PLATELET DISORDERS

Hemostatic System - general information

- **Normal hemostatic system**
  - **vessel wall**
  - **circulating blood platelets**
  - **blood coagulation and fibrynolysis**

Bleeding Diathesis

- **inherited or acquired defects of**
  - **vessel wall**
  - **platelets number and/or function**
  - **coagulation system**

PRIMARY HEMOSTASIS DISORDERS

- **Immediate bleeding after trauma, cuts and surgical and dental procedures**
- **Mucocutaneous bleeding: petechia, easy bruising, nosebleeds, gingival bleeding, heme-positive stools, hematuria, menorrhaga**

- **Secondary Hemostasis Disorders: delayed bleeding from cuts or injuris, hemarthroses and intramuscular hematomas, deep soft tissue bleeds, intracranial hemorrages**

PLATELETS

- Anucleate disc-shape cell fragments
- arise from megakariocytes in bone marrow
- 1/3 of platelets are sequestrated in the spleen
- other 2/3 circulate for 7-10 days
- responsible for primary hemostasis

- they adhere to damaged blood vessels, aggregate one with another and facilitate the generation of thrombin

- normal platelet count: 150-450 G/l

Platelet Disorders

- **Disorder of platelet number**
  - **thrombocytopenia**
  - **thrombocytosis**
- **Disorder of platelet function**

Platelet Disorders - signs and symptoms

- May be asymptomatic if platelets count > 50 G/l
- onset of bleeding after trauma - immediate
- sites of bleeding
  - superficial:
    skin, mucous membranes, nose, genitourinary tract

- physical finding - ***petechiae, ecchymoses***

Platelet structure

- **plasma (surface) membrane protein:**

  GPIIb-IIIa – fibrinogen receptor

  GP Ib-IX-V: vWF receptor

  GPIa-IIa: collagen receptor

- **secretory granules:**

  Alpha-Granules

  Dense granules

  Lysosomes

Platelet receptors in clinical practice

- Cyclooxygenase inhibitors
  (Thromboxane A2 –e.g. Aspirin)
- Adenosine diphosphate inhibitors

- ticlopidine hydrochloride (Ticlid), clopidogrel bisulfate (Plavix)

- GPIIb-IIIa receptor antagonists

- Abciximab, Epifibatide, Tirofiban

Disorder of platelet functions 1

- **defects of platelet adhesion**
  - **inherited:**

    vonWillebrand's disease,

    Bernard-Soulier syndrome
  - **acquired:**

    uremia

Disorder of platelet functions 2

- **defects of platelet aggregation**
  - **inherited:**

    Glantzmann's thrombasthenia
  - **acquired:**

    dysproteinemia, drug ingestion (ticlopidin)

Disorder of platelet functions 3

- **defects of platelet release**
  - **inherited:**

    grey-platelet, Hermansky-Pudlak, Chediac-Higashi syndr.
  - **acquired:**

cardiopulmonary bypass, myeloproliferative disorders, drugs

Platelet function tests

- Platelet count – in vitro clumping caused by EDTA-dependant agglutinins (pseudothrombocytopenia)
- Morphology
- Platelet aggregations with following inductors

  -ADP,

  - collagen,

  -ristocetin RIPA
- PFA-200

Therapy

- Platelet transfusion should be used only in severe bleeding episodes
- Recombinant factor VIIa
- Antifibrynolytic agents (tranexamic acid)
- Desmopressin (DDAVP)

Thrombocytopenia

A. Decreased marrow production of megakariocytes

- **congenital disorders**
- **acquired disorders**

B. Splenic sequestration of circulating platelets

C. Increased destruction of circulating platelets (congenital/acquired disorders)

- **immune destruction**
- **nonimmune destruction**

Thrombocytopenia (A)

