
The Duct

Bringing you news on PSC

research, education, and Support



PSC Partners Seeking a Cure Foundation

Summer 2008



Denise Harnois, DO, welcomed PSCers to the Mayo Clinic and to the conference. She gave an overview of the disease, setting the stage for other presentations.

Special Report: 2008 Annual Conference

Tom Brott, MD, Mayo Clinic Jacksonville liaison, with Ricky and Don Safer of the Foundation, discussed Mayo's commitment to education.



From the President of PSC Partners Seeking a Cure

Looking back on our fourth annual conference May 2-4 at the Jacksonville Mayo Clinic, I have to ask myself a few questions. Is there anywhere else where you could:

- meet and enjoy the company of 115 PSCers and caregivers from the U.S. and also from Canada, the UK, and Sweden who are eager to share their advice, experience and compassion?
- learn from world experts in PSC medical care and research?
- form strong and meaningful family bonds with people who understand what life is like with PSC?

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- be fed every three hours that you're awake?
 - scratch yourself in public and have no one notice or care?
 - laugh until you cried, thanks to our fast-talking banquet entertainer?
 - finish up the weekend feeling privileged to be an integral part of a group that outsiders would like to avoid?

If this appeals to you, then please read on.

Our conference weekend in Jacksonville Florida was a wild success for all who were able to attend. Jacksonville's sunny days and the beautifully landscaped Mayo campus set the scene. Our enthusiastic attendees set the warm and caring ambiance.

This year, we included two new popular additions to our agenda. Since our 2007 conference attendees had requested more social time together over the weekend, we put together two pre-conference activities for Friday morning: a golf tournament and an ecological boat tour on the St. John's River. These activities were a wonderful chance for the attendees to get to know each other in a casual setting before the conference began. On Saturday, our second addition was Lunch with a Physician breakout sessions. This was a special opportunity for each of us to interact individually with one Mayo physician in a small group setting. The Mayo physicians were very honest and caring in their feedback to our questions.

I think that the conference participants will agree with me when I say that the Mayo Clinic provided an amazing medical experience for all of us. PSC Partners Seeking a Cure was graciously welcomed by everyone from physicians to the AV staff. The unique Mayo culture prides itself in offering expert medical care and research while displaying sincere compassion towards their patients. I feel so fortunate to have experienced this personally!

All day Saturday, we had a varied roster of expert presenters speaking on pertinent topics, starting with Dr. Denise Harnois and Dr. Greg Gores, our keynote speaker. Dr. Gores' talk on cholangiocarcinoma relieved some of my fears about this possible dreaded consequence of PSC. Dr. Gores discussed his unique protocol for treating PSCers with cholangiocarcinoma, which includes the possibility of a liver transplant after cancer treatment. I was pleased to listen to Dr. Jaime Aranda-Michel, a rare hepatologist who is also trained in the vital field of nutrition. All the speakers were extremely well versed in their field, passionate about their work, and attuned to patient needs.

I'm very encouraged by the increase in PSC research going on internationally now. The winner of our



Dr. Stephen Lange, of Mayo Clinic presented a session on endoscopic therapy.

Dr Harnois moderated audience questions for Dr. Gores and Dr. Hewitt.



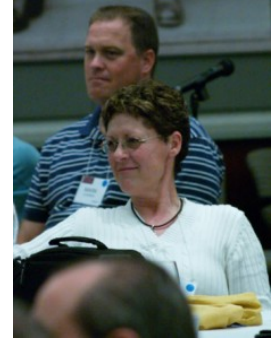


Ivor Sweigler, Ph.D., reported on the state of PSC research in the UK.



Dr. Adriana Vasquez reviewed family and patient psychological issues in chronic illness.

Audience members enjoyed the presentations.



AASLD prize for the best PSC research in 2007, Dr. Tom Hemming Karlsen from Oslo, Norway, discussed his promising research on PSC genetics. He also gave us an exciting update on the Norwegian PSC Center, which recently received a \$25 million contribution to be used for a ten year PSC research project! What a difference this could make for all of us. Ivor Sweigler updated us on Dr. Roger Chapman's continuing PSC research in the UK and Dr. Dennis Black of the Morgan Foundation described the STOPSC genetic registry which has recently been launched, with twenty participating centers in the U.S. On Sunday, David Rhodes announced that PSC Partners' Scientific Medical Advisory Committee is ready to present our very own research initiative by offering competitive grants to PSC researchers with a promising research project. We are definitely moving many steps ahead towards finding that cure for PSC!!

Here were a few more highlights of the weekend for me:

- Watching the first time attendees arrive on Friday

with great trepidation, then head home on Sunday smiling, with a wealth of knowledge under their belt and wonderful new friends to contact. So many of the new attendees told me that the weekend was life changing for them, as they now can put a more positive spin on their lives.

- Reestablishing old friendships and making new friendships with a group of phenomenal members.
- Experiencing the feelings of understanding, acceptance and hope that I have while we are all together. The positive energy of the group is amazing.
- Observing the large group of PSCers in their 20s and 30s form incredible bonds within their group while helping each other bravely face the challenges of living a successful life with PSC.
- Hearing Dave Rhodes' thoughts on Vitamin A, IBD and PSC.

- Watching Dave Rhodes present PSC Partners' \$20,000 contribution to the STOPSC registry to Musette Morgan.
- Cheering Lee Bria and Joanne Hatchett's announcement that our conference fundraisers raised close to \$90,000!!!
- Meeting Chuck and Joan Cooper of Hoops 4 Healing and hearing Chuck present their foundation's heartwarming story.
- Laughing so hard that I cried listening to Shelley Hussey's talk on the Power of Humor. I take great pride in the new PSC title that she bestowed upon me.

