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Hépatopathies auto-immunes

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Autoimmune Liver Diseases

- Autoimmune hepatitis
- Primary biliary cholangitis
- Primary sclerosing cholangitis
- Overlap syndromes
- IgG4-associated cholangitis

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Autoimmune Hepatitis

- Prevalence 15-25/100'000
- ♀ : ♂ = 3 : 1
- Clinical manifestations highly variable (asymptomatic - acute liver failure - chronic hepatitis - cirrhosis)
- May be associated with other auto-immune diseases
- Overlap syndromes (AIH-PBC, AIH-PSC)

AASLD Practice Guideline - Manns MP *et al.* Hepatology 2010;51:2193-2213.
EASL Clinical Practice Guideline. J Hepatol 2015;63:971-1004.

Autoimmune Hepatitis Diagnosis

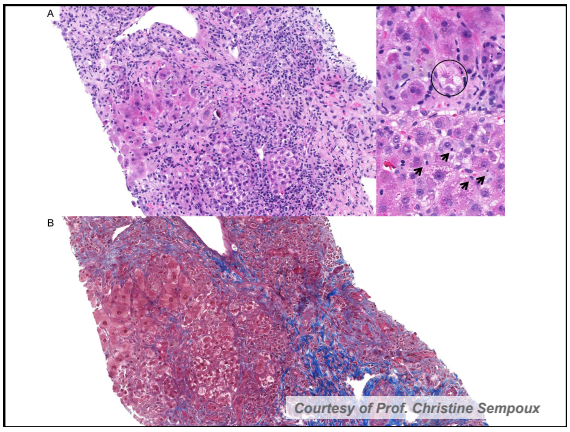
- Exclusion of other liver diseases
- Autoantibodies
  ANA, SMA (anti-actin) *Type 1*
  anti-LKM1 *Type 2*
  Others: SLA/LP, anti-LC1
- γ-globulins (IgG) ↑
- Liver biopsy
- Response to treatment

Autoimmune Hepatitis Simplified Diagnostic Criteria

		Points
Autoantibodies	ANA or SMA ≥ 1:40	1
	ANA or SMA ≥ 1:80 or LKM ≥ 1:40 or SLA/LP pos. (any titer)	2
IgG (or γ-globulins)	> ULN	1
	> 1.1 x ULN	2
Liver histology	Compatible with AIH	1
	Typical of AIH	2
Absence of viral hep.	Yes	2

6 points → probable AIH (sens. 88%, spec. 97%)
≥ 7 points → definite AIH (sens. 81%, spec. 99%)

Hennes EM *et al.* and the IAIHG. Hepatology 2008;48:169-176.



Autoimmune Hepatitis
Treatment

- **Predniso(lo)ne 0.5-1 mg/kg/d**
  → reduction to 10 mg/d by 10-12 wks and to 5 mg/d by 6 months
  → if possible, withdrawal by 1 year
- **Azathioprine 50 mg/d → 1-2 mg/kg/d**
- **Goal: complete remission** (ALT, IgG, histology)
- **Duration at least 3 years**

Autoimmune Hepatitis
Treatment

- **Alternative treatment options**
  - Budesonide (only in non-cirrhotic pts)
  - Intolerance to azathioprine: MMF
  - Insufficient response: i.v. corticosteroids, CsA, tacrolimus, infliximab, ...
- **Regular follow-up and treatment adherence are essential**

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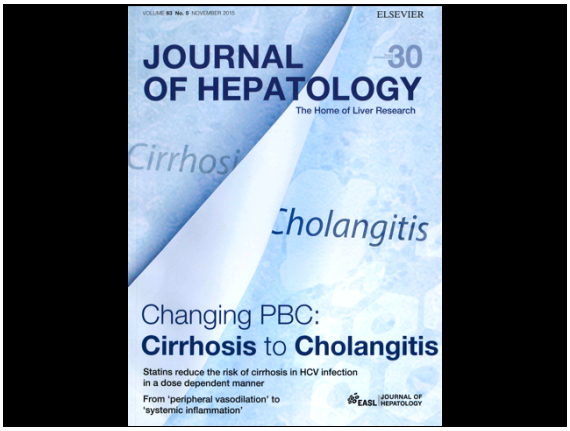


Primary Biliary Cholangitis

- **F.k.a. primary biliary cirrhosis**
- **Autoimmune disease with progressive destruction of small bile ducts**
- **Prevalence 2-40/100'000**
- **♀ : ♂ = 9 : 1, peak age 40-60 years**
- **May be associated with other autoimmune diseases** (Sjögren's syndrome, thyroiditis, celiac disease, RA, ...)

