

# ***Primary Sclerosing Cholangitis at the University of Colorado***

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# Objectives

- Describe liver program at the University of Colorado
- Describe our database
- Provide our basic PSC demographics
- Describe the natural history of IBD after liver transplant

# Liver Program at the University of Colorado

- Transplant Program established in 1988
- Follow over 4500 hepatology patients
  - >450 listed
- 1350 patients transplanted
- Follow 1005 post-transplant patients
- Database established in 1999
  - Complete records since 2002

# Liver Evaluation Database

Forms Reports HCV Follow-up HCC Follow-up Indiv. Reports Physician Page Clinic Flow Social Work Test

## Forms

Donor Intake Form	Patient Labs	Calculate Donor Score
Donor Master Form	Donor Labs	Study Review
Recipient Master Form	Hepatobiliary Agenda	<b>Blood Draw Queue</b>
Committee Presentation	Insurance Info	Lab Input with Encounters
Add/Edit Referring MD	Path Rounds	
Add/Edit Committee Member	Path Agenda	
Hepatobiliary	Evaluation Calendar	
Social Work Note	Schedule Update Review	
Agenda Edits	Edit/Add Study	
<b>Clinic Checkin</b>	Radiology Test Schedule	
Chart Crunching	Online Presentation	

Add Referring MDs

## Review

New Scanned Docs/Faxes

Radiology Review - All Pts	Lab Review - All Pts
Radiology Review - Rosen	Lab Review - Rosen
Radiology Review - Burton	Lab Review - Burton
Radiology Review - Everson	Lab Review - Everson
Radiology Review - Forman	Lab Review - Forman



Liver Evaluation Database

Home Create External Data Database Tools Add-Ins Acrobat

Hepatology Menu Clinic Checkin

**Last Name:** AAABogus **MRN:** 3 **Find by MRN:** 36797 **List Meld:**   
**First Name:** WrongPt **SSN:** 555-44-3333 **Diagnosis:** Primary Pulm Hypertension **Date:** 1/10/2008 **Lab MELD:** 17  
**DOB:** 1/2/1950 **Hepatologist:** LF  
**Status:** Transplanted **PA/NP:**

Photo

**Jump Menu** Medication List

**Vaccines**

Hepatitis A Immune  Hepatitis A Date:   
 Hepatitis B Immune  Hepatitis B Date:

**Allergies:** Prescription Meds: PCN - Rash, SOB, first in 1990  
Herbal: None  
Environmental: Work - anaphylactic - started at the age of 15  
Food: None  
OTC Meds: None

Record: 1 of 9131

**Medications**

Date Started	Medication	Dose	Frequency	Route	Mf
4/15/2009	Prograf		BID	PO	
8/26/2008	Prevacid	30mg	Daily	PO	
8/26/2008	Viagra	100mg	BID	PO	
3/10/2009	Lasix	20mg	Daily	PO	
6/11/2009	Naproxen	1gm	Daily	IV	
* 9/10/2009				PO	

Record: 1 of 5

Datasheet View Num Lock

Hepatology Menu Labs

Last Name:  First Name:  MRN:  Find by MRN  Add New Line  Status: Hepatology   
 SSN:  Hepatologist:   
 DOB:  Diagnosis:  PA/PP:

