



# Thrombocytopenia

## Find the cause to finalize the treatment approach

BY BONNIE MCCARRON, MD

Thrombocytopenia may be due to many causes, and the approach to a patient varies according to the diagnosis and the severity of the platelet deficiency. At the initial workup, medications should be ruled out as the primary cause. In most cases, it will then be helpful to follow the classic approach to the etiology of thrombocytopenia — decreased production, destruction and sequestration. Certain medical conditions associated with thrombocytopenia should not be missed, as they require urgent treatment. These include heparin-induced thrombocytopenia, thrombotic thrombocytopenic purpura (TTP), severe immune thrombocytopenia purpura (ITP), disseminated intravascular coagulation (DIC) and acute leukemia.

*Bonnie McCarron, MD, graduated from McMaster University and completed internal medicine and hematology training at the University of British Columbia, with a thrombosis fellowship at the University of Rochester. After practicing as an assistant professor at Dalhousie in the Division of Hematology, she is presently working as a hematologist at the Grand River Cancer Center in Kitchener, Ontario.*

### Symptoms and signs

- easy bruising
- mucosal bleeding
- petechial lesions
- excessive bleeding with trauma
- bleeding with invasive procedures

### Classic approach to cause

#### Decreased production

- myelodysplasia
- hematologic malignancies
- aplastic anemia
- metastatic cancers
- vitamin B<sub>12</sub> or folate deficiencies
- radiation treatment
- medications
- toxins, e.g. alcohol, cocaine
- congenital thrombocytopenia
- sepsis

#### Increased destruction and consumption

- drug-induced thrombocytopenia
- immune thrombocytopenia
- microangiopathic hemolytic anemias, including TTP, DIC
- pre-eclampsia
- sepsis

#### Sequestration

- splenomegaly due to various causes, e.g. liver disease, hematologic malignancies, infiltrative conditions

### Avoid platelet transfusions in:

- TTP — may worsen thrombosis
- ITP — use only in situations of life-threatening bleeding
- mild or moderate thrombocytopenia in a non-bleeding patient, unless invasive procedures are required

### Diagnostic workup

- history and physical examination — drug and medication history, alcohol intake, past illnesses, presence of splenomegaly
- peripheral smear — rule out platelet clumping; investigate for fragmentation seen with TTP, DIC
- complete blood count — determine if other cell lines are involved
- if leukopenia or anemia is also present, vitamin B<sub>12</sub> and folate deficiencies should be ruled out — if levels are normal, consider bone marrow aspirate and biopsy
- international normalized ratio, activated partial thromboplastin time and D-dimer tests — if abnormal, consider DIC
- creatinine level — to investigate for TTP
- liver function tests

### Conditions not to be missed

- severe ITP — if platelets are dropping, the platelet count should be followed closely; severe ITP with platelets < 10 x 10<sup>9</sup>/L requires treatment with steroids and/or intravenous gammaglobulin, urgently
- TTP — requires urgent plasma exchange
- DIC — generally associated with severe illnesses, e.g. sepsis, multi-trauma, obstetrical complications, malignancies
- heparin-induced thrombocytopenia — heparin must be stopped immediately and alternate anticoagulation considered, e.g. danaparoid or hirudin; warfarin must not be started until after the platelet count first recovers with another anticoagulant
- acute leukemia — if severe pancytopenia with circulating blasts are present, patients require urgent assessment by a hematologist

### Causes of thrombocytopenia in pregnancy

- gestational or incidental thrombocytopenia — mild, not associated with bleeding; occurs in third trimester; no treatment required
- pre-eclampsia
- immune thrombocytopenia — may be difficult to distinguish from incidental thrombocytopenia
- drugs, marrow infiltration, sepsis, etc., as in non-pregnant patients
- rare causes
  - DIC — may be seen with abruption or retained products
  - hemolysis, elevated liver enzymes, low platelets (HELLP) — part of the spectrum of pre-eclampsia
  - TTP/hemolytic uremic syndrome
  - acute fatty liver of pregnancy

### Immune thrombocytopenia purpura

- often a diagnosis of exclusion
- may be associated with viral illnesses, connective tissue diseases, lymphoproliferative disorders
- can be idiopathic
- normal hemoglobin and white cell count
- usually self-limiting in children, generally chronic in adults
- large platelet forms seen in peripheral smear
- bone marrow shows increased megakaryocytes
- requires treatment if platelets < 30 x 10<sup>9</sup>/L or if patient is actively bleeding
- main therapeutic agent — prednisone
- splenectomy — considered in patients who can't be weaned off prednisone; effective in approximately two-thirds of individuals
- intravenous gammaglobulin or anti-D antibody — can also be used for treatment