Haematological management of cyanotic congenital heart disease (CCHD).

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No disclosures
Outcomes have improved due to better diagnostics and better treatment.
Hematological management of cyanotic congenital heart disease

Which patients are we dealing with?

AortoPulmonary connections:
- PDA
- Central shunt
- MAPCAs

Shunt with normal or restricted pulmonary flow:
- Tetralogy of Fallot
- DORV/Taussig Bing anomaly
- Pulmonary atresia VSD MAPCAS
- Ebstein’s anomaly with ASD
- Univentricular heart with pulmonary outflow tract restriction

Pulmonary vascular disease due to a non restrictive shunt:
- Large non restrictive VSD
- Atrial shunt/ASD
- Univentricular heart without pulmonary outflow tract restriction
- Truncus arteriosus

5yr mortality of 12.6%. Highest of all ACHD patients

Oechslin E. Heart 2015;101:485–494. doi:10.1136/heartjnl-2012-301685

Management of adults with cyanotic congenital heart disease
Hematological management of cyanotic congenital heart disease: objectives of discussion:

The Good: Physiology

The Bad Complications & The Ugly Uncertainties

1) RBC Erythrocytosis: Inverse relation with platelets
   Hyperuricaemia
   Viscosity
   Phlebotomy
   Iron deficiency

2) Risk of bleeding - contributes to iron deficiency
3) Risk of thrombosis - wisdom of anticoagulation
4) Decreased immunity - contributors
   - risk of cerebral access related to hyperviscosity
   - risk of infective endocarditis
5) Vascular bed dysfunction / Atherosclerosis
The Good Management Steps and Therapies

1) Risk reduction:  
- Avoid destabilization of the equilibrium
- Treatment if iron deficiency
- Avoidance of dehydration
- Avoidance of paradoxical embolism
- Precise decisions on anticoagulation

2) Therapy:  
- Hyperviscosity
- Cerebrovascular complications
- Thrombosis
- Haemoptysis
- Gout
Hematological management of cyanotic congenital heart disease: The Good Adaptations

- Despite severe hypoxaemia, adverse cardiac hemodynamics, pulmonary hypertension & poor exercise tolerance, patients have good Q of L & reasonable prognosis.
- CCHD patients have beneficial physiological adaptations of cardiac & skeletal muscle.
- Chronic cyanosis leads to increase EPO production & an isolated rise in RBC count enhancing oxygen delivery.
- 2,3 DPG curve rightward shift enhances oxygenation.
- Cardiac output increases.
- Compensated erythrocytosis leads to new equilibrium. Appropriate EPO levels in response to hypoxia.
- Iron metabolism is preserved & hyperviscosity symptoms are absent.
Inverse relationship between platelet count & haematocrit!
In CCHD, the pulmonary circulation are bypassed by Right to Left shunt. Platelet production is dependent on fragmentation of megakaryocytes in lung vessels. Platelets

- Large shunt = fewer platelets + bad prognosis.
- Additional theories suggest decreased megakaryocytic production, increased platelet destruction and increased platelet activation contribute to low platelet counts.
- Thrombocytopenia seems independent of hemoglobin and iron levels.
Hematological management of cyanotic congenital heart disease: The Bad Effects on RBCs, Platelet function.

- **Decompensated erythrocytosis** leads to persistent EPO secretion, iron depletion & eventual iron deficiency anemia.
- Iron deficient red cells are microcytic and less deformable, leading to hyperviscosity.
- **Hyperuricaemia** occurs due to RBC breakdown & renal breakdown.
- Gout seldom clinically problem.
- Thrombosis & infarction are devastating complications of decompensated erythrocytosis.
- Cerebral blood flow is inversely related to hematocrit & viscosity.
- AF, hypertension & microcytosis are the perfect storm leading to CVA in adults with CCHD.

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Interplay of thrombocytopenia, shortened platelet survival, Von Willebrand factor deficiency & clotting factor deficiencies increases risk of bleeding.

- Bleeding contributes to iron deficiency.
- Despite low platelet counts the function of platelets seem preserved.
- Fibrinogen dysfunction inhibits normal clot formation.
- Chronic low grade DIC picture may contribute.
Reduced Vit K dependent coagulation factors are likely the result of poor cardiac output, hypoxia, & hepatic congestion.

Accelerated fibrinolysis adds to risk of bleeding.

Thrombotic events frequent. Thrombus in PA in up to 30% of Eisenmenger patients.

Hemoptysis is frequent & can be deadly.

Bleeding events are the most common cause of “non cardiac” death in CCHD.

Bleeding events seem to occur at approx 2.6% per patient yr. Mostly hemoptysis, mostly minor.

Hematological management of cyanotic congenital heart disease: The Bad Effects on Bleeding/Coagulation balance.
Hematological management of cyanotic congenital heart disease: The Bad Effects on Bleeding/Coagulation balance.