I'd like to share some compliments about our attendee group. As the Mayo physicians left on Saturday, many of them repeated the same comment to me--that this is the most knowledgeable patient group that they have ever seen. I also received several comments on the wonderful chatty nature of our group. Another person told me that she was impressed by the

amount of talking going on at each table and the depth of communication among the attendees. The power of our group truly is spectacular.

Once again I'd like to thank the many people who contributed to the success of the conference.

- Cordis Corporation, Astellas Pharma, Axcan Pharma, and Roche, our wonderful conference sponsors, whose support we all greatly appreciate.
- Dr. Tom Brott, who paved the way for Mayo to welcome us and Dr. Karen Brott, Conference Co-Chair who spent a year helping me with local logistics. Without them, this weekend would not have been possible. Karen and Tom are the best friends that anyone could have!
- Dr. Denise Harnois, who spent a year planning all the conference details with us and who hand picked our fantastic presenters.
- All the expert speakers who gave us brilliant presentations.
- All our attendees who took the time and effort to join us in Jacksonville.
- Lee Bria and Joanne Hatchett, who organized the Road to Jacksonville fundraiser and the silent auction. Thank you also to all those who contributed to our cause.
- Tim Wholey and Joanne Grieme, who organized and ran our successful golf tournament.
- Karen Brott, who suggested and organized the ecological boat trip-a great idea.
- Dike Ajiri, who did much behind the scenes work and filled in for Deb Wenthe, our Treasurer.
- Dave Rhodes, Aubrey Goldstein, Pat Bandy, Joanne Grieme, Ivor Sweigler and Shelley Hussey, who spoke at the conference.
- Jecy Belmont, who emerged as the natural leader of the 20s and 30s group.
- All our volunteers, who helped the conference run smoothly.

- Joanne Hatchett, who shared her practical medical forms and handouts with us.
- Arne Myrabo, who was our head photographer and who has created the CDs and 2008 conference web site for us.

The talents and enthusiasm in our group are greatly appreciated.

The planning for our 2009 conference in Chicago has already begun. I am grateful to Becky Long, our 2009 Conference Co-Chair who has already started planning with physicians at Northwestern. I am pleased to announce that our fifth annual conference will take place in Chicago the weekend of May 1-3, 2009 at a small hotel near O'Hare airport, a venue that is easily accessible. Becky also has many creative ideas for the weekend, so please mark these dates in your calendar, and we'll keep you updated. We have also kicked off the start of the Road to Chicago fundraiser.

When we started PSC Partners Seeking a Cure in 2005, I could never have imagined that our foundation could progress and expand so quickly in just four short years. Thank you all for your roles in our continuing success!

During each of our conferences, I am on an incredible high, just being surrounded by all of you. I soak up the positive energy of our group and try to hold on to that spirit all year long. Thank you all for your enthusiasm and passion for our shared cause. Together in the fight, whatever it takes! I miss my "PSC family" members greatly! Here's to good health for everyone!

Ricky Safer
President

Ricky and Don Safer,
founders of PSC
Partners
Seeking a Cure.



2008 Conference photo album



Winston Hewitt, MD, transplant surgeon at Mayo Clinic Jacksonville, explained the surgical consult for possible transplant.

Musette Morgan, of the Morgan Foundation, accepts \$20,000 from PSC Partners to support the STOP PSC initiative.



David Rhodes received a memento of the golf tournament, a caddy vest from Caddies for a Cure.



Dr. Dennis Black, of STOPSC, explained how the genetic database will assist in understanding PSC in adults as well as children.



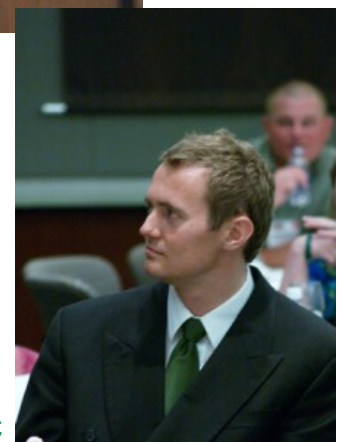
Shelly Hussey, humorist and author, as well as a PSC caregiver, entertained on Saturday night and proved that laughter really is the best medicine.



Lee Bria and Joanne Hatchett announced the successful conference fundraising results, close to \$90,000.



Dr. Tom Hemming Karlsen, of Oslo, Norway, the 2007 AALD prize winner, discussed research on PSC genetics.



We never ran out of something good to eat.





The 115 participants represented all ages and stages of life.

Dr. Greg Gores, of Mayo/Rochester, is an expert in cholangiocarcinoma.



Friday morning's pre-conference cruise on the St. John's River was a peaceful and educational event.



Dr. Michael Picco, of the Mayo Clinic, reviewed the relationship of IBD to PSC.



Chuck Cooper, a founder of Hoops for Healing in Ohio, related the story of the foundation that supports PSC research and organ donation.

Smiles from Joanne and Steve Grieme and Kathy Menuz.



Thanks, Sponsors!

We would like to thank our sponsors for making this weekend possible:

- Cordis Corporation - Platinum level sponsor
- Astellas Pharma - Silver level sponsor
- Axcan Pharma - Bronze level sponsor
- Roche Pharmaceuticals



Conference Session Summaries

by Ivor Sweigler, Chairman of the UK group, PSC Support

Ivor attended the Jacksonville Conference on behalf of his organization and graciously offered us his summaries of the proceedings. These proceedings also appear in that group's newsletter, PSC Support News, which is available by subscription at pscsupport@aol.com. The newsletter is not written by medical personnel and readers are advised to seek their doctor's advice concerning any changes in their treatment. The following summaries are written from a layman's understanding.

