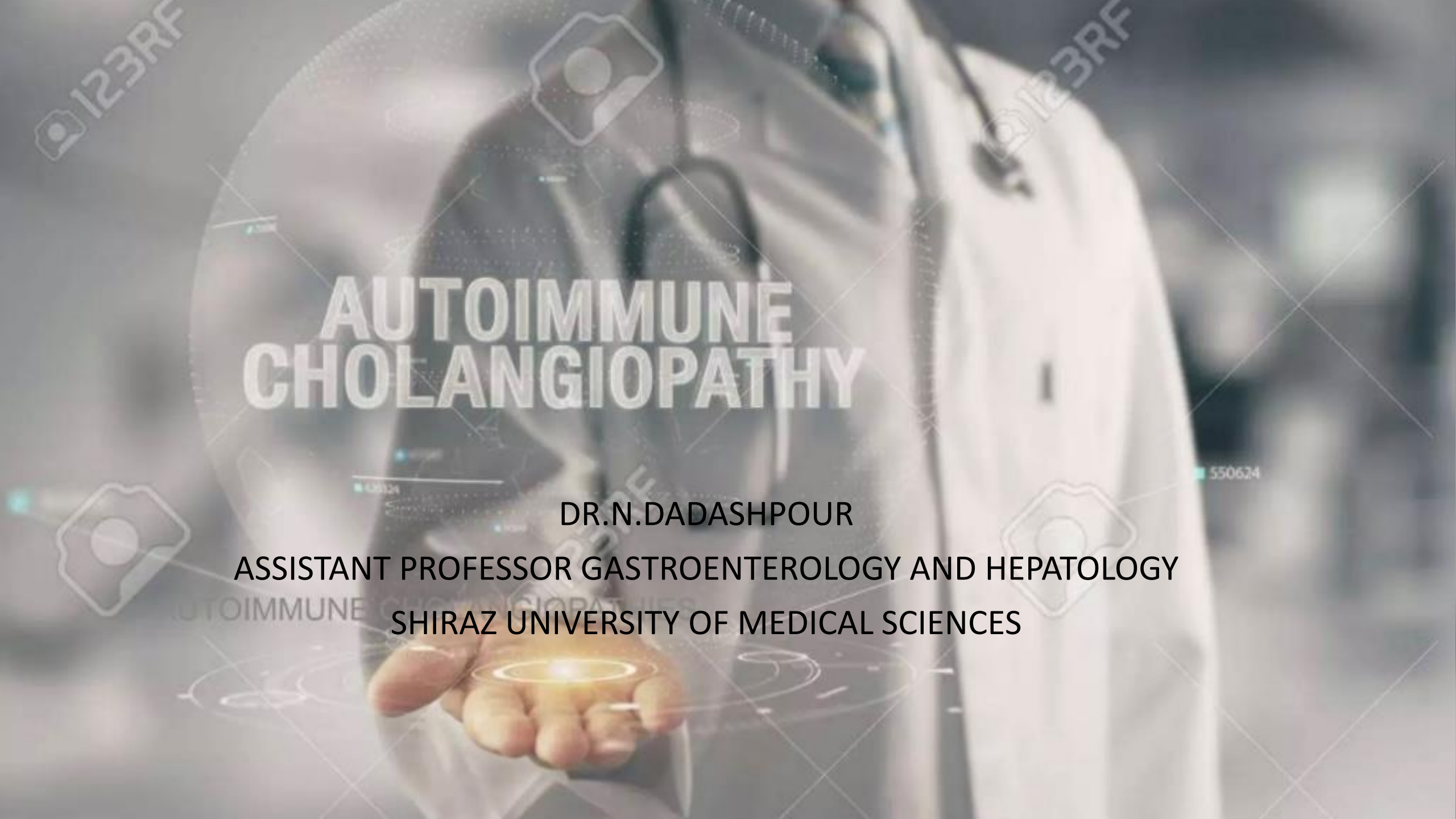


DR.N.DADASHPOUR

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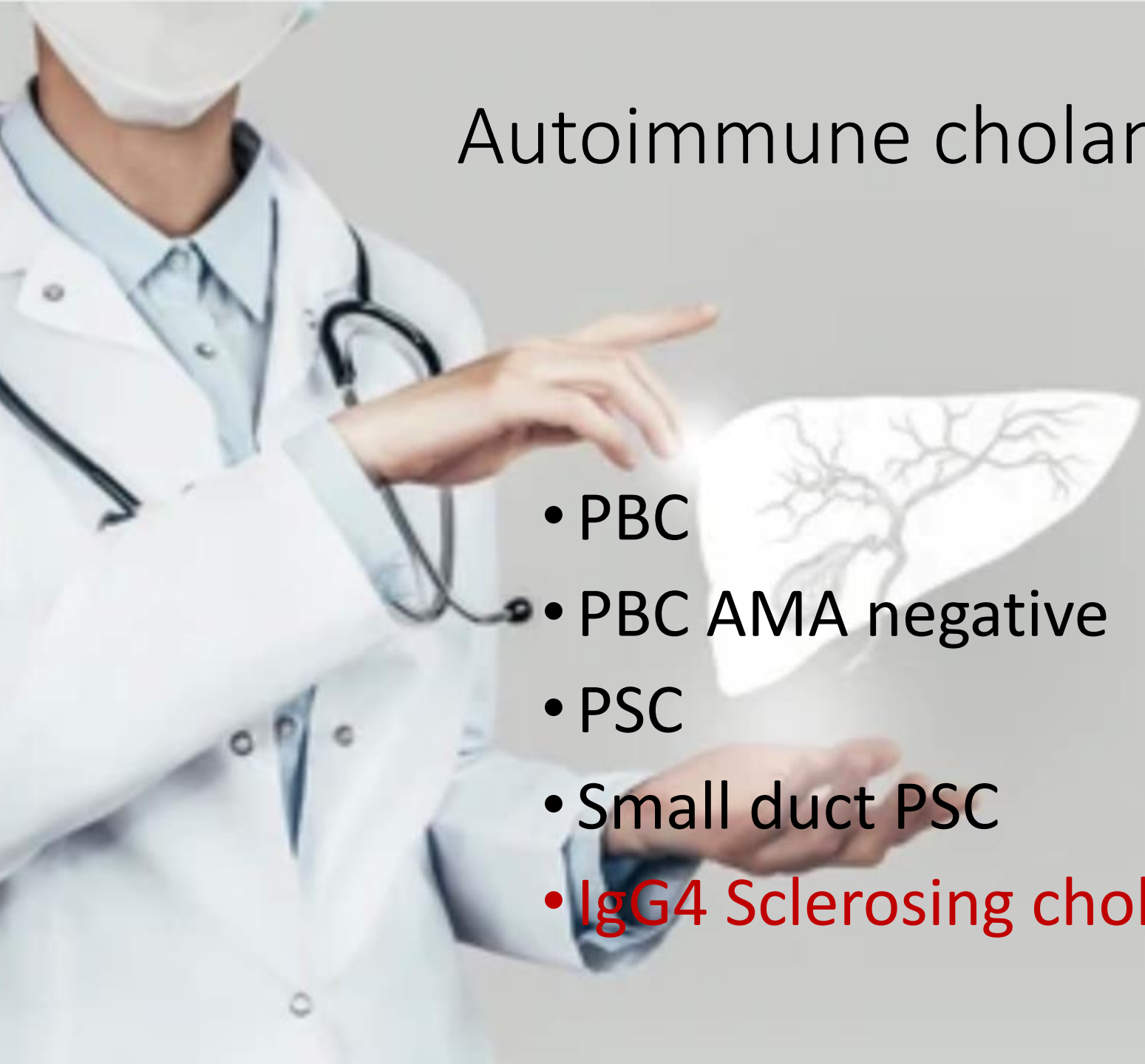
SHIRAZ UNIVERSITY OF MEDICAL SCIENCES



