Correlation of the Oxygen Saturation of the Blood and Changes in the Electrocardiogram, Blood Pressure, and Heart Rate During the Anoxemia Test

Observations on Normal Persons and Patients with Suspected and Manifest Coronary Heart Disease

By James A. L. Mathers, M.D., and Robert L. Levy, M.D.

During the performance of a series of anoxemia tests the oxygen saturation of the blood has been determined by means of the Millikan oximeter. The levels of hypoxemia induced have been correlated with various other factors. The results are considered with particular reference to a possible critical range, within which changes in the circulation occur.

The ANOXEMIA test for coronary insufficiency, as proposed by Levy, Bruenn, and Russell in 1939, has been subjected to thorough clinical trial by a number of observers. If properly performed on suitable subjects it is without hazard and yields results which are of value in clinical diagnosis. It has also been employed to study indirectly, in man, the action of various drugs on the coronary circulation. The result is determined by the effect of anoxia on the form of the electrocardiogram; criteria for a positive reaction have been established and widely used.

The range of optimal levels of anoxemia at which such electrocardiographic changes occur is not known although it has been shown that there is wide individual variation with respect to the degree of anoxemia obtained while breathing 10 per cent oxygen. This depends, in large part, on the rate and, particularly, the depth of respiration during inhalation of the low oxygen mixture. The present study was designed to ascertain whether there is a critical level of anoxemia at which significant alterations in the electrocardiogram are induced. The relationship of varying degrees of anoxia to changes in heart rate and blood pressure was also noted.

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Material, Procedure, and Methods

Observations were made in 97 individuals on whom 109 anoxemia tests were performed. The oxygen saturation was measured by the Millikan oximeter. The tests were performed according to the method described by Levy and his associates. At the end of the period of induced anoxemia the subject inhaled 100 per cent oxygen for two minutes; the final electrocardiogram and reading of oxygen saturation were made after the patient had then breathed room air for seven or eight minutes. Oximeter readings and observations of heart rate and blood pressure were recorded at one-minute intervals throughout each period of study. The criteria for a positive reaction were those previously outlined.

The 97 subjects included 45 with coronary sclerosis, ranging in age from 40 to 73 years; the average was 53 years. There were 14 in whom the diagnosis of coronary sclerosis was in doubt before and after the test; these patients ranged in age from 33 to 58 years, with an average of 46 years. In 38 individuals there was no evidence of cardiovascular disease; they are referred to as "normals." The range of age in this group was from 29 to 59 years; the average was 46 years.

The results of the oximeter readings and the observations on heart rate and blood pressure were submitted to statistical analysis. Those tests which were carried to completion were compared with twenty-two which were terminated in less than twenty minutes because of pain. No essential difference appeared to exist between the completed and the incompletely terminated tests for the duration of the observation. On this basis all the tests have been pooled for this period. In cases where repeat tests were available for the individual, only the first test has been included in the analysis.

* We are indebted to Dr. John W. Fertig and Miss Isabel McCaffrey of the Department of Biostatistics,
RESULTS

There were no significant differences in the average oximeter readings in the patients with coronary sclerosis, suspected coronary sclerosis, and in the normal subjects (table 1), so that for presentation all are considered as a single group (fig. 1).

Table 1.—Average Oximeter Readings for the Various Groups during the Test

<table>
<thead>
<tr>
<th>Classification</th>
<th>Room Air</th>
<th>10 Per Cent Oxygen</th>
<th>100 Per Cent Oxygen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>After 5 minutes</td>
<td>Start</td>
<td>5 minutes</td>
</tr>
<tr>
<td>Coronary Sclerosis</td>
<td>95</td>
<td>95</td>
<td>79</td>
</tr>
<tr>
<td>Suspected Coronary Sclerosis</td>
<td>95</td>
<td>95</td>
<td>82</td>
</tr>
<tr>
<td>Normals</td>
<td>95</td>
<td>95</td>
<td>78</td>
</tr>
<tr>
<td>All Individuals</td>
<td>95</td>
<td>95</td>
<td>79</td>
</tr>
</tbody>
</table>

During the control period, while the patient was breathing room air through the apparatus, the oxygen saturation of the arterial blood remained fairly constant, averaging 95 per cent, with a range from 92 to 98 per cent. The fall in saturation when the mixture of 10 per cent oxygen and 90 per cent nitrogen was administered was most marked in the first five minutes, the average falling from 95 to 79 per cent. It was less marked in the second five minutes (from 79 to 75 per cent) and minimal in the final ten minutes (from 75 per cent at ten minutes to 73 per cent at fifteen and twenty minutes).

