

Managing PSC Symptoms

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Early PSC

- **15-40% of patients are asymptomatic at presentation**
- **55% of patients have asymptomatic increase of liver enzymes (IBD)**

Symptomatic PSC

Prevalence of primary sclerosing cholangitis symptoms

Symptom	Frequency, %
None	15–55
Fatigue	50–75
Pruritus	40–70
Jaundice	9–69
Abdominal pain	16–60
Weight loss	10–34
Fevers and chills	5–28
Hyperpigmentation	25

* *Kaplan et al: Am J Gastroenterol. 2007;102:1042–1049*

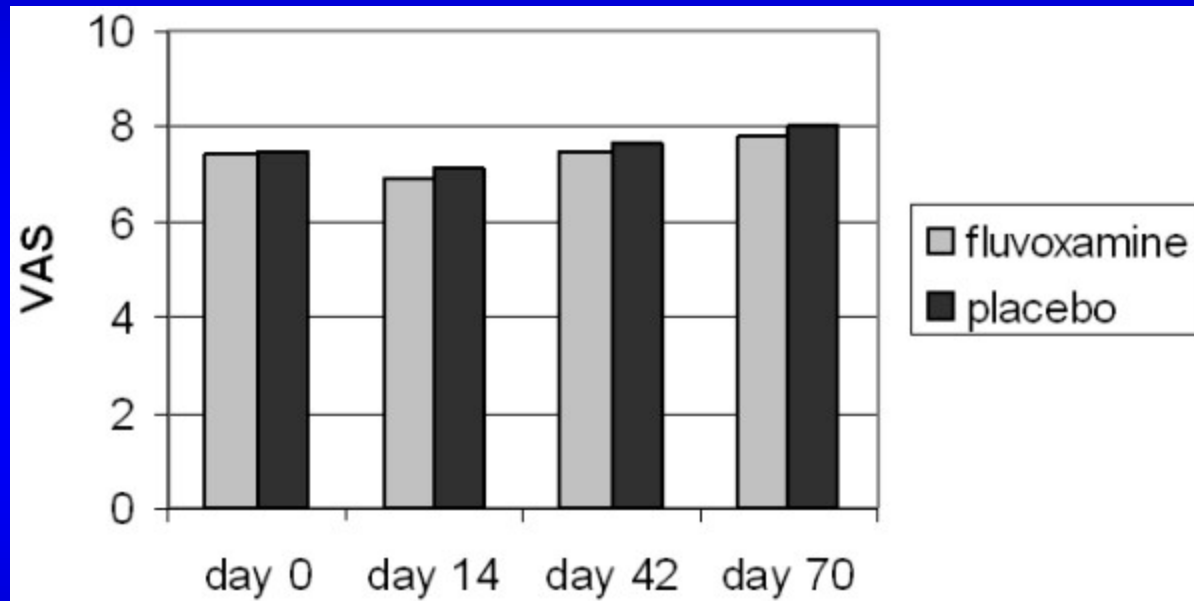
Fatigue/sleep disturbance

- Important to exclude hypothyroidism, anemia (IBD)
- fatigue may be centrally mediated by hormonal pathways (corticotrophin-releasing hormone or serotonergic neurotransmitter systems)*

