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RESISTANCE AND CAPACITANCE VESSELS OF THE SKIN IN PERMANENT AND TEMPORARY RESIDENTS AT HIGH ALTITUDE

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IT is well known that circulatory changes induced by living at high altitude not only affect the pulmonary circulation but probably involve the entire circulatory system, modifying the regional partition of both blood flow and volume. The following study was undertaken to provide quantitative information on the role played by the cutaneous circulation at altitude as a potential reserve for changing the flow and volume of blood during the process of acclimatization.

METHODS

Thirty-nine subjects, seven Europeans and 32 natives, were studied at low and/or high altitude, as shown in Table I.

The circulation in the right hand was chosen as a representative cutaneous vascular bed. Blood flow, volume and venous pressure were measured simultaneously: the pressure was measured by catheterizing a superficial

TABLE I

NUMBER OF SUBJECTS, ETHNIC BACKGROUND AND SITE OF STUDY

	Low altitude		*High altitude*	
Places	*Paris*	*Santa-Cruz*	*La Paz*	*Chorolque*
Elevation (approx.)	50 m	400 m	3750 m	5200 m
Barometric pressure (mean) in mmHg	759	725	480	403
Subjects				
Lowlanders:				
Europeans	4 →		4*	—
	3 →		3* →	3
Amerindians	—	5	—	—
Highlanders:				
Amerindians	—	—	15*	6
	—	6 →	6	—

Arrows indicate that the same subjects have been studied in several places.
*Experiments with CO_2 breathing and hyperventilation.

vein, the volume and the flow by means of a water-filled plethysmograph. The plethysmograph was specially built to obtain distensibility curves by altering the transmural pressure (Martineaud *et al.* 1966).

Experiments were done at the same room temperature ($22\cdot8 \pm 0\cdot2$°C) but at different hand temperatures, produced by varying the temperature of the water filling the plethysmograph (from 7·0 to 43·0°C); changes in the hand temperature were induced in order to explore the cutaneous circulation in different functional states.

To test the role played by the hypocapnia associated with altitude hypoxia, measurements were made in subjects during voluntary hyperventilation and while breathing a mixture containing 4–6 per cent CO_2. In the latter experiments the fractions of inspired O_2, N_2 and CO_2 were chosen by separate experiments in order to increase $P_{A_{CO_2}}$ without altering $P_{A_{O_2}}$.

Since increasing the $P_{A_{CO_2}}$ induced hyperpnoea, the effect of associated changes in intrathoracic pressure during this procedure was evaluated in the same subjects by the performance of voluntary hyperventilation up to the same minute volume induced by breathing CO_2. Since lowlanders were not able to increase their ventilation up to this level without discomfort, 2 per cent CO_2 was added to the inspired air for these subjects.

RESULTS

Resistance vessels

As shown in Fig. 1, blood flow in the hand ($\dot{Q}$) is lower at high altitude than at sea level in both residents and newcomers. The difference is statistically significant only when local skin temperature is above 33°C—that is, when local blood supply is high. In newcomers, $\dot{Q}$ is immediately reduced on arrival and then keeps an approximately steady level. Even after one month of residence, the $\dot{Q}$ of lowlanders is greater than that of highlanders.

Highlanders have the same $\dot{Q}$ values when residing at 3750 or 5200 m; by contrast, lowlanders exhibit a further and significant reduction at the highest altitude (Fig. 2).

As shown in Fig. 3, increasing or decreasing $P_{A_{CO_2}}$ does not appreciably affect skin perfusion in high altitude residents, but in newcomers there is a significant increase in flow when $P_{A_{CO_2}}$ is increased from 23 to 32 mmHg.

Since the mean arterial blood pressure is not significantly different at high altitude and at sea level and since there is no major alteration in venous blood pressure (Fig. 4), the reduction of $\dot{Q}$ at high altitude may be interpreted as the result of arteriolar vasoconstriction.

