Hemoglobin at High Altitude as Related to Age

D. B. Dill, J. W. Terman, and F. G. Hall

During the summer of 1962 the early phase of acclimatization to high altitude was studied in 6 of those who participated in the international high-altitude expedition to Chile in 1935. Ages of the 6 ranged from 58 to 71. Two also had taken part in a high-altitude study in 1929. In their earlier years these subjects had had an increase in hemoglobin concentration beginning with their arrival at high altitude. This response has been well established, especially by the Pike's Peak party led by Haldane and the work of Hurtado and associates in Peru. On the other hand, 5 of the 6 in the 1962 party exhibited a decrease in hemoglobin concentration during the first few days. The greatest decrease was observed in the oldest subject. His hemoglobin was 88% of his sea level value after 9 days at altitude and remained below his sea level value for another week. No observations were made on blood volume; hence, we can only speculate regarding possible related changes.

This report deals with the concentration of hemoglobin in the blood during the early phase of acclimatization to high altitudes.

The discovery that the concentration of hemoglobin in the blood increases at high altitude is credited to Paul Bert (1). His observations on animals from Bolivia were supported by Viault's observations in 1890—8 years later—on man as well as animals (2, 3). A review of these and other early studies (not all in agreement) by Schneider (4) covered the literature until shortly before the Barcroft Peruvian expedition. The Pike's Peak party, led by Haldane (5), gave clear-cut evidence of the early increase in hemoglobin concentration in the 4 male members of the party—Haldane, Y. Henderson, Schneider, and Douglas, whose ages ranged from 29 to 51. Their daily observations

From the Department of Anatomy and Physiology, Indiana University, Bloomington, Ind.

We are glad to acknowledge support of the study reported by the Federal Aviation Agency under Contract FA 2049. Our pleasant weeks at the laboratories of the White Mountain Research Station were made possible by Drs. Nello Pace and Raymond J. Hock and their staff. Mr. Jerry L. Newton assisted in the study.
using the Gowers-Haldane hemoglobinometer provided the first opportunity to examine the relation between age and the hematopoietic response to altitude.

No observations pertinent to our topic were made by the Barcroft study at Cerro de Pasco in Peru (6), except for the observation that the increase in red cell count over the sea level standard was twice as great in the Indian miners at Cerro than in either resident engineers or in the scientists 2 weeks after arriving.*

**Present Study**

*In this brief historical introduction it is fitting to recognize the contribution made in this field by Van Slyke and his numerous celebrated associates. First, the Van Slyke blood gas apparatus has been an invaluable tool in modern high-altitude studies. We first employed it in Colorado in 1929, later in Chile in 1935, and at White Mountain during the summer of 1962. It was our privilege in the Harvard Fatigue Laboratory to demonstrate to Hurtado, Astes-Salazar, and associates, from Peru, and to Chiodi from Argentina, the applicability of the Van Slyke blood gas apparatus as a prime tool in high-altitude laboratories such as they subsequently established. The two-volume work by Peters and Van Slyke (7) is as valuable as a handbook of basic methods as it is as a source of authoritative interpretations.

Methods

During the summer of 1962 the responses of 6 subjects—Keys, Forbes, Hall, McFarland, Talbott, and Dill—at high altitudes were observed and compared with observations made on some of them at high altitudes in 1929 and 1935. Details regarding the party, the locale—White Mountain Research Station—and respiratory responses have been reported (8, 9). In nearly all cases hemoglobin was determined by two methods. In the first, heparinized blood was equilibrated at 37° at a pO₂ of 172 mm. Hg and analyzed on the Van Slyke manometric apparatus. After correction for dissolved oxygen the concentration of hemoglobin was calculated on the assumption of a combining capacity of 1.34 ml. O₂ per gram of hemoglobin. In the second method hemoglobin was determined colorimetrically on the Evelyn apparatus by the cyanmethemoglobin method as described by Drabkin (10). As a convenient short-cut the blood sample used was that contained in the Van Slyke pipet below the lower graduation. This part of each pipet used was calibrated by weighing the mercury contained in it. Thus, after introducing blood into the Van Slyke apparatus the remainder was transferred to the colorimeter tube, the lower stem of the pipet being washed several times with the Drabkin reagent. In a few instances the hematocrit on the heparinized blood was observed.

