ALTITUDE-RELATED ILLNESS

I. PHYSIOLOGY AND ADAPTATION

The main physiologic effect of high altitude is hypoxia. As altitude increases, the barometric pressure decreases. This leads to a lowered PaO_2 and a decreased saturation of hemoglobin. Man can tolerate exposure to extremely high altitudes for short periods of time (e.g. the ascent of Everest's 29,028 feet without oxygen by Messner and Haebler). For prolonged stays at high altitude, man is more limited. Probably an altitude in the 16,000 to 18,000 foot range is the limit of man for prolonged residence at altitude. Beyond this altitude, progressive deterioration results

Certain physiologic changes occur with exposure to altitude. These changes are important because they are the basis for high altitude adaptation and also may be a predisposing factor to high altitude illness.

With acute ascent to high altitude, one gets a tachycardia which is probably due to an elevated sympathetic outflow. This leads to an elevation in cardiac output. The stroke volume remains unchanged at first but usually drops after two to three days. Systolic blood pressure decreases with exposure to altitude. The diastolic blood pressure tends to remain unchanged although some investigators have noted a slight decrease.

With rapid ascent to high altitude, one gets a prompt decrease in plasma volume. This decrease, to some degree, is due to diuresis. It is also due to a fluid shift from the extracellular space to the intracellular space. This change in plasma volume is approximately 10-20 percent. This decrease in plasma volume accounts for the initial increase in hematocrit with exposure to high altitude. Eventually, the red blood cell volume elevation occurs in a simple linear relation to decreased hemoglobin saturation. The critical oxygen tension stimulating the elevated red blood cell volume is 60 mmHg.

Other adaptations include a shift in the Hb-O_2 dissociation curve to the right. This is a theoretical advantage since oxygen delivery to tissues would be increased by this change. At extremely high altitudes (>20,000 feet), very little O_2 could be carried in the blood due to this adaptive shift. Thus, at extremely high altitudes, a left shift in the Hb-O_2 dissociation curve would be beneficial. This pattern has been seen in studies by Alpacas and Llamas. Also with an elevation in altitude one gets an increase in the 2,3 DPG content of the red blood cells. This effect appears within 24 hours of ascent and disappears rapidly after descent. There is an increase in serum erythropoietin concentration within 24 hours, which returns to near sea level values after three weeks.

Changes in lung function also occur with exposure to high altitude. Acutely one gets an increase in respiratory rate in response to hypoxia. Usually there is no effect on respiratory rate up to 10,000 feet and only minor increases up to 16,000 feet and a 20 percent increase at 20,000 feet. Chronic habitation at high altitude leads to a reduction in the hypoxic ventilatory drive. Pulmonary diffusing capacity is not increased in lowlanders who ascend to high altitude but it is increased in high altitude residents by 20-30 percent. During exercise at sea level, PaO_2 values tend to remain unchanged or perhaps increase slightly. However, with exercise at high altitude the PaO_2 drops. This change is due to a limitation of pulmonary diffusion capacity. Thus, at sea level, cardiac output is the limiting factor in heavy exercise while at high altitude it is the diffusing capacity of the lung that limits heavy exercise.

II. ACUTE MOUNTAIN SICKNESS (AMS)

Definition:
Acute Mountain Sickness is the constellation of symptoms that occur when someone is taken rapidly to altitude. AMS is rare below 8,000 feet. It will occur in most persons rapidly exposed to altitudes of 10,000-20,000 feet. The incidence of AMS is highly variable but on Mt. Rainier (approximately 14,400 feet) approximately 67 percent of climbers develop AMS.

Aerobic fitness is no predictor of not getting AMS with exposure to altitude. There is even more evidence that prior aerobic fitness leads to increased AMS incidence, most likely due to excessively rapid ascent. Prior ascents to altitude without symptoms of AMS are no guarantee of not having symptoms of AMS with reascent. Generally, there is no correlation between the severity of illness and increasing altitude. The incidence in males and females is the same and there is an increased incidence in younger patients.

Pathophysiology:
The development of acute mountain sickness has been linked to:

- Fluid retention
- Poor ventilatory response
- Increased alveolar-arterial oxygen gradient
- Increased CSF pressure

Several studies have noted increased fluid retention in subjects with AMS. Since ascent should be accompanied by diuresis, early weight gain is evidence of fluid retention. In addition, the occurrence of fluid shifts from the peripheral to the central circulation may be important.

