NHS
South Yorkshire
Integrated Care Board

Acute Management of Immune Thrombocytopenic Purpura (ITP)

Clinical Pathway

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Review on	July 2027

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Purpose of Guidance

This guideline is designed to guide general paediatricians in the investigation and management of children with suspected acute Immune Thrombocytopenia (ITP) aged 6 months to 16 years in South Yorkshire.

Scope of Guidance

This document contains information and clinical guidelines for management of children attending hospitals in South Yorkshire. It is to be used by staff within these Trusts and associated shared care areas whenever they are caring for children in hospital, in the community or at home. It uses the SCH ITP guideline and International Consensus document on management of ITP.

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Version Control

Date	Version	Comments	Changes Made
31/05/2023	1.0		

Key Definitions

Terminology	Description
Newly Diagnosed	< 3 months duration
Persistent	3-12 months duration
Chronic	>12 months duration
Severe	Clinically relevant bleeding requiring treatment, additional interventions or an increase in drug dose

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Introduction & Background

ITP may present with bleeding, bruising or a petechial rash. Children often have a platelet count of $<10x10^9/L$ and it often follows a self-limiting viral infection. In children the condition is normally short-lived and around two thirds will recover spontaneously within 6 months.

The incidence is around 4 in 100 000 children per year develop ITP. Children with ITP may be asymptomatic or having symptoms such as bruising, mucosal bleeding or in severe cases, gastrointestinal or intracranial bleeding. Up to 4% of children with ITP will have severe (Grade 4, see table) bleeding and <1% will have intracranial bleeding. Between 30 and 56% of newly diagnosed children will have bleeding that may require treatment (Provan et al., 2019).

Clinical Management: Acute Care

1. Basics of Diagnosis

There is usually an abrupt onset (24–48-hour history) of symptoms associated with a low platelet count - petechiae, ecchymoses and epistaxis - in an otherwise well child. Often there has been a viral infection in the preceding 2-3 weeks.

A diagnosis of ITP can be made when **ALL** the following criteria are fulfilled:

a. Isolated thrombocytopaenia with an otherwise **normal full blood count (FBC)**

b. A **normal blood film** other than thrombocytopaenia

c. **Absence of atypical features**, including

- Bone pain or limp
- Abnormal Lymphadenopathy
- Hepatosplenomegaly
- Persistent fever
- Macrocytosis – (Large red blood cells, e.g. MCV > 86fl (6m-2y) or >98fl (2-16y) BUT ensure to check local laboratory normal ranges)
- Family history of excessive bleeding
- Personal history of excessive bleeding, prior to this presentation

2. Differential Diagnoses

- **Acute leukaemia** – bone pain, hepatosplenomegaly, lymphadenopathy, anaemia
- **Current infection** – e.g. viral (mild) or bacterial illness (unwell, disseminated intravascular coagulation (DIC), abnormal clotting)
- **Non-accidental injury (NAI)** – pattern of bruising, other features of possible abuse/neglect
- **Henoch Schonlein purpura** – palpable purpura, distribution of lesions, abdominal/joint pain
- **Haemolytic uraemic syndrome (HUS)/Thrombotic Thrombocytopenic Purpura (TTP)** – renal failure, fever, CNS abnormalities, abnormal blood film
- **Drug induced** thrombocytopaenia – e.g. sodium valproate, antibiotics, heparin, quinine
- **Systemic Lupus Erythematosus** – ANA/dsDNA positive +/- symptoms malar rash, fatigue, mouth ulcers, arthralgia – consider especially in adolescents
- **Anti-phospholipid syndrome**
- **Other infections** – HIV, hepatitis C, H Pylori, CMV
- **Primary immunodeficiency** – e.g. common variable immunodeficiency, IgA deficiency
- **Liver disease**
- **Haemangioma** – DIC type picture with abnormal clotting
- **Mechanical/artificial heart valve**
- **Familial/inherited thrombocytopenia**
- **Bone Marrow failure syndromes** - Thrombocytopenia Absent Radii (TAR), Fanconi Anaemia, Wiskott-Aldrich syndrome

