8.0 HEMATOLOGY

8.1 ANEMIA

AEROMEDICAL CONCERNS: Anemia reduces tissue oxygenation and can be associated with widespread organ dysfunction, particularly when the hemoglobin concentration falls below 10 g/dl or the hematocrit is less than 30%. Work capacity and the compensation to conditions of hypoxia are also reduced. In acute blood loss, cardiovascular decompensation can occur from volume loss, leading to loss of +Gz tolerance and syncope.

WAIVER: The standards for aviation are derived from healthy aviators, not from hospital patients. Hence, our "abnormal" values are generally still within most hospital norms. Acceptable values for hematocrit are 40-52% in males and 37-47% in females. If the average of three hematocrits (*from three separate blood draws, not from the same sample analyzed three times*) falls below the normal range but between 38.0% and 39.9% for males (35.0% - 36.9% for females), the following work-up should be completed:

1. Thorough history (with emphasis on any personal or family history of anemia, ethnicity, blood loss, diet, menstruation, medications, and ETOH)
2. Focused physical (ensure no hepatosplenomegaly or lymphadenopathy)
3. CBC with RBC count, RBC indices, manual differential, RBC morphology, and reticulocyte count
4. Iron studies (serum iron, serum ferritin, and TIBC)
5. Chem 7
6. Liver function tests
7. TSH

If history, physical exam, and all labs are within normal limits as defined below (for labs not listed, use laboratory reference ranges), the member is PQ and no waiver is required. The accepted ranges are:

Acceptable Lab Values:

- RBC count - Male: 4.0-7.0, Female: 3.8-5.3
- Differential – Segs 40-80, Bands 0-10, Lymphs 20-50, Eos 0-10, Basos 0-3, Monos 0-10
- RBC indices - MCV 80-100 fl, MCH 26-36 pg, MCHC 31-38%, Retic count 0.5%-2.0%, RDW 11.0%–16.0%
- Iron studies - Ferritin 20-300 ng/ml, Iron 40-180 ug/dl, TIBC 240-460 ug/dl

If any abnormality exists, or if the average of three hematocrits falls below 38% or above 52% for males (below 35% or above 47% for females), the member is NPQ and a hematology or internal medicine consultation is required. Additional anemia work-up at that time may include hemoglobin electrophoresis, fecal occult blood tests, endoscopy, serum vitamin B12 level, serum or RBC folate level, and/or bone marrow biopsy depending upon the initial findings. This work-up may be initiated by the flight surgeon, depending upon his or her comfort level, so that

laboratory data will be available for the consulting physician. If unsure whether or not a test is indicated, do not order it. Waivers will be considered on a case-by-case basis in light of the underlying diagnosis.

NOTE: Blood donation of 450 cc (1 pint) requires grounding for at least 4 days. Flight personnel in combat or flying in a shipboard environment shall not donate blood within 4 weeks prior to such flying (per General NATOPS). Air Traffic Controllers who donate blood should only be in a down status for 24 hours immediately following blood donation.

INFORMATION REQUIRED:

1. Full clinical history
2. Physical examination
3. Laboratory evaluation as outlined above
4. Hematology and/or Internal Medicine consult

TREATMENT: Oral iron supplements are compatible with flying status, but require a waiver if needed to maintain a hematocrit within standards. Any cause that precipitated the iron deficiency must be rectified before a waiver recommendation would be considered.

DISCUSSION: The World Health Organization recommends that anemia should be considered to exist when hemoglobin levels fall below 13 g/dl in males and 12 g/dl in females. Chronic blood loss from the bowel or uterus of 15-20 ml/day will produce a state of negative iron balance in the body, which will eventually lead to anemia. A full hematological response to iron therapy is indicated by a rise in hemoglobin level of 1 g/dl/week.

