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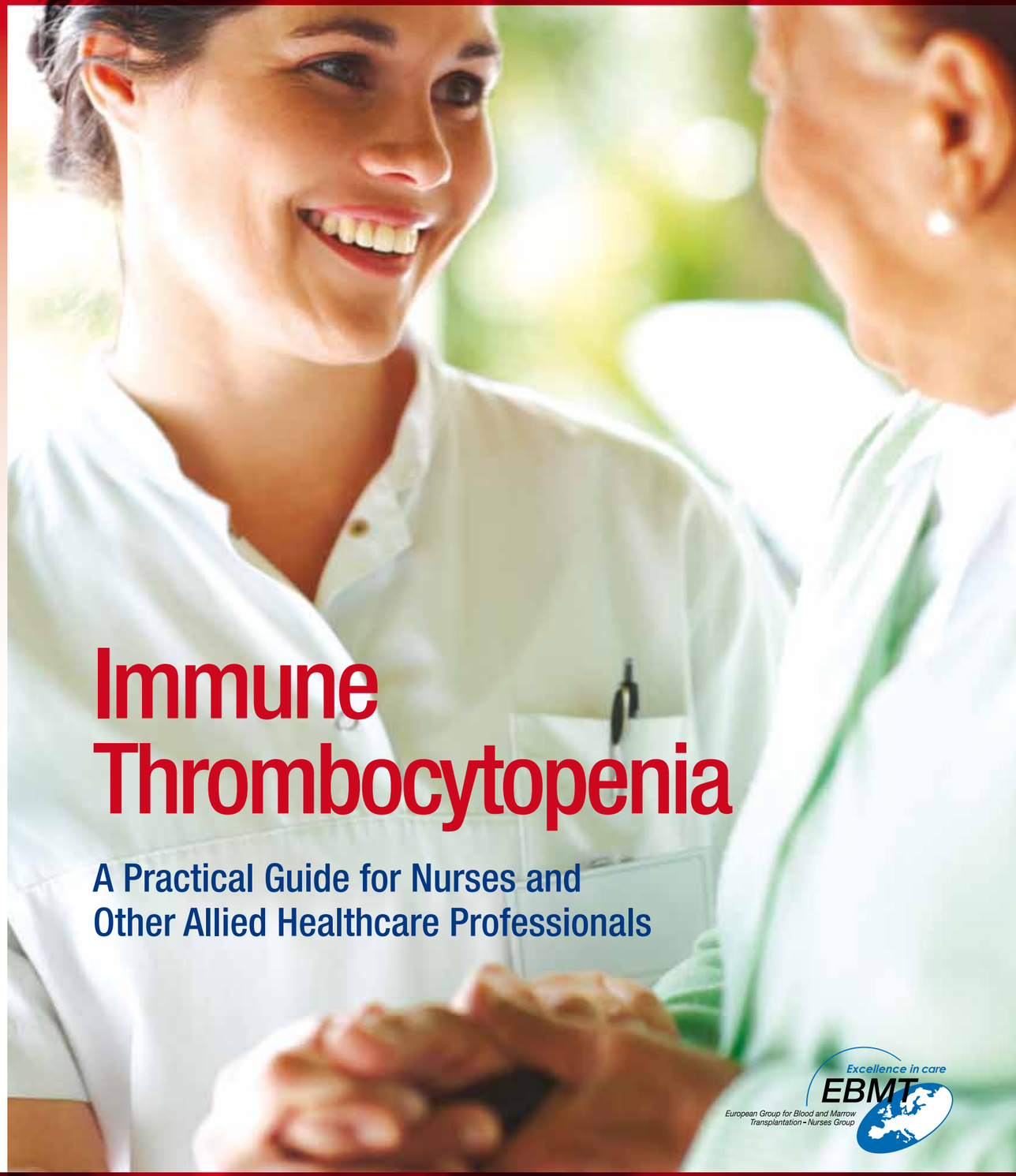

Immune Thrombocytopenia

A Practical Guide for Nurses and Other Allied Healthcare Professionals

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Contents

Chapter 1. Overview of immune thrombocytopenia

Immune thrombocytopenia (ITP) is an **autoimmune**-mediated haematological disorder affecting platelets. A patient's immune system produces **antibodies** directed against platelet antigens, resulting in platelet destruction and suppression of platelet production in the **bone marrow**. Patients with ITP are, therefore, at risk of serious bleeding events. In children, ITP is usually acute, with the majority of cases resolving spontaneously. In adults, ITP is more likely to be chronic, requiring individualised monitoring and treatment to maintain platelet counts at a safe level to prevent serious bleeding events.

History of ITP

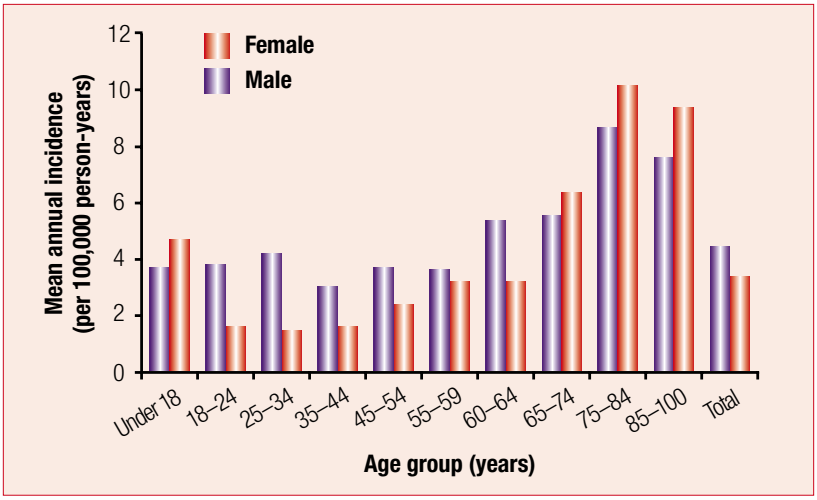
ITP was originally described in 1735 by a German physician, Paul Gottlieb Werlhof, and was therefore known as Werlhof's disease.[1] In 1916, Paul Kaznelson reported the first successful treatment for ITP after a patient showed a response to **splenectomy**.[2] Splenectomy was then used as the first-line therapy for ITP until 1950. In 1951, William J Harrington and James W Hollingsworth established that ITP was an autoimmune condition.[3] They postulated that the destruction of platelets in ITP was caused by a factor circulating in blood. Their experiment included Harrington receiving blood from an ITP patient which within 3 hours resulted in his **platelet count** dropping to a seriously low level, causing a seizure. It took 5 days for his platelet count to return to normal levels. Antibodies, usually immunoglobulin G, specific to platelet membrane glycoproteins (GPIIb-IIIa complex is the most common) have since been identified as the circulating blood factor involved in the destruction of platelets in ITP.[4–8]

ITP has until recently been termed **idiopathic** thrombocytopenic **purpura**, but was changed to immune thrombocytopenia to reflect the fact that many patients do not experience purpura and in the majority of cases it is an immune (autoimmune) rather than an idiopathic disorder.[9]

Epidemiology

ITP affects people of both sexes and all ages—there is no typical ITP patient (see Appendix for case examples). ITP is estimated to affect approximately 3.3/100,000 adults/year and between 1.9 and 6.4/100,000 children/year.[10] The incidence of ITP increases with age and, among adults between the ages of 18 and 65 years, is slightly higher in women than in men **(Figure 1)**.[11–13] The incidence rate of ITP is rising, partly due to the inclusion of automated platelet counts in routine blood tests. More than 20% of patients with ITP have other immune disorders (e.g. systemic lupus erythematosus, immune thyroid disease) or chronic infections.[14,15]

Figure 1. Incidence of ITP according to gender and age



ITP, immune thrombocytopenia. Reproduced with permission from the *British Journal of Haematology*.[12]

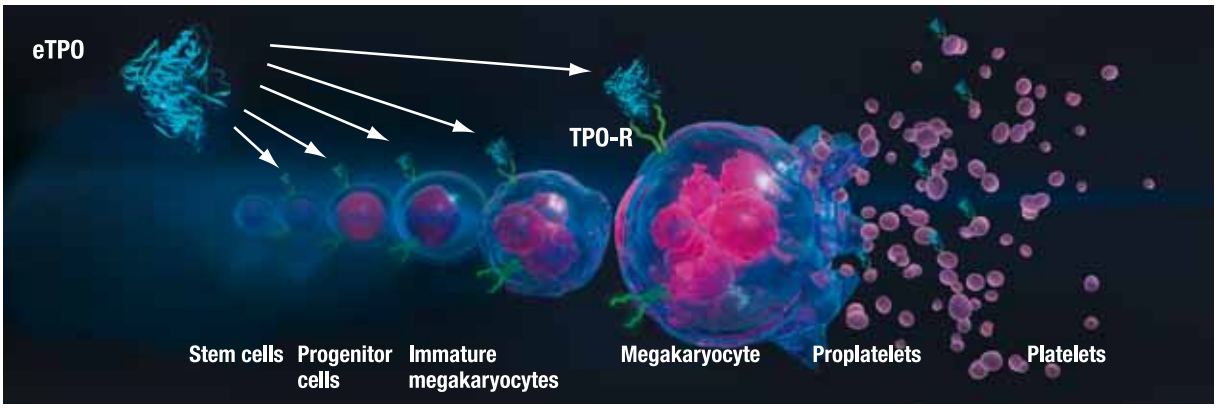
Pathophysiology

What triggers the immune system to produce autoantibodies directed against platelets is currently unknown. The key modulator of platelet production is **thrombopoietin**.[16] Endogenous thrombopoietin binds to receptors on **megakaryocytes** in the bone marrow, stimulating them to produce platelets **(Figure 2)**. Platelets are normally cleared from the circulation through the **spleen (Figure 3)**. The rate of platelet production is inversely related to the endogenous thrombopoietin level, but in ITP there is a functional deficiency in thrombopoietin that contributes to thrombocytopenia.[17]

