# Trust Guideline for the Management of Newly Diagnosed Immune Thrombocytopenia (ITP) in Children

A clinical guideline recommended for use

<table>
<thead>
<tr>
<th>For Use in:</th>
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<tbody>
<tr>
<td>By:</td>
<td>Paediatric Medical Staff</td>
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<tr>
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<td>Children under 16 years with Newly Diagnosed Immune Thrombocytopenia (ITP)</td>
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<tr>
<td>Name of document author:</td>
<td>Dr Jo Ponnampalam</td>
</tr>
<tr>
<td>Job title of document author:</td>
<td>Consultant Paediatrician/Shared Care Oncologist</td>
</tr>
<tr>
<td>Name of document author's Line Manager:</td>
<td>David Booth</td>
</tr>
<tr>
<td>Job title of author's Line Manager:</td>
<td>Chief of Division</td>
</tr>
<tr>
<td>Supported by:</td>
<td>Dr Hamish Lyall, Consultant Haematologist, NNUHFT Dr Emmy Dickens, Consultant in Paediatric Haematology, Addenbrookes Hospital</td>
</tr>
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This guideline has been approved by the Trust's Clinical Guidelines Assessment Panel as an aid to the diagnosis and management of relevant patients and clinical circumstances. Not every patient or situation fits neatly into a standard guideline scenario and the guideline must be interpreted and applied in practice in the light of prevailing clinical circumstances, the diagnostic and treatment options available and the professional judgement, knowledge and
expertise of relevant clinicians. It is advised that the rationale for any departure from relevant guidance should be
documented in the patient's case notes.

The Trust's guidelines are made publicly available as part of the collective endeavour to continuously improve the
quality of healthcare through sharing medical experience and knowledge. The Trust accepts no responsibility for any
misunderstanding or misapplication of this document.

Quick reference guideline
Trust Guideline for the Management of: Newly Diagnosed Immune Thrombocytopenia (ITP) in Children

- Children with ITP should not be admitted to hospital unless they have ongoing significant bleeding.
- A decision to treat should be based on severity of symptoms, not on platelet count alone.
- A decision to treat a child should be discussed with the duty Consultant Paediatrician and/or Consultant Haematologist.
- Platelet transfusions should be given only for significant haemorrhage and are more likely to be effective if given with IVIG.

Rationale

Childhood ITP is uncommon and causes much (generally unjustified) anxiety regarding mortality and morbidity. There have been significant differences in investigation and treatment practice throughout the UK as good quality evidence has been scant. In recent years, however, large surveys of practice and outcome as well as a few randomized trials of different treatment modalities have been conducted. Guidelines on best practice have been updated as a result, and this guideline draws on the most recent international guidelines. National audits of practice have been carried out and results have further informed this guideline. There is an ongoing data collection registry that should be offered to patients and families at diagnosis which will further enhance our understanding of the natural history of the disease.

Definitions

Nomenclature
- Newly diagnosed ITP – remission occurs before 3 months (50-70%)
- Persistent ITP – low platelet count beyond 3 months – 1 year (20-30%)
- Chronic ITP – symptoms persist beyond 1 year (10-20%)

Grading of Disease Severity
- Mild (77% of children) – Few petechiae and small (<5cm) bruises. Epistaxis, stopped by applied pressure
- Moderate (20% of children) – Numerous petechiae and large (>5cm) bruises. Epistaxis longer than 20 minutes. Intermittent bleeding from gums, lips, buccal, oropharynx or gastrointestinal tract. Hypermenorrhagia, haematemesis, haematuria, melena – without hypotension and falling Hb<20g/l
- Severe (3% of children) – Epistaxis requiring nasal packing or cautery. Continuous bleeding from gums, buccal, oropharynx. Suspected internal haemorrhage (lung, muscle, joint). Hypermenorrhagia, haematemesis, haematuria, melena – leading to hypotension and falling Hb>20g/l
- Life-threatening (rare, < 1% of children) – Intracranial haemorrhage or continuous or high volume bleeding resulting in hypotension or prolonged capillary refill and requiring fluid resuscitation or blood transfusion

Broad recommendations
1. **Pathophysiology**

ITP is an acute immune-mediated condition of platelet destruction most commonly affecting young children. 80-85% remit spontaneously within a few months; 15-20% run a chronic course of >12 months duration.