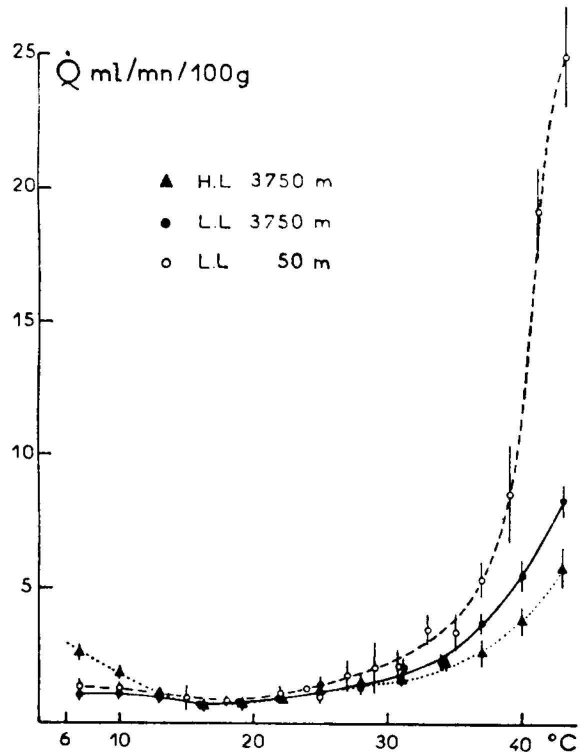

FIG. 1. Blood flow in the right hand (Q̇) plotted against local temperature (°C) in high altitude residents (HL, ▲) and in lowlanders (LL) at sea level (o) and after 1 month of acclimatization to altitude (●). Mean values and standard errors.

Capacitance vessels

Within the physiological range of skin temperature, there is no difference in the blood pressure in a superficial vein at sea level or at high altitude, in either highlanders or lowlanders. But for extreme temperatures, either warm or cold, there is an increase in venous pressure at high altitude (Fig. 4).

Volume changes induced by a given increase or decrease in transmural pressure are smaller at high altitude than at sea level. Since this decrease in vascular compliance could be due either to the presence of a larger volume of blood in the capacitance vessels or to active constriction of the walls of those vessels, it was necessary to determine the absolute value of the total volume of blood which can be shifted away from the hand by increasing the pressure in the plethysmograph up to the point where there was no further decrease in the volume of the hand. By this method the decrease in compliance appears to reflect an increase in capacitance vessel tone and is

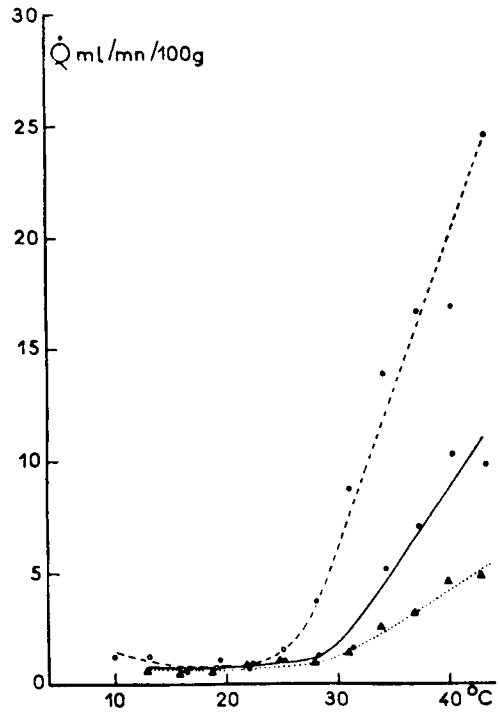

FIG. 2. Blood flow in the right hand (Q̇) plotted against local temperature (°C) in three lowlanders at sea level (o) and after six days of acclimatization at 3750 m (●) and 5200 m (▲). Mean values.

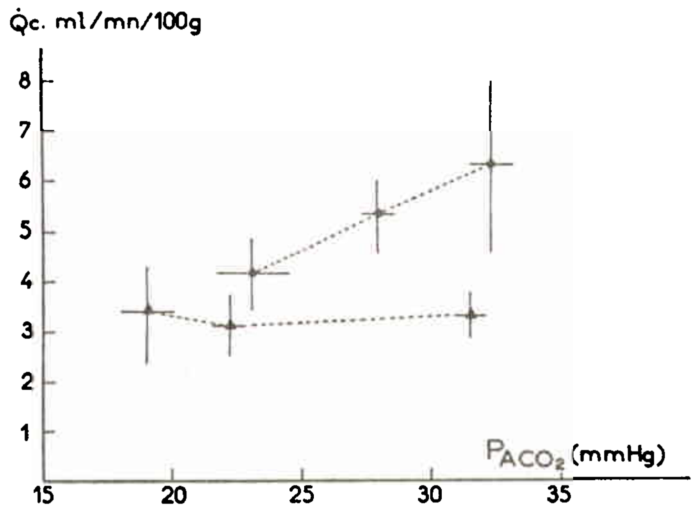

FIG. 3. Blood flow in the right hand (Q̇) as a function of end-tidal CO_2 tension ($P_{A_{CO_2}}$) in seven lowlanders (●) and 15 highlanders (▲) at 3750 m. Mean values and standard errors.

associated with a decrease of the volume of blood present in the skin (Fig. 5). This is observed both in residents and in sojourning subjects.