ITP was originally believed to be entirely the result of antibody-mediated platelet destruction; however, growing evidence indicates that the pathophysiology also involves other mechanisms such as T-cell mediated platelet destruction and suboptimal bone marrow production of platelets.[18] The antibodies that bind to platelets can also bind to and damage megakaryocytes, rendering them immature and less productive **(Figure 4)**. In up to 50% of ITP patients, there is no identifiable antibody-mediated cause.[19] In these cases, ITP may be related to cell-mediated mechanisms where platelets are destroyed by reactive cytotoxic CD8(+) or other T-regulatory cells.[20,21] In children, ITP may be triggered in response to a viral infection (e.g. chickenpox, rubella, mumps) or vaccinations using live viruses.[15,22]

Patients with ITP can develop additional antibodies to other tissues and organs; the most common target appears to be the thyroid gland.[23] Around 40% of patients have detectable antibodies directed at the thyroid tissue and nearly one-quarter may develop symptomatic or subclinical hyperthyroidism or hypothyroidism.[2]

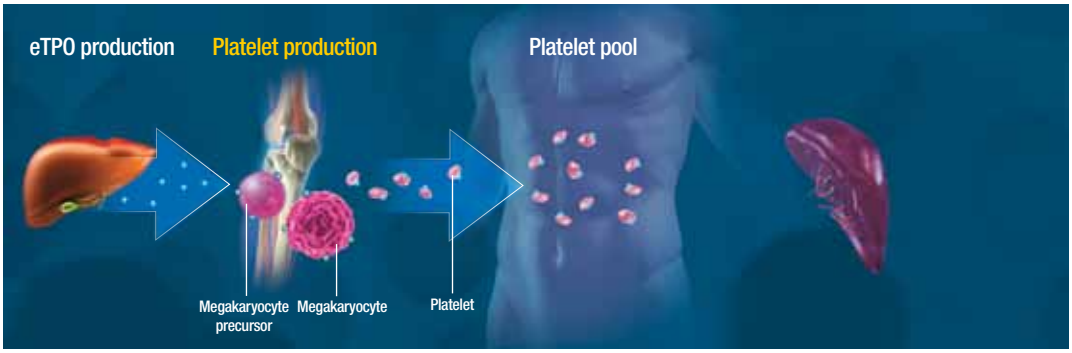
Figure 2. Natural platelet production



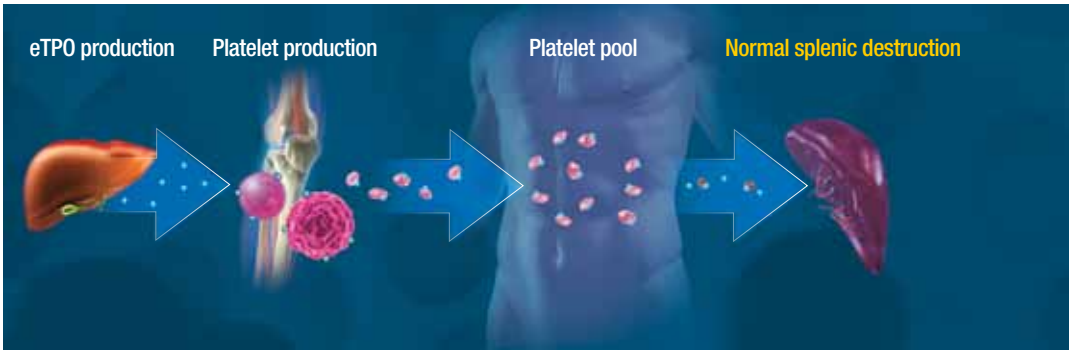
eTPO, endogenous thrombopoietin; TPO-R, thrombopoietin receptor. Image courtesy of Amgen.

Figure 3. Normal platelet homeostasis

Thrombopoietin, a hormone produced at a fixed rate in the liver, is the key regulator of platelet production

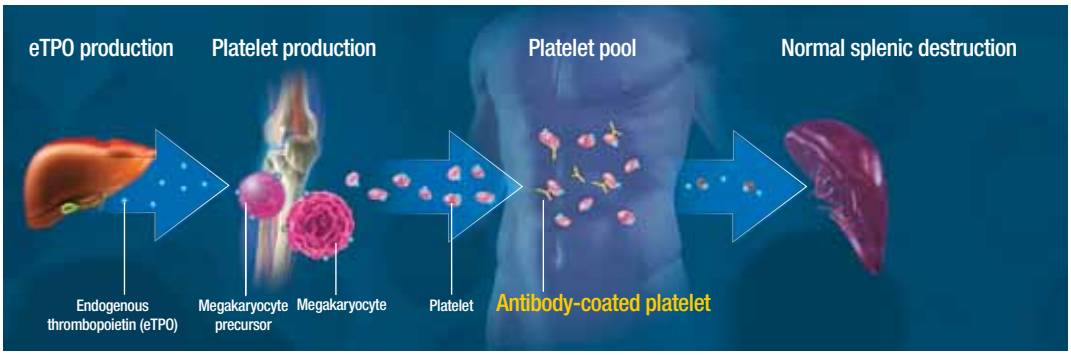


Endogenous thrombopoietin stimulates bone marrow megakaryocytes via the thrombopoietin receptor to produce platelets, which are released into the circulation and have a lifespan of ~10 days

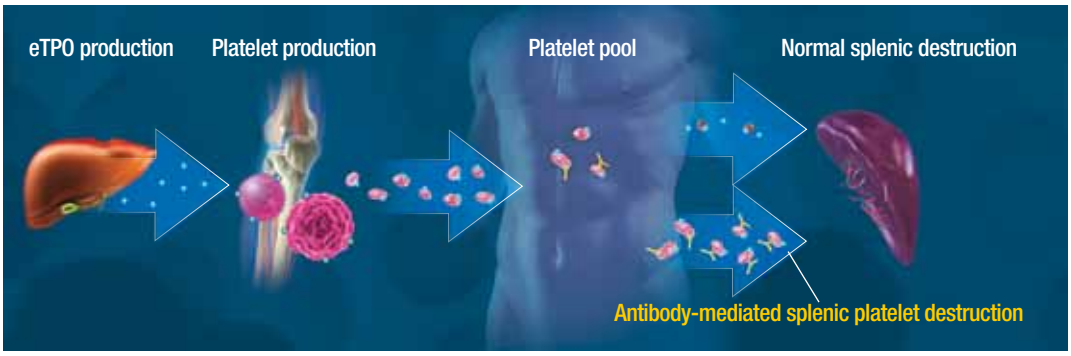


Ageing platelets are naturally cleared from circulation. They are phagocytosed by macrophages mainly in the spleen, but also in the liver and bone marrow

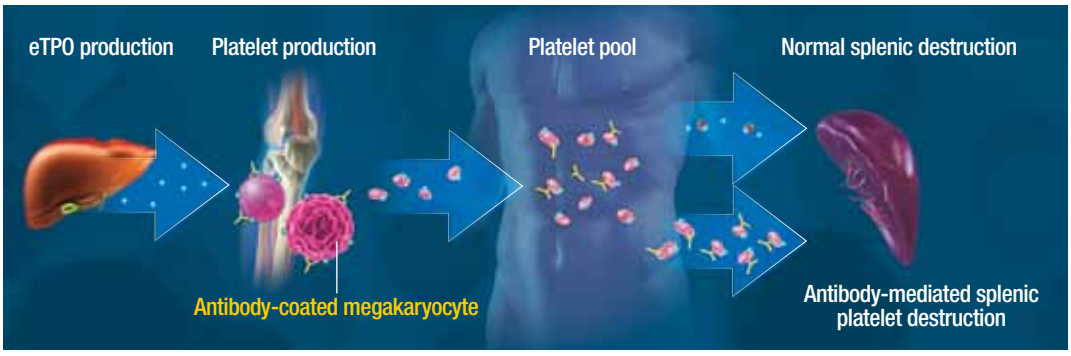
Figure 4: Current view of ITP – increased platelet destruction and suboptimal platelet production



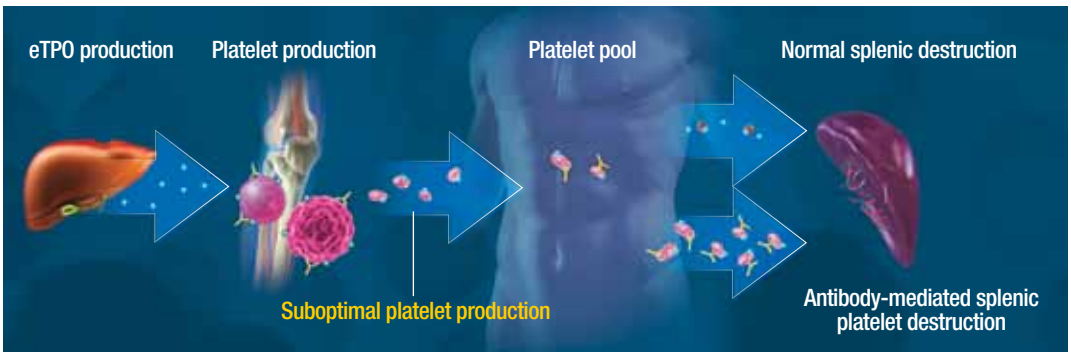
In ITP, antibodies bind to glycoproteins on healthy circulating platelets



