Acute immune thrombocytopenic purpura

To treat or not to treat?

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Summary
Immune thrombocytopenia in children is usually a self-limiting illness, but in adults the disease is likely to be chronic, and may be associated with other pathology which predisposes to bleeding. Despite very low platelet counts serious bleeding is rare in both adults and children. More than 80% of children have mild clinical manifestations. Intracranial haemorrhage is rare at all ages, is unpredictable and can occur at any time when the count is very low. Currently recommended therapies for both adults and children are associated with significant side effects and occasional deaths. Treatment may interfere with quality of life more than the illness itself. Drugs can be withheld in the majority of children with appropriate advice to child and family. Treatment can be individualised, taking into account the person’s needs and lifestyle as well as bleeding. In chronic ITP many need no active therapy. The situation with adults is more complex but those with a platelet count above 30 $\times$ 10^9/l usually need no treatment as bleeding is rare, and those adults with refractory ITP unresponsive to treatment live with very low counts for years without significant bleeding suggesting the need to re-evaluate the balance of risks of treatment versus bleeding. It is notable that adults with ITP may die from infection, probably related to therapy.

Minimum treatment
If treatment is required, either for more troublesome bleeding or for quality of life issues (activities, anxiety) then the minimum treatment should be given. Recent studies suggest that very short courses of high dose prednisolone (4 mg/kg/d for 4 days) are effective without running the risk of serious side effects (7). It is notable that in children with severe bleeding, the response to therapy was less effective than expected in raising the count, although bleeding ceased (16). Emergency treatment of serious bleeding is usually with IVIG together with steroids and platelet transfusions which may be more effective in the context of immune suppression.

Acute immune thrombocytopenic purpura (ITP) is a rare disorder occurring principally in children in whom the majority recover spontaneously and completely within a few days or weeks. Acute ITP (defined currently as having duration of up to 6 months) also occurs in adults, but it is more likely to have an insidious onset and a prolonged duration. Affected individuals usually present with purpura which can be dramatic; mucosal bleeding is the next commonest symptom, but it is a striking feature in both adults and children that serious, life-threatening bleeding is rare despite impressively low platelet counts (usually less than 20 $\times$ 10^9/l). The low platelet count has been used as a surrogate marker for a risk of serious bleeding, so that treatment is directed towards increasing the count and reducing the risk of bleeding. Clinical trials reflect this and until recently have not included any formal assessment of bleeding symptoms or quality of life (1, 12). In adults and children, the serious and sometimes life-threatening nature of side effects of treatment are increasingly recognised leading to a re-evaluation of the indications for platelet-enhancing therapy (2, 10).

ITP management
In many European countries children with ITP have been managed without platelet-enhancing therapy because of the short duration of the illness and rarity of bleeding (4, 19). In the USA normal practice has generally been to treat the count so that the ASH guideline (11) indicated that all children with counts less than 20 $\times$ 10^9/l require therapy because there was no evidence that no treatment was safe.

Neither approach has been tested in randomised trials, but numerous studies have demonstrated that the outcome of the illness is not altered by treatment, and that the incidence of severe bleeding is low, around 3% (3, 5, 13, 18). The most serious complication, intracranial haemorrhage, is rarer still estimated at about 0.2% (3, 15), and may occur at any time, despite treatment, when the count is very low.

Doctors who are not familiar with ITP are usually worried about very low platelet counts and transmit this to the child and family. A watchful waiting policy includes adequate education of the child and family, and provision of a 24 hour contact point in case of new bleeding problems. This approach avoids unnecessary drug treatment with its associated side effects. Platelet counts do not need frequent monitoring. As long as the child still has purpura the count will be low. It is advisable to repeat the count within the first 10 days to ensure that a more sinister condition is not developing (mainly aplastic anaemia), otherwise it is more beneficial to measure the count when symptoms have disappeared.

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was no different to the normal population. Among those with lower counts (9%) the mortality risk was increased but as many died from infection (probably related to therapy) as died from bleeding (17). There is a strong case for tailoring the treatment to the individual patient, avoiding the use of toxic medication in those with counts above $30 \times 10^9/l$. Analysis of patient views indicates that steroids are very unpopular because of the side effects (20). The selection of alternative agents is not straightforward as each works for some but not other patients, and it is very useful to discuss the side effect profile as well as potential benefits with individual patients.

**Splenectomy**

Splenectomy may be indicated for those whose count is persistently below $30 \times 10^9/l$ and who have bleeding symptoms, but accepting that about 25% will relapse. The place of splenectomy has been questioned in the light of success with newer agents such as rituximab (8, 9), and thrombopoietic agents (6, 14) which may provide long-term treatment with minimal side effects.

**References**