

# A&I

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**Hypoplastic left heart syndrome**  
**Immune thrombocytopenia (ITP)**

orphan**a**nesthesia

a project of the German Society  
of Anaesthesiology and Intensive Care Medicine

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## OrphanAnesthesia –

### ein krankheitsübergreifendes Projekt des Wissenschaftlichen Arbeitskreises Kinderanästhesie der Deutschen Gesellschaft für Anästhesiologie und Intensivmedizin e.V.

Ziel des Projektes ist die Veröffentlichung von Handlungsempfehlungen zur anästhesiologischen Betreuung von Patienten mit seltenen Erkrankungen. Damit will Orphan Anesthesia einen wichtigen Beitrag zur Erhöhung der Patientensicherheit leisten.

Patienten mit seltenen Erkrankungen benötigen für verschiedene diagnostische oder therapeutische Prozeduren eine anästhesiologische Betreuung, die mit einem erhöhten Risiko für anästhesieassoziierte Komplikationen einhergehen. Weil diese Erkrankungen selten auftreten, können Anästhesisten damit keine Erfahrungen gesammelt haben, so dass für die Planung der Narkose die Einholung weiterer Information unerlässlich ist. Durch vorhandene spezifische Informationen kann die Inzidenz von mit der Narkose assoziierten Komplikationen gesenkt werden. Zur Verfügung stehendes Wissen schafft Sicherheit im Prozess der Patientenversorgung.

Die Handlungsempfehlungen von OrphanAnesthesia sind standardisiert und durchlaufen nach ihrer Erstellung einen Peer-Review-Prozess, an dem ein Anästhesist sowie ein weiterer Krankheitsexperte (z.B. Pädiater oder Neurologe) beteiligt sind. Das Projekt ist international ausgerichtet, so dass die Handlungsempfehlungen grundsätzlich in englischer Sprache veröffentlicht werden.

Ab Heft 5/2014 werden im monatlichen Rhythmus je zwei Handlungsempfehlungen als Supplement der A&I unter [www.ai-online.info](http://www.ai-online.info) veröffentlicht. Als Bestandteil der A&I sind die Handlungsempfehlungen damit auch zitierfähig. Sonderdrucke können gegen Entgelt bestellt werden.

## OrphanAnesthesia –

### a common project of the Scientific Working Group of Paediatric Anaesthesia of the German Society of Anaesthesiology and Intensive Care Medicine

The target of OrphanAnesthesia is the publication of anaesthesia recommendations for patients suffering from rare diseases in order to improve patients' safety. When it comes to the management of patients with rare diseases, there are only sparse evidence-based facts and even far less knowledge in the anaesthetic outcome. OrphanAnesthesia would like to merge this knowledge based on scientific publications and proven experience of specialists making it available for physicians worldwide free of charge.

All OrphanAnesthesia recommendations are standardized and need to pass a peer review process. They are being reviewed by at least one anaesthesiologist and another disease expert (e.g. paediatrician or neurologist) involved in the treatment of this group of patients.

The project OrphanAnesthesia is internationally oriented. Thus all recommendations will be published in English.

Starting with issue 5/2014, we'll publish the OrphanAnesthesia recommendations as a monthly supplement of A&I (Anästhesiologie & Intensivmedizin). Thus they can be accessed and downloaded via [www.ai-online.info](http://www.ai-online.info). As being part of the journal, the recommendations will be quotable. Reprints can be ordered for payment.

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#### Projektleitung

**Prof. Dr. Tino Münster, MHBA**  
Geschäftsführender Oberarzt  
Facharzt für Anästhesie,  
Spezielle Schmerztherapie,  
Notfallmedizin  
Anästhesiologische Klinik  
Friedrich-Alexander-Universität  
Erlangen-Nürnberg  
Krankenhausstraße 12  
91054 Erlangen, Deutschland  
Tel.: 09131 8542441  
Fax: 09131 8536147  
E-Mail: [muenster@kfa.imed.uni-erlangen.de](mailto:muenster@kfa.imed.uni-erlangen.de)

# orphananesthesia

## Anaesthesia recommendations for patients suffering from **Immune thrombocytopenia (ITP)**

**Disease name:** Immune thrombocytopenia (ITP)

**ICD 10:** D69.3

**Synonyms:** Immune thrombocytopenic purpura, idiopathic thrombocytopenic purpura

Immune thrombocytopenia, previously known as idiopathic thrombocytopenic purpura (ITP), is an autoimmune disease that is related to anti-platelet immunoglobulin (IgG) production. The production of IgG autoantibodies is critically dependent on cellular immune mechanisms particularly relating to T cells. The production of these autoantibodies by B cells depends on a number of cellular mechanisms that form a network of modulation, with T cells playing a pivotal role in pathophysiology. T-cell-mediated cytotoxicity is an alternative mechanism for platelet destruction in ITP [1-3]. Other causes are included genetic factors (immune genes-FcR, immune syndromes, platelet antigens) and susceptibility to initial event (infection, inflammation) [4]. Immune thrombocytopenia is characterised by increased mucocutaneous haemorrhage risk with low platelet counts [5].