2. **Clinical features**

2.1 **History**

Typically a child with newly diagnosed ITP:

- Presents with a short (24-48 hour) history of easy/spontaneous bruising or mucosal bleeding
- Is well at presentation
- May have had a viral infection in preceding 2-3 weeks (50%)

Atypical features in a child with bruising or bleeding include:

- A much longer history
- Presentation before 6 months of age (congenital platelet disorders)
- A family history of bleeding problems (Von Willebrands or other coagulopathy)

2.2 **Examination**

Typical features:

- Purpura, petechiae and ecchymoses
- Occasionally mucosal bleeding e.g. nosebleeds (and occasionally melaena)
- Rarely, macroscopic haematuria

Look for atypical features associated with other causes of bleeding/bruising/purpura:

- Acute Leukaemia: Lymphadenopathy, anaemia or hepatosplenomegaly
- Aplastic anaemia: Features of anaemia, recurrent infections
- Non-accidental injury: bruising suggestive of physical abuse,, fractures, signs of neglect
- Henoch-Schonlein Purpura: Distribution of lesions, palpable purpura, abdominal/joint pain
- Sepsis (especially meningococcal): systemic upset, fever, shock
- Haemolytic Uraemic Syndrome: diarrhoeal illness, anaemia, oliguria +/- jaundice

2.3 **Outcome**

- 80-85% of newly diagnosed ITP in children remits spontaneously
- Older children (i.e. those over 10) are more likely to progress to a chronic course (symptoms persisting for over 12 months)
- Severe haemorrhage (including macroscopic haematuria, symptomatic GIT bleeding or epistaxis sufficient to cause fall in Hb >20g/l) occurs in 3% of cases
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- Intra-cranial haemorrhage occurs in 0.1-0.5% cases, is rarely fatal
- Severe haemorrhage can occur after treatment has commenced
- Without treatment, most children will have a platelet count > 20x10^9/L within 5 days and a normal platelet count by six months

3. Investigations

3.1 Typical clinical cases

In typical clinical cases, the only investigations required are a Full Blood Count (FBC), coagulation screen and Film, which shows normal coagulation screen and thrombocytopenia (platelet count usually <20x10^9/L) with an otherwise normal film and counts. A Direct Coombs test (DCT) and immunoglobulins should also be performed at baseline.

3.2 Atypical clinical cases (bone pain, failure to thrive, lymphadenopathy, additional cytopenias)

Atypical features on the FBC, which should prompt a review of the diagnosis, include:

- Hb <100g/L (in infant <12months); <110g/L (in child >12months)
- WBC <5x10^9/L in child <6yrs; <4x10^9/L in child >6yrs
- Neutrophils <1.5 x10^9/L
- Blast cells on peripheral blood film

Where the clinical picture is atypical other investigations should be performed appropriate to the differential diagnosis.

3.3 Bone Marrow Aspiration (BMA):

- Is not indicated in typical cases
- Is of no proven benefit when used to “rule out” leukaemia before treatment is commenced
  - Leukaemia is extremely rare in these circumstances (0/332 in one series)
  - There is no proven adverse effect on outcome when treatment is given without prior BMA
- May be considered when either the clinical picture or FBC + film are atypical, particularly if steroid treatment is contemplated

4. Management

4.1 Hospital admission: Only patients requiring active treatment or close monitoring for severe bleeding require admission

4.2 Care at discharge All parents should receive:

- A full explanation of the condition and its management (please give parent information leaflet from website www.itp.org.uk or appendix below)
- A written referral via the referral console to Dr Jo Ponnampalam, Consultant Paediatrician
5. Treatment

Treatment should be based on severity of symptoms not platelet count alone. The goal of all treatment strategies is to achieve a platelet count that is associated with adequate haemostasis rather than a “normal” platelet count. Treatment can be divided into the following:

Observation only

- Used for mild to moderate bleeding
- Advise children and parents to exert caution regarding activities associated with trauma e.g. ski-ing, any contact sport e.g. rugby, boxing. Helmets should be worn if cycling and if swimming, no diving is recommended in shallow end.

