

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

Here we are, the final edition of the Biliary Bulletin. First I would like to thank those people who have sent cards, emails or have telephoned to express their appreciation for the help that they have received through the Australian PBC Support Group.

I know that many are disappointed that the group will not be continuing, but please remember that you have Contact Lists so there is still no need to feel alone with PBC. So many people are willing to be in touch to help one another so please do not hesitate to use the lists.

For those with computers and online the Oz-PBCers email list will continue to run, also the PBCers Organisation online at <http://pbcers.org> is a great source of support and information - you can join from their website.

Since the last edition of the BB, three of our dear friends have received their new livers. My love and best wishes for continued good progress go to Jocelyn here in Victoria, Marlene and Mary in New South Wales, such wonderful news, may each day get better for you all.

I have many people to thank for their help and support during the time the group has been operating:

Thank you to all the doctors who gave their valuable time to talk to us at our meetings and for being interested in our group.

Thank you to Orphan Australia for their kind assistance with printing our newsletter, and to all the kind people who have donated to our group.

Thank you Jocelyn and John for our wonderful Biliary Bulletin, it has been a pleasure to work with you. Thank you Jocelyn for sharing your knowledge and wisdom, you have been a great inspiration for me and others who have PBC.

Dear Dr. Mackay, what can I say, you have been there from the beginning always ready to help and advise. I don't think the group would have started without you, you promised you would be there for us and I sincerely thank you for keeping that promise.

Gloria, thank you, you did a wonderful job with the sale of the Christmas cards, thank you to all who purchased the cards which sold so quickly this time.

Thank you Debbie and David for having us in your home once again for our final get together on November 23rd.

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Thank you to Bill and my family for your help along the way, folding and getting newsletters ready for posting, not forgetting little ones who loved to stamp the envelopes.

To know that we made a difference for people who have PBC in Australia is very rewarding. I am looking forward now to giving more time to myself and family. I wish everyone a very happy and safe Christmas, keep well and always try to keep positive.

Rosemary

From the Editor

I am very sad to be writing this, the last Biliary Bulletin. The first one was printed in October 1998, in the early days of our group and since then, finding material to publish has been a major focus in my life.

I would like to thank those of you who have been so supportive with positive feedback, letters and profiles etc. and I particularly thank Rosemary for the use of her brain when mine failed, and of course my resident computer expert and "sub editor" John.

I think the newsletter has been very helpful in getting information to our members and hope that this has stirred your desire to do more research and learn more about PBC. Remember that knowledge is power!

Good luck and best wishes to you all, Jocelyn

Member Profile

Doreen Donaldson

First of all I would like to thank Jocelyn for the newsletter that keeps us all informed about PBC and letting us get to know some of the members.

I have just received my Summer Issue of the BB newsletter and Jocelyn said she was short of material and profiles and did not have a profile for the next issue so since we have many new members I thought I would introduce myself, so here goes.

I first went to my GP in 1988 after fainting a couple of times and having pain in the liver region. I had not been feeling well for a long time. When the doctor examined me he found the liver to be enlarged, he then asked me could he ask a personal question which was, "do you drink?" I said yes but just socially, weddings, parties etc.

As you will have all experienced, then came the full gamut of tests, blood tests, bowel, gall bladder and numerous other x-rays. My LFT's were very high (Alk Phos 603) - (GGT 2047) -- (Alt 259), Bilirubin was good only 13.

I was put on Prednisolone 40mg per day, during all the tests I started to experience pain after meals and the burning sensation up into the shoulder and was referred to a surgeon who then booked me in to remove the gall bladder, which is when I had my first liver biopsy.

I was told I had Granulomatous Hepatitis and that I would need a liver transplant within 10 years. When I was first diagnosed with liver disease I was very ill and depressed for the first 2 years and as no support group existed here in Australia at that time my husband and I decided to return to England to be with family and friends for a while, that was Dec 1990. I had another liver biopsy in March 91 which confirmed PBC.

Whilst there, my husband Bill and I got involved in raising funds for the new liver Transplant Unit at the Freeman Hospital Newcastle upon Tyne, which I attended. During that time I met other people with PBC, especially one woman who had a liver transplant just before we left the UK. In returning to the UK and meeting others with PBC, I obtained a more positive attitude and was able to look forward to the future. We then returned to Australia in May 1993.