Dr. Gregory Gores: Cholangiocarcinoma

Dr. Gores was the keynote speaker at the conference and is a pioneer in the treatment of cancer of the bile ducts, cholangiocarcinoma (CC).

Cholangiocarcinoma is something that we all fear because it is very difficult to treat and by the time it is found it may be too late. Dr. Chapman (UK) is still saying that about a third of all PSCers will get it (1) although in his own clinic the figure is much lower. He thinks this may be a consequence of the fact that he's been prescribing high-dose Urso for many years.

Dr. Gores says that our life-time risk of getting CC is 8-10 percent. He explained that the problem with this cancer is that it doesn't grow like other cancers. It's not a bump. You can see this on the X-ray. You can't take a biopsy of it. It's really a scarring cancer and it obstructs the bile ducts. It looks just like PSC: like an area of narrowing of the bile ducts. By the time you can see it on an X-ray it's advanced.

So what is CC? What is my chance of getting CC?

There are a number of misconceptions. Dr. Gores sees a number of patients coming from really good doctors across the country and was intent on clarifying this. Your chances of getting CC are probably 8-10 percent in your lifetime. So you should not get a transplant to prevent CC.

When he really worries about CC it is in the first two or three years after diagnosis. After that it is a minimal risk, less than 1 percent annually.

The tumor markers used are not very good (the blood tests for CA19-9 and CEA-125). The specificity is not too good. If the test is positive is it really positive? A simple blood test – it's not specific for CC because, for example, it can go up if you have an infection or for other reasons. How high can it be for me to be worried?

Dr. Gores doesn't really look at it until it goes over 100. The

normal range is 30-40. He gets nervous when it goes over 130. People in Pittsburgh have looked at this: 130, 150, 180.

[There are some contradictory features here. Some of the literature suggests that the longer you've had PSC, the higher the risk of CC but not according to Dr. Gores. He also later told Joanne Grieme that the CA19-9 readings can vary by as much as 20-30 points a day. Ivor, Editor]

PSC, inflammatory disease of the bile ducts, is a lot like colitis, inflammatory disease of the bowel. We don't know if Urso works. If you have IBD Urso probably reduces the risk of getting cancer of the colon. The Germans think it does. Almost every patient Dr. Gores sees with CC is taking Urso so he is not convinced.

In detecting CC, we also use cytology with brushings (of bile duct cells). Even then it's really hard to diagnose. If you have cancer it's positive in about 80 percent of cases. That's probably acceptable.

Can we improve?

He also uses FISH (2) (Fluorescence in Situ Hybridization) which counts chromosomes, 23 from your mother, 2 from your father, 46. If you have more than that something's wrong with that cell – too many chromosomes have been duplicated—not good. This process shows 50 percent sensitivity – it's not what they would like to see but it's a dramatic improvement. Once we get 5 or 6 cells with too many chromosomes that's all that is needed. If the cytology's positive and/or the FISH is positive and the CA19-9 is very high and there's a dominant stricture, Dr. Gores becomes very worried. And if he sees something on MRI then he's really worried. PT scanning is not useful for this disease, he claims.

Therapies?

There are a couple of approaches which he uses. He can use light-sensitive drugs: place them near the tumor and use a laser beam to get rid of it. This gives the tumor a really good thundering.

This is therapy but not a transplant and this is not a definitive therapy. But he has also pioneered liver transplantation in this situation. He uses radiation and chemotherapy to remove the cancer right up to the time of transplantation. Seventy-five percent of patients treated in this way have survived 5 years or more, a dramatic increase in survival.

[It should be noted that there is a rigid protocol for procedure in terms of age and size of tumor. The tumor must have a diameter of less than 3 cm and there should be no signs that it has metastasized - spread – which it very often does, through the blood and lymphatic systems. Until now the presence of CC has ruled out having a liver transplant. This is because the experience with most patients has been dismal. CC spreads rapidly and the majority of patients have a survival time of months. In a time of increasing organ shortage, priority will go to those who do not have the complications of CC. But several centers are now beginning to follow the Mayo lead. Ivor, Editor]

Footnotes

1 - Chapman R, Cullen S, “Etiopathogenesis of primary sclerosing cholangitis. *World J Gastroenterol* 2008 June 7; 14(21): 3350-3359 (Full text accessed 16 07 08 from www.wjgnet.com)

2 - FISH (Fluorescence In Situ Hybridization): a lab technique to identify structurally abnormal chromosomes. A segment of DNA is chemically modified so that it will look fluorescent under a special microscope. This DNA is a “probe” which can find matching segments of DNA when added to cells. It can detect structural chromosome abnormalities. This can reveal extra chromosomes in CC cells which have been obtained from bile duct brushings. Dr. Gores showed this on the screen. The images showed 3 copies of chromosome per cell. There should only be two and they were therefore abnormal, indicating that they were cancerous.

Dr. Jaime Aranda-Michel: Lipids and Bone Disease/Nutrition for PSC

Much of what Dr. Aranda-Michel said applies to advanced stage PSC, especially Stage 4, PSC with cirrhosis. A liver patient with cirrhosis can still be stable for many years but you can get complications of cirrhosis and DECOMPENSATION (1) of the liver. You also have to be aware of the possibility of high levels of cholesterol with possible cardiovascular risks.

All liver patients, regardless of the type of liver disease, are prone to have bone disease.

There are many potential complications, which can also affect the eyes and bones. It is quite frequent for symptoms to involve deficiency in Vitamin A. This is the third most common vitamin deficiency worldwide. About half a million people go blind because of this every year. Skin problems, involving thickening of the skin, may develop. You can also have muscle wastage.

