Acta Andina (1996) 5:3-8 Vol. 5. N°.1

Printed in Perú

# NEW CONCEPTS ON CHRONIC MOUNTAIN SICKNESS

ZUBIETA-CASTILLO, G. AND ZUBIETA-CALLEJA, G.

High Altitude Pathology Institute (IPPA). La Paz, Bolivia

## ABSTRACT

The adaptation capacity of human beings to atmospheric pressure changes is remarkable. In high altitude adaptation (HAA) we should consider: that of normal man and that of the diseased. The acute HAA can be more dramatic and problematic than chronic HAA. The diseases are the same as those at sea level and have hypoxic physiognomies. The term Chronic Mountain Sickness (CMS), has created confusion, because it includes pulmonary diseases that cause Excessive Erythrocytosis (EE). EE, is a mechanism of adaptation that increases the oxygen carrying capacity of the blood by increasing the number of red blood cells. The term "dysadaptation to high altitude", for CMS patients that present with EE, seems inappropriate and does not provide a pathogenesis. Above 3000 m, in the Bolivian Andes, respiratory disease with EE affects thousand of persons. With the availability of pulmonary function tests and blood gas techniques, it is increasingly evident that EE is due to some ventilatory or respiratory alteration. Patients with EE show aberrations of one or more of the following: FVC; FEV.1/FVC;FEF 25-75%, Alveolar ventilation; $PaCO_2$; pulmonary shunts; uneven ventilation; TLC; CC/TLC; CV/VC; blood pressure; or chest x-ray. All of our patients had a $PaCO_2$ below 56 mmHg. In patients with EE there is a tendency for the hematocrit to increase with age (r = 0.35) with a plateau at around 60 years of age. We found an inverse relationship between FVC (r = 0.45) and RV/TLC (r = 0.10) with the hematocrit. In conclusion, EE (appearing as CMS) is an adaptation to hypoxia caused by disease at high altitude. **(Acta Andina 1996, 5:3-8)**

## RESUMEN

La capacidad de adaptación de los seres humanos a los cambios de la presión atmosférica es notable . En la adaptación a la altura (HAA) debemos considerar: la del sano y la del enfermo. La adaptación aguda puede ser mas dramática y peligrosa que la adaptación crónica. Las enfermedades son las mismas que las del nivel del mar pero con una fisonomía hipóxica. El termino Mal de Montaña Crónico (CMS) ha creado confusión, debido a que incluye enfermedades pulmonares que ocasionan la eritrocitosis excesiva (EE). Esta última es un mecanismo de adaptación que incrementa la capacidad de transporte de oxígeno de la sangre, incrementando los eritrocitos. El termino "desadaptación a la altura", para los pacientes con CMS que tienen EE, parece inadecuado y no explica la patogenesis. En los Andes Bolivianos por encima de los 3000 m., miles de pacientes son portadores de enfermedades respiratorias con EE. Con el acceso a técnicas de estudio de la función pulmonar y de los gases en sangre más eficientes, se hace mas evidente que la EE se deba a alguna alteración ventilatoria o respiratoria. Los pacientes con EE muestran alteraciones en uno o varios de los siguientes: FVC; FEV.1/ FVC; FEF 25-75%, ventilación alveolar; $PaCO_2$; shunts pulmonares; ventilación no uniforme; TLC; CC/TLC; CV/ VC; presión arterial ó radiografía de tórax. Todos nuestros pacientes tenían un $PaCO_2$ por debajo de 56 mmHg. En estos pacientes hay una tendencia a que el hematocrito aumente con la edad (r =0.35) estabilizándose alrededor de los 60 años de edad. También se encontró una relación inversa entre el FVC (r = 0.10) con el hematocrito. En conclusión, el mal de montaña crónico es una adaptación a la hipoxia, debido a enfermedad en la altura. **(Acta Andina 1996, 5:3-8)**

