AD-A188 348 MEDICAL PROBLEMS RELATED TO ALTITUDE IN HUMAN PERFORMANCE PHYSIOLOGY AND (U) ARMY RESEARCH INST OF ENVIRONMENTAL MEDICINE NATICK MA M K MALCONIAN ET AL 1/1

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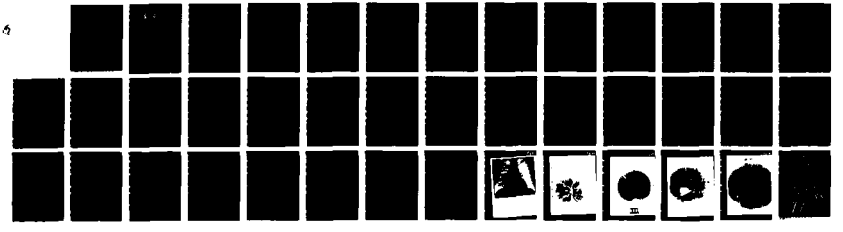

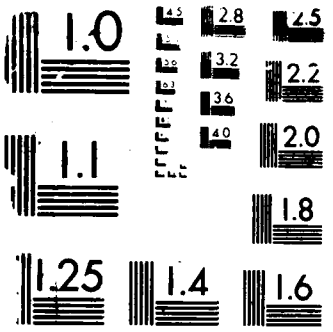

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AD-A188 340 DOCUMENTATION PAGE

Form Approved OMB No. 0704-0188

1a. REPORT SECURITY CLASSIFICATION: Unclassified	1b. RESTRICTIVE MARKINGS
2a. SECURITY CLASSIFICATION AUTHORITY	3. DISTRIBUTION/AVAILABILITY OF REPORT: Approved for public release; distribution is unlimited
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE	
4. PERFORMING ORGANIZATION REPORT NUMBER(S)	5. MONITORING ORGANIZATION REPORT NUMBER(S)
6a. NAME OF PERFORMING ORGANIZATION: U.S. Army Rsch Inst of Env Med; 6b. OFFICE SYMBOL (If applicable): SGRD-UE-ME	7a. NAME OF MONITORING ORGANIZATION: U.S. Army Rsch Inst of Env Med
6c. ADDRESS (City, State, and ZIP Code): Kansas St. Natick, MA 01760-5007	7b. ADDRESS (City, State, and ZIP Code): Kansas St. Natick, MA 01760-5007
8a. NAME OF FUNDING/SPONSORING ORGANIZATION: Same as 6a.; 8b. OFFICE SYMBOL (If applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER
8c. ADDRESS (City, State, and ZIP Code): Same as 6c.	10. SOURCE OF FUNDING NUMBERS: PROGRAM ELEMENT NO. / PROJECT NO. 3M1611 02BS10 / TASK NO. 879/BC / WORK UNIT ACCESSION NO. 126

11. TITLE (Include Security Classification): Medical Problems Related to Altitude.

12. PERSONAL AUTHOR(S): Mark K. Malconian, D.O. and Paul B. Rock, D.O., Ph.D.

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Year, Month, Day)	15. PAGE COUNT
Book Chapter	FROM _____ TO _____	October, 1987	38

16. SUPPLEMENTARY NOTATION

17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
FIELD	GROUP	SUB-GROUP	acute mountain sickness, high altitude cerebral edema, high altitude pulmonary edema, high altitude retinal hemorrhages, generalized peripheral edema, reentry pulmonary edema, chronic mountain sickness

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

This chapter discusses medical problems associated with the acute hypoxia of altitude including: acute mountain sickness, high altitude cerebral edema, high altitude pulmonary edema, high altitude retinal hemorrhages, generalized peripheral edema and disorders of coagulation. Medical problems associated with chronic hypoxia which are presented and discussed include reentry pulmonary edema and chronic mountain sickness. Preexisting medical problems aggravated by high altitude involve pulmonary disease, coronary artery disease and congestive heart failure. Cold injuries, dehydration, solar radiation injuries and nutritional problems are known to be associated with exposure to high altitude. Key words: [illegible] (physiology), [illegible] (physiology)

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT	21. ABSTRACT SECURITY CLASSIFICATION
☒ UNCLASSIFIED/UNLIMITED ☐ SAME AS RPT. ☐ DTIC USERS	UNCLASSIFIED

22a. NAME OF RESPONSIBLE INDIVIDUAL	22b. TELEPHONE (Include Area Code)	22c. OFFICE SYMBOL
Mark K. Malconian, D.O.	207/985-3293	SGRD-UE-ME

DD Form 1473, JUN 86 — Previous editions are obsolete. — SECURITY CLASSIFICATION OF THIS PAGE: UNCLASSIFIED

CHAPTER 14
MEDICAL PROBLEMS RELATED TO ALTITUDE
IN: HUMAN PERFORMANCE PHYSIOLOGY AND ENVIRONMENTAL MEDICINE AT TERRESTRIAL EXTREMES

Mark K. Malconian, D.O. and Paul B. Rock, D.O., Ph.D.
U.S. Army Research Institute of Environmental Medicine
Natick, Massachusetts 01760-5007

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INTRODUCTION

Each year large numbers of people from low altitude regions travel to areas of high terrestrial altitude for recreational activities including hiking, climbing, skiing and general sightseeing. Others such as miners, scientists and military personnel go to high altitude to work. In some areas of the world including the Tibetan Plateau and the Andean Altiplano, these high altitude sojourners are greeted by members of large indigenous populations which have been residing at lofty elevations for generations. All these people, both sojourners and permanent residents, are exposed to a variety of environmental conditions that have an adverse effect of their performance, health and well being.

Many of the environmental factors which cause medical problems in high altitude environments are not necessarily unique to high altitude, and most of them can be found in other environments. The particular combination of conditions and the nature of exposure to them is unique, however, and results in a distinct set of medical problems. The majority of these medical problems are in some way influenced by the progressively lower partial pressure of oxygen in the atmosphere which is a ubiquitous feature of all high altitude regions.

In this chapter we will review the present understanding of high altitude medical problems along with their treatment and prevention. The bulk of the chapter will concentrate on problems

related to hypobaric hypoxia, for most of those problems are unique to the high altitude environment. Many of the other problems are well discussed in other chapters of this book. In our description of hypoxia-related problems we will attempt to point out which information is based on the results of directed investigation and which is anecdotal. In spite of an increasing interest in high altitude medical problems, many are not well researched, and what is known of them relies heavily on scanty clinical reports, a fact that has not always been acknowledged in previous reviews.

