My Background
- From Lester, IA
- College: Augustana (now university)
- Medical School: Sanford School of Medicine at USD
- Residency: Omaha - UNMC/Children’s
- Now: Pediatrician with Avera McGreevy

Objectives
- What is ITP?
- How do we treat/manage ITP?
- Why is ITP important?
- What are the outcome of patients with ITP?

Case Study
- 8yo female comes to clinic with a rash x 1 days
- Pink/purple in color, started on upper back and had spread to legs/arms this morning
- Rash isn’t itchy or painful
- 1 week ago had fever and cough
  - Dx: viral URI

Case Study
- Other than the rash, feels good
- Denies N/V/D, wt loss, fatigue, night sweats
- PMHx: seasonal allergies
- PSHx: none
- Meds: none
- Allergies: NKDA
- Immunizations: UTD
- Development: normal
- No recent travel, no sick contacts, has a pet fish
Case Study

- VS: T 37.2  P 102  R 22  BP 100/76
- Wt: 39.7kg (94 percentile)  Ht 140cm (88 percentile)
- Skin: petechiae present over cheeks, neck, arms, back, chest, legs, non-blanchable; ecchymoses on right shin and arms; palms and soles are clear, no pallor or jaundice
- Exam otherwise normal

What is ITP?

ITP: 
Idiopathic Thrombocytopenic Purpura
Immune Thrombocytopenic Purpura
Immune ThrombocytoPenia

Differential normal

Immune Thrombocytopenia (ITP)

- Autoimmune disorder causing low platelet counts
- Discovered in 1951 by William Harrington and James Hollingsworth
  - Injected plasma from pts with ITP to healthy volunteers
  - Observed decrease platelet levels in volunteers
  - Years later, antibodies directed against platelets were identified

Immune Thrombocytopenia (ITP)

- May have a primary or secondary cause:
  - SLE
  - Medications
  - Viruses: hepatitis C, HIV
  - Bacteria: *H. pylori, Rickettsia*
  - Leukemia, lymphomas

**Pathogenesis:**

1. Antibody-mediated destruction of platelets
   - IgG targeting glycoprotein IIb/IIIa and/or Ib/IX on platelets
   - Antibodies only documented in 75% of cases
2. Decreased production of platelets
   - Increased clearance of thrombopoietin
   - Damaged megakaryocytes

**Acute vs Chronic:**
- Chronic – have ITP for > 12 months

2009: Vicenza Consensus Conference
- Renamed to Immune Thrombocytopenia
- Changed classification to newly diagnosed, persistent, and chronic
- Emphasized diagnosis of exclusion

**Estimated fraction of the various forms of secondary ITP based on clinical experience of the authors.**

![Image](http://www.nplatehcp.com/nplate/about-1p.html)


**Immune Thrombocytopenia (ITP)**

- Primary or secondary cause:
  - SLE
  - Medications
  - Viruses: hepatitis C, HIV
  - Bacteria: *H. pylori, Rickettsia*
  - Leukemia, lymphomas

**Pathogenesis:**

1. Antibody-mediated destruction of platelets
   - IgG targeting glycoprotein IIb/IIIa and/or Ib/IX on platelets
   - Antibodies only documented in 75% of cases
2. Decreased production of platelets
   - Increased clearance of thrombopoietin
   - Damaged megakaryocytes

**Acute vs Chronic:**
- Chronic – have ITP for > 12 months

2009: Vicenza Consensus Conference
- Renamed to Immune Thrombocytopenia
- Changed classification to newly diagnosed, persistent, and chronic
- Emphasized diagnosis of exclusion

**Estimated fraction of the various forms of secondary ITP based on clinical experience of the authors.**

![Image](http://www.nplatehcp.com/nplate/about-1p.html)


**Immune Thrombocytopenia (ITP)**

- Primary or secondary cause:
  - SLE
  - Medications
  - Viruses: hepatitis C, HIV
  - Bacteria: *H. pylori, Rickettsia*
  - Leukemia, lymphomas

**Pathogenesis:**

1. Antibody-mediated destruction of platelets
   - IgG targeting glycoprotein IIb/IIIa and/or Ib/IX on platelets
   - Antibodies only documented in 75% of cases
2. Decreased production of platelets
   - Increased clearance of thrombopoietin
   - Damaged megakaryocytes

**Acute vs Chronic:**
- Chronic – have ITP for > 12 months

2009: Vicenza Consensus Conference
- Renamed to Immune Thrombocytopenia
- Changed classification to newly diagnosed, persistent, and chronic
- Emphasized diagnosis of exclusion

**Estimated fraction of the various forms of secondary ITP based on clinical experience of the authors.**

![Image](http://www.nplatehcp.com/nplate/about-1p.html)