The hypoxic ventilatory response is the increased ventilation which occurs with hypoxia. Although it appears to be genetically determined, it is also a function of metabolic rate. As a result, drugs will effect this response. Training appears to have little effect on the hypoxic ventilatory response. Since most of the symptoms of AMS are cerebral, it is thought that this blunted hypoxic ventilatory response affects the cerebral circulation. The imbalance between

cerebral vasodilation from hypoxia and the cerebral vasoconstriction from hypocarbia may lead to altered cerebral blood flow. This impaired cerebrovascular regulation appears to lead to increased cerebral blood volume, increased CSF pressure or vasogenic edema. There is substantial circumstantial evidence to support this explanation. Several studies have demonstrated a 33-40 percent increase in cerebral blood flow. There is a lag period in its occurrence similar to that seen with AMS symptoms. Measures which affect cerebral blood flow, such as oxygen, affect symptoms. In addition, symptoms of AMS have been shown to increase with supplemental CO_2.

On ascent to altitude, there appears to be an increase in lung water. One study showed a 54 percent increase in estimated lung mass. In addition, many individuals show subclinical pulmonary edema. This causes a lower PaO_2 and a higher $PaCO_2$, than would be expected on the basis of barometric pressure alone.

The above events lead to a decreased arterial oxygen saturation. This hypoxia causes acceleration of cerebral vasodilatation and pulmonary edema, leading to further decrease in arterial PO_2. These events cause a dangerous progression of latitude related illnesses.

Signs and Symptoms: The symptoms of AMS tend to occur within the first 48 hours of ascent. Symptoms can consist of headache, dizziness, lassitude, anorexia, drowsiness, malaise, weakness, and DOE. Other symptoms include nausea, vomiting, warm and flushed sensation of the face, insomnia, palpitations, and vague pains in the posterolateral chest. Additionally, there may be decreased capacity for mental work, tinnitus, memory defects and vertigo. The symptoms tend to be most severe on the second and third days after ascent. Ataxia may occur and it may be progressive. The presence of ataxia is ominous and it is a clear indication for descent. The symptoms of AMS rarely last more than six days. Many patients with AMS will have either periodic or Cheyne-Stokes breathing. This is probably the cause of the insomnia often seen. By far, headache is the most common and prominent symptom of AMS.

Prevention:
The best prevention of AMS is staged ascent. Numerous studies have documented the protective benefits of this. For persons going to altitude from sea level a sojourn at the intermediate altitude (6,000-8,000 feet) for two to four days before going to higher altitude is recommended. In addition, a rest day ideally should be taken every second or third day.

Over 10,000 feet elevation, an ascent of no more than 1,000 feet per day is recommended. Above 14,000 feet, one should not ascend faster than 500 feet per day. Once altitude is reached, strenuous activity should be avoided for the first two to three days. Strenuous activity immediately after reaching altitude increases the chances of developing HAPE. Those individuals who develop symptoms should not continue to ascend.

The altitude at which one sleeps is probably more important than the altitude at which one works. Thus the concept of "work high" and "sleep low" becomes important. By sleeping at as low an altitude as possible, one reduces the likelihood of developing AMS or other high altitude illnesses.

The pharmacologic prevention and also the treatment of AMS is now possible with acetazolamide. Acetazolamide is a carbonic anhydrase inhibitor. Its mechanism of action is uncertain. Some investigators feel that if probably has its effect by causing a metabolic acidosis with resultant increase in respiratory drive and PaO_2. Others feel that it works due to its mild diuretic effects. Still others feel that it works by decreasing CSF formation and thus CSF pressure. It appears to also affect cerebral blood flow. Regardless of the mechanism, it works. The FDA has asked the manufacturer of Diamox to reliable the drug for use in AMS.

Controlled studies have shown that Diamox dramatically lowers the incidence of AMS when taken prophylactically. One study on Mt. Ranier showed a 67 percent incidence of AMS in subjects taking placebo while the subjects which took Diamox suffered only 17 percent incidence of AMS. The usual dose of Diamox for prophylaxis of AMS is 250mg po BID started 24-48 hours before ascent and continued for three to four days thereafter. Recent studies have shown that not only is Diamox effective for prophylaxis of AMS, it is also effective for the treatment of AMS even when symptoms have already begun. The dose and duration is the same as that for prophylaxis.

