



# ITP and Splenectomy

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# ITP AND SPLENECTOMY

## About the spleen and splenectomy

### Introduction

In certain instances a hospital consultant may suggest a splenectomy for a patient with ITP. This is the medical term used to define the removal of the patient's spleen by surgery. However, it is not an operation to be undertaken without due thought, since it cannot be reversed. Very importantly, patients will need to be immunised before the operation and also, in the UK, will have to take an antibiotic every day for the rest of their lives, to prevent infection. In the US, the typical care for adults after splenectomy is to have a supply of appropriate antibiotics at home to take immediately for signs of infection.

ITP is not the only condition which may require a splenectomy; it may be performed when the spleen becomes diseased, or immediately following a serious traffic accident or other injury – on the rare occasions when the spleen is severely damaged and bleeding cannot be controlled by any other method. If a patient's life is threatened in this way the need for a splenectomy can be urgent and unequivocal, but in the great majority of cases no immediate pressure exists and the patient is simply advised to consider splenectomy as an option.

People without a functioning spleen are described as asplenic – a term which may appear on emergency information cards that some patients carry about with them.

### About the spleen

So firstly, where is the spleen and what does it do? (If you have no taste for medical explanations feel free to ignore this section.) In a normal adult the spleen is an organ located in the abdomen on the left hand side, just beneath the diaphragm, but towards the back (if you place your left hand on your lower ribs on the left hand side you will be in the right area). It weighs about 150–200 grams (5–7oz) and is a purple, plump, sponge-like organ about 10cms (4 inches) long containing an intricate arrangement of arterial branches through which a large quantity of blood is pumped. In earlier times it was thought that the

spleen was an unimportant organ, in common with the appendix, but more recently it has been recognised that although not vital to life itself, it fulfils a significant role in helping to maintain the good health of the human individual.

Amongst its properties and functions, the construction of the spleen allows it to trap diseased or alien cells for disposal from the body by a process called phagocytosis – by engulfing and ingesting the target cells to prevent their continued circulation around the body. Additionally, the spleen separates iron from the haemoglobin in exhausted red cells for resynthesis by the bone marrow. Since the average life of a red blood cell is about 4 months, it follows that the entire body's red cells are replaced 3 times yearly – at an estimated rate of 5 million cells per second! In the developing embryo the spleen (in partnership with the liver) produces the early blood cells, but this is gradually superceded by the bone marrow once the bones are formed. The scene of no little activity therefore, the spleen also generates lymphocytes (a type of white blood cell), plasma cells (which are important to the body's immunity) and – of interest to the ITP sufferer – eliminates diseased or expended platelets.

Most ITP patients are aware that platelets are crucial to the clotting process and that, following an injury which allows bleeding, platelets are activated to become sticky at the point of trauma. This promotes a kind of platelet glue which thickens, forming a plug to prevent further blood leakage while the rest of the clotting process takes place, enabling the wound to heal. If insufficient numbers of platelets are present in the blood, prolonged bleeding can be a possibility.

In order to withstand infection and disease, special protein molecules called antibodies are generated by the body's white blood cells (the lymphocytes) to identify and adhere to unwanted material. Since the spleen is rich in phagocyte cells which, as observed above, capture and consume organisms marked, or coated, with antibodies, the spleen thus helps to ensure a healthy blood supply.

In a person with ITP platelets can become coated with antibodies as if they were alien to the body and, as such, become candidates for elimination. Healthy platelets may be removed from circulation in this way, even if the overall platelet content in the blood decreases beyond normal levels. Phagocytosis occurs throughout the body, not only in the spleen, and for this reason a splenectomy is not always be a successful remedy for ITP.

Splenectomy is no longer a routine procedure for patients with ITP as steroids and other drugs are now available, but it remains an option for those who have failed other

treatments and are at risk of bleeding.