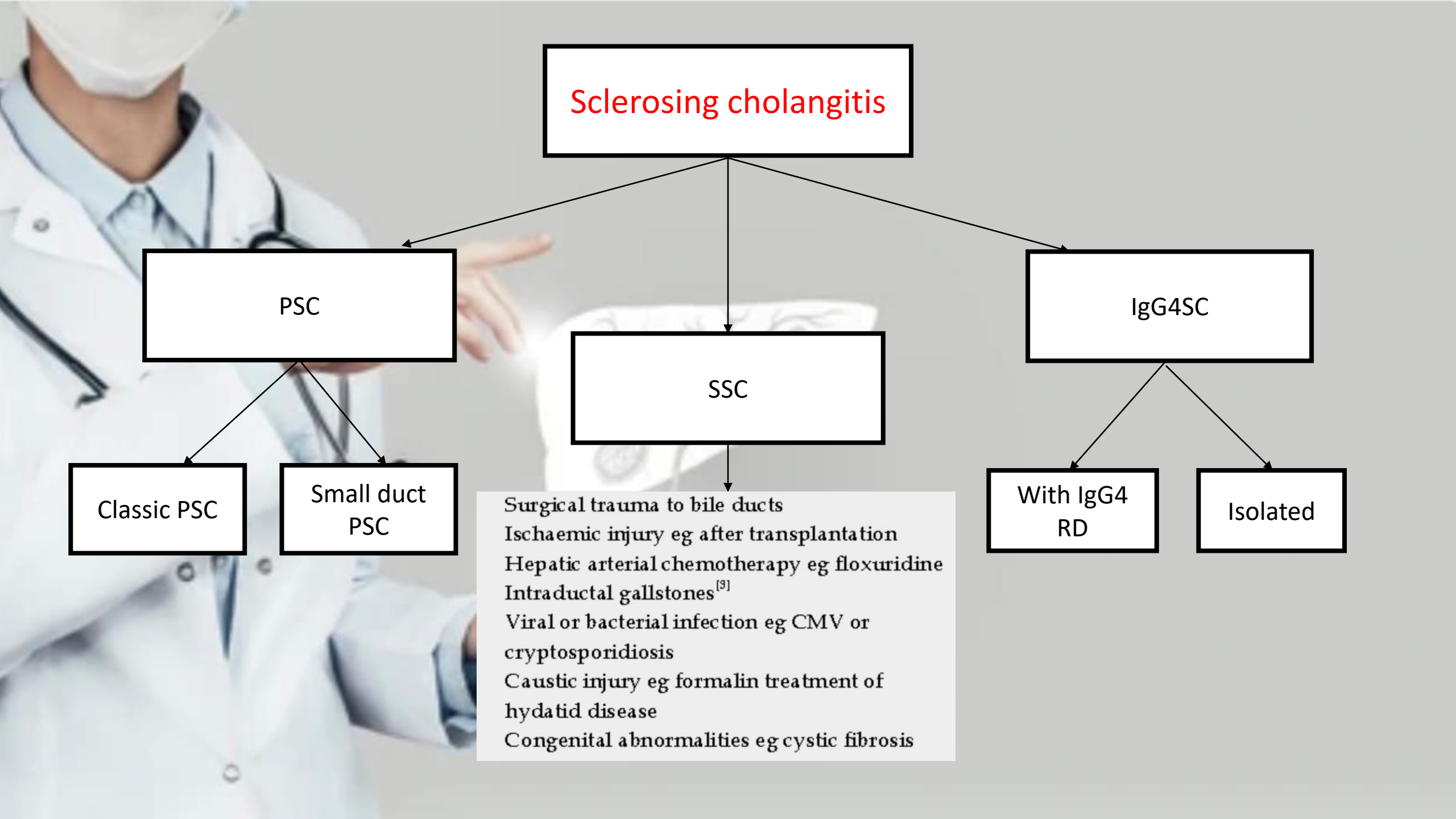
Goals:

- Definition of Autoimmune cholangiopaties
- When shoulde we doubt AIC/Clinical manifestations
- Diagnosis
- Treatment

Autoimmune cholangiopaties



- PBC
- PBC AMA negative
- PSC
- Small duct PSC
- IgG4 Sclerosing cholangitis


Sclerosing cholangitis
PSC
SSC
IgG4SC
Classic PSC
Small duct PSC
With IgG4 RD
Isolated
Surgical trauma to bile ducts
Ischaemic injury eg after transplantation
Hepatic arterial chemotherapy eg floxuridine
Intraductal gallstones[3]
Viral or bacterial infection eg CMV or cryptosporidiosis
Caustic injury eg formalin treatment of hydatid disease
Congenital abnormalities eg cystic fibrosis



IgG4 Related diseases:

- Immune-mediated fibroinflammatory disease
- Multiorgan involvement+elevated serum IgG4
- Typical imaging and histologic finding

- Common forms:

*AIP(Type 1)

