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Haematology and Erythrocyte Metabolism in Man at High Altitude: An Aymara-Quechua Comparison

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ABSTRACT In the course of haematological and biological investigations among Aymara and Quechua populations in Bolivia, an anthropological study of the erythrocytary respiratory function was carried out on the two groups at two altitudes: 3,600 m and 450 m.

A difference in the intensity of the biological variations of the two populations is observed at high altitude.

In the Quechuas, as in any lowland native, the adaptative phenomena are totally and quickly reversible.

In the Aymaras, we detected the existence of more marked haematological and biochemical characters: moderate polycythemia, hyperhaemoglobinemia, microcytosis, metabolical hyperactivity with accumulation of 2-3 di-phospho. glycerate and ATP, and methaemoglobinemia with a drop in the activity ofthe methaemoglobin reductases. The Aymaras preserve Sorne of those characters (methaemoglobinemia excepted) when they settle in lowlands.

The Andean high plateaux are a particularly suitable region for the study ofthe adaptative responses to high-altitude chronic hypoxia. It would seem that the plateaux were peopled Sorne 20,000 years ago (Vellard, 1976a). The c1assification ofthe human types now living on the Peruvian-Bolivian altiplano is based on the hypothesis of successive waves of immigrants (Vellard, 1976b): (i) a few groups are descended from the oldest Andean natives (the "Laguides") that were pushed back to the most inhospitable zones (Urus, Chipayas); (ii) the "Altiplanides" or Aymaras, who people the north zone of the inter-Andean corridor and have never wandered far away from it, go back to the great hunters who pushed back or assimilated the first populations of the high plateaux. They have preserved their linguistic, cultural and social uniqueness in the same ecological milieu; and (iii) the "Andides" or Quechuas, heirs to the great Inca culture, predominate numerically, territorially, and socially over the others. Their ecological milieu extends beyond the higher Andean zones to the neighboring valleys. They differ from the preceding two groups in that they appear less well adapted to high altitude and are far less homogeneous.

In the course of haemotypological and hiological investigations among those high-altítude populations, we carried out haematological and erythrobiological studies: (i) at 3,600 m (La Paz, Bolivia) on 452 adult Quechuas and 720 adult Aymaras (29 ± 11 years: sex ratio[1] = 1.85); and (ji) at 450 m (Santa Cruz, Bolivia) on 127 adult Quechuas and 163 adult Aymaras (26 ± 10 years: sex ratio = 2.03), who were born at high altitude and had been living for over 5 years in lowlands. The two populations do not differ significantly ($p < 0.001$) in either sex ratio (X^2 = 0.396) or mean age (t = 4.48).

Four types of laboratory examinations are performed on site: (1) haemogram (Fig. *lA);* (2) intra-erythrocytary metabolites affecting the haemoglobin affinity for oxygen (Fig. lB) studied by means of a colorimetric technique

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[1] = Number of men divided by the number of women.

for the reduced glutathione (GSH) (Kaplan and Dreyfus, 1964), a spectrophotometric method for the methaemoglobin (MetHb) (Kaplan, 1965) and enzymatic and photometric techniques for the ATP (Cartier et al., 1967a) and the 2-3 di-phospho-glycerate (2-3 DPG) (Keitt, 1971); (3) indirect tests to assess the function of the glycolysis, and pentose pathways, and the oxydo-reducing systems of the red blood cells (Fig. 2A,B) (Cartier, 1969, for glycolytic activity method; Brewer et al., 1960, for Brewer's test; Beutler, 1957, for Beutler's test; MilIs and Randall, 1958, for Mills and Randall's test); and (4) direct determination of the activity of 19 intra-erythrocytary enzyme systems (carried out on high-altitude residents only) (Fig. 3) by means of standardised enzymatic and photometric techniques (Cartier et al., 1967b; Kahn et al., 1971; Horn, 1973; Hegesh et al., 1968; Sass et al., 1967). The methods used are the ones described in our studies of the adaptive phenomena in the Quechua population (Arnaud et al., 1976, 1978, 1979, 1983).