There may be Vitamin K deficiency which affects clotting factors, causing bruising and easy bleeding. Vitamin D and calcium deficiency leads to bone disease. Even with plenty of sun (you can get Vitamin D from sunlight), in some warmer US states you can still find Vitamin D deficiency because of the use of sun protection creams.

Bone Density

You can measure bone density with a Dexa scan. But we're not very good at measuring bone quality. You can find patients who get bone fractures although they have normal bone density. So it's a lot more than just measuring with a Dexa scan. The bones are living tissues and go through different cycles of regeneration.

Osteoblasts (bone cells) produce mineralization to make bones strong. This process takes about three months, involving calcium and phosphorous. Genetic factors are important here; families with a history of bone disease.

Environmental factors and lifestyle also play a part: smoking, drinking, lack of exercise. And then there are the side effects of some medicines (like prednisolone, commonly used in treatment of colitis). Hormones are also involved.

Diagnostic tools

The bone structures may collapse resulting in fractures. X-rays can be taken and we need to make a diagnosis and then, if necessary, treat. We can use a simple tool – we can measure the spine, the hip etc. We can even measure the total body. That will give you a score, the T score. A negative score implies that you have lost a substantial amount of bone – osteopenia – early bone disease. And you can measure the calcium (2).

Treatment

Treatment involves trying to prevent further complications. With the aging process the T-score becomes more negative and the quality of bone worsens, irrespective of any liver disease. All liver patients,

regardless of the type of liver disease, are prone to have bone disease.

Malnutrition

Malnutrition is common but infrequently diagnosed. This is because there's greater concern with more serious life-threatening symptoms like varices, ascites, etc. You can have malnutrition for a long time without any apparent consequences.

The degree of malnutrition correlates closely with the severity of the liver disease. The problem is it's multifactorial and it's not a simple matter to get figures.

Often with cirrhosis you lose your appetite and you don't want to eat. This is connected with maldigestion and malabsorption – with the lack of bile flow. Chronic anorexia can develop: starvation, breakdown of muscle, and muscle wasting--which can be profound. Loss of weight occurs (also can be a consequence of colitis) and a lack of glucose.

Dr. Michel first gets to see this when the family tells him that the patient doesn't eat breakfast. You require fat and bile acids and need to eat snacks throughout the day. Eighty percent of patients awaiting a liver transplant have malnutrition (i.e., those with advanced liver disease).

You should have a sodium restricted diet – a diabetic type diet and **DON'T REDUCE PROTEIN – THAT IS A MISTAKE.** Take multivitamins and aggressively measure Vitamin D. You'll probably need a high dose plus calcium. There is disagreement on what is normal. This is still controversial.

What can you do?

First, be aware. There are various drugs available to treat bone problems. Don't stop doing weight-bearing exercises: get up and walk. A combination of different types of exercise is useful. Patients with cholestatic liver disease have malnutrition until proven otherwise.

Anorexia can be a major problem. Dr. Michel looks for malabsorption and for deficiency of Vitamins A, D, E and K. Some companies produce a pill which contains all of these fat-soluble vitamins.

Footnotes

1 - Decompensation: As we know, the liver is remarkable for its ability to repair itself and "compensate" for damage done to the liver cells but when a liver in advanced disease suffers too much injury it loses its ability to regenerate and decompensation occurs. You may then suffer from encephalopathy (mental confusion), bleeding varices, ascites, jaundice, etc.

2 - T-score : A bone mineral density measurement. It is the number of standard deviations (SD) from the young adult mean. The WHO defines normal bone density to be within 1 SD of the young adult mean, which is one. Thus osteopenia is defined by a T-score between -1 and -2.5. Osteoporosis is less than -2.5. Most patients will be elderly in this category.

Dr. Dennis Black: The Morgan Foundation and the STOPSC Program

Musette and Alan Morgan are fundraising and organizing a major and very important research initiative through the Morgan Foundation. The Foundation was sparked when their now-teenage son was diagnosed with PSC. He is currently doing well. The study they are funding includes adults and children. The major goal is to create a data and specimen storehouse and to make this information available to other researchers. Dr. Dennis Black, study chair of STOPSC and co-director of the Morgan Foundation, gave a presentation on the STOPSC Genetic Database. The number of medical centers involved in the endeavor has now reached 20 in the US and Canada.

The specific research objectives of STOPSC are:

- To identify risk factors, including genetic and environmental factors, in the development of PSC and to understand how PSC starts and worsens.
- To identify the role genetic factors play in the development and treatment of the disease.
- To help develop diagnostic tests and approaches that can diagnose the disease in its early stages, as well as indicators for the severity, progression and response to treatment of the disease.
- To evaluate and compare the effectiveness and safety of various treatments of PSC.
- To collect information that will help characterize the disease and clarify the relationship between childhood and adult forms of PSC.
- To study the natural history and clinical course of the disease in children and adults.
- To better understand the relationship of PSC with associated diseases such as autoimmune hepatitis, and inflammatory bowel disease.
- To identify risk factors and bio-markers for the development of cholangiocarcinoma.
- To develop and test models which predict patient outcomes (cirrhosis, portal hypertension, cholangiocarcinoma, death, transplantation, etc.).
- To characterize and follow trends in therapies of PSC.

(from <https://web.emmes.com/study/psc/index.html>)

Dr. Tom Hemming Karlsen: What Can Genetic Studies do for PSC?

When we say we have a genetic predisposition for PSC, and also colitis, what does this mean? This is the question behind the genome-wide research. Not an easy subject to understand with only a rudimentary scientific education which most of us have. But persevere if you want to know what medical scientists are trying to do in current PSC and colitis research. Dr. Karlsen presents as clear an account as you can find on this research.

