

The Biliary Bulletin

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Primary Biliary Cirrhosis (PBC) is an autoimmune disease which affects the liver and for which there is no known cause or cure. This newsletter communicates news and information to members of the Australian PBC Support Group and other sufferers of PBC.

From Rosemary

Dear Friends

I hope you are all as well as possible and not feeling the cold too much.

At the end of this year, Jocelyn and I will have been working for the support group for almost five years. A lot of time and hard work has been put in to keep the group running, but we both agree that we need to reclaim our lives in the near future - so from the end of this year unfortunately the support group will not continue to run.

I am sure you will all agree that so much has been achieved for PBC sufferers in Australia. We have brought more awareness of PBC, we have provided information and support and we have involved doctors in meetings so that patients have been able to understand their condition more easily.

We have helped bring people together, providing contact lists so that people can, if they wish, be in touch with others who have the same illness - so much better than being alone.

We were involved in helping to make Ursofalk accessible through the Pharmaceutical Benefits Scheme, so much better than having to travel to the hospitals to get our medication.

The Biliary Bulletin has been a huge success, thank you to Jocelyn and John who have done a wonderful job providing us with an excellent, informative newsletter.

I know the BB will be missed very much.

I am proud of what we have done, for me it has been a most worthwhile and rewarding experience, but due to the amount of time and work involved I feel that the time has come when I have to give more time to myself and my family.

I have plans, things to do and look forward to, which I could not possibly do if I continued to work for the group.

I know that many of you will be disappointed with the decision not to continue, but I hope you will understand.

Thank you once again to all those kind people who have donated so generously to our group. Funds remaining in the group at the end of the year will be donated to Liver Research; if any one is not happy with this decision please contact us.

IN THIS ISSUE

1	<i>From Rosemary</i>
1	<i>Chadstone Gathering July 27th</i>
2	<i>Member Profile</i>
2	<i>From the Editor</i>
3	<i>Identification of New Molecules in PBC</i>
3	<i>UK Centre Plans to Begin Liver Cell Transplants</i>
4	<i>PBC – Problems Outside the Liver (2)</i>

Many of the recent telephone calls I have received have been about the dreaded itch. Please look back at the Autumn edition of the Biliary Bulletin - PBC and Pruritus, there is lots of information in this excellent article.

It is still disappointing to find that some people are not being put on Ursofalk when diagnosed. If your doctor is not prescribing Ursofalk for you because of lack of information, please let me know.

There will be Christmas cards this year, thank you to Gloria Lahn for taking over this job for us. You can start to order now, just phone me.

I look forward to seeing many Victorian PBCers at Chadstone on July 27th.

Keep well and positive,

Rosemary.

Chadstone Gathering July 27th

Make a note in your diary to be at Zampellis, Chadstone, on Saturday 27th July at 12.30 for a stimulating and fun lunch with lots of other PBC buddies. We usually take over a portion of the upstairs section and it is a bit like having our own function room.

As this will probably be our penultimate gathering before the group disperses, you may not get another opportunity to gather and exchange information with other PBCers.

There are many "end of winter" sales at about this time, so you could combine lunch with some essential bargain hunting and have a really good day!

Bring your family and a smile – just be there.

Jocelyn.

Member Profile

Sylvia Freak

Hi Rosemary,

Well you asked for it so here goes:

My name is Sylvia Freak and I emigrated from England 32 years ago. I was diagnosed with an Underactive Thyroid 21 years ago when my second child was 10 months old. I just thought I was tired because of being a mother of two and was very relieved to know there was a medical reason why I was putting on weight and felt like a slug most of the time.

I was a very proud blood donor for many years having A Rh Negative blood, until September 1994 when the Blood Bank sent me a letter saying they could no longer accept my blood because for the last two donations my blood had tested a positive result to the Hepatitis C virus, but, when screened on a more specific supplementary test it then tested OK. So with the cost of quarantining my blood and retesting, it was decided they could no longer accept me as a blood donor.

I had never been sacked from anything, not a job or any organisation and here was the Blood Bank thanking me but saying no thanks. Anyway upon their advice I took the letter to my GP who looked at it and told me not to worry, these things happen!!!

I have never had much stamina and had always blamed this on my Thyroid problem even though I was on Thyroxine, but the tiredness remained even though I was a busy Mother of 2 and wife of 1 very patient hubby.

At this time I was working full time and our Company was going through many changes with a new Computer System being installed. I was working very long hours for week after week, so of course felt tired and worn out all of the time, until the crunch came and I knew I couldn't go on.

I had hit the wall and knew if I didn't give up work I would probably have a break down. My husband was totally supportive and after much crying and soul searching I handed in my notice. Even after I left work I felt totally exhausted and the stress was washing over me, but being the independent person that I am I decided I should try temping, that way there wouldn't be any stress. This lasted for about 3 months, by this time I was literally dragging my body around exhausted and gave up work entirely.

