



## Complete Summary

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### GUIDELINE TITLE

Thrombocytopenia.

### BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Thrombocytopenia. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2007 Apr 27 [Various].

### GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Finnish Medical Society Duodecim. Thrombocytopenia. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2005 Apr 17 [Various].

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## SCOPE

### DISEASE/CONDITION(S)

Thrombocytopenia

### GUIDELINE CATEGORY

Evaluation  
Management  
Treatment

### CLINICAL SPECIALTY

Family Practice  
Hematology  
Internal Medicine  
Pediatrics

## **INTENDED USERS**

Health Care Providers  
Physicians

## **GUIDELINE OBJECTIVE(S)**

Evidence-Based Medicine Guidelines collect, summarize, and update 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. Assessment of patient with and without symptoms
3. Laboratory studies, as indicated, such as haemoglobin, leucocyte count and differential, platelet count and bone marrow examination, platelet antibody assessment
4. Manual check of platelets when a low count has been detected by automatic counter

### **Treatment/Management**

1. Avoidance of or stopping possible thrombocytopenia-causing drugs
2. Monitoring of symptomless patients
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)  
(corticosteroids, including predniso[lo]ne; intravenous gamma globulin infusions; other drugs, including immunosuppressants and fibrinolysis inhibitors)
6. Splenectomy
7. Transfusions

## **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. Quality of Evidence: High**

Further research is very unlikely to change confidence in the estimate of effect

- Several high-quality studies with consistent results
- In special cases: one large, high-quality multi-centre trial

#### **B. Quality of Evidence: Moderate**

Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.

- One high-quality study
- Several studies with some limitations

#### **C. Quality of Evidence: Low**

Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.

- One or more studies with severe limitations

**D. Quality of Evidence: Very Low**

Any estimate of effect is very uncertain.

- Expert opinion
- No direct research evidence
- One or more studies with very severe limitations

**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**

- Stop drugs possibly causing thrombocytopenia unless vitally indicated.

- If the thrombocytopenic patient has symptoms of bleeding, immediate hospitalization is advisable.
- Remember the possibility of so-called pseudothrombocytopenia.

### Basic Rules

- The pathophysiological mechanism of thrombocytopenia (blood platelet count  $<150 \times 10^9/L$ , in late pregnancy  $<120 \times 10^9/L$ ) may be
  - Decreased production in the bone marrow
  - Increased consumption
  - Increased sequestration in the spleen
- Artificially low platelet counts are occasionally obtained when counted from ethylenediaminetetraacetic acid (EDTA)-anticoagulated blood (pseudothrombocytopenia). When thrombocytopenia ( $<100 \times 10^9/L$ ) is detected in a patient for the first time, the same blood sample should be checked manually for the presence of thrombocyte aggregates.
- Thrombocytopenia is 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  $100 \times 10^9/L$ . Platelet concentrations of 10 to  $50 \times 10^9/L$  are frequently associated with spontaneous bleeding, and haemorrhages are often severe with platelet counts of  $<10 \times 10^9/L$ . Drugs that affect the platelet function (aspirin [ASA], clopidogrel) increase bleeding tendency already in a rather moderate thrombocytopenia.

### Causes of Thrombocytopenia

#### Decreased Production

- Inborn causes
  - Inherited thrombocytopenias (rare)
  - Fanconi's anaemia
- Acquired causes
  - Aplastic anaemia
  - Bone marrow infiltrates (carcinoma, leukaemia, myelofibrosis, myelodysplasia, tuberculosis)
  - Ionizing radiation, other causes of myelosuppression (cytotoxic chemotherapy)
  - Drugs (trimethoprim-sulfamethoxazole, gold, thiazide diuretics, oestrogens, interferons)
  - Deficiency of vitamins and other essential trace elements or nutrients ( $B_{12}$ , folate, iron)
  - Viral infections
  - Heavy drinking
  - Pregnancy

#### Increased Consumption

- Inborn causes

- Non-immunological (haemolytic disease of the newborn, prematurity, maternal pre-eclampsia, infections)
- Immunological alloimmune 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, following blood transfusion, chronic and acute ITP) (see the Finnish Medical Society Duodecim guideline: "Bruises and purpura in children: ITP and its differential diagnosis")

### **Platelet Sequestration**

- Hypersplenism

### **Loss of Platelets**

- Acute haemorrhage
- 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 if possible. Alcohol consumption habits should be discussed.
- Many drugs cause thrombocytopenia relatively frequently (George et al., 1998) [C]. 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 bleeding tendency. This tendency is disproportionately strong among thrombocytopenic patients.
  - Paracetamol appears not to impair platelet function.

#### **Symptomless Patient, Platelet Count <100 x 10<sup>9</sup>/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.

## **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, a paediatrician, or haematologist.
- In adults, predniso(lo)ne 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. ITP in children is often a self-limited postinfectious condition (see the Finnish Medical Society Duodecim guideline: "Bruises and purpura in children: ITP and its differential diagnosis").
- Intravenous gammaglobulin infusions may induce a response faster than corticosteroids. Non-responders are treated with immunosuppressants or 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 Resources**

### **Other Evidence Summaries**

- Oprelvekin may accelerate platelet recovery and reduce the need for platelet transfusion in chemotherapy-induced thrombocytopenia (Wilde & Faulds, 1998) [C].

Refer to the original guideline document for other Internet resources and related literature.

### **Definitions:**

### **Levels of Evidence**

#### **A. Quality of Evidence: High**

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- Expert opinion
- No direct research evidence
- One or more studies with very severe limitations

### **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**

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)**

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### **ADAPTATION**

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

### **DATE RELEASED**

2001 Apr 30 (revised 2007 Apr 27)

### **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:* Esa Jantunen

## **FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST**

Not stated

## **GUIDELINE STATUS**

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This guideline updates a previous version: Finnish Medical Society Duodecim. Thrombocytopenia. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2005 Apr 17 [Various].

## **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, on October 5, 2004, and June 28, 2005. This summary was updated by ECRI on January 31, 2006, following release of a public health advisory from the U.S. Food and Drug Administration regarding the use of WinRho SDF (Rho(D) Immune Globulin Intravenous [Human]). This NGC summary was updated by ECRI Institute on January 7, 2008.

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Date Modified: 11/3/2008