In Figures 1, 2, and 3, we compare the parameters measured among the Aymaras with the ones obtained for the Quechuas (Student's t-test) at high altitude (3,600 m), then in the lowlands (450 m). The results for the Quechuas, chosen as reference group, are typical for the altitude under consideration and are reversible under altered altitude conditions (Arnaud, 1979).

As far as haematology is concerned, at 3,600 m (Fig. lA), the Aymaras enjoyan obvious adaptive advantage for the transport of oxygen by the blood as shown by (i) a significant increase in the number of cellular oxygen carriers, the red blood cells (higher Ht and RBC); and (ii) a very significant increase in the number of intra-erythrocytary oxygen carriers, haemoglobin (increased Hb and MHC). A microcytosis (decreased MCV) contributes to both increases. After moving to the lowlands (at 450 m), the Aymaras exhibit a general decrease in the values of haematological parameters, but retain sorne characters typical of their adaptation to life at high altitude: significant microcytosis and very significant erythrocytary hyperhaemoglobinemia.

Concentrations of the intra-erythrocytary metabolites influencing the affinity of the haemoglobin for oxygen (Benesh and Benesh, 1967; Darling and Roughton, 1942) vary with altitude (Fig. lB). At high altitude, in the Aymaras and the Quechuas, there is a tendency toward a decrease in the affinity, hence a better delivery of oxygen to the tissues (Grover and Weil, 1970). The ATP, 2-3 DPG, GSH, and even the MetHB values are significantly higher than lowland values. Glycolytic activity and the activity of anaerobic glycolysis are also significantly higher, but this metabolic response is more important than the haematological one; the production of 2-3 DPG is lower than that of Hb: the ratio 2-3 DPG to Hb increases significantly (Figs. lB, 2B). The variations with altitude are different in the Aymaras and the Quechuas. At high altitude, the Aymaras, with a greater intensity of erythrocytary gly-

A bbreviations

Ht, Haematocrit
Hb, Haemoglobin
RBC, Red blood cell
MCV, Mean corpuscular volume
MHC, Mean haemoglobin concentration
ATP, Adenosin tri phosphate
2-3 DPG, 2-3 di-phospho-glycerate
GSH, Reduced glutathione
Met Hb, Methaemoglobin
M.B., Methylene blue
G.A., Glycolytic activity
PHM, Phospho-hexo-mutase
DPGM, Di-phospho-glycerate mutase
AK, Adenylate kinase
G6PDH, Glucose-6-phosphate-dehydrogenase
6PGDH,6-phospho-gluconate-dehyrogenase
GSSG Red, Glutathione reductase
W.B., Whole blood
HK, Hexokinase
PHI, Phospho-hexo-isomerase
PFK, Phospho-fructo-kinase
ALDO, Aldolase
TPI, Triose-phosphate-isomerase
GAPDH Glyceraldehyde-phosphate-dehyrogenase
PGK, Phospho-glycerate-kinase
PGM Phospho-glycerate-mutase
ENO, Enolase
PK, Pyruvate-kinase
LDH, Lactico-dehyrogenase

.¿;.- = increase;
~ = decrease;
A = Aymara,
Q = Quechua.

= non-significant, $p > .05$;
.-A = significant, $.05 > p > .001$;
c~. = vcry significant. $p < .001$;