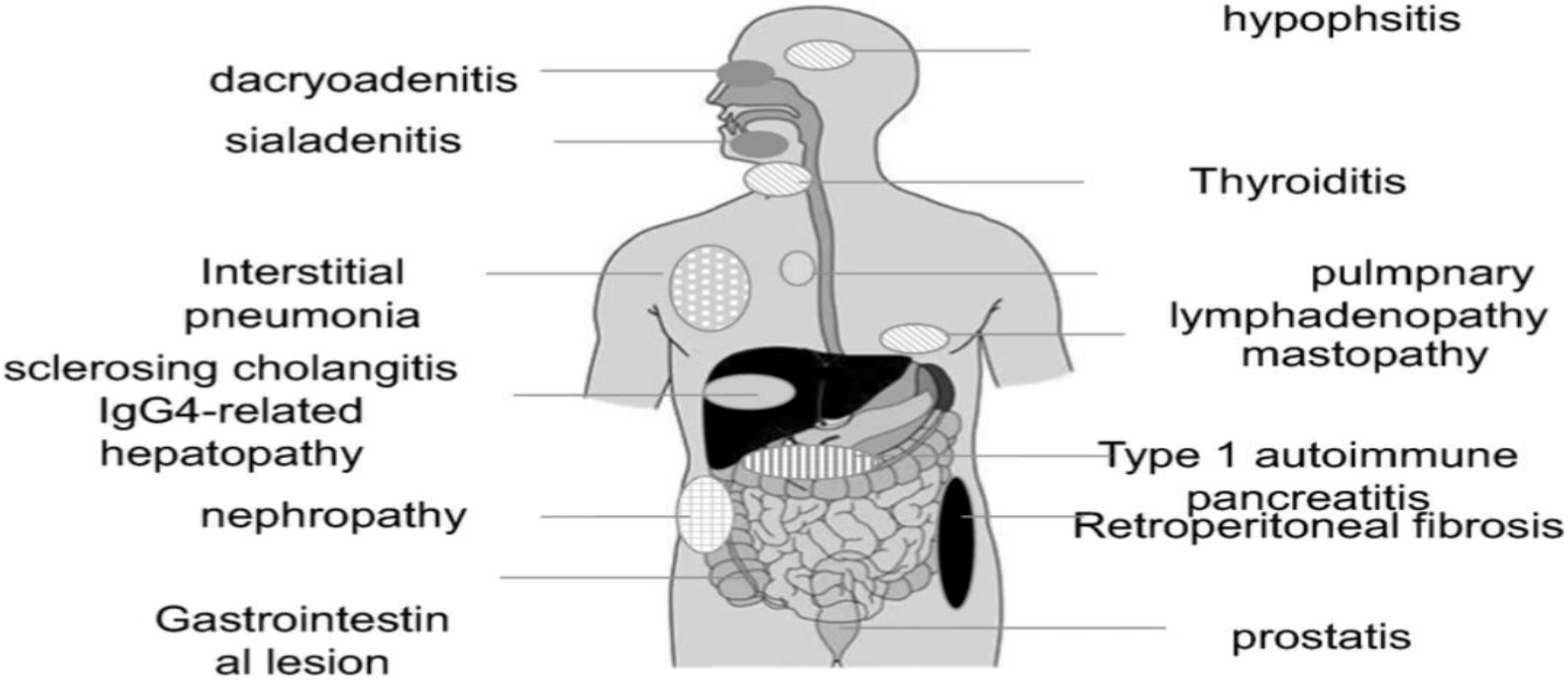
*IgG4 SC

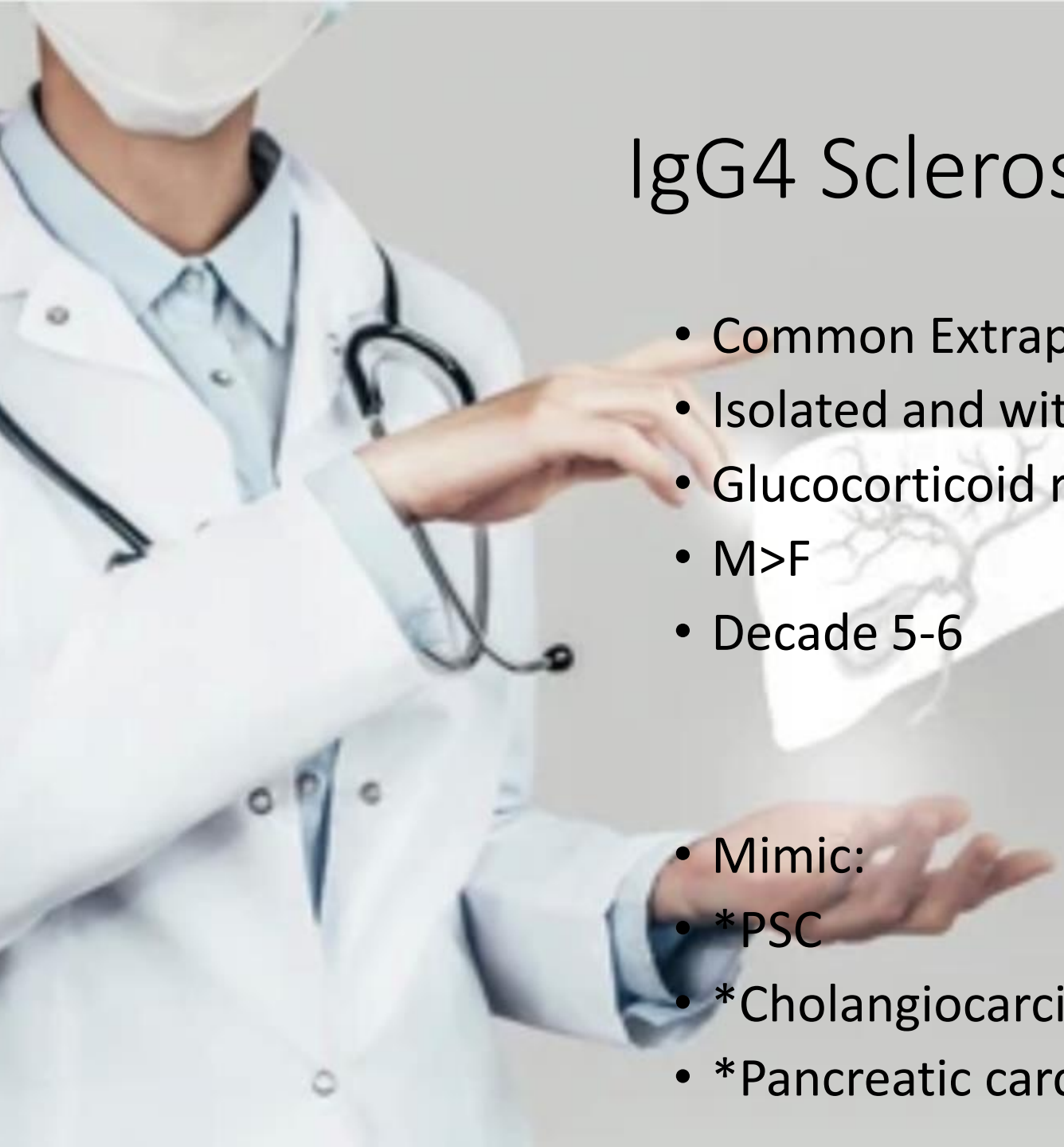
*Salivary gland diseasea

*Orbital diseases

*Retroperitoneal fibrosis

IgG4 Related diseases:





IgG4 Sclerosing cholangitis:

- Common Extrapancreatic manifestion of AIP(type 1)70%
- Isolated and without AIP(Rare)
- Glucocorticoid responsive Sclerosing cholangitis
- M>F
- Decade 5-6

- Mimic:
- *PSC
- *Cholangiocarcinoma
- *Pancreatic carcinoma



When shoulde we doubt IgG4 SC
Clinical manifestations:

- Painless obstructive jaundice
- Abdominal pain
- Weight loss

with Other organ involvement specialy AIP

- Asymptomatic patient with:

*Evaluation of Abnormal LFT(Cholestatic pathern)

*Pancrease enlargement or mass

*Duct stricture

*DM



Diagnosis

- Labolatory tests
- Imaging
- Tissue sampling and histology

HISORt Criteria:

*Histology

*Imaging

*Serology

*Other organ involvement

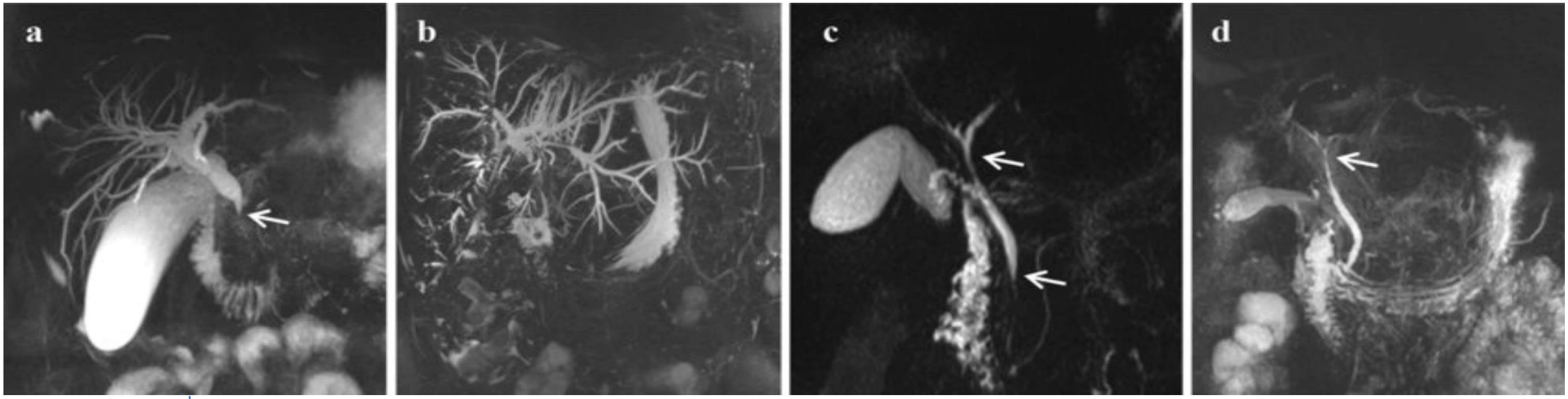
*Response to steroid therapy



Labolatory tests:

- Elevated ALP
- Polycolonal hypergammaglobunemia
- ANA(50%)
- Total serum IgG:Normal or elevated
- IgG4>2ULN(>280)
- Elevated IgE(60%)
- Peripheral eosinophilia

Imaging:
Choice:MRCP(4 types)



DDx:
Pancreatic cancer
CCA
IDUS/EUS+FNA/
ERCP cytology and
BX

DDx:
PSC

IBD/MRCP/Liver Bx

DDx:
CCA
ERCP cytology and
BX



Tissue sampling and histology:

- ERCP and brush cytology from strictures
- Intraductal FNA or EUS
- Intrabiliary biopsy
- Ampullary biopsy from major papilla

Histology:

IgG4>10/HPF +Two of the below histologic features:

1-Lymphoplasmacytic infiltrate

2-Obliterative phlebitis

3-Storiform fibrosis

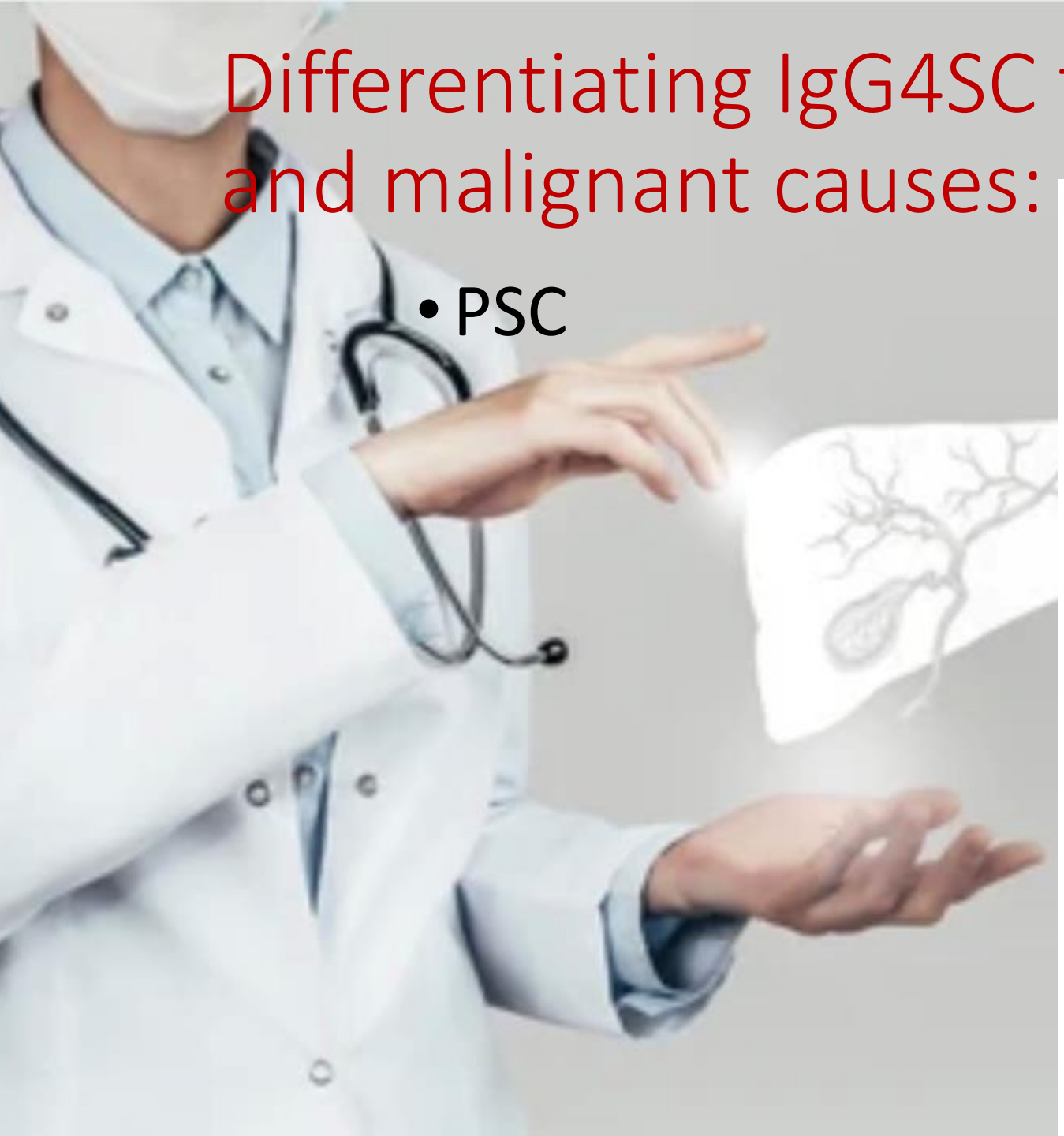


HISORt Critria:

Criterion H-Histology (at least one of the following)	1. Periductal lymphoplasmacytic infiltrate, obliterative phlebitis, storiform fibrosis 2. Lymphoplasmacytic infiltrate, storiform fibrosis, abundant IgG4+ cells (≥10 HPF)
Criterion I-Imaging of pancreas	1. Typical-diffusely enlarged gland with delayed (rim) enhancement; diffusely irregular, attenuated main pancreatic duct 2. Others-Focal pancreatic mass/enlargement; focal pancreatic duct stricture; pancreatic atrophy; pancreatic calcification; pancreatitis
Criterion S-Serology	Elevated serum IgG4 (normal: 8-140 mg/dL)
Criterion O-Other organ involvement (can be confirmed by biopsy or resolution/ improvement with steroid therapy)	Hilar/intrahepatic biliary strictures; persistent distal biliary stricture; parotid/lacrimal gland involvement; mediastinal lymphadenopathy; retroperitoneal fibrosis
Criterion R-Response to steroid therapy	Resolution or marked improvement of pancreatic/extrapancreatic manifestation with steroid therapy
Diagnostic of autoimmune pancreatitis when any of the following is fulfilled	1. Criterion H 2. Criterion I+S 3. Strong clinical suspicion of autoimmune pancreatitis (idiopathic pancreatic disease+Criterion S and/or O)+Criterion R

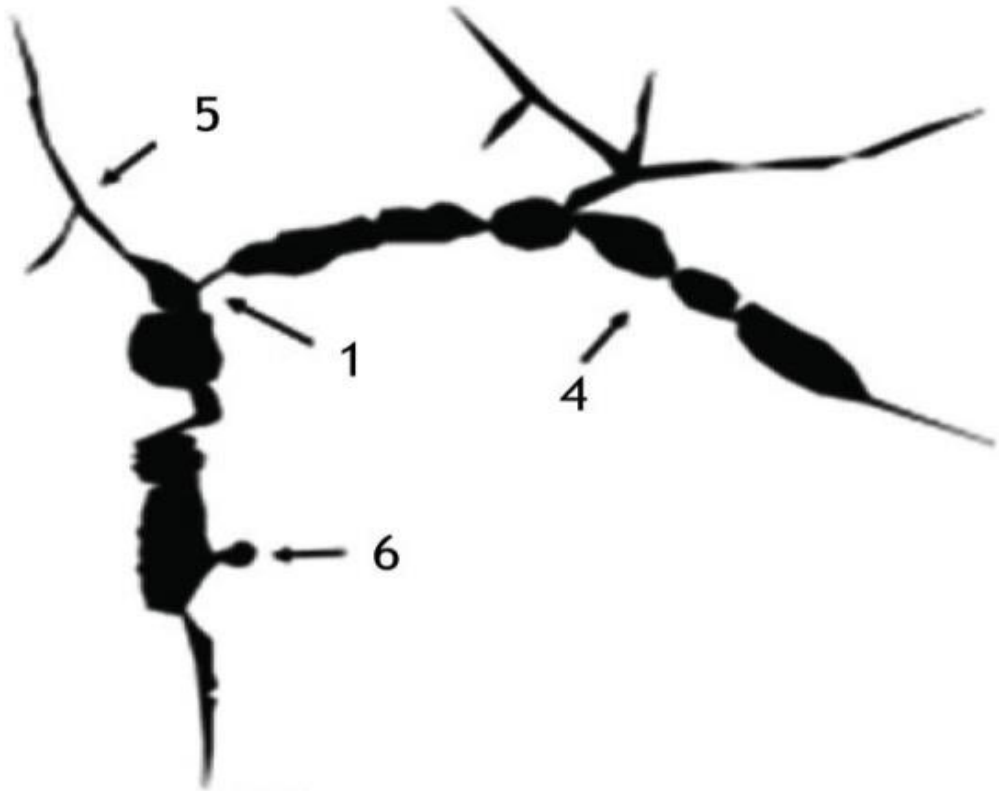
Differentiating IgG4SC from other benign and malignant causes:

- PSC



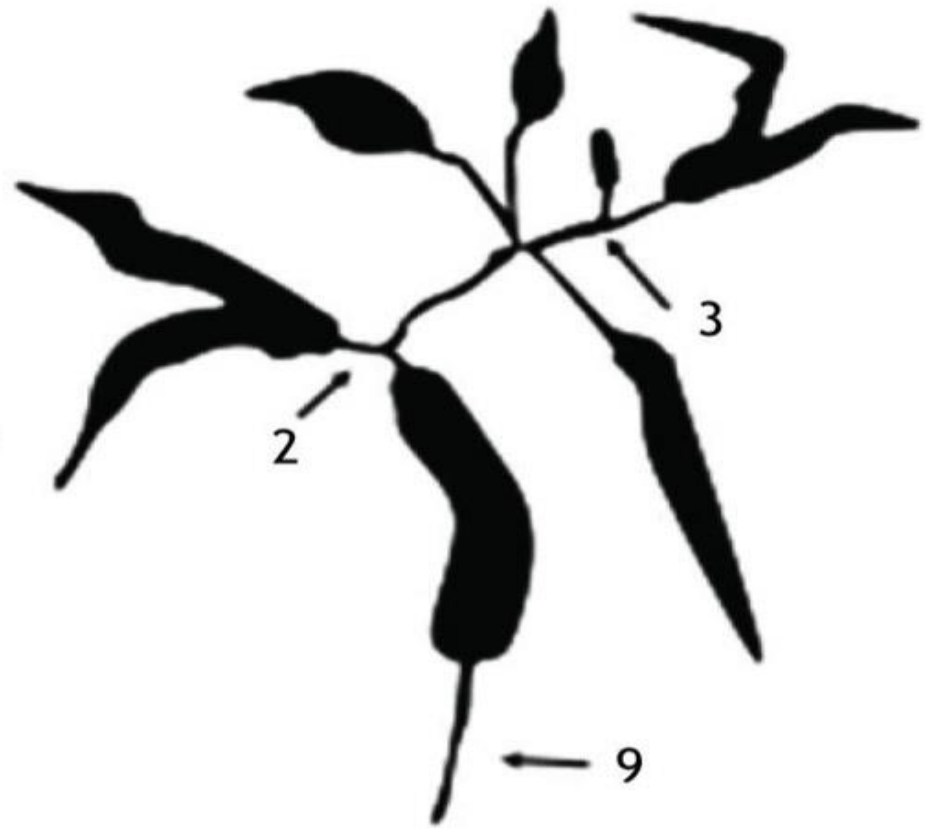
	IgG4-related sclerosing cholangitis	PSC
• Age	Elderly	Young
• Initial symptom	Obstructive jaundice	Liver dysfunction
• Associated diseases		
° Inflammatory bowel disease	Rare	Sometimes
° Sclerosing diseases	Frequent	Rare
• Elevation of serum IgG4	Frequent	Rare
• Infiltration of IgG4-positive cells	Many	Scarce
• Steroid responsiveness	Good	Poor
• Prognosis	Good	Progressive

PSC



1. Band-like stricture.
4. Beaded appearance.
5. Pruned-tree appearance
6. Diverticulum-like outpouching

Sclerosing cholangitis with AIP



2. Segmental stricture
3. Dilation after confluent stricture
9. Stricture of lower CBD



Pancreaticobiliary cancer:

- Age>60
- Focal involvement of pancrease and ducts
- Mildly elevated IgG4
- Without other organ involvement

Tissue sampling(biopsy)

Treatment:

- All patients

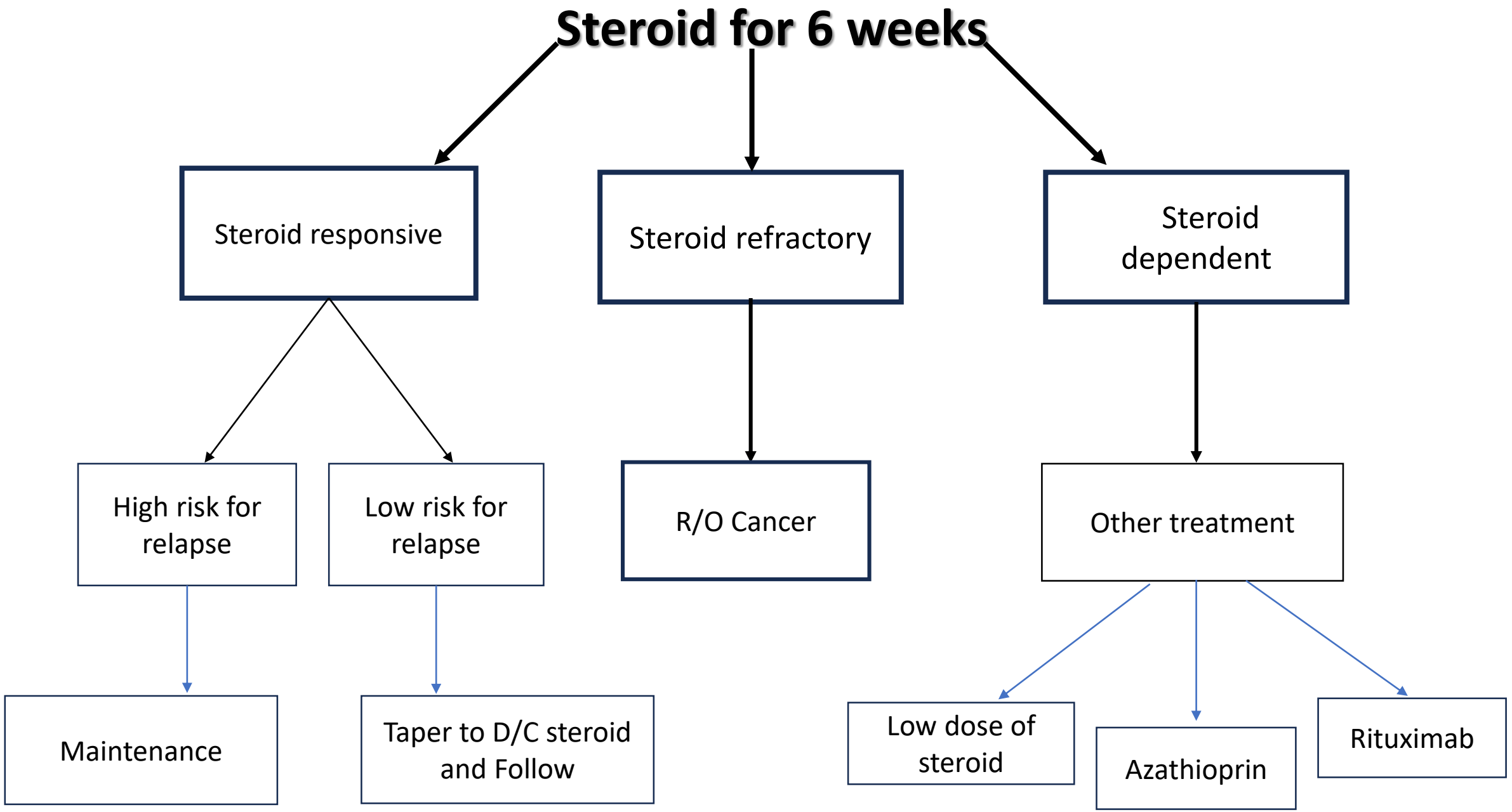
*prednisone/prednisolone(0/6 mg/kg/daily):30-40 mg/D