Fatigue

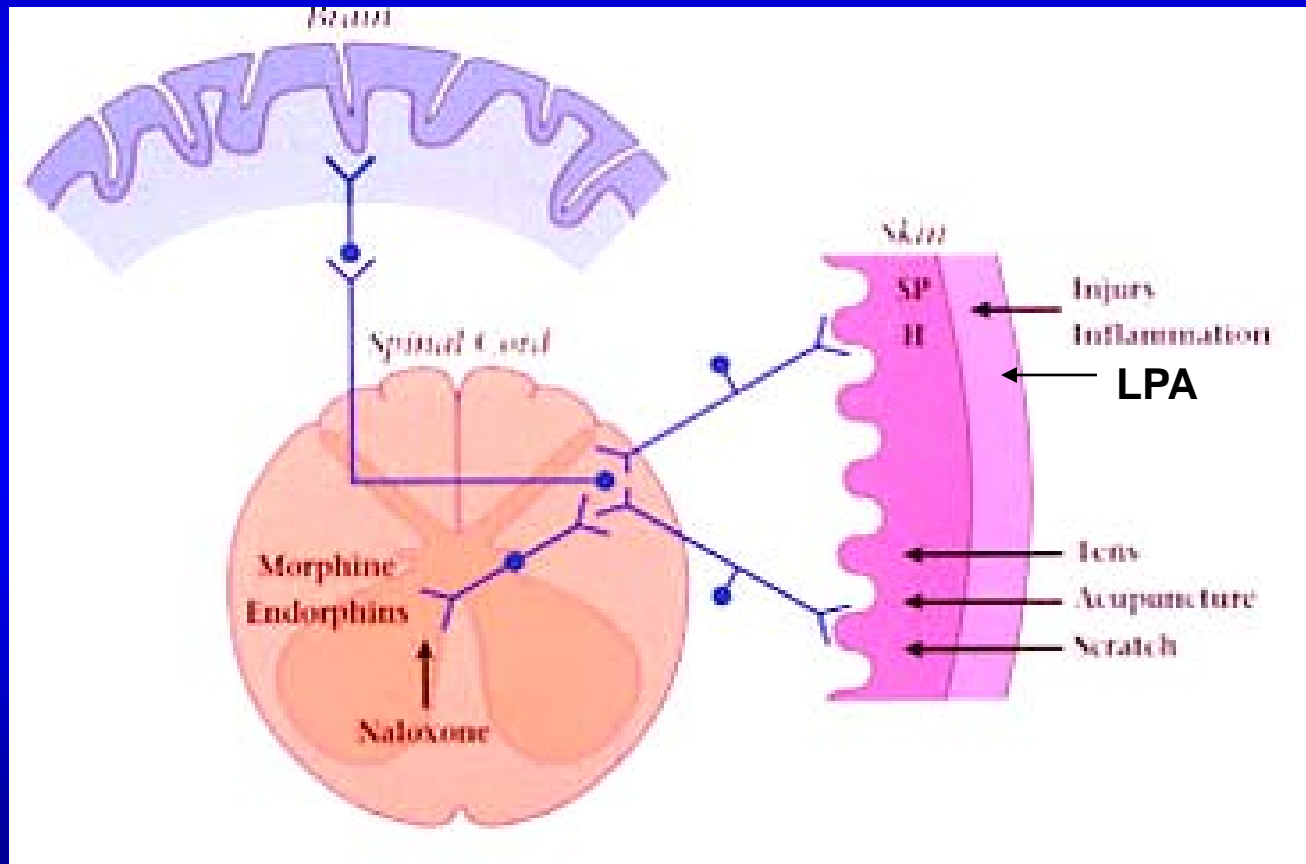
- **Urso does not seem to help with fatigue**
- **Fatigue can not be explained by depressive symptoms***