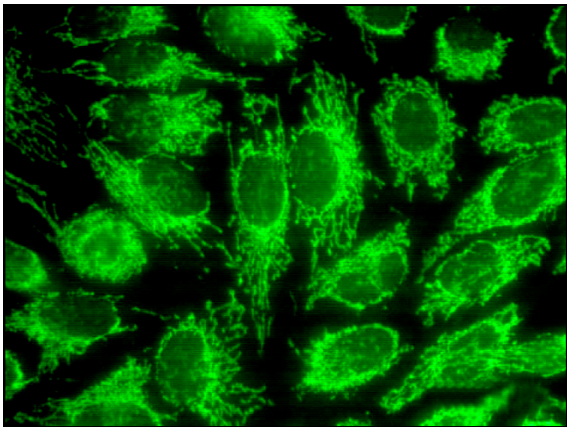
AASLD Practice Guideline - Lindor K *et al.* Hepatology 2009;50:291-308.
Beuers U *et al.* J Hepatol 2015;63:1285-1287.
EASL Clinical Practice Guidelines. J Hepatol 2017;67:145-172.

Primary Biliary Cholangitis
Clinical Manifestations

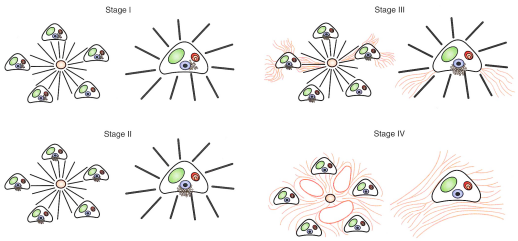
- **Initially asymptomatic** (AP ↑, γ-GT ↑)
- **Pruritus**
- **Fatigue**
- **Jaundice represents a late manifestation**
- **Xanthomas, osteopenia / osteoporosis, ...**
- **Complications of cirrhosis**

Primary Biliary Cholangitis
Diagnosis

- **Alkaline phosphatase ↑, γ-GT ↑**
- **Antimitochondrial antibodies (AMA)**
  (anti-M2 = E2 subunit of pyruvate dehydrogenase complex)
  Sensitivity and specificity > 95%
- **IgM ↑**
- **Liver biopsy** (not mandatory)



Primary Biliary Cholangitis
Histological Stages



Ludwig's classification

Lindor KD and Levy C. In: Zakim and Boyer's Hepatology. 6th ed. Elsevier 2012.

Primary Biliary Cholangitis
Management

- **Ursodeoxycholic acid 13-15 mg/kg/d**
- **Second line: obeticholic acid 5 → 10 mg/d**
- **Treatment of pruritus**
  (cholestyramine, rifampicin, naltrexone, sertraline, phototherapy, ...)
- **Prevention / therapy of osteoporosis**
- **Liver transplantation**
- **Investigational: fibrates, ...**

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Primary Sclerosing Cholangitis

- Chronic fibrosing inflammatory process of medium- and/or large-size, intra- and/or extrahepatic bile ducts
- Prevalence 5-10/100'000
- ♂:♀ = 2 : 1, median age at diagn. 40 yrs
- 80% associated with IBD (UC > CD)

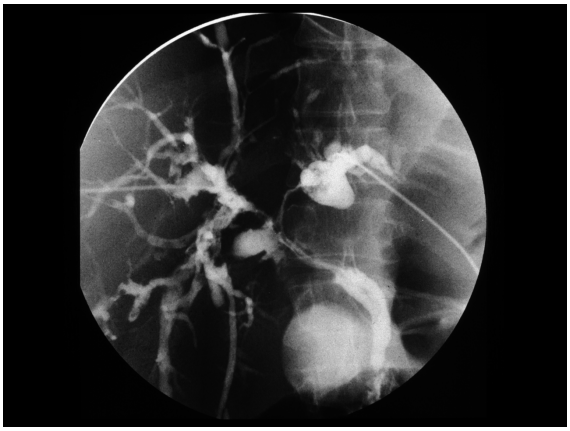
EASL Clinical Practice Guideline. J Hepatol 2009;51:237-267.
AASLD Practice Guideline - Chapman R *et al*. Hepatology 2010;51:660-678.
Karlsen TH and Boberg KM. J Hepatol 2013;59:571-581.
Lazaridis KN and LaRusso NF. N Engl J Med 2016;375:1161-1170.
ESGE-EASL Clinical Guidelines. J Hepatol 2017;66:1265-1281.

