Primary Care's Important Role in the Management of These Chronic Diseases

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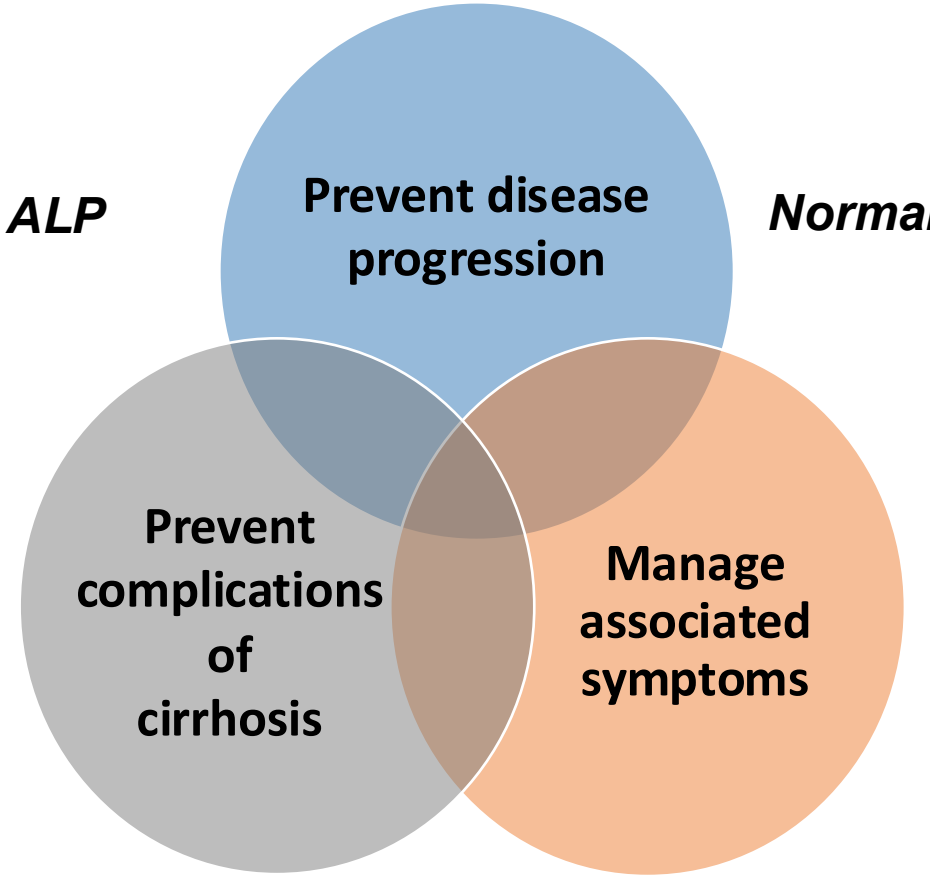
Key Differences in Autoimmune Diseases

- **AIH**: Primarily affects hepatocytes with inflammation and autoantibodies.
- **PBC**: Affects small bile ducts with a hallmark AMA positivity.
- **PSC**: Involves large and small bile ducts resulting in strictures and cholangitis. Strongly associated with IBD and hallmark feature is beading appearance on MRCP.

PBC: Treatment Goals

Reduce ALP → Normalize ALP



Normalize bilirubin → Bilirubin <0.6

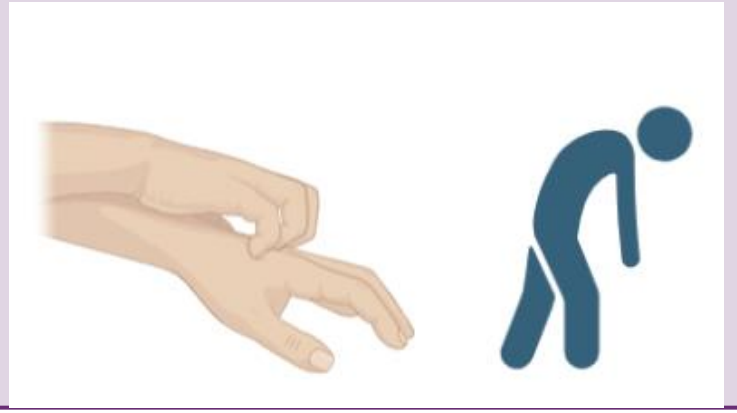
The goal of lifelong therapy is to prevent progressive liver disease and ameliorate disease-associated symptoms that reduce patient QoL[8]

8. European Association for the Study of the Liver. *J Hepatol*. 2017; 67:145–72; 9. Lindor KD et al. *Hepatology*. 2022; 75:1012-1013.