From over 50 years of experience, the success rate of a splenectomy in ITP to achieve a total and sustained response is given as 65–75%. Of these patients, a few may relapse at a later stage. Some additional patients will have a partial response with increased (but not normal) platelet levels. A limited number of hospitals in the UK can perform a test called The Indium Labelled Platelet Spleen Scan to identify whether the spleen is the main site of platelet destruction. This can help predict how successful the operation might be – see page 12 for further details.

## The operation

Apart from complications arising from general anaesthesia, which are rare, the main concern with an ITP patient undergoing surgery is to prevent excessive bleeding. To preclude this, precautionary measures (which may include treatment with prednisolone and/or immunoglobulin) may be given before surgery to raise the platelet count. In practice, serious bleeding following a splenectomy is uncommon and platelet transfusion is rarely required. Importantly, precautions against infection will also be necessary; pneumococcal, meningococcal (meningitis), *Haemophilus influenzae* (HiB) and hepatitis B vaccines should be given approximately two weeks in advance (or afterwards in cases of an emergency splenectomy) to protect from the time of the operation.

The operation itself can be performed in one of two ways; by either the 'open' or traditional technique, whereby the spleen is extracted through one incision 10–15 cms (4–5 inches) long in the abdomen on the upper left side, or by means of several smaller incisions assisted by a tiny video camera inserted into the abdominal cavity ('laparoscopic' technique – see page 7). The latter method is popularly known as keyhole surgery and is becoming increasingly favoured by surgeons because of the faster rate of recovery by the patient, but it is important that the entire spleen is removed since small 'seeds' of spleen left behind can regrow. The risks associated with a splenectomy by either method are not greater than from similar operations of this magnitude, such as the removal of the appendix or gall bladder.

During the operation nerves will have been cut which support the tissues surrounding the incision. Afterwards, some numbness of the skin in the area around the wound may be felt – this is normal. It is also usual to feel a little pain while the tissues are healing, sometimes for up to six weeks afterwards.

Immediately after the operation, it is not uncommon for the platelet count to rise beyond normal levels as the body adjusts to its asplenic condition. If this occurs a drug may be prescribed, such as aspirin, to prevent an adverse reaction to excessive platelet levels (thrombocytosis) until the situation settles.

Most patients are hospitalised for 5 to 7 days after open surgery or 2 to 3 days after keyhole surgery, and thereafter return to a normal life – usually without complications.

### **Life without a spleen**

Following a splenectomy, the immediate and long-term concern for the asplenic patient is to prevent infection. In addition to the tasks featured above, it is also the function of the spleen to filter out bacteria or protozoa which enter the bloodstream externally, often via the mouth or respiratory tract. Since this duty is not being performed after the spleen is removed, septicæmia (or sepsis) can arise because bacteria can multiply rapidly in the warm blood – particularly if antibodies antagonistic to that particular bacteria are at a low level.

Septicæmia must be treated immediately if it is not to prove fatal. The first sign of a raised temperature accompanied by headache, fever, hot and cold sweating or a rash, should alert every asplenic patient (or parent) to take urgent action. Often initial symptoms of septicæmia feel like the flu. Septicæmia is frequently induced by the *Streptococcus pneumoniae* bacteria (pneumococcus) which is the most common cause of bacterial pneumonia. However, pneumococcal vaccine as protection for splenectomy has dramatically reduced the risks and septicæmia is a complication very rarely seen (booster vaccinations against pneumococcal infections may be advised every 5 years). It also will be necessary to vaccinate against meningitis with the MenC vaccine (which gives life-long protection) and vaccinate annually against the influenza virus (complications of which can also lead to pneumonia).

Additional to vaccination, a daily antibiotic (penicillin, unless the patient is allergic to it) is usually prescribed to guard against septicæmia. In the UK it is now recommended that people without spleens should take life-long antibiotics but in many other countries they are given for a few years only. To some extent the wishes and the general health of the patient may be a guide, but for those who prefer not to take daily antibiotics it may be possible to obtain a small supply from the the GP to take at the first sign of infection, as an emergency precaution.

