

PSC Partners Seeking a Cure

Newsletter

Vol. 1, Issue 4, April 2005

Edited by David Rhodes and Ricky Safer



www.pscpartners.org

April 29, 2005

The Conference began with an informal get-together on the 37th floor of the Pinnacle Club at the Grand Hyatt Hotel, Denver, CO from 5:30 - 7:30 pm. We were served a delicious array of appetizers and beverages, and this was a perfect opportunity for all the attendees to meet (many for the very first time!) and get to know each other. This was a great bonding experience. As we registered we were each given a wonderful bag embossed with the PSC Partners logo, kindly donated by Joanne Grieme. Thank you Joanne! A poster was displayed of pictures sent in by members of the PSC Support Group who could not attend the conference.

Don Safer gave some welcoming remarks and thanked the organizing committee for all their efforts and dedication. We were all delighted to meet Dr. Aubrey Goldstein and his wife, Caroline. Aubrey truly holds a special place in the hearts and minds of the PSC Support Group! We were all delighted to meet Ivor Sweigler from the U.K. PSC Support Group!

April 30, 2005



Don Safer

Following breakfast, the conference was opened by our Master of Ceremonies, Don Safer at 8:00 am. We couldn't have asked for a more eloquent, thoughtful and witty host. His opening remarks set the stage for an incredibly informative day of talks and presentations. Don and Ricky Safer's son-in-law, Steve Deitch, played an important role in making sure that the audio-visual equipment was all set up correctly. Thank you Steve!

It was highly appropriate that a long-standing member of the PSC Support Group, Arne Myrabo, gave the first talk. Arne explained how he was first diagnosed with PSC. He spoke of the difficulty in learning a whole new language and new acronyms associated with

PSC, even for an engineer used to such terminology! He spoke of the underlying fears associated with being diagnosed with a disease for which the only treatment is a liver transplant. He explained how he stumbled upon the PSC Support Group, and how this helped him develop his knowledge of PSC and inflammatory bowel disease ... "Knowledge is Power." He described how he became a more informed patient and advocate for his own health, and for the health and well-being of his fellow PSCers, who are all living with a chronic disease. He spoke of optimism for the future, especially as a result of new advances in cadaveric, living donor and xeno transplantation, and stem cell research, and also as a result of the formation of the PSC Partners Seeking a Cure Foundation. He applauded those who have made this happen.



Arne Myrabo

In This Issue:

This issue of the newsletter is focused on the PSC Partners Seeking a Cure Conference, held in Denver, CO, April 29 - May 1, 2005:

CONFERENCE FOR PATIENTS AND CAREGIVERS

This is the first of two editions covering the conference. It includes brief synopses of several of the talks, and a few photographs from the conference. Additional articles will appear in the next issue of the Newsletter (Vol. 1, Issue 5, May 2005).

The conference was attended by 82 people from 21 different states, the United Kingdom and Canada. It was an incredibly informative meeting, and we are deeply indebted to all of the speakers for their contributions. We are especially thankful to the team of doctors from the University of Colorado Health Sciences Center.

The conference ran high with emotion and inspiration. Lee Bria has successfully captured the event in this poem:

The Conference (by Lee Bria)

To Denver each arrived
with questions on their minds,
hoping to change their lives
with the answers they would find.

Courage opened the door
anxious and ready to greet,
fellow soldiers in this war
brethren forever they would keep.

Stories shared from the heart
flowed down their river of tears,
their cores pierced by the dart
of pain, heartache, love and fears.

The tables all were filled
with listening and learning,
their thoughts and worries stilled
inquisitive and yearning.

From terrifying lows
to incredible heights,
they took the ride with vows
to bring forth the healing light.

Advice was freely shared
council from the wise to the new,
questions never before dared
were now voiced and answered too.

Cheers to the foundation
the positive word to send,
spread through out the nation
a pledge to save our friends.

Enlisting for the years
to destroy, not hit the wall
here's to the must / kateers
all for one and one for all !!

Thank you, thank you, thank you. I'm so proud to be a member of this group.

If you would like to contribute an article to a future issue of this Newsletter, please e-mail it to David Rhodes:

rhodesdavid@insightbb.com

One of our foundation goals is to increase organ donor awareness. We encourage U.S.A. readers to visit www.donatelife.net and click on their state. This site gives a state by state guide to the organ donation process. This would be a good place for our members to start thinking about how to help locally, if they are interested....“While donated organs and tissue are shared at the national level, the laws that govern donation vary from state to state. Therefore, it is important for you to know what you can do to ensure your decision to be a donor is carried out.”



Give
Life



Additional Contact Information

Ricky Safer is the principal contact person for our PSC Partners Seeking a Cure Foundation. She can be reached at:

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Dr. Gregory Everson and Don

April 30, 2005 (contd.)