Fast Print Flow Sheet  Find a Patient  Add New Patient

Date/Draw	Comments	WE	Hgl	HC	MCV	Neut%	Lymph%	PLT	PT	INR	N	K	CC	C	BU	C	G	Ar	Cl	Cr	PC	AS	AL	AP	L
6/27/2006 11:48:01 AM		4.5	10.6	32.2	98.9	80.5	11.5	41														68	35	154	
8/7/2006	will check data entry JE	5.8	15.3	45.5	92.7	50.4%	36.0	162	16.2	1.3	138	3.8	27	101	12	1.0	153		9.4			30	34	54	
11/1/2006 4:44:00 PM		5.6	14.7	45.8	99.3	62.2%	21.4	106			134	4.0	25	100	13	1.0	183		8.8			114	57	111	
11/2/2006 10:54:00 PM		6.9	15.2	47.6	99.6	57.3%	24.5	95	19.5	1.6	133	4.0	24	102	12	0.8	104		8.6			130	64	122	
11/3/2006 5:37:00 PM		8.3	12.1	37.1	100.0	67.6%	16.9	107	>120	16.0	133	4.3	20	105	16	1.2	144		6.9	1.6	3.9	49	19	34	
11/4/2006		4.9	9.8	31.0	100.0	51.8%	29.1	74	26.2	2.4	134	4.4	20	104	17	1.1	103		8.4	2.0	2.6	101	49	62	
11/5/2006		5.0	10.3	31.6	99.9	55.6%	24.6	86	25.2	2.3	134	3.6	24	101	10	1.0	88		9.1	1.9	2.3	115	52	67	
11/6/2006																									
11/6/2006	Pathology from 11/06/2006 was reviewed. The biopsy doesn't																								
11/7/2006		4.7	10.3	31.4	101.0	58.6%	21.3	81	26.1	2.4	134	3.5	18	102	8	1.1	89		8.3						
11/15/2006 4:10:00 PM		6.9	11.0	14.5	103.0	65.5%	18.3	77			130	3.8	20	96	24	2.4	175		9.3			131	53	74	
11/22/2006 11:29:00 PM											130	4.1	19	100	47	3.1	169		8.2	2.2	4.6				
11/6/2007		2.1	11.9	34.9	105.4			48			137	3.1	24	99	15	1.2	89		4.0			94	55	81	
11/27/2007		3.7	11.7	34.9	101.9	76.3	13.6	53			143	4.0	18	114	11	0.9	88		8.8			107	83	99	
11/15/2008		4.7	15.3	44.9	91.6	68.1	19.3	82			138	3.6	26	99	18	1.0	118		9.9			649	465	140	

Record: 1 of 29 | Search | [Navigation icons]

Misc Tests

Date/Time	Test	Result	refRange
12/2/2006 6:57:00 PM	LACT	18.0	
12/2/2006 6:57:00 PM	BILI IND	8.1	0.0-0.7

Record: 1 of 135 | Search | [Navigation icons]

More Serologies - only 1 line

Date	HIV	RPR	EBVIGG	EBVIGM	ANA	ACM	AMA	ASMA	CMV	Blood Antibody Type	Alpha1A	PtTyp
12:00:00 AM					<b>POSITIVE</b>	NEGATIVE					116	

Record: 1 of 1 | Search | [Navigation icons]

# PSC pre-transplant

- Follow 184 patients
- 78 listed
- 68.5% male
- 83.3% caucasian, 13.3% african american
- 51.1 +/- 14.5 years

# PSC post-transplant

- 155 transplanted, 5 relisted
- 9 cholangiocarcinoma
- 22 live donor transplants
- 74.8% male
- 91.6% caucasian, 6.3% african american
- 53 +/- 12.7 years
- 88.4% alive

***Inflammatory Bowel Disease  
Course in Patients Transplanted  
for Primary Sclerosing  
Cholangitis: a Patient Survey***

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# Background

- Natural history of IBD following liver transplant (LT) for PSC is unknown
- Variability in outcomes:
  - disease improvement 3-100%
  - worsening 0-51%
  - *de novo* IBD 2-27%

Shaked et al. Ann Surg 1992;215(6).  
Gavaler et al. Dig Dis Sci 1991;36(3).  
Fabry et al. Hepatology 1993;18(4).  
Papatheoridis et al. Gut 1998;43.

# Background

- **Studies have not shown factors consistently associated with disease activity**
- **Studies limited by small sample sizes**
- **Inconsistent designs:**
  - **inclusion/exclusion criteria**
  - **methods and extent of colitis assessment**
  - **follow-up duration**
  - **variables studied**

# Objective

- Describe our experience with IBD post-LT in patients with PSC
- Determine factors predictive of disease activity

# Study Design

Survey mailed to 115 recipients transplanted  
between 1988 - 2006

## Survey assessed:

- IBD diagnosis & timing
- medications
- frequency of flares
- opinion of disease course
- colonic neoplasia

## Transplant database:

- immunosuppression
- CMV status
- rejection
- recurrent PSC
- cholangiocarcinoma
- demographics
- labs

