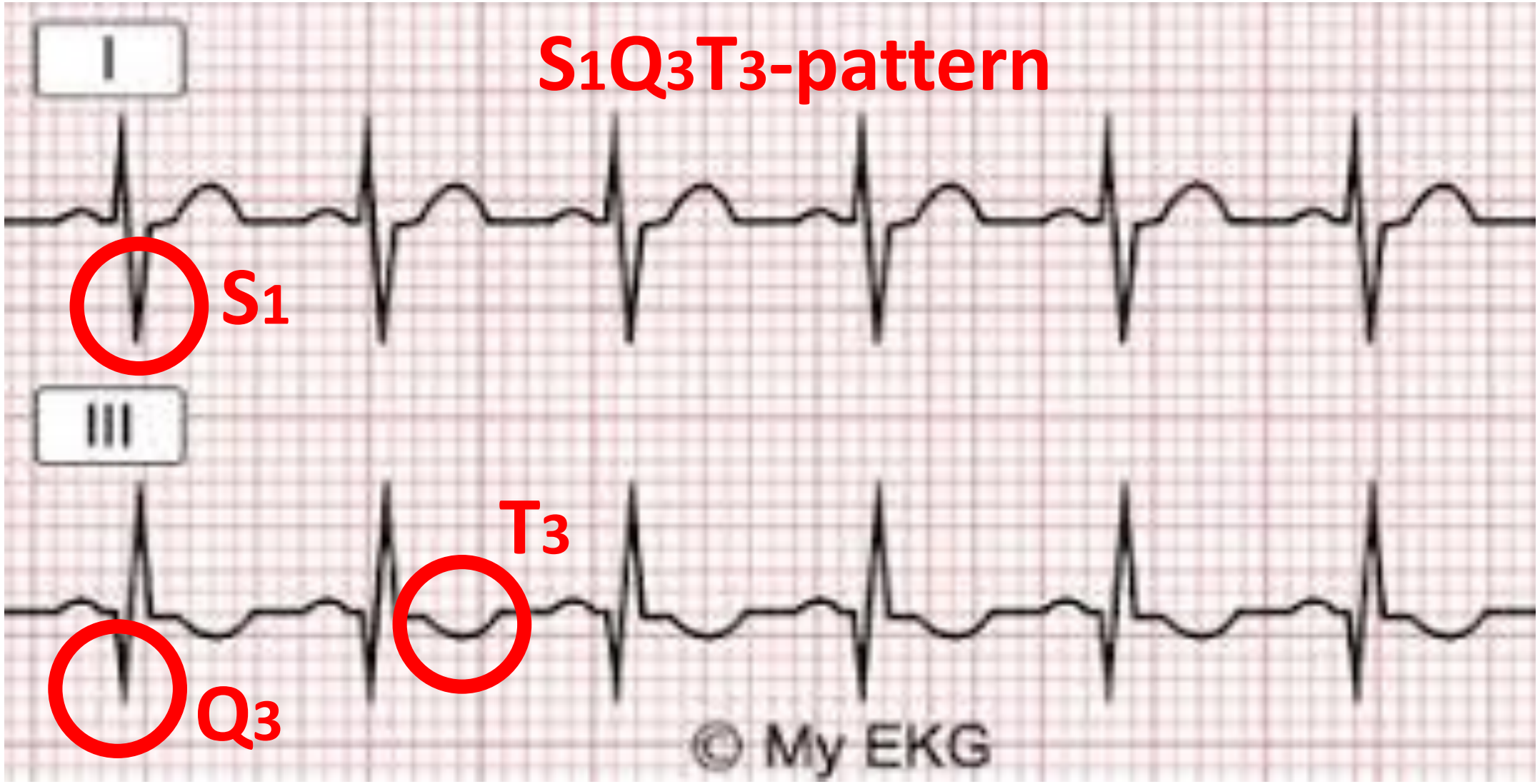
1. Cardiac ultrasonography
2. Chest radiography
3. D-dimer level
4. Electrocardiography (ECG)
5. Pulmonary angiography
6. Pulmonary computed tomographic angiography (CTA)
7. Ventilation–perfusion scanning

Diagnosis of VTE

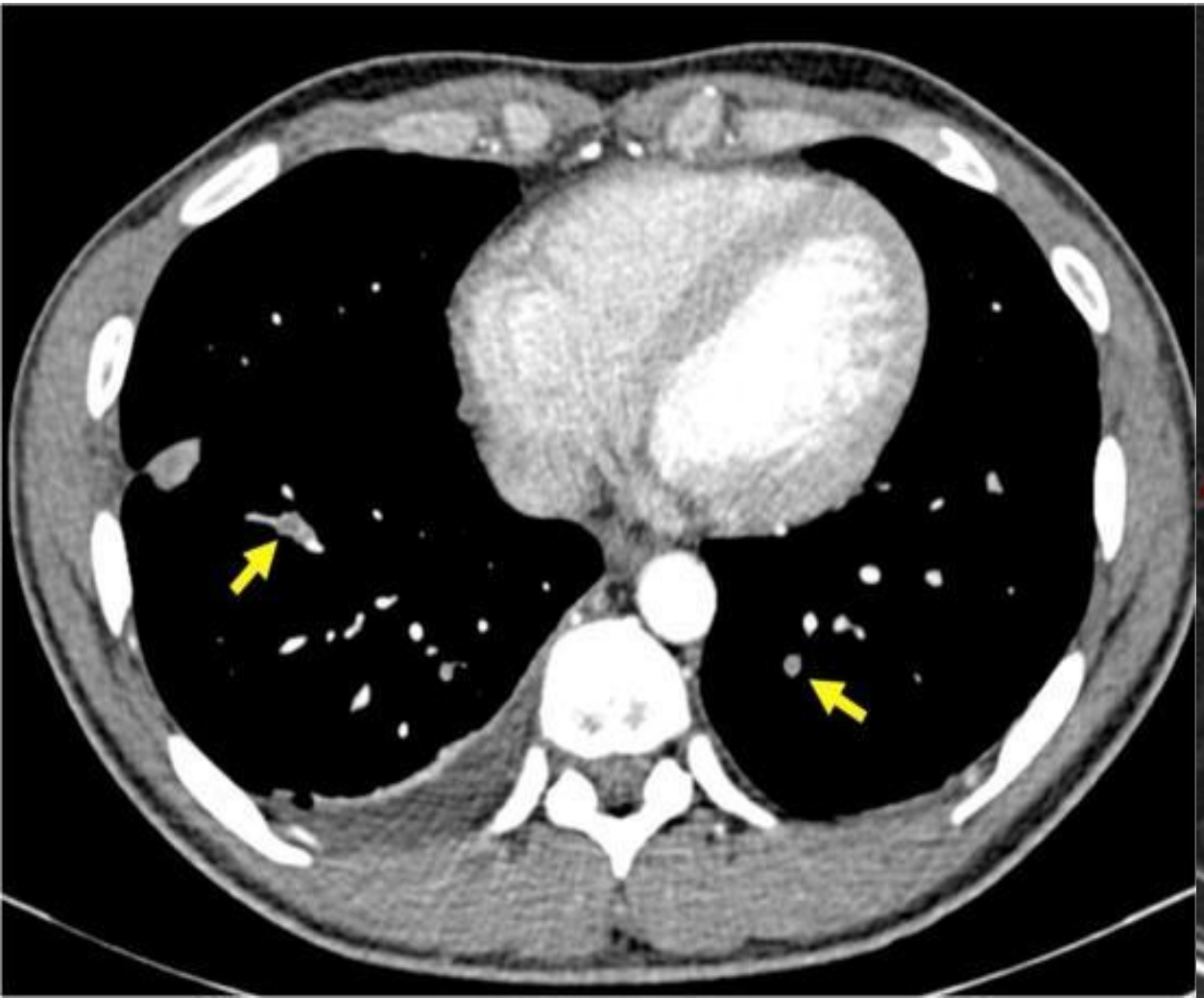
Combination of Clinical Probability and D-Dimer