3. Patient Assessment

As with all clinical conditions, a complete and thorough history and examination of the child is vital. This should include symptom **timeline**, **family history of bleeding** and **personal history of excessive bleeding**. A bleeding score such as Pediatric Bleeding Questionnaire (ahcdc.ca) or International Society of Thrombosis and Haemostasis Bleeding Assessment Tool ISTH BAT Score (practical-haemostasis.com) could be utilized.

Commented [SA(CNFT1]: Comment from the group- if macrocytosis means large white cells or platelets

Commented [PA2]: Typo - missing bracket

Commented [PA3]: Isn't term now "inflicted injury"?

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Patient Assessment Flow Chart

Patient presents with bleeding/bruising/petechiae:

- History
- Examination – check for hypersplenism.
- FBC – isolated thrombocytopenia
- Blood Film – normal aside from thrombocytopenia

Is the clinical picture that of typical ITP?

- Age > 6 months
- No bone pain
- No previous history of bleeding history
- No family history of excessive bleeding
- No organomegaly
- Isolated thrombocytopenia
- Normal blood film

YES

NO

Investigations

- FBC/Blood Film
- DAT (Direct antiglobulin test)
- U/E
- LFT
- Clotting Screen
- Immunoglobulins
- B12/folate

Abnormal or Uncertain Results

Atypical features or diagnostic uncertainty Discuss with Paediatric Haematology*

Atypical Features Reminder:

- Bone pain or limp
- Abnormal Lymphadenopathy
- Hepatosplenomegaly
- Persistent fever
- Macrocytosis
- Family history of excessive bleeding
- Personal history of excessive bleeding, prior to this

Supportive Treatment

- Oral Tranexamic acid (TXA) 25mg/kg (max 1.5g per dose) TDS if mucosal bleeding
- Avoid Aspirin and NSAIDS
- Avoid IM Injections
- Give patient information leaflet
- Arrange follow-up with a general paediatrician

*** Paediatric Haematology Contact on-call paediatric haematology registrar or consultant via Sheffield Children's Hospital Switchboard**

Acute Bleeding Severity Assessment

Mild/Moderate (with no risk factors*)	Moderate (with risk factors*) OR Severe	**Life-threatening**
• No treatment required • Watch and Monitor • Discharge with follow-up	• Discuss and refer to Paediatric Haematology	• **Discuss and refer urgently to Paediatric Haematology for emergency management**

*__Additional Risk Factors__:

- Bleeding from 3 or more sites
- Previous Severe bleed
- Marked social concerns

Table 1 - Acute Bleeding Assessment and Management

Severity Grade	Bleeding	Management
1 - Minor/Mild	• Few petechiae (<100) and bruises (<5 and <5cm in diameter • Epistaxis stops <15 minutes with pressure	Watch and monitor
2 - Moderate	• Numerous petechiae (>100) and large bruises (>5cm) • Epistaxis longer than 15 minutes • Intermittent bleeding from gums, lips, buccal, oropharynx or GI tract • Hypermenorrhagia, haematemesis, macroscopic haematuria, or melaena – without hypotension and Hb fall <20g/L	Watch and monitor Management is guided by bleeding symptoms i.e. nasal compression etc. Consider Tranexamic acid – see Section 4 Discuss with Paediatric Haematology* if additional risk factors, atypical features or bleeding concerns
3 - Severe	• Epistaxis requiring nasal packing or cautery • Continuous bleeding from gums, buccal, oropharynx • Suspected internal haemorrhage (lung, muscle, joint). • Hypermenorrhagia, haematemesis, macroscopic haematuria, melaena - without hypotension and falling Hb >20 g/L	Treatment as per Paediatric Haematology* advice
4 - Life-threatening	**Intracranial Haemorrhage (ICH)** **Or** **Continuous or high volume bleeding resulting in:** • **hypotension or prolonged capillary refill AND** • **requiring fluid resuscitation or blood transfusion**	**Urgent treatment as per Paediatric Haematology* – consider discussion with Embrace/PICU for transfer from DGH**

