Idiopathic Thrombocytopenic Purpura (ITP) in Children

Background
ITP is an acquired thrombocytopenia due to immune mediated shortened circulating platelet survival in the absence of other disturbances of haemostasis or coagulation. The body’s immune system destroys platelets in the blood. It may follow a viral infection or vaccination.

The normal platelet count is 150 - 400 x 10^9/l. In most cases of ITP the platelet count is less than 20 x 10^9/l. Platelets act as an initial plug to stop blood leakage before the rest of the blood clotting process begins. Low platelets in the blood results in petechiae, bruising or bleeding.

Patients fall broadly into two categories:
- Acute (90%): self-limiting disease with resolution within six months (usually within two months)
- Chronic (10%): does not remit within six months

Clinical presentation
- 4 / 100,000 children develop ITP each year; girls > boys
- Usually presents below 10 years, peak incidence 2 to 5 years
- Most children present with petechiae and bruising alone
- In some cases there is epistaxis, oral or rectal bleeding, or haematuria
- Morbidity is usually minimal, major bleeding is uncommon
- Intracranial haemorrhage is very rare (<1%) in ITP
- 1 in 24000 doses of the MMR vaccine may lead to ITP, usually within 6 weeks of vaccination, This is not a contraindication to a further MMR dose

Assessment
- Manifestations of thrombocytopenia without other abnormal findings - in particular no pallor, lymphadenopathy or hepatosplenomegaly
- Full blood count and film will usually confirm the diagnosis
- Confirmation rests on excluding other causes, particularly leukemia and aplastic anaemia
- Coagulation screening is unnecessary in a child with typical presentation

A bone marrow aspirate is an invasive procedure with morbidity in children who bruise easily. It is rarely needed, and only if there is uncertainty about the diagnosis.
Clinical classification

Mild: Bruising and petechiae; occasional minor epistaxis. Little or no interference with daily living.

Moderate: More severe skin manifestations with some mucosal lesions and more troublesome epistaxis or menorrhagia.

Severe: Bleeding episodes requiring hospital admission and/or blood transfusions. Symptoms seriously interfering with quality of life such as severe epistaxis, gastrointestinal haemorrhage or intracranial haemorrhage.

General Principles of Management

- Reassure patient/parents of the benign nature of ITP
- Usually no specific treatment is required other than monitoring
- Repeat full blood count within 7-10 days (to exclude other disorders, particularly aplasia)
- While purpura persist the platelet count will be low so does not need repeating
- Follow up until platelet count recovers (>150 x10^9/L)
- Hospital admission/enforced rest are not essential
- Admit only if there is significant bleeding
- Give parents the ITP Support Association web address [http://www.itpsupport.org.uk](http://www.itpsupport.org.uk)
- Seek consent for inclusion on the UK Paediatric ITP Registry [http://www.uk-itp.org/](http://www.uk-itp.org/)
- Inform Dr Breen, for entering on the ITP Registry

General advice

- Avoid contact sports (such as rugby or martial arts) until platelets >50x10^9/L
- Avoid aspirin and non-steroidal anti-inflammatory drugs such as ibuprofen
- Report to hospital if mucosal or other significant bleeding occurs

Suspected intracranial haemorrhage

All published cases had altered consciousness and/or neurological signs. If these signs are present or severe headache, arrange urgent CT head scan. Treatment includes IV high dose methyl prednisolone, intravenous immunoglobulin (IVIG) and massive platelet transfusion, so will be managed by senior staff in discussion with paediatric haematologists and neurosurgeons.
In-patient management
Several therapies raise the count faster than no treatment. However, all have significant side-effects and none alters the underlying pathology. Treatment should be discussed with the consultant on call and, if necessary, the paediatric haematologist. These strategies are appropriate for all children with severe symptoms and some of those with moderate symptoms.

In-patient treatment options:

1) No treatment
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 x10⁹/L within 5 days and a normal platelet count by six months.

2) 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. It can be given orally at 25mg/kg (maximum 1.5g), three times daily. For gum bleeds, it is best taken as a liquid (“swish and swallow”).
It must not be used if there is haematuria as clot retention may occur.

