



## Complete Summary

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### GUIDELINE TITLE

Thrombocytopenia.

### BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Thrombocytopenia. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2002 Feb 19 [Various]. [4 references]

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## SCOPE

### DISEASE/CONDITION(S)

Thrombocytopenia

### GUIDELINE CATEGORY

Evaluation  
Management

### CLINICAL SPECIALTY

Family Practice  
Internal Medicine

### INTENDED USERS

Health Care Providers  
Physicians

### GUIDELINE OBJECTIVE(S)

Evidence-Based Medicine Guidelines collects, summarizes, and updates the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given recommendations.

#### TARGET POPULATION

Adults and children with thrombocytopenia

#### INTERVENTIONS AND PRACTICES CONSIDERED

##### Evaluation

1. Assessment of causes of thrombocytopenia
2. Laboratory studies, as indicated, such as haemoglobin, leucocyte count and differential, platelet count and bone marrow examination, platelet antibody assessment, measurement of platelet life-span with radioactively labeled platelets
3. Manual check of platelets when a low count has been detected by automatic counter

##### Management

1. Avoidance of or stopping possible thrombocytopenia-causing drugs
2. Monitoring of symptomless patient
3. Referral, as indicated, to a specialist (in internal medicine or haematology)
4. Hospitalization, if symptoms of bleeding
5. Pharmacologic treatment of idiopathic thrombocytopenia (ITP) (prednisolone; intravenous gamma globulin infusions; other drugs, including immunosuppressants and fibrinolysis inhibitors)
6. Splenectomy in patients with idiopathic thrombocytopenia who are non-responders to pharmacologic treatment
7. Transfusions (platelet transfusions; for massive bleeding, transfusion of red cells, fresh-frozen plasma, and platelet concentrates)
8. Oprelvekin in chemotherapy-induced thrombocytopenia

#### MAJOR OUTCOMES CONSIDERED

- Incidence of drug-induced thrombocytopenia
- Need for platelet transfusion in chemotherapy-induced thrombocytopenia
- Platelet count and platelet recovery
- Adverse effects of treatment

## METHODOLOGY

#### METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)  
Hand-searches of Published Literature (Secondary Sources)  
Searches of Electronic Databases

## DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence reviewed was collected from the Cochrane database of systematic reviews and the Database of Abstracts of Reviews of Effectiveness (DARE). In addition, the Cochrane Library and medical journals were searched specifically for original publications.

## NUMBER OF SOURCE DOCUMENTS

Not stated

## METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

## RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

A: Strong research-based evidence. Several relevant, high-quality scientific studies with homogeneous results.

B: Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.

C: Limited research-based evidence. At least one adequate scientific study.

D: No scientific evidence. Expert panel evaluation of other information.

## METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

## COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

## METHOD OF GUIDELINE VALIDATION

Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

The levels of evidence [A-D] supporting the recommendations are defined at the end of the "Major Recommendations" field.

#### Clinical Approach

- Remember the possibility of so-called pseudothrombocytopenia.
- Stop drugs possibly causing thrombocytopenia unless vitally indicated.
- If the thrombocytopenic patient has symptoms of bleeding, immediate hospitalization is advisable.

#### Basic Rules

- The pathophysiological mechanism of thrombocytopenia (blood platelet count  $<150 \times 10^9/L$ ) may be
  - decreased production in the bone marrow
  - increased consumption peripherally
  - increased sequestration in the spleen
- Artificially low platelet counts are occasionally obtained when counted from ethylenediaminetetraacetic acid (EDTA)-anticoagulated blood using automatic counters (pseudothrombocytopenia). When thrombocytopenia ( $<100 \times 10^9/L$ ) is detected in a patient for the first time, check the same blood sample manually for the presence of thrombocyte aggregates.
- Thrombocytopenia is only a symptom, the cause of which should be clarified. Typical manifestations of thrombocytopenia are skin bruising and petechiae and mucous membrane bleeding. In particular, gum and nasal bleeding is common. Bleeding may also take place in the gastrointestinal and urinary tracts. Menorrhagia is also common.
- A tendency towards bleeding is uncommon if the platelet count is 50 to  $100 \times 10^9/L$ , although the bleeding time starts to lengthen with counts  $<80 \times 10^9/L$ . Platelet concentrations of 10 to  $50 \times 10^9/L$  are frequently associated with spontaneous bleeding, and haemorrhages are often severe with platelet counts  $<10 \times 10^9/L$ .