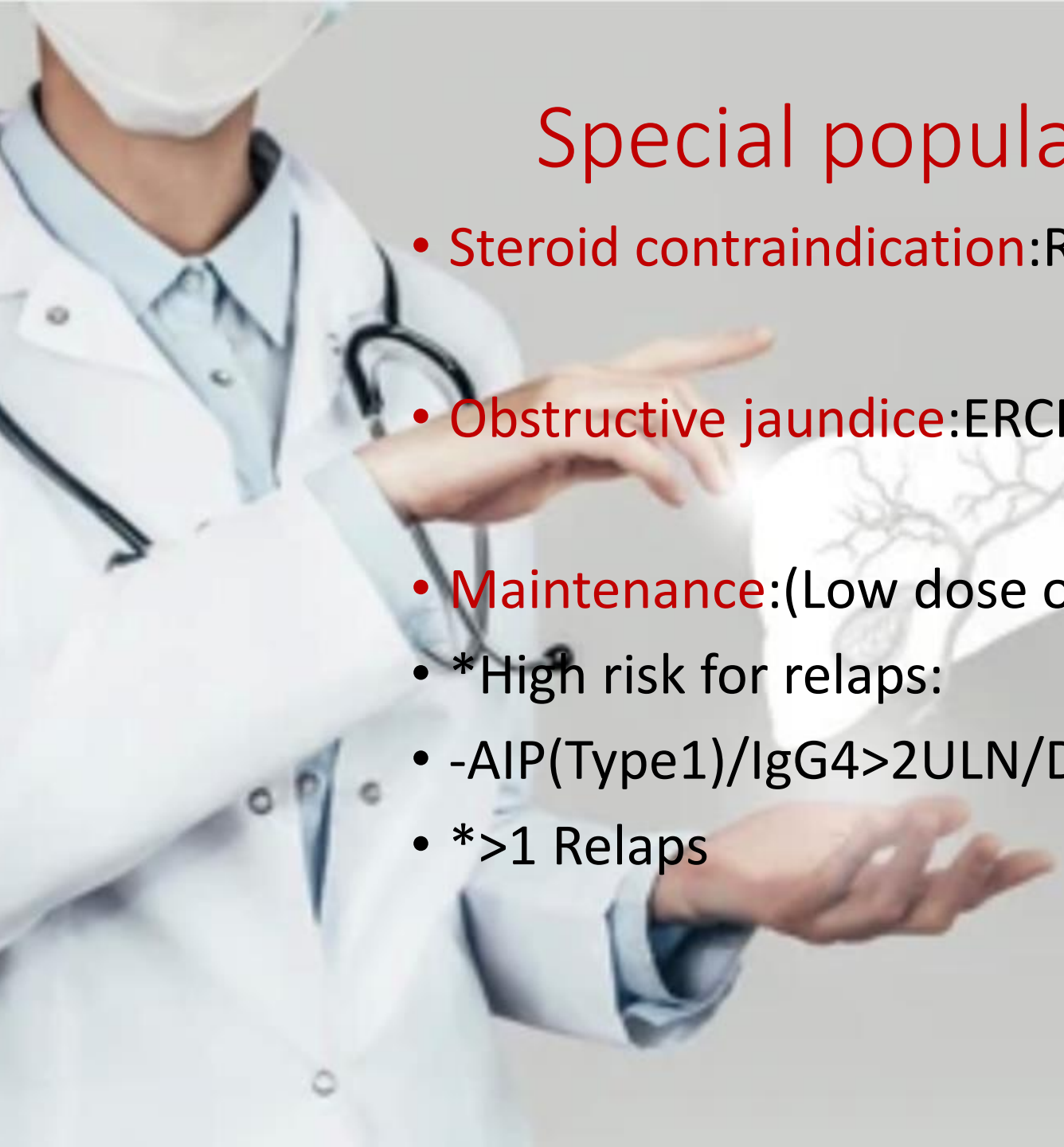
*4-6 weeks

Remission:(Clinical and imaging response)

Steroid refractory:Failure to respond to steroid

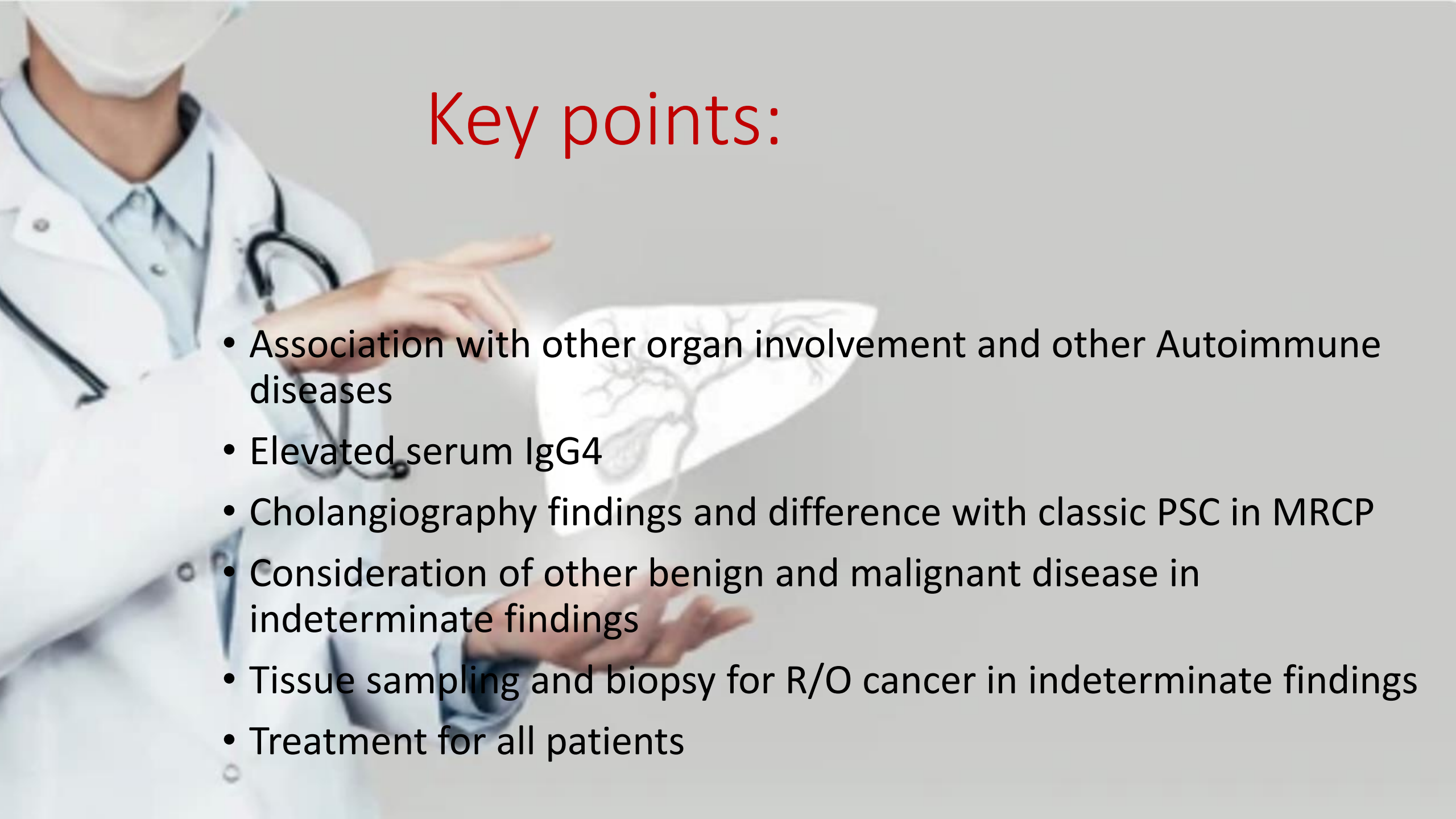
Steroid dependent:Worsening of disease or flare during steroid dose reduction or withdrawal


Steroid for 6 weeks
Steroid responsive
Steroid refractory
Steroid dependent
High risk for relapse
Low risk for relapse
R/O Cancer
Other treatment
Maintenance
Taper to D/C steroid and Follow
Low dose of steroid
Azathioprin
Rituximab



Special population

- Steroid contraindication:Rituximab
- Obstructive jaundice:ERCP+Stent
- Maintenance:(Low dose of steroid/MMF/Azaram/Rituximab)
- *High risk for relaps:
- -AIP(Type1)/IgG4>2ULN/Delay imaging response/>2OOI
- *>1 Relaps

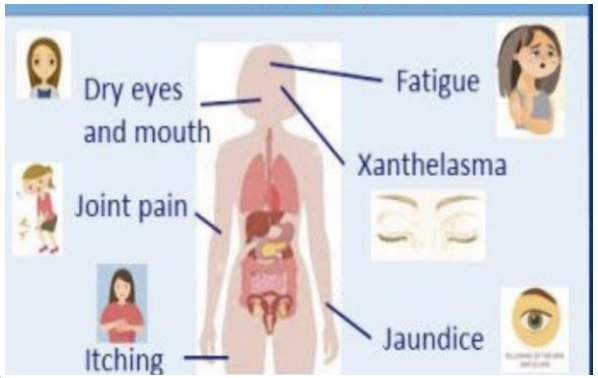


Key points:

- Association with other organ involvement and other Autoimmune diseases
- Elevated serum IgG4
- Cholangiography findings and difference with classic PSC in MRCP
- Consideration of other benign and malignant disease in indeterminate findings
- Tissue sampling and biopsy for R/O cancer in indeterminate findings
- Treatment for all patients

PBC

Cause:
T-lymphocyte mediated attack on intralubolar bile ducts/gradual destruction