When the first French medical books translated into Spanish, arrived in America, physicians studied medicine at high altitudes and compared the signs and symptoms of permanent residents with similar sea level illnesses. Treatments followed sea level guidelines. Clinicians making careful observations noted that at high altitude the normal inhabitants and their pathology had differences worthy of clarification. In 1928, Monge described an illness that he called high altitude erythremia, defined by markedly increased red blood cell levels (RBC). Initially he linkened it to Vaquez-Osler's disease [10]. He later modified this concept, attributing the disease to a loss of adaptation to high altitude, suffered by some subjects, who surprisingly returned RBC levels to normal upon descent to normal sea level [9,8]. This important discovery of illness at high altitude, is comparable to the observation of physiologic polycythemia in normals at high altitude by Viault [12]. Further reports,improved by quantity and quality gave more details of the characteristics of the disease, given the name of chronic mountain sickness (CMS), Monge's disease and more recently, excessive erythrocytosis (EE) [11,6]. At sea level, patients with cor pulmonale and chronic tissue hypoxia, also have been found to have erythrocytosis.

With time, patients at variable altitudes were studied, and it was concluded that adaptation is more difficult with higher altitudes and faster ascents [4,13,5]. It follows that one must consider the adaptation of normal man and that of the diseased man, since acute adaptation is much more dramatic and dangerous than chronic adaptation.

In the Bolivian Andes, where large populations live above 3000 m, pulmonary disease with EE is present in thousands of patients. With the arrival of improved pulmonary function and

Corresponding author:
Gustávo Zubieta-Castillo IPPA La Clinica del Instituto de Patologia en la Altura Av. Saavedra 2302 Casilla 2852, La Paz, Bolivia
Tel:591-2-368734
Fax:591-2-357159
E-mail: zubieta@oxygen.bo

blood gas equipment and with improved clinical experience, it seems to the authors more evident that EE results from some respiratory or ventilatory alterations. Our report substantiates this theory.

## Materials and Methods

Patients with EE who consulted us for treatment of cardio-pulmonary disease or because EE itself turned them cyanotic , were studied from 308 cases diagnosed as having secondary EE, 10 were chosen randomly and cardio-respiratory function studies were performed (Table 1) at High Altitude Pathology Institute (IPPA) in the city of La Paz, at 3600 m (PB x = 495 mmHg). The 10 patients were all male, born in and residents of this area. Control studies of patients' EE, age and pulmonary function studies for larger groups are also described.

Hematocrits were determined using the microhematocrit technique. Forced vital capacity (FVC), forced expiratory volume in 1 second (FEV.1) and forced expiratory flow (FEF) were obtained with the use of a Purittan Bennett Remac adapted through an analog-digital conversed to a PC, previously calibrated with a 3 liter syringe. Expired ventilation (VE) was obtained in a Tissot during 5 minutes and expired samples were analyzed along with blood gases in a Radiometer model MK2Phm Acid-Base analyzer.

Carbon dioxide production ($VCO_2$) and oxygen consumption ($VO_2$) were calculated using standard equations described elsewhere [2]. Alveolar ventilation was calculated from $VCO_2$ and alveolar $CO_2$ tension ($PACO_2$), that was sampled by the end-tidal method and analyzed in the same blood gas machine.Hyperoxic testing using the same method was performed where arterial oxygen tension ($PaO_2$) was measured from a blood sample taken from the radial artery at rest. Inability to achieve a $PaO_2$ above 200 mmHg was considered as an intra-pulmonary shunt. Nitrogen washout curves using the same Remac, were analyzed for uneven ventilation, where the slope of the alveolar plateau greater than 0.2 was considered abnormal. Blood pressure taken at rest in the supine position was also recorded in order to associate possible reno-vascular disorders. The chest x-ray was studied in each case.