PBC and PSC Management Goals

- **Prevent poor clinical outcomes**
  - Cirrhosis
  - Hepatic decompensation
  - Liver transplantation
  - Liver-related death

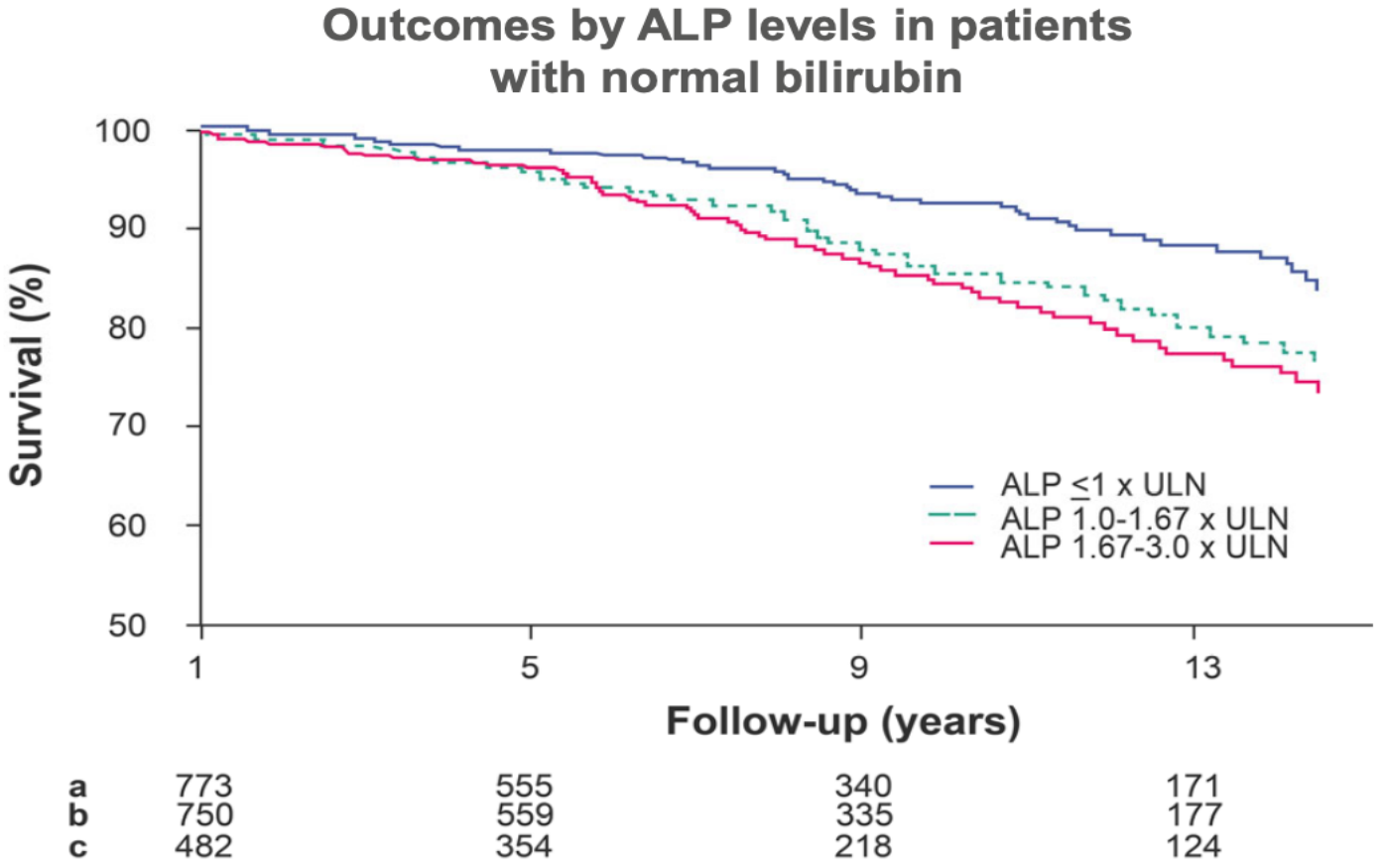
- **Improve quality of life**
  - Pruritus
  - Fatigue



Measuring Fatigue and Itch in the Clinic

- Important to **routinely ask** your PBC and PSC patients about itch and fatigue, and to use a scale (any scale; e.g., ask them to rate their fatigue on a scale of 0 to 10, where 0 = you can't get out of bed, and 10 = you can do whatever you want to do)
  - Gives an estimate of severity
  - Can follow changes over time.

