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Haematological Considerations in Patients with Cyanotic Congenital Heart Disease: A Review

Abstract: In patients with cyanotic congenital heart disease (CCHD), the need for prior antibiotic prophylaxis for infective endocarditis is well known to dentists, but not many dentists are aware of the associated haemorrhagic tendencies in such patients. Haemostatic abnormalities associated with CCHD are an important aspect that is often overlooked by both physicians and dentists. We briefly review the literature to highlight the importance of more elaborate haematological evaluation in patients with CCHD, prior to any oral surgical procedures.

Clinical Relevance: Patients with cyanotic congenital heart disease may have subclinical haemorrhagic tendencies. To detect these haemorrhagic tendencies and ensure the safe treatment of such patients, pre-operative haematological screening tests must be performed.

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Cardiac patients usually undergo dental treatment after a physician's consent, and in accordance with the established protocols for infective endocarditis antibiotic prophylaxis and withdrawal of anticoagulants, which are set, reviewed and updated by the scientific authorities periodically. But these alone cannot ensure safe extraction procedures in patients with cyanotic congenital heart disease (CCHD). In patients with cyanotic congenital cardiac defects, infective endocarditis prophylaxis and bleeding tendencies are the most relevant factors from a dental standpoint.[1] Coagulation abnormalities usually occur in CCHD patients with secondary polycythaemia. Bleeding tendencies are usually mild to moderate and are characterized by easy bruising, petechial haemorrhage and gingival bleeding.[2] In view of the increasing number of patients with CCHD surviving until adulthood,[3,4] it is more likely that such patients will be visiting dental clinics, which underlines the importance of knowledge about these potential subclinical haemorrhagic tendencies.

- Thrombocytopenia
- Qualitative platelet defects
- Disseminated intravascular coagulation
- Decreased production of coagulation factors due to impaired liver function
- Primary fibrinolysis

Table 1. List of haemostatic abnormalities in patients with CCHD.

Cyanotic	Acyanotic
■ Transposition of great vessels ■ Fallot's tetralogy (Ventricular septal defect, pulmonary stenosis, right ventricular hypertrophy, overriding aorta, tricuspid atresia, pulmonary atresia)	■ Ventricular septal defect ■ Atrial septal defect ■ Patent ductus arteriosis ■ Aortic coarctation

Table 2. Classification of congenital heart defects.

Review of the literature

A review of the literature was carried out using a computer (MEDLINE search with key words cyanotic congenital heart disease and dental considerations OR dental management in Eisenmenger's syndrome OR post extraction haemorrhage in cyanotic congenital heart disease)

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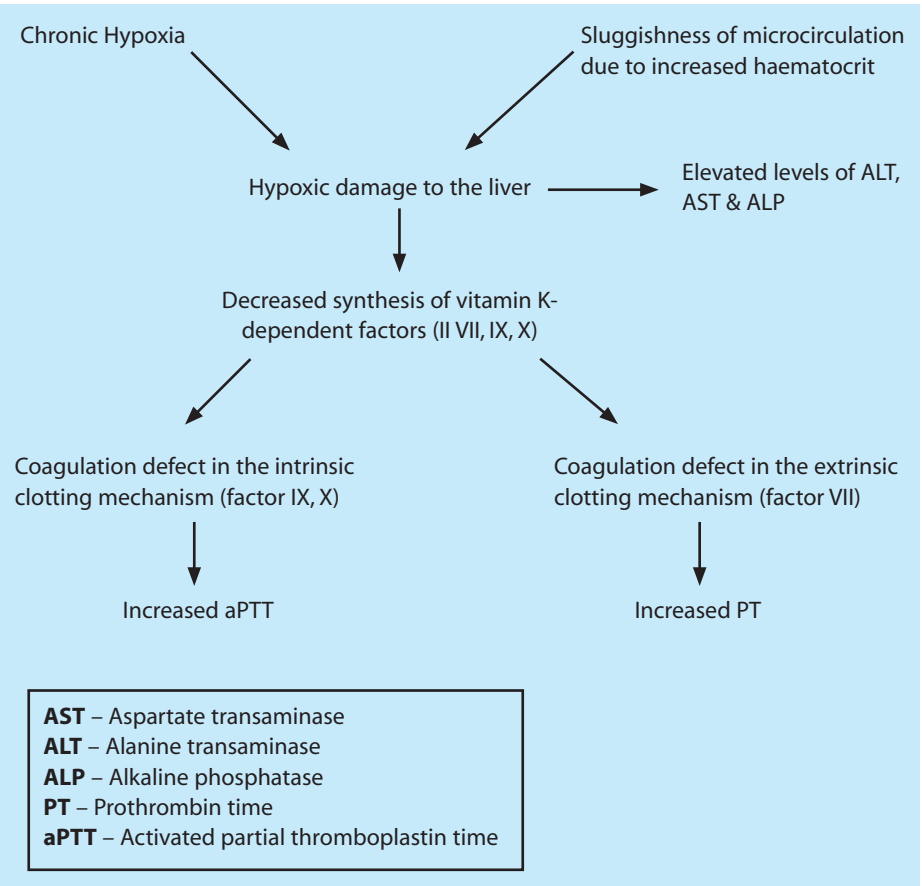