*** Paediatric Haematology**
Contact on-call paediatric haematology registrar or consultant via Sheffield Children's Hospital Switchboard

Commented [PA8]: Under "Moderate", could rephrase "Discuss….and refer" for clarity - presumably referral is to same team with whom case is being discussed. Why is there just a discussion and no referral with life-threatening cases?

Commented [PA9]: Table should have a title.

Commented [SA(CNFT10]: Query from the group- is there a treatment option for selected cases e.g IVIG?

Commented [SH11R10]: For this severity the expectation is generally to manage the specific bleeding symptoms as required i.e. nasal packing and TXA.
Any further treatment beyond this should really be discussed with paediatric haematology in tertiary centre - I've clarified this with the department. These patients may go on to receive IVIg/steroids/platelets in DGH but should ideally be after discussion with paeds haem

Commented [PA12]: Unclear how "Watch and monitor" relates to summary boxes above that suggest "Discharge with follow-up". Needs to be clearer.

Commented [PA13]: Initials should be defined before inclusion.

Commented [PA14]: In flow chart preceding table, discussion with haematology is advised in case of "atypical features". This is not captured in this table.

Commented [SA(CNFT15]: change to say paediatric haematolgy throughout guideline as its to be used in DGHs

Commented [PA16]: Suggested addition for clarity

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Commented [SA(CNFT18]: is there anything DGHs need to do before they consider discussion

Commented [SH19R18]: The main things would be to stabilise the child as needed with A-E assessment and volume replacement including blood if required. Discussion with embrace/PICU would be required depending in part on the advice from paediatric haematology/neurosurgery

4. Management of ITP

Platelet counts alone (even <10 x10^9/L) are not an indication for treatment. **Discuss with a Paediatric Haematologist* for Moderate bleeding with risk factors, Severe bleeding or Life-threatening bleeding** unless time does not allow.

If the patient has been assessed as suitable for **Watch and Monitor**:

- Provide Open Access to local hospital paediatric department
- Give patient leaflet to patients and or families – see Appendix 1. Signpost to websites such as:
  Information for Clinicians – UK-ITP Paediatric Registry (mdsas.com)
  Home - ITP Support Association
- **Oral Tranexamic acid (TXA)** can be given to patients with mucosal bleeding (e.g. epistaxis or menorrhagia) by local paediatric team without discussion with paediatric haematology:
  - Dose: 15-25mg/kg, 2-3 times a day, max 1.5g per dose.
  - Duration: up to 5 days (Usually requires less), prescribed as a short course
  - Caution: Do not prescribe if history of haematuria
  - If bleeding continues/worsens despite TXA then re-assess patient as per Section 3 and Table 1
- A repeat full blood count should be performed at **1 week**, and then every **2-4 weekly** depending on symptoms and platelet trend. **Re-assess the patient and grade bleeding severity as per table on each review**.
- If the patient remains thrombocytopenic at **3 months**, then a referral should be made to Haematology at Sheffield Children's Hospital to discuss possible treatment options for persistent or chronic ITP.
- Patient's whose platelet count **completely normalises on two consecutive FBCs** can be discharged.

Advice for parents: - *ensure documentation in notes*

- Avoid Aspirin and NSAIDS (ibuprofen)
- Avoid IM injections
- Avoidance advice for contact sports
- When to present with bleeding/head injuries and how to manage them initially at home
- Inform dentist if for dental procedures

Inform School and advise patient should avoid any activities that carry a risk of falls or head injuries. Advise to seek urgent medical attention for bleeding or head injuries.