The decrease in distensibility in sojourners appeared immediately after arriving at high altitude and grew more pronounced with time, although

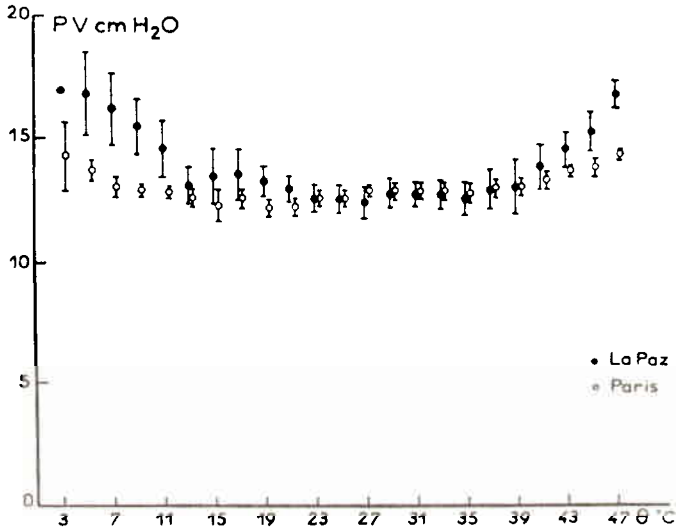

FIG. 4. Blood pressure in a superficial vein of the right hand (PV) plotted against local temperature (°C) in lowlanders at sea level (o) and at 3750 m (●). Mean values and standard errors.

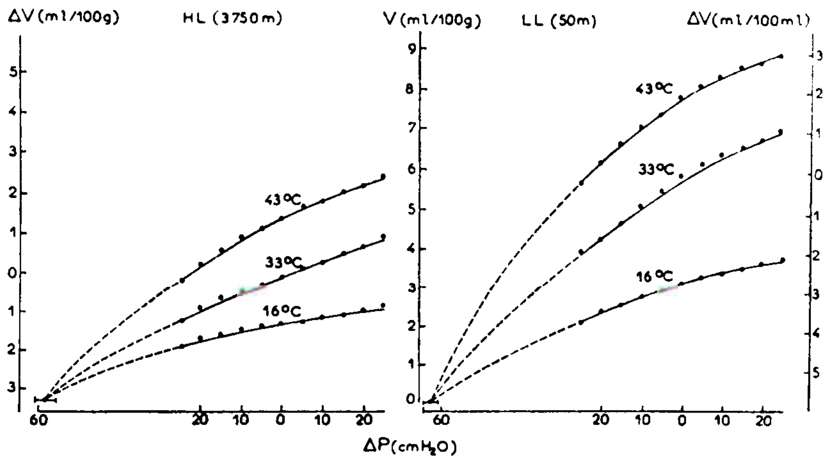

FIG. 5. Volume-pressure curves of capacitance vessels of the right hand in lowlanders (*right graph*, LL) and in highlanders (*left graph*, HL). Curves have been obtained for three different local temperatures: 16, 33 and 43°C. On the abscissa are shown the changes in venous transmural pressure (ΔP) and on the ordinate, volume changes (ΔV, right and left scales) and blood volume (V, middle scale), all expressed as ml/100 ml of hand volume.

the difference between the fourth and the thirtieth day was not statistically significant. Nevertheless, even after one month, distensibility in lowlanders was still larger than in highlanders (Fig. 6).