As I am now 50 years old, my enforced retirement had come a little sooner than I had planned, but sometimes we don't have a choice and at that stage I didn't. In July 1998 I received another letter from the Australian Red Cross advising me that they had improved their testing facilities and inviting me to donate.

I was so grateful to be reinstated that I happily gave blood, but again a letter came advising me that an additional test which is always done at the same time is to assess liver function and mine was not within the normal limits.

The liver enzyme ALT was elevated to 94 u/l (normal range is less than 45 u/l) and I was advised to see my GP. My previous doctor had died so I took the letter to my new GP along with the first letter, she advised I have an ultrasound done and then referred me to a Specialist Gastroenterologist and Physician.

So since 1998 after having a Liver Biopsy and being diagnosed with PBC I have regularly visited my Specialist. He only has 2 patients with PBC, the other lady is elderly so isn't on Urso, but luckily he put me on URSO straight away. To date my results are again showing Normal, having been up and down and when I try to tie my Doctor down as to Stages of PBC he has said I am in the early stage.

I know I should be grateful to be in the Early Stage, and the Doctor said I could possibly live with this and die of something else in 20 to 30 years, not bad eh, however the fatigue and nausea still haunt me and I have noticed other things like swelling of the abdomen, that lovely 6 month pregnant look, without the baby, heaven forbid been there, done that.

So now I never touch alcohol - I was only a rarely social drinker - and try to look after myself on the bad days. It's hard to sort out what is causing what symptoms, do I feel like this because of the PBC? Now I am working again 3 days a week (at the Company I left) but resist the urge to work full time again.

I simply cannot handle any more, and for me this is liberating. I am now feeling that I am once again in control of my life, whatever comes I will handle, be it Irritable Bowel Syndrome or the Asthma or PBC.

One good thing is I have met some lovely ladies due to our get-togethers here in SA. We are never alone and it's nice being able to pick up the phone or check the E-mails, whenever I think I wish I could be better, I try to remember I could be so much worse, so keep as well as you can everyone and thanks for listening.

Regards

Sylvia

From The Editor

I have really enjoyed my involvement with this group over the last several years. The best part has been talking to other sufferers – hearing their stories, helping them to work out ways of dealing with PBC, being able to gather and provide them with information and resources.

If you would like copies of tapes or videos for later reference you will need to arrange that over the next few months, after that they will probably be given to the transplant unit library at the Austin Hospital.

If you have any ideas about the winding up of the group, please ring Rosemary or myself, we would be happy to discuss them with you. Jocelyn.

Identification of New Molecules in PBC

Professor Geoff McCaughan

It is well known that Primary Biliary Cirrhosis is a long term illness as a result of persisting inflammation, damage and scarring to the liver. The inflammation is directed mainly at the small bile ducts within the liver but there is secondary damage to the major liver functioning cells themselves, the hepatocytes.

It has been known for many years that the immune system is heavily involved in this type of damage with recognition of mitochondrial antigens. It has also been postulated that PBC may be caused by a virus and this was discussed in the Biliary Bulletin of Summer 2002, volume 4, issue 1 by Dr Andrew Mason.

We have used modern genomic approaches to explore the damage to the liver in Primary Biliary Cirrhosis. This has led to the screening of approximately 1,000 genes in one single experiment that are expressed within the liver. The findings in our recent paper (GUT 2001;49:565) include identification of novel genes involved in liver damage.

These include new molecules previously thought to be associated with embryonic development, the so called "Wnt pathway" as well as inflammatory and fibrotic genes. The abstract of that paper is as follows:

Abstract

Background – Primary biliary cirrhosis (PBC) is an autoimmune disease in which the pathogenesis of progressive liver injury is poorly understood.

Aim – To provide novel insights into the pathogenesis of PBC related liver injury using cDNA array analysis, which simultaneously examines expression of many genes.

Methods – Utilising cDNA arrays of 874 genes, PBC was compared with primary sclerosing cholangitis (PSC) associated cirrhosis and non-diseased liver. Differential expression of 10 genes was confirmed by real time quantitative reverse transcriptase-polymerase chain reaction (RT-PCR).

Results – Array analysis identified many differentially expressed genes that are important in inflammation, fibrosis, proliferation, signaling, apoptosis, and oxidative stress. PBC was associated with increased expression of both Th1 and Th2 type molecules of the immune response.

Fibrosis related gene expression featured upregulation of connective tissue growth factor and transforming growth factor beta3. Many more apoptosis associated molecules exhibited increased expression, consistent with apoptosis being a more active and regulated process in PSC associated cirrhosis, than in PBC.

Increased expression of many genes of the Wnt and notch pathways implicated these highly conserved and linked pathways in PBC pathogenesis. The observed increases in

expression of c-jun, c-myc, and c-fos related antigen 1 are consistent with increased Wnt pathway activity in PBC.