## Results

In table 1, shadowed results identify abnormals in 10 patients with pulmonary volumes below 90% of predicted. Alveolar ventilation below 3000 ml/min/$m^2$ and arterial oxygen tension ($PaO_2$) below 56 mmHg were considered abnormal for this altitude.

| NM | Ht % | FVC % PR | FEV.1 % PR | FEF % PR | VA ml/min/m2 | PaO2 mmHg | PaCO2 mmHg | SHUNT PaO2 w/O2 | UNV Slope | B.P. mmHg | X-Ray |
|---|---|---|---|---|---|---|---|---|---|---|---|
| RC | 71 | 132 | 120 | 74 | 2445 | 46 | 27 | 75 | 0 | 109/80 | Abnor |
| FG | 67 | 79 | 77 | 59 | 2015 | 39 | 30 | 184 | 0.1 | 120/90 | Abnor |
| ET | 72 | 94 | 101 | 85 | 3535 | 45 | 33 | 114 | 0.1 | 130/95 | Abnor |
| CV | 78 | 90 | 93 | 80 | 2240 | 44 | 38 | 215 | 0.1 | 110/80 | Abnor |
| DB | 77 | 60 | 66 | 101 | 2262 | 50 | 26 | 115 | 0.1 | 160/105 | Abnor |
| RL | 69 | 97 | 103 | 118 | 3564 | 43 | 40 | 190 | 0.07 | 120/90 | Abnor |
| IC | 72 | 100 | 103 | 96 | 2456 | 49 | 31 | 200 | 0.1 | 139/84 | Abnor |
| LP | 83 | 45 | 43 | 23 | 2210 | 42 | 34 | 210 | 0.3 | 120/90 | Abnor |
| JV | 61 | 89 | 71 | 33 | 2720 | 43 | 35 | 230 | 0.27 | 140/90 | Abnor |
| HR | 65 | 93 | 95 | 87 | 3252 | 53 | 42 | 250 | 0.1 | 140/96 | Abnor |

Table 1. Excessive Erythrocytosis in 10 randomly chosen from 308 cases reveal pulmonary or blood pressure anomaly (shaded areas). NM = Name, Ht = hematocrit, FVC = forced vital capacity, FEV.1 = forced expired volume in 1 second, FEF 25-75% = forced expiratory Flow, VA = alveolar ventilation, PaO2 = arterial oxygen tension, PaCO2 = arterial carbon dioxide tension, SHUNT = PaO2 reached during breathing 100 % oxygen, UNV = uneven ventilation slope from nitrogen washout curve, B.P. = Blood Pressure, X-ray = chest x-ray, % Pr = % of Predicted

The existence of confluent nodules, scars, opacities, interstitial fibrosis, and patchy shadows on chest x-ray were considered abnormal. Age distribution in a large group of miners with EE compared to normals are shown in fig. 1.

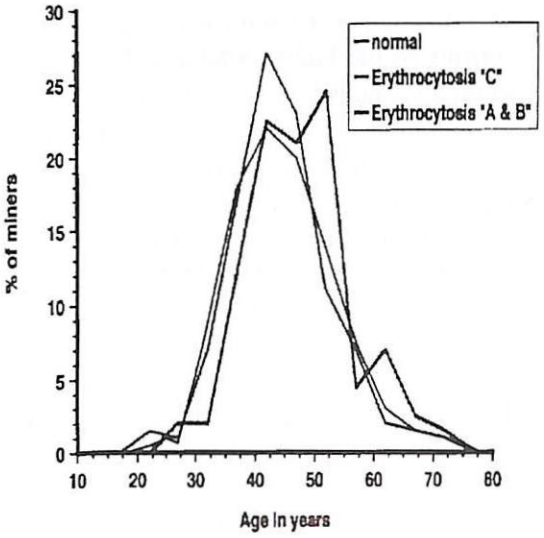


Fig. 1. Percentage distribution of ages for 129 miners with erythrocytosis types A & B, 395 miners with erythrocytosis type C and 1739 miners with no erythrocytosis at 3600 m. (From Zubieta et. al. Revista de la Academia Nacional de Ciencias de Bolivia 1985) [15].