In general terms, PSC is a complex disease. There isn't just one gene, but a number of genes involved, that act together in a complex way, leading to the clinical syndrome, which we call PSC. We search for variants in this DNA sequence that somehow alters the coding structure of the genes or the expression of the genes in one way or another. There are more than ten million such variants in the genes.

So how do we do this?

This is based on very fundamental questions for genetics. Those many variants that we find in the human genomes are somehow linked to each other. We look at various genetic markers until, at some point we are no longer able to detect them. We hunt through various genetic markers looking for disease-causing variables. We can focus on CC—this has something to do with the HLA complex, a genetic region. There are more than 250 genes and as many as one third are related to immunological functions. In 1983 Dr. Chapman (UK) discovered that HLA-DR2 was found to be closely associated with PSC and some researchers have found other variants (1). The possibility is that PSC has something to do with the HLA molecules themselves. They present small

molecular fragments to the immune system.

If you have particular variants of these HLA molecules, you may be particularly prone to the process that leads to PSC. The variants that are very close to each other are somehow linked and there are likely to be other genes in this region that may be causal to PSC. There is much research in this area.

The most likely scenario is that there are several genes in the region. We are working on this together with a group in Cambridge: and we also believe that associated antigens (2) and auto-antigens are important in the bile ducts.

Finally, we strongly believe that there is a region here which has nothing to do with the HLA complex but which is part of a cluster that acts together with these other genes to cause PSC. And then there are yet more genes that may be fueling this process. This is complex. Then we see (looking at a diagram on the screen) that in this region there are 250 genes. But in the human genome there are 30-40,000 genes.

Couldn't some of these genes have something to do with PSC as well?

Yes, obviously they could. As a consequence of this kind of analysis and these scientific developments there's been something of a rush to develop genome-wide associations.

[This has already led to an important new understanding of Crohn's disease and is influencing treatment. —Ivor, editor]

With this we use microchips and there are a few genetic markers. We try to find particular genetic regions of the genome where there is increased frequency of particular

genetic variant among PSC patients

HLA complex is important to PSC

There is a conceptually very important problem here and that is we are performing very tiny statistical tests and there are half a million genetic markers. There is a huge excess of associations. If we remove more genetic markers that have something to do with HLA, then suddenly almost all of these excess markers disappear and this astounded us.

So what we can say now, from looking at these features, is that the HLA complex is THE most important factor in PSC.

But is something else going on here?

We then proceed in a manner, which all genetic studies should do: test our findings on the population. We have our original study population of 289 patients and a similar control group, and we take their DNA using these markers. Some of these markers produce no results. Some of them were positive in the Swedish group but not the Dutch and vice versa. But the gene we found to be positive in the Dutch, Swedish, and Norwegian patients, which meant that this wasn't just chance, was a gene located in chromosome 13.

This is where the problem starts: because this new gene called GPC is something we know almost nothing about. We don't know what it does. This illustrates an important finding.

What this shows us is that this is not a conclusion; it is only the starting point. We must therefore do further studies.

We have also been studying ulcerative colitis (UC) and there we have a very different situation. We

followed a similar path with over 1,000 patients. We found a particular gene which is implicated and which we know a lot about. People with this gene have double the risk of UC. But to find this gene you have to do a combined analysis using 10,000 patients, with 10,000 controls, to be able to pinpoint it correctly. We have also been looking at cholangiocarcinoma and trying to identify those most at risk.

In conclusion we see that we are not yet able to produce conclusions. We are identifying biological processes which are related directly to disease and this underlines the need for collaboration between institutions for the research of such a disease.

We may not yet be able to treat PSC but with the understanding of the biological processes in the progression of liver fibrosis, treatment will become more effective in the future.

Footnotes

1 - HLA Human Leukocyte Antigens: A group of genes on chromosome 6 that code for the antigens that determine tissue and blood compatibility—obviously important in transplantation. HLA may mediate auto-immune disease. (A book which is ten years old but chapters are accessible on the internet is "Autoimmune Liver Diseases, E L Krawitt et al. 2nd edition. 1998, Ch 5, "The pathogenesis of PSC." S A Mitchell, R W Chapman ISBN: 0444828036)

2 - Antigens are substances that can trigger an immune response resulting in the production of antibodies as part of the body's defense.

Dr. Tom Hemming Karlsen: The Norwegian Research Fund

In a chat with Dr. Karlsen in the break after lunch, he provided me with more precise information on recent PSC philanthropy in Norway, for which I am grateful.

The donation in sterling terms is £10 million to which the Norwegian Government is adding £2.5 million. This will be distributed over 10 years at £1.25 million annually.

The management of the team has been planning not just to collect DNA samples from PSC patients, but also bile and biopsies from transplanted patients, as well as material for molecular studies and other tissues.

The philanthropist, Stein Erik Hagen, first approached the liver unit at the State Hospital in Oslo and simply asked them how much they needed for PSC research.

At first they were taken aback by the generosity of the donor and were at a loss to come up with a figure. The sum of £10 million was agreed. It appears to have been a notional or arbitrary figure. It could obviously have been more or less.

The general response in Norway has been mixed. In one of the most egalitarian societies in Europe many people wondered why so much money should be given to research a disease which is a very rare complaint suffered by a very small patient population. No doubt an element of envy is also present in such situations.

Dr. Karlsen explained that research into PSC has much wider implications for research into liver disease in general, autoimmune disease, and cancer.

The Norwegian group will direct a large European program for the study of PSC, involving patients in all Scandinavian countries, the UK, and Germany.