#### Causes of Thrombocytopenia

##### Decreased Production

- Inborn causes

- Pancytopenias and thrombocytopenias
- Bone marrow infiltrates
- Rubella
- Maternal use of thiazide diuretics during pregnancy
- Acquired causes
  - Aplastic anaemia
  - Bone marrow infiltrates (carcinoma, leukaemia, myelofibrosis, myelodysplasia, tuberculosis)
  - Ionising irradiation, other causes of myelosuppression
  - Drugs (trimethoprim-sulfamethoxazole, gold, quinidine (George et al., 1998; DARE-989740, 2000) [C], thiazide diuretics, alcohol, oestrogens, interferons)
  - Deficiency of vitamins and other essential trace elements or nutrients (B<sub>12</sub>, folate, iron)
  - Viral infections (in Henoch-Schonlein purpura, thrombocyte count is normal)
  - Uraemia
  - Heavy drinking
  - Pregnancy

#### Increased Consumption

- Inborn causes
  - Non-immunological (haemolytic disease of the newborn, prematurity, maternal pre-eclampsia, renal vein thrombosis, infections)
  - Immunological (drug-induced, isoimmune neonatal thrombocytopenia, maternal idiopathic thrombocytopenia purpura [ITP])
- Acquired causes
  - Non-immunological (infections, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, haemolytic-uraemic syndrome, drug-induced over-consumption of platelets)
  - Immunological (drug-induced, in connection with anaphylaxis, following blood transfusion, chronic and acute ITP)

#### Platelet Sequestration

- Hypersplenism and hypothermia

#### Loss of Platelets

- Haemorrhage and haemoperfusion

#### Clinical Approach

##### Symptomless Patient, Platelet Count 100-150 x 10<sup>9</sup>/L

- The general practitioner can safely follow the situation, initially at intervals of a few months. If no underlying disease becomes evident and thrombocytopenia remains stable, no further follow-up is required. All drugs causing thrombocytopenia should be avoided.

- Many drugs cause thrombocytopenia relatively frequently. These include heparin, quinidine, chloroquine, gold, salicylates, sulphonamides, thiazides, allopurinol, phenytoin, carbamazepine, and trimethoprim. Non-steroidal anti-inflammatory drugs (NSAIDs; especially acetylsalicylic acid) and some other medicines (clopidogrel) frequently impair platelet function and bring about a tendency to bleed. This tendency is disproportionately strong among thrombocytopenic patients. Paracetamol does not significantly worsen platelet function.

#### Symptomless Patient, Platelet Count $< 100 \times 10^9/L$

- Thrombocytopenia-causing drugs should be stopped. Basic investigations are performed: haemoglobin, leucocyte count and differential, platelet count, and bone marrow examination.
- If the situation does not improve, referral to a specialist in internal medicine or haematology is advisable.
- If there are no obvious reasons for thrombocytopenia, platelet antibody assessment should be carried out early.
- Sometimes it is necessary to measure platelet life-span with radioactively labeled platelets. This investigation gives information about the kinetic nature (poor platelet production or decreased survival) of thrombocytopenia.
- Pseudothrombocytopenia: thrombocytes are aggregated in an EDTA tube.

#### If a Thrombocytopenia Patient Has Symptoms of Bleeding

- He/she needs specialist care.
- It is important to detect the possible cause. Remember that the list of drugs possibly causing thrombocytopenia is very long. All these drugs should be avoided.