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Medicine in progress

Perhaps new knowledge



Every patient is unique

Perhaps the diagnostic is wrong

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### Disease summary

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Purpura are not seen in many patients, and ITP was shortened to immune thrombocytopenia. The diagnosis of immune thrombocytopenia is made via the exclusion of other factors that cause thrombocytopenia. The frequency of ITP in adults per year is 1.6-6.6 per 100,000 (6).

The incidence of ITP in adults is approximately equal for the sexes except in the mid-adult years (30-60 years), when the disease is more prevalent in women [7-9]. The initial hypothesized cause of ITP was increased platelet destruction at a rate that exceeded production by compensating bone marrow. New knowledge questions this model and provides evidence that platelet production is also decreased in many ITP patients [5]. There is no "gold standard" test that reliably establishes the diagnosis. However, a positive response to an ITP-specific therapy, e.g., intravenous immunoglobulin (IVIg) and/or steroids, is supportive of the diagnosis.

The stages of immune thrombocytopenia were re-defined:

- a) Newly diagnosed ITP covers the first 3 months after diagnosis
- b) Persistent ITP covers 3-12 months after diagnosis and cases that do not enter spontaneous remission or do not remain in remission after treatment cessation
- c) Chronic ITP encompasses the group with ITP that lasts 12 months or longer.

The primary target of ITP treatment is the prevention of major haemorrhage by attaining a safe thrombocyte count, but not the return of thrombocyte counts to normal. A level of  $50 \times 10^9/L$  may be sufficient in ITP patients with generally good functioning platelets. Adults with platelet counts less than  $30 \times 10^9/L$  are generally treated. Multiple large cohort studies reported that patients with platelet counts above that level were safely observed without treatment [10,11].

The incidence of haemorrhagic diathesis increases with age [12], and the effect of this condition on quality of life [3,14], mortality and morbidity should be considered [15,16]. Studies of co-morbidities and risk factors in large series of ITP patients with long follow-ups are rare [17,18]. Studies of surgical complications and mortality were only conducted for splenectomy procedures (19). The global features of adverse postoperative outcomes for ITP patients undergoing all types of surgical procedures have not been studied in a population-based cohort [20,21].

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### Typical surgery

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Splenectomy is a surgical procedure that is specific to ITP patients. Splenectomy should not be performed until 12 months from diagnosis if possible because of the possibility of spontaneous remission during this period [22]. However, the lack of response to more than one medication and findings of severe bleeding may add splenectomy to the agenda earlier in newly diagnosed or persistent ITP patients. Eighty percent of patients respond to splenectomy, and the response is permanent in 66% of patients, who do not require additional treatment for at least 5 years.

Emergency splenectomy may be performed in ITP patients with active haemorrhage and platelet counts  $<50 \times 10^9/L$ . Splenectomy may be performed as an open or laparoscopic surgery.

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All types of surgical procedures may be performed in patients with an ITP diagnosis. The critical factor is whether the decision for the surgical procedure is emergency or elective. An urgent increase in platelet count may be required for some thrombocytopenic patients who require surgical procedures but are at a high risk of bleeding. Switching from corticosteroids to IVIg, anti-D or recombinant factor VIIa (rFVIIa) may be effective in emergency settings, but a combination of first-line therapies is appropriate [23-28]. Subsequent maintenance therapy with the oral combination of danazol (10-15 mg/kg) and azathioprine (2 mg/kg). There is also some evidence of rapid response to vinca alkaloids [8]. Combination chemotherapy is a useful approach for patients with ITP refractory to conventional treatments both for acute induction and for long-term maintenance therapy [29]. Prednisone and IVIg are recommended for the emergency treatment of patients with uncontrolled bleeding. High-dose methylprednisolone (HDMP) may also be useful in this setting. Other therapies that work rapidly include platelet transfusion, possibly in combination with IVIg, and emergency splenectomy [23].