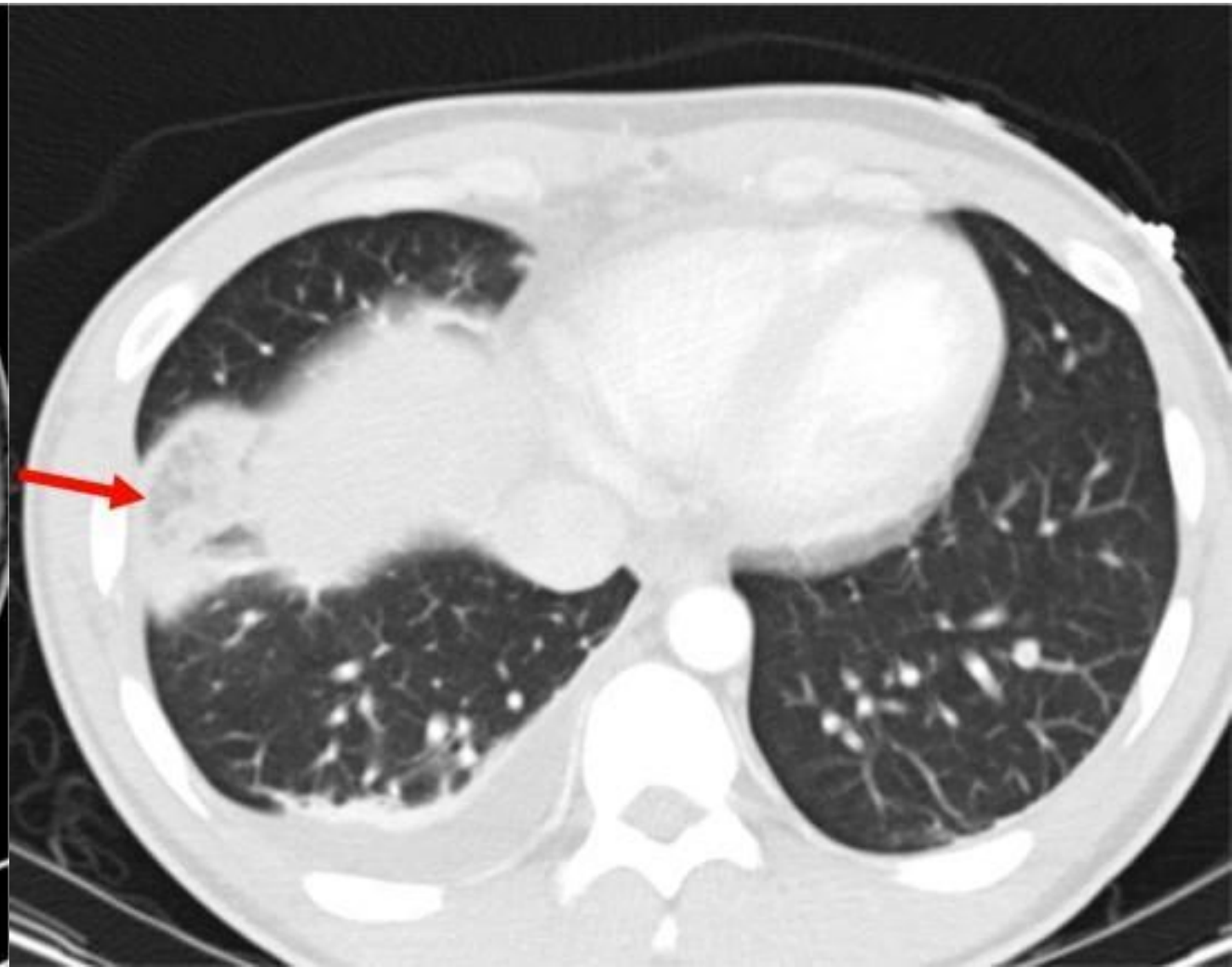


ECG



CT





Diagnosis

The diagnosis of pulmonary embolism have been confirmed

What should we do?

1) Embolectomy
2) Fibrinolytic therapy
3) Anticoagulant therapy
4) Antiplatelet therapy

Blood test

Variable	Result	Flag
RBC	4.26×10^{12}	N
Hb	114	Low
Ht	0.42	N
MCH	26	Low
MCV	74	low
WBC	6.39×10^{9}	N
Pt	378×10^{9}	N
ESR	32	High

What kind of anemia?

1) Hypochromic
2) Hyperchromic

1) Microcytic
2) Macrocytic

Urine test

Variable	Result	Flag
Protein	10.1	High
Albumin	924.4	High
Erythrocytes	1	N
Leukocytes	1-2	N
Bacterial cultures	0	N
Glucose	0	N
Ketone bodies	0	N
Bilirubin	0	N
Urobilinogen	0	N

What is the most likely diagnosis according to urine test?

1) Nephritic syndrome
2) Nephrotic syndrome

What is the most likely cause?

1) Goodpasture disease
2) IgA nephropathy (Bergers disease)
3) Membranous nephropathy
4) Poststreptoccocal glomerulonephritis
5) Lupus nephritis

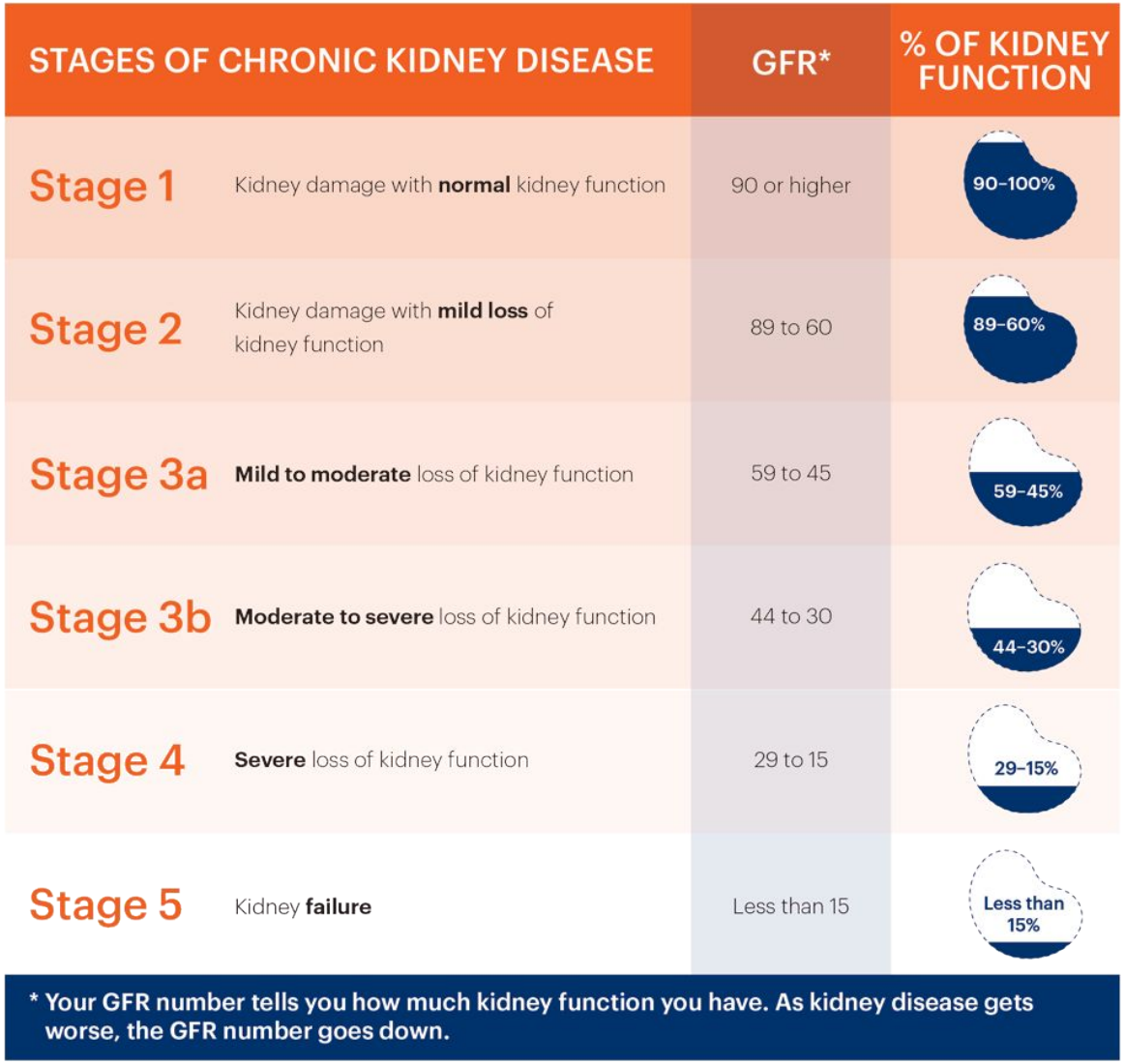
Biochemistry blood test

Variable	Result	Flag
AST	28	N
ALT	24	N
Alkaline phosphatase	410	High
GGTP	418	High
Glucose	5.6	N
Cholesterol	26.4	High
Total bilirubin	14	N
Total protein	45	Low
Albumin	8	Low
Creatinine	80	N
Ferritin	67	Low
C-reactive protein	12	High