Figure 1. Clinicopathological process depicting the clotting factor abnormality in patients with CCHD.

and a hand search of recent relevant cardiology and haematology journals. The literature review revealed numerous haemostatic abnormalities (Table 1) in patients with CCHD secondary to changes in the circulation.[5] Congenital heart disease can be cyanotic or acyanotic (Table 2). Haemorrhagic tendencies are usually observed in patients with cyanotic congenital heart disease with secondary polycythaemia.[5] This causes hyperviscosity of blood and sluggishness of the circulation, leading to haemostatic defects, which are explained in detail in the text.

Pathophysiology

In CCHD, the heart pumps deoxygenated blood, because desaturated venous blood returning to the heart is pumped out into the systemic circulation without having been passed through the lungs for oxygenation. In Fallot's tetralogy, tricuspid atresia and pulmonary atresia, the obstruction to the pulmonary flow results in right to left shunting of the blood. Systemic circulation of deoxygenated blood results in central cyanosis and chronic hypoxia. Chronic hypoxia triggers the release of erythropoietin hormone from the kidneys that results in compensatory erythrocytosis and polycythaemia.[6] Erythrocytosis is an adaptive response intended to compensate for inadequate tissue oxygenation. But an increase in the RBCs results in increased blood viscosity and sluggishness of microcirculation, resulting in hypoxic damage to the tissues. The haematological abnormalities are directly related to the degree of polycythaemia.[5]

Abnormality in the clotting factors

Hyperviscosity of the blood and sluggishness of the microcirculation causes hypoxic damage to the liver.[7] Impaired liver function can result in elevated levels of aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase. An abnormal liver function results in a decrease in the synthesis of vitamin K-dependent clotting factors (factor II, factor VII, factor IX and factor X). Deficient production of these clotting factors affects both the intrinsic and extrinsic mechanism of haemostasis. Therefore, an estimation of prothrombin time (PT) or activated partial thromboplastin time (aPTT) is required to exclude any abnormality in the extrinsic and intrinsic clotting mechanisms (Figure 1).

Platelet abnormalities

In patients with CCHD, platelets are shown to have both qualitative and quantitative abnormalities. Platelet count and haematocrit are inversely related to each other. Polycythaemia increases the blood viscosity and reduces the tissue perfusion. The resultant hypoxia of the marrow tissues causes inhibition of platelet production, causing thrombocytopenia.[8] Thrombocytopenia can also be a consequence of shortened half-life of platelets.[7] Therefore, an increased haematocrit is associated with thrombocytopenia in such patients[3,7,8] (Figure 2). Therefore, bleeding can be a consequence of thrombocytopenia, which underlines the importance of platelet count estimation.

Bhargava *et al*,[9] in their study of 33 patients, concluded that there was a reduction in platelet adhesiveness to glass and impaired availability of platelet factor 3 in nearly 50% of patients and poor clot retraction in 84% of patients, which highlights the qualitative platelet defects in such patients. There is also a deficit in the platelet adhesion receptor-like glycoprotein Ib that can lead to haemostatic complications.[10] Qualitative defects of platelets associated with cyanotic congenital heart disease include abnormal aggregation of platelets in response to adenosine diphosphate, epinephrine and collagen, which are principle haemostatic defects and directly related to the degree of polycythaemia.[3,5] Therefore, tests to rule out qualitative platelet defects need to be performed in such patients.