ICD-9 CODES:
280.1 Iron Deficiency Anemia
285.9 Anemia, unspecified

8.2 HEMOCHROMATOSIS

AEROMEDICAL CONCERNS: Symptomatic cases typically present with the classic triad of diabetes mellitus, hepatomegaly, and skin hyperpigmentation. Cardiac complications manifest primarily as congestive heart failure in young patients that can rapidly progress to death if untreated. CNS complications have been reported but, other than lethargy, are rare.

WAIVER: Waiver recommendations for hemochromatosis are not routinely made.

INFORMATION REQUIRED:

1. Internal medicine or hematology consult
2. Histocompatibility locus antigen (HLA) typing
3. Serum iron
4. Serum ferritin
5. Total iron body content
6. Transferritin saturation
7. Liver biopsy (if indicated)
8. Family studies (if indicated)
9. Cardiology consult
    a. Holter monitor
    b. Echocardiogram

TREATMENT: Frequent phlebotomy and/or treatment with chelating agents such as desferrioxamine are not compatible with waiver.

DISCUSSION: Phenotypic expression of the idiopathic hemochromatosis gene usually occurs between the ages of 20 and 40, with symptoms mainly occurring after the age of 50. Patients have the condition for an average of 3-5 years before the diagnosis is made. Hepatic fibrosis is unusual in patients younger than 35, but it will occur sooner and progress more rapidly to cirrhosis in heavy drinkers. Hypogonadism will occur in 25% of male patients and primary hypoaldosteronism in 10%. Cardiac failure and arrhythmias are common presenting features in younger patients. Up to 50% of patients over 40 years old have ECG irregularities and 43% of autopsied hearts from hemochromatosis patients show iron deposits in the AV node and conduction system.

Arthropathy is present in 30-50% (commonly in the proximal interphalangeal and metacarpophalangeal joints although 10% of patients have destructive arthropathy of the hip and knee joints). Phlebotomy 2-3 times a week until hemoglobin <10 g/dl, serum iron is less than normal, or ferritin is in the low normal range, followed by maintenance phlebotomy every 2-4 months, will reduce the incidence of complications other than arthropathy and the eventual appearance of hepatoma. However, this treatment is not compatible with waiver. The death rate at 5 and 10 years with phlebotomy is 66 and 32%, compared to 18 and 6% without treatment.

ICD-9 CODE:
275.0 Hemochromatosis

8.3 SICKLE CELL DISEASE/TRAIT

AEROMEDICAL CONCERNS: Patients with sickle cell disease have a severe risk of splenic infarct and other vaso-occlusive episodes involving the viscera, lungs, kidneys, or nervous system when exposed to hypoxia, infection, dehydration, or cold temperatures.

WAIVER: By direction from the SECNAV, sickle cell trait (SCT) is not disqualifying for any aviation, undersea or general duty program. Sickle Cell Disease and a history of sickling on exposure to altitude in flight or in a decompression chamber are disqualifying. A completed long form physical (SF-88) should be submitted to NOMI whenever an adverse physiologic event is recognized.

INFORMATION REQUIRED:

1. Hemoglobin electrophoresis documenting the percentage of hemoglobin S
   a. Hemoglobin S greater than hemoglobin A is disqualifying for general duty
2. Information on coexistent hemoglobinopathies.

TREATMENT: Patients requiring treatment for the condition are disqualified from flying.

DISCUSSION: The condition occurs often in African American populations, and sporadically in those of Mediterranean, Middle Eastern, or Indian descent. Between 7 and 9% of African Americans have sickle cell trait (SCT). Cases of sickling have been reported at altitudes as low as 2,500 feet, although patients with SCT are unlikely to sickle below 21,000 feet. Exercise and dehydration predispose to sickling. In addition to the classic sickle cell crisis, transient episodes of bone marrow aplasia can occur in response to infection and sequestration of erythrocytes in the liver and spleen that can also be life threatening. Patients with SCT should be counseled about the dangers of recreational diving and risks of anesthetics.