PROBLEMS ASSOCIATED WITH ACUTE HYPOXIA

Hypoxia at high altitude is a direct consequence of decreased barometric pressure of the atmosphere which causes a decreased partial pressure of oxygen. The partial pressure of oxygen in mountain areas ranges from 110mmg at 3000m (100000 ft) to 50mmg (1/3 of sea level) at the summit of Mt. Everest (29,000 feet) (65). Alveolar oxygen pressure at those altitudes ranges from approximately 58mmhg to 30mmhg (36,65). At the lower altitudes the decrease in barometric pressure and PIO2 results in little physiologic compromise, for the hemoglobin saturation changes little. At altitudes equivalent to the summit of Mt. Everest, the hemoglobin saturation has been measured as low as 40 % (62). The physiologic consequences of this profound hypoxia gives rise to many medical problems (62).

Acclimation to high altitude is the process by which an

individual adapts to low oxygen (Chapter 13). The physiologic changes which constitute acclimation are reversible and function primarily to increase oxygen availability at the tissue level. The most significant changes occur in the cardiovascular and pulmonary systems, but there may be adaptation at the cellular level as well. In a sense, hypoxia-induced medical problems at altitude can be viewed as related to acclimation. If acclimation is complete and the body successfully compensates for the hypoxia, no medical problems develop. Both incomplete acclimation and overcompensation result in characteristic physiologic states we recognize as altitude induced pathology.

Acute Mountain Sickness

Acute Mountain Sickness (AMS) is a symptom complex occurring in unacclimatized individuals who ascend rapidly to high altitude. It is self -limiting, but can be very debilitating. With appropriate measures it is preventable (7,9,11,14,15,47,56).

The symptoms of AMS include severe headache, lassitude, irritability, nausea, vomiting, anorexia, indigestion, flatus, constipation and sleep disturbances characterized by periodic breathing. In afflicted individuals 35 % may have localized rales and many have decreased urine output despite adequate hydration (12,14,19,50). Onset of symptoms usually begins 6-12 hours after ascent and peak in intensity in 24-48 hours, resolving in 3-7 days as acclimatization takes place. A small number of individuals may have symptoms longer (50).

The reported incidence of AMS varies from 8-100% of exposed individuals and is directly dependent on both the rate of ascent

and the final altitude reached (10,50). The highest incidence occurs in those sea level residents who fly into high mountain area because flying is the fastest means of ascent and allows no acclimatization. A few individuals experience symptoms as low as 2500m (8000ft), but it is much more common over 3000m (100000ft). Although there is some individual variation in susceptibility to AMS, virtually every one will experience some symptoms of AMS if they go rapidly over 4200m(14000ft) (50). Acclimatization at intermediate altitude decreases the incidence of AMS, but even well acclimatized individuals seem to get a headache upon reaching 5550m (18000ft).

The pathophysiology of AMS is not entirely clear (10,18,20,50,61). Although it is understood that hypoxia is the triggering factor in AMS, the myriad of effects of hypoxia on the human physiology make it difficult to delineate the exact pathophysiology. The symptoms and associated physiological changes resemble closely subclinical cerebral edema. It is known that hypoxia causes a marked increase in cerebral blood flow, that may lead to increased intracranial pressure (ICP). People with AMS show a decreased hypoxic ventilatory response (1,10,14,30,41,50,59). This may further increase cerebral blood flow by a more profound hypoxia and a relative hypercarbia when compared to controls. Hypoxia causes pulmonary hypertension which can lead to right ventricular overload and increased central venous pressure that may increase intracranial pressure leading to some cerebral edema. Hypoxia may cause cytotoxic injury to brain cells and the blood brain barrier leading to

intracellular and extracellular edema causing an increase in ICP. Thus there are several possible mechanisms to explain the occurence of mild cerebral edema in AMS (1,5,10,11,18,50,61). Research is being conducted in this area to define this pathophysiology.

Diagnosis of AMS is based upon the presence of symptoms in conjunction with a rapid ascent to altitudes over 3000m (10000ft). The differential diagnosis includes such things as dehydration, hangover, exhaustion, hypothermia, migraine, and hysteria (10,50) It is important to rule out full blown High Altitude Cerebral Edema and High Altitude Pulmonary Edema (see below) both of which can be rapidly fatal if left untreated.

Although AMS is selflimiting the symptoms are debilitating enough often to require treatment. Treatment consists of descent, oxygen, acetazolamide and in limited cases, furosemide (50). Descent is the treatment of choice and should continue until symptomatic improvement occurs. Often a descent as little as 300m will be all that is required (50). Oxygen administration for obvious reasons is equally effective however often impractical in mountain environments. Anecdotal reports of acetazolamide 250mg every six hours will relieve symptoms, although it is more effective if used prophylactically (2,3,8,10,13,50). Furosemide may be useful if antidiuresis is present, however care must be taken not to give furosemide to individuals who are dehydrated (a common condition in people at altitude). For mild cases symptomatic treatment may be all that is required. Analgesics have varying success in treating cephalgia of AMS. Any respiratory depressant is contraindicated.

Nausea and vomiting may be abated with compazine (10,50).

Many potential prophylactic measures have been formally or informally investigated for AMS. These include varying the rate of ascent, pharmacologic agents, dietary manipulations and various folk remedies. The ideal agent would prevent symptoms caused by a rapid ascent while allowing the body to acclimatize so that the prophylactic measure could be discontinued.

The use of gradual ascent, called staging allows the body to acclimatize and thus prevent AMS symptoms (13,21,50). The most widely recommended profile is to take one day of rest at 2500m (8000ft) and one additional day at rest for every 600m (2000ft) gain in altitude above that (13,50). Because the exaggerated desaturation and hypoxia occurring during sleep appears to contribute to symptoms, it is advisable to sleep as low as possible (10,50,60,61). This is reflected in the moutaineers's axiom, "climb high, sleep low".

Pharmacologic agents are useful in prophylaxis of AMS in individuals who do not have time for gradual ascent. Military personnel often fall into this category. Acetazolamide 250 mg every six hours is effective in preventing or reducing AMS symptoms in many people at altitude (2,3,8,9,13,33,56). Currently the Army recommends that acetazolamide be continued for 48 hours after initial ascent (50). It is common practice in mountaineering expeditions to continue acetazolamide throughout the ascent phase which may last many weeks. Acetazolamide does not prevent symptoms in all people and side effects such as paraesthesias are common. It is contraindicated in people with

sulfa allergies.

A number of other prophylactic agents have been recommended but none are in widespread use. Dexamethasone 4 mg every six hours has been shown recently to be effective in preventing AMS symptoms (29). Spironolactone has also been used experimentally with varying success (50). A number of other agents including naproxen, dilantin, ergotamine and furosemide have been shown not to be effective. The chewing of cocoa leaves is a folk remedy of the South American Indians, but can not be recommended for many reasons. Finally there is some evidence that a diet high in carbohydrates may be helpful in preventing AMS (22,50).