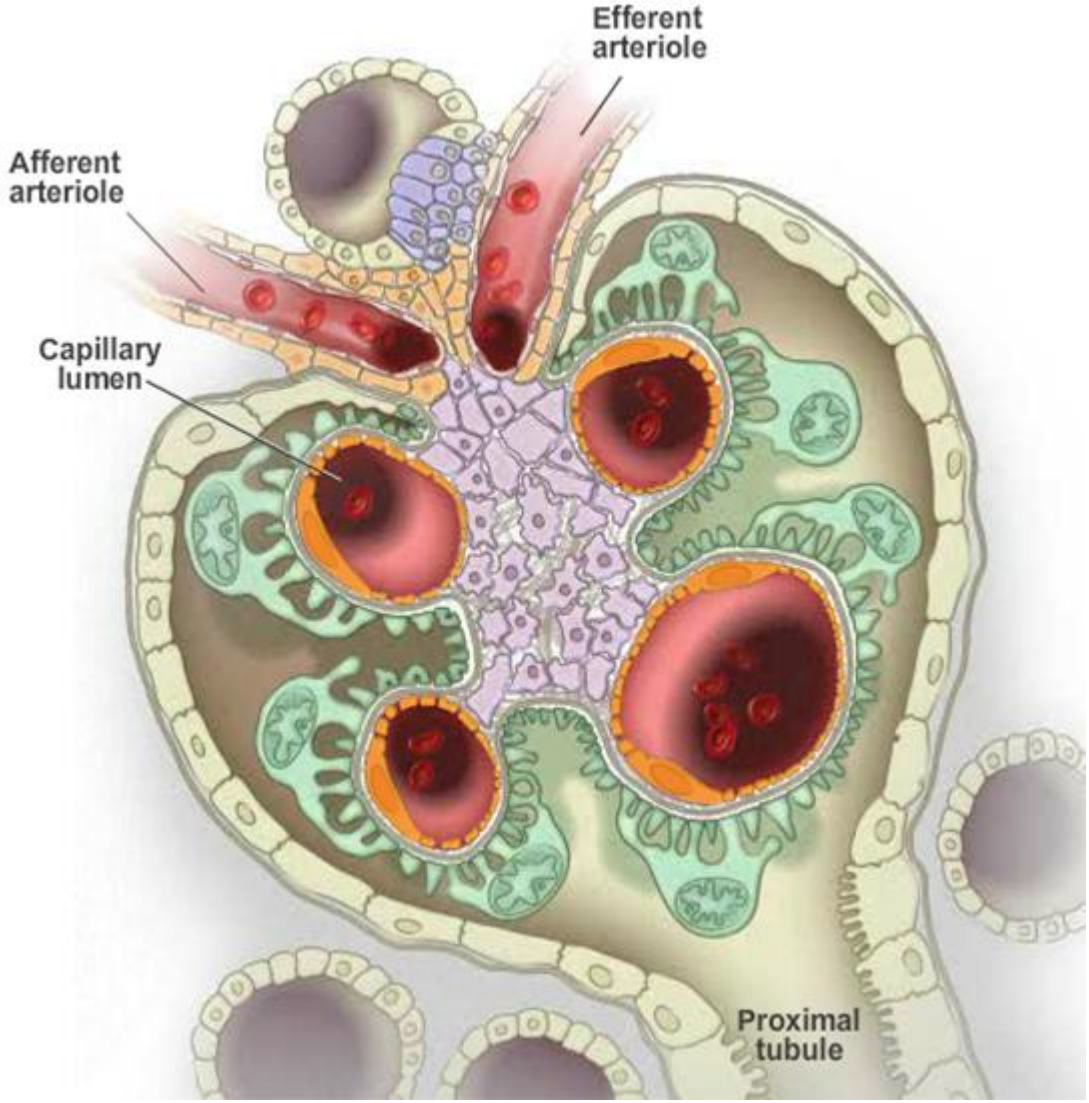
Glomerular filtration rate

- Male
- Negroid race
- 33-years-old
- Creatinine = 80 µmol/L

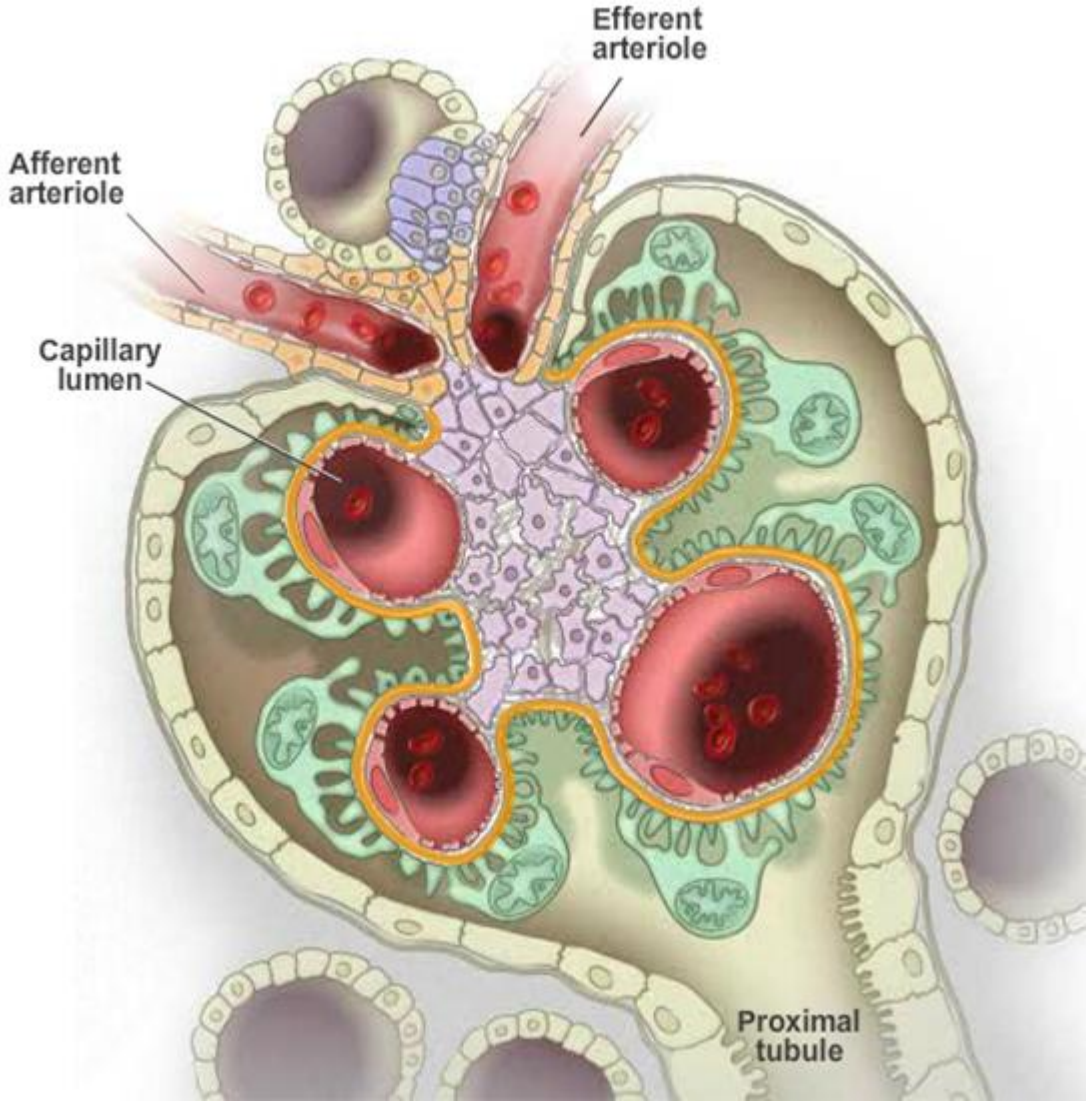
GFR = 129 ml/min



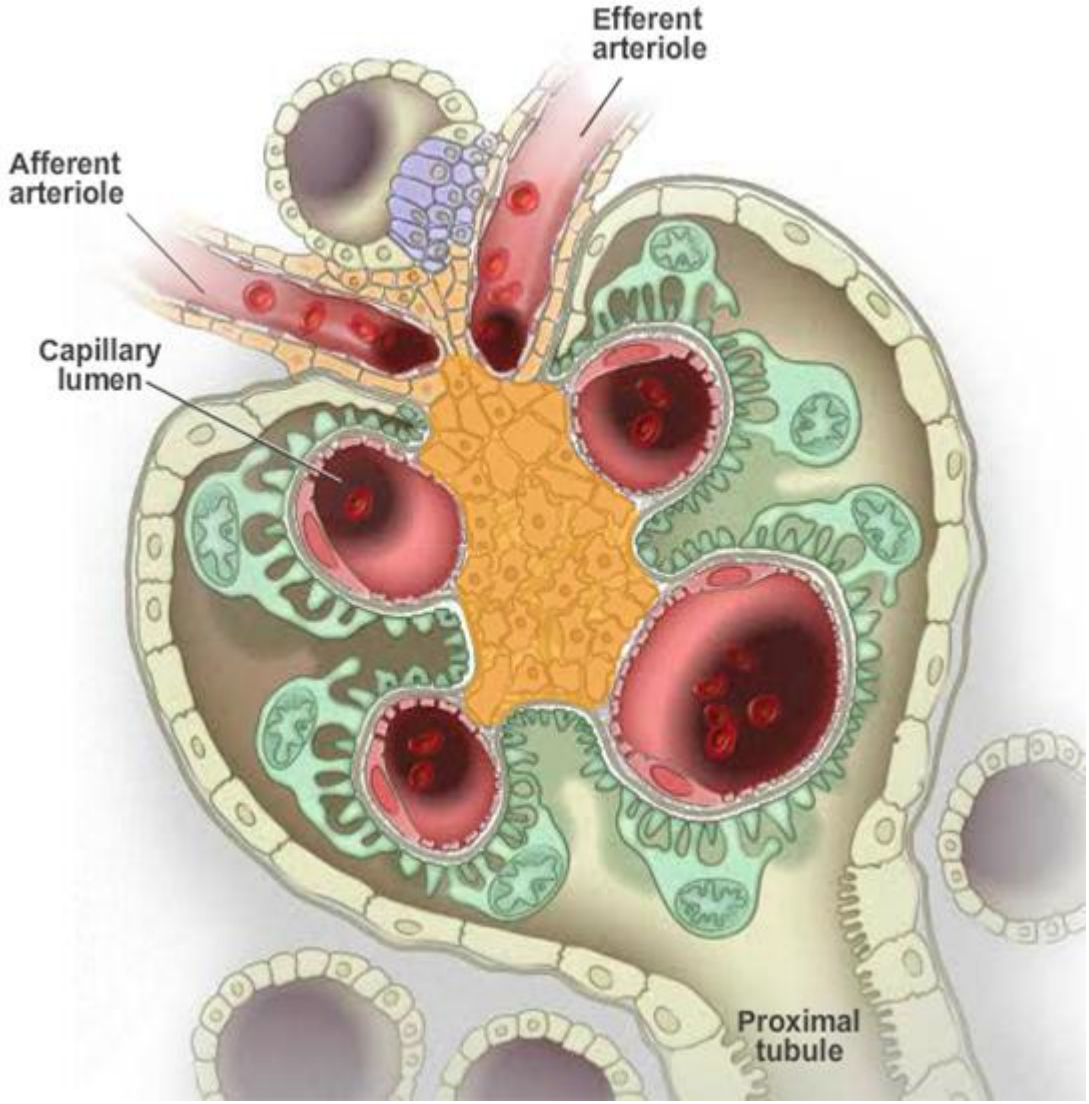
Fenestrated vascular endothelial cells



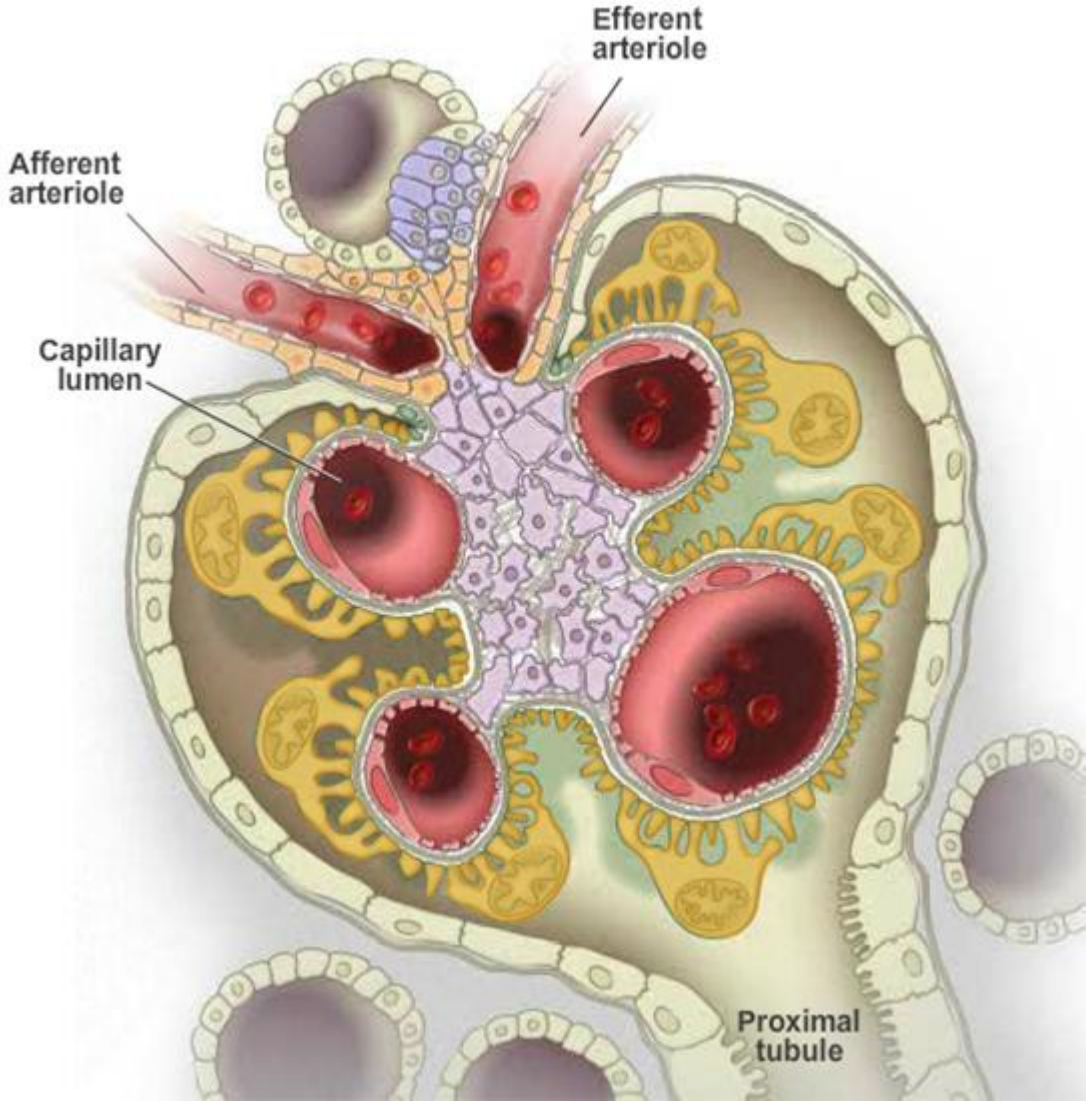
Glomerular basement membrane



Mesangium


Efferent arteriole
Afferent arteriole
Capillary lumen
Proximal tubule

Visceral epithelial cells (Podocytes)



Pathological Features	**Nephrotic syndrome**	**Nephritic syndrome**
Impairment	Podocytes	Endothelium, GBM, mesangium
IC deposition	Subepithelial space	Subendothelial space, mesangium
Contact with systemic circulation	-	+
Inflammation of glomerulus	-	+
Onset	Latent	Acute
Respond to therapy	+	+++
Recovering	Months to years	Days
