DIURNAL VARIATIONS OF HEMOGLOBIN IN THE BLOOD OF NORMAL MEN

BY EARL F. MCCARTHY AND DONALD D. VAN SLYKE
(From the Hospital of The Rockefeller Institute for Medical Research, New York)

(Received for publication, March 11, 1939)

The occurrence of diurnal variations of hemoglobin in the blood of normal people has been reported by a number of observers. Dreyer, Bazett, and Pierce (1) and Rabinowitch (2) have made determinations of the hemoglobin content of the blood of normal adults during the day and find a possible variation of 20 to 30 per cent of the average content. Short (3) finds a possible variation of 17 per cent as a result of his experiments. The methods employed by these investigators have not been so precise as those now available. The colorimetric methods used by Dreyer and his coworkers and by Short do not allow for the effect of variations in substances other than hemoglobin, such as lipids, which could affect the light absorption of the samples. Rabinowitch used the oxygen capacity method in his experiments, but employed an earlier and considerably less exact technique; also the inhalation of small amounts of CO by smokers may cause an appreciable alteration of the apparent hemoglobin content. His maximum variation during the day was more than double that observed by us.

Methods

The subjects in these experiments were healthy men from 20 to 30 years of age. They comprised laboratory technicians and medical students who were performing ordinary routine work. Blood was obtained by venipuncture from the arm veins at 2 to 3 hour intervals throughout the day. Precautions were taken to avoid stasis. The hemoglobin content was estimated from the CO-combining capacity according to the method of Van
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Slyke and Hiller (4). In this technique the blood sample mixed with water is saturated with CO in the 50 cc. chamber of the Van Slyke manometric apparatus. Subsequently the excess CO and the O₂ and N₂ extracted by the shaking are expelled from the chamber, and the HbCO is determined by measurement of the CO set free by acid ferricyanide solution.

We used samples of 1 cc. of blood, and measured the pressure of the CO gas at 1 cc. volume. (A Van Slyke-Neill chamber calibrated at 1.0 cc., in addition to the usual 0.5 and 2.0 cc. points, was used.) These conditions gave a desirable combination of accuracy with economy of blood. The mean difference between duplicate analyses was 0.06 volume per cent of CO capacity.

The CO capacity method has over the O₂ capacity two advantages with respect to immunity from error.

1. The correction for physically dissolved O₂ is replaced by a smaller and practically constant correction for physically dissolved CO. According to the solubility determinations of Sendroy, Dillon, and Van Slyke (5) normal blood saturated with air at 20° under 760 mm. of atmospheric pressure dissolves 0.70 per cent of O₂, and in blood of abnormal cell content the dissolved O₂ varies with the cell content. In comparison the correction for CO dissolved in the blood plus 2.5 volumes of water is only about 0.33 volume per cent of the blood in the technique of Van Slyke and Hiller, and is relatively independent of the cell content.

2. If the blood contains any preformed CO, as from tobacco smoke or the exhaust of automobiles, the O₂ capacity values are lowered, while the CO capacity is unaffected. The reason for this is that the CO is so strongly bound to the hemoglobin that agitation with air for the periods ordinarily used fails to replace the HbCO entirely with HbO₂. The O₂ subsequently determined in such a case therefore does not indicate all the Hb present. That the amount of CO in the blood of modern man can suffice to lower significantly the O₂ capacity values is indicated by the data on p. 112 of Enghoff's (6) monograph. He found O₂ capacities significantly lower than CO capacities in the bloods of seventeen out of 168 subjects; in these seventeen subjects the CO capacity exceeded the O₂ capacity by from 0.4 to 1.7 volume per cent.
### Table I