Antibody-coated platelets are recognised by macrophages primarily in the spleen leading to their destruction



Antibodies also bind to and damage megakaryocytes in bone marrow rendering them immature and less productive



Fewer megakaryocytes and an inappropriately low endogenous thrombopoietin level result in suboptimal platelet production

Chapter 2. Identifying immune thrombocytopenia

Definition

ITP is defined as isolated **thrombocytopenia** (platelet count <100 x 10^9/L) with no associated causes or disorders.[9] A normal platelet count in healthy individuals is between 150–450 x 10^9/L. Traditionally ITP has been classified as: acute, sudden onset, lasting less than 6 months; chronic, persisting more than 6 months; or refractory, persistently low platelet counts despite appropriate treatment or splenectomy. In 2009, a new nomenclature for the phases of ITP based on time from diagnosis was proposed **(Table 1)**.[9]

Table 1. Classification of ITP disease phases

ITP phase	Definition
Newly diagnosed	Within 3 months of diagnosis
Persistent	Between 3 to 12 months from diagnosis
Chronic	Longer than 12 months from diagnosis

ITP, immune thrombocytopenia. Data taken from Rodeghiero *et al. Blood* 2009.[9]

Signs and symptoms

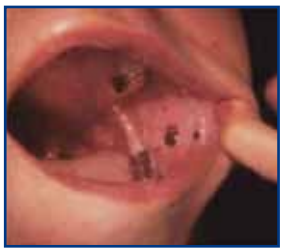
The signs and symptoms of ITP are highly variable. In adults, ITP usually has an insidious onset, with no preceding illness. Nearly one-quarter of patients present asymptomatically and receive a diagnosis of ITP through incidental routine blood tests.[24] Symptomatic patients can present with:[25]

- **Petechiae** or purpura **(Figure 5)**
- Unusual or easy bruising **(haematoma)**
- Persistent bleeding symptoms from cuts or other injuries
- Mucosal bleeding **(Figure 5)**
- Frequent or heavy nose bleeds (epistaxis)
- Haemorrhage from any site (usually gingival or **menorrhagia** in women)

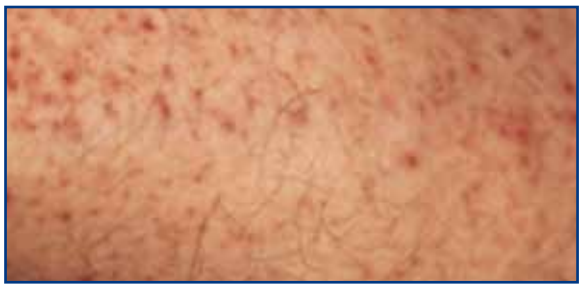
Figure 5. Signs of ITP

Purpura and haematomas

Conjunctival haemorrhage



Mucosal bleeding



Petechiae

Purpura and haematomas and conjunctival haemorrhage images courtesy of Douglas Cines and James Bussel. Mucosal bleeding and petechiae images courtesy of Drew Provan.

The platelet count is a surrogate marker for bleeding tendency. There is usually a good correlation between bleeding severity and the individual's platelet count, although a low platelet count may only cause minor bleeding in some patients.[26] Other factors that contribute to the bleeding risk that need to be considered when planning treatment and follow-up include: comorbidities that predispose to bleeding, complications of specific therapies, activity and lifestyle, potential interventions that may cause bleeding, and a patient's need for non-ITP medications that may affect bleeding.

Fatigue is a frequently overlooked symptom in ITP patients as until recently it was considered to be steroid-related rather than disease-related. A substantial number of patients, 90% in one survey, report experiencing fatigue, which has a significant impact on their quality of life.[27,28] Other symptoms that are often reported by patients include insomnia, heartburn, loss of appetite, loss of hair and, in adults in particular, anxiety related to the risk of uncontrolled bleeding.

Diagnosis

Diagnosis of ITP is one of exclusion; there is no standard test for ITP.[25,29] Diagnosis is usually made based on the patient's medical history, physical examination, **complete blood count** (CBC) and examination of a **peripheral blood smear (Table 2)**.[25] Occasionally further diagnostic studies may be required to exclude the most common causes of secondary ITP (e.g. hepatitis C, systemic lupus erythematous, human immunodeficiency virus [HIV], etc.). The medical history and physical examination are used to characterise the type, severity and duration of bleeding. A CBC will show normal blood counts except for low platelet counts, unless the patient has recently experienced significant bleeding. A peripheral blood smear can exclude pseudothrombocytopenia, which is an in-vitro artefact caused by platelets clumping in the test tube that can sometimes give rise to falsely low platelet counts when using automatic cell counters.

Table 2. Recommended diagnostic approaches for ITP

Basic evaluation	Tests of potential utility	Tests of unproven benefits
Patient history	Glycoprotein-specific antibody	Thrombopoietin
Family history	Antiphospholipid antibodies (including anticardiolipin and lupus anticoagulant)	Reticulated platelets
Physical examination	Anti-thyroid antibodies and thyroid function	Platelet-associated immunoglobulin G (PaIgG)
Complete blood count and reticulocyte count	Pregnancy test in women of childbearing potential	Bleeding time
Peripheral blood smear	Antinuclear antibodies	Platelet survival study
Quantitative immunoglobulin level measurement*	Viral polymerase chain reaction (PCR) for parvovirus and cytomegalovirus (CMV)	Serum complement
Bone marrow examination (in selected patients)		
Blood group (rhesus)		
Direct antiglobulin test		
Helicobacter pylori†		
Human immunodeficiency virus (HIV)†		
Hepatitis C virus (HCV)†		

*Quantitative immunoglobulin level measurement should be considered in children with immune thrombocytopenia (ITP) and is recommended in those children with persistent or chronic ITP as part of reassessment evaluation. †Recommended by the majority of the panel for adult patients regardless of geographic locale. Reproduced with permission from *Blood*.[25]

Bone marrow aspiration is used to exclude other diagnoses and is indicated in older patients (particularly those over 60 years of age to exclude myelodysplastic syndrome), in those with an atypical presentation (e.g. abnormalities observed on peripheral blood smear suggestive of other haematological disorders), in those with a poor response to first-line therapy and in those being considered for splenectomy.[25] In ITP, the bone marrow aspirate will show normal morphology, although there can be slightly increased numbers of megakaryocytes, with poor shedding of platelets.

HIV testing may also be required in at-risk cases to exclude a diagnosis of HIV-associated thrombocytopenia.[25]

Other causes of thrombocytopenia that need to be excluded include: reactions to medications, herbs, foods, or other substances such as quinine; giant platelets; inherited thrombocytopenia; and underlying disorders that may cause secondary ITP **(Figure 6)**.[11,15]

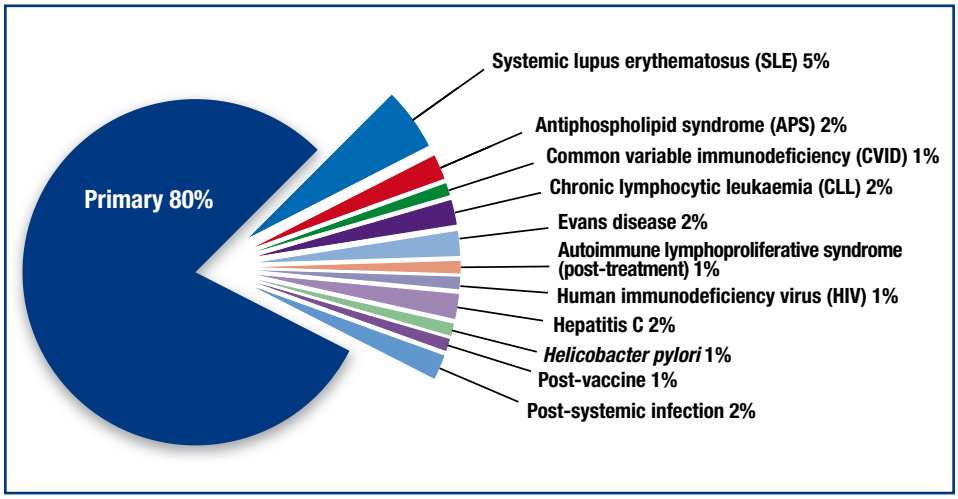
Prognosis

Overall the outcome of ITP is variable, highly individualised and there is no way to predict the course of the disease. Adults are more likely to develop chronic ITP and spontaneous recovery is uncommon.[27] Many adult ITP patients, however, experience mild and stable disease requiring no treatment.