In October 93 my doctor informed me about a 2-year trial of the drug Urso and as my LFT's were still elevated and the Prednisolone was not helping any more, he decided to put me in the trial and I had to sign permission forms etc. My LFT's did come down but are still high but not extreme like they were.

Having contact with others in the UK with PBC, I was determined to try and find others with PBC here in Australia. I had a story published in our local suburban newspaper and I was also interviewed on a local radio station in May 1994 about wishing to make contact with others that had PBC with the view to forming a support group. I got no response, yet Rosemary lived only around the corner from where I lived, she did not see the article.

We later made contact with each other in September 1996. In May 1998 we began talking about trying to locate other people with PBC Australia wide. Through a list of Gastroenterologists supplied by Jocelyn, (we met Jocelyn and Debbie through the PBC Foundation UK's contact list), Rosemary and I started writing to doctors, Gastroenterologists, local newspapers, magazines, stating our wish to make contact with others with the view of forming the group. We had our story published in the October 1998 issue of the Australian Women's Weekly, and also in the helpline of Woman's Day.

In July 98 we formed the Australian support group for people with PBC. When we decided to form the support group, I wrote to the Doctor in England who was my liver specialist for the 2 years from 1991-1993, for any information about PBC.

He informed us of the support group in England, The PBC Foundation, and also of a doctor here in Australia (who has since given a talk at one of the PBC meetings). The group's first meeting was held in my house in August 1998 and had about 28 people attend.

Literature which was sent to us from The PBC Foundation UK was photocopied (with permission from The PBC Foundation) and given out at the meeting.

I suffer from fatigue and have other autoimmune diseases, last year I had a very large cyst removed from my liver and ended up have 6 units of blood, 2 during my operation and the other 4 when complications set in when I was back on the ward when my blood pressure dropped to 65/45.

I am no longer in 24 hours of pain from the cyst and even though with the complications I am glad I went through the operation. I am now in stage 3-4 and feeling positive, I hope to have a few good years left before I will need a transplant.

It is good to know anyone diagnosed with PBC today in Australia is no longer alone and that medical literature and support is available. I am now involved in volunteer work at our local community centre where I teach computer classes and help on the reception desk. I spend time working on my Web Pages which are dedicated to PBC and I also distribute organ donor forms and booklets to doctors' surgeries, health centres and libraries. I ring each year to get a box of 600 mixed forms and booklets. If only more people could do this it would help to promote organ donor awareness to more people.

For my volunteer work at the community centre I was very honoured to have been nominated for City of Casey Citizen of the Year 2002 and was presented with a framed certificate and a paperweight desk clock for being one of the nominees. I am enjoying life and focused on other things aside from PBC and have learned how to LIVE with PBC.

Best wishes to all,

Take care and stay well (as well as we can with PBC)

Doreen Donaldson

Stages of PBC disease

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Stage 1

Portal Stage

Normal sized triads; portal inflammation, subtle duct damage.

Stage 2

Periportal Stage

Enlarged triads; periportal fibrosis and/or inflammation

Stage 3

Septal Stage

Active and/or passive fibrous septae

Stage 4

Biliary Cirrhosis

Nodules present; garland or jigsaw pattern

Although 4 typical stages of evolution have been defined, the disease initially is focal with considerable "overlap" between stages in any one case.

First is inflammation of the medium-sized bile ducts and chronic inflammation of the portal tracts. Granulomas may be found. With progression of PBC, the portal tracts become distorted, inflammation spreads into the parenchyma, bile ducts proliferate intensely, and periportal fibrosis develops.

Progressive scarring continues with less bile duct proliferation and less inflammation. Fibrous bands link the portal tracts, and zone 1 cholestasis and Mallory hyaline can become evident. The end product is a firm, regular, intensely bile-stained cirrhosis, difficult to distinguish from other cirrhotic processes in the absence of granulomas and the pathognomonic bile duct lesions.