Diagnosis:
ALK>1/5ULN
AMA+
Histologic evidence

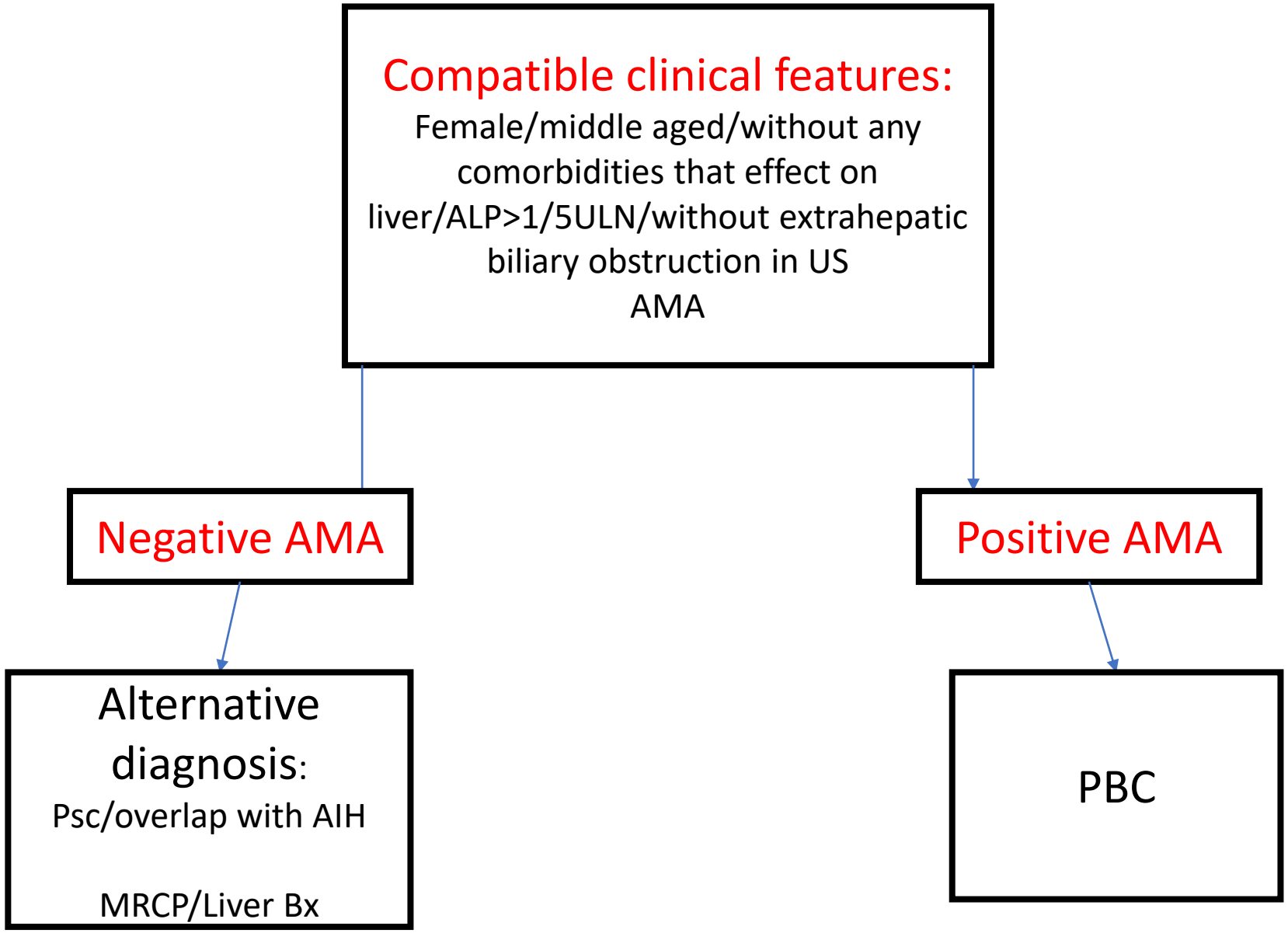
Clinical manifestations:
Mostly asymptomatic(60%)
Fatigue/pruritus/abdominal pain

Laboratory tests:
Elevated serum ALP
AMA+(95%)
ANA+(70%)
HLP

Physical examination:
Skin/hepatospelenomegaly/ ESLD



Associated autoimmune conditions


Compatible clinical features:
Female/middle aged/without any comorbidities that effect on liver/ALP>1/5ULN/without extrahepatic biliary obstruction in US
AMA
Negative AMA
Positive AMA
Alternative diagnosis:
Psc/overlap with AIH
MRCP/Liver Bx
PBC



Liver biopsy in PBC:

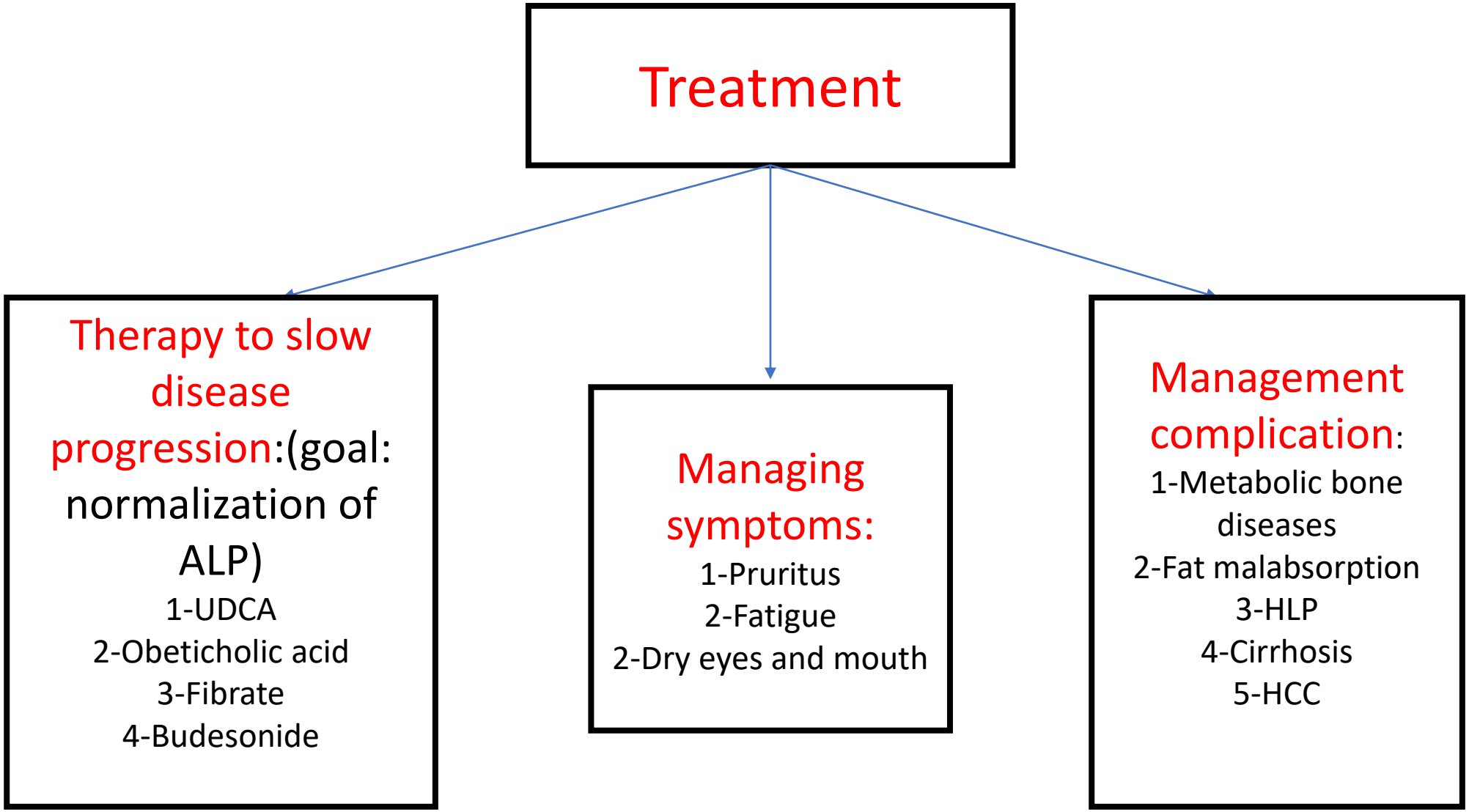
Often not required to make the diagnosis