In contrast, ITP is usually acute in children, particularly in those under 10 years of age, with recovery observed in the majority of cases even after several weeks to months of severe thrombocytopenia. Around 80% of children will spontaneously recover within 6 months with or without receiving treatment.[30] Some 15–20% of children will, however, develop chronic ITP.[30]

Among ITP patients who respond to therapy, mortality is similar to that of the general population.[31] Among those who do not respond within the first few years of receiving therapy there is a higher risk of morbidity and mortality.[31–33] Deaths are rare, but may be as high as 3% per year in refractory ITP patients and are usually related to **intracranial haemorrhage** or infection.[28,31,33]

Figure 6. Estimated proportion of different causes of secondary ITP



Reproduced with permission from *Blood*.[15]

Consequences of ITP

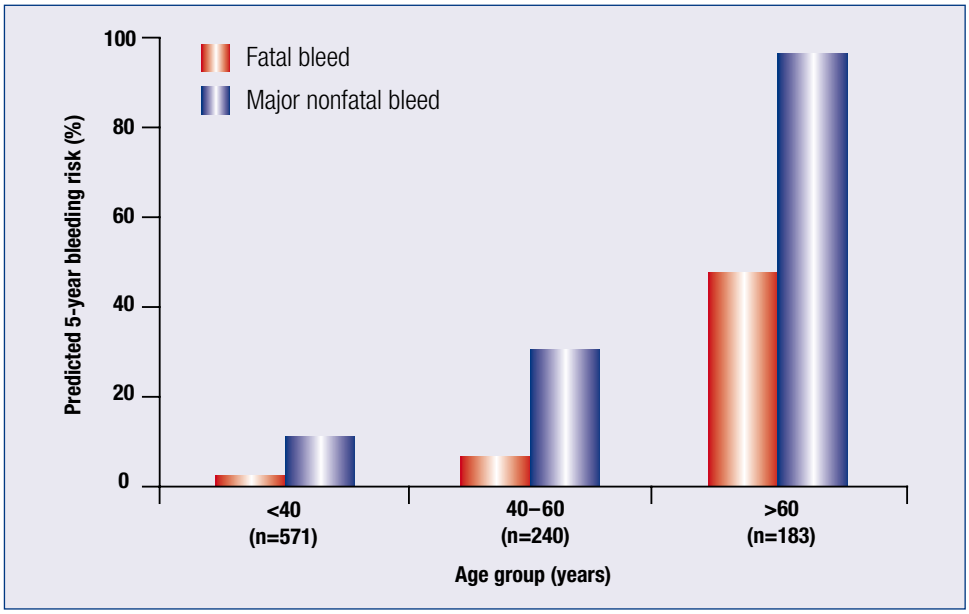
Patients with ITP have an increased risk of experiencing bruising and spontaneous bleeding events **(Table 3)**.[34,35] Patients with platelet counts less than 30 x 10^9/L are at increased risk of serious or life-threatening bleeding (e.g. intracranial haemorrhage, mucocutaneous bleeding, lower gastrointestinal bleeding, other internal bleeding and menorrhagia). Life-threatening bleeding, however, rarely occurs in patients with platelet counts above 10 x 10^9/L.[36] Age appears to be an independent risk factor for severe and/or fatal bleeding, with older people at higher risk **(Figure 7)**.[33,37]

Table 3. Consequences of low platelet counts

Platelet count (x 10^9/L)	Symptoms
>50	None
30–50	Excessive bruising with minor trauma
10–30	Spontaneous petechiae or bruising
<10	At risk of internal bleeding

Data taken from Cines & Blanchette. *N Engl J Med* 2002.[35]

Figure 7. Risk of bleeding increases with age



Adapted with permission from the *Archives of Internal Medicine*.[33]

Chapter 3. Managing patients with immune thrombocytopenia

Treatment guideline recommendations

The British Society for Haematology[30] and American Society of Hematology (ASH)[38] have developed treatment guidelines for ITP. In January 2010, new recommendations for the investigation and management of primary ITP were published by an international consensus group,[25] to reflect the introduction of new treatments, the greater understanding of the disease, and the availability of newer data.

Various treatment options are available for managing ITP, but the recommendations are mainly based on expert opinion rather than evidence based, due to the paucity of randomised controlled trials of standard therapies in adults with ITP. The choice of treatment(s) should be individualised and depends on a number of factors including the individual's signs, symptoms and comorbidities, tolerance, lifestyle and preference.[25]

Who and when to treat

Patients with a platelet count above 50 x 10^9/L usually do not require any treatment.[25] Those with lower platelet counts may require treatment depending on their symptoms or risk of bleeding **(Table 4)**.[25,39]

Table 4. When to treat

Platelet count (x 10^9/L)	Treatment
>50	No treatment
30–50	No treatment or prednisone (1–1.5 mg/kg/day) for patients at higher risk of haemorrhage (e.g. hypertensive, lifestyle factors, concomitant medication use, head trauma or scheduled for surgery)
<30	Prednisone (1–1.5 mg/kg/day)
Haemorrhage or life-threatening bleed	Emergency treatment: Platelet transfusion Intravenous immunoglobulin (IVIg; 1 g/kg/day for 2–3 days) Methylprednisolone (1 g/day for 3 days)

Data taken from Stasi. *Eur J Haematol* 2009.[39]

Current treatment options

First-line treatment

Corticosteroids

Corticosteroids are the standard initial treatment for patients with ITP **(Table 5)**. Corticosteroids prevent the destruction of platelets by macrophages within the spleen and liver thereby increasing platelet levels.[35] The first-line treatment option is prednisone 0.5–2 mg/kg/day until the platelet count increases to over 30–50 x 10^9/L. Response to treatment is usually observed within several days to weeks. If there is no response after 4 weeks, treatment is considered to have failed and should be stopped.[25] Corticosteroids are usually prescribed as a short-term treatment (3–4 weeks) because long-term use leads to significant side effects that outweigh the benefits of reducing the risk of serious bleeding.[25] When stopping treatment the dose should always be tapered. Patients receiving long-term corticosteroids (>6 months) require bone density monitoring or prophylactic treatment to avoid osteoporosis, particularly if they are over 60 years of age.[11] Other common side effects, such as diabetes, mood changes and sleeping difficulties, occur even with short-term use and should be discussed with patients.

Immunoglobulins

Immunoglobulins are used to desensitise the immune system. They are produced by collecting antibodies from human **plasma** and, therefore, carry the potential risk of transmitting infectious diseases.[40] There are two types available: intravenous immunoglobulin (IVIg) and intravenous anti-D immunoglobulin (IV anti-D Ig). The latter has been withdrawn from the European market due to safety concerns but is still included in the current recommendations.[25] IVIg is indicated for patients at high risk of bleeding or before surgery to increase platelet counts. In patients who are unresponsive to corticosteroids or if corticosteroids are contraindicated, response to IVIg is rapid but generally transient lasting between 2–4 weeks, although may persist for longer in some patients.[30] Repeat infusions of IVIg at regular intervals is common to maintain the platelet count at a safe level. Concomitant use with corticosteroids can attenuate the response. IVIg has been associated with rare but serious side effects including renal failure and thrombosis.[25]

Table 5. First-line treatment options for adult ITP patients

Management strategy		Initial response rate (time to response)	Toxicities	Duration of sustained response
Corticosteroids	Dexamethasone 40 mg daily for 4 days every 2–4 weeks for 1–4 cycles	Up to 90% (several days–weeks)	• Vary with length of administration: mood swings, weight gain, anger, anxiety, insomnia, Cushingoid face, dorsal fat, diabetes, fluid retention, osteoporosis, skin changes (e.g. thinning), alopecia, hirsutism, hypertension, gastrointestinal distress and ulcers, avascular bone necrosis, immunosuppression, psychosis, cataracts, opportunistic infections, adrenal insufficiency • Tolerability decreases with repeated dosing • Possibly lower rate of adverse events when used as short-term bolus therapy	As high as 50–80% reported during 2–5 years of follow-up
	Methylprednis(ol)one 30 mg/kg/day for 7 days	Up to 95% (4.7 vs. 8.4 days, HDMP vs. prednisone)		23% at 39 months
	Prednis(ol)one 0.5–2 mg/kg/day for 2–4 weeks	70–80% (several days–weeks)		Uncertain – estimated 10-year disease-free survival may persist for months (13–15%)
Intravenous anti-D* 50–75 µg/kg		Similar to IVIg – dose dependent (4–5 days)	• Common: haemolytic anaemia (dose-limiting), fever/chills • Rare: intravascular haemolysis, disseminated intravascular coagulation, renal failure, rare death	Typically 3–4 weeks but may persist for months
IVIg 0.4 g/kg/day for 5 days or infusions of 1 g/kg/day for 1–2 days		Up to 80%, half achieve normal platelet counts (rapid, many respond in 24 hours, typically 2–4 days)	• Headaches common (often moderate but sometimes severe) • Transient: neutropenia, renal insufficiency, aseptic meningitis, thrombosis, flushing, fever, chills, fatigue, nausea, diarrhoea, blood pressure changes and tachycardia • Occasional: anaphylactoid reactions in patients with IgA deficiency	Usually transient, returning to pre-treatment levels 2–4 weeks following treatment, although occasionally can persist for months

*Note: Intravenous anti-D was voluntarily withdrawn from the European market in August 2009 owing to safety concerns. HDMP, high-dose methylprednis(olone; IVIg, intravenous immunoglobulin; IgA, immunoglobulin A. Adapted with permission from *Blood*.[25]

Second-line therapy

Numerous second-line therapies with differing mechanisms of action are available **(Table 6)**, although many have not received an indication for use in ITP from the European Medicines Agency (EMA) or the Food and Drug Administration (FDA). The main aim of second-line therapy is to provide a safe platelet count (>50 x 10^9/L) that minimises a patient's risk of bleeding.[25]

Immunosuppressants

In patients with severe symptomatic ITP more intensive immunosuppression may be required.[25] Examples include azathioprine, cyclosporin A and mycophenolate mofetil, which are widely used in organ or tissue transplantation, and cyclophosphamide, which is used to treat cancers and other autoimmune disorders.[25]

Azathioprine response rates can be slow and patients should receive continuous treatment for at least 4 months before being considered unresponsive.[38] Sustained responses of several months to a few years after treatment discontinuation have been observed in around 20% of patients.[38] Patients who require continuous treatment should be monitored for potential toxic effects including disturbed liver function, bone marrow suppression and secondary malignancies (e.g. lymphoid malignancies).[41]

Cyclosporin A can be used alone or in combination with prednisone. It is, however, known to be toxic to the human kidney and long-term use can lead to permanent renal damage. It is, therefore, not recommended for patients with renal insufficiency and some older patients.[25]

Mycophenolate mofetil is an antiproliferative **immunosuppressant** that has been used in a limited number of studies.[25] Response rates of 39–78% have been reported, although whether the response is sustained remains to be determined.[25] It appears to be more useful in refractory patients.[30] Nausea and leukopaenia are common side effects and secondary malignancies, particularly skin cancer, have been reported.