3) Steroids
Consider use if significant clinical bleeding.
Give prednisolone 1-2 mg/kg/day for 5-7 days, and reduce dose to zero over 1 week.
Do not give for more than 14 days irrespective of platelet count.

4) Intravenous immunoglobulin (IVIG)
Consider for major bleeding problems not responding to steroids, or for operative/dental cover.
Give a single dose 0.8/kg.
If possible allow Vigam ® liquid to warm to room temperature for 2hours before use.
Immunoglobulin must be used in accord with ‘WUTH Intravenous Immunoglobulin Policy and procedure’. Note that this is a “red” indication, and so no approval is needed.
A hard copy of the IVIG request form should be sent to pharmacy along with a prescription. Due to the absence of any anti-microbial preservatives, administration must begin immediately after piercing the cap.

See Appendix 1 for use and prescription of immunoglobulin treatment for ITP.

5) Anti-D
In Rh positive children with a negative direct antiglobulin test (DAT) who have not had a splenectomy a single dose of anti-D can be considered as first line treatment.
This is for use only on recommendation of the haematologist. Do not use in children with a low haemoglobin secondary to bleeding or with evidence of autoimmune haemolysis.

6) Platelet transfusion
This is never indicated for a low platelet count alone. Life-threatening haemorrhage is the only indication.
Second Line Treatment: (Prescribed by Paediatric Haematologists)

1) **Rituximab**
Consider Rituximab in children who have significant on-going bleeding despite treatment with IVIG, anti-D or corticosteroids.

2) **High dose Dexamethasone**
Consider high dose dexamethasone in children with on-going bleeding despite treatment with IVIG, anti-D or conventional doses of corticosteroids.

**Chronic ITP**
Is defined as ongoing thrombocytopenia after a 6 month period. Such patients should be referred to a paediatric haematologist. A history of bruising from infancy should prompt suspicion of one of the rare congenital thrombocytopenias. Careful inspection of the blood film and tests of platelet function will serve to exclude other diagnoses. Bone marrow examination may be helpful in confirming chronic ITP.

Many children will run a low but adequate platelet count (eg >30 x10^9/L). In younger children spontaneous remission is likely to occur eventually; expectant management can continue. Older children are more likely to have a chronic course. Treatment is only required to raise the count for surgery, injuries or dental extraction. Particular problems may arise for menstruating girls for whom the oral contraceptive pill can be helpful. Children with chronic severe bleeding are very rare (estimated annual incidence of perhaps 1 in 2,500,000).

**Splenectomy**
Is rarely required (success rate 70-80%). It is only ever justified for severe bleeding and should not be considered before at least six and preferably twelve months from diagnosis.

Link to patient information leaflet:
http://www.uk-ipt.org/docs/ITP/whatIsITP.pdf

References:
4. UK ITP Support Association; 2013 http://www.itpsupport.org.uk
Idiopathic Thrombocytopenic Purpura (ITP) in Children Clinical Guideline - v3
Approved by: DCGSG & WiSCH CGDG

Auditable Standards

1. All children without significant bleeding are managed as out-patients
2. All treatments are given in accordance with the guideline
3. All children / parents are given information on the ITP registry

Version 3
Date of issue: January 2014
Date of review: January 2017
Review interval: 3 yearly
Author: Dr L Breen / Dr R. Lewin
Approved by: 1. DCGSG
2. WiSCH CGDG
Location of copies: 1. Intranet
2. Clinical Areas
Appendix 1

Intravenous immunoglobulin for Idiopathic Thrombocytopenic Purpura

See also the ‘WUTH Intravenous Immunoglobulin Policy and procedure’. Note that this is a “red” indication, and so no approval is needed. A hard copy of the IVIG request form should be sent to pharmacy along with a prescription.

Preparation Vigam – 5g immunoglobulin in 100mL (5%)
Dose 0.8g/kg (16mL/kg)
Rate Start at 0.01 – 0.02 mL/kg/minute. If well tolerated, this can be increased to 0.04 mL/kg/minute (to a maximum of 3mL/minute).

This table gives the infusion rate required in mL/hour
Rate Start at 0.01 – 0.02 mL/kg/minute. If well tolerated, this can be increased to 0.04mL/kg/minute (to a maximum of 3mL/minute).