- Advise parents to avoid the use of NSAIDs during disease course (no aspirin, ibuprofen/Nurofen/Calprofen). Parents can be reassured that paracetamol is safe to take
- Avoid herbal remedies that can increase the risk of bruising or bleeding
- Avoid intramuscular injections when platelets<100
- Monitor disease course with follow-up in outpatients

Pharmacological Treatment

- Use for severe bleeding and following life-threatening haemorrhage
  - Raises platelet count faster than no treatment [median time to achieve platelets over 20x10^9/L is 1 day for IVIg; 2 days for steroids]
  - Has no proven effect on the rate of serious or fatal haemorrhages
  - Has no effect on the incidence of chronic ITP (longer than 12 months); however can be useful to provide a transient benefit only-it is useful to document whether or not children respond to any given treatment as this can influence treatment options if they relapse later
  - Is associated with a significant risk of side effects
  - Tranexamic acid may be prescribed (in consultation with duty Consultant) for troublesome persistent symptoms - ensure no haematuria present when using tranexamic acid. Dose for oral tranexamic acid as per cBNF

Treatment with Blood Products
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- Platelet transfusions should only be used for life-threatening haemorrhages following consultation with a Consultant Paediatrician and/or Haematologist.
- Best practice suggests giving platelet transfusion – 1 complete unit (if child >15 kg) and re-check the count at 10 minutes post transfusion.
- Platelets are consumed extremely quickly in ITP; therefore, it is necessary to administer IV immunoglobulin concurrently.
- Please note that anti-D is not recommended in this trust.

5.1 Life-threatening haemorrhage

Attention to Airways, Breathing and Circulation as with any other emergency

- Give platelet transfusion and concurrent intravenous immunoglobulin and IV methylprednisolone (see below).

5.2 Severe haemorrhage

Attention to Airways, Breathing and Circulation as with any other emergency

- Persistent GIT haemorrhage or epistaxis causing fall in Hb >20g/l from baseline or to level below 80g/l.
- Give platelet transfusion concurrently with intravenous immunoglobulin and IV methylprednisolone (see below).

5.3 Specific therapies

5.3.1 Intravenous Immunoglobulin (IVIg): (please refer to Trust Immunoglobulin policy and fill in appropriate form-refer to hyperlinks below). Obtain verbal consent and document in medical notes.

**Standard Dose:** 1gram/kg per dose as a single dose by intravenous infusion. Repeat dose on Day 2 if no improvement.

- The second dose may be omitted if symptoms have remitted and the platelet count is >20x10^9/L on the second day.
- Ensure a full blood count is checked post treatment and at 1 week to document response.

The TRUST immunoglobulin guidelines are designed to help potential prescribers of immunoglobulin identify treatment indications for which its use is appropriate; the immunoglobulin request form helps inform local immunoglobulin assessment panels to approve and monitor the local prescribing of immunoglobulin, appropriate indications for use and also informing a national immunoglobulin database.

[www.ivig.nhs.uk](http://www.ivig.nhs.uk)

[http://intranet/committees/DTMM/docs/ImmunoglobulinRequestForm.doc](http://intranet/committees/DTMM/docs/ImmunoglobulinRequestForm.doc)

5.3.2 Steroids (to preferably be given via the oral route):

5.3.2.1 Prednisolone

Dose: 4mg/kg/day (maximum 200mg/day in divided doses) orally for 4 days,
then stop.
Alternately, a dose of 1-2mg/kg for 2 weeks, then wean(rapidly if non responder, more slowly if responder)

5.3.2.2 Methyl Prednisolone (MePred)- only to be administered in life threatening or severe haemorrhage, with IVIG
Some studies comparing high-dose MePred with IVIg show no difference in efficacy; others suggest IVIg is slightly faster and more effective at raising platelet counts.

Dose: 30mg/kg/day for 3 days p/o, followed by 20mg/kg/day for 4 days po

6. Follow-up

Patients discharged without treatment should be seen in the Jenny Lind Children’s Hospital within 7-10 days for a repeat full blood count. A written referral should be instigated by the admitting team at this stage for the child to be seen in the joint Paediatric Haematology clinic by Dr Jo Ponnampalam and Dr Hamish Lyall(Consultant Haematologist) and should appear on the referral console. The child should be given open access to CAU till seen in the Paediatric Haematology clinic and remain the responsibility of the admitting consultant till seen in the specialist clinic. Advice can be obtained from either Dr Ponnampalam or Dr Lyall in the interim. Parents should be given an information leaflet (see appendix or download from website www.itpsupport.org.uk) and the open access telephone number for CAU 01603-289774.

Parents should be asked to return the child to hospital if significant haemorrhage begins. Intracranial bleeds are very rare in ITP but should a child with ITP with a platelet count <50 develop headaches or any signs and symptoms suggesting intracranial pathology, parents should be advised to telephone CAU and/or attend for advice promptly as rarely this may indicate associated intracranial pathology.