Laboratory Findings

Early findings feature cholestasis with alkaline phosphatase elevated disproportionately greater than serum bilirubin and aminotransferases. In fact, the serum bilirubin is often normal early in the course of the disease.

Serum bile acid concentration and gamma-glutamyl transpeptidase activity are elevated. Serum cholesterol concentration and total lipids usually are increased. Serum lipoproteins are increased, mainly because lipoprotein-X is present.

Serum albumin is normal early in the course of the disease, but the globulins usually increase the serum IgM often to very high values. Antibodies against a component of the inner membrane of mitochondria (in 85 to 95% of patients) are important diagnostically, but they can also be found in some patients with HBsAg-negative chronic active hepatitis, making this differentiation difficult.

Prognosis

The course of PBC varies greatly. It may not diminish the quality or the duration of life. Of patients who present without symptoms, 50% show evidence of liver disease over the ensuing 15 years. Slow progression suggests prolonged survival. A rising serum bilirubin, associated with autoimmune disorders, and advanced histologic changes indicate a poor prognosis.

PBC is one of the best indications for liver transplantation.

Research Project

Funds remaining in the support group at the end of the year will be donated to the Austin Hospital Medical Research Foundation to help finance a research project:

Proposed Study of the Epidemiology of PBC in Victoria 1990-2002

Aims

We wish to repeat the epidemiology study of PBC in Victoria twelve years on. The aims of the study are to:

- 1) Determine whether our original finding that PBC in Victoria is rare is correct.
- 2) To determine the natural history of PBC in our cohort of 84 cases identified in 1990.
- 3) To determine whether patients have received ursodeoxycholic acid, a drug now commonly used internationally in the treatment of PBC, and what effect this has had on outcome.
- 4) To determine the incidence of end stage liver failure and the need for liver transplantation in this group over the period 1990-2002 and compare this with the European data.

We wish the Foundation every success with the project and look forward to seeing the results.

Letter

from Doreen Cheong

Dear Jocelyn

I have just received the latest BB and am so sorry to hear that the support group will not continue but I wanted to thank you and Rosemary for your wonderful efforts. I can only guess how time consuming such contributions from you both were, particularly, Jocelyn when you have been so ill. Both of you have given so much to so many people.

Personally, I am extremely grateful for your caring and support particularly when I was so ill, pre and post transplant. I looked so forward to reading each edition of the BB, from the overall content, to learning how others were coping with PBC, to the more technical contributions. I will miss it. However, I am sure that you are gladdened by the wonderful friendships that you facilitated which I am sure will continue in a much more informal manner.

Doreen Cheong

The Cause of Primary Biliary Cirrhosis

Professor Ian Mackay

When someone hears that they have a serious chronic disease, the likely first question to their doctor is “What caused it, and why should it happen to me?” Causes might not be discussed at length with patients presenting with a chronic disease, particularly primary biliary cirrhosis, because knowledge on causation remains scanty, and covering the various possibilities can be quite time-consuming.

Primary biliary cirrhosis, or PBC, acquired this name around 1950: “Primary” distinguished it from secondary bile duct diseases due, for example to gallstone obstruction; “biliary” signified that the disease affected biliary ductular rather than intrinsic liver cells; and “cirrhosis” signified that the liver became scarred and nodular.

In earlier times, PBC could be recognized only in the later cirrhosis stage, but nowadays many patients are diagnosed and treated much earlier, well before cirrhosis occurs. What happens in PBC is that cells lining the small bile ducts within the liver (ductules) are progressively damaged and disappear, so that bile secretion by the liver fails.

An attempt to explain causes of PBC to enquiring patients might begin with the general belief that it is due to an autoimmune reaction impacting on biliary ductules. Autoimmune diseases, of which there are many, are a catastrophic consequence of the normally protective immune system turning on a tissue of the body itself as if it were a foreign germ. Autoimmune diseases are known to depend on an unfortunate interaction between genes and environment.

In regard to genes, heredity clearly plays some part, since up to 1 of every 20 patients will have an affected relative. Also, there is something about being female that is relevant, since over 9 of every 10 patients are women. However, even in this modern era of high-level genomic research, the actual “disease genes” for PBC have proven hard to identify.