High Altitude Cerebral Edema

High Altitude Cerebral Edema (HACE) is a clinically apparent cerebral edema seen in individuals who ascend rapidly to high altitude. Although it has a low incidence of occurrence, HACE is potentially fatal if left untreated (5,10,18,25,50,56).

The early symptoms of HACE resemble those of AMS (5,10,18,50). In fact HACE may be a severe form of AMS (5,25,50). Early symptoms include severe headache, nausea, vomiting, and extreme lassitude. Truncal ataxia, and change of mental status help differentiate early HACE from AMS (5,9,18,50). Left untreated a variety of focal and generalized symptoms will manifest including visual changes, anesthesias , paresthesias, rigidity, hemiparesis, clonus, pathological reflexes, hyperreflexia, bladder and bowel dysfunction, hallucinations and seizures (5,10,15,18,25,50,56). Other clinical manifestations of increased intracranial pressure will be seen if one has the

appropriate diagnostic tools. Left untreated HACE will progress to obtundation, coma and death.

The incidence of HACE is low, occurring in about 1% of individuals exposed to altitude (5,10,15,18,50,56). Rapid ascent and lack of acclimatization are predisposing factors. It has been reported as low as 2700m (9000ft) (18,50), but the majority of cases occur above 3600m(12000ft). High altitude pulmonary edema (see below) often occurs with HACE.

Pathological examination of brain tissue from HACE patients reveals gross cerebral edema (10,18,50). The mechanism of edema formation may be cytotoxic (due to hypoxia), vasogenic (due to increased cerebral blood flow and increased blood pressure), or most likely a combination of above (5,10,11,18,25,50).

The diagnosis of HACE is based upon the presence of symptoms in conjunction with rapid exposure to high altitude (10,18,50). Differential diagnosis includes, cerebral thrombosis or hemorrhage, infections, migranous encephalopathy, and severe cerebral hypoxia from high altitude pulmonary edema. Because it is difficult to make a definitive diagnosis of HACE in mountainous conditions all suspected cases should be evacuated to lower altitudes without delay (10,18,50).

The definitive treatment of HACE is to descend. In general, the greater the descent the better, preferably to an altitude of less than 2500m(8000ft) (18,50). Descent of more than 300m (1000ft) may be required to cause any clinical improvement. Supplemental oxygen can be a useful adjunct but should not be used as a substitute for descent (9,10,18,50). Dexamethasone 4-6

mg q 4 hours is a recognized treatment (10,18,50). Furosemide and mannitol has also been used with some success (50). Their use must be tempered with the awareness that many HACE victims are dehydrated despite the presence of HACE.

While there is no definitive evidence for effective prophylactic measures for HACE, the close relation between HACE and AMS would suggest that the measures previously discussed for the prevention of AMS may also be effective for HACE (particularly gradual ascent) (18,50).

High Altitude Pulmonary Edema

High Altitude Pulmonary Edema (HAPE) is a noncardiogenic pulmonary edema caused by altitude exposure in unacclimitized but otherwise healthy individuals (10,24,26,38,50). Young active males seem particularly susceptible (10). Like HACE, HAPE can be rapidly fatal if left untreated, but usually responds to descent in altitude.

HAPE usually manifests itself 12-96 hours after a rapid ascent to high altitude (10,24,26,38,50). The onset is often subtle manifested by fatigue, dyspnea on exertion and nonproductive cough (10,24,26,38,50). Frequently AMS symptoms (nausea and headache) are also present (10,24,26,38,50). Early signs of HAPE include tachypnea, tachycardia and rales (10,24,50). As HAPE progresses, dyspnea at rest and orthopnea occur. The cough often becomes productive with blood tinged and eventually pink frothy sputum (10,50). Cyanosis becomes apparent. Mental status changes may occur indicative of severe hypoxia or HACE (10,18,50). Chest xray in the HAPE patient

reveals multiple small patchy infiltrates which are asymmetric and enlarged pulmonary vasculature with a normal size heart (Figure 1) (10,24,26,50). EKG may show tachycardia, right ventricular overload, right axis deviation, T wave inversions and other nonspecific ST-T wave changes (26,50). Without a previous EKG for comparison, an EKG may be of little useful information. If left untreated HAPE can run a fulminant course progressing to coma and death in less than 12 hours (10,50).

HAPE occurs in unacclimatized individuals who ascend rapidly to high altitude (10,24,26,38,50). The incidence is higher than that of HACE and appears to vary with age and activity. Children and young adults have a much higher incidence than older individuals (50). Exercise at altitude, by further increasing an already increased pulmonary artery pressure may increase susceptibility to HAPE or more likely exacerbate the condition (24,50,61). HAPE is also more likely to occur in individuals who have previously experienced HAPE (50). Subclinical HAPE evidenced by rales, may occur much more frequently than previously thought (12,50,56). Reports have described rales in one third to one half of persons at altitude higher than 3500m(11500ft) (10,24,38,61).

The pathophysiology of HAPE has recently become better understood. Recent findings in HAPE include high pulmonary artery pressure (compared to assymptomatic controls at altitude), normal left atrial filling pressure (4,10,48,50,51), normal cardiac function, blunted chemosensitivity and hypoxic ventilatory depression (17,28) and high protein pulmonary lavage

samples with predominance of macrophages and complement activators (52). These findings suggest a high pressure high permeability edema similar to neurogenic pulmonary edema (50). Other evidence indicates that HAPE may be a pure pressure edema due to redistributed blood flow away from microembolized vessels caused by hypoxia induced coagulopathy.

The diagnosis of HAPE is based upon the signs and symptoms of pulmonary edema in otherwise healthy individuals exposed to high altitude. The differential diagnosis includes pneumonia, congestive heart failure, pulmonary embolus and in the military setting, exposure to chemical warfare agents.

Treatment of HAPE depends on its severity, but virtually all cases will respond to descent (10,50). In severe cases descent is mandatory (10,50). Because exercise and hypoxia increases pulmonary artery pressure, descent should be via litter using supplemental oxygen if possible (50). Mild cases may be treated in place with bed rest and oxygen, but descent is mandatory for all but mild cases (10,24,38,50). Pharmacologic agents which have been useful in treating severe HAPE include furosemide and morphine sulphate (10,50). While morphine can depress respiration, its cautious use is justified similarly to its use in cardiogenic pulmonary edema (50). While using either of these agents it must be remembered that despite HAPE or HACE the person may be volume depleted and the addition of a diuretic and vasodilator may aggravate the presence of volume depletion (10,50). Aminophylline, ispoprterenol and digoxin are not useful (10,50). Dexamethasone is not useful unless HACE accompanies HAPE (10,50).

Prophylactic measures for HAPE involve avoiding the risk factors for all altitude illnesses, a gradual ascent to allow for acclimatization, limited physical activity until acclimatization occurs, and because arterial desaturation is greatest during sleep, sleep at as low an altitude as possible. Avoiding cold exposure is also helpful (4,10,50). Acetazolamide may also be useful in preventing HAPE especially in persons with a prior history of HAPE (10,14,50).