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<th>Time</th>
<th>0 to 30 minutes</th>
<th>30 to 60 minutes</th>
<th>60 to 90 minutes</th>
<th>90 minutes until complete</th>
<th>Time to complete if highest weight (hours)</th>
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<td>2</td>
<td>4</td>
<td>8</td>
<td>8.9</td>
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<td>4 to 5.9</td>
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<td>4</td>
<td>8</td>
<td>12</td>
<td>8.8</td>
</tr>
<tr>
<td>6 to 7.9</td>
<td>2</td>
<td>5</td>
<td>10</td>
<td>20</td>
<td>7.4</td>
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<td>8 to 9.9</td>
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<td>6</td>
<td>12</td>
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<td>50</td>
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<td>30 to 40</td>
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<td>70</td>
<td>120</td>
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### Appendix 2

#### Proforma for ITP registry

Please record the information in the table below

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</thead>
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<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Date of birth</td>
<td></td>
</tr>
<tr>
<td>Date of presentation</td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td></td>
</tr>
<tr>
<td>Preceding illness? (give details)</td>
<td></td>
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<tr>
<td>Recent medication? (including herbal)</td>
<td></td>
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<tr>
<td>Past medical history</td>
<td></td>
</tr>
<tr>
<td>Family history of thrombocytopenia?</td>
<td></td>
</tr>
<tr>
<td>Recent vaccinations? (last 3 months)</td>
<td></td>
</tr>
<tr>
<td>Any atypical features?</td>
<td></td>
</tr>
<tr>
<td>Symptoms :</td>
<td></td>
</tr>
<tr>
<td>Bruising (number, sites)</td>
<td></td>
</tr>
<tr>
<td>Bleeding (severity, intervention)</td>
<td></td>
</tr>
<tr>
<td>Petechiae (&lt;10, 10-100, &gt;100)</td>
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</tr>
<tr>
<td>Epistaxis (unilateral / bilateral, severity)</td>
<td></td>
</tr>
<tr>
<td>Other (give details)</td>
<td></td>
</tr>
<tr>
<td>Treatment given:</td>
<td></td>
</tr>
<tr>
<td>Tranexamic acid (and route)</td>
<td></td>
</tr>
<tr>
<td>Steroids</td>
<td></td>
</tr>
<tr>
<td>Immunoglobulin</td>
<td></td>
</tr>
<tr>
<td>Other (give details)</td>
<td></td>
</tr>
<tr>
<td>Any tests? (other than fbc) (give details)</td>
<td></td>
</tr>
</tbody>
</table>
Appendix 3

TO BE PRINTED ON LOCAL HEADED PAPER

Unique Consultant Number:
Patient Initials:
Patient Identification Number for this trial:

PARENT/ PATIENT RE-CONSENT FORM
(Version 2.0 – Nov2009)

As data will continue to be collected over several years a re-consent is required from the child when they are of an appropriate age to have the capacity to understand what is required of them, this is usually between the ages of 10-14.

Title of Project: UK childhood ITP registry
Principal Investigator: Dr J Grainger, Royal Manchester Children's Hospital

Please initial boxes

1. I confirm that I have read and understand the information sheet(s) dated ______/_____/______ (version ______) for the above study and have had the opportunity to ask questions.

2. I understand that my continued participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

3. I understand that anonymous information from my medical notes will be forwarded on to the secure electronic UK Childhood ITP database based in Manchester, UK.

4. I agree for anonymous information concerning me to be transferred from the UK database to be forwarded electronically to the intercontinental chronic ITP database based in Basel, Switzerland. The sharing of data with PARC is voluntary and does not exclude from the UK registry participation.

5. I agree for my General Practitioner to be informed about my entry into this study.

Information stored in the database may identify children from whom we would like to collect further information.

