Clinical Guideline
SUSPECTED IMMUNE THROMBOCYTOPENIA (ACUTE ITP) IN CHILDREN

SETTING  Division of Women and Children’s Services
FOR STAFF  All clinical staff
PATIENTS  Children with suspected ITP

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Introduction

Immune Thrombocytopenia (ITP) is a benign condition of childhood occurring in four to five children per 100,000, per year. There is usually an abrupt onset of symptoms. Platelet counts are frequently dramatically low (0-20 x 10⁹/l). It is a diagnosis of exclusion as there is no definitive diagnostic test. It can occur at any age from two months but does not usually affect neonates.
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 is based on severity of symptoms not on platelet count alone
- Decision to treat should be discussed with Paediatric Haematology Consultant
- 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.

Aetiology

Acute ITP is an immune-mediated condition. Autoantibody (IgG immunoglobulin) binds to platelets which are then destroyed in the spleen. It typically occurs following a viral illness or immunisations.

Clinical features

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 two to three weeks.

It is usually a self-limiting illness. Most cases resolve in six to eight weeks and 80 – 85% will have a normal platelet count within six months. 15 – 20% will develop chronic ITP (>12 months duration). Older children (>10 years of age) are more likely to develop a chronic course.

Life-threatening bleeding e.g. intracranial haemorrhage is rare (<1% of children).

Atypical features include a longer history, presentation before six months of age (congenital platelet disorders), less dramatic thrombocytopenia (>20 x 10^9/l), family history of bleeding or platelet problems (Von Willebrands or other inherited bleeding disorders), bone pain, failure to thrive, lymphadenopathy/hepatosplenomegaly or additional cytopenias (anaemia or low white cell count).

Investigations

For all suspected cases of ITP:

- Full blood count (FBC) & reticulocytes – isolated thrombocytopenia
- Blood film – normal, occasional large platelets, no blasts, no red cell fragmentation
- Clotting screen – normal
- Direct Coombs Test (DCT)
- Immunoglobulins (Igs)

Atypical cases – investigations directed according to differential diagnosis.

Bone Marrow Aspirate (BMA)

Not indicated in typical cases. No proven benefit in ruling out leukaemia before starting treatment. No proven adverse effect on outcome when treatment is given without prior BMA. May be considered when FBC/blood film is atypical especially if steroid treatment is being considered.
Traditionally a BMA was routinely performed. Evidence has now confirmed that BMA is rarely needed at presentation but must be reconsidered in the presence of excessive or persistent bleeding despite a platelet count of >20x10⁹/l, failure to respond to treatment or persistent disease.

Other causes of bleeding/bruising/thrombocytopenia to consider

- Acute leukaemia – bone pain, hepatosplenomegaly, lymphadenopathy, anaemia
- Current infection – e.g. viral (mild) or bacterial illness (unwell, disseminated intravascular coagulation (DIC), abnormal clotting
- Haemolytic uraemic syndrome (HUS)/TTP – renal failure, fever, CNS abnormalities, abnormal blood film
- Drug induced – 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
- Familial/inherited thrombocytopenia
- Bone Marrow failure syndromes - Thrombocytopenia Absent Radii (TAR), Fanconi Anaemia, Wiskott-Aldrich syndrome
- Autoimmune Lymphoproliferative Syndrome (ALPS) – splenomegaly, lymphadenopathy
- Primary immunodeficiency – e.g. common variable immunodeficiency, IgA deficiency
- Liver disease
- Hypersplenism – e.g. portal hypertension
- Haemangioma – DIC type picture with abnormal clotting
- Mechanical/artificial heart valve
- Non accidental injury (NAI) – pattern of bruising, other features of possible abuse/neglect
- Henoch Schonlein purpura – palpable purpura, distribution of lesions, abdominal/joint pain