In the case of the members of the Pike's Peak expedition, moving
averages have been employed in plotting their increments of hemoglobin concentrations; i.e., the Day 1 value is the average for Days 0, 1, and 2, and the Day 2 value, the average of Days 1, 2, and 3, etc. The results, plotted in Fig. 1, suggest both that the rate of increase in

hemoglobin decreases with age and also that the equilibrium value may be higher in youth than in middle age. The values for Henderson and Schneider were averaged, since they were about the same age—38 and 37, respectively. Aside from a 3-day period in the third week, their average response was below that of Douglas, aged 29. The response of Haldane, aged 51, in turn was below that of Henderson and Schneider. While they noted that the rise in hemoglobin and in the number of red corpuscles, "was especially rapid in the first two or three days in all of us except Haldane in whose case it was gradual," they did not consider age as a factor.

Results

Table 1 lists the results of 9 experiments in 1962 in which hemoglobin was determined by the two methods described, and in which the hematocrit was observed. These results give an indication of the errors in our determinations of hemoglobin and also provide evidence that the oxygen-combining capacity of red cells is a characteristic that changes little if any with age and with the process of acclimatization to high altitudes. The mean value, approximately 20 mM/L of red cells, is about the same as that found both at sea level and at high altitudes in 1935 (11-13).
Table 1. Hemoglobin Concentration in Blood and in Red Cells Obtained in 1962 (Present) Study

<table>
<thead>
<tr>
<th>Subject</th>
<th>Altitude (m.)</th>
<th>Hct. (%)</th>
<th>In blood</th>
<th>In red cells</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Van Slyke</td>
<td>Drabkin</td>
</tr>
<tr>
<td>Dill</td>
<td>3800</td>
<td>40</td>
<td>7.79</td>
<td>7.53</td>
</tr>
<tr>
<td>Dill</td>
<td>4343</td>
<td>45.5</td>
<td>8.56</td>
<td>8.43</td>
</tr>
<tr>
<td>Hall</td>
<td>3800</td>
<td>49.5</td>
<td>10.09</td>
<td>9.84</td>
</tr>
<tr>
<td>Keys</td>
<td>3800</td>
<td>40.3</td>
<td>7.99</td>
<td>7.60</td>
</tr>
<tr>
<td>Keys</td>
<td>3800</td>
<td>40</td>
<td>8.06</td>
<td>8.08</td>
</tr>
<tr>
<td>Keys</td>
<td>4343</td>
<td>41.5</td>
<td>8.32</td>
<td>8.25</td>
</tr>
<tr>
<td>Talbott</td>
<td>3093</td>
<td>46</td>
<td>9.31</td>
<td>9.15</td>
</tr>
<tr>
<td>Talbott</td>
<td>3800</td>
<td>41.5</td>
<td>8.38</td>
<td>8.38</td>
</tr>
<tr>
<td>Talbott</td>
<td>4343</td>
<td>44.4</td>
<td>8.64</td>
<td>8.38</td>
</tr>
</tbody>
</table>

All the observations on hemoglobin in 1962 on Dill and Forbes are shown in Fig. 2 together with the time-course of their stays at altitude. Both showed an initial decline in hemoglobin concentration; the minimum value for Forbes was observed on the fifth day, and for Dill, on the ninth day. Fig. 3A has the corresponding records for Hall and McFarland, and Fig. 3B for Keys and Talbott. After initial slight increases in McFarland, Hall and Talbott at the Crooked Creek laboratory, hemoglobin concentrations decreased, reaching the lowest values on the fifth, third, and fourth days, respectively. In Keys there was a slight upward trend from the beginning.