It is important to note that immunoglobulin (IVIG) and systemic corticosteroids should have been discontinued at least three months before any of the vaccinations. These work by suppressing the immune system and may cause the administered vaccines to be ineffective.

Presuming that adequate protection from infection is thus obtained (although no vaccine or antibiotic can guarantee 100% protection), risks from splenectomy are considered to be low. However, children are at a significantly greater risk than adults in this respect – if possible the operation is best deferred until the mid teens, when basic immunity will be established – which is another reason why many clinicians exercise great caution before performing splenectomy on children.

As the months pass and the patient's life returns to normal it can be easy to forget that certain safeguards continue to be necessary to avoid infection. Of course, try to live a normal life but, as stressed above, be aware of any changes to your usual healthy state – a raised temperature or fever, a chill, severe sore throat, a bad cough, skin rash, severe headache with drowsiness and/or vomiting, or severe abdominal pain are all indications to seek medical advice urgently. Doctors cannot be expected to know all about their patients' conditions without reference to their records (especially if you see a locum doctor), so it would be wise to remind him/her that you (or your child) is asplenic and may be at risk from overwhelming infection. To cover emergencies, such as a road traffic accident or other injury, it is sensible to carry an emergency warning card such as the ITP HealthCare card, or jewellery giving medical details, to alert those treating you of your condition. Splenectomy cards are issued from most hospitals.

Additional considerations apply when travelling to, or living in, tropical countries, which should be discussed with your doctor. Malaria is a particular problem and should be prevented by the use of insect repellent creams, mosquito nets etc. (try wearing long sleeved/trousered clothes whenever possible), and don't forget to take the antimalarial tablets prescribed by your doctor. In the same way, any animal bites (whether in this country or abroad) should be guarded against and if bitten, do see your doctor for advice. Dog bites can cause a rare infection – *C canimorus* and ticks can carry babesiosis and Lyme disease. Again, wear long sleeved/trousered clothes in the country or if staying in or near woodland areas, especially if deer are likely to pass nearby.

# Is splenectomy in ITP still a valid treatment option today?

by **Professor Adrian Newland CBE**

In Immune Thrombocytopenia (ITP) treatment should be considered on the patient's symptoms and signs rather than on the platelet count as up to 40% of patients will not require therapy. For those with significant bleeding or who are at risk of bleeding there are numerous treatments available, both medical and surgical. Non-surgical treatment includes steroids and immunosuppressant drugs and surgical management is by splenectomy, involving removal of the spleen. Splenectomy surgery has been shown to cause an immediate increase in platelet count in up to 80 % of patients. Despite this, the response is not always sustained and relapses often occur, overall results depending on the length of follow-up and in large studies are no better than 60%. In addition to the failure rate extra caution must be taken when splenectomies are carried out on ITP patients, as they are more likely to bleed during surgery due to the nature of the disease, usually requiring pre-operative preparation to increase the platelet count. There are other complications of splenectomy, based on the immune functions of the spleen. These include a higher risk of infections post-surgery and in the UK, the Department of Health recommends that antibiotic prophylaxis is taken for life after splenectomy surgery, although not all countries recommend this. Splenectomy surgery involves the removal of a healthy organ with the potential risks that entails and its early use has been questioned.

Splenectomy surgery was previously the "gold standard" of ITP treatment and has been carried out for over a century. Although it is considered as one of the few treatments that may lead to cure there has been a decrease in its popularity, primarily as a result of newer medical treatments which may be an effective alternative to surgery. Even though some of the drugs have a wide spectrum of side effects, they are preferred to surgery with its potential complications, including cardiovascular disease, plus the lifelong risk of infection.