6. I agree to be contacted about future ethically approved studies.

____________________________  ____________________  __________________
Name of child                  Date                        Signature

____________________________  ____________________  __________________
Name of parent/guardian       Date                        Signature

____________________________  ____________________  __________________
Name of person taking consent Date                        Signature

1 for patient; 1 to be kept with hospital notes

UK childhood ITP Registry (version 2 dated 07.11.2009)
Appendix 4

TO BE PRINTED ON LOCAL HEADED PAPER

Unique Consultant Number:
Patient Initials:
Patient Identification Number for this trial:

PARENT/PATIENT CONSENT FORM
(Version 2.0 – Nov2009)

Title of Project: UK childhood ITP registry

Principal Investigator: Dr J Grainger, Royal Manchester Children’s Hospital

Please initial boxes

1. I confirm that I have read and understand the information sheet(s) dated (version ) for the above study and have had the opportunity to ask questions.

2. I understand that my/my child’s participation is voluntary and that I am/my child is free to withdraw at any time, without giving any reason, without my/his/her medical care or legal rights being affected.

3. I understand that anonymous information from my/my child’s medical notes will be forwarded on to the secure electronic UK childhood ITP database based in Manchester, UK.

4. I agree for anonymous information concerning me/my child to be transferred from the UK database to be forwarded electronically to the intercontinental chronic ITP database based in Basel, Switzerland. The sharing of data with PARC is voluntary and does not exclude from the UK registry participation.

5. I agree for my/my child’s General Practitioner to be informed about my/his/her entry into this study.

Information stored in the database may identify children from whom we would like to collect further information.

6. I agree to be contacted about future ethically approved studies.

Name of child __________________________ Date __________________________ Signature __________________________

Name of parent/guardian __________________________ Date __________________________ Signature __________________________

Name of person taking consent __________________________ Date __________________________ Signature __________________________

1 for patient; 1 to be kept with hospital notes

UK childhood ITP Registry (version 2 dated 07.11.2009)
Appendix 5

TO BE PRINTED ON LOCAL HEADED PAPER

United Kingdom Childhood ITP Registry

INFORMATION FOR PARENTS

(Version 2.0, 07.11.2009)

We are asking you to consider the possibility of allowing information about your child to be included in an information registry. In doing this we are trying to gain more information about the medical condition Immune Thrombocytopenic Purpura.

Before you decide it is important for you to understand why the research is being done and what is involved. Please take time to read the following information carefully and discuss it with friends, relatives, doctors and nurses if you wish. Ask us if there is anything that is not clear or if you would like more information. Take the time to decide whether or not you wish your child to take part.

1. What is the purpose of the registry?

Immune thrombocytopenic purpura (ITP) is a blood condition characterised by a low platelet count. The platelet count drops because antibodies produced by the patient coat the platelets which are then recognised as abnormal and are removed from the blood stream by the normal body protection systems. There are many aspects of ITP that we do not fully understand, for instance why do people suddenly start producing antibodies against their own platelets, why do children with very low platelet counts rarely have serious bleeding, why some children get better quickly and others have a more long term disorder. We would also like to know more about the very best treatment for children with ITP.

To help us answer these questions we want to collect information about children with ITP in the UK in a systematic way to create a collection of information (or registry). This will form part of an international registry (PARC, Paediatric and Adult intercontinental Registry on Chronic ITP).

The main aims of this project are to try and understand when and why children with a low platelet count bleed, when and why there is a need for treatment and how having ITP impacts on the quality of life on the child and family.

2. Why has my child been chosen?

All children under the age of 16 years who present to hospital in the UK with ITP will be eligible to take part in this project.
3. Does my child have to take part?
No. Participation in the project is entirely voluntary. If you agree to your child taking part and then later change your mind, you are still free to withdraw at any time without giving a reason. This will not affect the standard of care received by your child.

4. What do I have to do?
If you agree for your child to take part in this project we will need you to sign a consent form. You will be given a copy of the consent form and this information sheet to keep.

