Acclimatisation to High Altitudes.¹

By Dr. J. S. HALDANE, F.R.S.

THERE is now general agreement among physiologists that, as was originally concluded by Paul Bert, the formidable group of symptoms known as 'mountain sickness' is due essentially to the lowered partial pressure of oxygen owing to the diminished barometric pressure of high altitudes; also that the symptoms depend upon the lowered oxygen pressure being insufficient to saturate with oxygen to a normal extent the hæmoglobin of the arterial blood, so that a normal pressure of oxygen is not maintained in the central nervous system. The defective saturation of the arterial blood shows itself by blueness, often extreme, of the lips and face. Persons who ascend by gradual stages to high altitudes are commonly found to be immune to mountain sickness; and this fact has been brought into extraordinary prominence by the experiences of the last Mount Everest expedition. Members of the expedition were completely immune to mountain sickness at a height of 27,000 feet, though persons going without acclimatisation to a similar barometric pressure in balloons or steel chambers lose consciousness rapidly, and would shortly be dead if they remained in the rarefied atmosphere.

Two expeditions have been made to high altitudes with the special object of investigating the nature of the acclimatisation. The first was to Pike's Peak in the Rocky Mountains in 1911 by Douglas, Yandell Henderson, Schneider, and myself, with supplementary investigations by Miss FitzGerald at mining villages, etc. The second was to Cerro de Pasco, Peru, in 1922 by Prof. Barcroft and associates. There have also been various observations in steel chambers under reduced barometric pressure, and in air-tight chambers in the air of which the oxygen percentage was allowed to fall without accumulation of carbon dioxide. These observations have shown that (1) for a given consumption of oxygen or production of carbon dioxide in acclimatised persons the volume of air breathed is increased in proportion to the fall in barometric pressure; (2) the percentage of hæmoglobin in the blood is similarly increased. Both of these changes will evidently act in the direction of diminishing the fall in oxygen pressure in the central nervous system. If the breathing were increased without compensatory changes in the body, the latter would be very abnormally alkaline, owing to excessive washing out of carbon dioxide. This extra alkalinity is, however, almost entirely compensated owing to the fact that as soon as the breathing begins to be increased owing to the stimulus of want of oxygen, the kidneys begin to excrete an increased amount of alkali, as was shown by Kellas, Kennaway, and myself. Hence in an acclimatised person the alkalinity of the body is scarcely increased at all.

So far, there appears to be agreement on the subject of acclimatisation; but on further points there is marked difference in opinion. The very careful, and apparently conclusive, experiments of Fredericq and of A. and M. Krogh had shown that, as measured with the aerotonometer, the oxygen pressure of the arterial blood is, under normal resting conditions, always lower

than that of the alveolar air in the lungs. On the other hand, the experiments of Douglas and myself by the carbon monoxide method had shown that the mean oxygen pressure of the blood leaving the lung alveoli is, under normal resting conditions, exactly the same as that of the alveolar air, so that diffusion equilibrium for oxygen between alveolar air and blood is complete. At the time we attributed the difference in results to there being a loss, during the conveyance of the arterial blood from the lungs, of a slight amount of oxygen owing to the presence in the blood of reducing substances which had not had time to be oxidised completely in the lungs. A later investigation by Meakins, Priestley, and myself in 1918 furnished, however, a much simpler and more satisfactory explanation, which at the same time cleared up a number of other clinical and physiological observations which had hitherto been unintelligible.

The alveolar air, as obtained by one form or another of the method introduced by Priestley and myself in 1905, is evidently a mixture of the samples of air from innumerable alveoli. In some alveoli the oxygen percentage will be lower, and in some higher, according as the blood supply is greater or less in relation to the air supply. The mixed arterial blood will reflect these conditions. Now the dissociation curve in the living body of the bicarbonate, in which form carbon dioxide is transported in the blood, is practically a straight line over the differences in carbon dioxide pressure which come into account in the lungs. This was shown by Christiansen, Douglas, and myself in 1914. Hence the effect on the mixed arterial blood of varying carbon dioxide pressure in the lung alveoli will be just the same as if the carbon dioxide pressures in all the lung alveoli were equal. On the other hand, the dissociation curve of oxyhæmoglobin is nothing like a straight line, and has the characteristic doubly inflected form discovered by Christian Bohr. The effect of the varying oxygen pressure in different alveoli will therefore be that the mixed arterial blood will have a lower oxygen pressure than that of the mixed alveolar air. This effect will, moreover, be exaggerated if the oxygen pressure of the alveolar air is abnormally low, as at high altitudes.

We have thus a complete explanation of the difference between the results by the aerotonometer and carbon monoxide methods, since the latter method gives the average of the oxygen pressures of the various streams of blood leaving different alveoli, and not the oxygen pressure of the mixed arterial blood. We have also the explanation of why, in unacclimatised persons, a quite moderate lowering of barometric pressure—for example to the pressure at 11,000 feet—may produce extreme symptoms of mountain sickness, with great blueness of the lips.