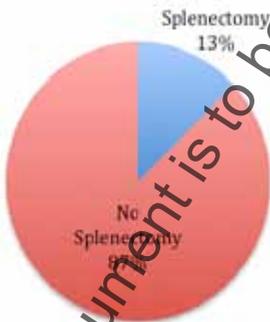
The 2010 International Consensus on ITP Diagnosis and Treatment, listed splenectomy as a second line therapeutic option but there has been considerable discussion since then about the clinical place of splenectomy surgery in the management of ITP, which

has led to a large discrepancy in practice. The UK ITP Registry has been collecting data on patients with ITP from multiple sites in the UK for many years. There are currently 48 active centres and data has been collected for 1369 patients. The Registry concentrates on adult patients with primary ITP, collecting data at presentation with long term follow-up. As ITP is a relatively rare disease the Registry allows the use of data from multiple hospital centres providing patient numbers which would not have otherwise been possible in the given timeframe.

Over the period covered by the Registry, based on the year of ITP diagnosis, there has been an increased time before splenectomy surgery is carried out and a reduction in the number of operations. The interval before surgery has increased from under one year to over three years. Whilst the mean interval between diagnosis and splenectomies carried out between 1970 and 1975 was approximately 6 months, the mean for splenectomies carried out in 2010 onwards was over 3 years.

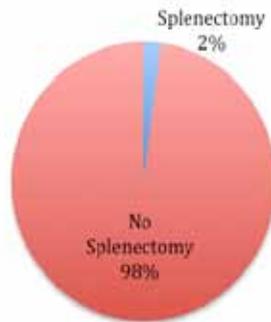
Since the publication of the 2010 guidelines there has also been a substantial (6.5-fold) decrease in splenectomy use. Both groups are of a large size however it should be noted that those diagnosed post-2010 guidelines, have had a smaller time frame for potential surgery.

**Diagnosed Pre-guidelines**



N=178

**Diagnosed Post-Guidelines**



N=857

The increasing interval to splenectomy tends to suggest that patients are being offered alternate therapies before splenectomy and the use of surgery is increasingly being downgraded in the option list. It is however arguably the only curative form of treatment and the question is whether patients likely to respond can be targeted.

Our own studies indicate that Indium labelled platelet scanning is of value before performing splenectomy in ITP. Platelets are extracted from the blood, labelled with a small amount of the radioactive label, Indium, and injected back into the blood stream and their fate followed. Around 60% of patients show a pure or predominant splenic uptake of platelets and they respond well to splenectomy. Among patients with a pure splenic pattern, 95% showed an excellent immediate response to splenectomy and 88% maintained a good long-term platelet count at six months post-surgery. In contrast, the patients with a mixed pattern of liver (hepatic) and spleen uptake displayed a good immediate response but only 16% maintained a platelet response at six months. We no longer offer splenectomy to patients with a pure liver (hepatic) pattern of uptake as the response rate in this group was very low. The 60% who show splenic uptake and are suitable for surgery have a success rate very similar to those who do not have the Indium studies but, of course, we do not see the 40-45% of failure rate as those are excluded from surgery. Interestingly many patients who could benefit from surgery from the studies now prefer to defer the operation and try the newer alternate treatments and keep their spleen intact. Our results with the predictive Indium studies have now been confirmed by groups in France, Spain and Italy.

Splenectomy clearly has a place in the management of ITP however its position as an early option in the steroid relapsed or refractory patient can be questioned and it is not as important as it has been. Alternate therapies are now available. Rituximab may show a response in nearly 60% with a significant proportion remaining in remission at 12 months. The thrombopoietin agonists (Nplate and Revolade) show responses in over 90% and at least a quarter are showing long term remission off all treatment. Both of these options may significantly delay or even completely avoid surgery and as their risk profile is increasingly understood may be a better alternative to the removal of a healthy organ. We believe that splenectomy should be reserved for those where predictive studies indicate an increased chance of long term response and even then other options need discussing.