Table 6. Second-line treatment options for adult ITP patients

Management strategy	Approximate response rate (time to response)	Toxicities	Sustained response
Azathioprine 1–2 mg/kg (maximum 150 mg/day)	Up to 65%; 40% in anecdotal reports (slow – may need to be continued for 3–6 months)	• Low incidence and generally mild: weakness, sweating, transaminase elevations, severe neutropenia with infection, pancreatitis	Up to 25%
Cyclosporin A 5 mg/kg/day for 6 days then 2.5–3 mg/kg/day	~50–80% in small series – dose dependent (3–4 weeks)	• Moderate but transient: increase in serum creatinine, hypertension, fatigue, paraesthesias, gingival hyperplasia, myalgia, dyspepsia, hypertrichosis, tremor	>50% of responders receiving low doses (at least 2 years)
Cyclophosphamide 1–2 mg/kg orally daily for at least 16 weeks or 0.3–1 g/m^2 intravenously for 1–3 days every 2–4 weeks	24–85% (1–16 weeks)	• Most are mild to moderate: neutropenia, acute deep venous thrombosis, nausea, vomiting	Up to 50%
Danazol 200 mg 2–4 times daily	67% complete or partial response; 40% anecdotal reports (3–6 months)	• Frequent side effects: acne, increased facial hair, increased cholesterol, amenorrhoea, transaminitis	46% remained in remission at a median of 119±45 months (mean duration of therapy 37 months)
Dapsone 75–100 mg	Up to 50% (3 weeks)	• Infrequent and treatable/reversible: abdominal distension, anorexia, nausea, methaemoglobinuria, haemolytic anaemia in glucose-6-phosphate-dehydrogenase-deficient patients • Severe: skin rash may require drug to be stopped	Sustained response in up to two-thirds of responders
Mycophenolate mofetil 1000 mg twice daily for at least 3–4 weeks	Up to 75% – complete response in up to 45% (4–6 weeks)	• Mild and infrequent: headache (most common and dose-limiting), backache, abdominal distension, anorexia, nausea	Sustained for short time
Rituximab 375 mg/m^2 weekly x4	60% – complete response in 40% (1–8 weeks)	• Low rate, usually mild to moderate • Severe: serum sickness and (rarely) bronchospasm, anaphylaxis, pulmonary embolism, retinal artery thrombosis, infection, development of fulminant hepatitis via reactivation of hepatitis B • Rare cases of progressive multifocal leukoencephalopathy	Sustained response >3–5 years in 15–20% of responders Responders may require retreatment months to years later
Splenectomy	80% – with ~65% achieve a lasting response (1–24 days)	• Haemorrhage, peripancreatic haematoma, subphrenic abscess, wound infection, death, pneumococcal infection, fever, overwhelming sepsis syndrome, thrombosis	Response sustained with no additional therapy in ~65% over 5–10 years
Thrombopoietin receptor agonist – eltrombopag 25–75 mg orally daily	For 50-mg dose 70%, for 75-mg dose 81% had platelet count >50 x 10^9/L on day 43 (By day 15, >80% of patients on 50 mg or 75 mg eltrombopag daily had an increased platelet count)	• Adverse events in ≥20% of patients: headache • Treatment-related serious adverse events: increased bone marrow reticulin, worsening thrombocytopenia upon discontinuation, thrombosis, liver function abnormalities (in 13%)	Up to 1.5 years*
Thrombopoietin receptor agonist – romiplostim 1–10 µg/kg subcutaneously weekly	Non-splenectomised: 88% Splenectomised: 79% (1–4 weeks to achieve platelet count >50 x 10^9/L from <30 x 10^9/L)	• Adverse events in ≥20% of patients: headache, fatigue, epistaxis, arthralgia and contusion (similar incidence to placebo group) • Treatment-related serious adverse events: increased bone marrow reticulin, worsening thrombocytopenia upon discontinuation, thrombosis	Up to 4 years*
Vinca alkaloid regimens	Highly variable transient response in 10–75% (5–7 days)	• Neuropathy, especially with repeated dose and in the elderly; neutropenia, fever, inflammation/thrombophlebitis at the infusion site	Average 10 months

*With continual drug administration. Adapted with permission from *Blood*.[25]

Cyclophosphamide can be given as a daily oral dose or intermittent intravenous dose. It has potentially severe side effects (e.g. bone marrow suppression, bladder cancer, leukaemia, sterility) and is, therefore, recommended only for patients with severe ITP, very low platelet counts and active bleeding.[25,42]

Corticosteroid-sparing agents

Danazol is an attenuated androgen originally developed to treat endometriosis.[25] The response rate is around 60%, with older patients appearing to respond better.[25] Side effects including acne and increased facial hair are usually reversible upon treatment discontinuation, but danazol is contraindicated in patients with pre-existing liver disease.[43]

Dapsone has anti-inflammatory and immunomodulatory effects. Response rates of around 50% have been reported.[30] Dapsone may be particularly useful in elderly patients or if splenectomy is contraindicated.[25]

Monoclonal antibodies

Rituximab is a chimeric **monoclonal antibody** that binds to the CD20 surface antigen present on B-cells and acts as an immunosuppressant. Rituximab is widely used even though it is not indicated for ITP and the optimal dose has not been established.[25] A response can occur in 60% of patients, and approximately one-third of patients have been reported to have a complete response that is maintained for at least 1 year.[44] Rituximab is contraindicated in patients with active hepatitis B infection. Some serious haematological and cardiovascular adverse effects have been reported (e.g. progressive multifocal leukoencephalopathy [PML], late-onset neutropenia) and more long-term safety data are needed.[25]

Splenectomy

Splenectomy is indicated for patients who are refractory or intolerant to corticosteroids and have severe thrombocytopenia, bleeding or both. It is recommended to wait at least 6 months from diagnosis before performing a splenectomy in case of spontaneous remission.[25] After splenectomy, durable remission is achieved in approximately 66% of patients.[45,46] Even after splenectomy some 20% of patients may relapse weeks, months or years later.[25] All patients need to be fully aware of the risks and benefits before making an informed decision regarding splenectomy. For example, patients must know that they will be susceptible to infections and must receive ongoing vaccination to prevent infection, prophylactic antibiotics before surgical procedures (e.g. dental work) and aggressive treatment for any infection. It is recommended that patients receive vaccines, such as prophylactic polyvalent pneumococcal, meningococcal C conjugate and *Haemophilus influenzae* b, at least 4 weeks prior to or 2 weeks after splenectomy.[25] Vaccinations may not be effective in patients who have received rituximab in the previous 6 months and vaccination requirements need to be addressed after B-cell recovery.

Thrombopoietin receptor agonists

Thrombopoietin receptor agonists mimic the action of the body's endogenous thrombopoietin to stimulate the production of platelets in bone marrow. Unlike other available therapies they are not immunosuppressive.[25] Two thrombopoietin receptor agonists are currently available: eltrombopag, a daily oral medication, and romiplostim, a once-weekly subcutaneous injection. Both are indicated for adult splenectomised patients who have ITP refractory to other treatments such as corticosteroids and immunoglobulins, and as second-line therapy for non-splenectomised patients in whom surgery is contraindicated.[47,48]

Thrombopoietin receptor agonists need to be administered continuously to keep platelet counts above 50 x 10^9/L.[25] A response (increase in platelet count) is usually seen within 1–2 weeks of treatment initiation in both splenectomised and non-splenectomised patients.[47,48] If there is no response to the highest dose after 4 weeks, the patient can be considered unresponsive.[47,48] Using eltrombopag or romiplostim can allow patients to reduce or discontinue their concurrent ITP therapy.[47,48] Patients receiving eltrombopag should avoid antacids, dairy products or polyvalent cation-containing mineral or vitamin supplements (i.e. iron, calcium, magnesium, aluminium, selenium, zinc) for at least 4 hours before and after administration to avoid significant reduction in eltrombopag absorption.[47] To date, no food or drug interactions have been reported for romiplostim.[48]

The side effects of thrombopoietin receptor agonists are generally mild; the most common is headache.[47,48] Concern has been raised over increased **reticulin** levels in the bone marrow, although the significance of this observation has yet to be established.[25] Patients should have peripheral blood smear and CBC tests before starting treatment, then weekly until the platelet count has stabilised and monthly thereafter. If cellular morphological abnormalities are observed treatment should be discontinued and a bone marrow biopsy performed using appropriate staining for reticulin.[47,48] Regular monitoring is also required to prevent platelet counts exceeding the normal range, as excessive numbers of platelets in the circulation can increase the risk of thrombotic and thromboembolic complications such as blood clots and stroke.[47,48]

Vinca alkaloids

Vinca alkaloids, such as vincristine and vinblastine, are used in cancer to inhibit tumour cell growth. In ITP, vinca alkaloids may inhibit phagocytic cell function through binding to platelet microtubules, which may help localise treatment to the platelet-destroying phagocytic cells.[49] Response to treatment is not sustained and vinca alkaloids may be more useful in providing short-term increases in platelet counts.[25] There is an upper cumulative dose limit for vinca alkaloids and neurotoxicity is a common side effect.

