Table 3. Uncommon Defects in Which Adult Survival Is Exceptional

<table>
<thead>
<tr>
<th>Defect</th>
<th>Anomalous Course of Coronary Arteries</th>
<th>Ventricular Septal Defect</th>
<th>Tetralogy of Fallot</th>
</tr>
</thead>
<tbody>
<tr>
<td>Double-outlet right ventricle</td>
<td>Compete transposition of great arteries with ventricular septal defect</td>
<td>Pulmonary atresia</td>
<td>Pulmonary atresia</td>
</tr>
<tr>
<td>Atrioventricular septal defect</td>
<td>Transposition of great arteries</td>
<td>Pulmonary stenosis</td>
<td>Pulmonary stenosis</td>
</tr>
<tr>
<td>Pulmonary venous obstruction</td>
<td>Sinus inversus with levocardia</td>
<td>Cyanotic left to right shunt</td>
<td>Cyanotic left to right shunt</td>
</tr>
<tr>
<td>Diaphragmatic defects</td>
<td>Acyanotic left to right shunt</td>
<td>Cyanotic left to right shunt</td>
<td>Cyanotic left to right shunt</td>
</tr>
<tr>
<td>Common atrioventricular septal defect</td>
<td>Cyanotic left to right shunt</td>
<td>Cyanotic left to right shunt</td>
<td>Cyanotic left to right shunt</td>
</tr>
</tbody>
</table>

The greatest risk is infective endocarditis, whereas beginning in the 3rd decade, heart failure is the major complication in patients with a sizable left to right shunt. Adult survival with a nonrestrictive patent ductus arteriosus is more likely to occur with suprasystolic pulmonary vascular resistance and reversed shunt.

Anomalous course of coronary arteries. Widespread use of coronary arteriography together with careful pathologic studies have disclosed the ectopic origins and anomalous course of the extramural coronary arteries. The proximal course of the anomalous coronary artery is clinically more important than an ectopic aortic origin. The greatest risk occurs when the left coronary artery arises from the right aortic sinus and passes between the aorta and right ventricular outflow tract, a disorder more common in males. The anomaly is generally not recognized until early to mid-adult life, when it announces itself by angina pectoris, myocardial infarction or sudden death, especially during or immediately after exercise.

Ventricular septal defect. Adult survivors generally fall into two groups: 1) those whose defects have either closed spontaneously or have remained small or have become small and clinically inapparent, and 2) those who have nonrestrictive defects with pulmonary vascular disease and reversed shunt. Adult survival with a moderately restrictive defect and significant left to right shunt is exceptional. Longevity is affected by coexisting aortic regurgitation or infective endocarditis.

Tetralogy of Fallot. Eleven percent of patients are alive at 20 years, 6% at 30 years and 3% at 40 years. In patients with tetralogy of Fallot and pulmonary atresia, pulmonary blood flow is maintained by aortic to pulmonary collateral vessels. Systemic hypertension is a special concern because increased afterload is imposed on both the right and left ventricles, with what appears to be more dire consequences on the right ventricle. Acquired calcific aortic stenosis produces similar effects. Infective endocarditis on an incompetent aortic valve can result in acute severe regurgitation into both ventricles, with catastrophic consequences.

References

If inappropriately employed, results in symptomatic iron deficiency and an increase in whole blood viscosity (microspherocytes). Patients with decompensated erythrocytosis exhibit unstable increasing hematocrit levels and recurrent symptoms attributable to sluggish tissue perfusion. Symptoms related to hyperviscosity include headache, fatigue, faintness, dizziness, visual disturbance, paresthesia, irritability, myalgia, reduced mental function and anorexia. Each symptom should be graded as mild, moderate, marked or severe to provide the basis for phlebotomy (3).