# Results: Study Sample

**1147 Total Transplanted**

**147 PSC**

**115 Alive**

**88 (77%) Responded**

# Patient Characteristics

<b>Median age at transplant (yrs)</b>	<b>46 (16 – 71)</b>
<b>Living donor transplant (%)</b>	<b>14.7</b>
<b>Gender (% male)</b>	<b>76</b>
<b>Race (% caucasian)</b>	<b>93</b>
<b>Median time since LT (yrs)</b>	<b>6.8 (0.6 – 17.9)</b>
<b>CMV mismatch (%)</b>	<b>24</b>
<b>IS (% Tacrolimus, Sirolimus)</b>	<b>59, 56</b>
<b>Prednisone (%)</b>	<b>13</b>
<b>Rejection (%)</b>	<b>72</b>
<b>Recurrent PSC (%)</b>	<b>16</b>
<b>Cholangiocarcinoma (%)</b>	<b>5</b>
<b>IBD (%)</b>	<b>74</b>
<b>Med. years with IBD</b>	<b>18 (0.5 – 48)</b>

# Outcomes: IBD

88 Responses

74% (65) IBD

89% (58) dx pre-LT

14 yrs. IBD pre-LT (0.5 – 48)

11% (7) *de novo*

71% dx >3 yrs post-LT

29% <1 yr post-LT

85% (55) UC

12% (8) Crohn's

3% (2) Indeterminate

# All IBD vs. No IBD

	All IBD (65)	No IBD (23)
<b>Med. time since LT (yrs)</b>	<b>6.8 (0.6 – 17.9)</b>	<b>6.8 (1.2 – 16.4)</b>
<b>Median age at LT (yrs)</b>	<b>46 (16-66)</b>	<b>46 (26 - 71)</b>
<b>Gender (% male)</b>	<b>72</b>	<b>87</b>
<b>Tacrolimus (%)</b>	<b>62</b>	<b>52</b>
<b>Prednisone (%)</b>	<b>14</b>	<b>9</b>
<b>CMV mismatch (%)</b>	<b>21</b>	<b>30</b>
<b>Med. rejection episodes</b>	<b>1.0 (0 – 9)</b>	<b>2 (0 – 8)</b>
<b>Recurrent PSC (%)</b>	<b>17</b>	<b>13</b>
<b>Median bilirubin</b>	<b>0.6 (0.2 – 6.6)</b>	<b>0.5 (0.2 – 2.5)</b>