**Hemoglobin Concentrations of Normal Young Men at Different Hours of the Day**

<table>
<thead>
<tr>
<th>Subject</th>
<th>9 a.m.</th>
<th>11 a.m.</th>
<th>2 p.m.</th>
<th>5 p.m.</th>
<th>8 p.m.</th>
<th>11 p.m.</th>
<th>Average for subject</th>
<th>Median for day</th>
<th>Range of day above and below median</th>
<th>Range of day in percent of median</th>
</tr>
</thead>
<tbody>
<tr>
<td>G. M.</td>
<td>20.03</td>
<td>19.00</td>
<td>19.26</td>
<td>19.24</td>
<td>18.93</td>
<td>18.46</td>
<td>19.16</td>
<td>19.25</td>
<td>±0.79</td>
<td>±4.1</td>
</tr>
<tr>
<td>F. W.</td>
<td>20.32</td>
<td>20.02</td>
<td>19.92</td>
<td>19.61</td>
<td>18.95</td>
<td>19.52</td>
<td>19.73</td>
<td>19.62</td>
<td>±0.70</td>
<td>±3.6</td>
</tr>
<tr>
<td>J. K.</td>
<td>18.84</td>
<td>19.97</td>
<td>18.82</td>
<td>19.27</td>
<td>18.12</td>
<td>18.45</td>
<td>18.92</td>
<td>19.05</td>
<td>±0.92</td>
<td>±4.8</td>
</tr>
<tr>
<td>F. R.</td>
<td>19.62</td>
<td>19.73</td>
<td>20.13</td>
<td>20.19</td>
<td>19.30</td>
<td>20.75</td>
<td>19.97</td>
<td>20.03</td>
<td>±0.72</td>
<td>±3.6</td>
</tr>
<tr>
<td>H. G. T.*</td>
<td>17.21</td>
<td>16.67</td>
<td>17.16</td>
<td>17.01</td>
<td>17.08</td>
<td>16.70</td>
<td>16.99*</td>
<td>16.94*</td>
<td>±0.27</td>
<td>±1.6</td>
</tr>
<tr>
<td>F. B.</td>
<td>19.58</td>
<td>19.45</td>
<td>19.90</td>
<td>18.89</td>
<td>19.21</td>
<td>18.86</td>
<td>19.38</td>
<td>19.90</td>
<td>±0.55</td>
<td>±2.8</td>
</tr>
<tr>
<td>J. F.</td>
<td>20.77</td>
<td>20.88</td>
<td>20.47</td>
<td>21.37</td>
<td>20.36</td>
<td>20.31</td>
<td>20.70</td>
<td>20.84</td>
<td>±0.53</td>
<td>±2.5</td>
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<td>J. M.</td>
<td>20.56</td>
<td>20.72</td>
<td>20.59</td>
<td>19.92</td>
<td>19.86</td>
<td></td>
<td>20.33</td>
<td>20.29</td>
<td>±0.43</td>
<td>±2.1</td>
</tr>
<tr>
<td>J. B.</td>
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<td>20.54</td>
<td>21.73</td>
<td>20.07</td>
<td>21.02</td>
<td>20.10</td>
<td>20.68</td>
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<td>±0.53</td>
<td>±3.5</td>
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<tr>
<td>A. C.</td>
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<td>20.33</td>
<td>19.36</td>
<td>19.52</td>
<td>19.59</td>
<td>19.31</td>
<td>19.95</td>
<td>20.50</td>
<td>±1.14</td>
<td>±5.4</td>
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<tr>
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<td>20.35</td>
<td>20.04</td>
<td>19.53</td>
<td>19.02</td>
<td>19.22</td>
<td>19.72</td>
<td>19.69</td>
<td>±0.67</td>
<td>±3.4</td>
</tr>
<tr>
<td>F. P.</td>
<td>19.38</td>
<td>18.93</td>
<td>18.83</td>
<td>19.14</td>
<td>18.87</td>
<td>18.61</td>
<td>18.96</td>
<td>19.00</td>
<td>±0.30</td>
<td>±2.0</td>
</tr>
<tr>
<td>R. S.</td>
<td>18.59</td>
<td>17.77</td>
<td>17.03</td>
<td>17.63</td>
<td>17.46</td>
<td></td>
<td>17.81</td>
<td>±0.78</td>
<td>±4.4</td>
<td></td>
</tr>
<tr>
<td>D. K.</td>
<td>18.65</td>
<td>18.23</td>
<td>17.93</td>
<td>18.26</td>
<td>18.63</td>
<td>18.24</td>
<td>18.02</td>
<td>18.29</td>
<td>±0.36</td>
<td>±2.0</td>
</tr>
<tr>
<td>E. J.</td>
<td>20.57</td>
<td>20.04</td>
<td>20.03</td>
<td>20.30</td>
<td>20.34</td>
<td>20.62</td>
<td>20.33</td>
<td>20.30</td>
<td>±0.30</td>
<td>±1.5</td>
</tr>
<tr>
<td>R. E.</td>
<td>21.30</td>
<td>20.21</td>
<td>20.56</td>
<td>20.39</td>
<td>20.31</td>
<td>20.04</td>
<td>20.48</td>
<td>20.67</td>
<td>±0.63</td>
<td>±3.1</td>
</tr>
<tr>
<td>L. A.</td>
<td>21.07</td>
<td>19.61</td>
<td>19.67</td>
<td>19.43</td>
<td>19.69</td>
<td></td>
<td>20.05</td>
<td>20.62</td>
<td>±0.62</td>
<td>±3.1</td>
</tr>
<tr>
<td></td>
<td>20.62</td>
<td>20.07</td>
<td>19.38</td>
<td>19.33</td>
<td>19.25</td>
<td>18.99</td>
<td>19.70</td>
<td>19.81</td>
<td>±0.82</td>
<td>±4.1</td>
</tr>
</tbody>
</table>