**Table 1. Suggested treatment algorithm for anaesthesia induction in patients with ITP**

	Operating setting	
	Elective operation	Emergency operation
<b>During anaesthesia induction</b>	<p>Assess using the current guideline treatment of ITP approach</p> <ul style="list-style-type: none"> <li>*Platelet transfusion is not necessarily</li> </ul> <p>Ensure that appropriate further expert (haematologist) help and advice is obtained at the most appropriate time for the patient</p> <ul style="list-style-type: none"> <li>The best time in operation is planned for the patient</li> </ul>	<p>Whatever the count of platelets was operated ensure that appropriate combination chemotherapy and/or *platelet transfusion treatment may be possible</p> <ul style="list-style-type: none"> <li>IVIg (1 g.kg<sup>-1</sup> or 2 g.kg<sup>-1</sup>)</li> <li>metilprednizolon (30 mg.kg<sup>-1</sup>)</li> <li>vinca alkaloids (0.03 mg.kg<sup>-1</sup>)</li> <li>anti-D (50-75 µg.kg<sup>-1</sup>)</li> <li>rFVIIa (50-122 µg.kg<sup>-1</sup>)</li> </ul> <p>Ensure that appropriate further expert (haematologist) help and advice is obtained at the most appropriate time for the patient.</p>

\* make decision of platelet transfusion

### Type of anaesthesia

A large body of literature references and guidelines aid the decision-making process, such as the recently updated evidence-based guidelines of the American Society of Regional Anesthesia and Pain Medicine for patients receiving antithrombotic or thrombolytic therapy. However, no explicit recommendations or guidelines exist for patients with haemorrhagic diathesis, such as von Willebrand disease (vWD), haemophilia A and B, and ITP. ITP patients often present with low platelet counts.

The primary concern for regional anaesthesia in thrombocytopenic patients is the risk of neuraxial haematoma development secondary to haemorrhage [30]. Spinal or epidural anaesthesia are generally considered safe when the platelet count is over 80 x 10<sup>9</sup>/L. However, the consistently low platelet counts in ITP seem less problematic than rapidly falling values due to other diseases, which are often accompanied by platelet dysfunction or coagulopathy. Neuraxial anaesthesia was successfully performed in several studies with platelet counts between 50 and 80 x 10<sup>9</sup>/L. (23).

Nevertheless, the minimum safe platelet count for neuraxial blockade is undefined in these patients. Evidence-based recommendations for neuraxial anaesthesia in patients with haemophilia, vWD or ITP cannot be offered.

Each patient must be treated individually. Veen et al. [31] reviewed the current guidelines, case series and case reports on epidural and spinal anaesthesia and lumbar punctures (LPs) in thrombocytopenic patients. This review reported that a platelet count of  $80 \times 10^9/L$  was a safe count for the placing/removing an epidural or spinal anaesthetic, and  $40 \times 10^9/L$  was a safe count for LP in the conclusion.