Environment provides tantalizing clues, since there are well recognized areas of high prevalence including Northern Europe, with even high prevalences in particular locations within single countries. Conversely, PBC is quite rare among Asian and African populations. Researchers at the University of Newcastle, UK, have ascertained prevalences in Northern England as high as one in every thousand women aged over 40.

But what exactly is the environment agent that starts the mischief? Dietary habits, water supplies, and environmental chemicals have been “incriminated but not convicted”. Researchers at the University of California at Davis in the USA are conducting an extensive survey in the USA to ascertain unsuspected environmental and life-

style factors in the background of patients with PBC, and results should be very informative.

Possibly, any one of several different environmental agents may trigger PBC, and this is why a comprehensive questionnaire on a large population is needed. Among the “usual suspects” are infections. There is evidence, not wholly convincing, for an unidentified virus, as discussed recently in the Melbourne Biliary Bulletin. Also blamed have been bacteria, particularly *E. coli*, either resident in the intestine or those causing recurrent urinary infections in women. Progress in the environmental direction is hindered because of the lack of a suitable laboratory animal model that closely resembles human PBC.

Whatever the genetic and environmental background, the immune system is very closely entangled with both the origins and the chronicity of PBC. Back in 1958, it was observed at the Hall Institute in Melbourne that the serum of a patient with PBC reacted immunologically with ground-up extracts of human tissues, a surprising finding because, normally, responses of the immune system are strictly limited to external stimuli: there is understandably an embargo on responses to tissues of the body itself.

This embargo, called immune tolerance, gets overridden in PBC, and the result is the production of autoantibodies and an accompanying autoimmune disease. In 1965 researchers in London identified mitochondria, the energy packages of cells, as the target of the autoantibodies in PBC and, even today, the laboratory test for anti-mitochondrial antibody (AMA) remains a cornerstone of diagnosis.

Finally, after much “hunting”, research at the Hall Institute in 1986, based on genetic engineering technologies, led to the identification of the actual molecule targetted by the AMA: this was an important mitochondrial enzyme with the cumbersome name of pyruvate dehydrogenase complex (PDC).

Next, more puzzles and more roadblocks! One puzzle is that mitochondrial PDC is present in every cell in the body, yet the disease itself is focussed mainly on the liver, although sometimes other organs can be affected as well. Another puzzle is to translate how the “start-up” environmental cause acts so as to direct the immune system to react mistakenly against a mitochondrial enzyme in the first place, and then how this reactivity actually damages the small bile ducts and causes them to shrink away.

Finally, to close on a high note. Research, primarily coming from France, led to a major innovation in therapy, namely the drug ursodeoxycholic acid (UDCA), which at least arrests the usual relentless progression of PBC on to liver failure, and the eventual need for liver transplantation. One would think, knowing of a treatment that “worked” for a particular disease, that this would give useful clues on its cause.

Not really! UDCA is known to change the composition of human bile such that it becomes less irritant when it leaks out from damaged bile ducts and, also, it may have some immune-modulating properties. But, unfortunately, we cannot clearly relate the efficacy of UDCA to the general immunological theories on the causation of PBC.

So, in conclusion, it is not surprising that there is some hesitancy by doctors to enter into deep discussions with patients on “causes” of PBC. As to where we stand today, it's like the half-full, half-empty glass. It is pleasing that so much has been discovered in recent decades about a hitherto quite mysterious disease, but disappointing that there is still so much more we need to know. But the present tempo of research around the world into PBC should soon change all that.

Professor Ian R Mackay
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Sourcebook for PBCers

ICON Health Publications has released *The Official Patient's Sourcebook on Primary Biliary Cirrhosis*, a comprehensive manual for anyone interested in self-directed research. Fully referenced with ample Internet listings and glossary. From the Press Release :

“This sourcebook has been created for patients who have decided to make education and Internet-based research an integral part of the treatment process. Although it gives information useful to doctors, caregivers and other health professionals, it also tells patients where and how to look for information covering virtually all topics related to primary biliary cirrhosis, from the essentials to the most advanced areas of research.”