A. Decreased marrow production of megakariocytes

- **congenital disorders**
  - **Fanconi's anemia**
  - **thrombocytopenia with absent radii (TAR)**
- **acquired disorders**
  - **marrow infiltration with malignant cells**
  - **marrow fibrosis**
  - **aplastic and hypoplastic anemias (idiopathic, drugs, toxins)**
  - **deficiency states (vitamin B12, folate, iron)**
  - **paroxysmal nocturnal hemoglobinuria**

Thrombocytopenia (B)

B. Splenic sequestration of circulating platelets (hypersplenism)

- **splenic enlargement due to tumor infiltration**
- **splenic enlargement due to portal hypertension**

Thrombocytopenia (C)

C. Increased destruction of circulating platelets

- **congenital disorder**
  - Wiscott-Aldrich syndrome, Bernard-Soulier syndrome
- **acquired disorders**

nonimmune destruction

  - DIC
  - hemolytic-uremic syndrome/thrombotic thrombocytopenic purpura
  - sepsis
  - vascular prostheses, cardiac valves

immune destruction

  - Primary immune thrombocytopenic (ITP)
  - drug-induced thrombocytopenia
  - chronic autoimmune disorders
  - infection (HIV)
  - Malignancies

PRIMARY IMMUNE THROMBOCYTOPENIA – ITP (Idiopathic Thrombocytopenic Purpura)

- The most common cause of isolated thrombocytopenia defined as a peripheral blood platelet count less than 100G/L
- No associated condition or other causes of thrombocytopenia
- Shortened intravascular survival of platelets due to destruction caused by antiplatelet antibodies

PRIMARY IMMUNE THROMBOCYTOPENIA

- **Clinical features**
  - **petechiae**
  - **ecchymoses**
  - **mucose membranes bleeding**
  - **menorrhagia**
  - **rare internal, intracranial bleeding**