Fatigue



***Fluvoxamine (anti depressant) did not help with fatigue (teBorg et al, BMC Gastroenterol. 2004 Jul 13;4:13)**

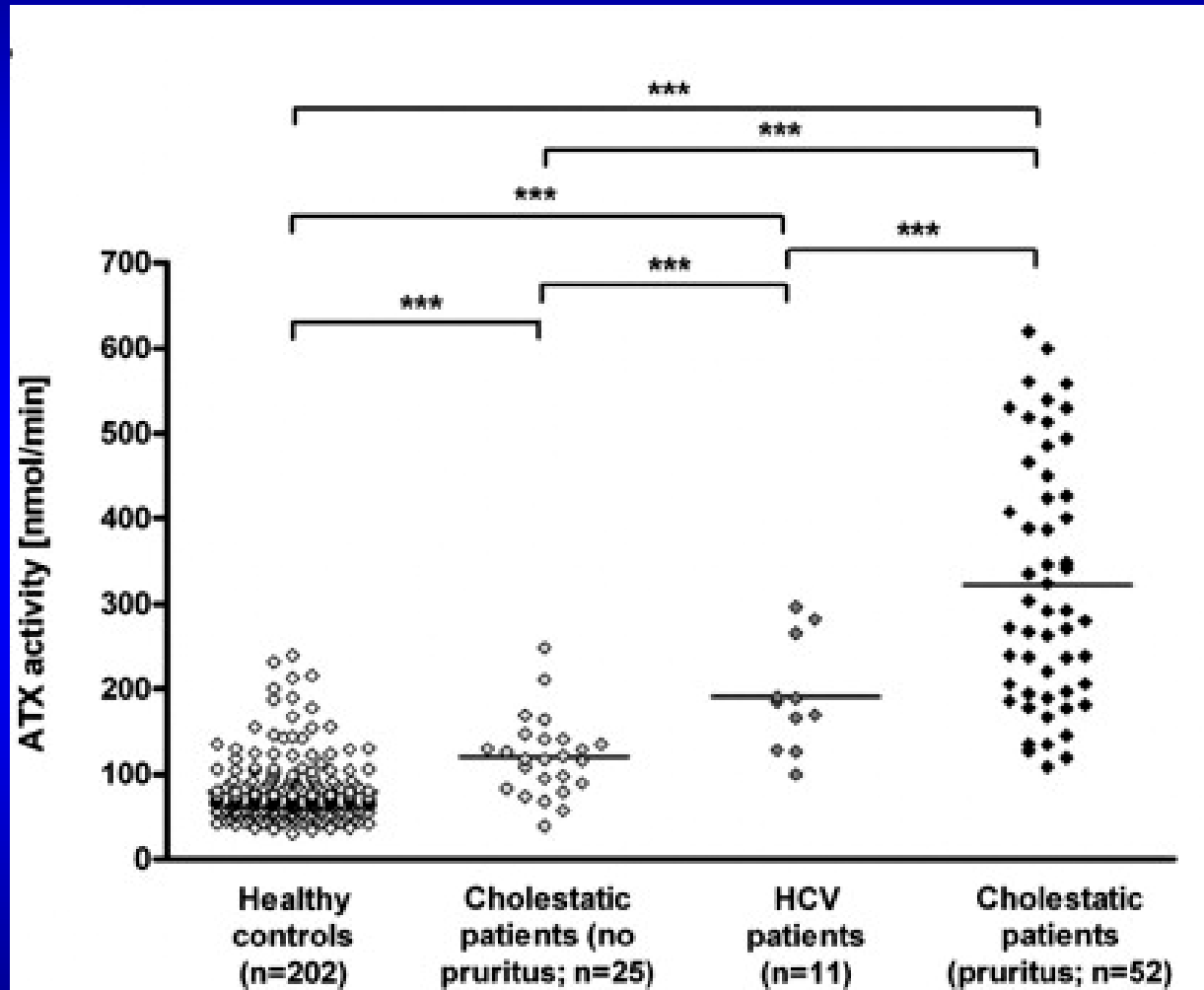
Pruritus (itching)



Causes of Pruritus

- **Bile acids**
- **Endogenous opioids**
- **? Histamine**
- **Autotaxin-LPA**

Autotaxin-LPA



Kremer et al: Gastroenterology. 2010 Sep;139(3):1008-18, 1018.e1. Epub 2010 Jun 19.

Autotaxin-LPA

- Pruritus is a very frequent symptom in patients with any form of cholestasis.
- The severity of cholestatic pruritus does not correlate with serum bile salt levels nor with serum endogenous opioid levels, histamine, tryptamine or Substance P levels.
- The severity of cholestatic pruritus strongly correlates with serum autotaxin levels.
- Autotaxin is an enzyme that produces lysophosphatidic acid (from lysophosphatidylcholine), which is a very potent signalling molecule.
- Intradermal injection of lysophosphatidic acid in mice produces scratching behaviour.