High Altitude Retinal Hemorrhages (HARH)

High Altitude Retinal Hemorrhages (HARH) are the result of an altitude induced retinopathy. Although common, they are self limited and are of little consequence unless they occur in the macula (6,10,37,58). Most likely they have a similar pathophysiologic mechanism as AMS and HACE (6,10,37,58).

HARH are normally asymptomatic unless they occur in the macula. Macular hemorrhage will result in blurred vision and scotomata (10). Fundoscopic exam will reveal disc hyperemia and engorgement and increased tortousity of vessels in virtually all personnel exposed to high altitude without supplemental oxygen. Typically retinal hemorrhages appear as flame type hemorrhages in the superficial layers of the retina, but hemorrhages in the deeper layers are possible. Multiple hemorrhages are common (Figure 2a, 2b, 3a, 3b).

The incidence of HARH varies directly with altitude. They are unknown below 3000m(100000 ft), but the incidence approaches 100% above 6800m(22000ft) (6,10,37,50,58). Strenuous exercise

may increase the risk of retinal hemorrhage by increased systolic blood pressure as well as a forced valsalva maneuver during a technical climb or while defacating. Unlike other altitude illnesses HARH are not related to the state of altitude acclimatization, and multiple occurrences are possible throughout any sojourn.

The exact mechanism of HARH is unknown. Most feel it results from pressure surges caused by exercise or other activity in retinal vessels which are maximally dilated due to hypoxia induced increases in cerebral blood flow (6,10,37,50,58).

HARH usually go unrecognized, but may be easily diagnosed by fundoscopic exam. The differential diagnosis includes hemorrhage from vascular disease, diabetes mellitis, septic infarcts and organic hypoxia from cardiac and respiratory disease.

HARH are self limited and resolve one to two weeks after descent. There is no treatment other than descent and there is no prophylaxis. Because non-macular hemorrhages are of little consequence, descent is not necessary. When a macular hemorrhage is diagnosed, descent is imperative in order to promote healing, prevent further hemorrhages and prevent visual deficits (6,37,58).

Generalized Peripheral Edema

Generalized edema occurs in some individuals when initially exposed to high altitude and with repeated exposure to high altitude. It is characterized by a pronounced edema of the face and upper extremities, decreased urine output and weight gain

(50). Although uncomfortable it is a benign condition. The edema resolves with descent but will reoccur with subsequent ascent. It is more common in females but is not related to menses or birth control pills (50). Furthermore it does not appear to have any relation with HACE or HAPE. The diagnosis is based on history and physical findings. The differential diagnosis includes cardiogenic edema and allergic reactions. Edema can be treated successfully with diuretics and salt restriction (50). Prophylaxis with the same regime is usually successful in preventing edema in susceptible individuals who must travel to high altitude.

Disorders Of Coagulation

People who ascend to high altitude appear to be at increased risk for venous thrombosis, pulmonary embolus and stroke (10,35,44,50,55). The possible causes for these phenomena include hypoxia induced clotting abnormalities, polycythemia, dehydration, cold and venous stasis during prolonged periods of inactivity during inclement weather (10). Clotting abnormalities observed include thrombocytopenia, decreased fibrinogen, decreased factor VIII and increased 2,3 DPG and FDP (10,35,44,50,55). What is puzzling is that people have been observed with abnormal clotting parameters with no clinical manifestations and also with clinical manifestations from a coagulation disorder with normal laboratory clotting parameters (50). There are no general trends in the clotting parameters upon ascent to high altitude, however there are numerous case

reports of markedly abnormal clotting parameters in some individuals. More studies are needed to delineate this problem.

PROBLEMS ASSOCIATED WITH CHRONIC HYPOXIA

Reentry Pulmonary Edema

Reentry Pulmonary Edema is HAPE that occurs in high altitude natives upon returning to high altitude after traveling to low altitude areas. The occurence of Reentry Pulmonary Edema may be related to the rate of ascent upon return to high altitude. Case reports are more frequent in high altitude areas where rapid ascent is possible and absent from areas where rapid ascent is not possible (10,27,53). It has been postulated that this occurs due to increased smooth muscle component of the chronically hypoxic pulmonary arteries that when rexposed to hypoxia develop abnormally high pulmonary artery pressure (10,27,50,53).

Chronic Mountain Sickness

Chronic Mountain Sickness (CMS) is an ailment of people who reside at high altitude for a prolonged period of time. It is characterized by an erythrocythemia in high altitude residents (hemoglobin > 20gm/dl) (10,31,39,40,50,66). It occurs most commonly in people born at low altitude who move to high altitude, but also occurs in people who have always resided at high altitude. It was first described by Monge in 1928 when studying inhabitants of the Andes, and is often referred to as Monge's disease (40). Incidence of the disease is low in women

and some populations living at high altitude have marked differences in incidence (10,42,50).

Symptoms are those of primary polycythemia: lethargy, dizziness, headache, sleep disturbances and mental status changes. Diagnosis is made by the presence of symptoms in high altitude residents with marked polycythemia (10).

Studies of CMS patients have shown excessive hypoxia for a given altitude when compared to other residents, blunted hypoxic ventilatory response, hypoventilation, widened A-a gradient and severe oxygen desaturation during sleep (10,16,31,32,39,46,50,64).

The surest form of treatment is relocation to lower altitude. When not practical, phlebotomy may provide subjective improvement. Low flow oxygen during sleep may also provide some improvement. Medroxyprogesterone acetate and acetazolamide have been shown to be successful, presumably due to the respiratory stimulant effect of these drugs (10,31,39,50).

PRE-EXISTING MEDICAL PROBLEMS AGGRAVATED BY HIGH ALTITUDE

There is little data available about the effect of altitude on pre-existing medical problems. Much of the following discussion is based on speculation. Pre-existing medical problems are however of great concern to many who journey to altitude.

Pulmonary Disease

The results of pulmonary disease at sea level may be

pulmonary hypertension, V/Q mismatch, impaired diffusion capacity, and decreased ventilatory muscle capacity. These impairments may cause illness at even modest altitudes.

People with pulmonary hypertension at sea level will experience further increases pulmonary artery pressure at altitude from hypoxia, and thus worsening there condition and perhaps making them more susceptible to other altitude illnesses.