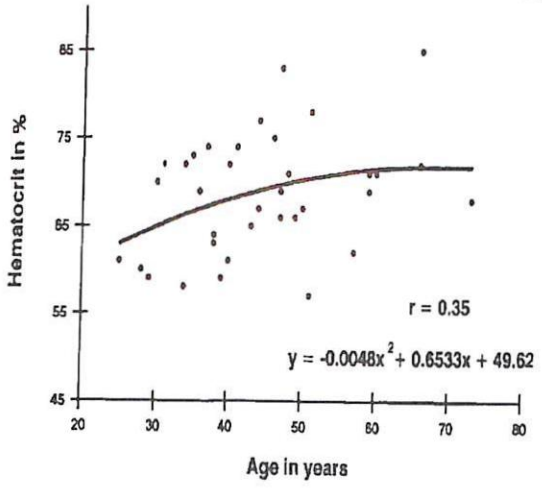


Fig. 2. Correlation between hematocrit and age in 35 patients with EE.

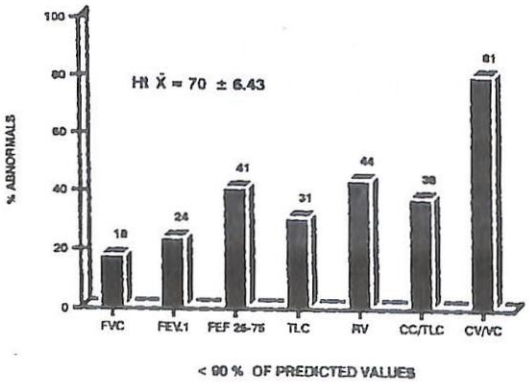


Fig. 3. Percentage of abnormals in pulmonary function testing in 17 patients with EE.

The tendency to increase EE with age in 35 patients with EE is shown in fig. 2. In fig. 3 abnormal pulmonary function tests are shown in 17 patients. FVC and RV/TLC in relation to hematocrit in 17 and 15 patients respectively are depicted in fig. 4 and 5. The correlation between $PaO_2$ breathing ambient air during hyperoxic tests in EE patients with pulmonary shunt is shown in fig 6.

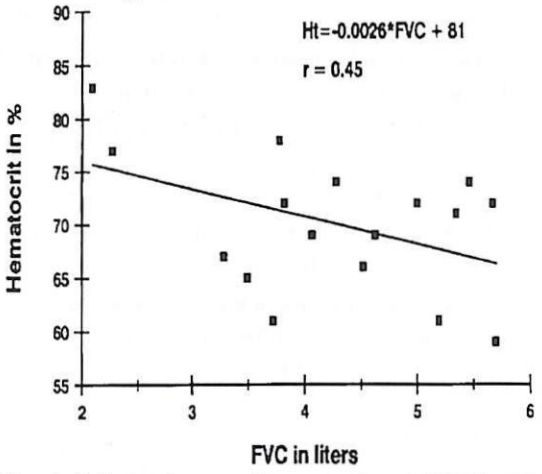


Fig. 4. Relation between hematocrit and FVC in 17 patients with EE.

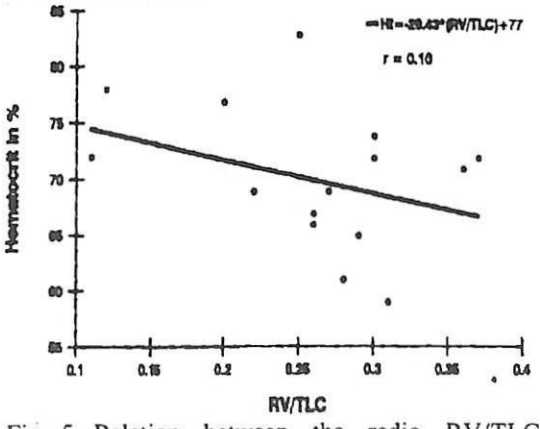


Fig. 5. Relation between the radio RV/TLC obtained from the nitrogen washout curve with the hematocrit in 15 patients with EE.