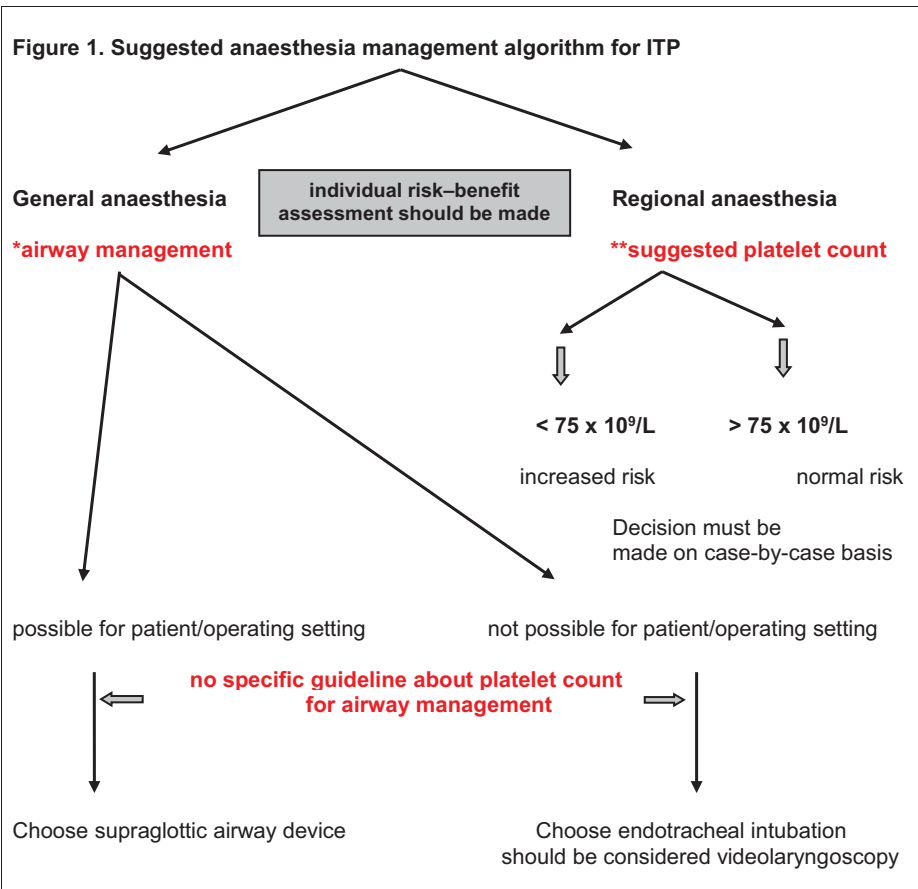
This topic emphasised the necessity to ensure the following points: platelet count should be stable; coagulopathy should not be congenital or acquired; the patient should have normal platelet functions without the use of an anti-platelet agent; and 12 h should have elapsed from the last dose of a prophylactic dose of low molecular weight heparin, or 24 h after a therapeutic dose before an epidural or spinal anaesthetic is placed [33]. However, Veen et al. [31] suggested for patients with platelet counts of  $50\text{--}80 \times 10^9/L$  requiring epidural or spinal anaesthesia and patients with a platelet count  $20\text{--}40 \times 10^9/L$  requiring a LPs, based on an individual risk assessment.

It is possible that lower platelet counts may also be safe but there is insufficient published evidence to make recommendations for lower levels at this stage [31]. Some degree of thrombocytopenia is a relatively common occurrence, but what number constitutes a safe platelet count for these techniques based on the occurrence of spinal haematomata is debated. The Association of Anaesthetists of Great Britain & Ireland, The Obstetric Anaesthetists' Association Regional Anaesthesia is published about regional anaesthesia and patients with abnormalities of coagulation [32].

In idiopathic thrombocytopenic purpura and gestational thrombocytopenia, there are reduced platelet numbers, but normal function. In these situations, expert opinion is that an experienced anaesthetist might reasonably perform a neuraxial blockade providing the platelet count is  $> 50 \times 10^9/L$  and stable, but an individual risk–benefit assessment should be made [32,36-39]. If platelets  $50\text{--}75 \times 10^9/L$  there are increased risk, if platelets  $20\text{--}50 \times 10^9/L$  there are high risk, if platelets  $<20 \times 10^9/L$  there are very high risk [32].

It is possible that spinal anaesthesia with platelet counts below this level may be safe if data are extrapolated from that derived from lumbar punctures in non-pregnant patients performed by haematologists using needles considerably larger than those used by obstetric anaesthetists [33].

All kind of general anaesthesia methods may be used for emergency and elective surgeries in patients with an ITP diagnosis.

**Notes to figure 1**

\* There is no consensus associated with control of platelet count for reducing the airway trauma and bleeding in ITP patients.

\*\* For lower platelet counts a careful analysis of benefit against risk of vertebral canal haematoma is needed, and multidisciplinary is discussion encouraged.

ITP patients have reduced platelet numbers, but normal function. In these situations, expert opinion is that an experienced anaesthetist might reasonably perform a neuraxial blockade providing the platelet count is  $> 50 \times 10^9/L$  and stable, but an individual risk-benefit assessment should be made (considered attempt insertion, needle size). [32,36-39].

Association of Anaesthetists of Great Britain & Ireland (2013); If platelets  $50-75 \times 10^9/L$  there are increased risk, if platelets  $20-50 \times 10^9/L$  there are high risk, if platelets  $<20 \times 10^9/L$  there are very high risk [32].  
 Veen, et al.(2010); they suggested for patients with platelet counts of  $50-80 \times 10^9/L$  for epidural and spinal anaesthesia [31].

Choi, et.al (2009); when the platelet count is more than  $50 \times 10^9/L$  before block performance. The minimum "safe" factor levels and platelet count for neuraxial blockade remain undefined in both the obstetric and general populations and evidence-based recommendations for neuraxial techniques in the setting of haemophilia, vWD, or ITP cannot be offered [41].