- No clear relation between bleeding or thrombosis and platelet count.
- CCHD patient have a point of balance between thrombogenicity and bleeding liability.
- Raised fibrinogen & raised factor VIII/ VonWillebrand factor complex due to chronic disease. Also raised PF4, P selectin and E selectin. This leads to platelet and endothelial activation.
- These increases compensate for the bleeding risk of low platelet numbers, and may lead to thrombogenicity.
- Thrombosis relatively common....perhaps 1% risk per patient yr.
- Despite risk of paradoxical stroke, PE’s and CVA uncommon at 0.06% and 0.12% per patient yr.
Hematological management of cyanotic congenital heart disease: The Ugly: Is it better to anticoagulate?

- Anti-coagulation strategies in patients with idiopathic PAH are proven.
- This can not be extrapolated to Eisenmenger patients.
- Eisenmenger patients do worse when anti-coagulated!
- No survival benefit, 16% risk of severe bleeding.
- Anecdotal best practice is to anticoagulate Eisenmenger patients only if thromboembolism is proven, or other clear indications such as valve prosthesis are present.

Does anticoagulation in Eisenmenger syndrome impact long-term survival?
Hematological management of cyanotic congenital heart disease: The Ugly: Is it better to anticoagulate?

- Anti coagulation strategies in patients after Fontan operation is a vastly different story!
- Guidelines not so clear!
- My feeling is to anticoagulant the Fontan patient with arrhythmia, end organ damage or proven thrombosis.
- Always consider anticoagulation benefit vs risk at each follow up.


Cyanotic congenital heart disease and atherosclerosis.
Tarp JB, Jensen AS, Engstroem T, Holstein-Rathilou NH, Søndergaard L.

Chronic cyanosis and vascular function: implications for patients with cyanotic congenital heart disease.
Cordina RL, Celermajer DS.

- High bilirubin, low iron, and low platelets lead to lower cholesterol levels and thus lower atherosclerosis risk.

- Potential target for medication.
Hematological management of cyanotic congenital heart disease: The Ugly Complications and Uncertainties.

Immunosuppression

- CCHD patient certainly have risk of infective endocarditis and brain abcess.
- Do survivors of Fontan Procedure have immune deficiency?
- Surgical thymectomy, thoracic duct manipulation & PLE contribute to low absolute lymphocyte counts.
- T-cell lymphopenia with low CD4+ and CD8+ counts & hypogammaglobulinaemia is demonstrated.
- Clinical effect is delayed clearance of cutaneous viral infections.
- Systemic opportunistic infections were not seen despite lab abnormalities.
- Theory is that lymphatic recirculation is defective, but T cell function is preserved at tissue level.

Risk Factors and Clinical Significance of Lymphopenia in Survivors of the Fontan Procedure for Single-Ventricle Congenital Cardiac Disease.
Morsheimer MM, Rychik J, Forbes L, Dodds K, Goldberg DJ, Sullivan K, Heimall JR.
Hematological management of cyanotic congenital heart disease: The Good Treatments for Hyperviscosity.

- Phlebotomy is exclusively used for hyperviscosity symptoms or pre operative autologous blood donation.

- Always rehydrate patients well.

- Consider cerebral access with appropriate imaging.

- No specific target hematocrit.
Hematological management of cyanotic congenital heart disease: The Good Treatments for Hyperuricaemia & Gout.

- Is it really gout? HPOA vs Periostitis vs Gout.
- Colchicine
- Allopurinol
- Rasburicase
Hematological management of cyanotic congenital heart disease: The Good Treatments for Iron Deficiency

- Iron supplementation is recommended especially for those with an inappropriately low Hb for severity of hypoxia.
- Perhaps as much as 45% of patients are iron deficient.
- Increased erythropoiesis, phlebotomy & bleeding contribute to iron deficiency.
- Age, kidney impairment, growth requirements & menorrhagia worsen iron loss.
- Iron replacement makes as much difference in 6MW test as Bosentan treatment. (BREATHE-5)
- No real data on type or duration of iron supplementation treatment
- Benefit of iron supplementation is more than risk.
Hematological management of cyanotic congenital heart disease:
Take home message

- Hematological system contributes to adaptations and complications in CCHD.
- Challenges include are erythrocytosis, iron deficiency, anemia, hyperviscocity, hemorrhage, thrombosis and hyperuricaemia.
- Risk reduction and prevention strategies avoid destabilization of the equilibrium.
- ACHD clinic systems are imperative!
The Good: “There are two kinds of people in the world: those with guns and those that dig. You dig?”

The Good: “There are two kinds of people in the world: those with hematological complications of cyanotic congenital heart disease, and those who complain. You complain?”