Bleeding severity

<table>
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<tr>
<th></th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Life-threatening (or ICH)</th>
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<tbody>
<tr>
<td></td>
<td>Few petechiae and small (&lt;5cm) bruises</td>
<td>Epistaxis stopped by applied pressure within 20 minutes</td>
<td>Epistaxis requiring nasal packing or cautery</td>
<td>Intracranial Haemorrhage (ICH) or Continuous or high volume bleeding resulting in hypotension or prolonged capillary refill and requiring fluid resuscitation or blood transfusion</td>
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<tr>
<td></td>
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<td></td>
<td>Continuous bleeding from gums, buccal, oropharynx</td>
<td>Continuous bleeding from gums, buccal, oropharynx</td>
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<tr>
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<td></td>
<td>Suspected internal haemorrhage (lung, muscle, joint)</td>
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<td>Hypermenorrhagia, haematemesis, macroscopic haematuria, melaena – without hypotension and falling Hb &lt;20 g/L</td>
<td>Hypermenorrhagia, haematemesis, macroscopic haematuria, melaena – without hypotension and falling Hb &gt;20 g/L</td>
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Management – see assessment flowchart page 7

Children with ITP usually have only mild or moderate symptoms and do not require treatment or admission to hospital.

Extended observation or treatment may be required if there are social concerns or additional risk factors for severe bleeding (multiple sites, exposure to aspirin, need for surgery, recent head injury).

It is generally safe to discharge home with appropriate advice.

Ensure a referral to Paediatric Haematology team is made and initial follow up will be arranged for seven to ten days.

Oral tranexamic acid can be used for mucosal bleeding or as a mouthwash for gum bleeding in the absence of macroscopic haematuria (risk of clot retention).

Treatment

This is based on the severity of bleeding symptoms. Low platelet counts alone (even counts <10x10^9/l) are not an indication to treat.

- Mild/moderate – watch and monitor
- Moderate – watch and monitor or treatment for selected cases
- Severe – treatment
- Life-threatening – urgent treatment

Discuss with a Paediatric Haematologist before starting treatment unless there is life-threatening bleeding when time does not allow.

Supportive

Tranexamic acid – for troublesome, persistent symptoms. Not if macroscopic haematuria.

Steroids – if no active infection or GI bleeding. Raises platelet count over 2-14 days. Prednisolone dose 4mg/kg/day (maximum 200mg) in divided doses for four days. Alternatively 1-2mg/kg/day for two weeks then wean. Consider giving with stomach protection e.g. ranitidine/omeprazole cover. Effect may last for up to six months but relapse is commonly seen after weaning.

Intravenous Immunoglobulin (IVIG) – raises platelet count more quickly than steroids (over 48 hours) by allowing the antibody coated platelets to remain in the circulation for longer but has higher risk of infusion-related side effects. The dose of IVIG for treating ITP in children is 0.8 – 1g/kg as a single infusion. A second dose may be required after 24 – 48 hours if there is severe or life-threatening bleeding, such as an intracranial bleed or pulmonary haemorrhage. Otherwise, if a haemostatically adequate platelet count is not achieved a second dose (1g/kg) may be considered at day five to seven. Check FBC post treatment and five to seven days later. Effect usually lasts two to four weeks.

The second dose of IVIG or maintenance treatment requires prior approval from the sub-regional immunoglobulin panel (immunoglobulinpanel@uhbristol.nhs.uk).

Blood products

Platelet transfusion for life-threatening haemorrhage. If child >15kg, give 1unit. Recheck platelet count 10 minutes post transfusion. Give in conjunction with IVIG and IV methylprednisolone.
If treatment is given:

- Daily FBC for first two to three days
- Discharged when symptoms improved
- Check FBC one week post treatment to assess for ongoing response
- Relapse is common especially after IVIG but re-treatment is often not required and again, should be guided by symptoms rather than platelet count alone

**When to discuss with a Paediatric Haematologist**

1) To consider other diagnoses if any of the following are present:
   - Atypical features or features suggestive of malignancy (bone pain, failure to thrive, lymphadenopathy)
   - Full blood count shows abnormalities other than just thrombocytopenia
   - Blood film shows abnormalities other than occasional large platelets and reactive lymphocytes
   - Any doubt about the diagnosis of acute ITP

2) If there is an indication to treat:
   - Prior to initiating treatment for ITP, please discuss with Paediatric Haematologist
   - If there is severe or life-threatening bleeding, start treatment and then discuss urgently with Paediatric Haematologist

**General advice for children with ITP**

Avoid aspirin or ibuprofen (NSAIDs). Avoid IM injections.