Provan, et al. (2009); Obstetric anaesthetists generally recommend a platelet count of at least  $75 \times 10^9/L$  to allow administration of spinal or epidural anaesthesia. Haematologists believe that a platelet count of at least  $50 \times 10^9/L$  is adequate to allow for cesarean section [9].

British Committee for Standards in Haematology General Haematology Task Force (2003) [54].

Orlikowski, et al. (1996); The authors suggested that parturients with platelet counts greater than  $75 \times 10^9/L$  should not be denied regional anaesthesia [36].

### Necessary additional diagnostic procedures (preoperative)

There is no need for diagnostic research beyond platelet count in the preoperative period. Blood group should be typed, and it may be beneficial to obtain information on peripheral smear platelet functions. A thrombocyte dysfunction evaluation should be performed in collaboration with haematology, anaesthesiology and surgery [34]. Preoperative thrombelastography (TEG) and a patient-specific evaluation may be beneficial for decisions on regional anaesthesia [34-39]. The maximum amplitude (MA) likely represents platelet function in TEG. Growing evidence indicates that measures to support and monitor coagulation, such as TEG and thrombelastometry (ROTEM), are important for quality improvement and may offer alternative effective approaches to limit blood transfusion and decrease perioperative bleeding [40].

Currently Platelet Function Analyzer is a rapid, easy, and sensitive test of platelet functions that is an alternative to a bleeding time test. It is frequently used to diagnose congenital or acquired platelet diseases like von Willebrand disease (vWD), Glanzman thromboasthenia and Bernard Soulier syndrome. Additionally, it is used to assess the efficacy of medication like acetyl salicylic acid, clopidogrel and ticlopidine used for antiplatelet treatment [42]. The Platelet Function Analyzer (PFA)-100 is a device for quantitative, rapid, in vitro measurement of platelet functions [43]. The PFA-200 is a newer version of the PFA-100 (44). The PFA-200 device includes a thin membrane covered with collagen/epinephrine or collagen/adenosine diphosphate (ADP). When blood flow passes through this membrane, adhesion activation and aggregation of platelets occurs forming a plug. The time for this plug to cover the membrane is named the "closure time (CT)" [45,46]. Generally, there is an inverse correlation between the reduction in platelet count and CT value.

Patient characteristics such as a platelet count  $<100 \times 10^9/L$  and haematocrit  $<30\%$  usually result in prolongation of the CT [47,48]. Slaughter et al. [49] found that normal collagen and ADP closure time was a good negative predictor of bleeding, but elevated closure time had little positive predictive value. Forestier, et al. [50] found that PFA-100 results correlated with postoperative bleeding. Publications related to PFA have mainly been completed on patients undergoing cardiac surgery. In the literature, there are insufficient studies comparing the correlation of platelet counts, prognosis, bleeding findings and laboratory findings for platelet function disorder in the presence of thrombocytopenia.

A study by Ugur, et al. [51] retrospectively compared clinical findings and laboratory values of patients with platelet function (collagen/epinephrine (coll/EPI) or collagen/ADP (coll/ADP)) studied due to thrombocytopenia with different etiologies and bleeding diathesis. Platelet function tests were assessed using a PFA-200 (INNOVANCE PFA-200 System Siemens Healthcare Global, Marburg, Germany). The diagnoses of thrombocytopenia patients included in the study were immune destruction (n=14), solid organ (n=19) and haematologic malignancy (n=9). Six of the patients with solid organ malignancy and one patient with haematologic malignancy had bleeding findings while none of the immune thrombocytopenia patients had bleeding findings. When patients are grouped in terms of pathogenesis of thrombocytopenia, 28 had bone marrow suppression, and 14 had destruction-linked



thrombocytopenia. When these two groups were compared, all seven patients with bleeding findings were in the group with bone marrow suppression-linked thrombocytopenia. In terms of collagen/ADP and collagen/epinephrine CT values, there was no significant difference observed between the two groups.

#### Particular preparation for airway management

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Bleeding after airway trauma and intubation is very important in ITP patients. There was concern that laryngoscopy and tracheal intubation may lead to damage of mucosal surfaces, particularly around the laryngeal inlet and trachea, with subsequent haemorrhage [23]. Consensus has not been reached concerning the selection of therapeutic method, and there is no specific guideline about platelet count concerning the trauma of airway in ITP patients.

Based on some research, increasing the platelet count by high-dose IVIg therapy or platelet transfusion is helpful to reduce the complications associated with airway trauma in ITP patients [52]. Additionally for airway management supraglottic airway devices, which allow less traumatic insertion compared to endotracheal intubation, should be considered [53]. If intubation is definitely necessary, the use of videolaryngoscopy allows easy and successful intubation with less traumatic intervention.