5. Indications for Discussion with Paediatric Haematology*

1. Patient with moderate with risk factors; severe or life-threatening bleeding
2. Patients with abnormalities of FBC or other investigations performed during initial assessment (other than co-existing iron deficiency which can be managed appropriately)
3. Patients with atypical features on history or examination
4. Chronic ITP – whilst the definition of 'Chronic ITP' is >12 months, discussion and probable referral is recommended if ITP is present for >3 months

*** Paediatric Haematology**
Contact on-call paediatric haematology registrar or consultant via Sheffield Children's Hospital Switchboard

Commented [PA20]: Is there any caution that should be exercised in prescription of tranexamic acid e.g. consideration of risks, duration of treatment, responsibility for ongoing monitoring of need for treatment?
My ignorance but is it correct that tranexamic acid would be prescribed in ITP without discussion with haematologist?
As written I have a concern that treatment with TXA could continue for longer than intended given that guidance doesn't contain advice on when to review and/or stop and who is responsible.

Commented [SH21]: I've added in the clarification that on each review the child should be graded on severity as per the table

Commented [SH22]: I've added in a clarification on chronic ITP

Commented [PA23]: This does not appear to include the additional risk factors detailed above table and which (according to table) trigger discussion (bleeding from 3 or more sites, previous severe bleed, social concerns).

6. Management of Life-threatening Bleeding in ITP

Any patient with a major or life-threatening bleed, including a suspected intracranial bleed should be discussed urgently with the haematology registrar or consultant on-call at Sheffield Children's Hospital. Management may need to be initiated at presenting centre and may include the following:

- **Airway, Breathing, Circulation** as appropriate, including red blood cell transfusions, intensive care support and other speciality involvement. Follow local guidelines for stabilization and management of major bleeding in children
- **Platelet transfusion** – Typically give 10-20ml/kg to max adult dose, however patients may require 20-30ml/kg. Platelet transfusions should **only be used in life-threatening bleeds and after discussion with Paediatric Haematology*. Ensure that IVIg is being given concurrently via a separate IV line as platelets are rapidly consumed in ITP.** Check FBC for platelet count 10-60 minutes after administration.
- **Intravenous Immunoglobulin (IVIg**) – Standard is 1g/kg as a single dose. Refer to local trust policy for prescription and approval. Platelet counts often rise to haemostatic levels within 24-48 hours of a single dose. A second dose can be given 24 hours after the first if required. Ensure IVIg administered in separate line to platelet transfusion
- **Steroids – IV Methyl-prednisolone**, dose 30mg/kg/day (up to 1g max dose). A second dose can be given 24 hours later.

7. Treatments Children may be having for ITP

Some children will be admitted to their local hospital whilst on longer term treatment for ITP. **If any of these patients attend with bleeding, they should be discussed with Paediatric Haematology* in Sheffield Children's Hospital.** Examples of ITP treatments:

1. Steroids – Typically prednisolone given at 4mg/kg/day (max 200mg/day) in divided dose for 4 days. Longer courses are not effective and have significant side effect profiles
2. Thrombopoietin- Receptor agonist (TPO-Ras) – Examples include Eltrombopag and Romiplostim. They are used in persistent or chronic ITP and may be used in combinations to keep platelet count >50 x10^9/L. (Avatrombopag is only available in clinical trials to paediatric patients)
3. Rituximab – CD20 monoclonal antibody. Used particularly in refractory ITP in adolescent females and ITP associated with autoimmune disorders
4. Mycophenolate Mofetil – immunosuppressive agent
5. Splenectomy – A very small proportion of children with ITP may have had a splenectomy and should be treated as all asplenic patients.

8. Summary

- Children with ITP do not necessarily need to be admitted to hospital unless they have significant bleeding or there are social concerns
- Decision to treat a patient with ITP is based on severity of symptoms not on platelet count alone
- Decision to treat a patient with ITP should be made after discussion with Paediatric Haematology Consultant (aside from cases of mild or moderate bleeding with no risk factors)
- Children with acute bleeding and ITP should be graded and managed as per Table 1
- In cases of life-threatening bleeding, treatment should be given urgently and if necessary prior to discussion with Paediatric Haematologist
- Platelet transfusions should be given only for significant life-threatening haemorrhage and are more likely to be effective if given with IVIG.

