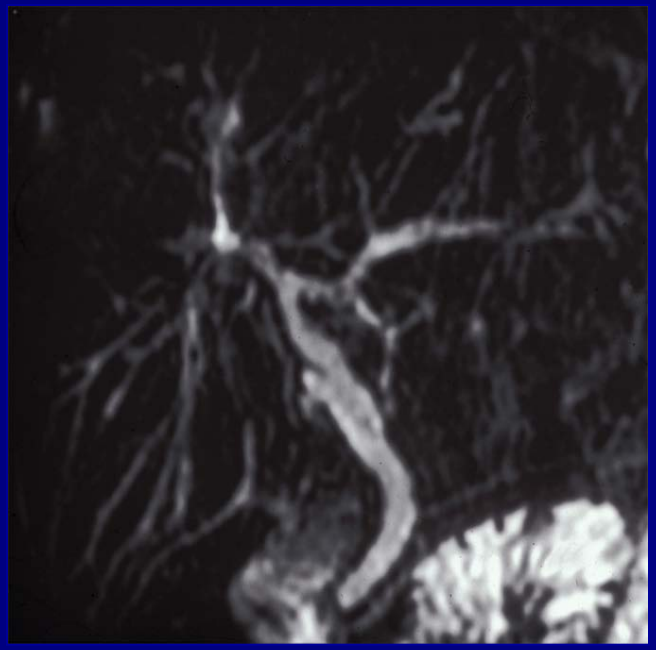
Adolescent and Pediatric Primary Sclerosing Cholangitis



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Outline

- Child and adolescent PSC vs Adult
  - Variations in the disease
  - Variations in the response
  - Need for transplant

Definition

- Chronic liver disease involving the bile ducts
- Cause unknown
- Diffuse inflammation of biliary ducts = scarring
  - Narrowing
  - Obstruction
  - Dilation
- Frequently associated with inflammatory bowel disease
- Can lead to cirrhosis and portal hypertension

Clinical Presentation

- Elevated bilirubin or liver function enzymes
- Elevated GGT
- Most often asymptomatic
- May present with colitis and find liver disease also ~40% of time
- Fatigue, Jaundice, weight loss common

Diagnostic Criteria

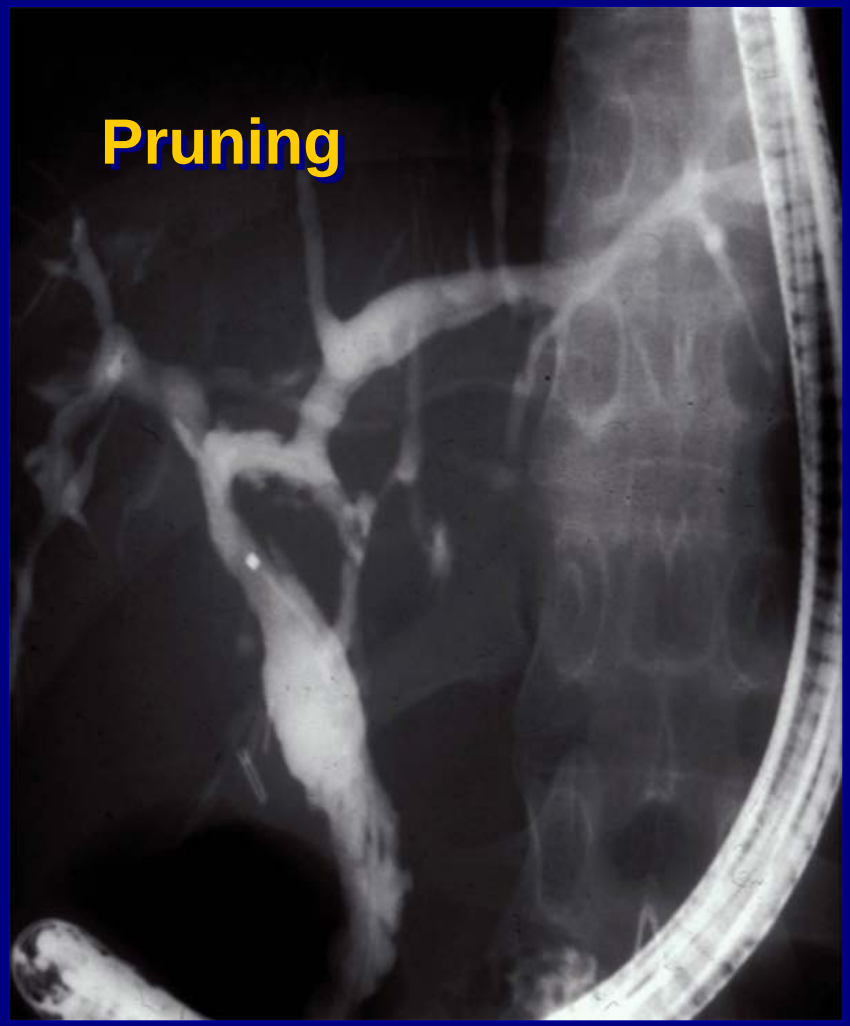
- Cholangiogram abnormalities involving any part of the biliary tree (ERCP or MRCP)
- Biopsy proven bile duct scarring
- Clinical and Laboratory findings
  - Cholestasis (elevated bilirubin, LFTs, GGT)
  - Alkaline phosphatase 2 to 3x normal
  - IBD
  - Autoantibodies