GFR	Normal	Decreased
Proteinuria	**> 3 g/l**	**1 – 3 g/l**
Erythrocyturia	-	+
Casts	-	+

Clinical features	**Nephrotic syndrome**	**Nephritic syndrome**
Proteinuria	**> 3 g/l**	**1 – 3 g/l**
Proteins in the blood	Decreased	Normal/ Decreased
Lipids in the blood	Elevated	Normal
Edema	+++	+
Micturition	Normal	Oliguria
Hypertension	-	+
Pain in loin	-	+

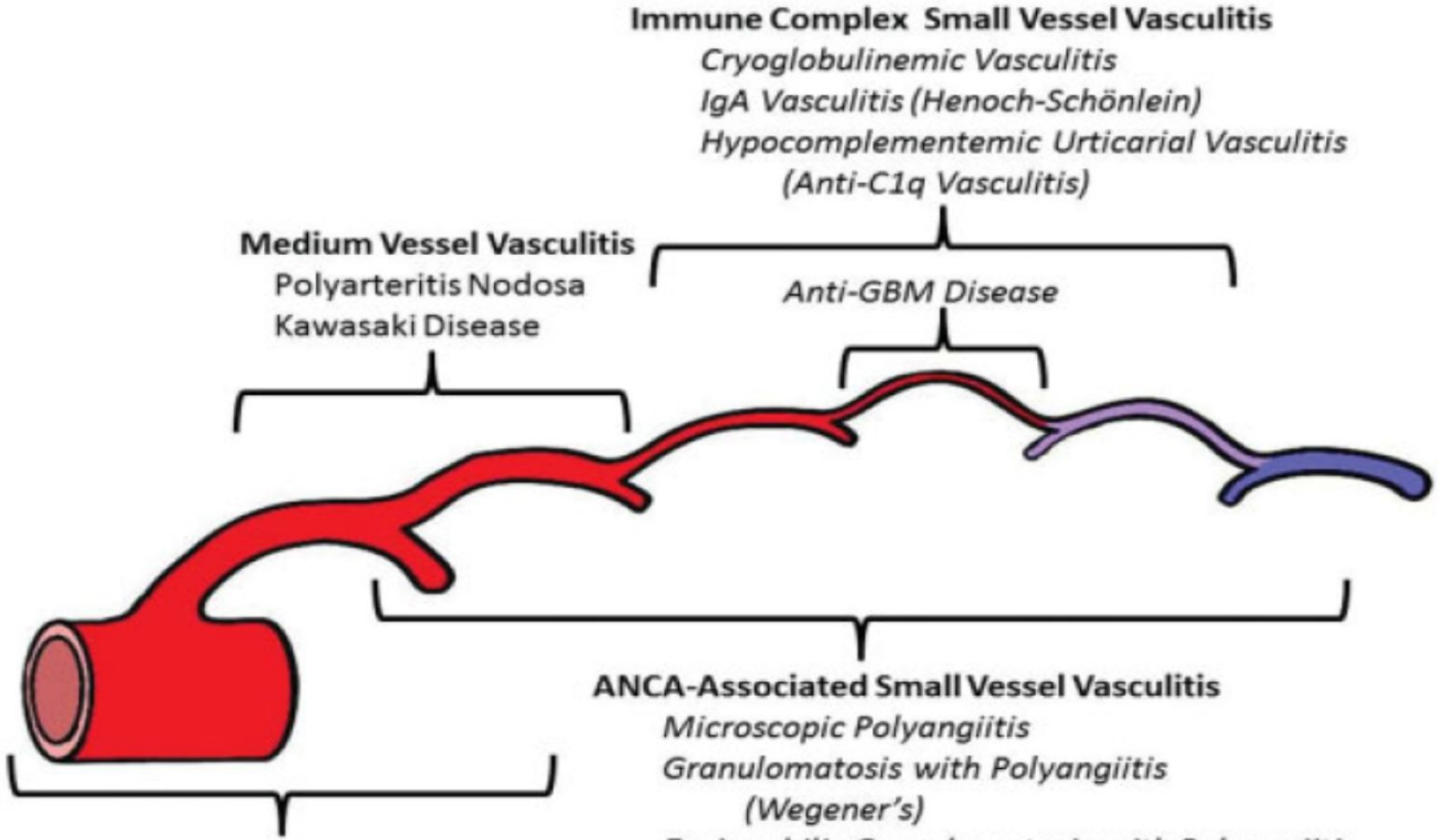
Nephrotic syndrome

- Minimal change disease
- Focal segmental glomerulocslerosis
- Membranous nephropathy
- Diabetic nephropathy
- Amyloid nephropathy
- Alport disease
- Membranoproliferative glomerulonephritis
- Thin basement membrane disease
- Mesangioproliferative glomerulonephritis
- Post-infectious glomerulonephritis
- Rapidly progressive glomerulonephritis (glomerulonephritis with crescents)