Dr. Gregory Everson

Dr. Gregory T. Everson M.D., Professor of Medicine and Director of Hepatology, UCHSC, Denver, CO, gave an excellent talk entitled “Introduction to PSC: The “Top Ten” Issues for Patients and Families”. He explained that PSC is: inflammation and destruction of intrahepatic and extrahepatic bile ducts (**cholangitis**). This leads to segmental scarring and strictures (**sclerosing**). There is no known cause; it is an autoimmune disease (**primary**). He described typical presentations of PSC, ranging from asymptomatic (with abnormal liver function tests (LFT’s)), to symptomatic (e.g. jaundice, hepatic mass, GI bleed, itching, inflammatory bowel disease). Dr. Everson described how to interpret the reports of blood tests, ERCP, PTC, and liver biopsy. He showed a table of normal liver function tests, and the types of strictures of the bile-ducts seen in ERCP and PTC. He also showed an image of a liver biopsy specimen from a PSC patient, and pointed out areas of inflammation and damage. Dr. Everson discussed the question of “How did I or my family member get PSC?”, and noted that there is evidence for a genetic predisposition for the disease, and that there may be an as yet unknown “inciting agent” that leads to inflammation and injury. He emphasized, however, that the disease is often characterized by periods of quiescence. Dr. Everson described the many important functions of the liver:

1. Regulates metabolism
 - a. Fat
 - b. Carbohydrate (sugar, starch)
 - c. Protein
 - d. Cholesterol
 - e. Vitamins
2. Maintains coagulation
3. Clears toxins
4. Produces enzymes and proteins
5. Excretes bile, pigments, and chemicals
6. Metabolizes drugs and chemicals

Abbreviations:

- ERCP = Endoscopic Retrograde Cholangiopancreatography
- PTC = Percutaneous Transhepatic Cholangiography
- PSC = Primary Sclerosing Cholangitis

In relation to abnormal cholesterol metabolism associated with liver disease, Dr. Everson showed examples of cholesterol deposits on the eye-lids (Xanthelasma) and elbows/palms (Xanthomata) that are characteristic of liver disease. Nutritional recommendations from Dr. Everson included avoiding use of alcohol and eating a well-balanced diet. Dr. Everson also addressed the question of “How can I best deal with the Emotional Roller-Coaster?” He stressed the importance of support systems:

1. One’s self
 - a. Education and knowledge
 - b. Know what to expect
 - c. Gain control
 - d. Develop coping skills
 - e. Maintain general health
2. Spouse or significant other
3. Family
4. Friends
5. Professionals
6. Medications

Mayo Model for PSC

- Useful in PSC only and not generalizable to other liver diseases and only predictive once lab tests become abnormal
- Model uses bilirubin, stage of fibrosis on liver biopsy, age, and spleen size
- Both internally (Mayo) and externally validated to predict survival in PSC

With respect to medical treatment, Dr. Everson discussed the use of antibiotics for infections, ERCP/PTC for treatment of stones, strictures and bile-duct cancers, the use of ursodeoxycholic acid (UDCA) to improve bile flow, and anti-pruritic agents to relieve itching. He described endoscopic and radiological approaches to stricture management, and noted the risk of colon and bile-duct cancer in PSC. Dr. Everson showed an image of cholangiocarcinoma associated with PSC, and stressed the importance of monitoring for colon cancer and liver tumors. Dr. Everson also discussed the question of “When is it time to consider liver transplantation?” He showed pictures of severe bile-duct injury/blockage, features of recurrent bacterial cholangitis, and esophageal varices that are all indications for transplantation. However, he closed by noting that the MELD system does not currently reflect the important features of PSC more accurately captured by the Mayo Clinic model (see lower inset; *Mayo Model for PSC*). We are deeply indebted to Dr. Everson for sharing his remarkable PSC expertise, and for his superb moderating skills.

April 30, 2005 (contd.)



Dr. James Trotter

James F. Trotter, M.D., Associate Professor of Medicine in Department of Hepatology and Associate Medical Director of Liver Transplantation at UCHSC, gave an excellent presentation on “Pre-transplant PSC treatment”. He specifically discussed the major symptoms; itching, cholangitis and weight loss. Dr. Trotter noted that itching is probably caused by accumulation of bile acids in the skin, but observed that no single treatment is uni-

formly effective for all patients. Itching generally becomes worse at bedtime, tends to drive others (e.g. spouses) crazy, and tends to come and go (over months). Dr. Trotter discussed the problem of cholangitis, which represents an infection in the bile tree, caused by stone or sludge build up blocking the bile tree, and then proceeded to discuss treatment options for cholangitis. Finally, Dr. Trotter addressed the problem of weight loss during end-stage PSC, and closed with some insightful observations on PSC. The audience was particularly struck by the concept of “**hitting the wall**”. The following are some key points from Dr. Trotter’s extremely thorough presentation:

Itching Treatments

- keep skin moist (esp. in Denver)
 - Neutrogeena (best, expensive)
- avoid narcotic pain pills
- topical (put directly on skin)
 - hydrocortisone cream
 - Sarna
 - citrus body lotion
 - Solarcaine spray/lotion
 - oatmeal bath
 - ice pack
- Benadryl/Atarax
 - often recommended, rarely helpful
- Rifampin
 - Interacts with some drugs
- ursodeoxycholic acid (Urso, Actigall)
- cholestyramine (Questran)
 - tastes bad, stomach upset
- Marinol
 - active component of “pot,” marijuana
- Ativan, Valium
 - only for short-term treatment
- Revia
- Phenobarbital
- other
 - tanning booth, phototherapy
 - hemodialysis with charcoal filter
 - ??

Cholangitis Symptoms

- vary patient-to-patient, learn your symptoms
- jaundice, abdominal pain, dark urine, fever
- can lead to life-threatening infection
- recurrent = weight loss, muscle loss

Cholangitis treatments

- prevention
 - ERCP in selected patients
 - take actigall or urso (800-1000 mg/d)
 - for recurrent episodes
- continuous low-dose antibiotic
- 1 – 3 pills per week
- selected patients change antibiotic to prevent emergence of “resistant” bacteria
- treatment of episode of infection
 - ERCP in selected patients
 - take antibiotics by mouth or IV 7 – 14 d
 - treat as early as possible

Weight loss

- caused by liver failure, recurrent infections
- > 10 % body weight
- occurs at very end-stage of PSC
- leads to loss of muscle, energy, quality-of-life

Weight loss - treatment

- testosterone cream
 - Testim, Androgel
 - apply directly to skin daily
 - goals: weight gain, increased energy
 - side-effects: ankle swelling
 - expensive (\$6 per day)
 - not always covered by insurance

Observations

- most PSC patients are stable for years
- then hit “**the wall**”
 - recurrent symptoms, hospitalizations
 - loss of muscle, weight, energy
 - time for transplant (if possible)
- deceased-donor from ICU
- living donor
- die waiting for transplant
- other center
 - 3 centers with faster transplant rate
- alternative/nutritional therapies
 - 1) more frequent for conditions poorly treated by conventional rx
 - 2) Dr. Trotter goes to an acupuncturist, open-minded
 - 3) most are ineffective
 - 4) MD’s are ignorant about the effects of nutrition (eat well)
- cholangiocarcinoma (bile duct cancer)
- affects about 10 % of PSC patients
- no viable way to screen
- frequently (usually) fatal
 - Walter Payton, Chris LeDoux

April 30, 2005 (contd.)

Joel S. Levine, MD FACP,
Professor of Medicine
and Interim Head, Division of
GI-Hepatology at the School of
Medicine at the University of
Colorado and Senior Associate
Dean for Clinical Affairs



Dr. Joel Levine

Dr. Joel Levine gave an outstanding presentation on “IBD in PSC”, addressing three central issues:

- Understanding current knowledge about the bowel disease associated with PSC.
- Understanding the relationship between IBD in PSC and colon cancer.
- Understanding current approaches to the medical and surgical treatment of IBD in PSC.

At the outset he raised some very interesting, fundamental questions about whether PSC is an uncommon extra-intestinal manifestation of colitis (2-4%) ... or whether it is a colitis that is a lot like ulcerative colitis and a little like Crohn's colitis, and as a very common extra-hepatobiliary manifestation of PSC (75%)?

The special features of the IBD associated with PSC are:

- A lot like CUC (Chronic Ulcerative Colitis)
 - Confluent disease ‘only’ involving the colon
 - No granulomas, + crypt abscesses
 - No fistulae or fissures
 - + pANCA in 80%; ASCA negative
- A little like Crohn's
 - Rectal sparing common (50% vs 5% in CUC)
 - Backwash ileitis common (50% vs 5% in CUC)
- The bowel disease:
 - Is clinically mild
 - Responds to the same medicines as CUC (at least pre-liver transplant)
 - Steroids, colon specific 5-ASA compounds
 - Uncertain about immunomodulators
 - Puts patients at greater risk (probably) of developing dysplasia and colon cancer

In relation to dysplasia and colon cancer, Dr. Levine noted that most would agree that the patient with PSC and IBD has an increased risk of developing colon cancer ... over and above the 0.5% per year in patients with CUC (>8-10 years). In one study the risk was increased 4 fold. A possible explanation is the secondary bile acids at increased concentrations in the colon of the patient with PSC. Dr. Levine discussed what can be done

about this risk, and gave several practical approaches, including primary and secondary prevention strategies:

- Primary Prevention (all evidence is epidemiologic not prospective trials)
 - UDCA (ursodeoxycholic acid)
 - 5-ASA compounds (decreased inflammation?)
 - Folic acid (1 mg per day)
- Secondary Prevention
 - Surveillance colonoscopy (done properly) every year after having colitis > 8 years
 - Colectomy for documented dysplasia

Dr. Levine finally discussed the types of colectomy in PSC patients, and the problems of pouchitis that can occur. He discussed treatment and prevention approaches for pouchitis, including use of antibiotics and probiotics, respectively:

Colectomy in the PSC Patient

- Total colectomy with ileostomy or ileoanal pull through with J pouch
 - Ileostomy
 - Requires ostomy appliance, simple, lower risk. Risk of varices at the ostomy site in patients with cirrhosis.
 - Ileoanal pull through – No ostomy or appliance. Good result is 5-6 continent BMs a day. However, inflammation of the pouch is increased in patients with PSC

Pouchitis in the Patient with PSC

- Pouchitis – inflammation with ulcers of the J pouch that causes increased frequency of BMs, urgency, and incontinence.
- Cause unknown but likely a combination of the bacterial flora in the pouch and the immunologic set up of the patient.
- Over 75% of patients with PSC get pouchitis (as opposed to 30% CUC)
- Diagnosis requires endoscopic evaluation of the pouch with biopsies
- Treatment
 - Antibiotics – metronidazole and ciprofloxacin are the mainstays but others are tried with varying success
 - Immunosuppressant Rx not helpful
- Prevention
 - Probiotics after surgery or after first episode
 - VSL #3 best data

April 30, 2005 (contd.)

Igal Kam, MD
Professor of Surgery
Chief of Transplant Surgery
University of Colorado
Health Sciences Center



Dr. Igal Kam

Living Donor Liver Transplant: Colorado's Experience

Dr. Igal Kam gave a brilliant talk and superbly illustrated presentation on the University of Colorado's experience with living donor liver transplants (LDLT). Dr. Kam's presentation began with a description of the anatomy of the liver, including the biliary tree and blood vessels of the liver. He then proceeded to discuss the history of living donor transplants and the great need for this technique because of the organ shortage and death of patients on the waiting list. He described the early use of left segment liver transplantation in pediatric patients in Japan, eventually leading up to the pioneering right lobe liver transplantation technique at Colorado.

Dr. Kam discussed the important principles of recipient selection for LDLT:

- Must meet UNOS criteria for liver transplantation
- Optimal candidates are UNOS status 2B, (> 10 child's points) especially with small hepatomas, not at the top of cadaveric list
- Status 1, 2A are possible candidates
- Recipient with a poor predicted outcome should be excluded (multiple-organ failure)
- Recipient listed as UNOS status 3 should be excluded

donor selection criteria:

- Voluntary
- Identical/compatible blood type
- No significant medical problems
- Long-term significant relationship with recipient

and donor evaluation criteria:

- Medical Evaluation
 - Physical exam
 - Blood tests, x-rays and EKG
 - Psychiatric evaluation if indicated
- Radiological evaluation
 - CTA, MRC

Dr. Kam described the surgical techniques involved in LDLT, including donor surgery, backtable preparation and recipient surgery. As he described the procedures in detail, he warned the audience that some of the images were graphic in nature, and not for the squeamish! We will not include these images in the newsletter. Although Dr. Kam's video clips of the procedures

did not display properly on the screen at the conference, we are pleased to include several of them on the conference CD.

Finally, Dr. Kam gave an overview of the excellent graft survival and patient survival rates associated with LDLT. He concluded his presentation with the following main points:

- Adult living donor liver transplant is safe and effective with careful donor and recipient selection.
- Application of this technique to some patients with end stage liver disease may significantly decrease waiting list mortality.
- Right lobe grafts provide adequate liver volume
- Right lobe grafts allow for easier vascular anastomoses .
- Right hepatectomy is well tolerated in the donor
- Bile duct complications still remain the Achilles heel of this procedure.
- More studies need to be done to assess the impact of this procedure on the outcome of liver transplant.
- Absolute contraindication: lack of team experience in major liver surgery.

Dr. Kam's surgical genius and sincere compassion for his patients were greatly appreciated by the audience. We were truly honored to have had the opportunity to hear and talk to this great man.

April 30, 2005 (contd.)

Lisa Forman, M.D., M.S.C.E.
Assistant Professor of Medicine and Associate Director of the GI and Hepatology Training Program at University of Colorado Health Sciences Center



Dr. Lisa Forman

PSC: Post-Transplant Issues

Dr. Lisa Forman focused appropriately on post-transplant issues in PSC, and broadly divided her talk into 4 areas: Case Presentation; Survival; Management; and Conclusions.