PBC: Normal ALP Levels are Associated with Improved Survival



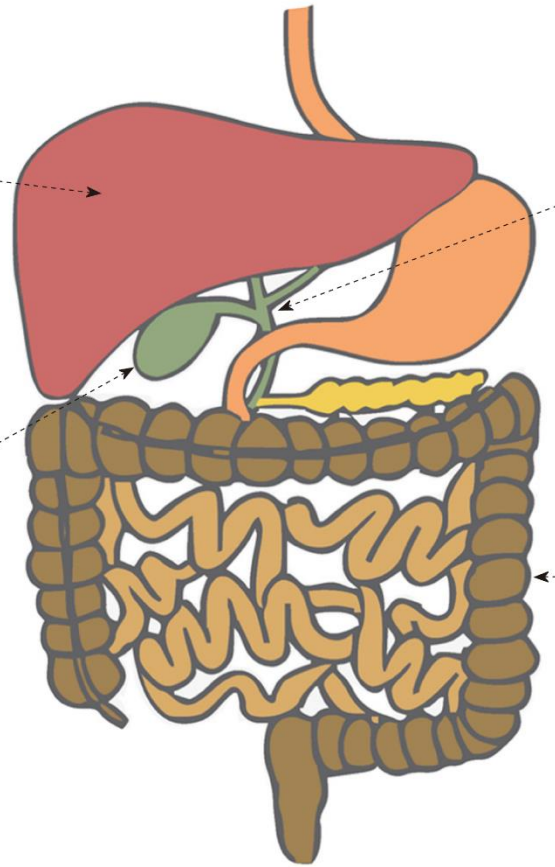
Normal ALP + Bilirubin < 0.7 mg/dL + LSM < 8 kPa = Deep Remission

Murrillo Perez CF et al. Am J Gastroenterol. 2020

Long-term Management of PBC Patients

- Liver tests every 3-6 months
- Thyroid status (TSH) annually
- Bone mineral densitometry at time of diagnosis and then every 2-4 years
- Vitamins A, D, K annually if bilirubin >2.0
- Upper endoscopy every 1-3 years if cirrhotic or Mayo risk score >4.1
- Ultrasound ± AFP every 6 months in patients with known or suspected cirrhosis

PSC: Malignancy Screening Critical



Hepatocellular carcinoma
0.3%-2.8% lifetime incidence
Unknown risk over general population

Q6 month screening if cirrhotic

Cholangiocarcinoma
Up to 20% lifetime incidence
400x-1500x risk over general population

Yearly MRCP & CA 19-9
**regular surveillance associated with a higher 5-year survival (68% vs. 20%, $p < 0.0061$)

Gallbladder carcinoma
1%-3.5% lifetime incidence
10x risk over general population

Yearly ultrasound
- Q6 month for polyps ≤8mm
- Cholecystectomy if polyps >8mm

Colorectal cancer
20%-30% lifetime incidence in PSC-IBD
10x risk[1] over general population
4x risk[1] over patients with UC

