



ITCHING

Itching, also known as pruritus, is a feature of Primary Biliary Cirrhosis, as it is of several other liver diseases. The severity of the itch can vary enormously between people with PBC with some people having no itching and others having very severe itching. Furthermore, the severity of the itching for each individual person can fluctuate greatly during the course of the

PBC. There is also variation in the severity of the itching both within the day and between days. For many people, the itching can be severe for several weeks or months and then improve. Studies have suggested that during the day itching is cyclical in intensity, becoming worse and then improving without obvious cause.

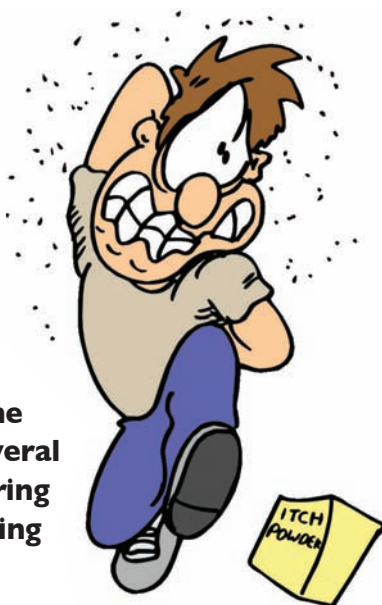
It is very important to appreciate that the severity of the itching bears no relationship to the severity of liver damage. Indeed, there are many people with very early disease and little, if any, damage in the liver yet have very severe itching; the opposite situation also exists where people with quite advanced disease have no itching. Thus, although the itching can have a major impact on symptoms and quality of life, it does not reflect the degree of liver damage.

CAUSE OF ITCHING

The cause of the itching in PBC is not really fully understood. It used to be thought that the bile acids that are retained in PBC were the cause of the itching but subsequent studies have suggested that this might not be the cause. More recently, a number of studies, based on those that were originally done in Leeds, have suggested that the itch may be related to retention of naturally occurring chemicals called opioids which are not that dissimilar to chemicals that are similar to the opium group of drugs. For instance, some drug addicts who take opiates do complain of severe itching and itching can also be associated with drugs such as Morphine. Thomas De Quincy, in his book 'Confessions of an Opium Addict' describes this well. It seems that many people with PBC do have increased levels of naturally occurring opioids and cells are thought to be more sensitive to the effect of these chemicals. This is not only of some academic interest but it has also allowed for new treatments to be introduced.

TREATMENT OF ITCHING

Symptomatic Treatment: Inevitably, people have found out what makes the itching worse and what makes it better and adopt various strategies in their lives to reduce the severity of the itching. Temperature can affect the itching and many people find a hot bath or locally applied heat will exacerbate the itching. Other people find clothes of certain materials make the itching worse. Physical activity and diet usually have little effect on itching. Creams and simple moisturisers are sometimes very effective.



MEDICATION

The only drug that is licensed for treatment of itching in people with PBC is Questran, also called by its 'proper' name Colestyramine. This is a resin which is taken by mouth and interferes with the re-absorption of those chemicals that cause itching.

It is very important to understand the mechanism of action of the drug as this affects how the drug can be taken most effectively. Colestyramine is not absorbed and remains in the gastrointestinal tract. In both the normal person and those with PBC, chemicals that cause the itch are released in the bile (which is made in the liver and stored in the gall bladder) in the duodenum and travel down the bowel to where they are re-absorbed and so the chemicals that cause the itch are recycled. Colestyramine binds to these chemicals (and also other molecules) and prevents their re-absorption.

The implications therefore are twofold: firstly, Colestyramine is more effective, when given, when there is most bile in the bowel. Bile is made continuously by the liver and stored in the gall bladder; when the stomach expresses its contents into the small bowel, signals are sent to the gall bladder to pump the bile into the bowel. Thus, the most effective time to take the Colestyramine is after a fast and when there is food in the bowel. This tends to be around the time of the first meal of the day and therefore Colestyramine is usually most effective when given just before and just after breakfast. Other doses should be given during the day just before lunch or the evening meal.