It seems obvious that persons who are hypoxic from COPD at sea level will have greater hypoxia and may be more symptomatic at high altitude than at sea level. These patients may want to avoid going to altitude. Further, people with COPD who are compensated or assymptomatic at sea level may experience symptoms upon ascending to altitude (50). An individual with COPD and modest sea level hypoxia, may experience a substantial decrease in oxygen saturation at a modest altitude due to hemoglobin oxygen affinity at lower plasma oxygen partial pressures (10,50). Also individuals with COPD may not be able to increase minute ventilation in response to the hypoxia of altitude the way a healthy individual would, thus causing them more profound hypoxia. In patients with COPD who might be able to increase ventilation upon ascending to altitude, and who have decreased respiratory muscle reserve might conceivably develop respiratory muscle fatigue and failure. Thus it would seem prudent that in people with COPD with sea level hypoxia or carbon dioxide retention that sojourns to high altitude be done with great care and possible supplemental oxygen. As stated previously much of the above is speculation and based on anecdotal reports.

It would seem likely that patients with obstructive sleep-

apnea at sea level, would be more symptomatic at altitude. Hypoxia during obstructive apneic periods would likely be more profound than at sea level. It is difficult to predict in central sleep-apnea the effect of sleeping at high altitude due to the changes in arterial pH, cerebral spinal fluid pH and chemoreceptor sensitivities that may take place at altitude.

Studies from Colorado has show lung disease to be more common at high altitude (42,43), and that elderly people with lung disease at altitude improve upon relocating to lower altitude (49).

Coronary Artery Disease

The question often arises as to the effect of going to altitude in patients with Coronary Artery Disease (CAD). It has been shown in healthy individuals performing maximal exercise at 29000 ft in an altitude chamber (after a six week gradual ascent), that there was no evidence of ischemia by EKG (51). Further during near maximal exercise there was no evidence of ischemia by echocardiogram (57) and cardiac output was maintained (when compared to sea level values) (48). It appears in the healthy heart there is not an increased risk of ischemia under severe hypoxia at altitude. One report of patients with CAD studied 11 patients with CAD at altitudes up to 3170m (45). In this study all patients who had normal exercise EKG's at sea level also did at 3170m. Only patients symptomatic at sea level were also symptomatic at altitude. Further studies need to be done. It is also worth considering patients with CAD who have a degree of coronary artery spasm. It is known that hypoxia can

induce spasm in these patients. Therefore they may be at risk for coronary artery spasm upon ascent to altitude. At the present time it is unclear as to the risk of patients with CAD who ascend to high altitude.

Congestive Heart Failure

Heart failure both right sided and left would be expected to decompensate at altitude due to fluid retention, hypoxia and its effect on the pulmonary vasculature. Hackett has observed repeatedly older people with CHF who are brought to 2000m, decompensate (10). Thus it would seem prudent for patients with CHF to avoid going to altitude.

PROBLEMS NOT ASSOCIATED WITH HYPOXIA

Cold Injuries

Cold injuries in high altitude environments are caused by a combination of environmental and physiological factors. In general the temperature decreases two degrees C for every 300m elevation (50). In addition the climate of mountains causes a high windchill factor and much lower effective temperatures. The low temperatures combined with peripheral vasoconstriction, dehydration and hemoconcentraion at high altitude causes the full spectrum of cold injury including, hypothermia, frost nip, frost bite and immersion foot (50). The diagnosis and treatment of cold injury is discussed in chapter 11. Prevention of cold

injury is based upon keeping personnel adequately hydrated, nourished and protected from cold exposure.

Dehydration

Dehydration at high altitudes results from the combination of low environmental humidity with a number of physiological and behavioral factors. There is an increased loss of fluids at altitude due to hypoxia induced fluid shifts, diuresis and hyperventilation (50). At the same time, personnel often have a decreased fluid intake due to blunted thirst sensation from cold, hypoxia, nausea from AMS and the lack of potable water. Dehydration is a serious problem in and of itself but also greatly increases susceptibility to cold injury. Dehydration can be prevented by a conscious effort to imbibe fluids in the absence of thirst (50).

Solar Radiation Injuries

Ultra-violet (UV) radiation injury at high altitude is the result of decreased UV wave filtering capacity of the thinner atmosphere and increased reflection of light from snow and rock surfaces. Injuries include sunburn and snowblindness. Sunburn can occur rapidly and can be severe. Treatment is the same as at low altitude and can be prevented with limiting skin exposure with clothes and sunscreens. Snow blindness (photophthalmia) can develop within 12 hours of sun exposure (50). It results from UV absorption by the eye. Although selflimiting it can be extremely painful and debilitating. Opthalmic steroid preparations may provide symptomatic relief (50). Proper eye protection will prevent its occurrence (50).

Nutrition

Like dehydration several physiological and behavioral factors contribute to poor nutrition at high altitude. Weight loss occurs due to decreased caloric intake secondary to AMS, and lack of energy to prepare and consume food. Evidence also exists for fat malabsorbtion at high altitude presumably due to hypoxia. Anecdotal and recent investigations suggest diets high in carbohydrates may be helpful due to ease of digestion and increased ventilation (50).

CONCLUSIONS

Exposure to high terrestrial altitude is associated with a distinct set of medical problems caused by a unique combination of environmental stressors including hypobaric hypoxia, cold, low humidity, increased solar radiation and rugged terrain. Many of the problems related to prolonged hypoxic exposure are unique to high altitude and can be viewed as resulting from inappropriate acclimation to the hypoxic stress. Little is known of the precise pathophysiologic mechanisms involved, but some guidelines for treatment and prevention exist none-the-less. The most effective treatments seem to involve decreasing the level of hypoxemia by descending to lower altitudes. Much research needs to be done in this area. The medical problems which are not primarily related to hypoxia are better understood in terms of their pathophysiology and are treated as they would be in any other environment.

REFERENCES

1. Anholm, J.D., C.S. Houston, and T.M. Hyers, The relationship between acute mountain sickness and pulmonary ventilation at 2,835 meters (9.300 feet). Chest 75(1):33-36, 1979.

2. Birmingham Medical Research Expeditionary Society Mountain Sickness Study Group: Acetazolamide in control of acute mountain sickness. Lancet 1:180-183, 1981.

3. Cain, S.M., and J.E. Dunn II. Low doses of acetazolamide to aid accomodation of men to altitude. J. Appl. Physiol. 21:1195-1200, 1965.

4. Chauca, D. and J. Bligh. An additive effect of cold exposure and hypoxia on pulmonary artery pressure in sheep. Res. Vety Sci. 21: 1976.

5. Dickinson, J.G. High altitude cerebral edema: Cerebral acute mountain sickness. Sem. Resp. Med. 5:151-158, 1983.

6. Frayser, R., C.S. Houston, A.C. Bryan, I.D. Rennie and G. Gray. Retinal hemorrhage at high altitude. N. Engl. J. Med. 282:1183-1184, 1970.

7. Gray, G.W., A.C. Bryan, R. Frayser, C.S. Houston, and I.D.B. Rennie. Control of acute mountain sickness. Aerospace Med. 42:81-84, 1971.