Survival issues were of great interest to the audience. Dr. Forman presented evidence that both patient and graft survival were greater in cholestatic than in non-cholestatic transplantations. However, PSC has a tendency to recur following transplantation (5-10%). While the majority of these patients with recurrent PSC do well, and recurrent PSC does not influence patient or graft survival, risk factors for recurrent PSC remain obscure. Diagnostic testing for recurrent PSC is similar to pre-transplant diagnostic testing, with the exception that ERCP is substituted by PTC (see abbreviations on p. 2). Post-transplant PSC is managed with antibiotics, actigall (UDCA), and biliary drains. Dr. Forman addressed the issue of post-transplant IBD, and noted that the course was variable, with new diagnosis of IBD (especially UC) occurring rarely. Transplantation does not appear to affect the incidence of colorectal cancer.

April 30, 2005 (contd.)

David Rhodes (PSC Support Group member and Professor of Horticulture at Purdue University) gave a talk on "PSC: A Care-Giver's Perspective". He described his son's diagnosis of PSC/UC in the summer of 2003, and how this led to establishment of the PSC Literature web site as a resource for PSC patients and care-givers. He then proceeded to discuss the medications and supplements that his son has been taking since diagnosis (stage 2 PSC), including ursodiol (UDCA), rifampin, asacol, vitamins, folic acid, fish oils and spinach. David described the probable mechanisms of action of these compounds, with emphasis on their effects on liver metabolism, and bile transport processes. He presented evidence that ursodiol may be protecting the bile-salt export pump in hepatocytes against impairment by toxic bile acids such as deoxycholic acid. He showed how rifampin and fish oils may also be affecting the activity of bile transport systems, and bile metabolism, by activating molecular switches; the pregnane X receptor (PXR) and peroxisome proliferator-activated receptor alpha (PPARα). He also discussed the anti-inflammatory effects of fish oils and how several of the medications (ursodiol, asacol, fish oils) may inhibit the inflammation pathways in inflammatory bowel disease. He described how folic acid and betaine (found at high levels in fresh spinach leaves) may be beneficial in maintaining the methylation cycle in the liver, and in keeping homocysteine levels low. Finally, David briefly discussed the rapid progress being made in identifying inflammatory bowel disease genes, and understanding the genetic basis of IBD. He expressed enthusiasm for the recently published NIDDK action plan on autoimmune liver diseases, and the forthcoming PSC research workshop in Bethesda, MD, sponsored by NIDDK and the Morgan Foundation. He closed by dedicating his talk to Shauna Saunders, a PSC support group member, and graduate student at Duke University, who died in Dec. 2004 while awaiting a liver transplant.



David Rhodes

April 30, 2005 (contd.)

Dr. Aubrey Goldstein gave the closing talk of the Conference on April 30. His talk was entitled "PSC: Perspectives from a PSC Transplant Recipient and M.D." Dr. Goldstein was the mainstay of the PSC Support Group for many years, and he is a Chronic Care Physician at St. Vincents Hospital in Ottawa, Canada. Last, but by no means least, this was considered by many in the audience to be the most moving speech of the conference. Aubrey described his very personal experience with PSC, from initial diagnosis, though dreadful, life-threatening, and painful complications, such as GI bleeds and pancreatitis, eventually leading to liver transplantation. He described his life-style changes implemented to battle PSC, including exercise, and a switch to a vegetarian diet; a move that he is certain resulted in minimal hepatic encephalopathy prior to his liver transplant. Aubrey conveyed to his audience the critical importance of the support system for the PSC patient, and relayed his own personal battles with the mental and physical toll of this disease, both pre- and post-transplant. Aubrey touched upon the side-effects of immunosuppressants and other medications, and the dread of PSC recurrence. Overall, Aubrey's talk captured the essence of "the wall" and the emotional "roller-coaster" in a quiet, thoughtful, yet riveting fashion. His talk was greatly appreciated by the audience, and we thank him profusely for his unique perspective and contribution.



Dr. Aubrey Goldstein and his wife, Caroline

May 1, 2005

We were thrilled to have Ivor Sweigler from PSC Support (U.K.) join us at the conference. Ivor gave a brief history of his own PSC diagnosis in 1991, and noted that his PSC has progressed very slowly since then. He described how he went to the medical library to read up about the disease, and how he discovered that medical texts on PSC have changed little over the years. He relayed to us his experience in co-ordinating the U.K.



Ivor Sweigler

PSC Support Group, now with 320 members, and the central role that his "PSC News" newsletter plays in keeping members informed. Ivor expressed enthusiasm for our fund-raising efforts on this side of the Atlantic, but lamented that on the other side of the Atlantic they have been unsuccessful in this endeavor. Ivor is eager to build bridges with PSC Partners and continue our fruitful collaboration and dialogue. He encouraged us to attend the next meeting with Dr. Roger Chapman, in Oxford on July 9, 2005. It is expected that Dr. Chapman will release results of the latest high-dose ursodiol trial in PSC at this meeting. Ivor plans to give a full report of this meeting in July.