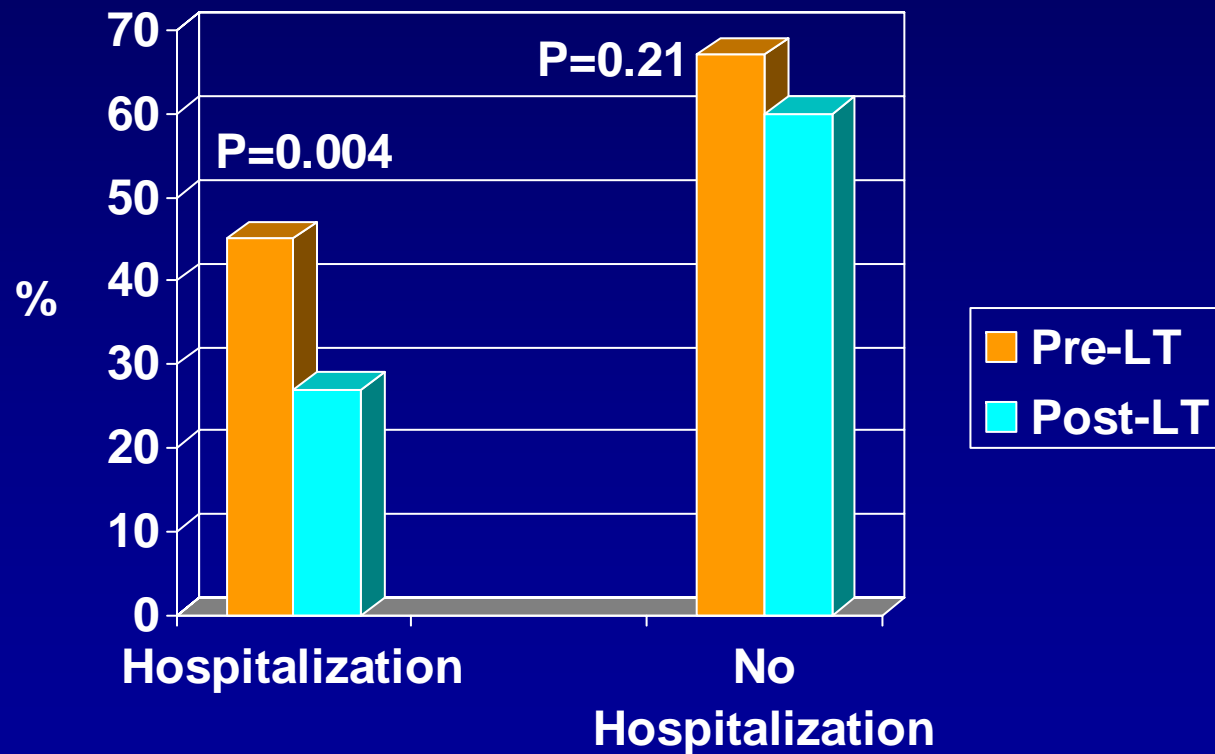
# No IBD vs. *De Novo* IBD

	No IBD (23)	<i>De Novo</i> IBD (7)
Med. time since LT (yrs)	6.8 (1.2 – 16.4)	7.8 (2.7 – 17.9)
Median age at LT (yrs)	46 (26 - 71)	45 (39 - 57)
Gender (% male)	87	43 <b>p=0.03</b>
Tacrolimus (%)	52	86
Prednisone (%)	9	29
CMV mismatch (%)	30	29
Med. rejection episodes	2 (0 – 8)	2 (0 – 7)
Recurrent PSC (%)	13	0
Median bilirubin	0.5 (0.2 – 2.5)	0.6 (0.3 – 1.6)

# Pre-LT IBD vs. *De Novo* IBD

	Pre-LT IBD (58)	<i>De Novo</i> IBD (7)
Med. time since LT (yrs)	6.7 (0.6 – 16)	7.8 (2.7 – 17.9)
Median age at LT (yrs)	47 (16 - 66)	45 (39 - 57)
Gender (% male)	76	43
Tacrolimus (%)	59	86
Prednisone (%)	12	29
CMV mismatch (%)	20	29
Med. rejection episodes	1.0 (0 – 9)	2.0 (0 – 7)
Recurrent PSC (%)	19	0
Median bilirubin	0.7 (0.2 – 6.6)	0.6 (0.3 – 1.6)
Ulcerative Colitis (%)	88	57 <b>p=0.0008</b>