PSC-IBD: Yearly colonoscopy beginning age 15 yrs

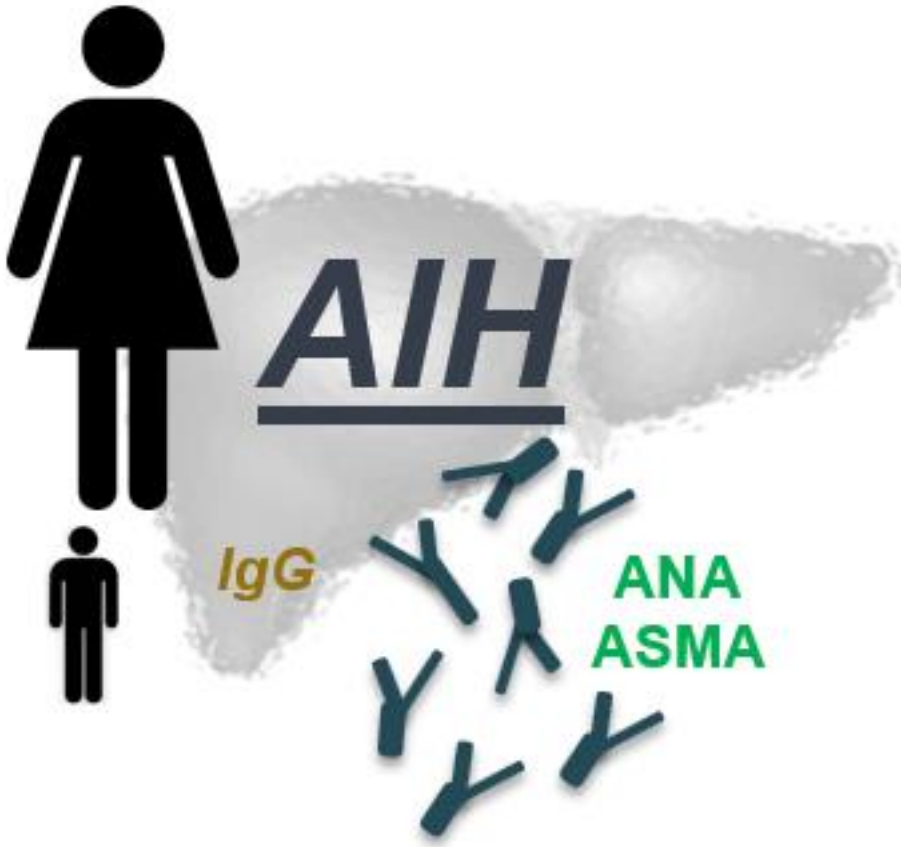
Ali AH et al. *Hepatology*. 2018; Hirschfield et al. *Lancet*. 2013.

Treatment of PSC

- There is no proven pharmacotherapy for the treatment of PSC that can reduce disease progression or improve mortality
- Treatment is directed at complications ***and symptoms*** if and when they occur
- No therapies have been proven to prolong survival or change the natural history
- IBD therapy has little effect on PSC course and vice versa
- Monitor for malignancies
- Liver transplantation, especially living donor
- Clinical trials opportunity