8. Greene, M.K., A.M. Kerr, I.B. Mcintosh, and R.J. Prescott.

Acetazolamide in prevention of acute mountain sickness: a double blind controlled cross-over study. Br. Med. J. 233:811-813, 1981.

9. Hackett, P.H. Mountain Sickness: Prevention, Recognition and Treatment. New York: American Alpine Club, 1980.

10. Hackett, P.H. and T.F. Hornbein. Disorders of High Altitude. In Murray, J.F. and J.A., Nadel (eds), Textbook of Resiratory Medicine. Saunders, Philadelphia, 1988.

11. Hackett, P.H., and D. Rennie. Acute mountain sickness. Sem. Resp. Med. 5:132-140, 1983.

12. Hackett, P.H., and D. Rennie. Rales, peripheral edema, retinal hemorrhage and acute mountain sickness. Am. J. Med. 67:214-218, 1979.

13. Hackett, P.H., and D. Rennie. Avoiding mountain sickness. Lancet 2:938, 1978.

14. Hackett, P.H., D. Rennie, S.E. Hofmeister, R.F. Grover, E.B. Grover, and J.T. Reeves. Fluid retention and relative hypoventilation in acute mountain sickness. Respiration 43:321-329, 1982.

15. Hackett, P.H., D. Rennie and H.D. Levine. The incidence, importance, and prophylaxis of acute mountain sickness. Lancet 2:1149-1154, 1976.

16. Hackett, P.H., J.T. Reeves, R.F. Grover and J.V. Weil.

Ventilation in human populations native to high altitude. In West, J.B., Lahiri, S. (eds.): High Altitude and Man, Washington, D.C.: American Physiological Society, 1984, pp. 179-191.

17. Hackett, P.H., R. Roach, R.B. Schoene, G. Harrison and W. Mills. Blunted chemosensitivity and hypoxic ventilatory depression in high altitude pulmonary edema. Fed. Proc. 44:1563, 1985.

18. Hamilton, A.J., A. Cymerman and P. Black. High Altitude Cerebral Edema. Neurosurgery 19:841-849, 1986.

19. Hannon, J.P., K.S.K. Chinn and J.L. Shields. Effects of acute high altitude exposure on body fluids. Fed. Proc. 283:1178-1184, 1969.

20. Hansen, J.E., and W.O. Evans. A hypothesis regarding the pathophysiology of acute mountain sickness. Arch. Environ. Health 21:666-669, 1970.

21. Hansen, J.E., C.W. Harris, W.O. Evans. Influence of elevation of origin, rate of ascent and a physical conditioning program on symptoms of acute mountain sickness. Military Med. 132:585-592, 1967.

22. Hansen, J.E., L.H. Hartley, and R.P. Hogan. Arterial oxygen increase by high carbohydrate diet at altitude. J. Appl. Physiol. 33:441-445, 1972.

23. Heath, D., and D.R. Williams. Man at High Altitude.

Churchill livingstone, Edinburgh, 1981.

24. Houston, C.S. Acute pulmonary edema of high altitude. N. Engl. J. Med. 263:478-480, 1960.

25. Houston, C.S., and J.D. Dickinson. Cerebral form of high altitude illness. Lancet 2:758-761, 1975.

26. Hultgren, H.N. High Altitude Pulmonary Edema. Biomedical Problems of High Terrestrial Altitudes. Springfield, VA. Federal Scientific and Technical Information, 1967, pp.131-141.

27. Hultgren, H.N., and E.A. Marticorena. High altitude pulmonary edema: Epidemiologic observations in Peru. Chest 74:372-376, 1978.

28. Hyers, T.M., C.H. Scoggin, D.H. Will, R.F. Grover and J.T. Reeves. Accentuated hypoxia at high altitude in subjects susceptible to high altitude pulmonary edema. J. Appl. Physiol. 46:41-46, 1979.

29. Johnson,T.S., P.B. Rock, C.S. Fulco, L.A. Trad, R.F. Spark, and J.T. Maher. Prevention of acute mountain sickness by dexamethasone. N. Engl. J. Med. 310:683-686, 1984.

30. King, A.B., and S.M. Robinson. Ventilation response to hypoxia and acute mountain sickness. Aerospace Med. 43:419-421, 1972.

31. Kryger, M.H., and R.F. Grover. Chronic mountain sickness. Sem. Resp. Med. 5:164-168, 1983.

32. Kryger, M., R. McCullough, R. Doekel, D. Collins, J.V. Weil, and R.F. Grover. Excessive polycythemia of high altitude: Role of ventilatory drive and lung disease. Am. Rev. Resp. Dis. 118:659-665, 1978.

33. Larson, E.B., R.C. Roach, R.B. Schoene and T.F. Hornbein. Acute mountain sickness and acetaazolamide: Clinical efficacy and effect on ventilation: J. Amer. Med. Assoc. 248:328-332, 1982.

34. Lassen, N. Factors limiting performance at extreme altitude: Acute mountain sickness. In Houston, C., and Sutton, J. (eds.). Prodeedings of the Fourth International Hypoxia Symposium, 1985 (in press).

35. Maher, J.T., P.H. Levine and A. Cymermen. Human coagulation abnormalities during acute exposure to hypobaric hypoxia. J. Appl. Physiol. 41:702-707, 1976.

36. Malconian, M.K., P.B. Rock, J.T. Reeves, A. Cymerman, J.R. Sutton, B.M. Groves, P.D. Wagner, H. Donner, L. Trad, V. Forte, P.M. Young, and C.S. Houston. Operation Everest II: Alveolar and arterial gases at extreme altitude. Submitted.

37. McFadden, D.M., C.S. Houston, J.R. Sutton, A.C.P. Powles, G.W. Gray and R.S. Roberts. ' High altitude retinopathy. J Amer. Med. Assoc. 245:581-586, 1981.

38. Menon, N.D. High altitude pulmonary edema. N. Engl. J. Med. 273:66-72, 1965.

39. Monge, C.C. and M.C. Monge. Natural acclimatization to high altitudes: Clinical conditions in life at high altitudes. Scientific Publ. No. 140, Washington, D.C., Pan American Health Organization, 1966, pp. 46-52.

40. Monge, M.C. La Enfermedad de Los Andes. Sindromes Eritremicos. Ann. Fac. Med. (Peru) 11:1, 1928.

41. Moore, L.G., G.L. Harrison, R.E. McCullough, R.G. McCullough, A.J. Micco, A. Tucker, J.V. Weil, and J.T. Reeves. Low acute hypoxic ventilatory response and hypoxic depression in acute altitude sickness. J. Appl. Physiol., 60: 1401-1406, 1986.