Comparable observations were made on 3 of us—Dill, McFarland and Talbott—in 1935 (11) and also on Dill and Talbott in 1929 (14). The findings in 1929 and those in 1935 at the first three stations are shown in Fig. 4 together with records of the time-course of stays at altitude. There is excellent agreement between the responses of Dill

Fig. 2. Blood hemoglobin concentration during acclimatization to high altitude in summer of 1962. Solid circles indicate values for Dill; open circles, Forbes.
and Talbott in 1935 and their responses in 1929. Each started about 1 mM apart and showed a similar upward trend, with the exception of the 6-day value for Dill in 1929. Comparison of findings on the 3 subjects in 1935 with those of 1962 is even more clear-cut. All show a drop in 1962 and none a drop in 1935. There was a roughly parallel upward trend in the 3 subjects in 1935. An additional point is worth making: Dill has a relatively low hemoglobin concentration. This persists at altitude and it has persisted over a 33-year period at sea level.

**Discussion**

There have not been many comparable observations in the literature, even in young men, since those of Douglas, Haldane, Henderson, and Schneider (5) illustrated in Fig. 1. One series has been reported by Hurtado et al. (15), and he has kindly furnished additional unpublished observations. All his subjects, Peruvian medical students, went directly to Morococha, which has an elevation of 4540 m. His results for each individual have been calculated to the sea level base line of

---

**Fig. 3.** Blood hemoglobin concentration during acclimatization to high altitude, summer of 1962. A. Solid circles, indicate values for MacFarland; open circles, Hall. B. Solid circles indicate values for Keys; open circles, Talbott.

**Fig. 4.** Blood hemoglobin concentration during acclimatization to high altitudes. DBD indicates Dill; JHT, Talbott; McF, McFarland. Year of study is shown for each.
100 and the same has been done for our observations in the summer of 1962. The mean hemoglobin concentrations at the various times of exposure are plotted in Fig. 4. In a few cases scattered observations have been consolidated; e.g., Hurtado had a measurement on one individual at 18 days, another at 20, and a third at 22 days; the three have been averaged and the mean appears in the figure at 20 days (Fig. 5).

The results demonstrate a marked difference in the response of hemoglobin concentration to oxygen lack between young men and men ranging in age from 58 to 71. Young men from the day of arrival at altitude generally show an increase in hemoglobin. This was observed by the Pike’s Peak party, in members of our group in 1929 and 1935, and in the Hurtado’s medical students. On the other hand, 5 of 6 members of our group in 1962 exhibited a decreased concentration during the first days at altitude. The sixth showed a small upward trend through the first 5 days. Of the 3 subjects who spent 2 weeks or more at altitude, hemoglobin concentration eventually rose above the sea level values at 23 days (Dill), at 8 days (Hall), and at 11 days (Forbes).

We do not have observations on blood volume and hence can only speculate on the nature of related responses to high altitude. One possible interpretation of our findings is that, in the early stages of adaptation in our age range, plasma volume increases faster than red cell volume. It does not seem likely that a high rate of red cell destruction was involved, since we did not engage in much exercise during the first week. Neither is it likely that there was an upset in water balance since body weight changed little from day to day, ranging from a gain of 2.5 kg. by Talbott to a loss of 2.2 kg. by Forbes.

The novelty of our findings points to the need for further study. Frequent measurement of red cell and plasma volumes should be
coupled with daily observations of hemoglobin concentrations. Cardiac output measurements might be useful in interpreting observations on work capacity and other criteria of acclimatization. The daily urinary erythropoietin might prove quite significant. The method described by Hodgson et al. (16) has been applied by Scarò (17) on newcomers at 3990 m. and residents at 1260, 3990, and 4515 m. The content of erythropoietin was somewhat higher in residents at high altitude than in residents at low altitudes. It was several times higher in recent arrivals at high altitude than in residents. This approach coupled with the others mentioned above might lead to a better understanding of the relation of age to adaptation to high altitudes.

References