5. What will happen if my child takes part?
This information sheet has been sent out from the study headquarters (based at Royal Manchester Children’s Hospital). A doctor looking after your child in your hospital will discuss the project with you and you will also be able to speak with one of the chief researchers by telephone if you have any additional questions before signing the consent form. If you consent to participate your doctor will read your child’s medical notes and complete a form about your child’s condition including symptoms, how often they bleed and what treatment is required. These forms are returned to the central data manager without any information that could identify your child (anonymised information) and stored securely. If you agree this information will also be shared with the international PARC study group (head quarters in Basel, Switzerland) by secure electronic transfer.
Six months after your child first developed ITP further information will be collected by means of a second form again filled in by your local hospital doctor. However at this stage the majority of children will have recovered fully. The registry will continue to follow up only those with ITP that does not get better quickly (about 20% of patients). Information will then be collected every twelve months until either the ITP gets better or the project closes.
The database may pick out individual children whose bleeding pattern or clinical course may teach us more about ITP. Such individuals may be approached regarding other ethically approved studies. You will also be asked to complete a 10 minute online questionnaire regarding how ITP has affected your child’s daily life. If your child is 7 years or older we will also ask them to complete the same questionnaire on their own. We will ask you to complete these questionnaires within the first two weeks of the ITP being diagnosed, at 6 weeks, at 6 months and then if the ITP is persisting again on a yearly basis until the ITP goes away.

6. Are there any disadvantages or risks involved in my child’s participation in the project?
No.
7. What are the possible benefits of taking part?
The information we obtain will not be of direct benefit to your child at the moment but may improve the way we treat other children with ITP in the future. However if your child has ITP for a long time information gained from this project may help their future treatment.

8. Will my child’s participation in this study be kept confidential?
Your child will be allocated a unique case number that will be kept by your hospital doctor. This will be used to identify the information sent to the information co-ordinators. They will not be able to know your child’s name and will therefore not be able to disclose identifying information to anyone else.

9. What will happen to the results of the study?
Anonymous information from the registry will be stored electronically on a secure database. Analysis will be carried every six to twelve months. The results will be published in medical journals and possibly used to modify future treatment. Information from the database will be fed back to families via the ITP support association. Your child will not be identified in any report or publication.

10. Who is organising and funding the research?
This project is being undertaken by The UK Paediatric ITP Working Party led by Dr. John Grainger, Consultant Paediatric Haematologist in the Manchester Children’s Hospital. The study is funded by the ITP Patient Support Organisation. There will be no payments to researchers for conducting the project.

11. What if I have any concerns?
If you have any concerns or other questions about this project or the way it has been carried out, you should contact a member of the working party

12. Contact for further information
If you require any further information please contact a member of the working party:

<table>
<thead>
<tr>
<th>Name</th>
<th>Hospital</th>
<th>Telephone No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr John Grainger</td>
<td>Royal Manchester Children's</td>
<td>0161 7018418</td>
</tr>
<tr>
<td>Dr Paula Bolton-Maggs</td>
<td>Manchester Royal Infirmary</td>
<td>0161 2764811</td>
</tr>
<tr>
<td>Dr Mike Richards</td>
<td>St. James’ Hospital, Leeds</td>
<td>0113 2066295</td>
</tr>
<tr>
<td>Dr Mike Williams</td>
<td>Birmingham Children's Hospital</td>
<td>0121 333 9843</td>
</tr>
<tr>
<td>Dr Nichola Cooper</td>
<td>Hammersmith Hospital</td>
<td>0208 383 5182</td>
</tr>
</tbody>
</table>

Thank you for reading this information sheet.
Appendix 6

TO BE PRINTED ON LOCAL HEADED PAPER

United Kingdom Childhood ITP Registry

INFORMATION SHEET TO BE READ TO PATIENTS UNDER 10 YEARS.

(Version 2.0, 07.11.2009)

You have something wrong with your blood that can make you bleed or bruise this is called ITP. Other children get ITP too! Sometimes they have it a long time and sometimes it goes away quickly.

The doctors know a lot about ITP, but they would like to find out more so they can get better at looking after children who have it.

To find out more about it we need to ask questions to all the doctors looking after children with ITP. We can then collect together all the answers and look at them carefully.

Before we can ask the doctors any questions about you we have to ask your mum and dad if we can do it to make sure that they are happy about it.

We will keep on asking the doctors questions about you until your ITP goes away, or we think we have got enough information.

If you are over 7 years old, we will ask you to answer some questions on the computer. This will be about how having ITP makes you feel.

If you want to ask us anything that you are not sure about then we will be very happy to talk to you.

If you or your mum and dad don’t want to take part then this is OK and no one will be upset.

Thank you.