The benefits of acetazolamide are many. It increases minute ventilation, ameliorates sleep apnea and maintains oxygenation during sleep. It has been shown to reduce the frequency and incidence of periodic breathing from 85 to 35 percent. This occurs because the additional ventilatory stimulus shifts the apneic threshold to a lower $PaCO_2$. The side effects of acetazolamide include paresthesias, malaise, myopia, anorexia, alteration in the taste of beer or carbonated drinks, nausea, and drowsiness. These side effects tend to occur only if the drug is taken for greater than five days. Contraindication to the use of acetazolamide are those conditions of preexisting metabolic acidosis. During the apneic periods, arterial oxygen may drop sharply, aggravating tissues which are already oxygen deficient.

Other pharmacologic methods for prophylaxis of AMS have been tried with varying degrees of success. Furosemide, furosemide plus morphine, and furosemide plus betamethasone have been noted to be successful by some investigators. The majority opinion states that none of the above combinations are truly effective. A recent controlled trial of antacids (Rolaids) showed that it was not effective for AMS prophylaxis. Several recent controlled studies point to drugs other than Diamox which may be effective for prophylaxis of AMS. One recent study showed that Decadron (4mg po every six hours) started 48 hours prior to ascent was more effective than placebo for prophylaxis. Likewise, another study found spironolactone (25mg po QID) to be more effective than placebo for the prophylaxis of AMS. It is not clear if the mechanism is due to aldosterone inhibition or via extra renal (ie. CSF) action. One other study found methazolamide is a carbonic anhydrase inhibitor which has a longer half-life, lower protein binding, less renal excretion, and reportedly less side effects than Diamox.

Many other medications have been suggested. Dilantin has been studied in a small group. This study on Mt. Everest, although no strong conclusions could be made promoting its use, additional

studies may be useful. Inderal has been used in the treatment of migraines. It does not cause substantial change in the headaches of AMS, and may affect overall performance. Cocaine or amphetamines may prevent fatigue, but their effect as respiratory stimulants is not clear. Methylprogesterone is a respiratory stimulant which has been used in sleep apnea and COPD. Due to its side effects, it has not been adequately studied. Testosterone is known to increase red cell mass, a process that occurs naturally in man at higher altitudes. This has also not been studied due to its slow effects.

Treatment:
As noted before, Diamox can also be used to acutely treat AMS. Mild or moderate AMS can be treated with light duty, light diet, and symptomatic measures. The use of aspirin or tylenol is usually adequate for headaches. Some clinicians Valium or Dalmane to treat the insomnia but most would refrain from the use of hypnotics. When Valium was studied at higher elevations, it appeared to decrease stage IV sleep and O_2 saturation. Halcion would be the most recommended of all sleep medications due to its short half-life. Benadryl 50-100mg HS has been used, but it is less tranquilizing than Halcion. Its effects on respiratory drive have not been studied. The drug of choice for sleeping is Diamox. Voluntary hyperventilation for 10-15 minutes may be helpful. Compazine has been used for control of nausea and vomiting. Continuous O_2 (1-2 L/Min) during sleep may be helpful. Mild to moderate AMS will respond to the above measures after a few days. More sever AMS, or if ataxia is noted, should be treated with O_2 and descent.

Any patient with AMS have a lung, fundoscopic and neurologic exam to look for signs of more severe altitude illness such as HAPE or HACE. As will be noted below, rales maybe found in a high percentage of cases of AMS. This alone does not indicate that the patient has HAPE. The other signs/symptoms found in HAPE must be present before a diagnosis of HAPE can be made. The presence of cerebral ataxia, however, is a good predictor that the AMS is severe and that it may go on to HACE.

Once acclimatization occurs, troops may return to sea level for periods of 10-14 days then return to altitude without running the risk of AMS on return.

III. HAPE

Definition:
HAPE is a high altitude illness in which the lungs are the main target organ.

Patients with HAPE usually have the symptoms of AMS but occasionally one encounters HAPE in a patient without the symptoms of AMS. HAPE only rarely occurs at less than 8,000 feet and usually occurs at more than 12,000 feet. The incidence of HAPE is 13 times greater in the 1-20 year age group than in the > 20 year old age group. Persons with a history of previous attacks of HAPE are likely to have recurrent episodes of HAPE with later exposures to altitude.

Also, HAPE is more common in high altitude residents who go to sea level then return to altitude.