Much of the information relates to the USA, however there does not seem to be a similarly-comprehensive resource for Australian PBCers available. The book is available from on-line retailers such as Barnes and Noble or Amazon, or from the publishers:

ICON Health Publications 4370 La Jolla Village Dr. 4th Floor San Diego, CA 92122

For more information, please visit:

www.icongrouponline.com/health/Primary_Biliary_Cirrhosis.html

Christmas Get-Together

In case anyone didn't get the flyer, there will be a 'final' get-together Saturday 23rd November, at 19 Godfrey St. Bentleigh. Please bring a salad if your last name starts A-M, dessert if your last name starts N-Z. BYO drinks. Children welcome, call Rosemary on (03) 9700-2981

If you can't make it don't worry, there will be a standing arrangement to meet for lunch at Zampelis, Chadstone Shopping Centre on the first Saturday in June and December. Everyone is welcome. Jocelyn

Member Profile

Sue Flatt

On 15th December 1999, the day after my 52nd birthday, I underwent the liver biopsy that confirmed the diagnosis that, yes indeed, I have Stage One PBC. This was the culmination of a process that had taken five months of blood tests, wait and see, another blood test, consultation with different specialist, and yet more blood tests. The GP was diligent and determined, hunting down the reason for my elevated LFT's despite my airy dismissals “Oh, it'll be nothing; I feel fine!”, and I owe him many thanks for his persistence.

It was after the diagnosis that I went into a decline; an emotional trough, not a physical one. Me, the person who had always been fit and healthy; who loved bushwalking, and gardening; who liked exercise and being active. How could I, this fit and healthy person, be someone with a chronic, progressive liver disease? The two ideas just didn't fit.

I remember how long it took me to join the PBC support group. I'd log on to the web-site, and re-read the information there, and remind myself how to join the group - then quickly log off again in a flurry.

I'd often seen this reluctance in my clinical work. A child would be diagnosed with ADHD, or Asperger's Disorder, or autistic features. I'd busy myself getting information and contact details for the parents about the support group for their child's condition. Then I'd be surprised, perplexed, by their wary acceptance of the information I'd gathered for them, and their sluggishness in following it through.

Now I understood it better. Yes, reality says, a support group is a good thing. It helps a person affected by a condition connect with other people with the self-same condition; it provides an avenue for sharing, understanding and a feeling of being supported. Before that, however, has to come that cognitive shift, that reshaping of the self-concept, that move from “I belong in the group of the population that is ‘normal’ and healthy” to “I belong to the group that is defined by having this condition”. It can be a difficult transition to make, and I certainly found it so.

However, I did manage to make the shift, and I did join the support group, although not till six months after that liver biopsy.

Now, two years later, I'm well and confident. Thanks to URSO and various natural remedies, my LFT's are good, and I manage to limit the effects of the illness to as small an area of my life as I can (that is, I've given up alcohol, eat pretty much a fat-free diet, make three monthly visits to the doctor, and have lots of tablets to swallow). I'm hopeful that the PBC and I can co-exist in a relatively cordial way (though in my heart of hearts I still want it to go away altogether, of course!).

So, that's me. Just for the record, my biographical details are : by profession I'm a Clinical Psychologist. I work with children and adolescents and their parents. I work for a government health care service, and find the restrictions

and politics and under-funding of public service frustrating and annoying. However, I love the work, the clients, the therapy, and that keeps me going.

I'm single, but was married for 15 years, and I have two lovely children (a son and a daughter, both now in their 30's), a three and a half year old grandson, and a granddaughter who was born on the last day of June. I still go bushwalking and potter in the garden, and I still love reading and classical music, and I've recently taken up creative writing as a new interest.

Sue Flatt

Ursodeoxycholic Acid Enhances Calcium Absorption in Patients with Primary Biliary Cirrhosis

A DGReview of: "Ursodeoxycholic Acid Enhances Fractional Calcium Absorption in Primary Biliary Cirrhosis"

Osteoporosis International

08/15/2002

By Mark Greener

Researchers from Calderdale Royal Hospital, Halifax, and other centres in the United Kingdom and the United States, compared fractional calcium absorption in female patients with an average age of 60 suffering from primary biliary cirrhosis with that in sex- and age-matched controls.