#### Idiopathic Thrombocytopenic Purpura (ITP)

- Treatment is planned by a specialist (in internal medicine, or a paediatrician or haematologist).
- In adults, prednisolone continues to be the first-line therapy. The starting dose is 1 to 2 mg/kg/day. Response to treatment is often achieved in 1 to 4 weeks. At least a partial response is observed in 70 to 90% of cases, but a good one (i.e. platelet count  $> 100 \times 10^9/L$ ) in only 30 to 50% of the patients. After a maximal response is observed, the drug is slowly (over weeks) tapered to the smallest dose resulting in an acceptable clinical situation, say a platelet count  $> 50 \times 10^9/L$ , with no symptoms of bleeding. Among paediatric haematologists the use of corticosteroids in ITP has been more controversial, because spontaneous remissions are very frequent (George et al., 1998).
- Intravenous gamma globulin infusions may induce a response faster than do corticosteroids. Non-responders are treated with immunosuppressants or by splenectomy.
- Fibrinolysis inhibitors may be used to reduce excessive mucous membrane haemorrhages, such as nasal, gastrointestinal, and urinary tract bleeding and menorrhagia. Platelet transfusions are effective if no platelet antibodies are present. Massive bleeding is compensated with red cells, fresh-frozen plasma, and platelet concentrates.

## Related Evidence

- Oprelvekin accelerates platelet recovery and reduces the need for platelet transfusion in chemotherapy-induced thrombocytopenia (Wilde & Faulds, 1998; DARE-981457, 2001) [C].

## Definitions:

### Levels of Evidence

A: Strong research-based evidence. Several relevant, high-quality scientific studies with homogeneous results.

B: Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.

C: Limited research-based evidence. At least one adequate scientific study.

D: No scientific evidence. Expert panel evaluation of other information.

### CLINICAL ALGORITHM(S)

None provided

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### REFERENCES SUPPORTING THE RECOMMENDATIONS

[References open in a new window](#)

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Concise summaries of scientific evidence attached to the individual guidelines are the unique feature of the Evidence-Based Medicine Guidelines. The evidence summaries allow the clinician to judge how well-founded the treatment recommendations are. The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field).

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

Effective evaluation and management of thrombocytopenia

### POTENTIAL HARMS

- In a systematic review, the most frequent adverse effects of oprelvekin were oedema and dyspnoea.

- Artificially low platelet counts are occasionally obtained when counted from ethylenediaminetetraacetic acid (EDTA)-anticoagulated blood using automatic counters (pseudothrombocytopenia).

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better  
Living with Illness

### IOM DOMAIN

Effectiveness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Thrombocytopenia. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2002 Feb 19 [Various]. [4 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2001 Apr 30 (revised 2002 Feb 19)

### GUIDELINE DEVELOPER(S)

Finnish Medical Society Duodecim - Professional Association

### SOURCE(S) OF FUNDING

Finnish Medical Society Duodecim

### GUIDELINE COMMITTEE

Editorial Team of EBM Guidelines

#### COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Author: Editors

#### FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

#### GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Finnish Medical Society Duodecim. Thrombocytopenia. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2001 Apr 30. Various p.

#### GUIDELINE AVAILABILITY

This guideline is included in a CD-ROM titled "EBM Guidelines. Evidence-Based Medicine" available from Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: [info@ebm-guidelines.com](mailto:info@ebm-guidelines.com); Web site: [www.ebm-guidelines.com](http://www.ebm-guidelines.com).

#### AVAILABILITY OF COMPANION DOCUMENTS

None available

#### PATIENT RESOURCES

None available

#### NGC STATUS

This summary was completed by ECRI on December 17, 2002. The information was verified by the guideline developer as of February 7, 2003. The summary was updated by ECRI on April 2, 2004.

#### COPYRIGHT STATEMENT

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