The incidence of HAPE is greater if persons arriving at altitude participate in heavy exercise on arrival. In fact, episodes of HAPE occurring at 8,000-10,000 feet are usually related to heavy physical exertion.

Pathologic Findings:
Postmortem studies of patients with HAPE have yielded some interesting results. Grossly, the lungs are congested and swollen with protein rich exudate filling the alveoli. In some cases one sees fibrinous intra-alveolar exudates for hyaline membranes. There may be hemorrhage into the alveolar spaces and dilation of the pulmonary lymphatics and interstitial pulmonary edema. Indian investigators have found thrombi and fibrin clumps in the vascular bed to be a prominent feature of HAPE. Investigators elsewhere have not found this as an important feature of the pathology of HAPE.

Pathophysiology:
The exact pathophysiology of HAPE is not well known. It is known that pulmonary arterial pressure (PAP) increases upon exposure to hypoxia. The magnitude of this response is dependent upon the degree of hypoxic stimulus and upon the individual. The previously discussed hypoxic ventilatory response (HVR) occurs with hypoxic stimulus. The pulmonary vascular pressor response is the degree of constrictor response which occurs with hypoxia. An individual with a blunted HVR and a strong pulmonary vascular pressor response may be more likely to have increased pulmonary pressures, and subsequently develop HAPE.

Much research has been directed at the pulmonary vasculature. Normally the blood flow response to hypoxia is regional, allowing diversion to improve oxygenation. At high altitudes, alveolar hypoxia throughout the lung contributes to ventilation perfusion mismatch. Radio active labeled albumin showed increased perfusion in HAPE patients, with localized areas showing significantly different flow rates. This becomes particularly important during stresses such as strenuous exercise or sleep hypoxia. The presence of a restricted pulmonary vascular bed leads to non-uniform overperfusion.

In recent studies of the bronchoalveolar lavage fluids in climbers with HAPE on Mt. McKinley, the fluids contained increases in high MW proteins, RBCs, and leukocytes, primarily alveolar macrophages. This high protein concentration suggests this process is an increased permeability type of pulmonary edema. The increased pressure may cause mechanical distention of endothelial pores. In addition, this pressure may initiate an inflammatory response leading to increased permeability of the vascular endothelium. The isolation of locally vasoactive leukotrienes, complement fragments, and an overall increase in the absolute neutrophilic number suggest there is an inflammatory response. The process is different from ARDS in that the cells are alveolar macrophages not neutrophils. The role of thrombin, platelets, and microemboli are not clear but may mediate the endothelial damage.

Neurogenic pulmonary edema may also exist secondary to increased cerebral pressure. In one HAPE victim, an opening pressure of 300 cm H_2O was noted.

Clinical Presentation:
The symptoms of HAPE tend to occur within 24-48 hours after arrival at altitude. Usually the symptoms of AMS are present before or occur with the symptoms of HAPE. The symptoms of HAPE are fatigue, dyspnea, dry cough, hemoptysis, and mild fever. Gurgling from the lungs may be heard without a stethoscope and the patient may actually produce pink, frothy sputum. Non-medical observers who have seen patients with HAPE have often described them as drowning in their own juices. Signs of HAPE include rales on auscultation and a loud pulmonic second sound. Hemoptysis is present in approximately 20 percent of cases. In severe cases, there can be tachycardia, tachypnea, cyanosis, and hypotension. Eventually the patient will become incoherent, irrational and may even have hallucinations. Once the classic signs and symptoms of HAPE set in, death is imminent (usually within 6-12 hours) unless treatment is begun.

In mild cases of HAPE, the chest x-ray may show small patchy infiltrates. In more severe cases the infiltrates may nearly fill both lungs. The infiltrates are rarely confluent and spaces are usually present, especially at the lung bases. The central pulmonary arteries are usually prominent because of the marked pulmonary hypertension. The edema is especially common in the right mid lung field and often localizes at first. It is not usually distributed in a "bat wing" pattern. Pleural effusion is rare. Left atrial enlargement and pulmonary venous congestion are rarely present.

EKG changes taken in HAPE victims usually suggest acute pulmonary hypertension with right ventricular overload. As noted earlier, rales on auscultation of the lungs of patients with AMS is fairly common. One study on Mt. Ranier (14,408 feet) found rales on auscultation in 15 percent of all climbers. Thus, a large percentage of persons at altitude probably develop subclinical HAPE. Persons with symptoms of AMS alone with rales should be treated for AMS only and should not be treated as if they have HAPE.