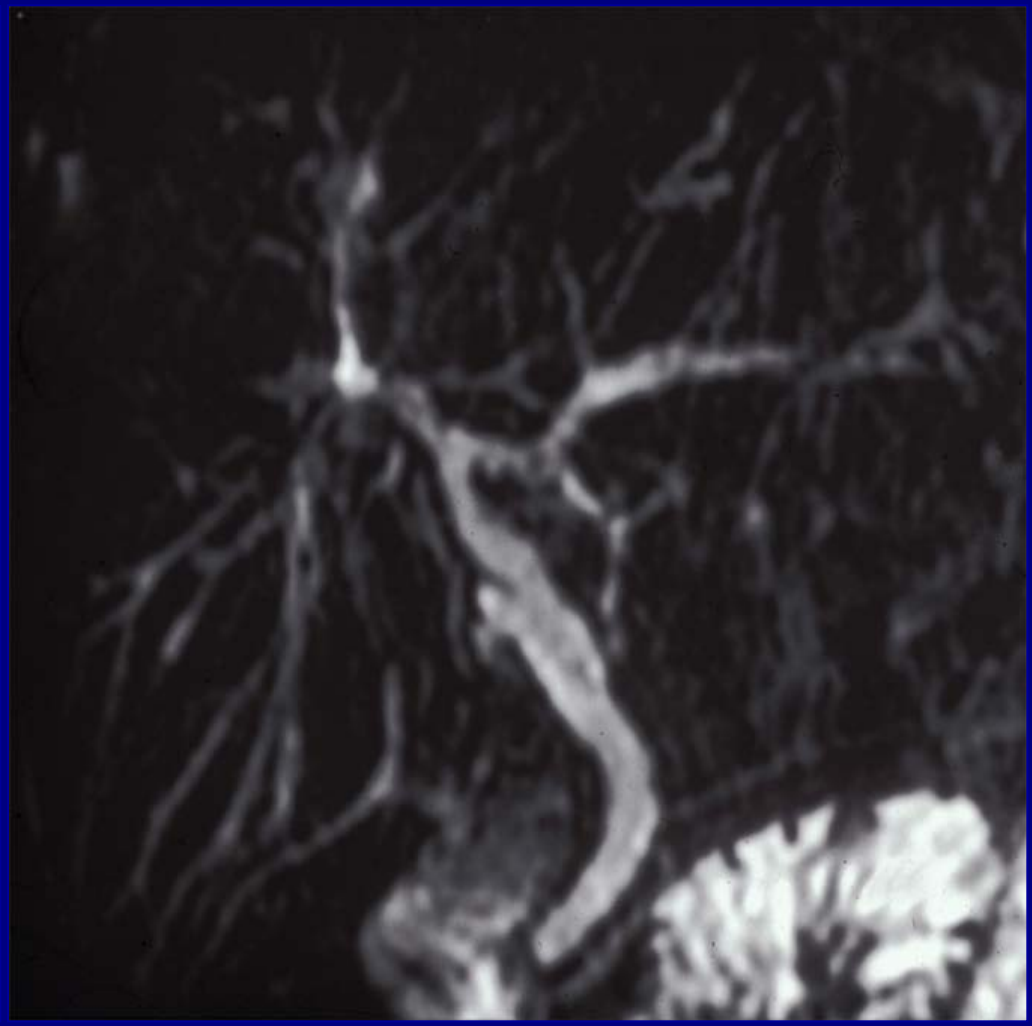
Prevalence of Autoantibodies

- Autoantibodies
  - P-ANCA 80%
  - AMA <2%
  - ANA 50-60%
  - SMA 35%

Primary Sclerosing Cholangitis

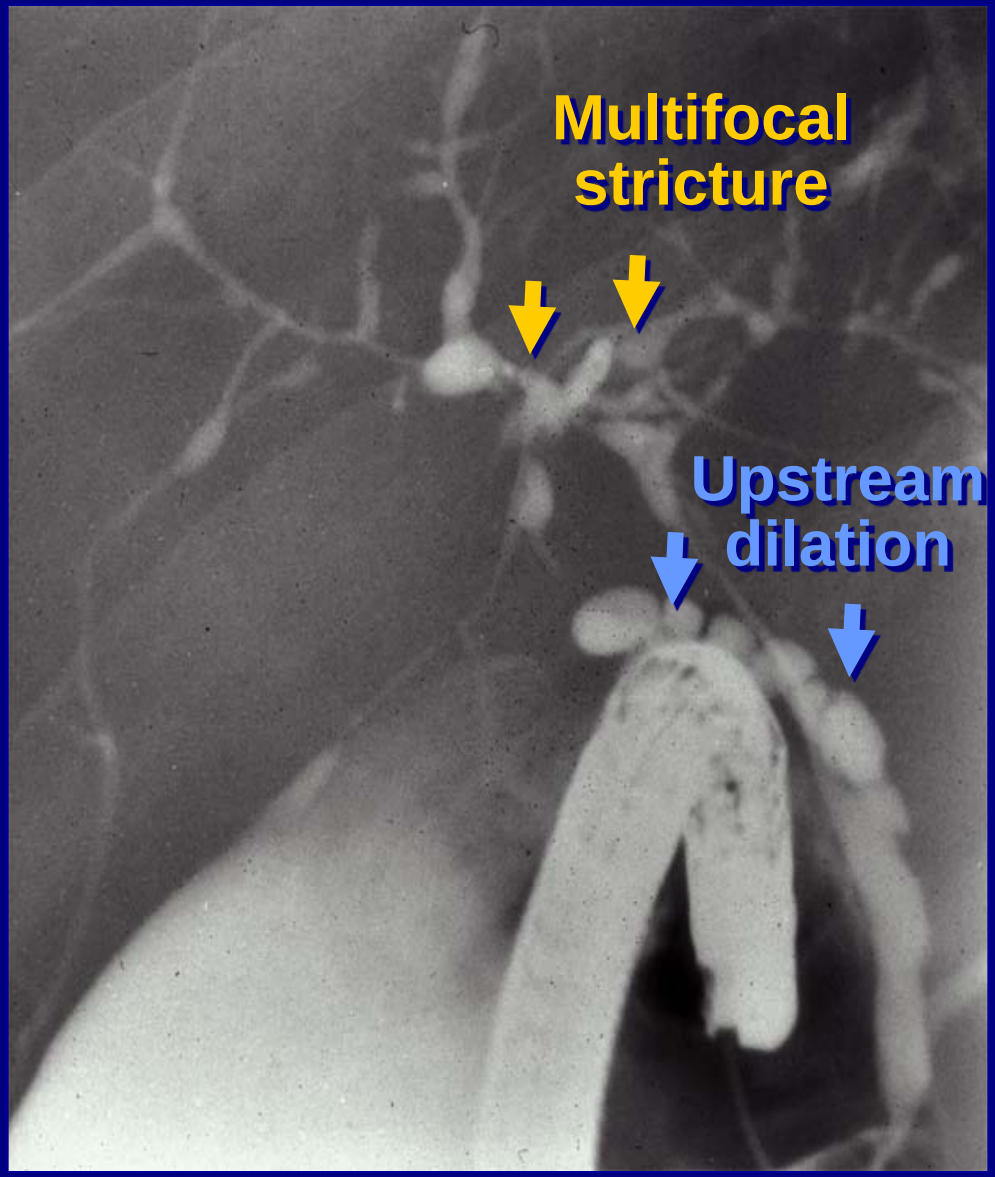
Comparison of ERCP and MRCP

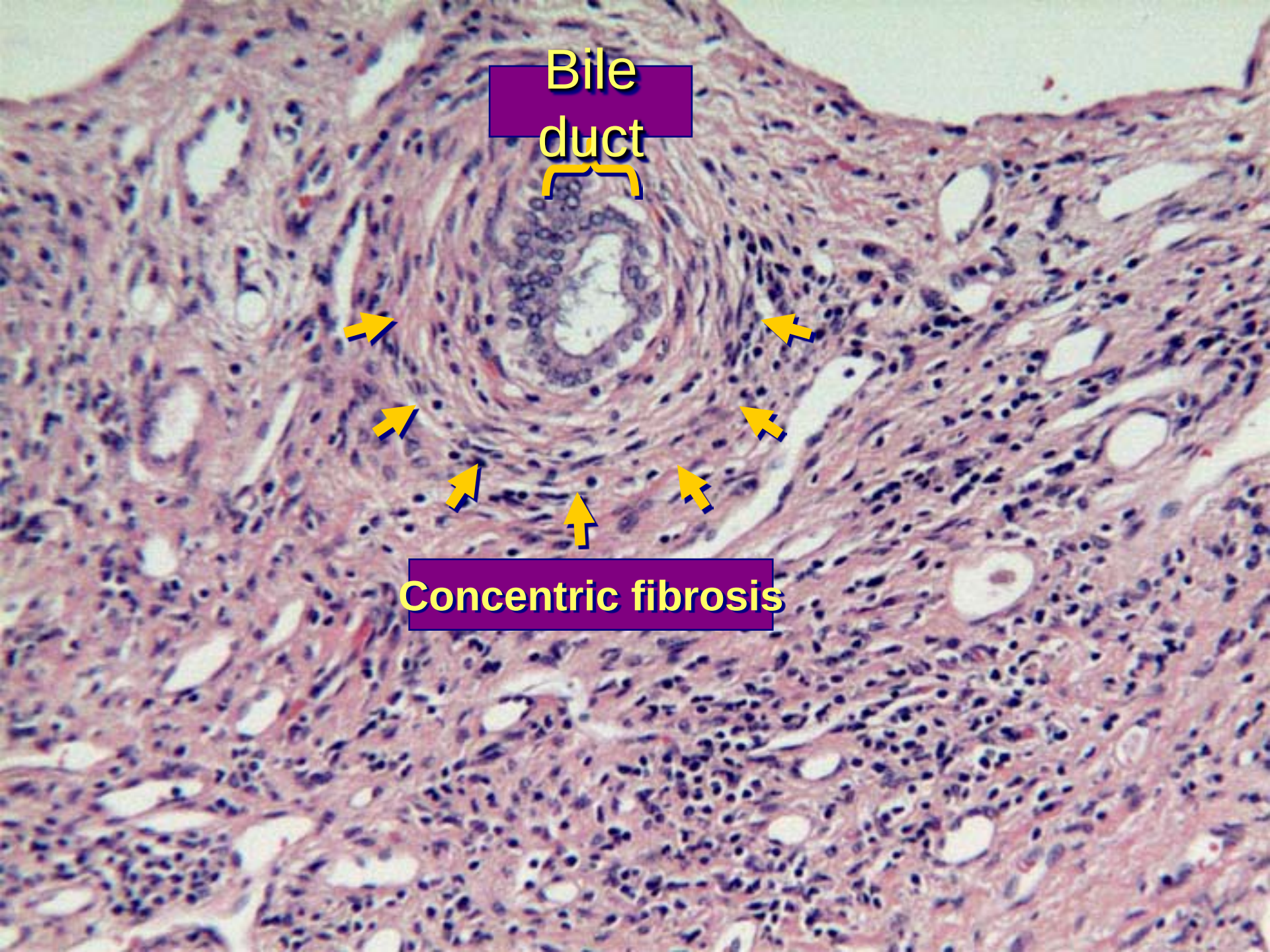




Primary Sclerosing Cholangitis

Classic Case of PSC




Bile duct
Concentric fibrosis

Relationship to Inflammatory Bowel Disease

- IBD in 60-80% of PSC patients
- Ulcerative colitis more common than Crohn’s disease (2:1)
- 4-5% of UC patients have PSC

PSC Associations

- Majority of adults with PSC have an associated non-liver disease
  - IBD