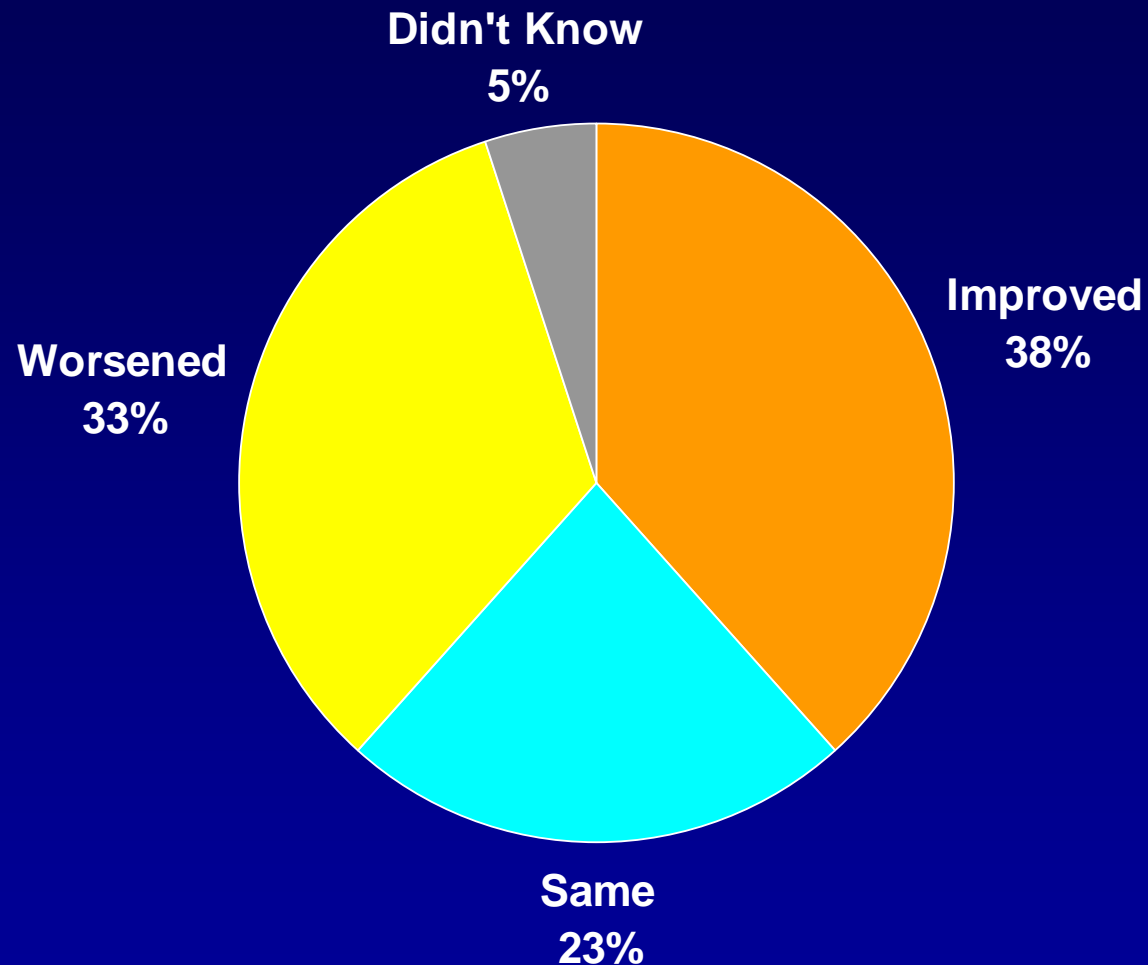
# Outcomes: IBD Flares



# Outcomes: Medications

	Pre-LT (%)	Post-LT (%)	P Value
None	9	25	<b>0.02</b>
5-ASA	79	63	<b>0.03</b>
Prednisone	31	14	<b>0.03</b>
Azathioprine	3	11	0.38
Infliximab	2	5	0.63