*** Paediatric Haematology**
Contact on-call paediatric haematology registrar or consultant via Sheffield Children's Hospital Switchboard

Commented [PA24]: Would it be helpful to reference resuscitation guideline?

Commented [PA25]: Suggested edit for clarity.

Commented [PA26]: Reference please.

Commented [PA27]: This section could be written with more detail and care given potential risks of administration of various items.

Commented [PA28]: I do not think that all this detail is necessary e.g. doses of prednisolone.

Commented [SA(CNFT29]: Made after discussion with rather than discussed

Commented [PA30]: Not the case - as written suggests that decision to treat with TXA is independent of any haematology consultation. Does it mean decision to treat with platelets?

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Appendix 1: Patient and Parent Information Sheet

Commented [PA31]: Could this just be referenced and exist as stand alone PIS with usual governance?

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Sheffield Children's Hospital
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Sheffield
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Acute ITP: Information for Patients and Parents

Background

The blood contains tiny cells called platelets, which help to prevent bruising and bleeding. If there are not enough platelets in your blood, cuts in your skin can carry on bleeding longer than usual, your gums can bleed when you clean your teeth and you can bruise without even being aware that you have knocked yourself. You may also develop little red dots on the skin.

Platelets are produced in the bone marrow and travel around in the circulation until they are needed at a site of injury (such as a cut or bang). If they are not needed in this way they normally survive for about 10 days before being removed from the bloodstream and replaced with new ones from the bone marrow.

What is ITP?

ITP is an acquired illness (you are not born with it) in which the body's own immune system removes normal platelets from the bloodstream by mistake. The immune system usually protects you by finding, labelling and getting rid of things that don't belong in your body – such as germs. In ITP the immune system mistakenly gets rid of your own platelets by attaching a special protein to them, called an antibody, so that they are attacked and destroyed. Although you are making plenty of platelets, they are being 'used up' more quickly than usual and you become 'thrombocytopenic' which just means you have a low number of platelets. It is not known why the body begins to produce antibodies against its own platelets. It may be that an infection such as a cold or sore throat a few weeks beforehand may trigger the immune system to behave in this way.

The problems you may notice are bruises, also known as 'purpura', tiny red dots on the skin, known as 'petechiae', nose bleeds, and sometimes other bleeding such as gum bleeding when you clean your teeth. Girls can have heavy, prolonged periods.

A normal platelet count is between about 150 and 450 depending on age. Often people with ITP have platelet counts of less than 20 when they are first diagnosed with the condition. Experience has shown us that although there may be easy bruising, children with platelet counts around 20 rarely have any serious bleeding.

What are the symptoms to expect in ITP?

Most children seem perfectly normal, happy, active and well apart from the bruises and sometimes little red spots on the skin. The child will not have any pain or fever and will usually just be their normal selves.

Some children may have nose bleeds which may take quite a while to stop, or they may have bleeding or 'blood blisters' in the mouth. Serious bleeding is very rare.

Is it very dangerous to have a low platelet count?

Although the numbers of platelets are reduced, the bone marrow is working hard supplying new platelets to replace the ones being removed by the immune system and the platelets that are present work very well. Although the symptoms described above can be alarming at first, they are usually not dangerous and the safest thing to do once the correct diagnosis has been made, is to just wait for the platelet count to recover on its own.

One important and serious problem that can occur very rarely is bleeding inside the head. This is called an **intracranial haemorrhage**. It is important to contact your hospital if your child has a head injury whilst their platelets are low so that they can be assessed and observed on a ward if necessary. It is also important to contact a doctor if you feel your child is not themselves, with drowsiness, vomiting weakness or fits.