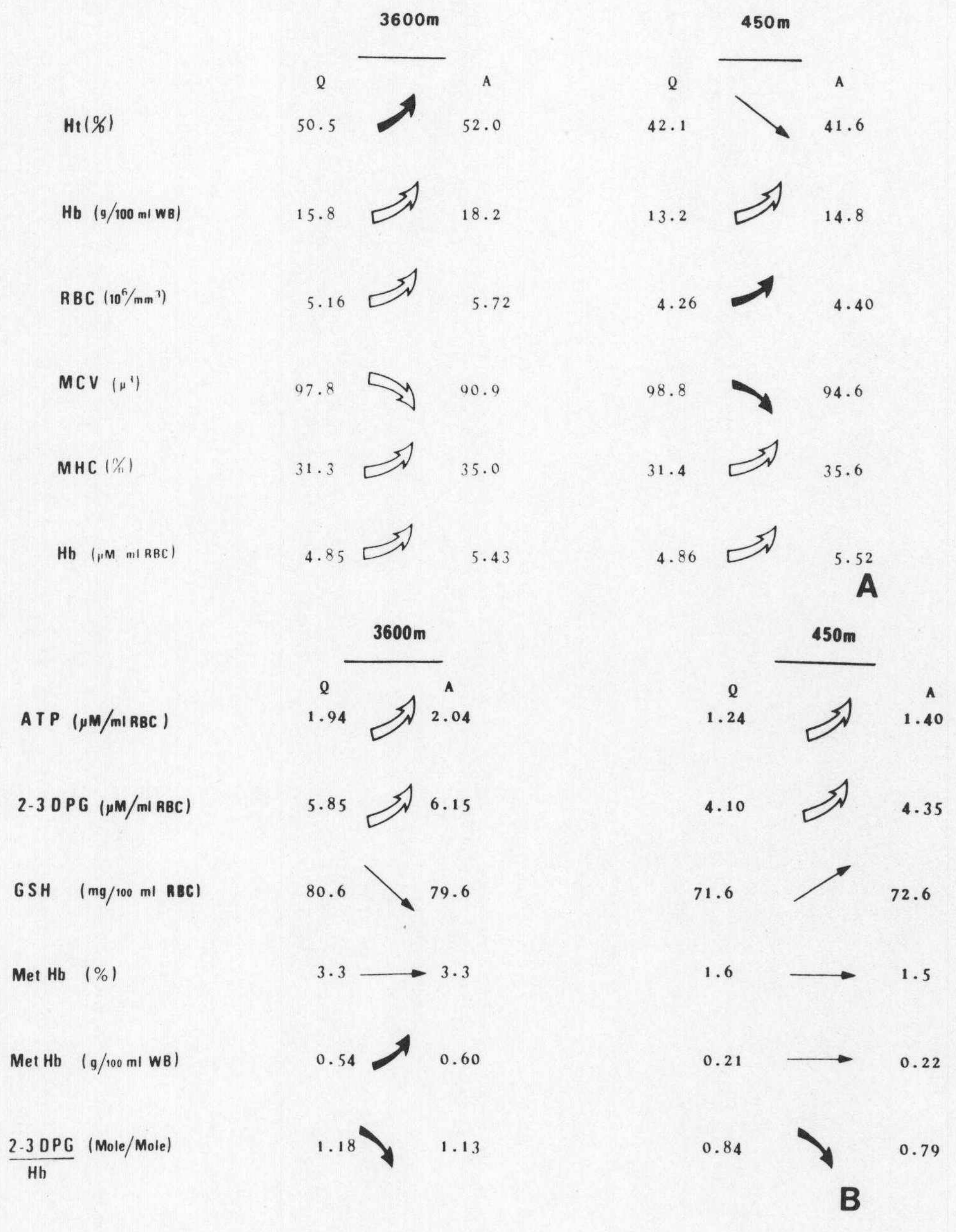

Fig. 1. Comparison of variation of haematological and erythrometabolical parameters in the Aymaras and the Quechuas at 3,600 m and 450 m. A. Haemogram. B. Intra-erythrocytary metabolites.

colytic activity than the Quechuas, accumulate more ATP and 2-3 DPG. The hyperhaemoglobinemia of the Aymaras results in better transport of oxygen by the blood, while the metabolic hyperactivity responsible for the production of 2-3 DPG (Arnaud and Gutierrez, 1984) improves tissue oxygenation. Under normal conditions of oxygenation at 450 m, the Aymaras preserve sorne of their metabolic hyperactivity, resulting in an accumulation of ATP and 2-3 DPG, whereas the Quechuas revert to the normal values of