Management of Pruritus

- **Rule out biliary obstruction: increase in serum bilirubin and/or worsening pruritus:**
 - progressive bile duct dilatation on imaging studies,
 - Recommend performing an ERC

Treatment of Pruritus*

- Decrease water temperature of shower or bath.
- Use a moisturizing soap such as Dove and avoid deodorant soaps.
- Do not dry off completely after shower/bath.
- After shower/bath, while skin is still damp, apply EUCERIN CREAM to all skin that is itching. EUCERIN CREAM can be bought almost anywhere
- Wear fewer/lighter clothes.
- Sleep with fewer clothes and blankets.
- **Cholestyramine powder** (Questran, Cholestipol), a prescription medication that binds with bile salts in the intestine to decrease the absorption of bile salts, is taken one scoop/packet twice a day initially and may be increased to a total of six scoops/packets a day.
- All other medications should be taken one hour before and four hours after taking Questran.

Treatment cont.*

- **Doxepin** is a prescription medication. It is given at a very low dose (10-20 mg) for pruritus. Since this medication may cause drowsiness, it should be taken only at bedtime.
- **Ursodeoxycholic acid** : 20 mg/kg/d qhs.
- **Rifampin** (10% liver toxicity)

** Courtesy of Dr. Marion Peters, UCSF*

Difficult to Treat Pruritus

1. **Naloxone**-admit

0.4mg iv push

then 0.2 ug/kg/minute in 100cc for 4 hours if no problems

then 0.4 ug/kg/minute in 100cc for 4 hours if no problems

then 0.8 ug/kg/minute in 100cc for 2 hours

- then add Naltrexone 12.5 mg per day for 3 days
 - 12.5 mg bid for 3 days
 - 25 mg bid for 3 days
 - maximum dose 100 mg per day

2. **Dranabinol** case reports

5 mg take ½ pill per day

increase to 5 mg per day

maximum 20 mg per day

3. **Gabapentin** 300 mg per day- research only Dr Nora Bergassa 212-305-1021

4. **MARS dialysis against albumin column**- binds anything under 50KD

used for encephalopathy and intractable pruritus, 6-8 hours run requires line

Dr. Spangler in San Diego

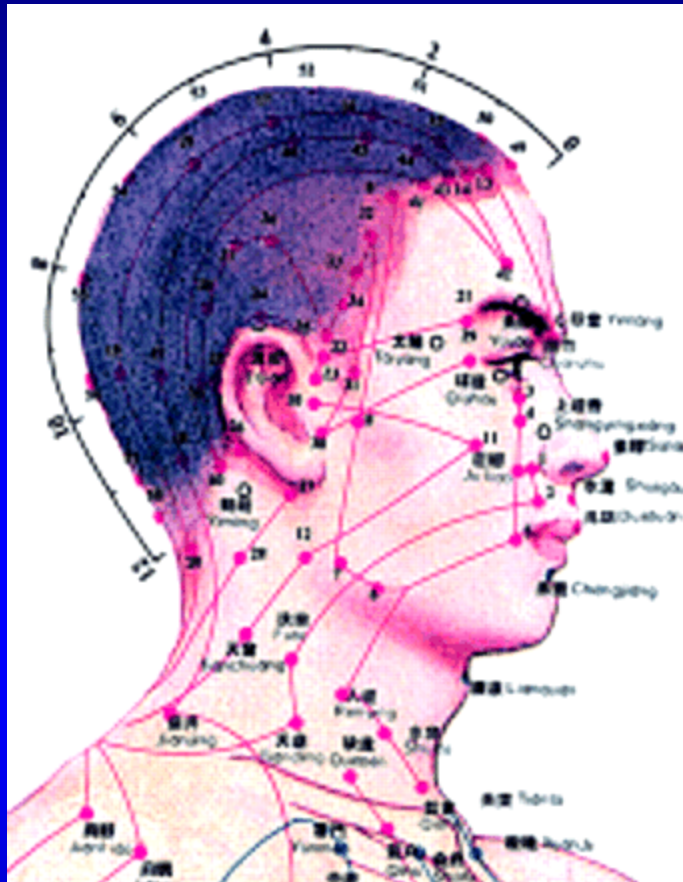
5. **Zoloft (sertraline)**. Limited data but improved pruritus in patients taking for depression

6. **Liver transplant**

Alternative Medicine

- ? Reduction of bile acids: yin shi huang used in China to treat neonatal jaundice (*Artemisia capillaris*)
- 6-ECDCA: some inhibition of fibrosis
- Grape fruit juice (?)