42. Moore, L.G. and J.G. Regensteiner. Adaptation to high altitude. Ann. Rev. Anthropol. 12:285-304, 1983.

43. Moore, L.G., A.L. Rohr, J.K. Maisenbach and J.T. Reeves. Emphysema mortality is increased in Colorado residents of high altitude. Am. Rev. Resp. Dis. 126:225-228, 1982.

44. O'Bradovich, H., M. Andrew, G.W. Gray and G. Coates. Hypoxia alters blood coagulation during acute decompression in humans. Physiologist 25:276, 1982.

45. Okin, J.T. Response of patients with coronary heart disease to exercise at varying altitudes. In Vogel, J.H.K. (ed.): Hypoxia, High Altitude and the Heart. A monograph in the series: "Advances in Cardiology," Basel: S. Karger., 1970.

46. Penaloza, D., and F. Sime. Chronic cor pulmonale due to

loss of altitude acclimatization (chronic mountain sickness). Am.J. Med. 50:728-743, 1971.

47. Ravenhill, T.H. Some experiences of mountain sickness in the Andes. J. Trop. Med. and Hygiene. 20:313-320, 1913.

48. Reeves, J.T., B.M. Groves, J.R. Sutton, P.D. Wagner, A. Cymerman, M.K. Malconian, P.B. Rock, P.M. Young, and C.S. Houston. Operation Everest II: Preservation of cardiac function at extreme altitude. Submitted.

49. Regensteiner, J.G., and L.G. Moore. Migration of the elderly from high altitudes in Colorado. J. Amer. Med. Assoc. 253:3124-3128, 1985.

50. Rock, P.B. Medical problems of High Terrestrial Altitudes. U.S. Army Flight Surgeons Manual, 1986.

51. Rock P, M. Malconian, H. Donner, B. Groves, J. Reeves, J. Sutton, J. Alexander, H. Hultgren, A. Cymerman, and C. Houston. Operation Everest II: Electrocardiography During Maximal Exercise At Extreme Altitude. Medicine and Science in Sports and Exercise. 18: S74, 1986.

52. Schoene, R.B., P.B. Hackett, W.R. Henderson, E.H. Sage, M. Chow, R.C. Roach, W.J. Mills and T.R. Martin. High Altitude Pulmonary Edema; Characteristics of Lung Lavage Fluid. JAMA 256:1 1986.

53. Scoggin, C.E., T.M. Hyers, J.T. Reeves and R.F. Grover. High altitude pulmonary edema in the children and young adults of Leadville, Colorado. N. Engl. J. Med. 297:1269-1273, 1977.

54. Severinghaus, J.W., H. Chiodi, E.I. Eger II, B. Brandstater, and T.F. Hornbein. Cerebral blood flow in man at high altitude. Circ. Res. 19:274-282, 1966.

55. Singh, I., I.S. Chohan, and N.T. Matthew. Fibrinolytic activity in high altitude pulmonary edema. Indian J. Med. Res. 57:210, 1969.

56. Singh, I., P.K. Khanna, M.C. Srivastava, M. Lal, S.B. Roy and C.S.V. Subramanyam. Acute mountain sickness. N. Engl. J. Med. 280:175-184, 1969.

57. Suarez, J.M., J.K. Alexander, and C.S. Houston. Operation Everest II: Left ventricular systolic function in man at high altitude assessed by two dimensional echocardiography. Submitted.

58. Sutton, J.R. High altitude retinal hemorrhage. Sem. Resp. Med. 5:159-168, 1983.

59. Sutton, J.R., A.C. Bryan, G.W. Gray, E.S. Horton, A.S. Rebuck, W. Woodley, I.D. Rennie, and C.S. Houston. Pulmonary gas exchange in acute mountain sickness. Aviat. Space Environ. Med. 47:1032-1037, 1976.

60. Sutton, J.R., C.S. Houston, A.L. Marnsell, M.D. McFadden, P.H. Hackett, J.R.A. Rigg, and A.C.P. Powles. Effect of

acetozolmide on hypoxia during sleep at high altitude. N. Engl. J. Med. 301:1329-1331, 1979.

61. Sutton, J.R., and N. Lassen. Pathophysiology of acute mountain sickness and high altitude pulmonary edema. Bull. Europ. Physiopath. Resp. 15:1045-1052, 1979.

62. Sutton J, Reeves J, Wagner P, Groves B, Cymerman A, Young P, Malconian M, and Houston C. Oxygen Uptake During Exercise At Extreme Simulated Altitude Maintained By Marked Reduction In Mixed Venous Oxygen Tension. Federation Proceedings, 45: 882, 1986.

63. Wagner,P, .J.Reeves, J.Sutton, A.Cymerman, B. Groves, M. Malconian, and P.Young. Possible Limitation Of Maximal O2 Uptake By Peripheral Diffusion. Am. Rev. Resp. Dis., 131: A207, 1986.

64. Weil, J.V., M.H. Kryger and C.H. Scoggin. Sleep and breathing at high altitude. In Sleep Apnea Syndromes. Guilleminault, C., and W.C. Dement (eds): New York; Liss, 1978, 99 119-136.

65. West, J.B. Man on the Summit of Mount Everest. In West, J.B. and S. Lahiri (eds.): High Altitude and Man. Bethesda American Physiological Society, Bethesda, , 1984, pp. 5-17.

66. Winslow, R.M. High altitude polycythemia. In West, J.B., and S. Lahiri, (eds.): High Altitude and Man. Bethesda, American Physiological Society, 1984, pp. 163-172.

Legend

Figure 1. High Altitude Pulmonary Edema (HAPE). (Courtesy of Charles S. Houston, M.D.)

Figure 2. High Altitude Retinal Hemorrhages (HARH)

A. Photo taken immediately upon return to sea level after a six week gradual ascent to 25000 ft. in an altitude chamber.

B. Same subject 10 days later.

Figure 3. High Altitude Retinal Hemorrhages (HARH) (Courtesy of Charles S. Houston, M.D.)