Prior to discharge from CAU, contact research nurse (Louise Coke) ext 4530 or email louise.coke@nnuh.nhs.uk for information on UK Database Study information and Consent. This should not delay discharge but please send an email, if not, so that the research team can contact the family after discharge.

Patients receiving treatment:
- Should have daily FBC for the first 2-3 days(usually still an inpatient) and thereafter at the direction of the Consultant (usually regular FBC until recovery of platelet count >50x10⁹/L)
- Should be discharged when clinical symptoms have remitted, Hb levels are stable and platelet count is rising
- Check a FBC at 1 week post treatment to check for response

Child should have open access to CAU and be advised to return urgently in the presence of any of the following:

i. A prolonged (over 20 minutes) nosebleed which will not stop despite pinching the nose
ii. Prolonged gum bleeding
iii. Blood in the poo or urine
iv. Following a heavy blow to the head, particularly if the child is stunned or sickly
v. Persistent or severe headache
vi. Vomiting or drowsiness
vii. Children on steroids are at a greater risk of a severe form of chickenpox. If your child has not had chickenpox then contact the hospital. If your child is in direct contact with someone who has chickenpox or who develops chickenpox within 7 days of being with your child.

**Clinical audit standards**

1. All children admitted with suspected ITP should have:
   - a clear history detailing onset of bruising, presence/absence of mucosal bleeding and a family history relating to bleeding disorders
   - recorded examination findings to confirm/exclude anaemia, lymphadenopathy, organomegaly and signs of sepsis
   - No investigations other than FBC + Film, coagulation, DCT and Immunoglobulins should be performed unless there are documented atypical features in history and/or examination

2. All children who receive specific treatment for ITP (IVIG or Steroids) should have documented evidence of life-threatening or severe haemorrhage. Also an assessment of response to treatment should be clearly documented.

3. All children who receive platelet transfusion for ITP should have evidence of life-threatening haemorrhage.

4. All children who receive specific treatment for ITP (IVIG or Steroids) should have daily FBC monitoring for minimum of 2 days and ongoing monitoring demonstrating recovery of platelet count >50x10^9/L.

5. All children with ITP should have at discharge, documentation of:
   - follow-up arrangements in the Paediatric Haematology clinic (cases of chronic ITP, the need for any secondary investigations or treatment options for chronic cases, should only be performed in the clinic setting)
   - information given to parents (also available on the ITP support website [www.itpsupport.org.uk](http://www.itpsupport.org.uk))

**Summary of development and consultation process undertaken before registration and dissemination**

This guideline has been updated by Dr Jo Ponnampalam, Consultant Paediatrician, NNUHFT; it has been circulated for comments to Dr Hamish Lyall, Consultant Haematologist, NNUHFT, Dr Emmy Dickens Consultant Paediatric Haematologist at Addenbrookes Hospital, Cambridge. This guideline was also circulated via email to Dr John Grainger, Consultant Paediatric Haematologist, Central Manchester University Hospitals NHS Foundation Trust, UK National ITP database Chief Investigator and his comments incorporated into guideline.

It had also been circulated for comments to all the Paediatric Medicine Consultants within the Jenny Lind Hospital when first written, not during updating.

More recent publications have again been reviewed and the guideline modified accordingly in January 2018.
Trust Guideline for the Management of:
Newly Diagnosed Immune Thrombocytopenia (ITP) in Children

This version has been endorsed by the Clinical Guidelines Assessment Panel and reviewed by Dr Emmy Dickens, Paediatric Haematology Consultant, Addenbrookes Hospital.

Distribution list/ dissemination method

CAU, Buxton ward, Haematology department, Trust Intranet

References/ source documents


Grainger JD et al. Changing trends in the UK management of childhood ITP. Arch Dis Child 2012;97:8-11


Trust Guideline for the Management of: Newly Diagnosed Immune Thrombocytopenia (ITP) in Children


Kessler, C.M. Advances in the Management of ITP in Children and Adults. Clinical Advances in Hematology and Oncology Volume 12, Issue 6, June 2014

J.D.Grainger :Guideline ‘Suspected or Known Immune Thrombocytopenia Management in Children’ March 2015
Introduction
This explains about immune thrombocytopenic purpura (ITP), which is a blood disorder affecting the platelets. It also explains what to expect when your child is diagnosed with the condition.