Editorial Note

We have attempted to cover the main points covered by many of the speakers, primarily for the benefit of those who could not attend the conference. Because of space constraints, however, we have not been able to include every word spoken, nor cover all talks in equal depth. We apologize if we have not done justice to each of the valuable contributions, and if we have omitted important points. More detailed slide presentations will be included on the Compact Disk (CD) that will shortly become available.

Each conference attendee will receive a free complimentary copy of the CD. The CD will be for sale on our website for those who couldn't attend the conference this year. The CD will include photographs from the conference, PowerPoint presentations, and Dr. Kam's transplant surgery movies. Please see Issue 5 (Vol 1, Issue 5, May 2005) of this newsletter for additional coverage of the conference.

Fundraising News

\$5,033.50 Donated by the Department of Risk Management at the University of Michigan Health System (UMHS)
(by Lee Bria)

PSC Partners now has fifteen very special new friends, the team "Risky Business". They are:

Julie Larsen
Karen Adkins-Bley
Kathy Lanava
Carol Ziegler
Susan Anderson
Kelly Saran
Mary Beth Crandall - Team Captain
Deborah Gordon
Vicki Young
Ellen Mckeown
Elaine Commiskey
Jane Brehmer
Patti Reynolds
Kylie Welling
Terry Headly



Thank you "Risky Business"

Thanks to all of these wonderful people who worked hard for nine weeks in the "PAL Charity Challenge" sponsored by the UMHS to raise money for our PSC Partners Seeking a Cure foundation. Together for nine weeks they walked hundreds of miles and exercised many, many minutes to earn first place over 156 other teams. I was very proud to accept a check for their efforts in the amount of \$5,033.50. I know that all of our members appreciate what they have done to help us and we can not thank them enough. We will make sure to keep all of our new friends informed of our foundation's progress. They have boosted the spirits of our members and given all of us much needed encouragement by their generosity. Little do they know how many lives they have already touched and how many more that they will touch. Thank you to each and every one of them.

May 1, 2005 (contd.)

Following Ivor Sweigler's talk on the morning of May 1, Lee Bria held a workshop/discussion period on fund-raising. She described current fund-raising activities (including the wristband project, and notecard project; giving thanks to Bill Wise and Ali for their significant efforts in these endeavors). Lee conveyed how we can all help in various ways, and encouraged us to "think outside the box." Conference attendees were given a form that can be used to suggest new fund-raising projects (this form will soon be available on our web site). Participants were asked to complete volunteer forms outlining their various skills, with the view to forming future committees of talented individuals who would be willing to address our various foundation activities, including: medical/scientific advisory; fund-raising; conference planning; technology; legal policy; and financial committees.



Lee Bria

Elissa Deitch gave a brief report of funds raised thus far, and noted that our first financial report will be available in May, 2005. A big thank you to Elissa for all her pro bono legal work that she has done for us to form the foundation, to file the 501(c)3 application, and to continue every week answering our legal questions. It was suggested that the foundation board members should be listed on the pscpartners.org web site, and that a 2 page brochure of the foundation, and its mission, should be developed.

May 1, 2005 (contd.)

Conference attendees kindly completed feedback sheets. Here are some answers from the question: "What did you like most about the conference?"

- The excellent contributions from the UCHSC team.
- Medical team from Denver was top flight.
- The wealth of information presented.
- I gained so much information from so many different perspectives.
- Extremely knowledgeable speakers, all very committed to the resolution of some of the issues that are presenting themselves to PSC patients, ie. recurrence, new mediation protocols, etc.
- Breadth of knowledge of all speakers-very up to date information.
- The doctors were great in explaining complicated issues to laymen.
- The variety and knowledge of all the speakers were excellent.

Some thoughts and reflections from one of the conference attendees

Made it Down From the Mountains

(by Bill Wise)

Gang,

Wow... where to begin?! First things first, thanks so much to Ricky, Don, Lee, Dave, and Judy for being the instigators of the foundation and the organizers and driving force behind the conference. For those of you who weren't able to attend, no matter how great we make it sound, it was better! Do whatever you have to so that you can join us next year.

Some observations and a brief recap from my perspective...

- Until Friday night I'd never met another person with PSC. Now I know about forty.

- I was stunned to find out that about half the attendees were made aware of the conference by the University of Colorado and had no idea there was an online support group. We owe Dr. Everson and his colleagues a hearty "Thank You" as well.