The study confirmed that low bone mineral density is common among primary biliary cirrhosis patients. Indeed, bone mineral density in patients with primary biliary cirrhosis was significantly lower compared to controls at both the lumbar spine and femoral neck.

Moreover, the study offers some of the first evidence that ursodeoxycholic acid, the treatment of choice for primary biliary cirrhosis, influences calcium absorption.

Twenty-two of the patients with primary biliary cirrhosis received ursodeoxycholic acid for approximately eight weeks, with around one month off therapy. Before receiving ursodeoxycholic acid, patients with primary biliary cirrhosis showed lower fractional calcium absorption than controls: 33.8 and 52.0 per cent respectively. However, ursodeoxycholic acid increased fractional calcium absorption from 33.1 per cent off-treatment to 36.6 per cent while taking therapy.

Patients suffering from primary biliary cirrhosis expressed higher osteocalcin levels than controls. However, levels of neither parathyroid hormone nor 25-hydroxyvitamin D differed between patients and controls.

Ursodeoxycholic acid did not alter levels of either parathyroid hormone or 25-hydroxyvitamin D.

The authors concluded that primary biliary cirrhosis is associated with low spinal and femoral neck bone mineral density, impaired calcium absorption and raised levels of osteocalcin in plasma. However, ursodeoxycholic acid partly corrects calcium malabsorption in patients with

primary biliary cirrhosis. Therefore, the authors called for studies to determine whether ursodeoxycholic acid's effects are sustained over longer follow up and whether bone mineral density also increases.

Thank You

Just after midnight on September 17th the phone rang and at last, after a long wait, I was told that it was time to come in for my transplant. I was wheeled away for the pre-op at about 8 am. and re-united with my family in Intensive Care about 7.30pm.

Now, several weeks later I would like to let you know how much I appreciate all the messages of care and support that many of you sent. Your interest and affection was inspirational to me and often, when the going got a bit tough, I thought of all my PBC friends who had "been there" before me and were urging me on, and it gave me strength and optimism. Thank you all!

The medical team and staff at the Austin Hospital are absolutely wonderful. As well as being expert in their field they are also warm, compassionate and dedicated people. My grateful thanks go to them too for their care.

I am recovering well, regaining strength and stamina and still finding it hard to believe that I was so unwell just a short time ago. I am very aware of my great good fortune at getting another chance at life and urge you all to make it part of your life's work to spread awareness about organ donation and its life saving potential whenever you can.

Wouldn't you feel great if you were responsible for saving a life?

Cheers, Jocelyn

PBC Questions and Answers

Reprinted by kind permission of the PBCers Organisation

Question

I understand that there are at least two different variants of PBC: One that is more rapidly progressing & that is likely to result in transplant or death within about 5-8 years of the onset of symptoms.

The other a more slowly progressing form that may never require transplant. Is there any difference in the antibodies, genetic information, or reactivity to particular enzymes or proteins that can be identified between these 2 variants?

Is there any way to predict which form of PBC a patient has?

Answer

I do not think that there is convincing evidence for two distinct extreme types of PBC. Rather, there appears to be a continuum of disease severity. In other words, PBC

progresses in most cases, but the rate of progression varies greatly among individual patients.

Asymptomatic patients have substantially longer life expectancies than symptomatic ones, but their survival is still less than that of healthy individuals. The likelihood that a patient will progress rapidly or will need a liver transplant will most clearly depend upon the severity of disease at the time of presentation (e.g., a patient presenting with jaundice or ascites has advanced disease), and the rate of disease progression as monitored over a period of time.

There are scoring systems such as the Mayo PBC Prognostic Index or the new MELD Score which a physician can use to determine an individual patient's general prognosis or likelihood of mortality from the disease over a given time period.

These scoring systems are not crystal balls, however, and only provide a statistical probability of an individual's prognosis. The key factors in these scoring systems are age and liver function including serum bilirubin level, serum albumin level, prothrombin time and signs of fluid retention such as edema fluid. The MELD score also looks at kidney function.

Your question about other clinical or biochemical markers of more rapidly progressive disease is interesting as there is some evidence for this. Interestingly, patients whose disease presents with the very frightening symptom of bleeding from varices often have less in the way of signs of cholestasis, and may actually preserve their liver function for longer.