1. AASLD Practice Guidelines. *Hepatology*. 2009; 2. Lindor KD et al. *Hepatology*. 2009.

AIH: Complex, Immune Mediated Inflammation



Heterogeneity of AIH is what makes it so challenging

ALL

Populations

Age ranges

Ethnicities

VARIABLE

Clinical presentations

Treatment responses

Outcomes

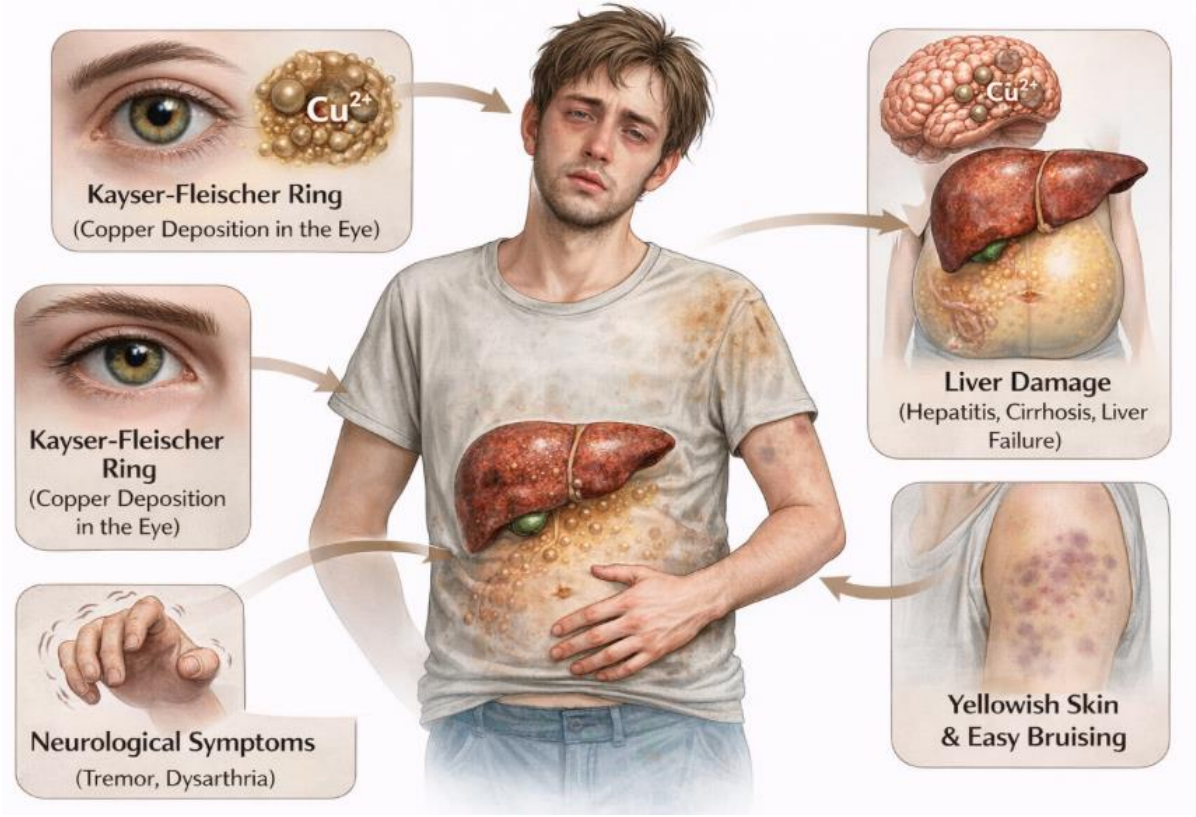
Disease side effects

AIH: Key Takeaways

- Chronic liver disease with an immune-mediated pathogenesis.
- Characterized by elevated liver enzymes, autoantibodies (ANA, SMA, LKM, SLA), and liver histology with inflammatory changes.
- Treated with immunosuppressive therapy (prednisone, azathioprine or MMF).

Key Differences in Genetic Diseases

Wilson Disease



Hemochromatosis

Diagnostic Challenges in Wilson Disease

- Patients with WD experience inaccurate or late diagnoses[1,2]; WD is often “brushed off”

- One study noted that 72% (129/179) of patients with WD were misdiagnosed with other diseases such as[2]:
  - Hepatitis, cirrhosis, splenomegaly, hepatomegaly, encephalitis, encephalopathy, peripheral neuropathy, psychosis, osteoarthrosis, nephrosis and anemia

- A misdiagnosis of depression is particularly common, especially in teenagers
  - These patients are not correctly diagnosed until they eventually experience severe WD symptoms.

1. Ferenci P. *Handb Clin Neurol.* 2017; 142:171-180; 2. Yu M et al. *Front Neurol*. 2022; 13:884840.

Wilson Disease: Clinical Pearls

- Always consider in young patients with unexplained liver disease
- Look for psychiatric + neurologic + hepatic combination
- Low ceruloplasmin is helpful but not diagnostic alone
- Early treatment is life-saving and prevents irreversible damage

Hemochromatosis: Who Should be Offered Genetic Testing?

- Any adult with biochemical evidence of iron overload
  - >45% transferrin saturation (TS) and >300mg/L serum ferritin (SF) in men and post-menopausal women or >200mg/L SF in pre-menopausal women
- Unexplained chronic liver disease and increased TS
- An adult with a first-degree relative (sibling, parent or child) with a known genetic mutation
- Family history of iron overload, liver disease, type II diabetes, arthritis, heart disease (relatives with symptoms of *HFE*-hereditary hemochromatosis)