#### Particular preparation for transfusion or administration of blood products

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Transfusions of platelet concentrates are helpful at the time of induction. The exact platelet count that is needed for any procedure is not known, but the following counts are offered for guidance [54]:

- Dentistry (scaling, deep cleaning)  $\geq 20\text{-}30 \times 10^9/\text{L}$
- Simple extractions  $\geq 30 \times 10^9/\text{L}$
- Complex extractions  $\geq 50 \times 10^9/\text{L}$
- Regional dental block  $\geq 30 \times 10^9/\text{L}$
- Minor surgery  $\geq 50 \times 10^9/\text{L}$
- Major surgery  $\geq 80 \times 10^9/\text{L}$
- Vaginal delivery and caesarean section  $\geq 50 \times 10^9/\text{L}$
- Spinal or epidural anaesthesia  $\geq 80 \times 10^9/\text{L}$

Rapid-effect medication should be used if the operation is an emergency, and it is necessary to urgently increase the platelet count in the preoperative period. IVIg (1 g/kg single dose or 2 doses if necessary) + corticosteroids (pulse or moderate-high dose) followed by thrombocyte suspension support is the most frequently chosen combination. Thrombocyte suspensions should not be used in ITP patients to resolve thrombocytopenia except in cases of emergency, life-threatening haemorrhages because these suspensions produce a rapid disintegration of platelets. If thrombocyte suspension use is necessary, then it should be administered after IVIg and/or pulse corticosteroid administration to increase the life span of transfused platelets. Plasmapheresis treatment should not be used in these patients [55]. Treatment is rarely indicated in patients with platelet counts above  $50 \times 10^9/\text{L}$  in the absence of the following conditions: bleeding due to platelet dysfunction or another haemostatic defect, trauma, surgery [56]; clearly identified comorbidities for bleeding; mandated anticoagulation therapy; or in persons whose profession or lifestyle predisposes them to trauma. Patient preference must also be considered when discussing treatment options. Detailed consensus-based recommendations for target platelet counts during surgery in adults were provided previously [57].

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### Particular preparation for anticoagulation

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There is no evidence to support the need of a particular anticoagulation strategy. Anticoagulant agents may be used in ITP patients for other comorbidity reasons, such as thrombosis, stents or heart valve disease. Planning before an elective surgery in an ITP patient using anticoagulants should include the regulation of anticoagulant medication treatment and/or low molecular weight heparin, which should be evaluated with the current disease and characteristics of the planned surgery, and any decisions made should be specific to the patient.

Antifibrinolytic agents, such as oral or IV tranexamic acid and epsilon-aminocaproic acid, may be useful in preventing recurrent bleeding in patients with severe thrombocytopenia. However, the efficacy of these agents has not been evaluated using randomized trials in ITP patients. Tranexamic acid (1 g, 3 times daily, orally) and epsilon-aminocaproic acid (1-4 g every 4-6 hours, maximum dose, 24 g/day) may be especially valuable in certain dental or surgical procedures [9].

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### Particular precautions for positioning, transport or mobilisation

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No special position or mobilisation is defined for ITP patients. Postoperative haemorrhage monitoring should include the clamping of surgical drains during transport, and extra care and attention should be paid to prevent drain loosening.

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### Probable interaction between anaesthetic agents and patient's long-term medication

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No specific interactions are known. The use of aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs) in patients with any of thrombocytopenic disorders can dramatically shift the relationship between platelet count and platelet function. Therefore, these drugs should not be used in patients with thrombocytopenia. Data from compatibility and interaction studies with other drugs are not available.

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### Anaesthesiologic procedure

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Emergency surgeries should proceed regardless of platelet count. Platelet transfusion may be given to rapidly increase platelet count during anaesthesia induction if the platelet count is low.

ITP diagnoses should be defined as acute or chronic for non-emergency surgeries. Treatment stages of the American Society of Hematology guidelines [62] or the country's own haematology society guidelines should be followed. ITP patients who respond to treatment should complete surgery preparations and undergo surgery.

The anaesthesiologist should make the decision for general or regional anaesthesia based on the patient's clinical characteristics, current platelet count and function, type of surgery to be performed, and characteristics, such as the scale and possibility of bleeding. It is appropriate for the anaesthesiologist to evaluate an ITP patient undergoing surgery with a haematologist and the surgeon. However, final judgment for the care of individual patients should lie with the responsible health care professional and be based on the careful investigation of individual circumstances.