A particular feature was observed in six subjects who usually lived at high altitude but who had dwelt for a while at a lower level. When they returned to altitude, the recurrence of the cutaneous vascular pattern

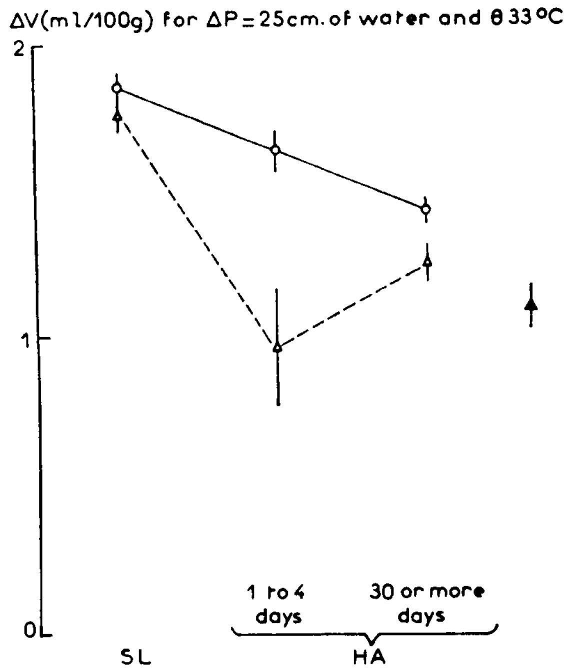

FIG. 6. Comparison of the reduction of cutaneous vascular distensibility during acclimatization at 3750 m in sea level residents (o) and in high altitude residents returning from sea level (△). Values obtained in resident highlanders (▲) are given for reference. Mean values and standard errors.

characteristic of high altitude was preceded by a marked overshoot during the first few days (Fig. 6).

Breathing CO_2 does not significantly affect vascular compliance, in either highlanders or lowlanders.

DISCUSSION

This work extends previous studies on the effect of high altitude on cutaneous circulation reported by this group (Durand *et al.* 1967, 1969).

It is generally agreed that blood flow in the hand, as measured by venous occlusion plethysmography, represents mainly, if not only, the perfusion of the skin. Increasing or lowering the pressure around the hand probably only affects the distensible vessels (capillaries and veins) of superficial tissues, deep vascular beds in bones or muscles being protected from external pressure (Martineaud *et al.* 1966).

The first work on the cutaneous circulation at high altitude, as far as we know, was done on visitors at Pike's Peak by Schneider and Sisco (1914) by a calorimetric technique. Their results are contrary to those reported later. They found an increased blood flow in the hand, and also a decrease in peripheral venous pressure. Later, Rotta (1947) and Alarcon-Castillo (1956) claimed that peripheral venous pressure was higher at high altitude than at sea level, while mean right atrial pressure is not altered (Peñaloza and Sime 1968). The data of Elsner, Bolstad and Forno (1964) also suggest that skin blood flow in the lower limbs is reduced at high altitude. More recently Roy and co-workers (1968) also found a reduction of skin perfusion in sojourners at high altitude. Weil and co-workers (1969) and Wood and Roy (1970) studying sojourners described a venoconstriction at high altitude and in the latter paper the authors concluded that blood shifted toward the central circulation. Thus at present, a reduction in cutaneous blood flow and volume at high altitude can be considered to be well established.

In this study, a significant reduction in blood flow by comparison with control subjects is only observed when skin temperature is above 33°C (that is, when the subject is in an ambient temperature of more than 24°C). At this temperature skin perfusion in the hand decreases from 12·0 ml/min/100 ml at sea level to 2·5 at 5200 m; if one accepts a rough extrapolation to the entire skin surface, this will yield a redistribution of less than 100 ml/min or about 2 per cent of the total resting cardiac output. Furthermore, during muscular exercise, reduction in cutaneous blood flow at high altitude compared to sea level is equal in percentage but less in absolute amount (Martineaud *et al.* 1970). Hence the effect of high altitude on skin perfusion should not play any significant physiological role except for unusual heat exposures.

It is also interesting to note that 'hunting' appears at a greater skin temperature at high altitude than at sea level, although so far no interpretation of this fact can be given.

The increase in capacitance vessel tone seems to be the most important physiological feature of the skin circulation at high altitude. By this mechanism, about 2·5 ml of blood per 100 ml is mobilized, which is almost half the blood present in the skin of the hand at a room temperature of 24°C and would represent roughly 300 ml for the whole skin area.