While these figures give the curve of the averages it is readily apparent from the graph (fig. 1) that there was a wide range of individual variability after the low oxygen mixture was inhaled. When 100 per cent oxygen was administered at the termination of the period, the saturation of the blood rapidly returned to an average figure of 98 per cent in about forty-five seconds. In a small number of cases the patient was changed directly from the 10 per cent oxygen mixture to room air, and in these instances the return to normal saturation was slightly slower, or there was a rapid return to a saturation of 86 to 90 per cent, with a subsequent slow rise to normal saturation. The average points of the depth of respiration more than the rate. In those instances in which the patient was apprehensive of the procedure, hyperventilation was more apt to occur and the resultant degree of unsaturation was less marked. In this series, one individual hyperventilated to such a degree in the original test that the arterial saturation never fell below 90 per cent. When the test was repeated at a later date the patient had become accustomed to the procedure and more normal respiration prevailed. This resulted in an average curve of anoxemia which

on this curve and the great individual variation from the average were similar to those found by other workers whose method involved the use of an equivalent partial pressure of oxygen.\(^5\)\(^-\)\(^11\)

The degree of unsaturation obtained in each case in all probability depends on the volume of gas inhaled by the individual and is a factor


showed 82 per cent at five minutes, 79 per cent at ten minutes, and 75 per cent at fifteen minutes. In both tests the electrocardiograms failed to reveal significant changes although the clinical diagnosis of coronary sclerosis had been made.

<table>
<thead>
<tr>
<th>Classification</th>
<th>Room Air</th>
<th>10 Per cent Oxygen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>After 5 minutes</td>
<td>Start</td>
</tr>
<tr>
<td>Coronary Sclerosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive Test</td>
<td>80</td>
<td>82</td>
</tr>
<tr>
<td>Negative Test</td>
<td>67</td>
<td>69</td>
</tr>
<tr>
<td>Suspected Coronary Sclerosis</td>
<td>74</td>
<td>75</td>
</tr>
<tr>
<td>Normals</td>
<td>76</td>
<td>76</td>
</tr>
</tbody>
</table>

Table 2.—Average Heart Rate for the Various Groups during the Test

In the total series, 16 individuals had an oxygen saturation curve which remained above 80 per cent in the original test. In 3 of these the reaction was positive within the first ten minutes, with the oxygen saturation at the time ranging from 83 to 85 per cent. In two types of patient a high degree of saturation was observed. The first was the apprehensive individual who obviously hyperventilated even during the control period and in whom the level never fell below 88 to 93 per cent. This type of patient increased both depth and rate of respiration to a marked degree and with one deep inspiration often caused a change in saturation of 5 to 10 per cent. The second type was the well-conditioned, athletic person who compensated readily to the low oxygen mixture by a very slight increase in the respiratory rate and a barely noticeable increase in the depth of respiration. The form of the curve of oxygen saturation was similar in character to the average but was maintained at a higher level, the lowest point reached being about 85 per cent.

In 4 individuals a drop in saturation to levels ranging from 55 to 60 per cent was obtained; of these 2 were normal subjects, one had coronary sclerosis, and in one the diagnosis of coronary sclerosis was suspected. In all 4 the respiration was slow and shallow throughout the test. The drop in saturation was rapid and associated with a definite increase in the heart rate of 20 to 40 beats per minute. None of these individuals experienced unpleasant symptoms or disturbing signs at this low degree of arterial oxygen saturation.