Secondly, because the Colestyramine acts by preventing re-absorption of the chemicals that cause the itch, it is therefore clear that it will take several days or weeks before the excess chemicals are depleted and Colestyramine becomes effective. Colestyramine does have other side effects: firstly, it may interfere with the absorption of some vitamins and some medications and therefore, it is important to take such medicines at different times from the Colestyramine. If in doubt,

talk to your pharmacist, nurse or doctor. Colestyramine does have some side effects including bloating and diarrhoea. This is lessened by the use of Questran light rather than Questran. The dose of Cholestyramine needs to be adjusted to the severity of the itching.

A number of other drugs have also been shown to be effective in some people with itching associated with PBC:

UDCA: In general, Ursodeoxycholic acid (Urso) has no effect on the itching.

Rifampicin: An antibiotic type of drug which is used particularly in the treatment of tuberculosis. Several studies have suggested that it has an effect in 30-40% of people with itching in PBC. Not only does it colour the urine a bright orange, but it has side effects in that it may damage the liver, so monitoring of liver tests is important after the introduction of the Rifampicin. It also interacts with other drug metabolism so you would need to be very careful as to which medications you are taking although usually it is well tolerated.

Naltrexone: A drug that was used for drug and alcohol dependency. Because it interferes with the opium-type drugs it has been shown to be effective in people with PBC and itching. The medication has to be given carefully as psychological side effects may occur especially in the first few days. In effect, a cold turkey-like reaction may occur. Usually, a small dose is needed to start with and the dose is gradually increased but caution must be taken in the first few days to make sure there are no adverse effects. Again, it works in about one quarter of people.

Sertraline: More recently, the antidepressant drug, Sertraline has been shown as being effective in relieving the itching in some people. The effect is unrelated to the antidepressant impact and it must not be assumed that, because the drug is used as an antidepressant, the treatment is effective via treating the depression and that the doctor believes the person is depressed. Again, one in four people have a good response.

Other Treatments: Sometimes cleaning the blood can be effective. There are several devices including plasmapheresis that have been shown to be of help in some people. This is quite an invasive technique and a little bit like haemodialysis. There are significant risks to it but it can be used to good effect on occasions.

Liver Transplantation: A very effective treatment for itching. Usually, it is used as a last resort in those with early disease but, in those with advancing disease, transplantation is highly effective.

Prednisolone: In small doses may help a minority of people with PBC but side effects are significant.

Overall then, itching or pruritus can be a major problem in people with PBC. However, adjustment of treatment usually allows good control of this problem.

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The Health Partnership

Primary Biliary Cirrhosis is a long-term condition and PBC patients can expect to remain under follow up for many years. Most PBC patients are reviewed by hospital doctors



(gastroenterologists or hepatologists). However, many PBC patients are cared for by their GP. Either way, the PBC patient and their doctor should aim to develop a health partnership, in which both partners have responsibilities.

The doctor has the following responsibilities:

- He or she should explain the diagnosis and what it means for the patient.
- He or she should look for typical symptoms and help the patient understand these symptoms.
- If a treatment is recommended, the doctor should explain why the treatment is necessary. He or she should explain what the treatment will do and what the treatment will not do (for example, ursodeoxycholic acid will slow down the rate of progression of PBC but it will not cure the disease). The doctor should describe the common side-effects which may occur; he or she should also describe any extra monitoring which may be required.
- If treatments are not available, the doctor should help the patient develop suitable coping strategies.
- He or she should monitor the progress of the disease using blood tests, scans, and other investigations as appropriate. Many guidelines have been published and most hospitals have their own protocols – the doctor should be aware of these, bearing in mind that guidelines are not dogma.

It is important to remember that the doctor and patient are health partners. The patient also has responsibilities. Some of these responsibilities are listed below:

- There are simple courtesies, like attending appointments (or, if it is impossible to attend the appointment, cancelling it). It is surprising how many patients simply don't turn up.
- Patients should try to understand their PBC. If something is not clear – ask and ask again.
- Patients should know what medications they are taking and why they are taking them.
- Honesty is the best policy. This is particularly important when it comes to treatments. Be honest about the effect on symptoms; be honest about the side-effects, and be honest about whether the treatment has been taken.

Dr George Mells