Nephritic syndrome

Disease	Causes	Mechanism	Syndrome
Minimal change disease	1. Idiopathic	Defectiveness of podocytes	Nephrotic
Focal segmental glomerulosclerosis	1. Idiopathic 2. HIV	Sclerosis	Nephrotic
Membranous nephropathy	1. Idiopathic 2. Cancers 3. Autoimmune diseases	Subepithelial deposition of IC	Nephrotic
Diabetic nephropathy	1. Diabetes mellitus	Sclerosis	Nephrotic
Amyloid nephropathy	1. AL-amyloidosis (Gammopathies) 2. AA-amyloidosis (Chronic inflammatory process)	Amyloid deposition	Nephrotic

Disease	Causes	Mechanism	Syndrome
Alport syndrome	1. Genetic	Collagen 4 mutation -> Defectiveness of GBM	Nephritic-nephrotic
Thin basement membrane disease	1. Idiopathic	Defectiveness of GBM	Nephritic-nephrotic
Membranoproliferative glomerulonephritis	1. HCV, HCB 2. Autoimmune diseases 3. C3-glomerulonephritis (Dense deposite disease)	Subendothelial deposition of IC	Nephritic-nephrotic
Mesangioproliferative glomerulonephritis	1. IgA-nephropathy, Henoch-Shonlein purpura 2. Autoimmune diseases	Mesangial deposition of IC	Nephritic-nephrotic
Post-infectious glomerulonephritis	1. Infections (especially Streptococcus)	Subendothelial deposition of IC	Nephritic
Rapidly progressive glomerulonephritis (glomerulonehritis with crescents)	1. Goodpasture disease 2. Autoimmune diseases 3. Vasculitis	1. Antibodies to GBM 2. Subendothelial deposition of IC 3. Vasculitis of glomerulus	Nephritic



Jennette, A&R 2013;65(1):1

Lupus nephritis

Acute

Rapidly progressive glomerulonephritis

Chronic

Stage 1-4	Mesangioproliferative glomerulonephritis, Membranoproliferative glomerulonephritis	Mesangial and subendothelial deposition of IC
Stage 5	Membranous nephropathy	Subepithelial deposition of IC
Stage 6	Chronic kidney disease	Sclerosis

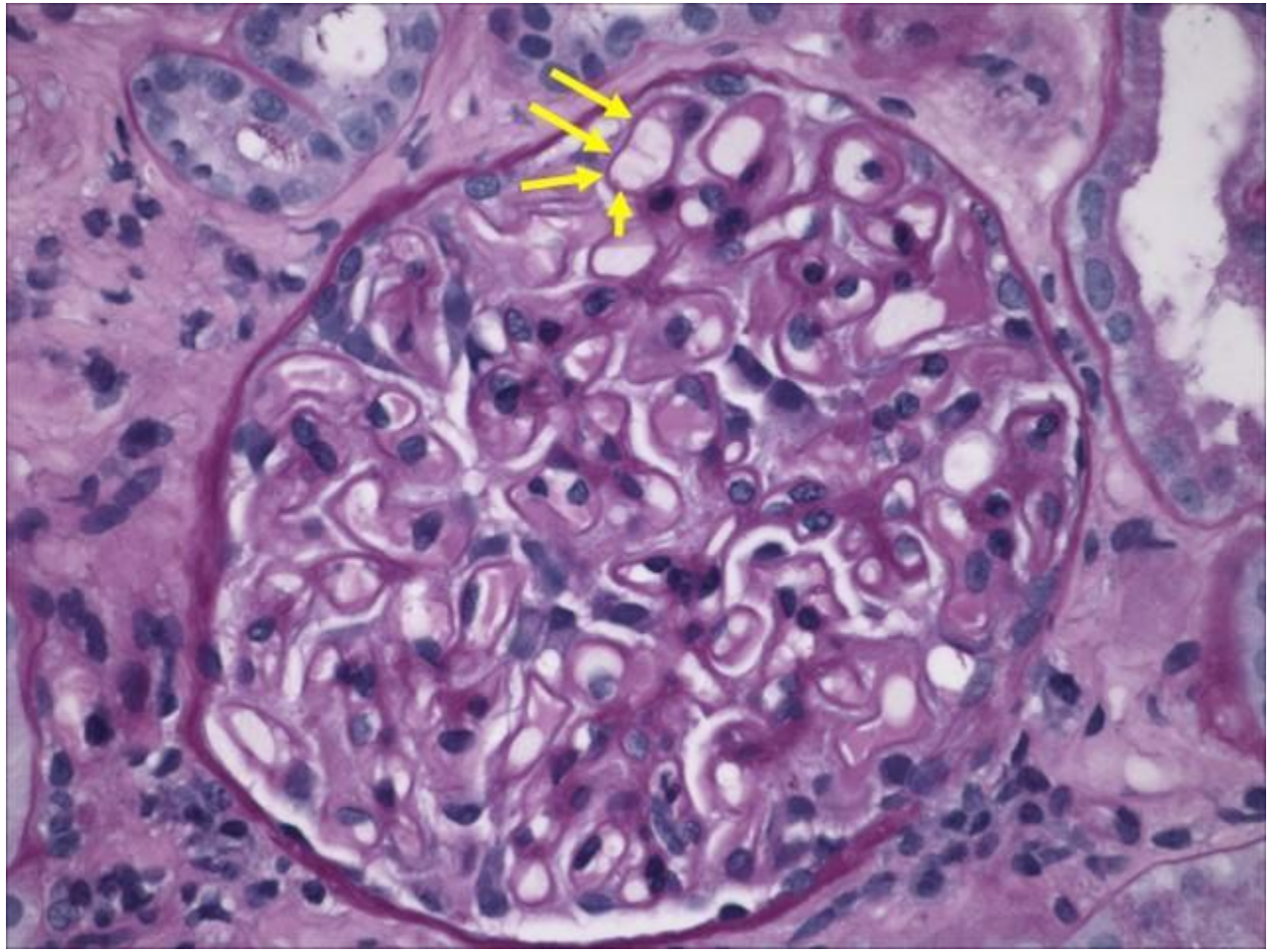
Which of the following tests or procedures should be performed to further evaluate the cause of nephrotic syndrome? (1-9)

1) Antinuclear antibody testing
2) Testing for complement level
3) Testing for cryoglobulins
4) CT of the abdomen
5) Testing for hepatitis B
6) Testing for hepatitis C
7) Testing for HIV
8) Renal biopsy
9) Testing for ANCA

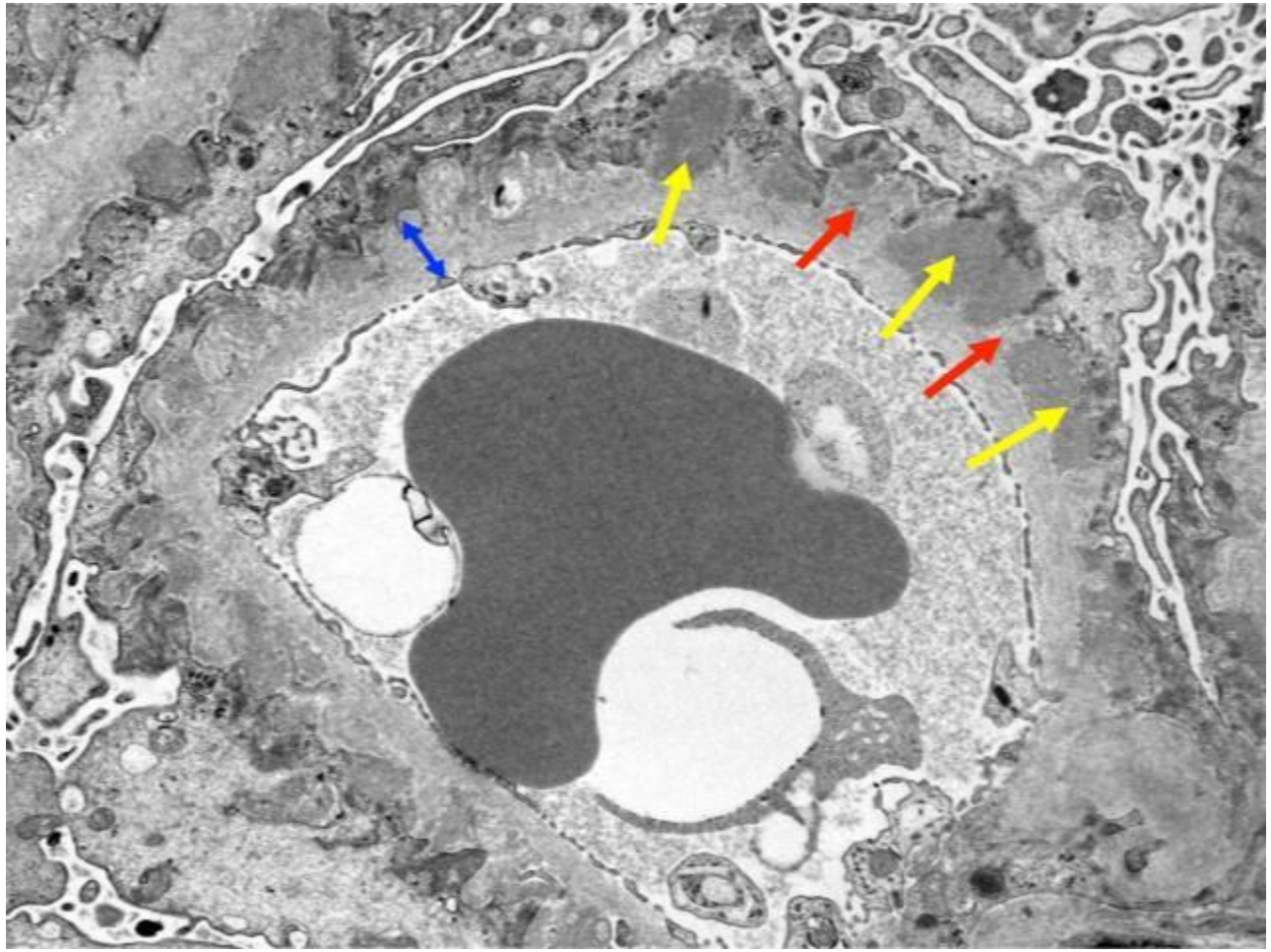
Serological blood test

Variable	Result	Flag
HCV surface antigen	negative	N
HCV surface Ig	negative	N
HCV core IgG	negative	N
HCV core IgM	negative	N
HBV Ig	negative	N
Cryoglobulins	negative	N
HIV Ig	negative	N
Antinuclear antibodies	negative	N
C3-complement	0.7	Low
ANCA	1:640	High