Prevention:
Generally the methods of prevention of HAPE are similar to those outlined for the prevention of AMS. Ascent to high altitude from sea level should be staged with a planned sojourn at an intermediate altitude and a limit on the amount of ascent per day. The procedure for staged ascent outlined for AMS should be followed. Heavy physical activity should be avoided for the first two to five days after ascent. Remember to "work high" and "sleep low". The incidence of HAPE tends to increase when the sleeping altitude is greater than 7,000 feet. Acetazolamide is also thought to be useful in preventing HAPE.

Treatment:
HAPE, once discovered, should be treated immediately since it will lead to progressive deterioration and usually death within 6-12 hours. The patient should be placed at absolute bedrest and given oxygen. Descent is the definitive treatment and it should be done immediately. Usually a descent of only 2,000 to 3,000 feet will result in improvement. The patient should be medevaced to a medical facility as soon as possible. Some investigators have used Lasix

effectively but it carries the risk of causing hypovolemic shock if diuresis is profuse. Digitalis is ineffective since the left atrial pressure is normal or even low. Some investigators promote morphine to shunt blood from the pulmonary circuit and reduce the preload. Nitrates have not been adequately studied to date. Other drugs useful in reducing vasoconstriction such as nifedipine or phentolamine need additional study. The cardiac output and systemic blood pressure are often low in HAPE. Also, there is no left ventricular failure in HAPE.

IV. HIGH ALTITUDE CEREBRAL EDEMA

Definition:
At high altitudes some patients may develop an encephalopathic type picture. This is known as High Altitude Cerebral Edema (HACE) or High Altitude Encephalopathy (HAE).

HACE can occur at altitudes as low as 8,000 feet but it more typically occurs at elevations greater than 12,000 feet. The incidence of HACE in persons brought rapidly to high altitude is approximately 2 percent.

Pathophysiology:
Alterations in cerebral blood flow probably play the major role in the development of HACE. Hypoxia results in cerebral vasodilatation, and an increase in cerebral blood volume. The increase in partial pressure of arterial CO_2 would also inhibit cerebral vasoconstriction. These changes would become particularly pronounced during periods of hypoventilation such as during sleep. At high pressures, there is impaired regulation of cerebral vasculature at the capillary levels. These elevated brain microvascular pressures result in frank cerebral edema. A malfunction in the cellular membrane sodium pump due to hypoxia has also been proposed as a possible cause of this edema. Since both events have been postulated for AMS, HACE appears to be the severe end of the AMS spectrum.

Clinical Presentation:
The coexistence of symptoms of AMS and HAPE are common but the symptoms of HACE can present alone. Early signs and symptoms include headache, vertigo, vomiting, confusion, truncal ataxia, poor judgment, irrational behavior, emotional liability, and hallucinations. Focal neurologic defects have been recorded. On physical exam, one can see papilledema, retinal hemorrhages, and increased CSF pressure. Testing of the patients gait similar to that used in alcohol tests is very useful. In some cases the symptoms may be suggestive of subdural hematoma. Hypothermia with its neurological symptoms must be considered in the differential diagnosis.

Treatment:
Once diagnosed as having HACE, the patient should be treated with oxygen, bedrest and descent. This treatment should be fairly emergent as death can occur within several hours. Some investigators have noted success with Decadron usually in a dose of 4mg IV, PO or IM q4H, but additional studies are needed. Decadron was shown to reduce the width of the retinal arteries at

36 hours, probably due to reduction in vasogenic interstitial edema. Since HACE appears to be a severe manifestation in the AMS spectrum, Diamox is probably useful as a prophylactic measure. Decadron, staged ascent and other measures such as described for the prevention of HAPE and AMS are helpful. Late neurologic complications are rare, except in patients who remain comatose for long periods.