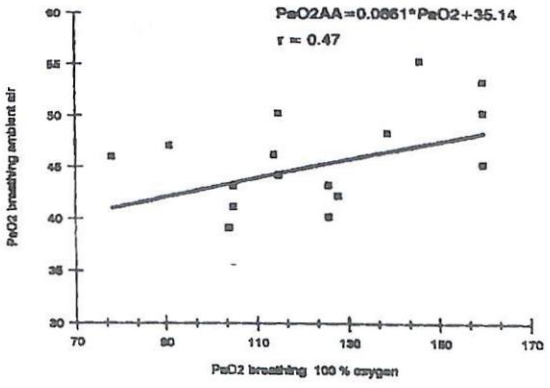


Fig. 6. Relation between the pulmonary shunt determined by breathing 100 % oxygen at 3600 PB = 495mmHg, and the PaO2 breathing ambient.

## Discussion

Previous studies [15,16,14] in 2263 patients with silico-tuberculosis, with evident pulmonary lesions, whose diagnosis was based solely on the physical exam, chest radiology and increase of RBCs; showed 5.7% with severe erythrocytosis (types "A" & "B"): $> 7.5 \times 10^6$ GR and 17.45% with moderate erythrocytosis (type "C") $> 6.5 \times 10^6$ and $< 7.5 \times 10^6$ GR.

They all had the same characteristics typical of "chronic mountain sickness", that is, over 40 years old and overweight (fig. 1) [14,15].

With respect to the relation between hematocrit and age in 35 patients with EE there is a tendency for the hematocrit to increase with age ($r = 0.35$) with a plateau at around 60 years of age (fig. 2), showing the adaptation to disease without reaching extremely high levels of the hematocrit. Multiple observations were made by other authors [7].

In another group of 17 subjects with a mean hematocrit of $70 \pm 6.43\%$, the results of pulmonary function tests below 90% of predicted are shown in fig. 3. The greater percentage of abnormals corresponds to the relation closing volume/vital capacity (81%), which merits further observations and analysis.

Fig. 4, confirms the observations of other authors of lower FVCs and larger hematocrits [6,7]. A further observation is that there is an inverse relation between RV/TLC and hematocrit in patients with EE (fig.5).

A direct relation ($r = 0.45$) was obtained between pulmonary shunt determined by hyperoxic tests, expressed as the $PaO_2$ reached while breathing 100% oxygen and the $PaO_2$ while breathing room air (fig.6).

From all this data it can be appreciated that the EE is due to some form of pulmonary function abnormality. Adequate technology and experience in chest x-ray interpretation is required. All 10 subjects have a low $PaO_2$, with or without $CO_2$ retention.

It is evident that pulmonary lesions of any origin, give rise to an accentuated erythrocytosis, depending on the severity of the lesions, the altitude, and time of residence at altitude, with an awareness that some subjects are more susceptible than others to this accentuation. On the other hand, obvious lesions although not extensive on the chest x-ray, may create pulmonary shunts evident during pulmonary function testing, and cause a severe EE, attributed to ventilation-perfusion mismatch in lobes or segments of the lungs. Analogously, lesions that preserve pulmonary vessels, create shunts that are more erythrogenic than the total destruction of the bronco-alveolar and vascular structure. This leads us to propose the theory that a lobectomy of a compromised lobe, may eliminate the hypoxic stimulus to the kidney and therefore overcome secondary erythrocytosis.

Chronic diseases at high altitude, are the same as those at sea level but with hypoxic physiognomies. When the term "chronic mountain sickness" was originally coined, it created confusion because it included diverse pulmonary diseases that have an increased hematocrit, which is a mechanism of adaptation, that increases the oxygen transportation capacity of blood. In the patients suffering from "chronic mountain sickness" with EE, seems inappropriate and does not explain the pathogenesis of this chronic disease. In our experience, it is always due to some form of pulmonary, cardiac or renal disease, improperly diagnosed at high altitude. Accordingly, the terms secondary erythrocytosis,excessive erythrocytosis and increased polycythemia [1] have been created for diseases whose etiologies are clearly identified. The Cudkowicz scientific mission to La Paz in 1971, which we witnessed, studied 20 patients with CMS. In our opinion, all of them had pulmonary disease [3].