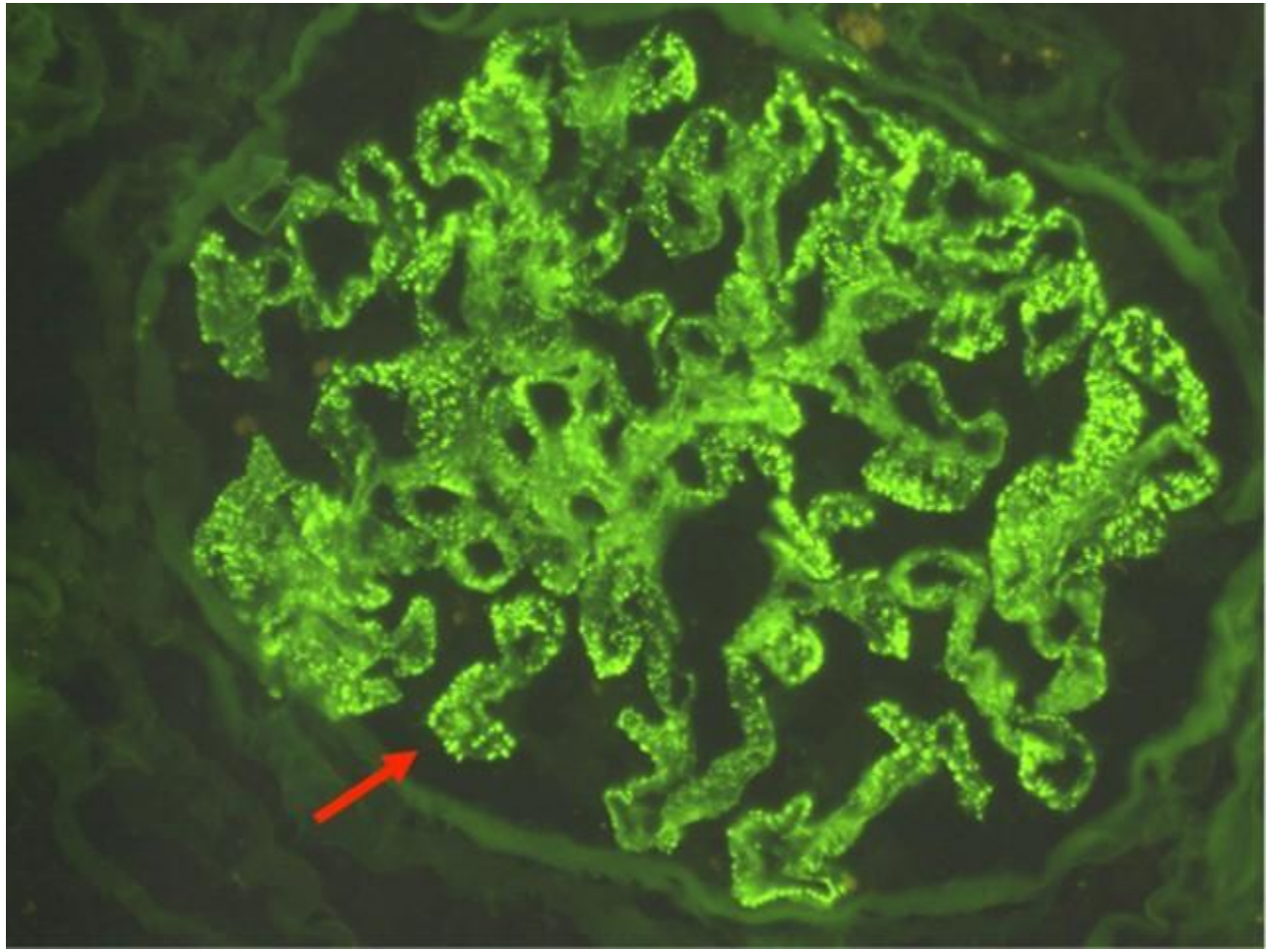
Renal biopsy



Renal biopsy - electron microscopy

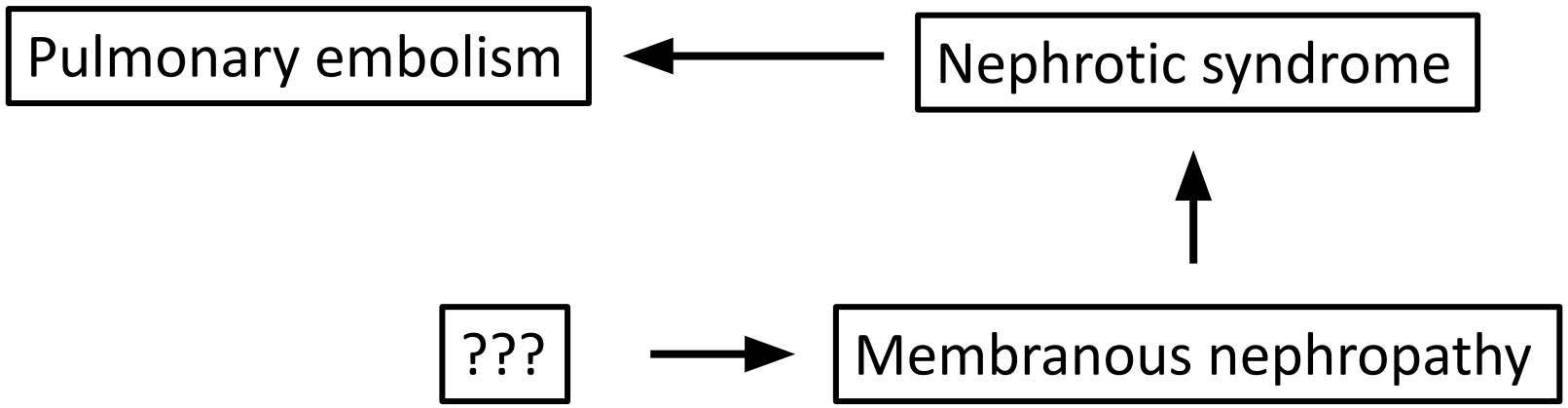


Renal biopsy - immunofluorescence microscopy



Renal biopsy

The biopsy specimens reveal a membranous pattern of injury that is consistent with the diagnosis of membranous nephropathy.



Ulcerative colitis

Hypochromic microcytic anemia

Elevated alkaline phosphatase and GGTP

High anti neutrophil cytoplasmic antibody

The patient's abnormal level of alkaline phosphatase is most suggestive of which one of the following conditions? (1)

1) Budd-Chiary disease
2) Pagets disease
3) Portal vein trombosis
4) Primary biliary cirrhosis
5) Primary sclerosing cholangitis

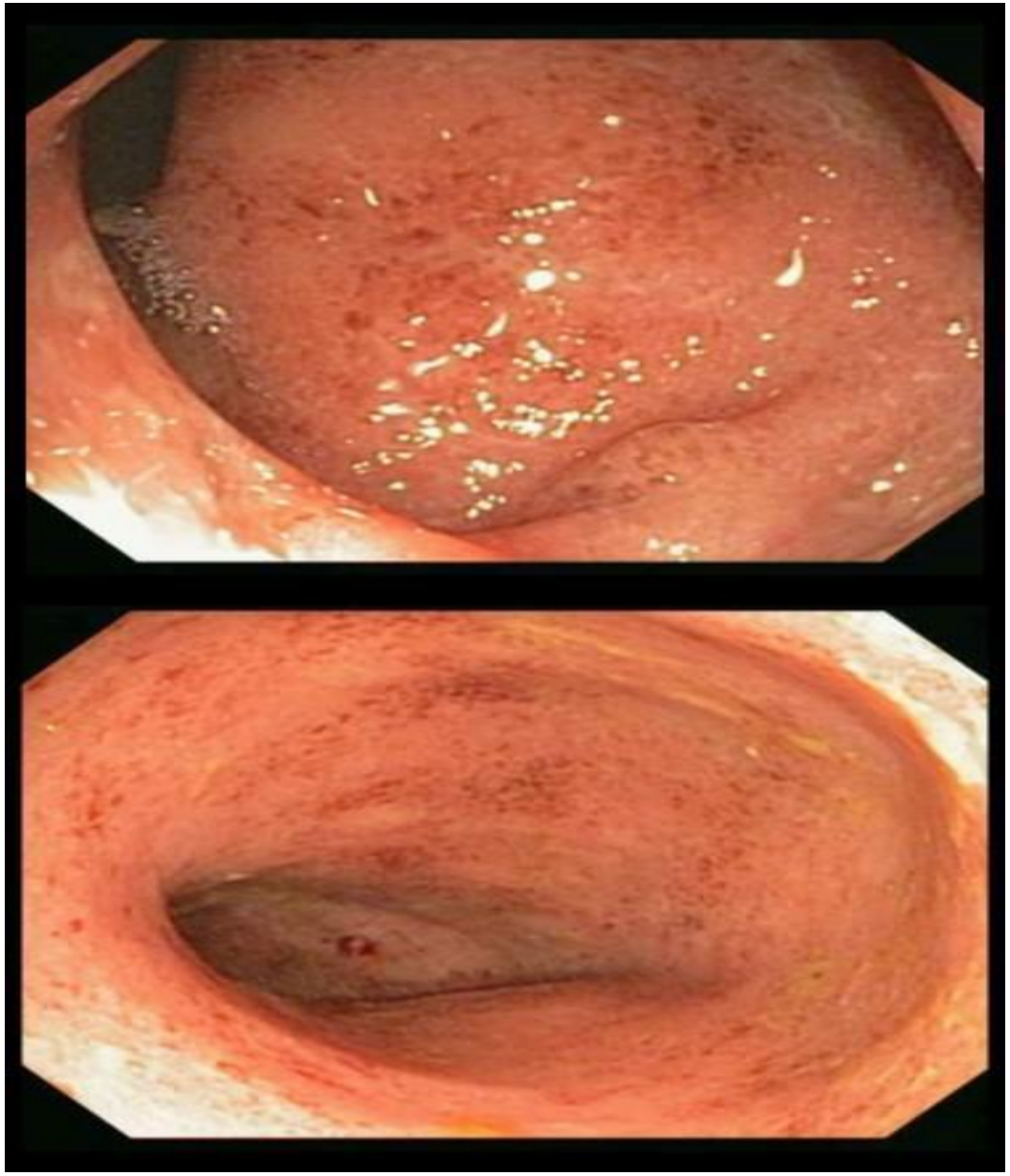
Which of the following procedures are now indicated? (2)