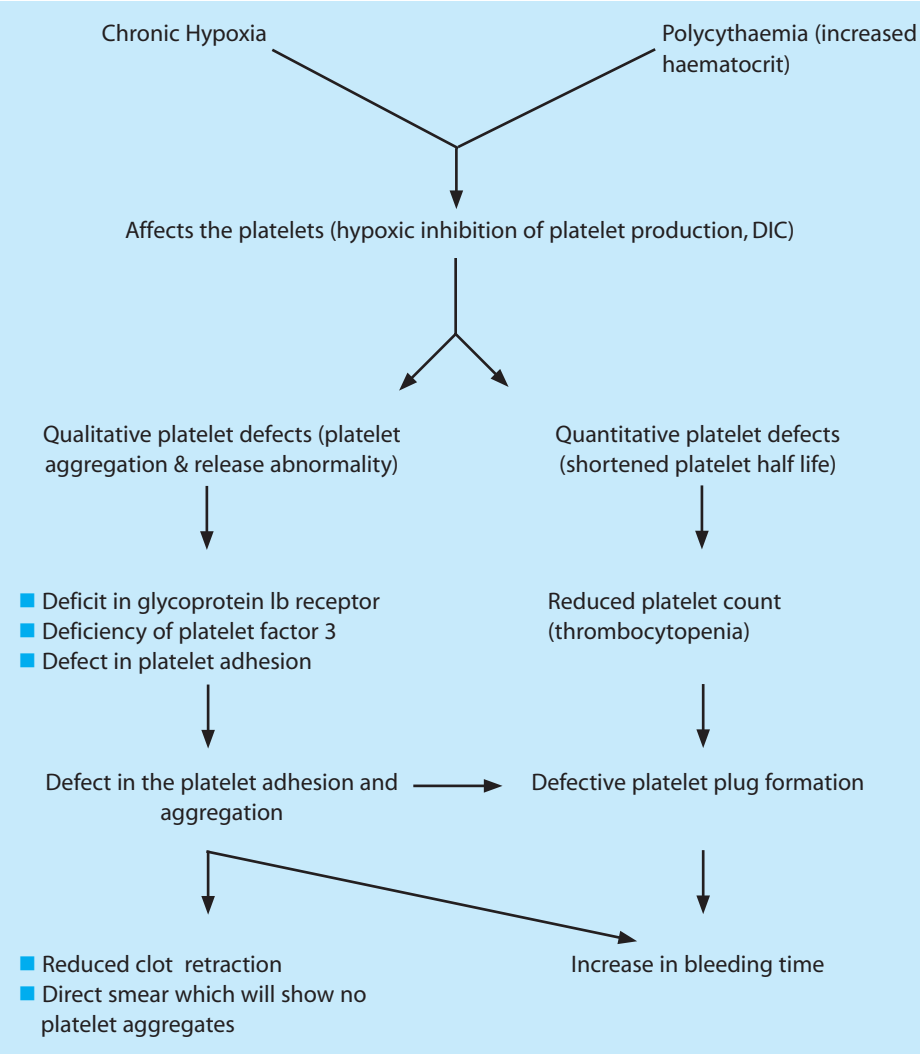

Figure 2. Clinicopathological process depicting the defects in the platelets observed in the patients with CCHD.

Disseminated intravascular coagulation

In CCHD, polycythaemia is associated with an increase in the blood viscosity, which affects blood flow and tissue perfusion.[3] The resultant vascular stasis makes these patients susceptible to widespread intravascular deposition of fibrin and platelet thrombi; this leads to consumption of sufficient quantities of platelets and coagulation factors involved in the formation of fibrin (fibrinogen, factor V, VII) to deplete the circulating blood and leave it haemostatically weak. This results in disseminated intravascular coagulation. The circulating blood becomes hypercoagulable and patients are at increased risk of haemorrhage.

Other causes

Although rare, there are reports of von Willebrand's disease[2] and primary fibrinolysis[3] in such patients, which emphasizes the need for consultation with a physician in cases of prolonged postoperative bleeding following any oral surgical procedures.

Clinical relevance

When a known cardiac patient reports for dental treatment, a dentist must take a detailed history to ascertain whether the patient has congenital cardiac defect. If CCHD is suspected, look for the following:

- Signs of peri-oral cyanosis;
- Bluish discoloration of skin; and
- Clubbing of the fingers.

A history of frequent headaches, tinnitus, fatigue, dizziness and stroke can also be useful to establish hyperviscosity syndrome in such patients. Positive history and clinical signs may indicate towards subclinical haemorrhagic tendencies, which can be the result of any of the causes listed in Table 1.

Hence, screening tests should be performed which include both haematological and biochemical investigations. Haematological investigations, like haematocrit, can be used to estimate the extent circulatory derangements cause haemostatic abnormalities. The following screening is recommended for all patients with CCHD:

- Full blood count;
- Platelet count;
- Prothrombin time;
- Activated partial thromboplastin time.