A. HARH after several days at 18500 ft.

B. Same subject two weeks later.


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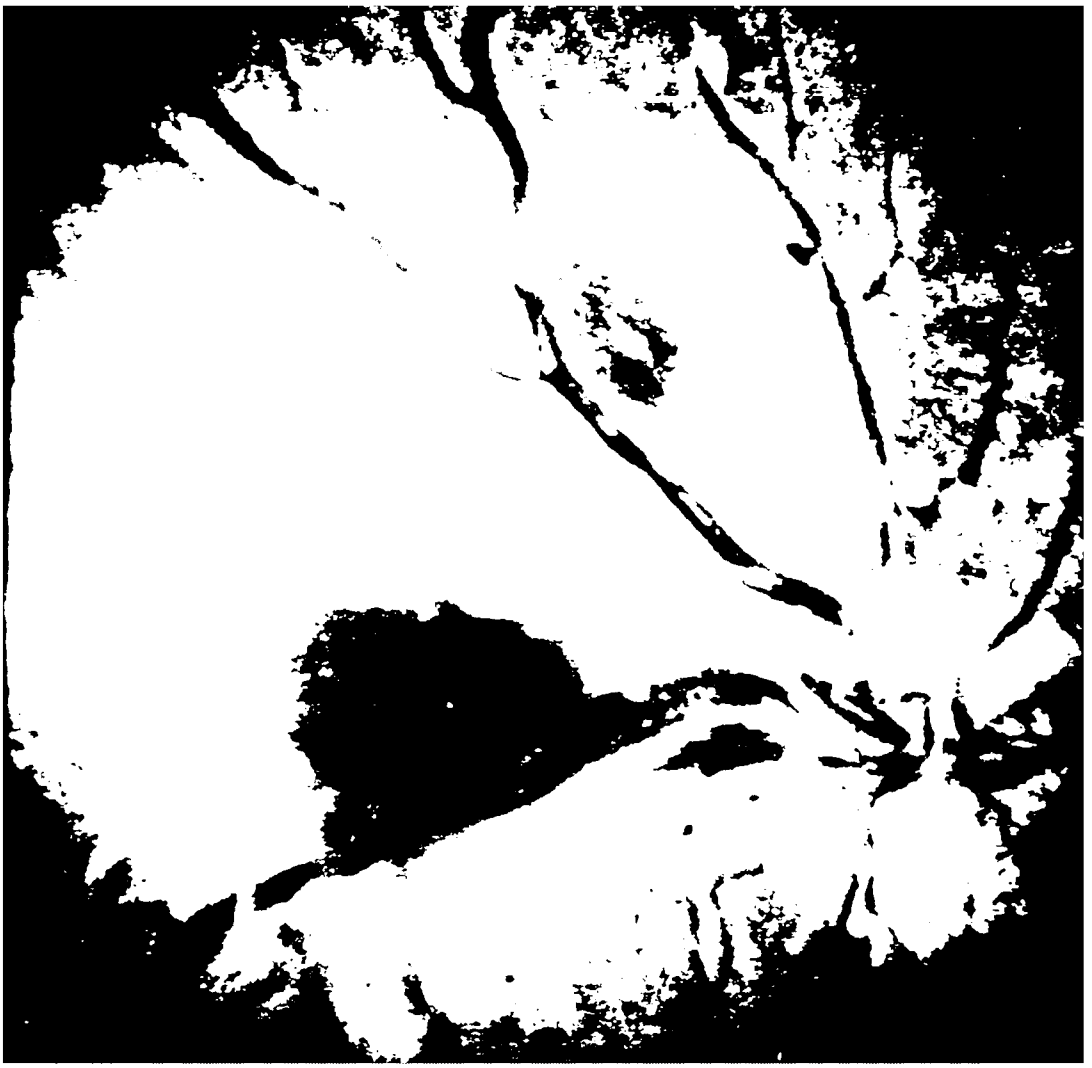

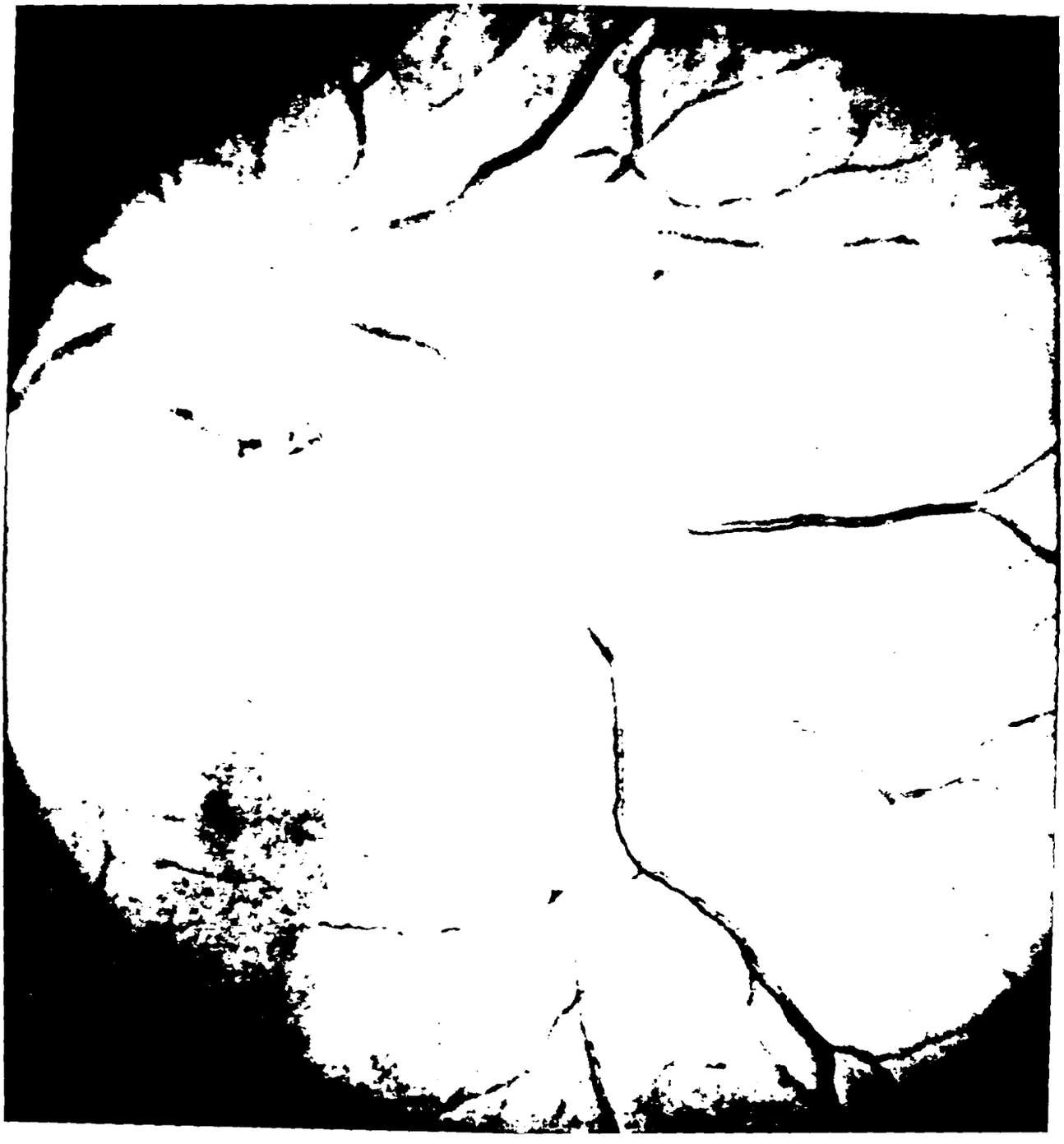

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