- Jason Drasner is every bit as funny as he seems here. Thanks a bunch for sharing your bunk space, Jason. Your wife has nothing to worry about... but if she's got a thing for bald guys, you might be in trouble. ;-)

- Melanie (MO) and her daughter Andrea have one of the wildest mother/daughter relationships I've ever seen. It's metered insanity, yet it works so well for them. Two of the most charming ladies I know.

- Monte... if you're out there, give a shout. Thanks for being our tourguide for the weekend. I apologize to you and Jason both for suggesting that stinker of a movie Saturday night. I saw "Sahara" Monday night and it was MUCH more entertaining. Best of luck to you... hope the call comes soon!

- Ricky Safer is the single most organized person on the planet.

- All the presenters from the University of Colorado were top notch. I was particularly interested in Dr. Levine's thoughts on PSC colitis as a different animal from Crohn's or CUC. Heady stuff.

- We couldn't ask for a better poster boy for our disease than Chris Klug. What an inspiration that guy is, not to mention charming, approachable, sincere... and a damn fine athlete to boot.

- Dave and Judy Rhodes have really big brains, and yet somehow Dave was able to make us all understand. If he'd had a Fish Oil, Folic Acid, and Spinach stand set up, he'd have sold out. That they've dedicated themselves to this cause is a big boon to us all.

- Don Safer can tie a bow tie.

- Words can't do justice to the power of Dr. Aubrey's presentation. Other attendees know what I mean and I won't cheapen it by trying to describe it. Suffice to say, hands down, the most moving experience of the weekend. Thanks,

Aubrey.

- If you could bottle Lee Bria, we'd all have our fatigue problems fixed.

- Omaha Tim, Denise/Deb, Sam Edney, Arne, Joanne, Deb Wente, Ali, and all the rest from this group... it was such a pleasure to meet all of you. My only regret is that we didn't have more time to get to know each other.

- Ivor is a man to be reckoned with. To assemble a newsletter of such exceptional quality and head a group of patients with not as much drive as was apparent in our group requires a singular dedication to his purpose. We should all be so tenacious.

On to some of the things happening here in my absence...

- To add another data point, I'm 37 yo and had first indications of PSC at age 32. I was listed for transplant last fall at age 36. I currently take 1800mg/day Urso and occasionally use Cholestyramine or Hydroxyzine for pruritis and Cipro as needed for infections.

- Lee, what took you so long? The conference ended on Sunday and you waited until Wednesday to get another \$5k donation?!?! Bless your heart! BTW... check out Watson Pharmaceutical. My last batch of generic Urso had their name on it.

- Andi, fabulous that you could represent us with Dr. Gershwin's group. You were a common topic of discussion this weekend. Please keep us posted.

- To all the new members, WELCOME! You're joining us at an exciting time. You won't find a kinder, more genuine, or more knowledgeable group of individuals on the 'net. Make yourselves at home.

I'm sure I'll think of more stuff I want to add, so stay tuned for further updates as events (and memory) warrant. Already looking forward to next year.

Very Best Regards,

Bill Wise

Additional comments from conference attendees:

- I enjoyed every moment. It was upbeat, fun, serious and informational.
- The conference was by far the BEST I have attended. GREAT JOB!
- Well organized. You all did an incredible job in putting together the program. I am truly amazed and very impressed.
- I have learned some things that will positively change my lifestyle/life.
- I loved meeting the people and feeling the enthusiasm and optimism of the group.
- It was a great opportunity to meet others and break the isolation.
- Extraordinary planning, execution and quality of program and speakers.
- This is the beginning of something that will change lives and the outcome of medical care and research. Gives great purpose to all.

We are very pleased to include the following article from Dr. Christopher A. Aoki, Fellow, Division of Gastroenterology, UC Davis Medical Center, describing Dr. Eric Gershwin's Research on PSC and other autoimmune liver diseases:

Primary Sclerosing Cholangitis has been designated by the National Institute of Health as an "orphaned" disease due to the inadequate knowledge and research being done for patients with PSC. Here at UC Davis we are striving to put an end to this glaring deficiency. Although this is a new area of investigation for us, we are lucky to have an expert in autoimmune liver disease at our institution. Dr. Eric Gershwin has made many important discoveries in Primary Biliary Cirrhosis, a very similar autoimmune liver disease. We hope to take what he has learned and the techniques he has used to study this disease and apply it to PSC. We believe by studying these two diseases simultaneously we will be able to exploit not only the similarities between them but also the differences in hopes of discovering why the immune system attacks the bile ducts and what can be done to stop it.

Although we have many ideas, we are beginning to investigate the autoantibody found in PSC, the atypical p-ANCA. Antibodies are a normal part of our immune system that attacks foreign organisms when they invade our system. However, in many autoimmune diseases, these antibodies bind to normal host tissue or proteins and are termed autoantibodies. In the case of PSC, this autoantibody binds to the nucleus of neutrophils and has been named the atypical perinuclear antineutrophil antibody or p-ANCA. The identity of the specific protein that these autoantibodies bind is unknown. We believe that by identifying the protein that this autoantibody binds it will help us to determine whether or not these autoantibodies may be contributing to the chronic inflammation and destruction of

the bile ducts. It may also give us clues as to what may have initiated the disease and possibly new methods of diagnosing this disease at an earlier stage than what is currently available.