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### Particular or additional monitoring

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Additional monitoring is dependent on the type of surgery. Arterial and central venous lines should be considered in patients with expected bleeding due to surgery.

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### Possible complications

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The risk of fatal haemorrhage is very low, but the risk of severe bleeding is increased in the very old, patients with additional diseases that cause haemorrhage (>65 years with a previous history of haemorrhage, gastrointestinal problems, liver cirrhosis, uncontrolled hypertension), and patients using medication (aspirin, Coumadin, NSAID, etc.). Bleeding prevention should be normally accomplished for the given surgical procedure.

Postoperative complications of splenectomy include bleeding, infection, thrombosis, prolonged hospitalisation, hospital readmission, and the requirement for additional intervention [58]. Reported complication rates vary considerably [59-62] and may be greater in patients aged 65 years or older [63]. A recent systematic analysis reported that splenectomy complication rates were 12.9% with laparotomy and 9.6% with laparoscopy, and mortality was 1.0% with laparotomy and 0.2% with laparoscopy [58]. ITP [64] and splenectomy [65] are related to the risk of thromboembolism. Appropriate thromboembolism prophylaxis should be provided for these patients. Caution is advised for postoperative complications in patients suffering from prolonged immobilisation and/or hospitalisation.

Postoperative infection risk is increased, especially in ITP patients receiving immune suppressive treatment. Splenectomised patients are at a lifelong risk for uncontrolled infection with poor outcome from *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae*. Immunisation with polyvalent pneumococcal, *Haemophilus influenzae* (B) and meningococcal vaccines should be administered at least 2 weeks before surgery to reduce the risk of overwhelming postoperative bacterial sepsis [66].

There is a relationship between postoperative complications after any type of surgery in ITP patients and preoperative ITP history, emergency application, hospital stay, and preoperative platelet, and/or red blood cell transfusion. The administration of blood products to these patients before surgery is one cause of a negative prognosis that is independent of ITP itself [67].

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### Postoperative care

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The degree of postoperative monitoring is dependent on the surgical procedure and preoperative condition of the patient. Intensive care and ventilator support may be necessary in the postoperative period despite the selection of appropriate anaesthesia methods that account for bleeding risk from the interventions to the patient.

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### Information about emergency-like situations / Differential diagnostics

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Situations of unexpected bleeding during surgery must be analysed to determine whether the bleeding is related to thrombocytopenia linked to ITP or other reasons that increase intraoperative bleeding (e.g., hypothermia, surgical procedures, such as liver resection, cardiac surgery, and neurosurgery, NSAID use, massive blood transfusion, and disseminated intravascular coagulopathy). The ESA management of severe perioperative

bleeding guidelines recommend that a treatment protocol should be initiated using a goal-directed approach that is appropriate to the patient.

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### Ambulatory anaesthesia

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Ambulatory anaesthesia guidelines may be generally followed in ITP patients who are controlled by treatment with no additional predicted haemostasis problems in the preoperative period and platelet counts within recommended limits for the planned surgery (57). However, there is no evidence-based approach that is defined for ambulatory anaesthesia for elective minor and day-case surgeries [68].

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### Obstetrical anaesthesia

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The decision for caesarean section or vaginal birth for mothers with ITP should be based on obstetric indications. The incidence of pregnant women with ITP is 1-2/1000, but ITP comprises 5% of pregnancy-related thrombocytopenia cases, and 15% of pregnant women with ITP had platelet counts lower than  $50 \times 10^9/L$  at the time of birth [69,70]. Women with immune thrombocytopenia may become pregnant, or the disease may occur for the first time during pregnancy. The pathogenesis of ITP in pregnancy is similar to non-pregnant patients. Laboratory findings consist of isolated thrombocytopenia before pregnancy and during early pregnancy. Clinical signs of altered coagulation, such as petechiae and easy bruising, despite normal haemostasis or the prevention of bleeding in pregnant women with ITP who have a platelet count  $\leq 20 \times 10^9/L$  comprise the most important issues for anaesthesia practice, and these patients require urgent management [71,72]. Foetuses of these mothers are also at increased risk for thrombocytopenia and bleeding.

The management of anaesthesia in caesarean section should not be based on a single parameter in pregnant women with severe thrombocytopenia. Platelet count and other laboratory findings should be paired with TEG and clinical findings to render a decision after considering the patient-specific risks and benefits for the use of general or regional anaesthesia.