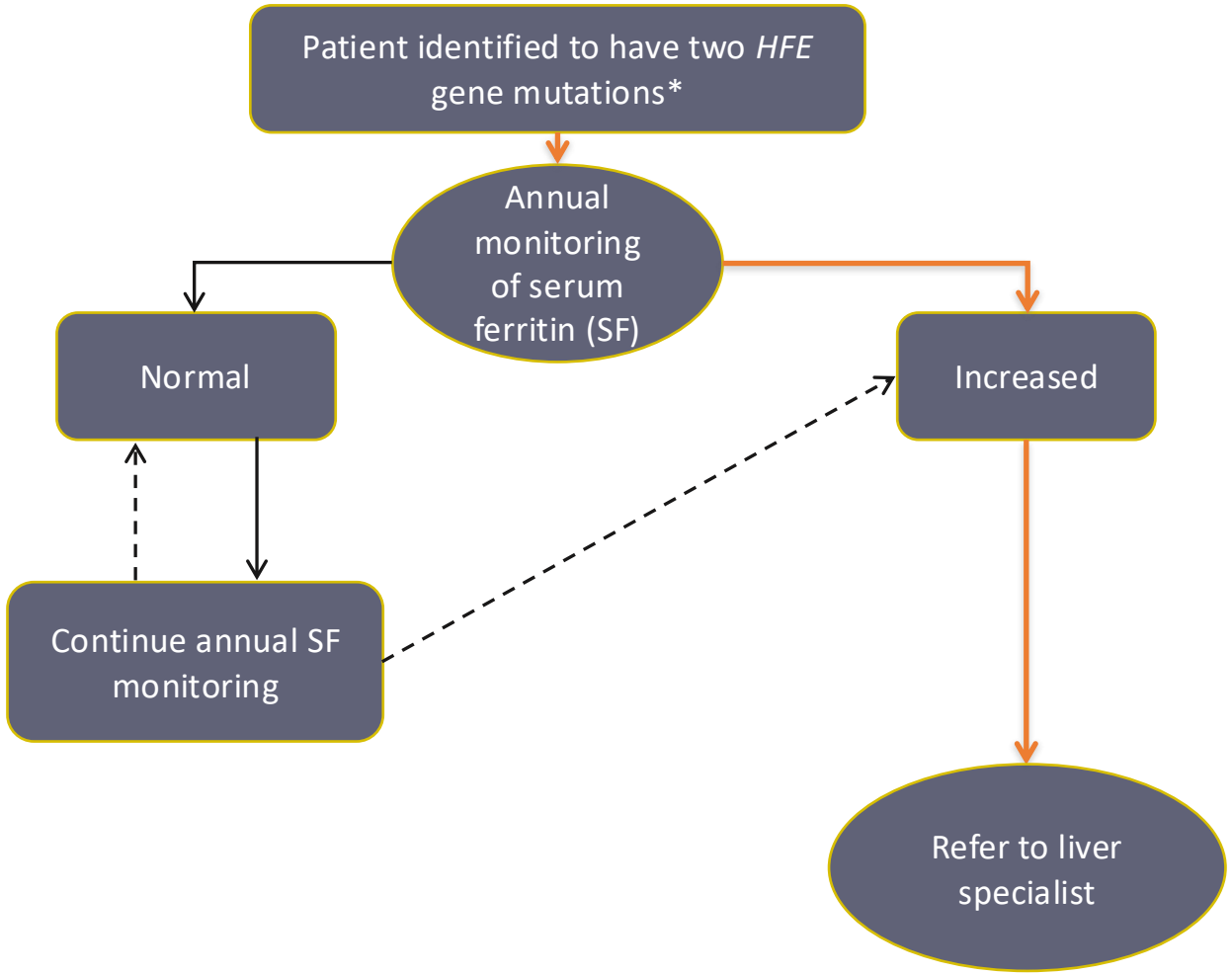
HH: What Does the Genetic Test Result Mean?

- The actual risk to develop iron overload is dependent on how many and which gene mutations have been inherited, in addition to other genetic and non-genetic factors
  - Gender
  - Alcohol intake
  - Use of iron and vitamin C supplements
  - Menstrual/pregnancy-associated iron losses

HH: How Will Genetic Testing Help You and Your Patient?

- *If mutations are identified*
  - Appropriate surveillance and management of risk of iron overload
- *If no mutations are identified*
  - If your patient was tested because of a known family mutation, he/she no longer needs frequent monitoring of iron indices and is not at increased risk to develop iron overload. The test has ruled out HH
  - If your patient was tested because of a reported positive family history, more information is needed before ruling out HH in this individual. Your patient should be encouraged to obtain confirmation of the familial mutations and/or diagnosis
  - If your patient was tested because of persistently high iron indices, additional investigations should be considered

HH: Surveillance and Management



Primary Care's Role

- All these diseases are lifelong diseases that require surveillance.
- Critical for primary care to work together with liver specialists to ensure follow up completed.
- In PBC and PSC, ongoing management of fatigue and pruritus important for patient's quality of life.

Final Reminder

- Referral to a liver specialist is important for any unexplained abnormalities in laboratory results or imaging relating to liver.
- Diagnosing these incurable diseases early is important to slow the progression.

Session II: Q&A