Acupuncture



- Small studies in histamine-induced pruritus showed some benefit
- In cholestasis-induced pruritus the effect is questionable

“Smart” advice from the web:

- **Sweating (Primary Sclerosing Cholangitis (PSC))**
- **Sweating is powerful way to cleanse your body from accumulated toxins.**
examples:
 - **exercise with a lot of clothes**
 - **Sauna**
 - **drink warm tea in a hot room ...**
 - **eat CAYENNE pepper! ...**
- **It is known that some modern industrial toxins and pesticides can leave your body only through sweat glands!**

Dominant Strictures-Cholangitis

- **Dominant strictures can induce stagnation of bile, resulting in bacterial colonization and secondary cholangitis.**
- **This can be the first presentation of the disease occurring in 6.1% of PSC patients.**

Cholangitis

- pain in the right upper quarter of the abdomen (pain may also occur in the chest, in the upper back, or the right shoulder)
- nausea and vomiting
- belching
- fever
- chills
- jaundice - yellowing of the skin and eyes
- low blood pressure
- lethargy
- decreased level of alertness
- itching
- pale stools
- dark urine

Treatment

- **Most patients respond to therapeutic drainage of the obstruction plus antibiotics.**
- **Occasional patients with recurrent bacterial cholangitis may benefit from prophylactic long term antibiotics.**
- **Recurrent cholangitis can be so severe as to become the primary indication for OLT.**

Portal Hypertension

- In a cohort, 36% of patients (n =102) had varices, of these 56% were moderate/large varices
- Independent predictors of esophageal varices were the platelet count, albumin level, and advanced histologic disease.
- Evaluation by endoscopy.

Metabolic Bone Disease

- Osteopenia is characterized by a T-score between 1 and 2.5 standard deviations below the density
- Osteoporosis as a T-score beneath 2.5. The incidence of osteoporosis in PSC is between 4 and 10%.
- Initial screening for osteopenia is recommended and thereafter at 2-3 year intervals.

Treatment of osteoporosis

- Calcium 1.0-1.5 g and vitamin D 1,000 IU daily for therapy
- vitamin D to promote calcium absorption is recommended
- in patients with proven osteoporosis bisphosphonates may be added.

Fat Soluble Vitamin Deficiency

- **A, D, E, K**
- **Vitamin levels and INR need to be checked**
- **If severe deficiencies, celiac disease needs to be ruled out**

Pregnancy and PSC

- *De novo* pruritus and abdominal pain during pregnancy may occur in PSC patients.
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- Pruritus may be so intense as to warrant early delivery via induction. No serious deterioration of liver function during or after pregnancy has been reported.
- Outcome has been satisfactory for both patients and children

Chapman et al: Diagnosis and management of PSC, AASLD Guidelines, Hepatology, [51: 660-678 \(2010\).](#)

Unique Liver Transplant Indications

- for patients with PSC these include intractable pruritus, recurrent bacterial cholangitis, and localized cholangiocarcinoma (Mayo study).

appealed MELD score may be granted by this process to help prioritize the PSC patient with these complications for liver transplantation.

Summary

Disease-associated complications of primary sclerosing cholangitis and their treatments

Complication	Treatment
Pruritus	Cholestyramine Rifampin Other agents: opioid antagonists, sertraline, ondansetron Refractory pruritus: liver transplantation
Fatigue	No specific treatment available
Vitamin deficiencies	Vitamin supplementation
Metabolic bone disease	Calcium and vitamin D supplementation Bisphosphonates?