  - Diabetes Mellitus
  - Pancreatitis
  - Thyroid disease
  - Other autoimmune disease
- In children is mostly associated with IBD

Primary Sclerosing Cholangitis

Features Used in Prognostic Models

Mayo Clinic (n=174)	King's College (n=126)	Multicenter (n=426)	Swedish (n=305)	New Mayo Model (n=405)
Age	Age	Age	Age	Age
Bilirubin	Hepatomegaly	Bilirubin	Bilirubin	Bilirubin
Biopsy Stage	Biopsy Stage	Biopsy Stage	Biopsy Stage	AST
Hemoglobin	Splenomegaly	Splenomegaly		Variceal Bleed
Inflammatory Bowel disease	Alkaline Phosphatase			Albumin

Disease Therapy

- Dilation of dominant strictures
- No proven medical therapy
  - Management of fat-soluble vitamin deficiencies = A, D, E, K
  - Screening for cancer
    - Lifetime risk for cholangiocarcinoma 7-15%
    - Incidence 0.5 to 1%
    - Smoking and IBD may increase risk
  - Screen for portal hypertension
  - Antibiotics for cholangitis

Primary Sclerosing Cholangitis

Medical Therapy Tested to Date

Medical Therapy Tested to Date

Penicillamine	Colchicine	Mycophenolate Mofetil
Cyclosporine	Methotrexate	Silymarin
Pentoxifylline	Budesonide	Tacrolimus
Nicotine	Pirfenidone	Ursodeoxycholic acid **(possible benefit)**
Azathioprine	Etanercept	

Liver transplantation

- Survival
  - 1 year 90-95%
  - 5 year 85-88%
- Slight increase in problems with rejection and infection compared to other liver diseases
- PSC can reoccur post-transplant

Patterns of PSC in Children

- AIH/PSC overlap
  - “Autoimmune Sclerosing Cholangitis (ASC)”
- Small duct PSC
- Classic PSC

ASC

- Strong autoimmune features
  - Autoantibodies: ANA, SMA, IgG
  - Sometimes looks like AIH but progresses to PSC
  - 60% have perinuclear antineutrophil cytoplasmic antibodies (p-ANCA)
- Bile duct damage – inflammation of bile ducts
- Also inflammation attacking hepatocytes as well called “interface hepatitis”
- Usually bile duct damage less advanced may not be evident on cholangiogram