Maximum .................................. 21.20 21.31 ±1.14 ±5.4
Minimum .................................. 18.02 17.81 ±0.27 ±1.6
Mean ...................................... 19.86 19.94 ±0.64 ±3.2
Standard deviation √Σd²/n ............ ±0.74 ±0.92 ±0.21 ±1.0

* The exceptionally low data for H. G. T. are excluded in calculating means, minima, and standard deviations for "average for subject" and "median for day."

### Results

The results from eighteen subjects are shown in Table I. In thirteen of the subjects the observations covered 1 day each; in
five subjects observations were made on 2 separate days about a week apart. Fig. 1 illustrates the changes observed in the five subjects who provided two curves each. From Fig. 1 there seems to be a tendency for the blood of each subject to follow a daily course typical of the individual.

The greatest range between the highest and lowest values for 1 day was 2.3 volumes per cent of CO capacity, or 11 per cent of the mean value. The average range was 1.3 volumes per cent of CO capacity, or 6.4 per cent of the mean.

These ranges of variation are narrower than those reported with earlier, and probably less exact, methods for hemoglobin measurement.

![Fig. 1. Diurnal hemoglobin variations observed on 2 different days, about 1 week apart, in five young men.](http://www.jbc.org/)
The direction of change in hemoglobin concentration during the day is not predictable from our data. There seems to be a tendency for the concentration to decrease during the waking hours: in 20 of the 23 days observed the hemoglobin at 11 in the evening was less than at 9 in the morning. The variation in behavior is such, however, that on a given day one could not predict even the direction of the change. Thus subject R. E. showed, from the earliest to the latest blood sample on 1 day, a decrease from 21.48 to 20.70, and on another day an increase from 20.24 to 21.17 volumes per cent.

The mean hemoglobin content of our eighteen subjects is represented by 19.9 volumes per cent of CO capacity. It appears that most of our subjects were in the lower half of the range, 20.7 ± about 2.0, for normal men, which was estimated from data available in 1930 by Peters and Van Slyke (7), and has been confirmed recently by Enghoff’s (6) precise study, with the CO capacity method applied to 95 men between 18 and 59 years of age.

SUMMARY

In eighteen young men hemoglobin determinations by Van Slyke and Hiller’s manometric CO capacity method were performed at intervals of 2 to 3 hours from 9 a.m. to 11 p.m. on 1 or more days. The accuracy is indicated by a mean difference between duplicate analyses of 0.06 volume per cent of CO capacity.

The range between highest and lowest values in an individual through a day averaged 1.3 volumes per cent; the greatest range seen in any of the 23 observed days was 2.3 volumes per cent, equivalent to 11 per cent of the mean hemoglobin content for the day. Usually the hemoglobin content was lower in the evening than in the morning; but a subject showing this change on one day reversed it on another.

The much greater ranges of diurnal hemoglobin variation reported in the past literature appear attributable to methods of analysis which provided a significant part of the variations.

BIBLIOGRAPHY

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