# Laparoscopic splenectomy

by **Mr Richard Hardwick MBBS, MD, FRCS**

## Introduction

Laparoscopic splenectomy is the removal of the spleen by keyhole surgery. It is now an established procedure for removing the spleen but is technically demanding and only a limited number of surgeons have the training and experience to perform it. Patients with ITP are ideally suited to keyhole surgery as their spleen is rarely enlarged. The normal spleen weighs 150-200 grams and is about the size of the patient's hand. Enlarged spleens are more difficult to remove laparoscopically.

## How do I get to see the surgeon?

Almost all patients are sent for a splenectomy by their hæmatology consultant. You will therefore already be under the care of a hospital specialist and after discussion of the various options will be sent to see the surgeon. The surgeon's role is to let you know what to expect from surgery, warn you about possible complications and then to do a good job! It is a wise to ask your surgeon how many of these procedures he or she does each year, how long they have been offering this service and how often they have had to convert to an open operation. Specialists will not be offended being asked these questions.

## What does having a laparoscopic splenectomy involve?

Having met with your surgeon and agreeing to proceed with surgery you will have some vaccinations to protect you against some common bacteria (pneumococcus, Hæmophilus influenzae, hepatitis B and meningococcus). This is because you are more susceptible to these without your spleen. You may need some treatment from your haematologist just prior to your surgery to boost your platelet count, depending on how low it is. You will visit the hospital within two weeks of your surgery for pre-assessment. This is when blood tests will be done and a full medical examination performed to check that you are fit for a general anaesthetic and the procedure. Most hospitals now have 'procedure specific consent forms' giving lots of detail about each operation. Ask your consultant if they have one as it may answer many of your questions. Many hospitals will admit you early in the morning on the day of your surgery rather than the night before. Make sure you know where you are to report to and any specific instructions such as when you must stop eating and drinking. If in doubt, call the

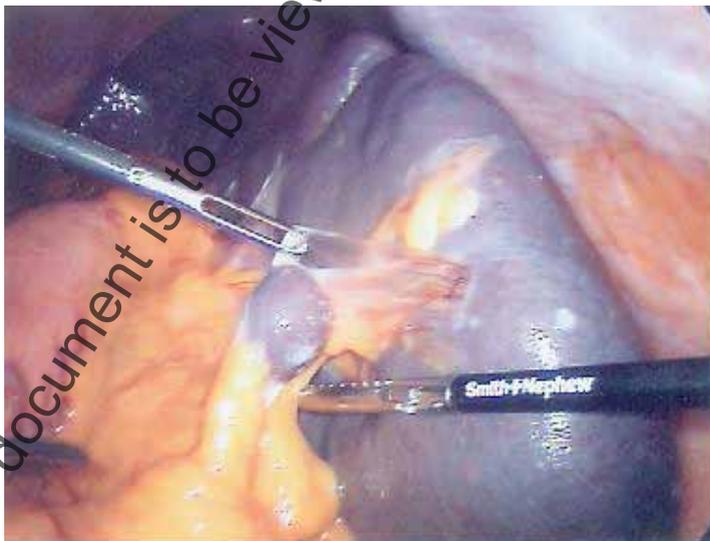
consultant surgeon's secretary or the specialist nurse looking after you (this person is likely to be based in Haematology but there may be one in the surgical team as well).

The operation will be under a general anaesthetic and you will meet the anaesthetist usually on the day of your operation before you go to theatre. You may have some waiting around depending on where you are on the operating list so take something to read with you. The surgery takes about 90 minutes to do and an average of a 2-3 days stay thereafter. You can reasonably expect to be back at work within 10-14 days after an uncomplicated operation. You will be given an intravenous dose of antibiotics during your surgery and started on penicillin tablets before you go home. Without your spleen you are at increased risk of certain infections and therefore most patients are advised to take penicillin daily for life.

### What does the operation itself involve?

A surgeon may choose three, four or five holes depending upon how large your spleen is; some holes will be small (5mm), some a little larger (10mm) and one is usually bigger still (about 30mm). The biggest wound is the one that the spleen is removed through.