**Immune Thrombocytopenia (ITP)**

- Primary or secondary cause:
  - SLE
  - Medications
  - Viruses: hepatitis C, HIV
  - Bacteria: *H. pylori, Rickettsia*
  - Leukemia, lymphomas

**Pathogenesis:**

1. Antibody-mediated destruction of platelets
   - IgG targeting glycoprotein IIb/IIIa and/or Ib/IX on platelets
   - Antibodies only documented in 75% of cases
2. Decreased production of platelets
   - Increased clearance of thrombopoietin
   - Damaged megakaryocytes

**Acute vs Chronic:**
- Chronic – have ITP for > 12 months

2009: Vicenza Consensus Conference
- Renamed to Immune Thrombocytopenia
- Changed classification to newly diagnosed, persistent, and chronic
- Emphasized diagnosis of exclusion

**Estimated fraction of the various forms of secondary ITP based on clinical experience of the authors.**

![Image](http://www.nplatehcp.com/nplate/about-1p.html)


**Immune Thrombocytopenia (ITP)**

- Primary or secondary cause:
  - SLE
  - Medications
  - Viruses: hepatitis C, HIV
  - Bacteria: *H. pylori, Rickettsia*
  - Leukemia, lymphomas

**Pathogenesis:**

1. Antibody-mediated destruction of platelets
   - IgG targeting glycoprotein IIb/IIIa and/or Ib/IX on platelets
   - Antibodies only documented in 75% of cases
2. Decreased production of platelets
   - Increased clearance of thrombopoietin
   - Damaged megakaryocytes

**Acute vs Chronic:**
- Chronic – have ITP for > 12 months

2009: Vicenza Consensus Conference
- Renamed to Immune Thrombocytopenia
- Changed classification to newly diagnosed, persistent, and chronic
- Emphasized diagnosis of exclusion

**Estimated fraction of the various forms of secondary ITP based on clinical experience of the authors.**

![Image](http://www.nplatehcp.com/nplate/about-1p.html)


**Immune Thrombocytopenia (ITP)**

- Primary or secondary cause:
  - SLE
  - Medications
  - Viruses: hepatitis C, HIV
  - Bacteria: *H. pylori, Rickettsia*
  - Leukemia, lymphomas

**Pathogenesis:**

1. Antibody-mediated destruction of platelets
   - IgG targeting glycoprotein IIb/IIIa and/or Ib/IX on platelets
   - Antibodies only documented in 75% of cases
2. Decreased production of platelets
   - Increased clearance of thrombopoietin
   - Damaged megakaryocytes

**Acute vs Chronic:**
- Chronic – have ITP for > 12 months

2009: Vicenza Consensus Conference
- Renamed to Immune Thrombocytopenia
- Changed classification to newly diagnosed, persistent, and chronic
- Emphasized diagnosis of exclusion

**Estimated fraction of the various forms of secondary ITP based on clinical experience of the authors.**

![Image](http://www.nplatehcp.com/nplate/about-1p.html)

Differential Diagnosis

- ID
  - Tick-borne illnesses
  - Meningococcal meningitis
  - Parvo virus
- Hematology
  - ITP
  - DIC
  - Aplastic anemia
  - Evans syndrome
  - Autoimmune lymphoproliferative syndrome
- Oncology
  - Leukemia
  - Lymphoma
  - Neuroblastoma
  - Rhabdomyosarcoma
  - Drug reaction
  - SLE
  - Lab error

How to Treat ITP?

Treatments

- Observation and education
- First Line Therapies
  - IVIG
  - Steroids
  - IV Anti-D Therapy: Rh+, negative DAT, Hgb > 10
- Second Line Therapies
  - Rituximab
  - Splenectomy
  - Recombinant thrombopoietin


Treatments

- Giving platelets is not effective but is needed for life-threatening hemorrhages
- Primary reason for treatment:
  - Prevent intracranial hemorrhages
  - Treatment increases platelet levels > 20 more rapidly
- No data shows treatment effects outcomes of ITP


Treatments

- Proven et al (2010, Blood): Attempt to provide consensus based recommendations for diagnosis/treatment of ITP
  - Majority can avoid treatment
    - must be counseled on risks of hemorrhages and life-style changes
    - must have follow up
  - Admit: clinically significant hemorrhages, social concerns
  - Treat all children with severe hemorrhages and consider treating moderate hemorrhages/increased risk of hemorrhages
    - IVIG, anti-Rhesus, steroids


Treatments

- Lo and Deane (2014, Autoimmunity Reviews):
  - No bleeding or only mild bleeding: observe, follow plts level 5-7 days, avoid traumatic activities
  - Moderate/Severe bleeding: first-line therapy
    - Steroids, IVIG, anti-Rhesus
    - Goal: minimize risk of ICH until remission occurs
  - Life-threatening bleeds: platelets + first-line txs
  - Non-responders:
    - Avoid trauma, minimize side effects of treatments
    - Rituximab, splenectomy


Treatments

  - 2314 patients: 72.2% IVIG, 9.4% no treatment, 7.8% steroids
  - Only 12% pts admitted had non-cutaneous bleeding
  - Average cost: $8,984 (50% cost from pharmacy)
  - Average length of stay: 2 days

Why is ITP Important?