The genome-wide study of even 1,000 patients is not thought to be enough and it is hoped to multiply this several-fold.

Even such a widespread effort has limitations and may reveal only fragments of the truth but it will

result in better treatment and care of patients and bring us closer to the cause of PSC.

It was good to see such a young PSC researcher (he's 36). Such doctors will be urgently needed to replace the older researchers most of whom are not very far from retirement age. Dr. Karlsen is also the first to receive the \$3,000 award from PSC Partners Seeking a Cure, the aim being to encourage young liver specialists to research PSC. We need more Dr. Karlsens as well as Stein Erick Hagens!

An Advisory Board has been established for the new PSC Research Centre, the only research unit in the world exclusively concerned with the study of PSC. Professor Erik Schrumppf is the Director and the Management Team also includes doctors Kirsten Boberg and Tom Karlsen. This development crowns 25 years of PSC Research at the Rikshospitalet, Oslo.

Six research areas will cover: genetics of PSC, cholangiocarcinoma, IBD in PSC, liver transplant in PSC, bile acid toxicity, and autoimmunity in PSC.

It is remarkable what some well-placed philanthropy can accomplish. Oslo becomes the world centre of PSC Research.

Mark your
calendar!!!

Next year's
PSCPartners Seeking a Cure
Conference

Chicago, May 1-3, 2009

Together in the fight,
whatever it takes!

Dr. Winston Hewitt: The Surgical Consult— Surgical Approaches to PSC and CC

Dr. Hewitt is Assistant Professor of Surgery at Jacksonville. But he didn't speak a great deal about surgery: he went over much of the ground covered by Dr. Gores but some of this is worth repeating for greater clarity.

Surgery has a limited role

The surgical approaches to PSC, as well as cholangiocarcinoma (CC), are really interrelated. From the surgical standpoint we are frequently asked to evaluate dominant strictures and other suspicious areas in the liver. Apart from liver transplantation, surgery has a relatively limited role in the management of PSC. Surgery will not alter the course of PSC. He then went over some of the familiar details of PSC which it isn't necessary to repeat.

Detecting tumors

The surgeon needs to know the results of the procedures for detecting tumors: FISH and brush cytology. You're looking for abnormalities in the chromosomes. You take what looks like a tiny wire brush and brush the bile ducts, take the cells and smear them on a slide. The cells are digitized to produce a digital image. This is then analyzed and compared to normal cells. With FISH you look for fluorescent abnormalities present on the cell and these would be indicative of cancer.

With all this information it's still not as simple as you might think to establish the presence of CC.

In PSC the dominant strictures will present with abnormalities which are not carcinomic, but now you're able to define the location of the dominant stricture or carcinoma as well as whether it has spread beyond the liver. The resectable possibilities of the liver depend on whether the tumor has invaded the surrounding veins in that area and other surrounding structures (stomach, colon, etc.). If it has, the liver is non-resectable for CC. The surgeons then plan according to the location of the tumor. There are various staging criteria for CC: those without cirrhosis, how much the right and left hepatic ducts are affected, etc.

Recent success of liver transplant for CC has been changing the paradigm. Many centers have not yet accepted the utility of liver transplant for CC: 25-30 percent of patients will be ruled out because it is found that they have small metastases (i.e. spreading cancer) on the lining of the inside of their abdomen wall which were not appreciated beforehand, when they were considered appropriate patients for transplant.

The goal is to remove the cancer entirely as well as any surrounding tissue involved. The gallbladder is removed and it's clinically important

What attendees said about the conference . . .

The presentations were all wonderfully useful, scary as usual, but not to be missed. We all need to review our knowledge regularly, even though it hurts again to do so. It helps us make sure we are doing everything we need to be doing to cope and move on. We absolutely loved the networking time and arrangements. It was so helpful.

&

I didn't know what to expect and I found everyone to be so warm and welcoming. The conference was very well run and I was impressed.

&

SPEAKERS WERE VERY
INFORMATIVE AND
EXCELLENT PRESENTERS.

&

**It was a conference
with soul.**

that the bile duct margins that you're leaving in place do not have evidence of tumors under the microscope.

Apart from these concerns OLT (cadaver liver transplant) is the only established long-term treatment for PSC for patients in end-stage liver disease. Long-term results are excellent. At one year post-op, survival is 90 percent. Around 10 percent of all liver transplants are for PSC patients. As with most liver diseases there can be recurrence of PSC in the liver graft. It may affect as many as 20-40 percent long-term (it usually returns, however, in milder form).

In summary, surgical procedures will not alter the course of PSC. Percutaneous and endoscopic interventions have supplanted much surgery. Surgery, apart from transplantation, is reserved for complications, e.g., suspicious strictures, cholecystitis (acute chronic inflammation of the gallbladder). Cirrhotics are best served with liver transplant. In CC, surgical resection remains the gold standard therapy. But the protocol is strict and most patients will not be surgical candidates.

The treatment protocol for CC in PSC involves the latest procedures in the eradication of cancerous cells:

- External beam radiation therapy brachytherapy (inserting radioactive material into the growth or into neighboring tissue)
- Staging laparotomy (in which the abdomen is opened for surgical treatment)
- Capecitabine (an anti-cancer drug found to be effective in treating several cancers including metastatic breast cancer)
- Liver transplant

Order Your Copy of 2008 Conference Presentations at:

<http://www.pscpartners.org/CD2008.htm>.

A huge thank you goes out to Arne Myrabo for creating the 2008 conference website and to Dave Rhodes for creating the 2007 conference website!

... about the conference ...