In the Pike's Peak expedition we used the carbon monoxide method, and found, in every subject investigated, that after acclimatisation, the average oxygen pressure of the blood leaving the alveoli was much higher than that of the alveolar air. But this was not the case in an unacclimatised control, who was still blue when examined, and shortly afterwards became mountain-sick, though after he was acclimatised, and

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his lips were again normal in colour, he reacted just like the other acclimatised subjects. We therefore concluded that active secretion of oxygen is an essential part of acclimatisation. Later experiments by Kellas, Kennaway, and myself in 1918 on acclimatisation in a steel chamber gave strong confirmation to this conclusion.

In the Peru expedition no experiments were made by the carbon monoxide method, but Prof. Barcroft and his associates made determinations of the percentage oxygen saturation of the arterial hæmoglobin. From the results of these analyses they drew the conclusion that the oxygen pressure of the arterial blood is never higher than that of the alveolar air. This conclusion, however, depended on a further conclusion that in all the subjects investigated the dissociation curve of the oxyhæmoglobin in the blood was greatly altered in such a way that the blood passing through the lungs would take up more oxygen than at sea-level. This result is in direct contradiction of careful experiments made previously by Barcroft himself on the Peak of Teneriffe and on Monte Rosa, and of particularly careful confirmatory experiments made by Douglas and myself on Pike's Peak, at practically the same height as in the Peru expedition. No explanation is given of the contradiction, and it seems quite incredible that a real difference could have existed. Until, at least, confirmatory evidence is forthcoming, I can only conclude

that there was some error of experiment in the Peru determinations. The analyses of the arterial blood gave just such results as we should have expected from the Pike's Peak experiments; and if, as I must still believe, the dissociation curves were practically the same as at sea-level, these blood-gas analyses prove, by themselves, our conclusion that oxygen secretion is an essential element in acclimatisation.

Prof. Barcroft unfortunately failed to understand the nature of our conclusions as to oxygen secretion, or the significance of previous work as to the relation between the mean alveolar oxygen pressure and the oxygen pressure of the mixed arterial blood. He has thus been unwittingly led, particularly in his recently published book on "The Respiratory Functions of the Blood," into a complete misrepresentation of my own views on the subject. On reviewing the whole of the existing evidence, including the very important data from the Everest expeditions, I can see no way of interpreting the phenomena of acclimatisation without the assumption of oxygen secretion in addition to the other known factors.

(The lecture contained a review of the evidence bearing on oxygen secretion by the lungs, since the time when its occurrence was first suggested by Ludwig; and at the end there was a discussion of the reason, now evident enough, why so little benefit was obtained in the last Everest expedition from the use of oxygen.)

Obituary.

PROF. EDOUARD NAVILLE.

THE late Prof. Edouard Naville, who died recently at Geneva in his eighty-third year, was a typical representative of the older generation of Egyptologists. The son of a distinguished Genevese family, of strong Evangelical tenets, he came to England when young to study at King's College, London, and here imbibed the liking for England and all things English that was characteristic of him through life. He went on to Bonn, and later studied Egyptology under Lepsius. He and Maspero both began their scientific work at the same time, round about the year 1870. In spite of great differences of temperament and style, their work shows resemblances characteristic of their time, especially in purely archaeological matters; neither was able quite to enter into the spirit of the newer science of archæology or to understand its insistence on the importance of small things equally with great. The men of that generation thought only of great, beautiful, and fine things, and could see nothing of importance in a bead or a scarab. They were scholars and connoisseurs, not anthropologists.

Naville began to excavate in the early 'eighties for the Egypt Exploration Fund, shortly after its foundation (as also did Prof. Sir Flinders Petrie), and his work at Bubastis and at Deir el-bahri for the Fund will always be notable; that at Deir el-bahri being indeed among the most important excavations carried on by the Society. His work on the supposed site of Pithom and on the route of the Exodus was the most important, and in its time certainly interested a large body of subscribers. But his views on this subject are not now so generally accepted as they were then. The placing of the Exodus in the reign of Menephtah is

no longer regarded as a *chose jugée*, and Naville's views on the actual route of the Exodus have undergone some modification at the hands of younger scholars. For their time, however, his theories were very advanced, and of great importance. At Deir el-bahri he uncovered the great temple of Hatshepsut, and in later years (1903-7) that of Mentuhotep IV., this time assisted by the present writer, Mr. E. R. Ayrton, Mr. C. T. Currelly, and others. His earlier work had been done almost entirely alone, except that for one season at the Hatshepsut temple he had had the assistance of Mr. D. G. Hogarth. His plans and architectural descriptions were made for him chiefly by the late Mr. Somers Clarke, though in the Mentuhotep temple Mr. C. R. Peers and one of Naville's relations, M. Edmond Fatio, also helped.

Later on, Naville began the excavation of the Osireion, the great subterranean building behind the temple of Abydos, thought by him to be of the time of the Old Kingdom, but proved by his successor in the work, Mr. H. Frankfort, to be the funerary temple and cenotaph of Seti I. (XIXth Dynasty), thus confirming a surmise of Borchardt's published in *Klio* several years ago. This building was discovered by Sir Flinders Petrie and Miss M. A. Murray so long ago as 1902, but on account of the enormous labour and expense required for its excavation had been abandoned until Naville and the Exploration Fund took it up. Naville's work, in which he was assisted by Mr. T. E. (now Prof.) Peet and Mr. G. A. Wainwright, resulted in the clearance of practically the whole of this extraordinary building. Then the War came and closed down operations. Naville, after it, was too old to resume the work, which could not in any case be