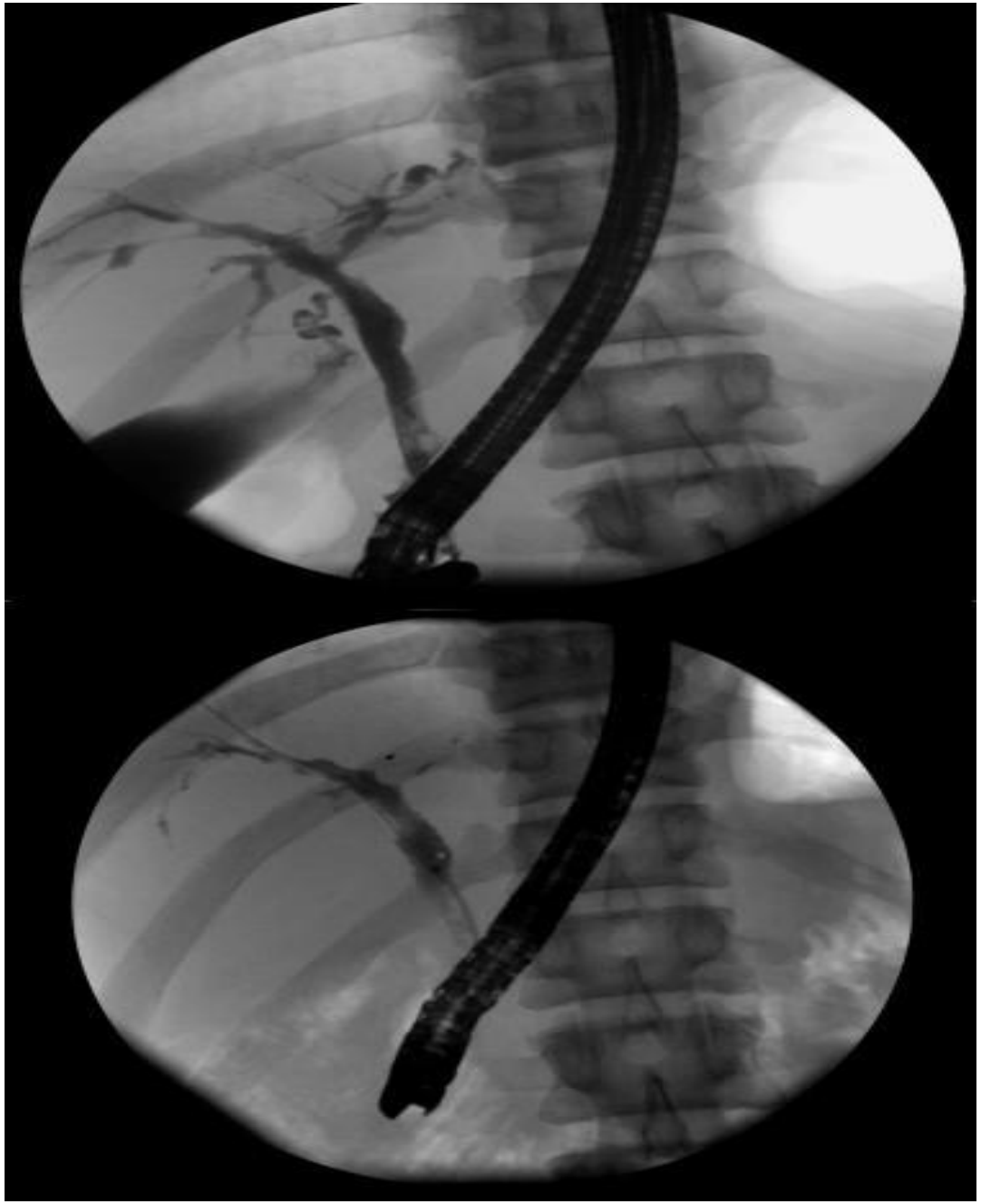
1) Cholangiopgraphy
2) Endoscopic ultrasonography of the pancreas and biliary tree
3) Liver biopsy
4) Transabdominal hepatobiliary ultrasonography
5) Upper gastrointestinal endoscopy
6) Colonoscopy

Which of these methods of cholangiography is more preferred?

1) Endoscopic retrograde cholangiopancreatography
2) Magnetic resonance cholangiopancreatography