A marked overshoot of this venomotor response is observed in highlanders returning from a lower altitude. It is appealing to think that this response could be related to high altitude pulmonary oedema occurring in these same circumstances: pulmonary hypertension being favoured by the shift of blood from the skin to the lungs. Wood and Roy (1970) recently reported some evidence in support of this assumption, by showing that vascular compliance of the forearm was less in patients with high altitude pulmonary oedema.

Living at high altitude not only exposes the subjects to hypoxia but imposes various other stresses, such as hypocapnia, which can enhance the cardiovascular action of hypoxia. In the present study it is surprising to note that breathing CO_2 increases the skin blood flow in visitors only. This relative insensitivity of high altitude residents is comparable to that reported by Lefrançois, Gautier and Pasquis (1968) in studies on the control of ventilation at high altitude.

Other experiments, however, should be done before we can conclude that increases in $P_{A_{CO_2}}$ do not affect the venous compliance of lowlanders at high altitude. It cannot be concluded from the present data that the lack of change of compliance on breathing CO_2 reflects a totally unchanged pressure–volume relationship or, rather, a similar point on a new pressure–volume curve. Moreover, hyperpnoea induced by breathing CO_2 produced a large scattering of the values for compliance and a large number of measurements is therefore necessary to obtain statistically significant results.

The present study was not designed to find the site of action of P_{O_2} or P_{CO_2}, but other experiments on isolated veins and on paraplegic subjects (Bidart *et al.* 1969; Bidart, Durand and Martineaud 1970) suggest that blood gases can act centrally to alter the capacitance and resistance of the vessels of the skin.

SUMMARY

Blood flow, pressure and volume have been measured in the right hand as a representative cutaneous vascular bed. Measurements have been made at sea level and at high altitude on residents and newcomers.

Blood flow is lower at high altitude than at sea level in both highlanders and lowlanders. The reduction in flow is detectable immediately on arrival at altitude. However, after one month, sojourners still have a larger blood flow than highlanders.

Correction of hypocapnia by breathing an appropriate mixture of CO_2 does not alter the cutaneous blood flow in natives but partially corrects that of lowlanders.

Vascular pressure–volume curves obtained by plethysmography show a decrease both in volume and in compliance at high altitude; again, distensibility is less in highlanders than in lowlanders. A marked overshoot of this venomotor response is observed in highlanders returning from a lower altitude. Breathing CO_2 does not significantly affect distensibility in either highlanders or lowlanders.

From these findings it can be concluded that the cutaneous circulation acts as a quantitatively important reservoir in the redistribution of blood volume induced by high altitude, being able to expel about 250 ml of blood when skin temperature is 33°C or above.

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DISCUSSION

Pugh: Dr Durand, do you feel justified in applying your results for the skin of the hand to the rest of the skin surface?

Durand: Yes, most of the skin should behave like the skin of the hand, at least as far as blood flow is concerned. The cutaneous blood volume, as far as I am aware, has never been measured elsewhere than in the extremities.

But since flow and volume in the skin usually vary in the same direction, if one excepts pathological circumstances, it is reasonable to think that blood volume behaves in the overall skin as in the hand.

West: The reduction in skin blood flow doesn't help to explain the fall in pulmonary blood volume that Dr Severinghaus showed and that we found to some extent.

Durand: I don't know where the blood goes. When one measures local blood flow—cerebral, cutaneous, renal or coronary—it is found to be reduced at high altitude and nevertheless the cardiac output is the same as at sea level. It seems to be the same for the blood volume. One may suppose that at least part of the blood flow and volume removed from other organs or tissues goes to the muscles.

Milledge: Dr West was measuring capillary blood volume; the pulmonary blood volume might be increased even though capillary blood volume is slightly reduced. Dr S. B. Roy found the pulmonary blood volume to be increased by 80 per cent between 48 and 72 hours after arrival at altitude (Roy *et al.* 1968). It would help to explain the dangerous period for hypoxic pulmonary oedema, and also possibly the beneficial effect of morphia in this condition, which would drain blood back again into the periphery.

Durand: S. B. Roy certainly found a fantastic increase in pulmonary blood volume in soldiers coming back to altitude. He interpreted these findings as the result of a peripheral venoconstriction or an increased blood volume. I don't think that more than 100 ml can be accommodated as a supplement within the arterial side of the pulmonary circuit. Perhaps more if one includes the right ventricle.