Emergency treatments and hospitalisation

Urgent increases in platelet count may be required, for example, in those requiring surgical procedures at high risk of bleeding or with current central nervous system, gastrointestinal or genitourinary bleeding.[25] Increases in platelet counts can be achieved by changing to IVIg either alone or in combination with corticosteroids **(Table 7)**. Platelet transfusion is indicated for patients who are experiencing severe bleeding or about to undergo surgery to increase their platelet count for a short period.[25] Anti-fibrinolytics (e.g. tranexamic acid) can be used to prevent recurrent bleeding in patients with severe thrombocytopenia, but there are no randomised studies of their efficacy in ITP.[25]

Table 7. Emergency treatments

- Combination of first-line treatments, e.g. high-dose intravenous corticosteroids and IVIg
- Platelet transfusions with or without IVIg
- Vinca alkaloids
- Splenectomy
- Anti-fibrinolytics

IVIg, intravenous immunoglobulin. Data taken from Provan *et al. Blood* 2010.[25]

For most patients hospitalisation is usually not required, but is indicated in those with: severe mucocutaneous or internal bleeding; platelet counts less than 20 x 10^9/L and a history of significant bleeding; compliance issues; or no demonstrable response to therapy with comorbid conditions.[11]

Failing first- and second-line therapies

Around 20% of ITP patients are unable to maintain haemostatic platelet counts after receiving first- and second-line therapies or splenectomy.[25] In many cases patients learn to live with low platelet counts. For those who continue to be symptomatic with increased risk of bleeding, the options are limited **(Table 8)**.[25] Thrombopoietin receptor agonists are the most effective option, with an overall response rate of nearly 80% in splenectomised patients, and are well tolerated.[25] Thrombopoietin receptor agonists have undergone rigorous controlled clinical trials, however, treatment needs to be continuous to maintain platelet counts. The other treatment options have not been extensively studied and are associated with considerable toxicities.

Table 8. Management of ITP in patients failing first- and second-line therapy

Management strategy	Approximate response rate (time to response)	Toxicities	Sustained response
Category A: treatment options with sufficient data			
Thrombopoietin receptor agonist – eltrombopag 25–75 mg orally daily	For 50-mg dose 70%, for 75-mg dose 81% had platelet count >50 x 10^9/L on day 43 (By day 15, >80% of patients on 50 mg or 75 mg eltrombopag daily had an increased platelet count)	• Adverse events in ≥20% of patients: headache • Treatment-related serious adverse events: increased bone marrow reticulin, worsening thrombocytopenia upon discontinuation, thrombosis, liver function abnormalities (in 13%)	Up to 1.5 years*
Thrombopoietin receptor agonist – romiplostim 1–10 µg/kg subcutaneously weekly	Non-splenectomised: 88% Splenectomised: 79% (1–4 weeks to achieve platelet count >50 x 10^9/L from <30 x 10^9/L)	• Adverse events in ≥20% of patients: headache, fatigue, epistaxis, arthralgia and contusion (similar incidence to placebo group) • Treatment-related serious adverse events: increased bone marrow reticulin, worsening thrombocytopenia upon discontinuation, thrombosis	Up to 4 years*
Category B: options with minimal data, considered to have potential for considerable toxicity			
Campath-1H	Initial response in 67% of patients (1 week–9 months)	• Fever, rigors, chills, intracranial haemorrhage, cerebral vein thrombosis, severe intravascular haemolysis, death, infection, transfusion-associated graft versus host disease	All but one patient relapsed within 24 months
Combination chemotherapy: various regimens	Response in >65% (2–3 months)	• Risk of second malignancies including acute leukaemia, mild nausea and vomiting, alopecia, acne, haemorrhagic cystitis, neuropathy, pancytopenia	Durable response rate seen in two-thirds of patients achieving complete remission (~40% of patients)
Autologous stem cell transplantation (ASCT)	Of 14 patients, 6 achieved remission (5 weeks)	• Frequent serious toxicities reported in peri- and post-transplant period: infection, mucocutaneous bleeding, myelosuppression, death	Long-term complete remission in one-third of patients

*With continual drug administration. ITP, immune thrombocytopenia. Adapted with permission from *Blood*.[25]

Special considerations

Pregnancy

Platelet levels can naturally decrease by approximately 10% towards the end of the third trimester.[25] In most cases this will have no effect on the patient, but in some cases may cause incidental thrombocytopenia of pregnancy. This benign condition resolves within 2 months of delivery, but may cause an exacerbation in those with pre-existing ITP.[25] Presentation and diagnosis of new ITP in a pregnant woman is similar to that of non-pregnant individuals, although other pregnancy-related causes of thrombocytopenia (e.g. preeclampsia; haemolysis, elevated liver tests and low platelet count [HELLP]; pregnancy associated thrombotic thrombocytopenic purpura [TTP]) need to be excluded.[50]

There is no medical reason why women with existing ITP cannot become pregnant and have children, although a number of factors need to be considered first, such as platelet count, symptoms and overall health.[50]

Women with mild stable ITP can usually go through pregnancy without requiring treatment. For women with symptomatic ITP, treatment will depend on platelet count and risk of maternal haemorrhage **(Table 9)**.[25] Regular monitoring is required throughout the pregnancy—monthly during the first two trimesters, every 2 weeks after 28 weeks and weekly after 36 weeks—and early consultation with the obstetrician is recommended.[50] More caution may be needed during and after delivery in women with ITP, to prevent excessive bleeding, therefore, delivery in hospital is advised. Current guidelines suggest that platelet counts are maintained at above 20 x 10^9/L during the first two trimesters with a higher level of above 50 x 10^9/L near term or if a caesarean section is required.[25] If a patient needs spinal or epidural anaesthesia then their platelet count should be over 75 x 10^9/L.[25]

Table 9. Managing ITP through pregnancy

First-line treatment	Failing first-line treatment	Treatments to be avoided
Corticosteroids Low-dose prednisone (10–20 mg/day) IVIg	Combination of a corticosteroid and IVIg Combination of IVIg with azathioprine	Danazol Immunosuppressives (except azathioprine) Rituximab Thrombopoietin receptor agonists Vinca alkaloids

IVIg, intravenous immunoglobulin. Data taken from Provan *et al. Blood* 2010.[25]

ITP usually does not affect the foetus, although some infants may be born with or develop low platelet counts soon after birth (within 2–5 days).[25] However, platelet counts frequently return to normal without any treatment. Approximately 5–10% of newborn infants can develop severe thrombocytopenia, but the incidence of intracranial haemorrhage is very low.[50] Invasive procedures to establish the foetal platelet count present a greater risk to the foetus than the risk of intracranial haemorrhage.[50] There also appears to be no difference in the risk of intracranial haemorrhage between caesarean section and vaginal delivery.[25]

Table 10. Key educational opportunities for nurses involved in managing patients with ITP

Stage	Educational opportunity
At diagnosis	• Give general overview of ITP (e.g. what is ITP?) • Clarify the impact of the disease and overall prognosis • Dispel common myths and reassure patients (e.g. ITP is not contagious, congenital or inheritable) • Advise on lifestyle considerations (e.g. activities to avoid) • Review all treatment options particularly first-line options – benefits, side effects • Give overview of routine laboratory assessments (e.g. platelet counts) • Outline resources available to assist patients with psychosocial support and coping mechanisms
Symptomatic disease	• Describe dosing, administration and duration of treatment • Assist with managing side effects of treatment • Advise on second-line treatment options, particularly splenectomy (procedure, benefits, risks, long-term consequences) • Reduce risk of complications (e.g. detail what medicines to avoid) • Give options for patients with chronic ITP who have failed first- and second-line therapies
Pregnancy	• Detail any safety concerns for mother and foetus • Explain outcomes of worsening maternal disease • Describe risks of pregnancy itself
Ongoing monitoring and follow-up	• Provide appointment schedules • Explain how to monitor signs and symptoms of falling platelet count • Clarify when to seek medical attention • Encourage patients to join a support group

ITP, immune thrombocytopenia.

Key role of nurses in managing ITP patients

Two of the key roles of nurses managing patients with ITP include:

1. Patient education **(Table 10)** – in particular to explain what ITP is, how it can affect the patient and the treatment options, including benefits and side effects, dosing, administration and duration of treatment and how to manage side effects **(Table 11)**.
2. Providing support – to enable patients and their families to cope with the physiological and psychological effects of ITP.