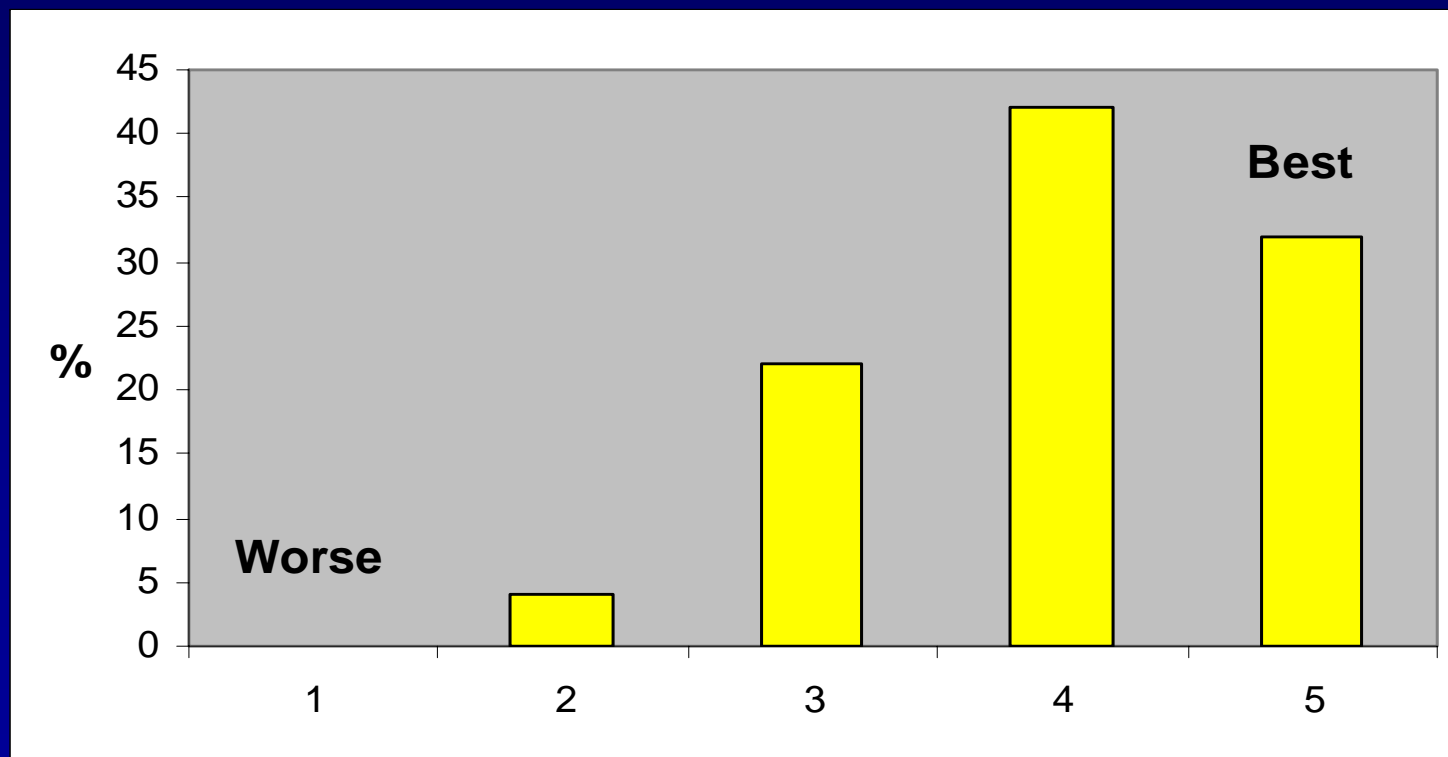
# Outcomes: Opinions



**No factors associated with subjective disease activity ( $p > 0.05$ )**  
(age, gender, transplant type, IS, CMV status, rejection, recurrent PSC, f/u from transplant)

# Outcomes: Quality of Health

73% rated current quality of health 4-5 on scale of 1-5



# Limitations

- **Not prospective**
- **Survey design subject to recall bias**
- **Subjective assessment of disease activity (no endoscopic documentation)**
- **We did not account for follow-up time from transplant when assessing colitis activity**
- **Although largest cohort, small sample size**

# Conclusions

- **Course of IBD post-LT variable with trend toward clinical improvement**
- **Medication reduction, fewer flares**
- **No overall subjective change**
- **No factors were associated with disease activity**

# Conclusions – *De Novo*

- *De novo* IBD occurs in 23% post-LT
- Female gender associated with development of *de novo* IBD
- Less ulcerative colitis
- Trend towards more females compared to cohort with pre-existing IBD

# Conclusions

Prospective multi-center studies  
needed to:

- further characterize the natural history of IBD post-LT
- identify predictive factors
- elucidate reasons for development of *de novo* or worsening IBD in face of immunosuppression

# Ongoing Theories

- T-cell dysfunction in liver disease protective to bowel in IBD. Post-LT immune reconstitution syndrome
- IS doses lower than those used in severe IBD (Azathioprine, CSA)
- Presence/absence of steroids accounts for disease activity
- *De Novo*: IBD may eventually develop in those whose death prevented by OLT
- Direct relationship between colitis course and IBD control at time of transplant

# Colonic Surgery

16% diagnosed with pre-malignant or cancerous lesion.

22% had colectomy

- 50% Pre-LT
- 50% Post-LT
- 46% Ileostomy
- 46% Ileoanal Pull-Through

12% had other type of colonic surgery

- 50% for obstruction
- 25% for unspecified
- 13% for perforation
- 13% for toxic megacolon