In cases in which the above investigations are normal but the patient is bleeding, a qualitative platelet disorder should be suspected, which can be confirmed by abnormalities in bleeding time, peripheral smear and clot retraction tests (after consultation with a physician, if required). Biochemical investigations include estimation of aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase to check for hypoxic liver damage in all patients with CCHD.

The existing protocols are concerned with the management and prevention of infective endocarditis prophylaxis and iatrogenic bleeding tendencies due to administration of anticoagulants and aspirin. However, in the patients with CCHD, there are subclinical haemorrhagic tendencies caused by factors other than aspirin and anticoagulant therapy. Hence, the standard protocol for management of such patients prior to surgical intervention is not ideal. In view of the possible subclinical haemorrhagic tendency in patients with CCHD, recognition of haemorrhagic tendencies and modification in the management approach (Figure 3) is needed.

If the screening tests are normal, or minor procedures like

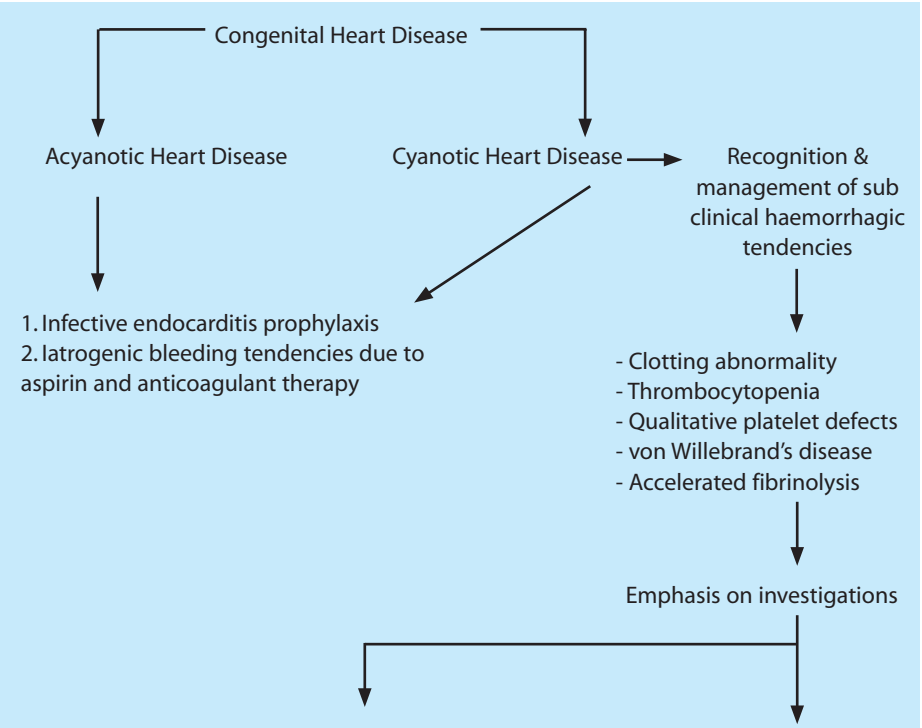

Figure 3. Highlights the modification in treatment protocol for management of patients with cyanotic congenital heart disease.

deep gingival scaling or extraction of mobile tooth is required, it can be safely performed and managed in the dental clinic. However, the patient must be followed up at least for the next 24–48 hours to check for any secondary haemorrhage. But, in cases of significant abnormalities in screening test or major surgical procedure, or the extraction of a deeply impacted tooth, it must be carried out after consultation with a physician in a hospital set-up. In patients with CCHD and Eisenmenger's syndrome, the use of general anaesthesia is recommended.[11,12] Consideration should be given to prevent any cyanotic episodes due to increase in stress as well as possible dehydration.[11]

Management of such patients is by a team approach between a dentist and physician. As the haemorrhagic tendencies have a systemic cause, the dentist can control only minor bleeding through the application of local haemostatics like tranexamic acid or epsilon amino caproic acid. In the case of uncontrolled bleeding, a physician/cardiologist should be consulted who may perform platelet transfusion, infusion of clotting factors, etc, to control the bleeding.

Conclusion

We emphasize the need and importance of performing pre-operative haematological screening tests in all patients with CCHD to prevent postoperative bleeding by predicting any subclinical haemorrhagic tendencies. An elevated haematocrit in patients with CCHD is an indicator of haematological derangement and associated bleeding tendencies. A detailed case history, symptoms of CCHD and abnormality in the screening tests like FBC, haematocrit, prothrombin time and activated partial thromboplastin time should alert the dentist of haemorrhagic tendencies. In conclusion, pre-operative screening will ensure better and safe care for patients with CCHD.