I feel that coming away from the conference there has been a huge weight lifted off my shoulders. Before the conference, I seemed more focused on what I thought the disease would not allow me to complete. However now, I feel like all the doors are back open even though life will be more of a challenge than for the average person.

&

As a first time attendee, it was comforting and educational sharing and learning what possible future changes to expect.

&

Excellent conference. Our level of awareness has increased tremendously. The conference was very positive, upbeat, funny, and very hopeful.

The 20-30 Somethings

FOCUS ON YOUNG ADULTS AT THE MAYO CONFERENCE

by Jecy Belmont, a 20-30-something, who lives in Connecticut.

At the conference this year there was a 20-30-year old discussion group. The object of this group was to give those who are dealing with PSC in this age group a climate in which to vent their problems, concerns, and questions to their peers. Often times there are different problems that concern this age group. They include questions such as social interaction, dating, alcohol, when to tell a significant other about PSC, and questions of this sort.

It was nice to see new faces to the conference in the group and a wide range of ages from 18 to late 30's, and some came from as far away as Sweden. The members of the group quickly found each other even before we went into our breakout sessions and friendships were formed immediately.

During the lunchtime breakout session on Saturday many questions were asked of Dr. Gores, many of which seemed to deal not so much with the physical problems associated with PSC but the psychological ones that go with being young and diagnosed with the disease. Dr. Gores reinforced the idea that you must continue to live your life and not to let the disease run your life for you.

During the lunchtime breakout session on Sunday we discussed many of the issues we deal with as young adults handling PSC. People shared their ways of dealing with fatigue, itching, alcohol, medications, social situations and other concerns when it came to friendships, work, insurance, love, and life in general.

The conference was a great success, especially for those of us in the young adult group. We made bonds and became fast friends. A Facebook group site was started to help us stay in touch with each other. We all look forward to next year's conference, hoping to expand on our group size.

More Details of Conference Presentations Are Online

We are pleased to announce that courtesy of web-hosting by PSC Partners Seeking a Cure, the 2008 and 2007 PSC conference websites are now available.

If you attended the 2008 or 2007 conference, you will receive an email providing you with the URL, username and password to access these websites.

If you are a non-attendee and would like to send in a \$10 donation to access a website, please go to our website at <http://www.pscpartners.org>, click on Conferences and then on Conference content online.

Financial Report of PSC Partners Seeking a Cure

Following is an update of the current financial position through May 31, 2008 of PSC Partners Seeking a Cure Foundation.

--Total net income for 2008 through May 31 is \$84,164, compared to last year's annual total of \$143,684.

--YTD donations are \$11,745 compared to a total for 2007 of \$63,821.

--Fundraising projects have raised \$66,460 YTD, compared to \$69,679 in 2007.

--Total raised since the PSC Conference 2007 for the Road to Jacksonville was \$89,128.

--Total assets through May 2008 are \$368,504, an increase of \$84,201 from Dec. 31, 2007.

As always, please direct any questions/comments to Deborah Wentz, Treasurer at debs_3@charter.net

“The Power of Humor” Brought Down the House

Author and caregiver Shelley Hussey’s presentation at the PSC conference on Saturday night was so hilarious that, due to our own raucous laughter taking up so much time, Shelley was unable to share the more informative points of her “laughter lecture.”

This article is the first of two in which Shelley seriously discusses humor and healing. In the next issue we will print her ten steps for developing a sense of humor.

Laughter’s Health Benefits

Laughter is so therapeutic. It releases brain chemicals called endorphins that promote a feeling of well-being. Laughter also relaxes and unwinds your stress knots, lowers your blood pressure, strengthens your immune system, and improves your circulation.

Laughter studies show that laughing can relieve allergy and arthritis symptoms, increase memory retention and creativity in the workplace, lessen pain from chronic diseases, and strengthen the immune system. Interest in humor’s effects has grown so much that the field has a name—psychoneuroimmunology; the study of how psychological factors, the brain, and the immune system interact to influence health.

Norman Cousins wrote in *Biology of Hope* that ten minutes of belly laughter (just counting the laughing time) would give him two hours of pain-free sleep. The reason laughter relieves pain is because it produces endorphins, one of the body’s natural painkillers.

Laughter is by no means a cure-all for illnesses, but some researchers say that people who laugh are less likely to get sick. Lee Berk, a pioneer in laughter studies and associate director of the Center of Neuroimmunology at Loma Linda University School of Medicine, maintains that laughter beefs up the immune system. In his 1989 study, published in the *American Journal of Medical Sciences*, he found laughter reduces blood levels of cortisol, epinephrine, and other substances which, when at high levels, tend to suppress the immune system. Decreasing these levels is believed to be beneficial.

Research has shown that laughter boosts immune function by raising levels of T-cells, Gamma-interferon, and B-cells that fight disease and infection. Laughing also forces moisture from the lungs so they don’t harbor disease as much. There are secretions in the tears that only happen after

laughter that clear the eyes. Laughing even raises your energy levels and body temperature.

Laughter’s Workplace Benefits

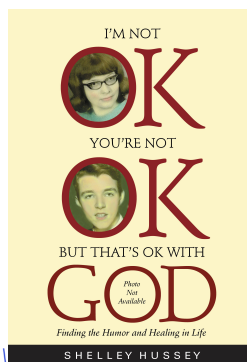
You need laughter for creativity especially in the workplace because it fully engages the brain. It’s also a great team-building tool; encouraging better communication.

Laughter’s Social Benefits

Humor draws attention away from the source of discomfort. Laughter is just good for our psychology because people regress to a childlike state and, socially. . . it’s contagious. It’s been called the universal language because no matter what language you speak, if people are laughing you can laugh with them. Humor is a coping tool that can minimize our suffering by giving us power in a powerless situation.