ASC vs Classic PSC

- Younger age
- More females
- High ALT and IgG
- Less IBD
- If IBD present does not correlate with liver activity
- Good response to immunosuppression and Ursodiol
- Decreased need for OLT and less cancer than classic PSC in 8 year f/u

Floreani et al. Am J Gastroenterol 2005;100:1516-1522

Small duct PSC

- 5% of PSC
- Normal Cholangiogram but biopsy shows PSC
- Can progress to classic PSC
- +/- colitis

Small Duct PSC

- Findings of bile duct damage on liver biopsy
- No biliary abnormalities on MRCP or ERCP

Reports on Pedi/Adol PSC

	Mount Sinai 2009	Mayo Clinic 2003	King's College 2001
Patients (M:F)	43 (3:2)	52 (2:1)	27 (1:1)
Age at dx	11	13.8	11.8
IBD	59%	81%	44%
Classic PSC	40%	56%	9/27
AIH/PSC	25%	35%	18/27
Small Duct PSC	34%	8%	

Reports on Pedi/Adol PSC

	Mount Sinai 2009	Mayo Clinic 2003	King's College 2001
Transplant	9/43 (19% within 7 to 19 yrs of dx)	11/52 (% within 20 years)	4/27
Reccurence	1 patient 10 yrs after OLT	3/11 within 6 years of transplant	-
Survival post-OLT	89% at 10 years		100%
Dilation of strictures	6/43		-
Colectomy	5		-

Child vs Adult PSC

	Child/Adolescent	Adult
Gender	F>M	M>F
Presentation	0.23 per 100,000	1.11 per 100,000
IBD at presentation	40 to 60%	70%
Overlap with AIH	35%	7-10%
Response to treatment	UDCA good Immunosuppression -good	UDCA moderate Immunosuppression - rare
Prognosis	Best for small duct dx Depends on stage at presentation	Depends on stage at presentation
Transplant	50% transplanted 12 yrs from time of diagnosis	50% transplanted 12 yrs from time of diagnosis
Recurrence after OLT	27%	20%

Recurance after Transplant

- Report from the most experienced Living related Donor program
- all PSC patients transplanted over 10 years 30 total, 10 excluded
- 11/20 had recurrence from 26-71 months post trplt
  - Risk factors were related donor, early CMV infection and age