IV. HIGH ALTITUDE RETINAL HEMORRHAGE

A high percentage of all persons at high altitude will develop asymptomatic retinal hemorrhages. The incidence of these is as high as 30-60 percent at 17,000 feet. At altitude, the appearance of the fundus is changed from that at sea level with hyperemia of the disc, tortuosity of the vessels, and increased diameter of the fundal arteries and veins. Evidence suggests that retinal hemorrhages are due to capillary rupture or leakage on the arterial side of the retinal vasculature. The principles of prevention are the same as previously discussed for AMS. Strenuous exercise increases the incidence of retinal hemorrhages, while slow ascent decreases the likelihood of occurrence. Normally, retinal hemorrhages are asymptomatic and only noticed if the fundus is examined. The visual fields are normal. On examination, one usually sees flame shaped hemorrhages but "cotton wool" exudates and vitreous hemorrhages have also been reported. Hemorrhages which are extremely large, involve the macula (estimated to be 5 percent in one study), or interfere with visual acuity, are indications for descent. If any of the above conditions occur, the patient should be given oxygen and brought to a lower elevation as soon as possible. There is no known pharmacologic agent to prevent or treat retinal hemorrhage. It is important to remember in the differential diagnosis that subacute cases of carbon monoxide poisoning are frequently accompanied by retinal hemorrhage.

V. CHRONIC MOUNTAIN SICKNESS (MONGE'S DISEASE)

Monge's Disease occurs only in long-term residents at high altitudes and thus is not of great importance in military operations. The mechanism of the disease is not certain. The symptoms include fatigue, dyspnea, somnolence, and slowed intellectual functions. Physical findings include cyanosis, clubbing, plethora, and physical signs of pulmonary arterial hypertension. Signs of right heart failure may be seen. The HCT is elevated (usually to more than 70) but polycythemia alone is not an adequate diagnostic criterion since certain persons at high altitude will have polycythemia without the signs and symptoms of Chronic Mountain Sickness. Patients with Chronic Mountain Sickness have abnormal elevation of PAP and no evidence of structural disease of the lung or heart. Pulmonary blood volume is reported to be decreased. Some investigators feel that this disorder is due to alveolar hypoventilation secondary to a decreased response to hypoxia. Regardless of the cause, the only correct treatment is descent to sea level on a permanent basis. Although this entity has traditionally been described at very high altitudes, a case has been reported from Lake Tahoe, California.

VI. SYSTEMIC EDEMA AT HIGH ALTITUDE

Occasionally certain persons, especially women, will develop edema of the face, hands, and feet at high altitudes. This edema usually tends to occur in the absence of other symptoms. In susceptible persons, repeat episodes are common. The edema goes away at lower altitude. There is no need for descent for systemic edema at high altitude. The patient should be examined carefully to rule out the presence of HAPE or HACE. Some investigators advocate Lasix for this condition but most would not use it. It is probably reasonable to restrict salt intake. The patient is usually able to tolerate the edema and continue to function well.

VII. SICKLE CRISIS

Blacks with sickle cell trait are prone to develop sickling attacks when exposed to a low PaO_2, as might occur at high altitudes. An elevation of 15,000 feet must be attained to reduce the capillary oxygen tension to the level where a sickle crisis may occur. However, sickling has occurred at lower elevations. The above refers to patients with sickle cell trait which is a minority of blacks. Also, Mediterraneans must be considered as possibly having sickle cell trait. A recent study showed six cases of splenic syndrome at altitudes of 5,280 to 7,000 feet, all in patients phenotypically non-black. In fact some studies have suggested that whites with sickle cell trait may have a greater susceptibility to splenic syndrome at moderate to high altitudes. In any event, pain, shortness of breath, or arthralgias in a patient at altitude should have sickle cell crisis included in the differential diagnosis regardless of race.

VIII. SUBACUTE MOUNTAIN SICKNESS

Subacute Mountain Sickness refers to the presence of the constellation of AMS symptoms which persists for weeks. These patients should be treated by descent.

IX. THROMBOEMBOLIC DISEASE

Thromboembolic Disease occurs with increased frequency at high altitude. Predisposing conditions for these entities include volume depletion and polycythemia which are common at high altitude. The incidence increase with prolonged inactivity is often related to alpine storms. Perhaps most important is that cerebral circulatory disturbances can also be produced by high altitude. Cerebral edema appears to play a major role in the development of cerebral thrombosis. The danger of cerebral thrombosis increases as the stay at altitude becomes longer. Females are usually advised not to use oral contraceptives at altitude to prevent cerebral edema.

X. POLYCYTHEMIA

Many long term residence at high altitude will develop polycythemia, often without associated symptoms. A hematocrit of 59 percent is not unusual at 14,000 feet. Hematocrits may be 60-70 percent in asymptomatic individuals. Polycythemia occurs to compensate for the decline in oxygen saturation.