Robert Provine, a behavioral neurobiologist at the University of Maryland, found that laughter functions as some kind of social signal. Studies have shown that people are 30 times more likely to laugh in social settings than when they are alone, in the absence of pseudosocial stimuli like television. Even nitrous oxide, or laughing gas, loses much of its potency if taken in solitude.

Says Willibald Ruch, a psychologist at the University of Dusseldorf: “To many researchers, laughter is about strengthening social bonds. Laughter occurs when people are comfortable with one another, when they feel open and free. And the more laughter, the more bonding within the group. This feedback ‘loop’ of bonding-laughter-more bonding, plus the desire not to be singled out from the group, may explain why laughter is often contagious—dramatically so. In 1962, for example, an epidemic of laughter among schoolgirls in Tanganyika lasted for six months and forced officials to close schools.”



Shelley Hussey is the wife of Fred, PSC, 03/04 and the author of *I'm Not OK, You're Not OK, But That's OK With God*. Email: shelleyhussey@bellsouth.net for ordering information; \$7.50 per book is being donated to PSC Partners Seeking a Cure.

MY WORDS, MY STORY

What Attending the Conference Meant to Me

by Rachel – mother of a PSCer

Medical alerts had been my connection to PSC. Words flying at me, cruelly erasing the hope I felt with each click on a new article, heartless, injurious statements that showed no compassion – that had been my world of PSC. Searching the internet, I discovered a different world through a name I could write to. Ricky Safer's. A series of exchanges with Ricky led me into a new direction. My husband and I were no longer alone in our quest.

The intensity of my mission, though pursued in solitude, was no different than the mission led by this special person and all the names she brought along with her. I sensed that along with Ricky stood a group of special people who were deeply connected to each other with a sense of solidarity, with compassion and a desire to help each other.

For several months, I cherished the window opened to me by Ricky. Then arrived the Jacksonville conference. Instantly, our story became one of many stories, and surrounded by the warmth of people who generously welcomed us among them, in no time, we felt fused into this tight community through ties that I could not describe to anyone outside. It was not about discovering other stories. It was about being pulled in by the kindness and openness of the PSC family, and surprisingly, by the hopefulness that this powerful group generated in me.

Regardless of how distant a definitive cure may be, and though medicine does not announce anything new, the feeling that Jacksonville produced in me was one of palpable hope. At the vertiginous speed science is moving, I was filled with faith that our fearless and enlightened PSCers and caregivers would witness a solution coming from a most unexpected source.

We all belong to this group of the selected few – the intensity in Room 1007 in Mayo, Jacksonville, the room filled with those wearing the blue dots (the caregivers) was no different from that of Room 1006, the red and green dots (PSCers and transplanted PSCers), and the same passion wove through each one of us *listening* to those committed researchers. As heavy as it all is, the knowledge that each of us will make a difference in one way or another fills us with strength and hope.

We feel privileged to be part of this incredible group.

The Newsletter's New Look

I'm sure you've noticed the new look and feel of our newsletter, beginning with our moniker, *The Duct*. For the first four years of our existence, our amazing guru Dave Rhodes has been in charge of the newsletter. We have all looked forward to each fantastic newsletter edition, but now Dave needs more time to focus on the PSC Literature site, writing our new brochures, and keeping track of PSC research internationally. As luck would have it, Pat Bandy of Maryland, joined PSC Partners Seeking a Cure at the right moment, and she has kindly agreed to take over Dave's newsletter position. Dave is a very hard act to follow, but I know that Pat will do a great job. Pat is an energetic and talented post-transplant PSCer with a passion for helping others. She's also had a long career in nonprofit publishing.

The center of our newsletter will still be Dave's scientific and research articles, but in addition, we would love articles of a personal nature written by our PSCers and caregivers. Please feel free to send in an article of any length, a poem or a drawing on any topic related to living with PSC. You, our members, display diverse backgrounds, talents and expertise, so if you share your thoughts with us, it will enhance the value of our newsletter. Please submit articles, questions or suggestions to newsletter@pscpartners.org.

If you would like to be notified each time that a new edition is ready, please go to our website at www.pscpartners.org, click on Newsletters and then on Join our Mailing List.

I'd like to thank Pat Bandy for all the planning, organizing, and writing that has gone into the creation of this new edition. Together in the fight, whatever it takes!

Ricky Safer

Note to Readers:

Articles in this newsletter have been written by persons without formal medical training. Therefore, the information in this newsletter is not intended nor implied to be a substitute for professional medical advice.

Please consult with your doctor before using any information presented here for treatment. Nothing contained in this newsletter is intended to be for medical diagnosis or treatment. The views and opinions expressed in the newsletter are not intended to endorse any product or procedure.



PSC Partners Seeking a Cure is a 501(c)3 nonprofit foundation that endeavors to find a cure for Primary Sclerosing Cholangitis.

The three-fold purpose of the **PSC Partners Seeking a Cure** foundation is to: raise funds for research on the causes and cures of PSC, promote PSC and organ donation awareness, and provide education and support to PSC patients and their families.

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

Tax-deductible donations can be sent to: PSC Partners Seeking a Cure, 5237 South Kenton Way, Englewood, CO 80111 with a check made out to: PSC Partners Seeking a Cure.

PSC Partners Seeking a Cure Board Members

Dike Ajiri, Lee Bria, Dr. Gregory Everson, Joanne Grieme, Chris Klug, Beccy Long, Scott Malat, David Rhodes, Ricky Safer, and Deb Wentz

The Duct Newsletter

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PSC Partners Web site

<http://www.pscpartners.org>