The operation involves carefully dividing all the attachments and blood vessels to the spleen. (Fig 1)



Many surgeons use a special device called a harmonic scalpel to seal and divide the smaller vessels and a vascular stapling device to cut and seal the large splenic artery and vein. Once the spleen has been completely mobilized and all its blood vessels divided, it is placed in a strong waterproof bag inside your abdomen. The edges of this bag are then brought out through the largest of the wounds (usually in the uppermost part of the left side of your abdominal wall) and the spleen is broken up into many small fragments inside the bag and these are pulled out piece by piece. This is how an organ the size of a grapefruit can be removed through a 3cm hole. It is important that no spleen tissue is spilt inside your abdomen as it can (rarely) re-form a new mini-spleen, so great care is taken to remove all the spleen tissue.

The wounds are closed with dissolvable stitches; some surgeons use skin glue to close the incisions (Fig 2).



You will receive clear instructions about wound care but usually you will be able to shower as soon as your intravenous drip is removed. This happens about 12-18hrs after surgery. Many surgeons will leave a small suction drain in your abdomen running from the space left where your spleen used to be, through one of the small keyhole incisions and into a bottle or bag hanging by the bed. This is to ensure that any small collection of blood is drained away. Not all surgeons use drains though.

The wounds will have been infiltrated with local anaesthetic while you are still asleep so they should not be too sore when you first wake up. However, despite the keyhole approach to splenectomy, your abdomen can be quite sore during the first 24 hrs after surgery and it is

sometime necessary to give you morphine. This is commonly done using a device called a PCA or Patient Controlled Analgesic device. You will be shown how to press a small hand-held button which administers a dose of morphine down your drip. Your anaesthetist will discuss pain control with you before your surgery. Many patients manage with tablet pain killers only but it is very variable as to how sore you will be. You will be encouraged to start drinking as soon as you feel like it and to get out of bed and go to the bathroom. If you have a drain this can usually be removed within 48hrs unless there has been some bleeding, in which case it will stay in longer and your discharge might be a little delayed. Commonly patients stay in hospital for 2-3 nights.

### **Are there any complications to laparoscopic splenectomy?**

Whilst laparoscopic splenectomy is undoubtedly an advance as far as the patient is concerned, it still carries with it many of the same risks and complications as open splenectomy. The main risk is bleeding. Some patients will need to have a platelet infusion as soon as their spleen has been disconnected from its blood vessels to ensure that the blood clots normally. There is a small risk that organs adjacent to the spleen may be damaged during the division of tissue connecting them to the spleen. The tail of the pancreas in particular is within a few millimetres of the splenic artery and vein. The stomach, colon and diaphragm too are all intimately connected to the spleen and may also be damaged, especially if there are adhesions from previous radiotherapy or surgery.

Rarely it is necessary to convert the operation to an open one (through a conventional cut in the abdominal wall). Obviously this must be done immediately, and it is important to be aware that if it is not safe to persist with the keyhole route, you may wake up with a bigger scar than you had anticipated! Having said this, conversion to open surgery runs at less than 5% (or 1 in 20 patients) in most centres where a lot of keyhole surgery to the spleen is undertaken.

Infections, particularly involved the lungs (pneumonia), are another risk. Getting mobile soon after surgery and being able to cough up any phlegm helps to reduce this risk and laparoscopic surgery is good for enabling patients to mobilize quickly after their operations as it is less painful than open surgery.