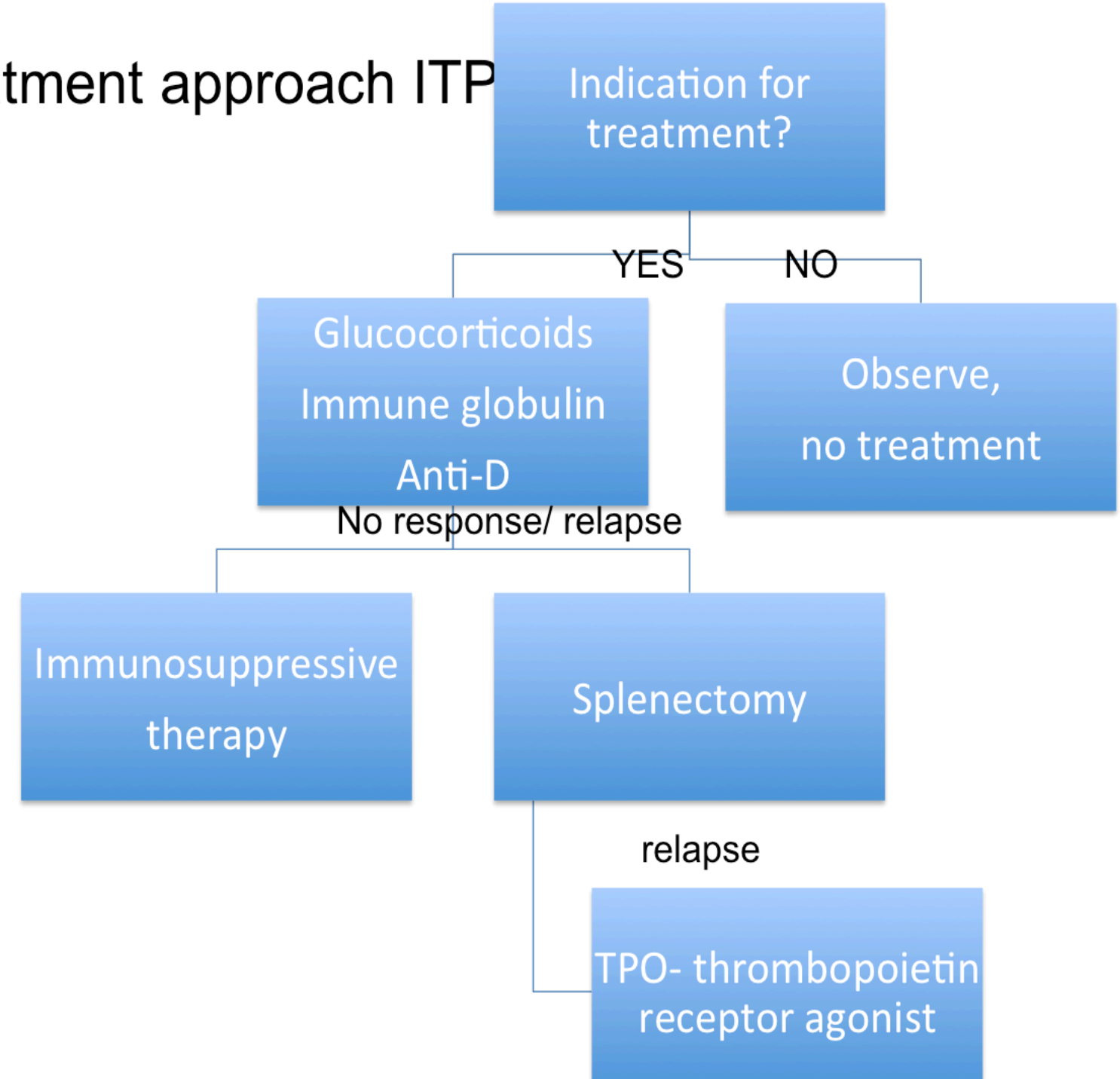
PRIMARY IMMUNE THROMBOCYTOPENIA

- Diagnosis is one of exclusion
  - platelet count <100G/l
  - bleeding time - usually normal
  - peripheral blood smear - large platelets
  - bone marrow examination - normal or increased number of megakariocytes
  - H. pylori (-), HIV (-), HCV (-)

Treatment of ITP

- **not necessary unless platelets count > 30G/L or there is extensive bleeding**
- **corticosteroids permanent responses - 30%**
  – prednisone 1mg/kg for 4-6 weeks
- **In steroid resistant patient splenectomy- permanent responses - 60%**
- **immunosuppresive drugs**
- **rituximab**
- **intravenous immunoglobulins**
- **anti-Rh (D) Immune Globulin**
- **other – danazol**
- **Thrombopoietin (TPO) receptor agonists**
  (romiplostim, eltrombopag)

Treatment approach ITP



HEPARIN-INDUCED THROMBOCYTOPENIA (HIT)

- caused by antibodies directed against heparin in complex with platelet factor 4 – **The 4Ts**
- **T – Thrombocytopenia**: 50% or more reduction in platelet count
- **T – Timing of platelet count fall**: Beginning 5 or more days after first exposure to heparin
- **T – Thrombosis** –New thrombotic complications
- **oTher causes of thrombocytopenia** – None apparent
- Therapy – to discontinue all forms of heparin
- Direct IIa inhibitors (lepirudin, argatroban) and Xa (danaparoid)

Thrombotic Thrombocytopenic Purpura (TTP)

- Syndrome of consumptive thrombocytopenia, pentad abnormalities:

1/ thrombocytopenia
2/ microangiopathic hemolitic anemia
3/ renal failure
4/ neurologic abnormalities
5/ fever

- Causing abnormality:
  Deficiency of metalloprotease ADAMTS 13
- Treatment:
- Prompt plasma exchange, Glucocorticoids, Recombinant ADAMTS 13

Thrombocytosis

- **Thrombocytosis resulting from myeloproliferation**
  - **essential thrombocythemia**
  - **polycythemia vera**
  - **chronic myelogenous leukemia**
- **Secondary (reactive) thrombocytosis**
  - **systemic inflammation**
  - **malignancy**
  - **iron deficiency**
  - **hemorrhage**
  - **postsplenectomy**