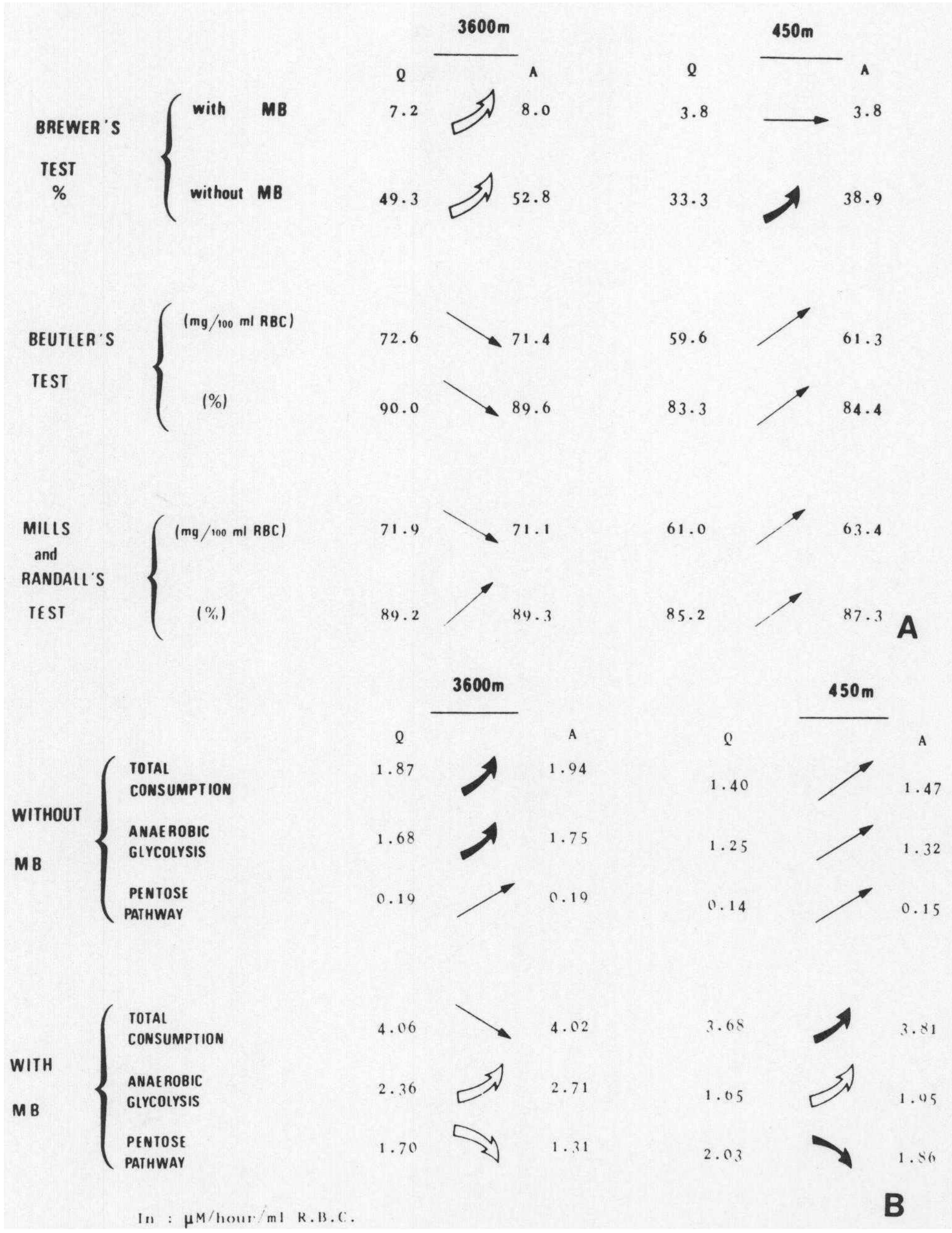

Fig. 2. Comparison of variation of erythrometabolical parameters in the Aymaras and the Quechuas at 3,600 m and 450 m. A. oxydation-reduction metabolism B. glycolytic activity.

the lowland residents (Arnaud, 1979). At high altitude, in both populations, the examination ofthe oxydo-reducing pathways (Fig. 2A) reveals a decrease in the activity of the two methaemoglobin reductase systems (Brewer's test). From a complete methaemoglobinisation of the blood at the beginning of the test, the values obtained at the end and shown in our tables correspond to the residual methaemoglobin not reduced by en-