Severinghaus: We don't have to look for where the blood goes. Henry Price and co-workers (1966) haemorrhaged normal supine individuals and were able to show no change in central venous pressure, pulmonary artery pressure, arteriolar pressure or anything that they could measure, but there was a decrease in splanchnic blood volume with no measurable signal. They were able to haemorrhage up to 1500 ml of blood and then replace it. It all came out of the splanchnic blood volume with no changes in the filling pressures in the right or left side of the heart.

Fejfar: I don't think we know much about the regional distribution of the blood flow, particularly in the splanchnic area, in the high altitude subject.

Durand: Another possibility to explain the decrease in blood volume is the augmentation of diuresis, which would explain the rapid increase of haematocrit in newcomers.

Severinghaus: Another place for water to go is into cells, which take up water and sodium because they don't have enough ATP to pump sodium out.

Harris: What is the size of the evaporative water loss from the lungs in these circumstances? It is a drying atmosphere.

Severinghaus: The ventilation at rest is only increased by 25 per cent, which is a very small fraction.

Tenney: The immediate effect at high altitude is anti-diuretic, isn't it?

Durand: In the first 48 hours it is, but then there is an increasing diuresis over the next few days.

Pugh: What work rates have you studied, Dr Durand?

Durand: In experiments not reported here, subjects exercised on an ergometer bicycle, for up to and over 1½ hours. Their oxygen uptake was 1·3 l/min, more or less. This constituted about 70 per cent of the low-landers' maximal oxygen uptake, and 55 to 60 per cent of the high-landers'.

Pugh: You did measure body temperature, I take it, to assure yourself that the central thermal state was comparable in all subjects?

Durand: Yes; we measured rectal and oesophageal temperatures.

Pugh: Was there any secondary rise in skin temperature as they got hot?

Durand: When they stopped exercising there was a rise in skin temperature, but not during exercise. We measured 25 different skin temperatures, and none of them increased. But the central temperature increased.

Pugh: This is interesting, because the level of exercise is very important. There is competition between the demand for blood by the working muscles and the demand for thermoregulation. Of course at very high work intensities there is persistent cutaneous vasoconstriction, even when people are hyperthermic, but normally at lower exercise rates cutaneous vasoconstriction passes off and is succeeded by normal rises in skin temperature and blood flow. In interpreting these results one has to be careful about what the exercise stress was, and whether there was some influence because low altitude people going to high altitude doing the same work will be working nearer to capacity.

Durand: It is difficult to compare exercise at sea level and at high altitude, even if one expresses the power as a fraction of the local maximal performance of the subject.

Peñaloza: On the question of the systemic circulation, it is interesting that systemic blood pressure at high altitude is lower than at sea level. This clinical impression, widely held for many years in Andean populations, has been confirmed recently in epidemiological studies by Ruiz and co-workers (1968). Vasodilatation and hypervascularization in response to chronic hypoxia are responsible for the diminished peripheral resistances. Marticorena and co-workers (1969) have demonstrated a lowering in blood pressure of sea level white males after a long residence at high altitudes. This observation emphasizes the effect of the environmental hypoxic stimulus on blood pressure, since these people obviously had a different genetic makeup from the altitude natives, and, in addition, they did not vary their diet and other habits.

I would also like to mention the role of polycythaemia in the regulation of diastolic blood pressure at high altitudes. This role is generally neglected at sea level, despite the fact that a direct partial relationship between haematocrit and diastolic pressure has been demonstrated (McDonough *et al.* 1965). At great altitudes, where the prevalence of polycythaemia is very high, this relation becomes evident and several recent observations made at our laboratory point in this direction. (1) In contrast to what happens to systolic pressure at altitude, diastolic values in men are not significantly different from those at sea level. Polycythaemia, increasing blood viscosity and peripheral resistances counteract the vascular effects of hypoxia, giving as the final result low systolic pressures associated with similar diastolic pressures values to those at sea level (Ruiz *et al.* 1968). (2) The behaviour of systemic blood pressure in females over 40 years is similar to that of males; however, below 40 years both systolic and diastolic pressures are lower than at sea level. This is ascribed to the slight degree of polycythaemia in younger females due to menstrual losses (Ruiz *et al.* 1968). (3) Diastolic hypertension is often seen in cases of Monge's disease, which is characterized by a severe degree of polycythaemia. Values of diastolic pressure in these patients become nearly normal after bleeding (Ruiz and Peñaloza 1970).

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