The guidelines of British Committee for Standards in Haematology recommend a platelet count of at least  $>80 \times 10^9/L$  for the use of neuraxial techniques in pregnant women with ITP [19]. However, most anaesthesiologists and authors reported that they used neuraxial blockade techniques, particularly spinal anaesthesia, in healthy asymptomatic pregnant women with ITP who had platelet counts  $>50 \times 10^9/L$  [54,73,74]. The use of TEG, which may also be used bedside, is currently recommended [36-38]. A maximal amplitude of 53 mm in TEG may indicate that the platelet count is  $54 \times 10^9/L$ , and coagulation will be sufficient. Some authors concluded that coagulation tests alone do not effectively predict the risk of epidural or spinal haematoma following neuraxial block. However, a normal TEG tracing, if supported by laboratory findings that are consistent with normal clinical findings, may facilitate a decision to conduct a neuraxial technique [37]. Steer [38] suggested that TEG may be used as a rapid, reliable and cost-effective tool to obtain coagulation data, which is required in obstetric patients for optimal obstetric and anaesthetic management. Platelet function analyser test measures the speed of formation of a platelet plug in-vitro, expressed as closure time in seconds. Studies in parturients suggest that it is an effective bedside test of platelet function [75]; however, evidence is lacking to support its routine use [76].

Platelet transfusion alone is generally not effective in ITP, but platelet transfusion in conjunction with IVIg may be considered if an adequate platelet count has not been achieved, and delivery is emergency. Also posttransfusion increments may be inadequate or short-lived and should be reserved to treat bleeding only [77]. Oral prednisone (or

prednisolone) may be initiated 10 days prior to the anticipated delivery at a dose of 10-20 mg daily and titrated as necessary in women whose platelet counts are  $< 80 \times 10^9/L$  and who have not required therapy during pregnancy.

Obstetric indications should determine the mode of delivery because of the difficulty in predicting severe thrombocytopenia in neonates and the very low risk of intracranial haemorrhage ( $<1.5\%$ ) or mortality ( $<1\%$ ) [54]. Percutaneous umbilical blood sampling or foetal scalp blood sampling is not helpful in predicting neonatal thrombocytopenia, and it is potentially harmful. Therefore, these procedures are not recommended. Infant platelet count occurs 2-5 days after delivery, and a spontaneous rise occurs by day 7.

Pregnant women with ITP should be aware of VTE despite thrombocytopenia. Post-partum mechanical precautions against VTE should be performed (e.g., compression stockings, pneumatic compression at intervals).

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*This guideline has been prepared by:*

**Author**

**Şule Özbilgin**, Department of Anaesthesiology and Reanimation, Faculty of Medicine,  
Dokuz Eylül University, Izmir, Turkey  
[sule.ozbilgin@deu.edu.tr](mailto:sule.ozbilgin@deu.edu.tr)

**Peer revision 1**

**Tanu Mehta**, Department of Anaesthesia and Critical Care, Doshi Institute of Kidney  
Diseases and Research Center, Civil Hospital Campus, Asarwa, Ahmedabad, Gujarat, India  
[tanu.khushi@yahoo.com](mailto:tanu.khushi@yahoo.com)

**Peer revision 2**

**James B. Bussel**, Departments of Pediatrics, Medicine, and Obstetrics and Gynecology,  
New York Presbyterian Hospital, Weill Cornell Medical Center, New York, USA  
[jbussel@med.cornell.edu](mailto:jbussel@med.cornell.edu)

**Dimitri Poddighe**, U.O. Pediatria, P.O. Vizzolo Predabissi, ASST Melegnano e Martesana,  
Milano Cultore della Materia in Pediatria Generale e Specialistica, Università degli Studi di  
Pavia, Italy  
[dimimedpv@yahoo.it](mailto:dimimedpv@yahoo.it)

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Alexandra Hisom M.A. &  
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Korrespondenzadresse: Roritzerstraße 27 |  
90419 Nürnberg | Deutschland  
Tel.: 0911 9337812 | Fax: 0911 3938195  
E-Mail: anaesth.intensivmed@dgai-ev.de

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Nadja Schwarz  
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Pia Engelhardt  
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Manfred Wuttke | Stefanie Triebert  
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## ADDRESS

German Society of Anaesthesiology and  
Intensive Care Medicine  
Nina Schnabel  
Roritzerstrasse 27 | 90419 Nuremberg | Germany  
Tel.: +49-911-9337822 | Fax: +49-911-3938195  
Email: nschnabel@orphananesthesia.eu