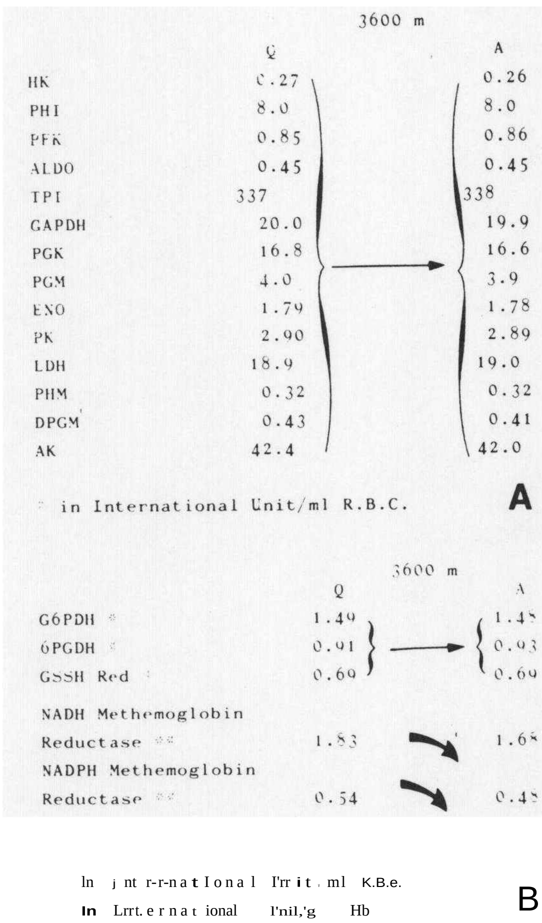

Fig. 3. Comparison of variation of the erythrocytary enzyme activities in the Aymaras and the Quechuas. A. enzymes of the anaerobic glycolysis. B. enzymes of the erythrocyte reducing system.

zymes. As the test lasts a fixed time, it is possible to check the activity of the NADH methemoglobin reductase and the NADPH methemoglobin reductase. For the latter, the presence of methylene blue is necessary. A confirmation of that significant decrease is obtained by measuring the glycolytic activity in the presence of methylene blue (Fig. 2B) as well as by determining the activity of the two enzymes at 3,600 m (Fig. 3B). The decrease accounts for the accumulation of MetHb in the red blood cells of people residing at high altitude (Arnaud et al., 1979). At high altitude, the Aymaras show an accumulation of MetHb greater than that of the Quechuas owing to weaker methaernoglobin-reducing enzymatic systems under normal working conditions (Arnaud et al., 1979). In the lowlands, the Aymaras lose the high-altítude methaemoglobinemia while keeping a methaemoglobin reductase activity lower than the Quechuas'. Beutler's test (to check the G6PDH, the 6PGDH and the GSSG Red.), Mills and RandalI's test (to check the GSH Per.), and the direct determinations of the activities of 17 other enzyme systems do not reveal any significant difIerence between Quechuas and Aymaras (Figs. 2A, 3A,B). Besides, both groups are subject to the same reversible characters owing to high-altitude hypoxia, which we have already described at length (Arnaud et al., 1978, 1979; Arnaud, 1979) and which are responsible for the accumulations of ATP, 2-3 DPG, MetHb, and GSH.

This anthropobiological study of the respiratory function of the red blood cells in the Quechuas and the Aymaras under two different conditions of oxygenation (450 m and 3,600 m) demonstrates the presence of acquired adaptive characters in the Aymaras. BiochemicalIy and haematologicalIy the Quechuas respond to high-altitude hypoxia like any lowlander. In the Aymaras, the adaptive characters are exacerbated: moderate polycythemia, hyperhaemoglobinemia, microcytosis, metabolical hyperactivity with accumulation of ATP and 2-3 DPG, methaemoglobinemia with a drop in the activity of the methaemoglobin reductase enzymes.

More important still, the Aymaras preserve sorne of those characters (methaemoglobinemia excepted) when they come to live in the lowlands.

Here we have an example of the acquisition of haematological and biochemical functional adaptive characters by a population that has been permanently exposed for numerous generations to constraining and selective environmental conditions.

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