Give parents/carers a copy of the BRHC “ITP - information for parents” sheet with contact details (Appendix B) and “What is ITP?” – Parent Leaflet (Appendix C and available from [www.uk-ipt.org](http://www.uk-ipt.org)).

Inform school and ensure teachers are aware of diagnosis.

If platelet count <50x10^9/l – avoid activities with a risk of head injury e.g. trampolining, fighting, martial arts, skateboarding/roller-skating etc.

If platelet count <20x10^9/l – as above and no outdoor playtime at school

**Websites for families:**
- [www.uk-ipt.org](http://www.uk-ipt.org)
- [www.itpsupport.org.uk](http://www.itpsupport.org.uk)
- Send letter to GP – Appendix A

**How to refer to Paediatric Haematology Team**

- Please email Anna Farrell and Caroline Bickerton (Paediatric Benign Haematology CNSs) [anna.farrell@uhbristol.nhs.uk, caroline.bickerton@uhbristol.nhs.uk](mailto:anna.farrell@uhbristol.nhs.uk, caroline.bickerton@uhbristol.nhs.uk)
- Include name of child, date of birth, hospital number, address/contact phone number for parent/carer and brief clinical details.
- The Paediatric Haematology team will aim to pick up the case on the next working day and review the blood film.
- The child remains the responsibility of the admitting team until an email response to the initial referral is sent.
Suspected Acute Childhood ITP Assessment
(Adapted from Central Manchester University Hospitals Guideline)

“Typical ITP”
Over 6 Months of age
No bone pain
No previous bleeding history → NO – Discuss with Paediatric Haematologist
No FHx of excessive bleeding
No LNs/organomegaly
FBC isolated thrombocytopenia
Normal blood film
Clotting screen & biochemistry normal

↓ YES

↓ Supportive therapy
Oral tranexamic acid if mucosal bleeding
Avoid aspirin/NSAIDs & IM injections

↓ CALCULATE BLEEDING SEVERITY

Mild/Moderate (& no risk factors)  Moderate (with additional risk factor*) or Severe
Normally discharge with follow-up & advice
Provide parents with information leaflets
Send letter to GP

Treat
If no active GI bleeding/chickenpox or other infection → start prednisolone
If yes to above → IVIG

Life-threatening
Start treatment
Platelet transfusion & IVIG & methylprednisolone
Discuss with Paediatric Haematologist urgently

↓

E-mail referral to Paediatric Haematology team

Review & repeat FBC/blood film at seven to ten days
• to ensure correct diagnosis, further opportunity for advice and reassurance

Follow-up in Paediatric Haematology clinic in two months

*Additional risk factors include – three or more bleeding sites, previous severe bleeding, marked social concerns
Table A

REFERENCES

<table>
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<tr>
<th>Guideline ‘Suspected or known Immune Thrombocytopenia Management Plan (Children)’ Grainger JD. Central Manchester University Hospitals March 2015</th>
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<td>Guideline ‘Management of Newly Diagnosed Immune Thrombocytopenia (ITP) in Children’ Ponnampalam J. Norfolk &amp; Norwich University Hospitals February 2018</td>
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</tbody>
</table>

RELATED DOCUMENTS AND PAGES

None

AUTHORISING BODY

Paediatric Haematology, Oncology and BMT Quality Assurance Forum (Quaf)

SAFETY

Nil

QUERIES AND CONTACT

Any queries should be directed to Anna Farrell/Caroline Bickerton, Paediatric Benign Haematology CNSs on ext. 28721 (Monday to Friday) or the on call Paediatric Haematology Registrar/Consultant.
APPENDIX 1

Advice for GPs – new diagnosis ITP

Your patient:

INSERT ADDRESSOGRAPh LABEL

has been diagnosed with ITP or Immune Thrombocytopenia.