Another project that is currently underway is the use of microarray to determine which genes are abnormally activated or deactivated in patients with PSC. As many of you know, some of our genes predispose us or protect us from certain diseases. Microarray is the latest in biotechnology advances that allows us to search almost the entire human genome (approximately 50,000 genes) for any abnormally expressed genes from just a few milliliters of donated blood. This powerful tool will allow us to look for possible pathways that may be abnormally turned on or off that lead to the disease. Hopefully this information can be used to find new ways of disrupting these pathways and develop new therapies for this disease. In addition, we may find ways to prevent the disease as well as new methods of diagnosis.

The third approach we are taking toward understanding PSC is headed by Dr. Chris Bowlus, an expert on genetic liver diseases. This project will investigate genetic differences between PSC patients and IBD patients without PSC as well as unaffected family members. Similar studies are taking place in the United Kingdom, Norway and Sweden but have been lacking in the US. Because the genetic basis of PSC may vary between ethnic groups, studying PSC in different populations is imperative. The first step in performing these studies requires the collection of DNA from PSC patients, family members and IBD patients without PSC. Our goal is to collect DNA from at least 400 PSC patients throughout the US.

These studies are not possible unless we have people like you who can donate their blood to make these projects a reality. A large part of Dr. Gershwin's success in Primary Biliary Cirrhosis has been due to the amount of patients with PBC from all over the country that have donated their blood to his various

	PSC	PBC
Sex	Affects predominantly men (2:1)	Affects predominantly women (9:1)
Age at diagnosis	25-45 years old	50 years old
Racial Predisposition	Northern European Descent	Northern European Descent
Diseases associated	IBD, Celiac Sprue, RA	SLE, Sicca syndrome, scleroderma
Autoantibodies	Atypical p-ANCA	AMA
Pathology	Strictures/fibrosis of the large and small bile ducts	Strictures/fibrosis of the small ducts only, granulomas
Treatment	? Ursodiol/liver transplant	Ursodiol/liver transplant

(continued from p. 9)

projects. Similar to PBC, PSC is a relatively rare disease and therefore large studies are not possible from one location or one medical center. Instead, they take an organized effort from patient groups such as yours who are able to reach a large number of patients.

In order to assist with this process we are developing a PSC Registry and a DNA and Serum Bank. The Registry and DNA/Serum Bank will be open to PSC patients, family members and IBD patients without PSC. These resources will allow us to perform the genetic and immunologic studies we have planned. In addition, the Registry will be used to keep a detailed record, and to inform participants of new projects and clinical trials which are used to develop new therapies.

Big breakthroughs in this disease will require a concerted effort not only from medical researchers, but also from PSC patients from all over the country to participate in these studies. As practicing hepatologists we care for many patients like you and we share your frustration with the limited knowledge and treatment options available to patients with PSC. This has motivated us to perform research in this area and we hope that you will help us on our quest to find a cure for this disease. We look forward to hearing from you soon!

Dr. M. Eric Gershwin, Distinguished Professor of Medicine, Chief Division of Rheumatology, Allergy and Clinical Immunology UC Davis Medical Center

Dr. Christopher L. Bowlus, Assistant Professor of Medicine, Division of Gastroenterology, UC Davis Medical Center

Dr. Christopher A. Aoki, Fellow, Division of Gastroenterology, UC Davis Medical Center

Please contact Marcy Crees at mlcrees@ucdavis.edu

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Laughter is the best medicine

Some of the comments we have received about the previous issues of the newsletter are that we should be less serious, and include a little humor. It's hard not to be deadly serious when talking about a dreadful disease such as PSC. However, we will try to oblige, recognizing that laughter is often a great medicine, but acknowledging that we have no experience as stand-up comedians:

Q. What do you call an opera singer participating in a clinical trial?

A. Placebo Domingo

Q. What is the correct medical term for word slurring?

A. Inflammatory vowel disease

Q. What do you call a bile acid prescribed for movie stars with liver disease?

A. Actorgall

O.K. enough already! Jason and Bill, if you are reading this, you can see we definitely need your input here!

**Better to light a
candle than to
curse the
darkness.**

Chinese Proverb

We are indebted to all the speakers who contributed to this conference, especially Dr. Gregory T. Everson and his colleagues from the University of Colorado Health Sciences Center.

We also thank all those members of the PSC support group, and their family, friends and caregivers, who have generously donated their time and funds to the PSC Partners Seeking a Cure foundation.