Table 11. Managing side effects of treatment*

Treatment	Side effect	Management options
Corticosteroids	Weight gain (can be rapid and lead to Cushingoid appearance)	• Avoid salt to decrease fluid retention • Avoid high-fat and high-sugar foods • Eat complex carbohydrates
	Muscle loss	• Increase exercise
	Gastrointestinal	• Administer early in the day after food • Proton pump inhibitors may be required
	Oedema	• Use diuretics • Avoid excess dietary sodium • Wear compression stockings
	Fatigue	• Manage activities carefully • Manage administration timing – give either early in the morning or late at night • Ensure patient has enough sleep
	Hyperglycaemia/diabetes	• Modify diet • Avoid carbohydrates and sugars • Regular monitoring of blood glucose levels • Oral hypoglycaemic or subcutaneous insulin may be required
	Acneiform rash	• Use non-irritating soaps • Topical or oral antibiotics may need to be prescribed
	Immunosuppression	• Monitor for infections • Educate patients to report signs and symptoms
	Other	• Advise patients of possible mood changes • Check blood pressure • Monitor for signs of osteoporosis
IVIg	Infusion reactions	• Slow rate of infusion, particularly first two occasions • Advise patients of possible allergic reactions
Immunosuppressants	Immunosuppression	• Monitor for infections • Educate patients to report signs and symptoms
	Liver function disturbances (for azathioprine)	• Monitor liver enzymes weekly for first 8 weeks and then monthly
	Bone marrow suppression (for azathioprine)	• Monitor thiopurine methyltransferase levels
Splenectomy	Infections	• Antibiotics may need to be prescribed • Vaccinations pre-splenectomy and every 5 years thereafter against pneumococci and haemophilus • If travelling abroad ensure immunisations are up-to-date
Thrombopoietin receptor agonists	Headaches	• Use paracetamol rather than aspirin or anti-inflammatory agents as these can interfere with platelet function

*Recommendations based on expert opinion.

Chapter 4. Immune thrombocytopenia – patient considerations

The ITP patient journey

Many ITP patients will experience a range of emotions that can differ according to the disease course and their stage of life. These emotions can be the result of the disease itself, because of treatments they are taking, or part of coping with the disease. The 10–20% of children who develop chronic ITP may struggle with the burden of disease and side effects of treatment. Children tend to be more concerned about their appearance and restrictions on their lifestyle than adults.[28] For example, some ITP treatments can cause significant weight gain, which can lead to depression in many patients. Children can also feel isolated by not being able to take part in everyday activities with their friends. In adults, ITP is associated with fear and anxiety about uncontrolled bleeding and long-term consequences of treatments such as splenectomy.[28] The symptoms of ITP can have a significant impact on a patient's quality of life and can affect their work productivity.[51] Providing appropriate support and counselling is essential to help patients and their families cope with ITP.

Living with ITP

ITP is manageable and patients can take steps to prevent complications **(Table 12)**.[52] The initial goal of treatment is to attain a haemostatically safe platelet count (>50 x 10^9/L) that prevents or minimises a patient's risk of serious bleeding by using the least possible intervention to reduce likelihood of potential toxicities. Generally treatment should be tailored to the individual patient.[25] To achieve this target, patients with low platelet counts must take therapy when necessary and as prescribed, and will in most cases be required to undergo continual monitoring of platelet counts.

Table 12. Patient recommendations*

Medications	Avoid medicines that affect platelet function: • Blood-thinning pharmaceuticals – aspirin, warfarin • Anti-inflammatory agents – ibuprofen, naproxen • Platelet aggregation inhibitors – glycerol guaiacolate Use acetaminophen-containing medications for pain or fever If aspirin, NSAIDS, warfarin or other antithrombotics are essential, maintain platelet counts at 40–50 x 10^9/L[11]
Activities	Most activities can be undertaken Sexual activity is not restricted, although care may be needed if a patient's platelet count is low and have active bleeding Avoid any activities with high risk of injury, particularly to head and neck – including contact sports (e.g. football, rugby, boxing) Wear gloves when working with knives or other tools Wear protective clothing such as helmets, knee, elbow or wrist pads as appropriate For children, provide soft surfaces in play areas
Personal hygiene	Brush teeth with a soft toothbrush Avoid dental flossing when platelet count <50 x 10^9/L Visit dentist regularly to avoid bleeding gums and gum disease Use an electric shaver rather than a razor for shaving
Travel	Ensure patient has adequate travel insurance If flying: • Undertake the recommended in-flight exercises for preventing deep vein thrombosis • Wear support stockings • Avoid alcohol and drink plenty of water
Other	Wear a medical identification tag or bracelet to alert healthcare professionals to their condition in case of emergency, particularly if the patient has undergone a splenectomy Carry an identification or health card that states their illness and lists their medications and dosages

NSAIDS, nonsteroidal anti-inflammetary drugs.*Recommendations based on expert opinion.

For women, menstruation can be an issue, with some experiencing heavy and prolonged bleeding that may lead to anaemia. The frequency and amount of menstrual bleeding can be managed using oral contraceptives or progesterone-containing intrauterine devices that induce endometrial atrophy.[39] Anti-fibrinolytic agents (e.g. tranexamic acid) can also be helpful to reduce menstrual blood loss. In cases of anaemia it may be necessary to monitor the patient's iron levels and provide iron supplementation.

If a patient needs to undergo a dental or surgical procedure, recommendations for safe platelet counts have been devised **(Table 13)**.[25] In these situations, tranexamic acid (25 mg/kg) can be used to prevent excessive postoperative bleeding.[39]

Table 13. Recommendations for platelet counts for dental and surgical procedures

Procedure	Platelet count (x 10^9/L)
Dentistry	≥20
Tooth extractions	
Simple	≥30
Complex	≥50
Local anaesthesia	≥30
Minor surgery	≥50
Major surgery	≥80
Major neurosurgery	≥100

Data taken from Provan *et al. Blood* 2010.[25]

Lifestyle considerations

In general, it is important for ITP patients to maintain a healthy lifestyle and balanced diet **(Table 14)**.[52] Lifestyle considerations include moderating caffeine intake, smoking cessation, and getting adequate sleep and exercise.[52] It is recommended that patients are exposed to at least 10–15 minutes of sunlight per day to increase vitamin D absorption to prevent osteoporosis. Patients should be encouraged to keep a diary to monitor how they are feeling to determine if there are any connections between their platelet count and lifestyle factors.

Table 14. Dietary recommendations

Drink plenty of water (at least 2 L/day) and eat fibre	To avoid constipation
Eat organic foods	Pesticides and herbicides can exacerbate autoimmune disorders
Eat dark, leafy green vegetables (e.g. kale)	Contain calcium, minerals and vitamin K, which promote clotting
Reduce intake of blueberries, red/ purple grape products, garlic, ginseng, tomatoes	Interfere with blood clotting
Reduce intake of dairy products (e.g. milk, cheese, yoghurt)	Contribute to mucus formation and exacerbate some autoimmune diseases
Avoid alcoholic drinks	Can damage bone marrow, where platelets are produced, and the liver, where clotting factors and thrombopoietics are produced
Avoid products containing quinine	Can lower platelet count

These recommendations are the opinion of the Platelet Disorder Support Association.[52]

Common patient questions

Below are some typical questions that a patient with ITP might ask and corresponding answers.

Question	**What is ITP?**
Answer	ITP is an autoimmune-mediated haematological disorder affecting platelets. The immune system produces antibodies directed against platelet antigens, resulting in platelet destruction and suppression of platelet production in the bone marrow, leading to an increased risk of serious bleeding events. [See Chapter 1]

Question	**What are platelets?**
Answer	Platelets are disc-shaped cell fragments that play an essential role in blood clotting. People with low platelet counts are at increased risk of spontaneous bleeding and/or bruising.

Question	**Who gets ITP?**
Answer	There is no typical ITP patient. ITP affects people of both sexes and all ages. [See Chapter 1 and Appendix]

Question	**Is ITP contagious? Can it spread to my family and others?**
Answer	No, ITP is not contagious, congenital or inheritable.

Question	**How long will I have ITP?**
Answer	In some cases ITP can resolve spontaneously, although in most adults ITP will be a lifelong illness. For many patients the difficult part is finding a treatment that works without causing unwanted side effects. [See Chapter 2]

Question	**What symptoms can I expect?**
Answer	Symptoms of ITP are highly variable. Symptomatic patients can experience petechiae, purpura, unusual or easy bruising and persistent bleeding. [See Chapter 2]

Question	**What are my treatment options?**
Answer	Various treatment options are available for managing ITP. First-line therapies include corticosteroids and immunoglobulins. Second-line therapies include immunosuppressants, corticosteroid-sparing agents, monoclonal antibodies, splenectomy, thrombopoietin-receptor agonists and vinca alkaloids. The choice of treatment(s) will depend on your signs, symptoms and comorbidities, how well the treatment is tolerated, lifestyle and preference [See Chapter 3]

Question	**How long will I need to be on these treatments?**
Answer	Many patients experience mild, stable disease that requires no treatment, while in those with symptomatic disease treatment may be required for short periods to increase platelet counts or long-term to maintain haemostatic platelet levels that prevent bleeding.

Question	**How long will it take to know the treatment is working?**
Answer	The length of time to determine whether a treatment is working will depend on the medication prescribed. [See Chapter 3]

Question	**What side effects could I have?**
Answer	All treatments used to manage ITP have been reported to have side effects, although the type and extent differ according to the treatment and from person to person. [See Chapter 3]

Question	**Are there any precautions that I can take to minimise side effects?**
Answer	Some side effects of treatment can be minimised. For example, monitoring and controlling your diet if receiving corticosteroids or taking paracetamol rather than aspirin for headaches if receiving thrombopoietin receptor agonists. [See Chapter 3]

Question	**How often do I have to get my platelet count checked?**
Answer	If your disease is stable you may not need to have frequent platelet counts. If you are symptomatic or receiving certain treatments you will need to have your platelet count checked more frequently. If you require dental or surgical procedures you should have your platelet count checked to ensure it is within a safe range. [See Chapter 3]

Question	**When should I contact my healthcare provider?**
Answer	Immediately if you hit your head or have a serious accident. If you are experiencing large number of bruises or petechiae, nosebleeds, bleeding gums, or blood in your urine, stool or vomit. Experiencing any of the following symptoms that are suggestive of intracranial haemorrhage: a persistent headache, dizziness, vomiting, unusual tiredness, confusion, slurred speech, discordant eye movement, weakness particularly on one side of the body, numbness/tingling hands or feet, a stiff neck or back, seizures, loss of hearing or sight.