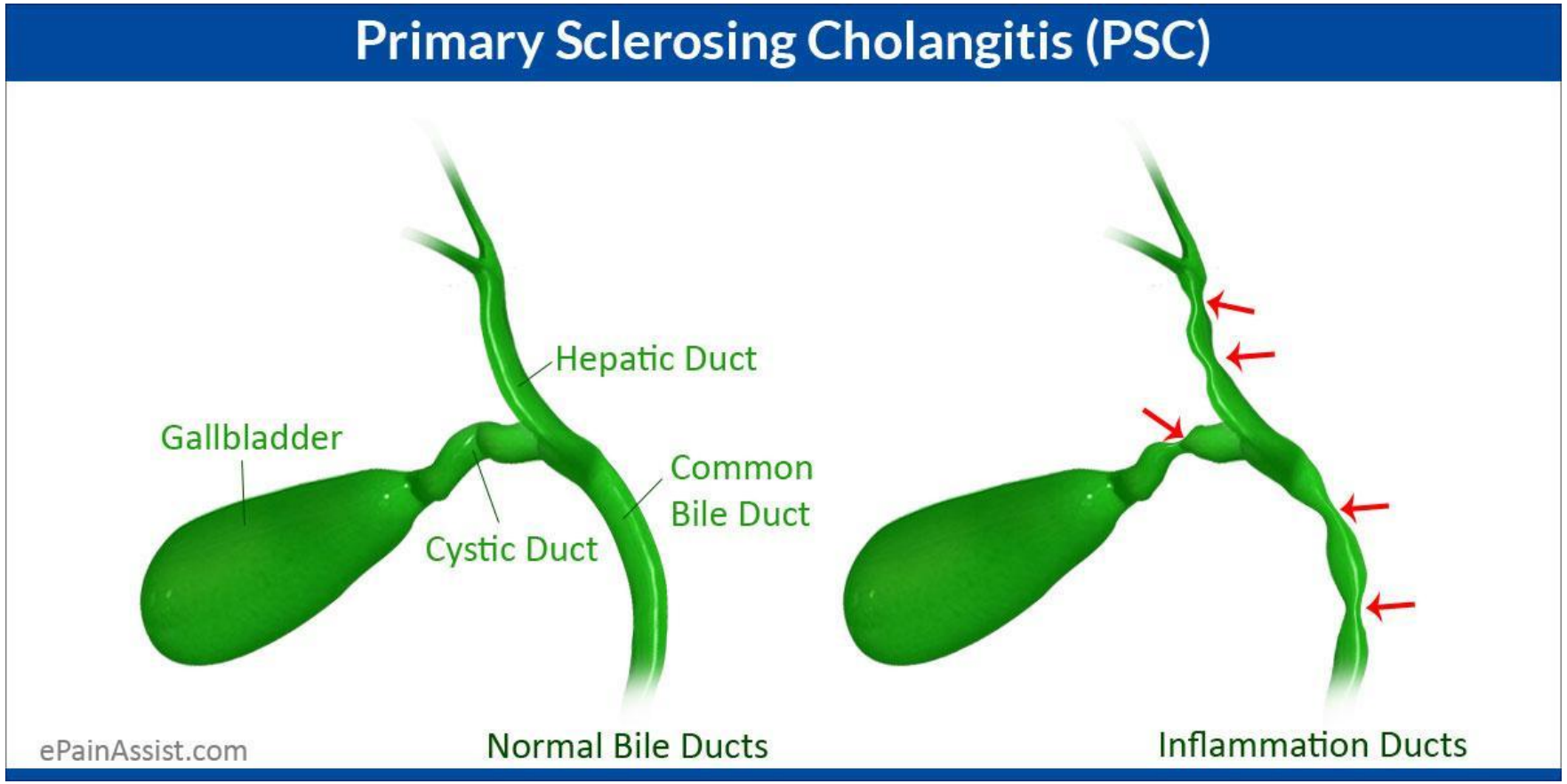
Colonoscopy





ERCP

Primary sclerosing cholangitis



Primary sclerosing cholangitis

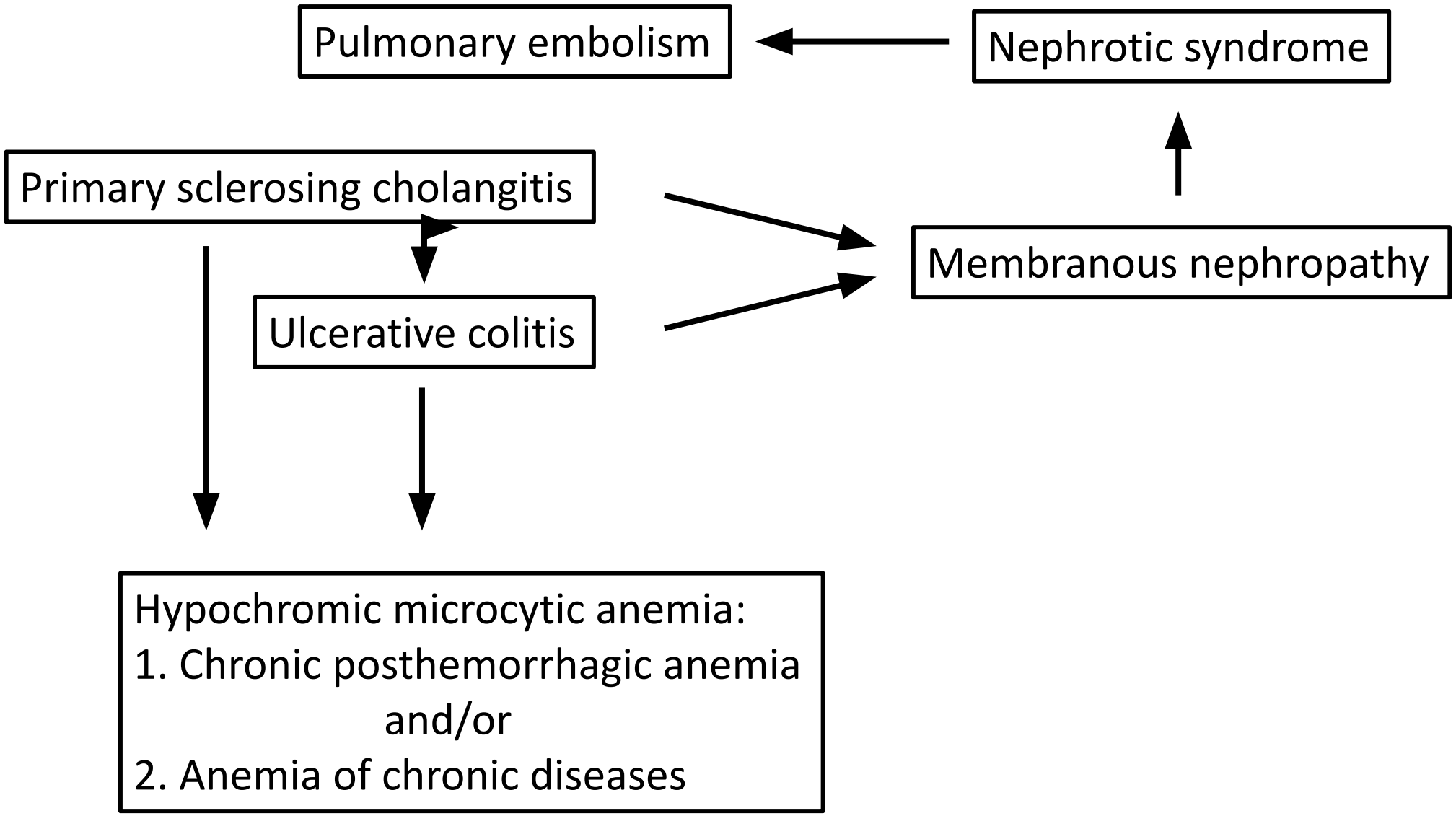
- Autoimmune disease
- Progressive inflammation and fibrosis of the intrahepatic and extrahepatic bile ducts
- As a result - biliary strictures, obstruction, cirrhosis and liver failure.
- Most patients are asymptomatic in the early stages of the disease
- Cholestatic syndrome prevails in clinical picture of advance stage
- Approximately 80 % of patients with primary sclerosing cholangitis have or will have ulcerative colitis

Primary sclerosing cholangitis

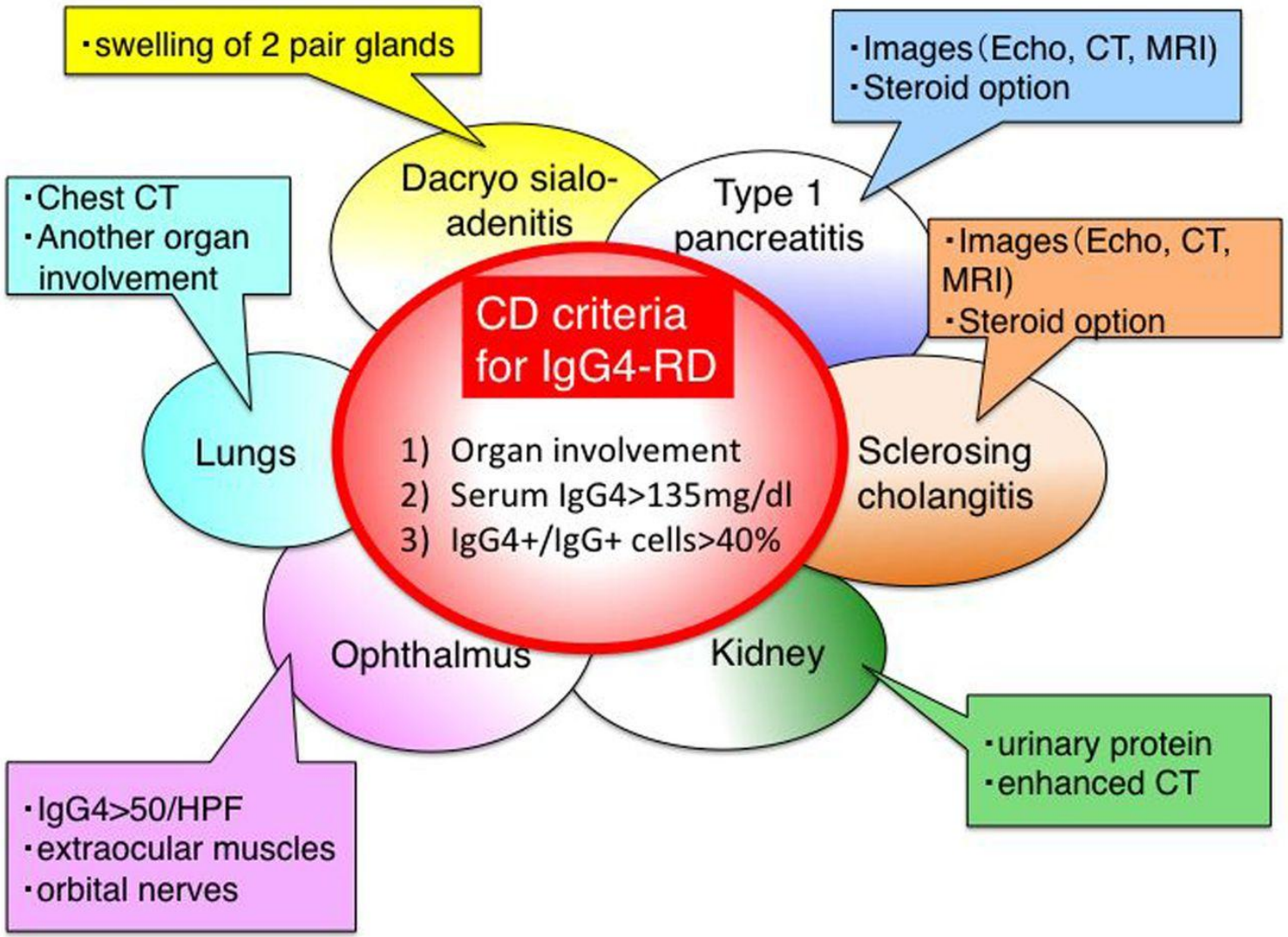
- Elevated level of alkaline phosphatase is very common, even in early stages
- > 65 % of patients have ANCA (as well as patients with UC)
- Cholangiography is compulsory for diagnostic

- Immunosuppressive therapy is useless
- Anticholestatic medications and surgical interventions can partially reduce symptoms
- The only one effective treatment is liver transplantation

- Without transplantation death in 10 years


Pulmonary embolism
Nephrotic syndrome
Primary sclerosing cholangitis
Membranous nephropathy
Ulcerative colitis
Hypochromic microcytic anemia:
1. Chronic posthemorrhagic anemia
and/or
2. Anemia of chronic diseases

Ig4-related diseases



Outcomes

- The level of IgG4 was elevated
- The diagnosis has been changed to IgG4-related sclerosing cholangitis
- In this case immunosuppressive therapy is effective

- Patient underwent immunosuppressive therapy with glucocorticoids
- He continued to get warfarin, mesalamine and lisinopril
- Two years after presentation, he had nephrotic-range proteinuria, but tests showed that the colitis and liver function were well controlled

Thank you for your attention!