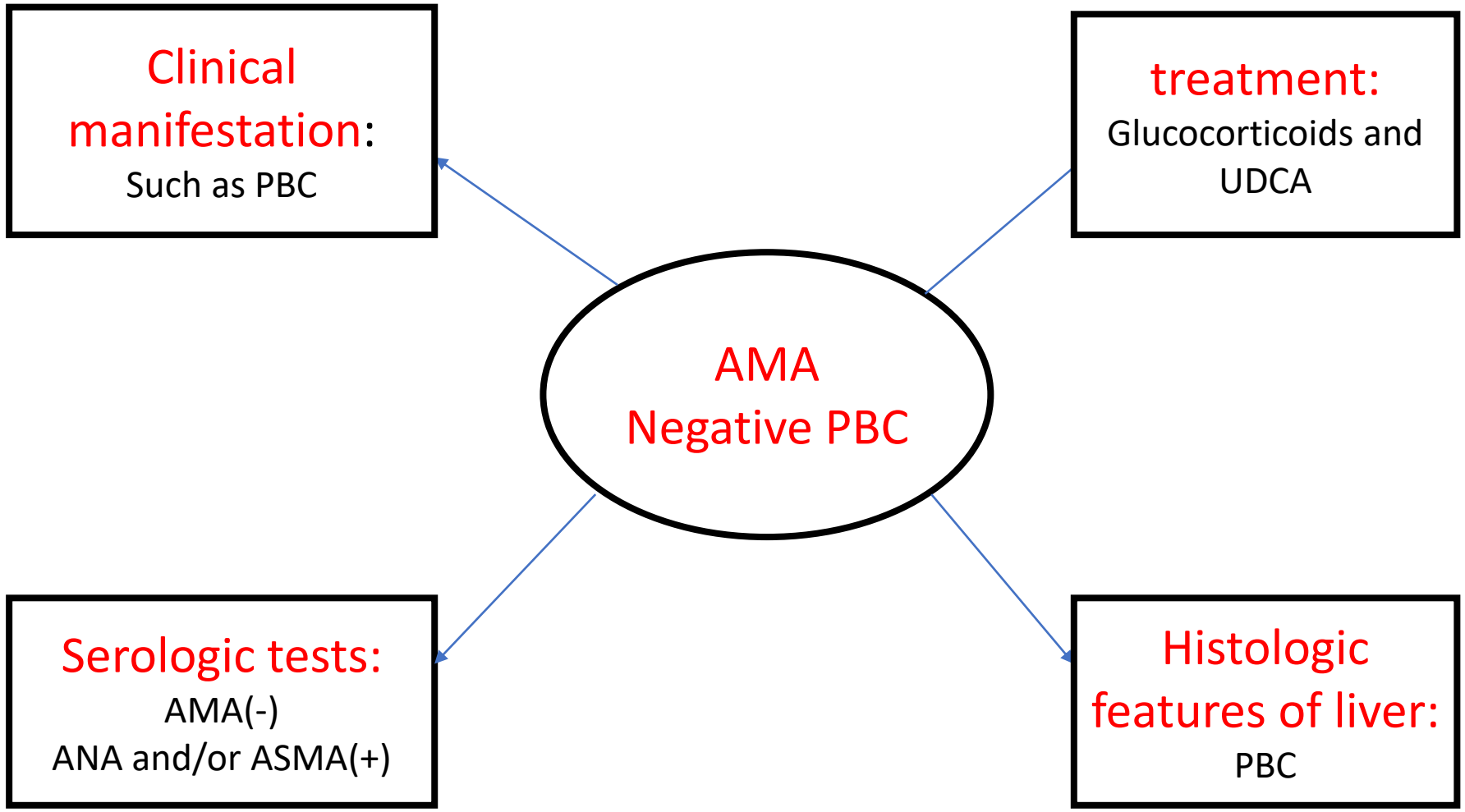
BUT It useful for:

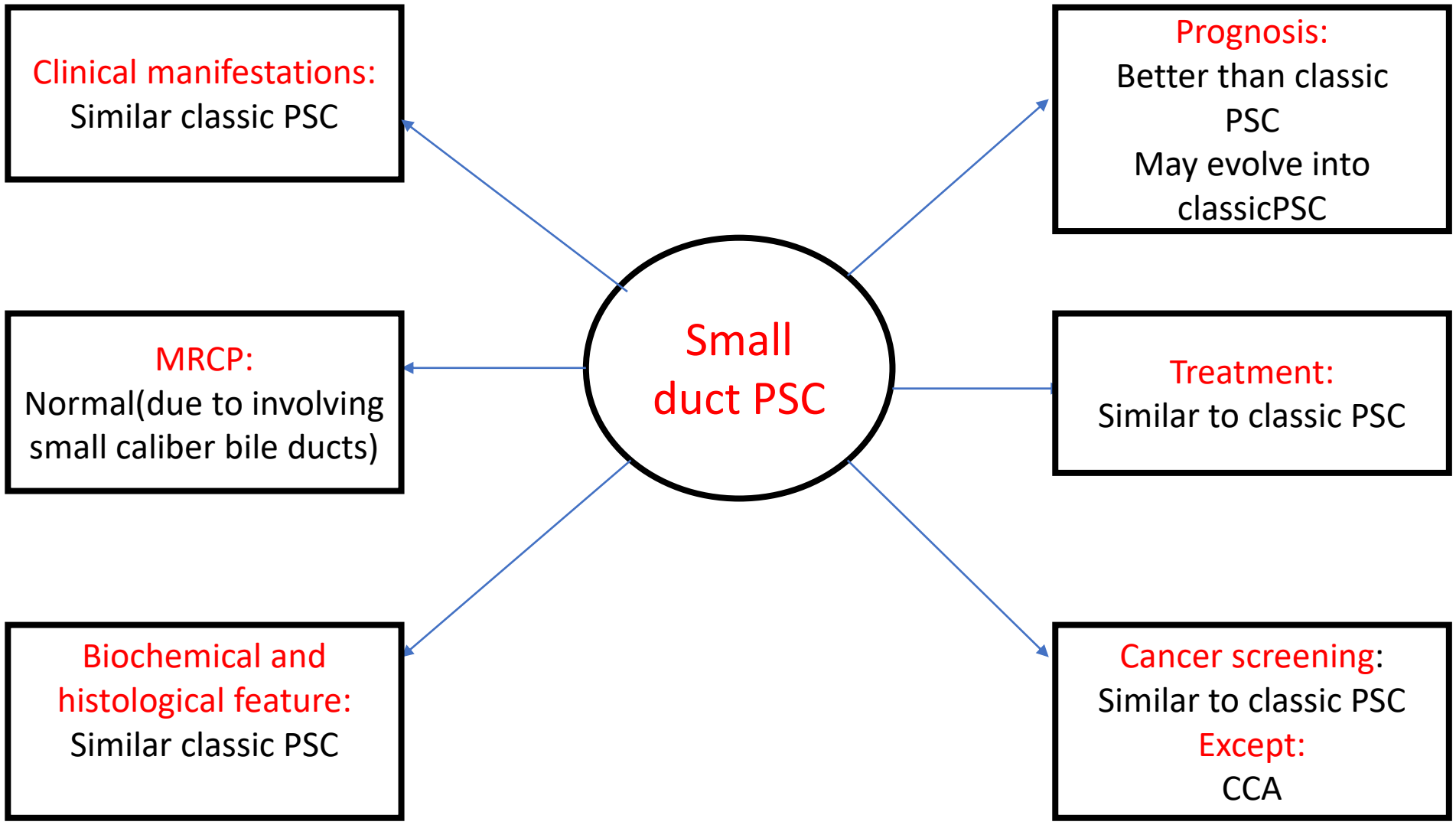
1-Staging and prognosis

2-Evidence of AIH(ALT>5ULN/ASMA+)

3-Patient dose not respond optimally to therapy with UDCA


Treatment
Therapy to slow disease progression:(goal: normalization of ALP)
1-UDCA
2-Obeticholic acid
3-Fibrate
4-Budesonide
Managing symptoms:
1-Pruritus
2-Fatigue
2-Dry eyes and mouth
Management complication:
1-Metabolic bone diseases
2-Fat malabsorption
3-HLP
4-Cirrhosis
5-HCC


Clinical manifestation:
Such as PBC
treatment:
Glucocorticoids and UDCA
AMA
Negative PBC
Serologic tests:
AMA(-)
ANA and/or ASMA(+)
Histologic features of liver:
PBC


Small duct PSC
Clinical manifestations: Similar classic PSC
MRCP: Normal(due to involving small caliber bile ducts)
Biochemical and histological feature: Similar classic PSC
Prognosis: Better than classic PSC May evolve into classicPSC
Treatment: Similar to classic PSC
Cancer screening: Similar to classic PSC Except: CCA