Cerebrovascular accidents. These sometimes occur in cyanotic infants and young children, especially those with iron deficiency. In cyanotic adult patients, however, erythrocytosis itself does not appear to be a significant risk factor for stroke, even when the hematocrit level is >65% and even in the decompensated setting (3). The relation between elevated hematocrit levels and cerebral blood flow is an important and incompletely resolved question (4–6), but phlebotomy is not advised if the objective is to reduce the perceived risk of stroke. Phlebotomy is recommended only in patients with symptomatic hyperviscosity when hematocrit levels exceed 65%, provided dehydration is not the cause. Dehydration can result in a rapid increase in the hematocrit level, provoking hyperviscosity symptoms. Treatment is volume replacement, not phlebotomy.

Phlebotomy, volume replacement and iron replacement. Symptoms of iron deficiency can be indistinguishable from hyperviscosity, but symptomatic hyperviscosity rarely occurs in iron-replete cyanotic patients with hematocrit levels <65%. Accordingly, when "hyperviscosity" symptoms are present with hematocrit levels <65%, iron deficiency should be suspected as the cause. Under these circumstances, phlebotomy aggravates rather than alleviates the symptoms and iron replacement should be considered (2).

Phlebotomy without quantitative volume replacement is potentially hazardous. To minimize the risk of phlebotomy-induced iron deficiency, the volume of blood withdrawn should be the least required to achieve symptomatic relief. With very few exceptions, phlebotomy is an outpatient procedure. Various techniques have been recommended. A reasonably simple and safe method for adults in an outpatient setting is the removal of 500 ml of blood over a 30 to 45 min period, followed by quantitative volume replacement with isotonic saline solution or salt-free dextran in patients with heart failure. Blood pressure is monitored at 15 min intervals for 1 h (3). The beneficial effects of phlebotomy are usually evident within 24 h and reflect increased systemic blood flow induced by the volumetric reduction in the erythrocyte mass. If the desired symptomatic relief is not achieved, the phlebotomy procedure can be repeated. Removal of >2 units of blood over a 2 day period is rarely required to achieve adequate symptomatic relief. If symptoms do not decrease, the possibility that concomitant iron deficiency is present should be considered.

Iron therapy must be monitored carefully because a prompt increase in the hematocrit level can be induced and result in hyperviscosity symptoms. The initial dose of iron should be small (325 mg of ferrous sulfate) and should be discontinued at the first increase in the hematocrit level, even if slight, which is usually discernible within 1 week.

Bleeding tendency. An excessive bleeding tendency can be present in cyanotic patients (7,8). Oral anticoagulant agents, heparin and aspirin exacerbate existing hemorrhagic derangements and should be avoided. For the most part, the bleeding diathesis tends to be mild and includes easy bruising, petechial hemorrhages in the skin and mucous membranes, epistaxis, gingival bleeding and hemoptysis. Serious and sometimes fatal bleeding can occur after trauma or with surgical procedures, and hemoptyses and epistaxes are occasionally copious and inordinately recurrent. The mechanisms responsible for the hemorrhagic disorder remain poorly defined. In general, the severity of the bleeding diathesis seems to correlate with the degree of erythrocytosis, especially in patients with hematocrit levels >65%. When the hematocrit level is >65%, phlebotomy to just below that level is often accompanied by lessening of the bleeding tendency.

Thrombocytopenia as well as abnormalities of the prothrombin time and the partial thromboplastin time may be present. Specific deficiencies of several coagulation factors have also been reported (8–10). Certain congenital hematologic disorders are sometimes found in association with congenital heart diseases and specific treatment of the primary hematologic disease is required. Spurious results of laboratory tests for coagulation occur in patients with a hematocrit value >55%, so adjustments must be made in the amount of anticoagulant added to the tubes in which blood is collected.