This is a benign autoimmune condition of childhood in which the immune system clears circulating platelets. Typically it resolves spontaneously within a few weeks or months without any treatment.

Treatment is reserved for cases where there is problematic bleeding.

A very low platelet count without bleeding is not an indication to treat.

Children with ITP diagnosed at BRHC are followed up by the Paediatric Haematology team.

After the initial diagnosis, they will be asked to attend for a nurse-led consultation and repeat FBC 7-10 days later.

If there are no specific concerns, they will be seen in Haematology outpatient clinic about 2 months from diagnosis.

If you or the family have any concerns in the interim, please contact:

- Paediatric Haematology Clinical Nurse Specialists - Anna Farrell/Caroline Bickerton
  - 0117 342 8721

Or

- Paediatric Haematology Registrar or Consultant via the hospital switchboard
  - 0117 923 0000.

Or

- Paediatric Haematology Secretary
  - 0117 342 8752
APPENDIX 2

ITP – Information for Parents

Your child has been diagnosed with Immune (Idiopathic) Thrombocytopenia or ITP.

This is a benign condition in childhood which typically resolves in 2-3 months without needing any treatment.

You will receive a separate leaflet about ITP produced by the UK ITP working party. This provides information about the condition and how it is managed.

What happens next?

Your child will be reviewed by one of the Haematology team within 7–10 days of the initial diagnosis. They will have a repeat blood test at this appointment.

If you are not given the time of the appointment before your child is discharged, you will be contacted by a member of the Haematology team usually within 3 days. If you have not heard from the hospital in this time please contact us on one of the numbers below.

The review usually takes place in Ocean Day Unit on level 6 at Bristol Royal Hospital for Children. Children with other blood disorders, leukaemia and cancer are also seen in this department. For this reason, if your child has been in contact with chickenpox or any other infectious diseases, please let the Haematology team know before you attend.

If there are no concerns, a follow up appointment will be made for Haematology outpatient clinic 4-6 weeks later.

What to do in an emergency?

If your child has any of the symptoms below, contact the hospital:

- Blood in the urine, poo or vomit
- Nosebleed lasting more than 15 minutes despite continued direct pressure
- Persistent bleeding from the gums or elsewhere
- Any head injury/severe headache/unusual sleepiness or vomiting

Contact information:

- Monday-Friday 8.30am-5pm Phone the Clinical Nurse Specialists on 0117 342 8721 or Ocean Day Unit on 0117 342 8145.
- After 5pm, at the weekend or on a Bank Holiday Call 0117 923 0000 and ask the switchboard to bleep the Paediatric Haematology/Oncology registrar on call
- After 10.30pm Contact the Children’s Emergency Department on 0117 324 8210.

Other concerns:

If you have any other non-urgent queries or concerns, please contact the Haematology Clinical Nurse Specialists on 0117 342 8721. Alternatively you can contact the Haematology Secretaries on 0117 342 8752.
APPENDIX 3

What is ITP? –parent leaflet

Introduction

This leaflet 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 x 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 x10^9/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.

4) 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.

5) Splenectomy

In ITP the majority of platelets are destroyed in the spleen. Removing the spleen (splenectomy) is often effective in early prevention 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. Other treatments to suppress the immune system (e.g. Rituximab, Ciclosporin) or to stimulate platelet production (eg Eltrombopag) are usually tried prior to splenectomy.

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 can not 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 and an emergency number (usually the phone number to the children’s ward). You should contact the hospital in the following circumstances:

- A prolonged (over 20 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
• 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 support group?

The ITP Support Association
‘Synehurste’
Kimbolton Road
Bolnhurst
Bedfors MK44 2EW
Tel 0870 7770559
Website: www.itpsupport.org.uk

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-itp.org) Families may be routinely asked to consent for anonymous data to be stored on the registry.