Some information that suggests that if an asymptomatic patient has other diseases, such as thyroiditis, sicca syndrome, and scleroderma, survival may be compromised, although not clearly just from liver disease. Granulomas seen on a liver biopsy have been associated with better survival. Neither the presence of antimitochondrial antibodies nor their level affects survival.

There have been many studies attempting to identify genes that determine susceptibility to PBC, but few studies have attempted to identify genes that affect the rate of progression or natural history of the disease. Recent studies suggest that a variant in the gene that produces a protein that is important in the process of inflammation (tumor necrosis factor alpha) but this needs to be confirmed.

Question

We have been told that taking Actigall or Urso can lower our lab results but the PBC still progress.

If this is true, how would we know our PBC is progressing?

Can PBC progress without other symptoms appearing?

Answer

This is an important question that has been discussed and debated extensively. I think most experts now believe that Ursodiol (aka Urso, Actigall) significantly slows but does not stop the progression of PBC. Available studies support the view that improvement in laboratory tests is indeed associated with an improvement in life expectancy, but the process of PBC still continues.

Disease progression occurs first at the level of liver cell and tissue structure and function and more often than not, is asymptomatic or not perceived through a change in symptoms until these changes are quite advanced.

Liver biopsy is not a completely reliable (or necessary) way to monitor disease progression. Early warnings of disease progression are usually provided by laboratory tests of liver function such as serum bilirubin and albumin levels.

Nathan M. Bass, MD, Ph.D.,
Professor of Medicine
Medical Director Liver Transplantation Service
University of California
San Francisco, CA

Question

In reading many of the digest notes from other PBCers, I see that often their LFTs go down into the normal range after starting Actigall or Urso.

My LFTs, after 10 1/2 years of Actigall have never been in the normal range although my bilirubin continues to be in the normal range and my only symptoms are Sjogren's and mild itching and arthritis.

Is this what is considered normal for those with PBC?

Answer

Ursodeoxycholic acid has been shown to delay the need for transplantation and perhaps to improve survival in several controlled trials. The beneficial effect is probably the greatest in individuals whose liver chemistry tests show the most improvement. However, several studies suggest that a patient with a normal serum bilirubin has a rather good prognosis, although perhaps not so good as an individual whose liver chemistry tests are entirely normal after treatment.

For patients who do not have an optimal response to ursodeoxycholic acid, additional treatments may be available, particularly by way of ongoing clinical trials. Patients who have continuing symptoms and abnormal liver chemistry tests related to PBC should consult their physician about the need for additional evaluation and the possibility of further treatment.

Alfred Baker, M.D.
Professor of Medicine, Gastroenterology
Director of the Liver Study Unit (PBC included)
University of Chicago Hospitals

Internet Stuff

John Holman

Domain Change

The Australian domain name system has unfortunately been privatised, like much else, and the immediate result is that **oz-pbc.org.au**, formerly free of charge to our not-for-profit group, would now cost \$50 per year to re-register. The plan is therefore to allow this domain to lapse, and to take advantage of the free web space offered by VICNET to local, non-profit groups such as the Oz-PBCers.

Website

The new Home Page address for the Australian PBC Support Group website has therefore become:

www.vicnet.net.au/~ozpbc/

(Note the **tilde** ~character, found at the upper left of most keyboards, and also that the hyphen has been removed.)

This website will continue to be maintained as an information resource - don't forget all previous Biliary Bulletin editions are archived there - and it is hoped that those on the email list will continue to respond to new subscribers with help and encouragement.

Transplant Emails

During the 5-week course of Joc's transplant a series of emails and information updates were sent to the Oz-PBCers mailing list. These proved to be popular with overseas readers too, but because many of these people

were unable to receive the attached photos, the complete series has been placed on the Oz-PBCers website at:

www.vicnet.net.au/~ozpbc/transplant/

If you don't have a computer or Internet connection you can still visit this site at your local library or Internet Café.

John Holman

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Australian PBC Support Group - www.vicnet.net.au/~ozpbc/

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You people really should keep up with the news — it says here that one in four people suffer from depression.



Leung