Immune Thrombocytopenia (ITP)
- ITP is managed by primary care physicians
- Epidemiology:
  - Most commonly affects ages 1-4
  - Affects 1/20,000 children
  - 2/3 cases have a history of a recent viral illness
  - Occurs most often late winter and spring
  - Affects males and females equally
  - Increased risk after MMR immunization


Immune Thrombocytopenia (ITP)
- Platelets are important to prevent bleeding
- Low platelets cause or contribute to:
  - Easy bruising
  - Nose bleeds
  - Bleeding gums
  - Hematuria
  - Intracranial hemmorhages

Intracranial Hemorrhage
- Risk of intracranial hemorrhage is extremely low: 0.1-1% of patients
- 25% mortality rate
- 33% with neurologic sequelae
- Increased risk:
  - Severe thrombocytopenia (< 10-20)
  - Bleeding manifestations other than skin
  - Head trauma
- Treatment does not decrease chance of developing ICH nor of developing chronic ITP


Intracranial Hemorrhage
- Psaila (2009. Blood): 40 pts with ITP and ICH (study group); 80 pts with ITP; no ICH (control)
  - No difference in age, sex, or duration of ITP
  - Median plt counts: study – 5; control – 8
    - 4 with ICH had counts of 35 at time of bleed
    - Half of control pts have counts < 10
  - 45% had ICH w/in 7 days, 20% after 1 week, 25% 1wk-6 months, 30% > 6 months
  - Risk factors: head trauma (33%), hematuria (22%), younger age, severe thrombocytopenia
  - Effect of treatment: unknown


Intracranial Hemorrhage
- Elalfy et al, 2010: reviewed medical records from patients with ITP from 1997-2007 in Egypt
  - Found 1840 patients
  - 56% male, 44% female
  - 10 developed ICH (0.54%)
  - ICH occurred from 1 week from onset to over a year
  - 4 had acute ITP; 2 persistent ITP; 4 chronic ITP
  - Median plt count 12
    - < 10 in 7pts with ICH; 10-20 in the other 3
  - 7 received treatment
    - 2 died, 3 residual seizures

Intracranial Hemorrhage

- Elalfy et al, 2010
- ICH can neither be anticipated or prevented
  - Steroids had limited effect in acute period
- Risk factors: plt count < 10, non-cutaneous bleeding, head trauma
- Counseling is essential
  - Avoid situations causing head trauma
  - ICH risk is present as long as patient has ITP
  - Regular follow up is needed

Outcomes of ITP

Immune Thrombocytopenia (ITP)

- Outcomes:
  - Self-limiting course, most resolve spontaneously by 6 months (70-85%)
  - 12% later developed autoimmune disease
    - SLE, CVID, autoimmune lymphoproliferative syndrome
  - 20% develop chronic ITP
    - More likely in teenagers (50%)
  - 0.1-1% develop intracranial hemorrhage (ICH)
    - 25% mortality
    - 13% life-long neurologic sequelae

Chronic ITP

- Managed by hematologist
- Lifestyle modifications
- Re-evaluate for secondary cause
- Treatment to prevent serious bleeding
  - Usually chronic steroids
  - Splenectomy: complete remission 64-88%
  - Rituximab: complete remission 30-50%

Case Study

- Treatment:
  - Gave IVIG 1gram/kg over 6 hours
  - Repeat CBC in AM

Labs (after IVIG x1)

<table>
<thead>
<tr>
<th></th>
<th>7</th>
<th>10.5</th>
<th>30.6</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>9.8</td>
<td>28.5</td>
<td>60</td>
</tr>
<tr>
<td>73</td>
<td>10.6</td>
<td>30.2</td>
<td>123</td>
</tr>
</tbody>
</table>
Summary

- Guidelines for treatment are unclear
- If treating, start with IVIG
- Be aware of potential risk factors for ICH
- Parental/Patient education
  - Anticipatory guidance
  - http://www.itpkids.org/content/itp_sports.html
  - Close follow up
  - Discussing risk of ICH and signs/symptoms
  - When in doubt, call for guidance

References


Thank You!

- Dr. Kara Bruning
- Dr. Stephanie Lowas (H/O Omaha)
- Dr. Nicholas Torbert
- Dr. Heidi Johnson