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BookReview

Essential Skills For Dentists. Edited by Gareth J Holsgrove, Peter A Mossey, David R Stirrups and Elizabeth S Davenport. Oxford: Oxford University Press, 2006. ISBN 9780198526193.

This extremely detailed book is aimed at undergraduate students and newly qualified graduates, although its style and content make it equally suitable for those involved in the provision of dental education. It is closely aligned with, and makes detailed reference to, the General Dental Council's (2002) *The First Five Years: A Framework for Undergraduate Dental Education* and the Quality Assurance Agency's (2002) *Dentistry: Academic Standards*.

The book is divided into three sections. Section 1 covers 'generic' skills, such as patient management and diagnosis, as well as clinically orientated practice management, with significant emphasis on the legal, ethical and moral obligations incumbent on members of our profession. Section 2 covers skills within the various specific dental disciplines. (Chapter numbering becomes a little confused at this point.) Section 3 seeks to illustrate how the first two sections interrelate, how to develop a team approach and to guide the student in the skills required to enhance their life-long learning.

Individual chapters are written by specialists in their specific fields and follow a set format. Each chapter starts with a list of key points and an introduction which includes references to the GDC and QAA documents referred to above. Information is conveyed by headlining the various learning outcomes and giving detail in the form of bullet points or short paragraphs. This is accompanied by a number of checklists or assessments which can be either self-administered or used by teaching staff. The chapters conclude with one or more mind maps, which provide an excellent revision aid, together with a list of references and suggested further reading.

This book appears to be aimed at enabling students to learn, rather than spoon-feeding information, and the structure of the individual chapters facilitates this. The language used, particularly in the early chapters, seems to be aimed more towards fellow educationalists than students – as such it is not always an easy read and may be somewhat daunting to the new undergraduate (and possibly to those of us who graduated many years ago!).

Overall, this is an invaluable guide to what is expected of undergraduates as they work towards becoming competent, ethical and caring members of our profession. It can also provide a very useful reference for existing practitioners as they seek to appreciate and implement the requirements of clinical governance.

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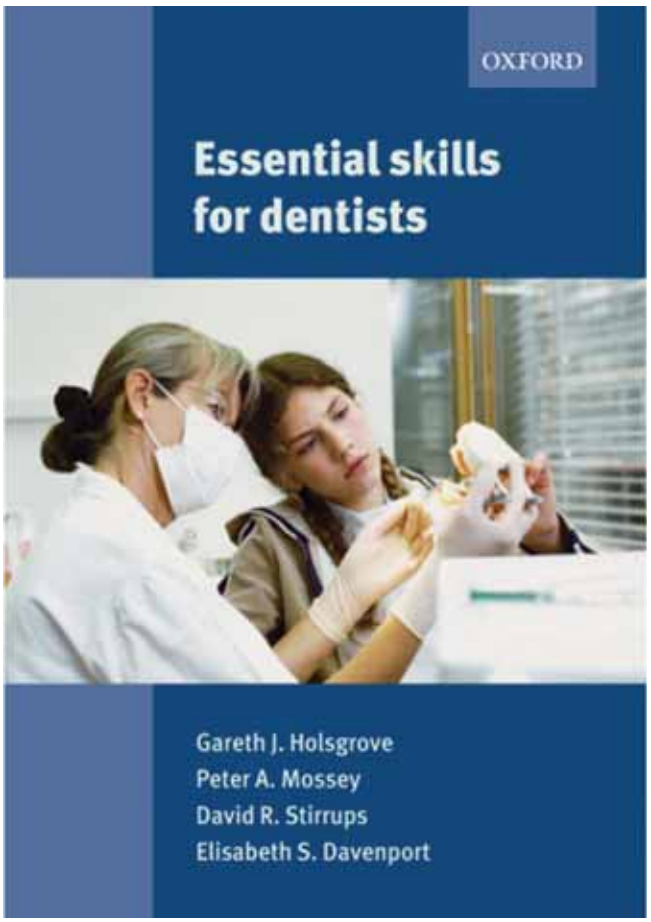

CPD ANSWERS

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1. A, B, C	6. A, B
2. A, B, D	7. A, D
3. A, C, D	8. A, C, D
4. C, D	9. A, B, C
5. A, B, D	10. B, D