### **How quickly will I recover from laparoscopic splenectomy?**

The average hospital stay after laparoscopic splenectomy is 2-3 days. This is followed by a recuperation period of 5-10 days at home before return to work and normal activities. During this early recuperation phase, it is safe to drive so long as you feel comfortable and

are in complete control of the car. You may feel tired in the afternoons and need an extra snooze, but should very quickly find you can eat and drink completely normally. Once back at work, the scars fade rapidly so that within a couple of months it will be difficult to tell that you have had major surgery. If the operation needed to be done by the open route, then the hospital stay will be 5-7 days and recovery at home 4-6 weeks. You will have your platelet count checked before you leave hospital and again soon after discharge to check that the operation has been successful. Despite splenectomy, not all patients with ITP get a normal platelet count again. The causes for this can be complicated and the likelihood of success for each individual patient should have been discussed with them by the consultant haematologist who has referred them for the operation.

## Conclusion

Patients with ITP are ideally suited to laparoscopic splenectomy. The advantages of this type of surgery are much smaller scars and a more rapid recovery than open splenectomy. Nevertheless, there are still complications in 5% of people and another 5% of patients may need to be converted to an open operation.

## Dosing regimens for antibiotic prophylaxis

Penicillin	
Adult	250-500 mg 12 hourly
Child aged 5-14 years	250 mg 12 hourly
Child under 5 years	125 mg 12 hourly
Erythromycin (base)	
Adult	250-500 mg daily
Child over 8 years	250-500 mg daily
Child aged 2-8 years	250 mg daily
Child under 2 years	125 mg daily
Amoxicillin/co-amoxiclav (doses according to amoxicillin content)	
Adult	250-500 mg daily
Child aged 5-14 years	125 mg daily
Child aged 1-5 years	10 mg/kg body weight daily
Child under 1 year	10 mg/kg body weight daily

# Indium labelled platelet spleen scan

by **Dr J.D. Cavenagh MD FRCP, FRCPath**  
& **Dr Drew Provan BSc, MBChB, MD, FRCP, FRCPath**

## Background

Most patients with ITP are initially treated with steroids. Some patients fail to respond to such therapy or relapse when the steroid dose is reduced. For such patients splenectomy is often recommended. Approximately two thirds of patients with ITP who undergo splenectomy will have a satisfactory response. Unfortunately, there are no definite criteria which help tell patients and their doctors whether splenectomy will be effective in any particular case. We believe that the best test currently available which helps predict response to surgery is the Indium Labelled Platelet Spleen Scan. We have now studied over 256 patients with this test and nearly 600 patients have been studied in France although it should be noted that it is technically difficult in patients with very low platelet counts and may not always give clear cut results. However, if the scan shows that the spleen is the major site of platelet destruction, then over 90% of patients will respond satisfactorily to splenectomy. However if the scan shows that the platelets are being destroyed elsewhere then the chances of a successful outcome are much lower. We believe that this test therefore helps doctors and patients make the best plans in the treatment of ITP.

## About the scan

We perform this scan at Barts Hospital. Patients need to attend the hospital for three consecutive days, usually Tuesday to Thursday. On the first day, the patient will spend most of the day on the Day Ward. To start with a blood sample is taken and a tracer dose of radioactivity is used to label the platelets. The platelets are then re-injected and blood tests are performed on several occasions during the course of the day. In addition we scan over the liver and spleen to see where the radioactively labelled platelets are accumulating. The patient needs to attend for a blood test and scan on the next two days. This only takes about half an hour. Using the results of the blood tests and scans we are able to work out the platelet life span and the major site of platelet destruction. Using this information we are able to determine whether the spleen the liver or a mixture of both is the major site of platelet destruction. We are then able to advise the patient and their doctor about the potential outcome from splenectomy.

We hope you found this booklet useful. If you have any questions e-mail us at [info@itpsupport.org.uk](mailto:info@itpsupport.org.uk) and we will do our best to answer them.

The ITP Support Association is always looking for ways to promote ITP awareness and raise funds for ITP research. If you can help us by holding or taking part in a fundraising or sponsored event in aid of our charity we would be delighted to hear from you. Anyone who raises money for our cause receives a certificate and if they send a photo it will appear in our quarterly journal "The Platelet".

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