Question	What is an intracranial haemorrhage?
Answer	An intracranial haemorrhage is bleeding that occurs in the skull as a result of either a ruptured or leaking blood vessel. Patients with ITP are at increased risk of intracranial haemorrhage if they receive any injury to the head.

Question	Are there any medications that I should avoid?
Answer	A number of medications such as aspirin and ibuprofen affect platelet functioning. Before taking any new medication always check the label or consult a healthcare professional. [See Chapter 4].

Question	Does having ITP require me to stay on a special diet?
Answer	There is no special diet for patients with ITP, although it is advisable to maintain a healthy balanced diet and lifestyle. [See Chapter 4]

Question	Can any of the treatments interact with my nutritional supplements or medications I'm receiving for other health conditions?
Answer	Some nutritional supplements and medications can affect platelets and, therefore, increase your chance of bleeding. It is important that you discuss all supplements and medications with a healthcare professional. [See Chapter 4].

Question	What can I do or not do now that I have ITP?
Answer	ITP should not stop you doing anything, although if your platelet count is low you may need to restrict some activities such as those that have a higher risk of injury (e.g. contact sports).

Question	Can I have children?
Answer	Women with ITP can have children, although there are some potential maternal and foetal complications that can occur, such as an increased risk of bleeding during delivery. It is important that patients are carefully monitored throughout pregnancy and during delivery, as some patients may require additional therapy. [See Chapter 3]

Question	What should my platelet count be during pregnancy?
Answer	It is recommended that platelet counts are maintained above 20 x 10^9/L during the first two trimesters, with a higher level of above 50 x 10^9/L near term or if a caesarean section is required. Counts above 75 x 10^9/L are needed for spinal or epidural anaesthesia. [See Chapter 3]

Question	Will I be able to have a natural and/or home birth?
Answer	Women with ITP can have a natural vaginal delivery depending on their platelet count. Home deliveries are not advised because of the increased risk of bleeding complications for the mother and the possibility of low platelet counts in the newborn. [See Chapter 3]

Question	What should I tell other people about my condition?
Answer	If you wish, you may want to explain to people that you have a blood clotting disorder that causes you to bruise easily and increases your risk of bleeding, but it is not contagious.

Question	Can I still go on holiday or travel for business?
Answer	Yes, you can still travel for business or leisure, although this may require some preparation. If you are symptomatic you must ensure you have enough medication for your trip and you may need to organise treatment in the country you are travelling to. For those who have had a splenectomy it is important to receive appropriate vaccinations to prevent infections. You will also require adequate travel insurance and should undertake the recommended in-flight exercises to prevent deep vein thrombosis.

Question	Will it affect my employment opportunities?
Answer	ITP should not affect your employment opportunities, although certain professions may have a higher risk of injury, which could increase your risk of serious bleeding.

Question	How will this affect my life insurance?
Answer	ITP may affect your life insurance but will depend on the individual insurer.

Glossary

Antibodies	Proteins produced by the immune system that attack foreign antigens (e.g. bacteria, viruses)
Autoimmune (disorder)	The body's immune system reacts against its own tissue to produce antibodies that attack itself
Bone marrow	Tissue inside of bones that produces blood cells
Bone marrow aspiration	Extraction of bone marrow from bones, usually the posterior iliac crest, using an aspiration needle
Complete blood count	A measure of the number of blood cells including platelets
Corticosteroids	Medicines that act on the immune system
Haematoma	Raised purple areas (bruise) on the skin caused by blood collecting under the skin
Idiopathic	A disease of unknown cause
Immune thrombocytopenia	A blood disease in which platelets are destroyed by the immune system
Immunosuppressants	Medicines that act to reduce the activity of the immune system
Intracranial haemorrhage	Bleeding that occurs in the skull as a result of either a ruptured or leaking blood vessel
Megakaryocyte	A bone marrow cell that produces platelets
Menorrhagia	Abnormally heavy and prolonged menstrual bleeding
Monoclonal antibody	An antibody produced from a single clone of cells
Peripheral blood smear	A blood drop on a glass slide used to examine blood cells under the microscope

Glossary continued

Petechiae	A type of bleeding in the skin. Tiny red or purple dots (<3 mm in diameter) on the skin caused by broken blood vessels that can resemble a rash
Plasma	The yellow liquid component of blood in which blood cells are suspended
Platelet count	A measure of the number of platelets contained in the blood
Platelets	The small cells that form blood clots when blood vessels are damaged. Otherwise known as thrombocytes
Purpura	A type of haematoma. Purple bruises about 1 cm in diameter that are generally round in shape and caused by bleeding under the skin
Reticulin	A network-forming fibre that acts to support soft tissues such as the bone marrow
Spleen	An organ that is part of the immune system, which filters and stores blood cells. Normally weighs 150 g and is located under the left costal margin
Splenectomy	Surgery to remove the spleen
Thrombocytopenia	Low platelet count (<100 x 10^9/L)
Thrombopoietin	A protein produced at a fixed rate in the liver that is the key regulator of platelet production
Thrombopoietin receptor antagonists	Medicines that mimic the action of endogenous thrombopoietin to stimulate the production of platelets

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Additional resources

American Society of Hematology	www.hematology.org/
European Hematology Association (EHA)	www.ehaweb.org
European Society for Immunodeficiencies (ESID)	www.esid.org
International Patient Organisation for Primary Immunodeficiencies (IPOPI)	www.ipopi.org
ITP Foundation	www.itpfoundation.org
ITP Support Association	www.itpsupport.org.uk
ITP Village	www.ITPVillage.com
Platelet Disorder Support Association	www.pdsa.org
Platelets on the Web	www.ouhsc.edu/platelets/index.html
The Daily Strength	www.dailystrength.org/c/Thrombocytopenic-Purpura/support-group

Appendix: Case examples

Mr K	
Patient details	• 23 years old • Recently graduated from university
Time since ITP diagnosis	• 11 years
Medical history	• Chronic ITP with persistently low platelet count (<10 x 10^9/L)
Presentation	• Initially presented with mild/moderate mucocutaneous bleeding
Laboratory results	• Platelet count <5 x 10^9/L
Clinical course and management	• At 17 years of age admitted to emergency department semi-conscious after being hit on the head by a bottle thrown during an argument • Experienced a traumatic epidural and intracerebral haematoma as a consequence of the head trauma • Underwent surgery for haematoma and recovered but with paresis in left arm • Following the accident, he received conservative treatment (i.e. no active ITP treatments) at the wish of the patient and his parents • At age 19 years underwent splenectomy after a period of intense counselling with the responsible haematologist. Experienced complete remission with platelet counts >150 x 10^9/L • Four years after splenectomy he has stable platelet count (>200 x 10^9/L) and living a fairly normal life. He has not needed any further ITP treatments during this time

Miss N	
Patient details	• 26 years old • Enjoys music and amateur dramatics
Time since ITP diagnosis	• 6 years
Medical history	• Chronic cyclical ITP • Splenectomised • Corticosteroid intolerant
Presentation	• Sudden drop in platelet count with bleeding
Laboratory results	• Platelet count <50 x 10^9L
Clinical course and management	• At new presentation she received moderate doses of corticosteroids and IVIg followed by romiplostim allowing corticosteroids and IVIg to be tapered and discontinued • Currently platelet count maintained using romiplostim 2 µg/kg weekly

Mr J	
Patient details	• 45 years old • Married and father of twin girls aged 13 years
Time since ITP diagnosis	• 10 years
Medical history	• Chronic lymphocytic leukaemia
Presentation	• Glandular fever, abnormal CBC
Laboratory results	• Routine CBC performed as recovering from glandular fever
Clinical course and management	• Responded to steroids for >6 years • Relapsed 13 weeks after finishing steroid treatment • ITP developed a cyclical pattern • Received IVIg 0.4 g/kg for 3 days with initial response • Relapsed after 18 months • Underwent splenectomy • Relapsed after 1 year • Received rituximab 100 mg once weekly for 4 weeks but no response • Currently responding to romiplostim

Mrs N	
Patient details	• 60 years old • Enjoys reading and going to the theatre
Time since ITP diagnosis	• ~5 years
Medical history	• None
Presentation	• No symptoms, routine blood test indicated ITP
Laboratory results	• Initial platelet count 30 x 10^9/L
Clinical course and management	• Initially prescribed prednisolone, her platelet count increased to 70 x 10^9/L but fell to 20 x 10^9/L when steroids discontinued • After discussion, it was decided to hold off further treatment • 8 weeks later her platelet count dropped to 8 x 10^9/L and she received IVIg, which was effective for a few weeks • After further discussion it was decided to watch and wait and she has not experienced haemorrhagic events even with low platelet counts • When platelet count dropped she also received a short course of IV anti-D Ig • She has travelled throughout Europe and to Australia without complications • Continues to enjoy an active life with a platelet count usually below ≤10 x 10^9/L with few bleeding problems