Although intracranial haemorrhages are very rare, it is important to avoid activities that carry a risk of head injury, until the platelet count begins to recover. Depending on the age of your child, these might include climbing frames, rollerblading, horse riding, trampolining, contact sports etc. If swimming then no diving in the shallow end! Individual activities can be discussed with your doctor.

Make sure any sports teachers are aware of your children's need to avoid contact sport and activities.

Is ITP common?

ITP affects about 4 in every 100,000 children each year. It happens most frequently in both boys and girls aged between 2 and 6 years but any age can be affected.

How is the diagnosis made?

This is done by listening to your description of your child's symptoms examining your child and taking a blood test to exclude other causes of low platelets. Occasionally if the platelet count is taking longer than usual to recover or if there are any symptoms that are unusual a bone marrow test may need to be done. The reasons for this and the procedure itself would be explained fully by your doctor.

How do you treat ITP?

Mostly ITP just gets better on its own, so the most important thing to do is to reduce the risk of any serious bleeding whilst waiting for recovery to happen. Medicines such as Ibuprofen and aspirin should be avoided as they stop the platelets working effectively. It is safe to use Paracetamol if it is needed.

Intramuscular injections should be avoided – usually they can wait until the child has recovered, if not they can be given subcutaneously (just under the skin, not deep into the muscle). Activities should be restricted as described earlier and the child may temporarily need closer supervision, depending on their

age. Any head injuries should be reported to the hospital. The child can continue attending school or nursery as previously but the staff should be made aware of the information on this fact sheet.

You will be given a 24hr/day contact phone number to ring if you ever need advice or reassurance.

If there is no important bleeding we usually just wait for your child's platelets to come back up to normal on their own. Minor mouth and nose bleeding can be helped by a medicine called **tranexamic acid** which makes any blood clots that do form stronger and less likely to dissolve away. It doesn't have any effect on the platelet count itself.

If there is important bleeding, or your child needs an operation (for some unrelated condition) it may be necessary to give specific treatment for the ITP to try to raise the platelet more quickly. If this was required, your doctor would discuss the treatments available with you.

How long does ITP last?

Most children have acute ITP which lasts for less than 3 months. In fact most are showing signs of recovery within a month and a few within a week. Children who have platelets which remain low between 3-12 months have persistent ITP. There are some children (10-20%) who still have low platelets longer than 12 months after diagnosis. This is called chronic ITP. The chronic form is commoner in girls and in older children but it is not possible to tell from the outset who will recover quickly and who will not. A very few children make a full recovery but then their platelet count falls again weeks or months later, often following a viral infection, and then the platelets usually return to normal again. This can be repeated several times and is known as relapsing ITP.

Eighty to ninety percent of children will have a normal platelet count a year after diagnosis without requiring treatment. Any child who still has low platelets 3 months after the initial diagnosis, will be referred to the haematology team at Sheffield Children's Hospital.

Can you catch ITP?

No**.** No one will catch ITP from your child and your child did not catch it from anyone.

What should I do if I'm worried?

At home watch your child for new bruises and bleeding. These should gradually improve and the old bruises and petechiae will completely disappear. If your child has a head injury or develops bleeding that will not stop with simple measures you should contact the hospital via the telephone numbers you were given. There is a space to write these numbers at the bottom of this leaflet.

Contact Details:

Ward: _____

Telephone Number: _____

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References

D Provan, D Arnold, J Bussel et al. Updated international consensus report on the investigation and management of primary immune thrombocytopenia. Blood Advances 2019;3(22):3780-3817

Grainger J. Suspected or known Immune Thrombocytopenia Management Plan (Children). North West Guideline. http://www.uk-itp.org/docs/ITP/suspected_or_known_immune thrombocytopenia_management_plan__children_.pdf [date of access 31/05/2023]

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Neunert et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Advances 2019;3(23): 3829-3866