Differential expression of four components of the Wnt pathway, Wnt-5a, Wnt-13, FRITZ and beta-catenin, was confirmed by quantitative RT-PCR.

Conclusion – Many genes implicated in intrahepatic inflammation, fibrosis and regeneration were upregulated in PBC cirrhosis. In particular, increased expression of a number of Drosophila homologues was seen in PBC (Gut 2001;49:565-576)

We look forward to further and continuing these experiments by repeating some of investigations on isolated cells within the liver, particularly the damaged bile ducts. This work will lead to progressive understanding of PBC as opposed to other forms of liver injury. Perhaps new therapeutic targets at a molecular basis can be developed and understood.

Geoff McCaughan.

Royal Prince Alfred Hospital, Camperdown NSW.

UK Center Plans to Begin Liver Cell Transplants

LONDON (Reuters) Apr 08 - A leading British liver transplant centre said on Monday it would start trials of liver cell injections as a possible alternative to transplantation in children with rare but potentially life-threatening conditions.

"We can start within 6 months," said Dr. Anil Dhawan, of King's College Hospital, London, who is heading the research.

A shortage of donors means around 60 patients die in Britain each year while waiting for a liver transplant, so there is great interest in developing alternatives to transplantation.

Instead of transplanting entire organs, the new procedure involves transfusing only 3% to 5% of the billions of cells present in the liver, Dr. Dhawan said.

Research in animals and reports from other centres provided "reasons for optimism" that the technique would work, he added.

The specially prepared donor cells will be taken from sections of liver not used during transplantation.

They will be given to children with metabolic disorders and may also be used to "buy time" in patients with acute liver failure.

As with organ transplantation, patients would still require immunosuppressive agents.

However, they would be spared the major surgery involved in transplantation and because they would still have their

own liver, they would also be able to take advantage of any future advances in gene therapy.

"It is a very exciting project though it is very much in the early stages," said Catherine Arkley, chief executive of the Children's Liver Disease Foundation, which is helping to fund the project with National Lottery money.

"Long term, the researchers hope to have a frozen bank of liver cells that they can call on when needed," she added.

PBC- problems outside the liver (2) - Metabolic Bone Disease

Dr Katrina Watson

People with liver complaints like PBC can be at risk of 'weak bones'. The technical term for this is 'metabolic bone disease'. It is not really a separate disease, but is a consequence of liver problems.

Metabolic bone disease includes two conditions called osteoporosis and osteomalacia. Both of these conditions cause 'weak' or 'thin' bones and can lead to fractures.

The liver is an important organ for the function of vitamin D. Vitamin D is the vitamin which helps calcium get into the body from food, and helps the calcium get into the bones. The liver converts inactive vitamin D into active forms. If the liver is very sick there can be low levels of active vitamin D.

Apart from abnormal vitamin D metabolism there are other factors that can contribute to 'weak bones'. These include:

- ? poor diet eg. lack of calcium
- ? lack of exercise
- ? lack of sunlight (sunlight is also essential to convert inactive to active vitamin D)
- ? chronic diarrhoea and impaired absorption of calcium and vitamin D (sometimes a problem in PBC)
- ? smoking
- ? family history of osteoporosis
- ? use of prednisolone (cortisone treatment)
- ? infrequent menstrual periods or early menopause

People who are most at risk of metabolic bone disease are those with actual cirrhosis (scarring) of the liver. If these people are going to be candidates for liver transplantation at some stage in the future, it is crucial to keep their bones as strong as possible.

The reason for this is that high doses of prednisolone are used for a period after liver transplantation, and this can further weaken the bones.

How do you know if you have metabolic bone disease?

There are usually no symptoms at all, and the only way is to have a bone mineral density scan (DEXA scan). Many liver clinics arrange this every 1 or 2 years for their PBC patients.

Can I prevent or treat metabolic bone disease?

Yes, you can. Firstly the doctor will look at the results of the DEXA scan and blood tests (for calcium, vitamin D and parathyroid hormone). The doctor may recommend some or all of the following, depending on your results:

- ? referral to a bone mineral density specialist
- ? adequate calcium intake (1000-1200 mg/day). May need to add Caltrate tablets. A single serve of dairy is about 300g of calcium – low fat dairy products are fine.
- ? additional vitamin D intake is sometimes needed (calcitriol tablets)
- ? stop smoking
- ? exercise regularly
- ? sometimes hormone replacement therapy (HRT) can restore menstrual periods, which helps the bones
- ? sometimes a special bone strengthening tablet (or injection) is used. These medications stop the bone destroying cells, and encourage bone-building cells
- ? a little sunlight each day.

Fortunately metabolic bone disease can be prevented or improved in the majority of cases, so that fractures are rare.

Katrina Watson.

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