Preoperative and postoperative management. In the usual clinical setting, the problems related to hemorrhagic tendencies in cyanotic patients require specific treatment. However, cyanotic patients can develop significant and even life-threatening bleeding with surgical procedures. Phlebotomy has been shown to reduce the bleeding tendency in erythrocytotic cyanotic patients and should be utilized preoperatively. An initial 500-ml isovolumetric phlebotomy is followed each 24 h by an additional 500-ml phlebotomy until a hematocrit level of just <65% is achieved. Blood units obtained by phlebotomy are reserved for possible autologous transfusion. When factor deficiencies are evident, fresh frozen plasma should be utilized as the vehicle for volume replacement. Patients in whom a true congenital coagulopathy (such as hemophilia or von Willebrand's disease) or thrombocytopenia (such as the thrombocytopenia-absent radius [TAR] syndrome) are identified are treated with the appropriate factor or platelet infusions.

Cardiopulmonary bypass may be associated with a reduction in platelet counts and in platelet dysfunction regardless of the preoperative hematocrit level (11,12). Accordingly, intraoperative platelet transfusions are frequently given empirically when patients with excessive bleeding undergo cardiopulmonary bypass. Other abnormalities that have been reported after cardiopulmonary bypass include coagulation factor deficiencies, disseminated intravascular coagulation, ex-
Cyanotic Congenital Heart Disease: Dynamics of Oxygen Uptake and Ventilation

KATHY E. SIETSEMA, MD

The matching oxygen and carbon dioxide exchange between the lungs and atmosphere to the rate of utilization and production of these gases by cellular metabolism is accomplished by tightly integrated circulatory and ventilatory function. Intracardiac shunts allow left- and right-sided cardiac output to change unequally, resulting in “uncoupling” of the otherwise closely coupled processes of external and internal gas exchange. Exercise testing with measurement of gas exchange provides valuable information about the physiologic significance of cyanotic and acyanotic congenital lesions and about the functional capabilities of patients.

Oxygen uptake in cyanotic congenital heart disease. Oxygen uptake (VO2) normally reaches a steady state level within 2 to 3 min after the onset of moderate exercise (1). The dynamic increase in VO2 can be divided into two components: the brief (10 to 20 s) rapid increase at exercise onset (phase I), followed by an exponential increase (phase II) to the steady state. The cumulative difference between the oxygen cost of the exercise and VO2 during the nonsteady state is the “oxygen deficit,” which reflects work performed with use of preformed sources of high energy phosphates, nonoxidative pathways of metabolism and depletion of local oxygen stores (2). The pattern of increase in ventilation (VE) is similar, although slightly slower than that of VO2. Distortion of these responses occurs in patients with cyanotic congenital heart disease, reflecting altered physiologic relations as a result of right to left shunting (3,4).

Because VO2 is measured from expired gases, its immediate determinants are pulmonary blood flow and the arteriovenous difference in oxygen content (a-vO2) across the pulmonary circulation (Fick relation): VO2 = Q × (a-vO2). Normally, VO2 doubles or triples relative to levels at rest during phase I (1,3), reflecting an abrupt increase in pulmonary blood flow (5). However, with cyanotic congenital heart disease, there may be little or no increase in VO2 in phase I and the attainment of a steady state is delayed (3). These findings undoubtedly reflect the effects of pulmonary blood flow and impaired ability to widen the arterial oxygen content due to progressively decreasing systemic arterial oxygen content. Similarly, prolonged recovery times for return of VO2 to rest levels have been reported (6) in children with cyanotic heart disease.

Slow adaptation to changes in metabolic rate dictates that cyanotic patients spend a great deal of time in nonsteady states, depleting and repleting oxygen and high energy phosphate stores. It is likely that this derangement imposes an abnormal dependence on nonoxidative metabolism. Consistent with this assumption, lactate acidosis develops at lower levels of exercise in cyanotic patients than in normal subjects (7,8) and muscle lactate levels are reported (9) to be higher in patients with tetralogy of Fallot than in normal subjects during maximal exercise. Blood lactate levels may underestimate the degree of tissue acidosis in cyanotic

References