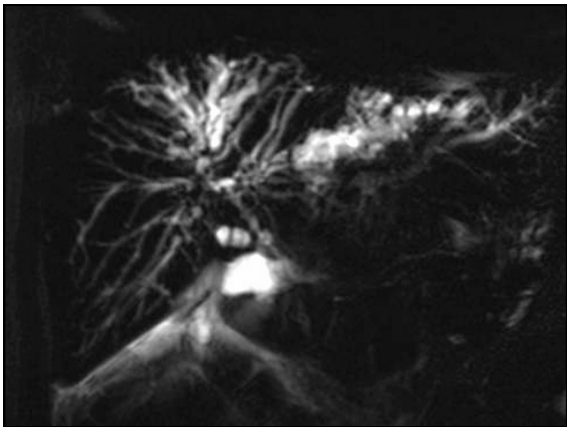
Primary Sclerosing Cholangitis
Clinical Manifestations

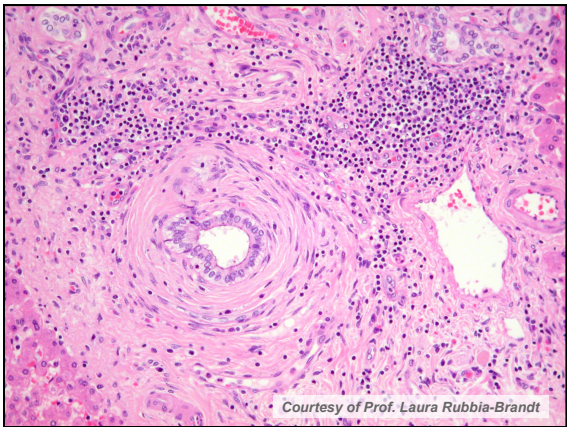
- Initially asymptomatic (AP ↑, γ-GT ↑)
- Pruritus, pain, fatigue, jaundice
- Complications:
  - bacterial cholangitis
  - cholangiocarcinoma (1.5% per year)
  - complications of chronic cholestasis
  - complications of cirrhosis
  - colorectal cancer

Primary Sclerosing Cholangitis
Diagnosis

- Alkaline phosphatase ↑, γ-GT ↑
- MRCP
- "Atypical" pANCA pos. in 50-80% but not sufficiently specific
- Evtl. ERCP (antibiotic prophylaxis!)
- Evtl. liver biopsy (staging)
- Colonoscopy







Primary Sclerosing Cholangitis
Management

- Ursodeoxycholic acid 13-15 mg/kg/d (?)
- Endoscopic dilation of dominant stenoses
- Treatment of pruritus
- Prevention / therapy of osteoporosis
- CCA and CRC surveillance
- Liver transplantation

DD PSC-PBC

PSC	PBC
- Medium and large BD	- Small bile ducts
- ♂ > ♀	- ♀ > ♂
- ~ 40 years	- 40-60 years
- Association with IBD	- No association with IBD
- MRCP	- AMA (M2)
- Recurrent bacterial cholangitis	- Progressive cholestasis, pruritus
- Cholangiocarcinoma	- No cholangiocarcinoma
- UDCA 13-15 mg/kg/d ?	- UDCA 13-15 mg/kg/d

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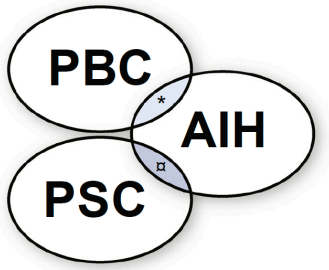
Autoimmune Liver Diseases
Overlap Syndromes



Boberg KM *et al.* on behalf of the IAIHG. J Hepatol 2011;54:374-385.

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IgG4-Associated Cholangitis

- Steroid-responsive sclerosing cholangitis
- ♂>♀, median age ~ 60 years
- Associated with autoimmune pancreatitis and diverse fibrosing conditions
- Often presents with obstructive jaundice; no association with IBD and CCA
- Serum IgG4 ↑
- IgG4-positive plasma cells
- Corticosteroids, evtl. azathioprine

Björnsson E *et al.* Hepatology 2007;45:1547-1554; EASL CPG. J Hepatol 2009;51:237-267; Stone JH *et al.* NEJM 2012;366:539-551.

Take Home Messages

- Consider autoimmune liver disease in the differential diagnosis of elevated LFTs
  → ANA, AMA, SMA, IgG
  → MRCP
- Regular follow-up and treatment adherence are crucial
- Collaboration between GP and specialist
- Progress in the understanding of the patho-genesis and management to be expected