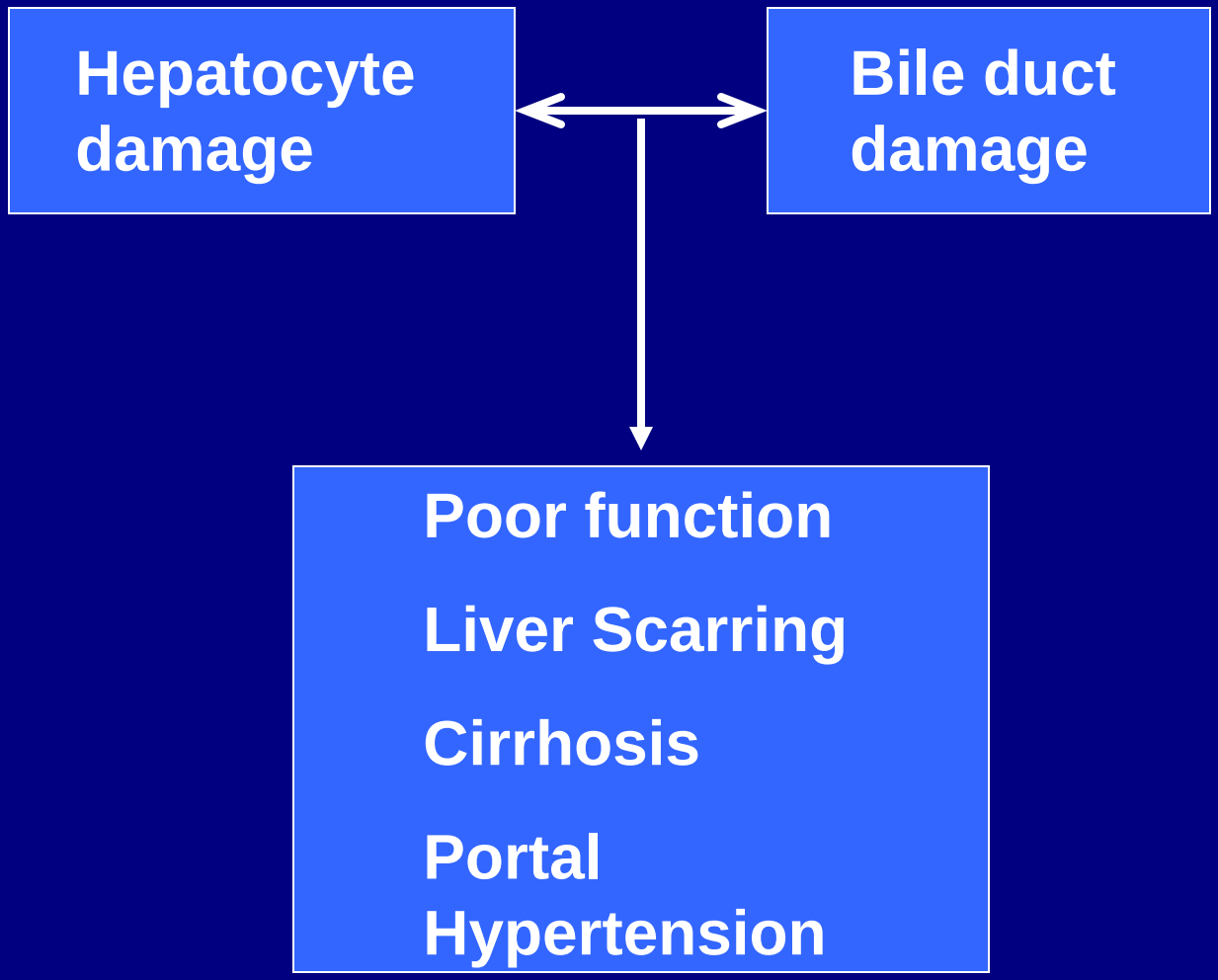
Egawa H, et al, Dig Dis Sci. 2009

Impact of Related Donor to Relapse of PSC

Egawa H, et al, Dig Dis Sci. 2009

Donor	Number pt (% of pt)	Relapse %	Relative Risk
Non-related	5 (25)	20%	1
Parents	10(50)	80%	17
Son	2(10)	50%	11
Sibling	3(15)	33%	3

Consequences of Liver Disease



Consequences of Liver Disease
Poor function

- Jaundice
- Fatigue
- Poor weight gain and muscle mass
- Weak bones
- Deficiencies in Fat-soluble vitamins
- Itching

Monitoring of Liver Disease

- Nutrition
- Bone health
- Medications for itching

Monitoring of Liver Disease

- Monitor for portal hypertension
  - Endoscopies
  - Banding varices
  - Beta-blockers to prevent bleeding
  - Shunts to prevent bleeding
- Monitor for cancer
  - Check serum markers
  - Radiologic studies

Different Care for PSC in Children - Not Small Adults?

- Vigilant for bile duct involvement in IBD
  - If elevated LFTS or GGT
  - Need liver biopsy and MRCP
- Vigilant for bile duct involvement in Autoimmune hepatitis
- Vigilant for IBD in PSC
  - Need endoscopy and colonoscopy for screening

Different Care for PSC in Children?

- If Autoimmune features (ASC) present will use immunosuppression
- All get Ursodiol
- Screen for IBD regardless of symptoms
- Focus on nutrition and growth
- Focus on bone health
- Less focus on cancer

Conclusion

- Speak to your Doctor about what you read
- Very little data in children – not “small adults”
- Controversies in care are not black and white – wide spectrum of disease

Conclusion

- Research leads to improvements in therapy for liver disease each year – especially in children
- The future is bright
- Keep looking ahead……

- **Thank you for coming**