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Blood Doping

Background

1. Definition:
    - "Blood doping" or "blood boosting" originally:
        - Transfusion of blood that had been withdrawn and stored (autologous)
        - Transfusion of another's blood (allogenic or heterologous)
            - To increase athlete's RBC count
    - Currently other technology exists to incr RBC count and capacity to carry and deliver oxygen
        - Recombinant human erythropoietin (rhEPO)
        - Other forms of artificial EPO
        - Artificial blood substitutes
            - Modified hemoglobin solutions
            - Perfluorocarbon-based emulsions
        - Novel erythropoiesis-stimulating protein (darbepoetin /Aranesp®)
        - Gene-activated erythropoietin (Dynepo®)
        - Encapsulated recombinant human erythropoietin
        - Gene therapy for alteration of endogenous erythropoietin production
        - Erythropoietin mimetics
        - Haematopoietic cell phosphatase inhibitors
2. Not considered blood doping:
    - Altitude training
    - Altitude tents
    - High altitude (nitrogen) house
3. General information
    - VO2max = max oxygen uptake
        - Major determinant of performance in endurance events
        - Affected by
            - Pulmonary respiratory fxn
            - Diffusion capacity of lung
            - Oxygen transport capacity
                - Fxn of hemoglobin concentration and cardiac output
            - Tissue ability to absorb and utilize delivered oxygen
    - Training protocols for endurance athletes often aim to improve VO2max
        - Legal
            - Exercise at low altitude, live at higher altitude ("live high-train low")
            - Exercising and living at high altitude ("live high-train high")
            - Altitude tents, altitude (nitrogen) houses, supplemental oxygen delivery
        - Illegal
            - Recombinant human erythropoietin (rhEPO)
            - Other forms of artificial EPO
            - Artificial blood substitutes
            - Autologous or heterologous blood transfusion

- Performance improvement from blood transfusion may be small but significant in elite competition
  - Study in two sets of cross-country skiers
    - Group that received autologous blood transfusion performed 5.3% better immediately after transfusion & 3.1% better 14 days after transfusion vs control group

Pathophysiology

1. Incidence/prevalence
   - Unknown how commonly this is used in sports
2. Risk factors
   - More benefit for endurance athletes
3. Morbidity/mortality
   - Autologous blood transfusion
     - Large quantity transfusions associated w/hypercalcemia and coagulopathy
       - Due to citrate preservative used in blood storage
   - Allogenic/Heterologous blood transfusion
     - Hypercalcemia and coagulopathy if blood is stored in preservative prior to infusion
     - HIV, Hepatitis B, and Hepatitis C transmission is possible
     - Transfusion reactions
       - Mild fever and hives
       - Severe hemolysis and DIC
   - Recombinant Human Erythropoietin
     - Numerous risks, see prescribing info
       - Hyperviscosity
       - Thrombosis
       - HTN
       - Post-tx blunted endogenous erythropoietic response w/secondary anemia
       - Development of anti-EPO antibodies
       - Pure red cell aplasia
   - Modified hemoglobin solns exist, complications include:
     - Incr pulmonary and peripheral arterial pressures
     - GI symptoms: pylorospasm, pancreatitis
     - Solutions from human or animal hemoglobin can contain and transmit infective agents or induce antibodies
     - Renal cell necrosis
   - Perfluorocarbon-based emulsions
     - Chemically inert and highly soluble chemicals that incr blood solubility of gases, incl oxygen
     - Perfluorocarbon is exhaled through lung and can be measured w/chromatography, complications include:
       - Myalgia and fever
       - Thrombocytopenia
       - Some forms produced w/egg; can induce allergic reaction
       - Phagocytosis can lead to engorgement of hepatic system by:
         - Microclots

        - Inhibition of white blood cells
        - Complement activation
        - Immune system disturbance
    - EPO gene therapy
        - Early studies have demonstrated difficulties in regulating rate of EPO production

Diagnostics

1. History
    - No specific symptoms
    - May see improved performance
    - Hyperviscosity symptoms
        - Fatigue
        - Headaches
        - Malaise
2. Physical exam
    - No physical changes usually noted
3. Diagnostic testing
    - Continuing to evolve
    - Appropriate testing depends on doping method
    - Screening hematocrit used to determine athletes with "at risk" level
        - Hematocrit >50%
    - DNA testing, spectrometry, other methods in development
    - Guidelines and recommendations
        - International Olympic Committee (IOC)
        - National Collegiate Athletic Association (NCAA)
        - World Anti-Doping Agency (WADA)
        - United States Anti-Doping Agency (USADA)

Differential Diagnosis

1. Polycythemia Rubra Vera
2. Severe dehydration

Therapeutics

1. If doping is suspected and pt has hyperviscosity symptoms
    - Phlebotomy is indicated
2. Discourage use of blood doping
3. Follow-Up
    - Follow-up should be based on individual pts symptoms and MDs request

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