ICD-9 CODES:
282 Sickle Cell
282.5 Sickle Cell Trait
282.6 Sickle Cell Disease

8.4 SPLENECTOMY

AEROMEDICAL CONCERNS: There is risk of serious, overwhelming infection in patients with co-morbid diseases who have had a splenectomy. Examples include ITP and lymphoproliferative diseases (leukemia, etc.). In such cases, the time between onset of symptoms and death can be rapid (i.e. just a few hours). In cases where splenectomy is performed due to traumatic rupture, these serious complications occur much less frequently.

WAIVER: Waivers are considered on a case-by-case basis after splenectomy, provided there is full recovery from the condition necessitating the operation. This includes splenectomy following traumatic splenic rupture and diagnostic splenectomy for Hodgkin's disease (see section 9.7 – Hodgkin's disease for further waiver requirements).

INFORMATION REQUIRED:

Initial Waiver:

1. Detailed history of the circumstances that led to splenectomy
2. Focused physical exam
3. CBC
4. Confirmation of the absence of malaria, infectious mononucleosis, and leukemia (in cases of spontaneous rupture of the spleen)
5. Fit for Full Duty determination from surgeon

Follow-up:

1. CBC (when co-morbid conditions exist)

Note: In cases where traumatic rupture necessitated splenectomy, no specific follow-up is required, provided there is no resulting compromise of the immune system.

TREATMENT: Prophylactic antibiotics may be acceptable in certain circumstances. Immunizations against pneumococcus, meningitis, and Hemophilus B are compatible with flying status, and should be administered before elective splenectomy if at all possible.

DISCUSSION: Following therapeutic splenectomy, the course is that of the disease requiring the splenectomy. The overall mortality rate is around 3%, of which infections account for 11% of the deaths. Mortality for isolated injury to the spleen is <1%. Late sepsis after splenectomy for Hodgkin's disease occurs in 11.5% of patients, with a 5% mortality rate. This is related to the chemotherapy rather than the splenectomy. In adults who have had a splenectomy, the mortality from pneumococcal pneumonia is 17% despite administration of antibiotics. If the patient is older than 50, the mortality rate is 28%.

ICD-9 CODES:
P41 Splenectomy
P41.5 Splenectomy (complete)
P41.43 Splenectomy (partial)

8.5 THALASSEMIAS

AEROMEDICAL CONCERNS: Thalassemias produce a low-grade anemia that can cause problems at altitude. Splenic enlargement and worsening of the anemia can occur under conditions of stress.

WAIVER: Aviation personnel must meet the hematocrit standards previously listed in the Anemia section (section 8.1). Personnel with beta thalassemia minor (heterozygous carriers – beta thalassemia trait) or with alpha thalassemia minor (1 or 2 gene loci absent) may be considered for waiver provided there are no other hemoglobinopathies present. Any anemia must be limited to a mild, microcytic anemia. Patients who have required splenectomy because of their thalassemia are permanently disqualified from military flying.

INFORMATION REQUIRED:

1. Establishment of the detailed diagnosis
   a. Estimation of HbA2, HbF, serum Fe and ferritin and by quantitative electrophoresis
2. Focused physical exam
3. Internal medicine or hematology consult (if obtained)

NOTE: The diagnosis of thalassemia cannot reliably be made in the face of iron deficiency, hence iron studies must be provided that document normal iron status with submission of the waiver request.

TREATMENT: N/A.

DISCUSSION: The thalassemias probably constitute the world's largest genetic disorder. Beta thalassemia occurs widely in a belt extending from Southeast Asia, through India, the Middle East, the Mediterranean (as far north as Romania and Yugoslavia), and to north and west Africa. Carrier frequencies can vary from 2 to 30% in these populations. Beta thalassemia also occurs sporadically in all racial groups. Splenectomy results in a greater risk of overwhelming infection and of severe malaria, which can affect an aviator's fitness to deploy. The flight surgeon will often make the diagnosis of thalassemia after chart review turns up a chronic, low grade microcytic anemia that does not respond to iron therapy. Patients with homozygous beta thalassemia or deletions in more than two of the alfa chains are almost always severely symptomatic or anemic, and as such rarely make it into the military.

ICD-9 CODE:
282 Thalassemias