What are platelets?
Platelets are one of the three types of blood cell, along with red and white blood cells. Platelets are small and sticky and their job is to prevent bruising and stop bleeding after an injury. Platelets, like red and white blood cells, are formed in the bone marrow. A rough idea of how many platelets are circulating in the bloodstream (platelet count) can be made using a sample of blood. The normal platelet count is between is 150 to 400 x 10^9/l. In most cases of ITP the platelet count is less than 20 x 10^9/l. A low platelet count is called ‘thrombocytopenia’.

What is immune thrombocytopenic purpura?
Immune thrombocytopenic purpura is a medical term for a condition in which there is bruising (purpura) because there are fewer platelets in the blood than usual (thrombocytopenic) and is usually caused by something going wrong with the immune system (the body’s defence against infection) or an allergic reaction of some kind.

Chronic ITP is the term for ITP that has not gone away on its own after 6 months. Only 1 in 4 children with ITP will develop chronic ITP. The majority of children with "chronic" ITP will still have some recovery of the platelet count at a later date and the majority of younger children will still completely recover after a few years even if the ITP is still present at 6 months.

How common is ITP and who does it affect?
About four in every 100,000 children develop ITP each year. There seem to be two groups who develop ITP: young children and young adults. It is more common in girls than boys.

What are the symptoms of ITP?
Most children with a platelet count of under 20 x 10^9/l will have petechiae (pinprick blood spots under the skin) and limited bruising. Bruising most commonly follows minor knocks ("easy bruising") but may also occur spontaneously without trauma. Apart from the bruising/bleeding the children are otherwise well. Common sites of spontaneous bleeding are the gums and nose. Girls may be troubled with heavy periods.

Less common and potentially serious are spontaneous bleeds occurring from the gut or brain. Data from international studies suggests that the risk of serious bleeds is about 3 in 100 children and the risk of brain bleeds is about 1 in 300 children. These bleeds most often occurred in the first week of ITP and were often caused by a rare pre-existing abnormality of the blood vessels in the head. The risk of serious bleeding is much lower when the platelet count recovers to over 20 x 10^9/l.

What causes ITP?
ITP commonly results due to the immune system mistaking platelets as being foreign and attacking the platelets. In many cases this may follow a viral infection or vaccination during which time the immune system attacks the virus but the immune system then goes on to think that the platelets are viral material and starts to attack the platelets.

How is ITP diagnosed?
ITP is usually diagnosed using a blood test called a ‘full blood count’. When a sample of your child’s blood is examined under a microscope, a haematologist can examine each
blood cell type closely. This is to rule out other conditions that may cause similar symptoms to ITP. If the platelets, red blood cells and white blood cells all look normal, this rules out leukaemia. If the low platelet count improves quickly and no treatment is needed, your child will not need any further tests.

If the platelet count is not showing signs of recovery by 3 to 6 months then a small sample of bone marrow will need to be taken and examined under the microscope. Additional blood tests may be taken at this time to exclude rare clotting or immune diseases that can mimic ITP. If the bone marrow looks normal, with the usual or higher number of platelet parent cells (megakaryocytes) and other blood tests are normal then the doctor will diagnose chronic ITP.

**What is the outlook for children with ITP?**

Many children, particularly younger ones, suddenly improve within six weeks, whether or not treatment has been given. Three out of four children will have improved by 6 months after the start of ITP. Even those who fail to recover completely will reach a platelet count over \(20 \times 10^9/l\) and have fewer bleeding problems. After six months about 25% of children will fully recover over the following year and over half will recover over several years.

When ITP recovers about one in 20 children will have a further occurrence in the future.

**How is ITP treated?**

Most children do not need any treatment unless they have severe bleeding, and most children improve whether or not treatment is given. The type of treatment recommended depends on your child’s symptoms rather than their platelet count. All the various forms of treatment aim to temporarily improve the platelet count and do not cure the condition itself. When treatments are considered, you will have the chance to discuss the risks and benefits of these, as opposed to no treatment, with the doctor. The options for treating ITP include:

1) **No treatment**

The majority of children with ITP have a low platelet count but do not have dangerous bleeding. If severe bleeding is not present at the time of diagnosis then it is very rare for dangerous bleeding to develop later. Without treatment most children will have a platelet count > \(20 \times 10^9/l\) within 5 days and a normal platelet count by six months.