Therefore, it is important not to loose perspective, that adaptation of the human organism to changes in atmospheric pressure and hypoxia are remarkable, both for normal subjects as well as for the diseased.

We believe diseased persons have a slower and more progressive adaptation than residents of high altitude, and we should not consider this a "loss of adaptation". On the contrary they are well adapted to withstand even advanced degress of their disease and its limitations in the hypoxic environment of high altitude

### Acknowledgement

Dr. John C. Triplett for the English correction of the manuscript.

## References

**1.-Cudkowicz L., Spielvogel H. & Zubieta G.**(1972) Respiratory studies in women at high altitude (3,600m or 12,200 ft and 5,200m or 17,200 ft). Respiration; 29: 393-426.

**2.-Dejours, P.**(1966) Respiration. Oxford University Press.

**3.-Ergueta J., Spielvogel H., Cudkowics L.**(1971) Cardio-respiratory studies in chronic mountain sickness (Monges`s syndrome. Respiration; 28: 485-517.

**4.-Houston C.S.**(1983) Altitude illness; the dangers of the heights and how to avoid them. Travel medicine.; 74: 231-237.

**5.-Kayser B.**(1994) Factors Limiting Exercise Performance in man at high altitude. Ph. D. Thesis. University de Geneve Press.

**6.-Leon-Velarde F. y Arregui A.**(1993) Hipoxia: Investigaciones Basicas y Clinicas. IFEA-UPCH, Lima, Peru.

**7.-Leon-Velarde F., Arregui, A., Monge, C. & Ruiz y Ruiz, H.**(1993) Aging at high altitudes and the risk of chronic mountain sickness. Journal of Wilderness Medicine.; 4(2): 183.

**8.-Monge C.**(1943) Chronic mountain sickness. Physiological Review; 23: 166-183.

**9.-Monge C.**(1937) High altitude disease. Arch Intern Med.;59: 32.

**10.-Monge C.**(1928) La enfermedad de los andes (sindrome eritremicos). Anales de la Facultad de Medicina. Lima, Peru.

**11.-Monge C., Arregui A. & Leon-Velarde F.**(1992) Pathophysiology and epidemiology of chronic mountain sickness. Int. J. Sports Med; 13: S79-S81.
(sindrome eritremicos). Anales de la Facultad de Medicina. Lima, Peru.

**11.-Monge C., Arregui A. & Leon-Velarde F.**(1992) Pathophysiology and epidemiology of chronic mountain sickness. Int. J. Sports Med; 13: S79-S81.

**12.-Vialut, F.**(1890) Sur l'augmentation considerable des globules rouge dans le sang chez les habitants des haut plateau de l'Amerique du sud. Compte Rendu hebdomaire Des Seances de L'Academ Science, Paris; 111: 917-18.

**13.-West J.B**(1984) High living: lessons from extreme altitude. Am. Rev. Respir. Dis.; 130: 917-923.

**14.-Zubieta-Calleja G.R. & Zubieta-Castillo G.**(1989) High altitude pathology at 12000 ft. Imprenta publicidad Papiro, La Paz, Bolivia.

**15.-Zubieta-Castillo G., & Zubieta-Calleja G.R.**(1985) El mal de montaña crónico y los mineros. Revista de la Academia Nacional de Ciencias de Bolivia. 4: 109-116.

**16.-Zubieta-Castillo G., & Zubieta-Calleja G.R.**(1986) Las enfermedades pulmonares y el mal de montaña crónico. Revista de la Academia Nacional de Ciencias de Bolivia. 5: 47-54.