2) **Tranexamic acid**

Tranexamic acid does not increase the platelet count but does help the blood to produce clots. It is particularly useful for gum bleeds, nose bleeds or heavy periods and helps the blood to form clots without altering the platelet count. It is best taken as a liquid ("swish and swallow") three times per day. It must not be used if there is any blood in the urine.

3) **Steroid treatment**

Steroids are sometimes given to children with ITP on a short-term basis in an attempt to increase their platelet count. However, when the steroid dose is reduced, the platelet count will drop again after a few days. Steroids should only be given for a short period of between 4 to 7 days. Side effects such as weight gain and mood changes are common. Longer courses of steroids may dampen the immune system, weaken bones, cause diabetes or obesity and stunt growth.

3) **Intravenous immunoglobulin**

Immunoglobulins are antibodies which can reduce platelet destruction. They are a blood product produced from many donors and have a theoretical but very low risk of transmitting blood-borne infections. One course of treatment with immunoglobulin takes two to five days as an in-patient in the hospital and the benefit will usually last about a month. Side effects such as fever and headaches are common.

4) **Anti – D (WinRho)**
WinRho can be used in Rhesus positive children (about 85% of children). WinRho is similar to immunoglobulin in producing antibodies which the immune system targets rather than the platelets. Anti-D is also a blood product but produced from a small number of donors. A small drop in the haemoglobin is common, rarely (1 in 40000 recipients) a severe and dangerous drop in the haemoglobin is seen. Anti-D can be given as a day case over about ten minutes and the benefit may last for several weeks.

5) Splenectomy

In ITP the majority of platelets are destroyed in the spleen. Removing the spleen (splenectomy) is often effective in preventing early destruction of the platelets and allows the count to rise. In children however this is rarely necessary unless the ITP persists and the child has recurrent severe bleeds. Splenectomy is a major surgical procedure and carries a long term risk of severe infection.

What about school, sport and holidays?

Most severe bleeds tend to occur in the first week and in children with a platelet count under 20 x10^9/l. In those children with a count over 20 x10^9/l they can return to school immediately after the head teacher has been informed about the ITP. In children with a lower platelet count school can resume after the first week and when the school have been informed. For primary school aged children it may be best if they take breaks inside if these cannot be supervised. The ITP Support Association produces a document for schools, clubs and playgroups.

If your child is on steroids and has not had chicken pox then school will need to inform you if anyone in your child’s class/nursery comes down with chicken pox.

At home it is best to take sensible precautions which all children should follow such only cycling with a helmet and if swimming no diving into the shallow end! It is sensible to avoid sports where there is a risk of head injury whilst the platelet count is below 50 x10^9/l. Make sure any sports teachers are aware. With a platelet count between 50 and 100 x10^9/l there will still be more bruising so encourage the use of shin pads etc. For further details discuss with your consultant.

It is best not to take any holidays abroad in the first three months of ITP as it may be difficult to get insurance. After this time most cases of ITP will have resolved. If the ITP does persist you will need to discuss further with your doctor and you will need specialist medical insurance. A list of recommended insurance companies can be obtained from ITP Support Association (details below)

What else can I do?

Your child should also avoid drugs like aspirin, ibuprofen or herbal medication which can increase the risk of bruising and bleeding. Finally, you should make sure that doctors and dentists know that your child has a low platelet count if they are due to have an operation.

When to seek help?

When your child is sent home you will be given a clinic appointment for review at the hospital, open access to the Children’s Assessment Unit and an emergency number (Children’s Assessment Unit, Jenny Lind Children’s Hospital: 01603 289774). You should contact the hospital in the following circumstances:

- A prolonged (over 30 minutes) nosebleed which will not stop despite pinching the nose
- Prolonged gum bleeding
- Blood in the poo or urine
- Following a heavy blow to the head, particularly if the child is stunned or sickly
- Persistent or severe headache
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- Vomiting or drowsiness
- Children on steroids are at a greater risk of a severe form of chickenpox. If your child has not had chickenpox then contact the hospital. If your child is in direct contact with someone who has chickenpox or who develops chickenpox within 7 days of being with your child.

Is there a UK registry?

To maintain accurate numbers of cases of childhood ITP and investigate possible markers for risk of severe bleeding a UK registry has been established (www.uk-iptp.org). Families may be routinely asked to consent for anonymous data to be stored on the registry.