The average response of the heart rate is similar in the four groups (table 2 and fig. 2), namely, coronary sclerosis with a positive reaction to the test, coronary sclerosis with a negative reaction, suspected coronary sclerosis, and normal. Although the curves are similar, the average heart rate for the coronary sclerosis group with a positive reaction stays at a higher level throughout the test than for the coronary sclerosis group with a negative reaction. The curves for the suspected coronary and normal groups fall between the first two. The heart rate curve obtained is the inverse of that of the oxygen saturation. As the saturation of
the blood diminishes the heart rate increases; the rate and degree of increase are related to the rate and degree of fall in the arterial oxygen saturation. The average rise for all the cases studied as a single group was 12 beats per minute in the first five minutes with only a slight additional increase in the last fifteen minutes of the test. If the patient experienced pain in the chest there was usually an associated increase in the heart rate over that which was present when the pain first appeared. In whom the systolic blood pressure may increase 10 to 15 mm. Hg at the time of the pain.

Observations on the degree of anoxemia and the changes in the electrocardiogram in the individuals with coronary sclerosis have been studied in an attempt to determine four points: (1) the optimal level of anoxemia which one should attempt to attain in order to decrease the number of false negative results; (2) the time at which significant changes occur related to the degree of anoxia. In no instances were any abnormal cardiac rhythms encountered.

The average systolic (table 3) and diastolic (table 4) blood pressure curves for the four groups are essentially horizontal, showing little or no change as the test proceeds. The systolic pressure of the coronary sclerosis group with positive reaction shows a higher level throughout than those with a negative reaction. The normal individuals have about the same level as the group with coronary sclerosis with a negative reaction and those with suspected coronary sclerosis, and are intermediate between the positive and negative groups. Although there is no change in average blood pressure as the test proceeds, there are some individuals who experience pain during the test.

\begin{table}
\centering
\caption{Average Systolic Blood Pressure for the Various Groups during the Test}
\begin{tabular}{|l|c|c|c|c|c|}
\hline
Classification & Room Air & 10 Per Cent Oxygen \\
& After 5 minutes & Start & 5 minutes & 10 minutes & 15 minutes & 20 minutes \\
\hline
Coronary Sclerosis & & & & & & \\
Positive Test & 147 & 148 & 152 & 148 & 148 & 143 \\
Negative Test & 129 & 127 & 130 & 129 & 132 & 129 \\
Suspected Coronary Sclerosis & 139 & 139 & 143 & 143 & 138 & 140 \\
Normals & 130 & 129 & 135 & 137 & 136 & 135 \\
\hline
\end{tabular}
\end{table}

\begin{table}
\centering
\caption{Average Diastolic Blood Pressure for the Various Groups during the Test}
\begin{tabular}{|l|c|c|c|c|c|}
\hline
Classification & Room Air & 10 Per Cent Oxygen \\
& After 5 minutes & Start & 5 minutes & 10 minutes & 15 minutes & 20 minutes \\
\hline
Coronary Sclerosis & & & & & & \\
Positive Test & 84 & 84 & 89 & 85 & 84 & 83 \\
Negative Test & 79 & 78 & 80 & 79 & 79 & 79 \\
Suspected Coronary Sclerosis & 86 & 86 & 87 & 83 & 82 & 82 \\
Normals & 81 & 81 & 83 & 82 & 81 & 78 \\
\hline
\end{tabular}
\end{table}

in the electrocardiogram; (3) the number of individuals who are able to complete the twenty-minute test; and (4) the value of the final ten minutes of the test (table 5).

As had been expected there was a wide range of saturation (63 to 84 per cent) at which the reaction was first noted to be positive, and no optimal point of saturation could be defined. The positive reactions in which the patient experienced pain during the first ten minutes were positive at a higher degree of oxygen saturation than in complete tests in which a positive result was obtained in the final ten minutes. This is in agreement with the oxygen saturation curve presented earlier and is a factor of the time at which the test was discontinued because of pain. It also indicates a greater degree of coronary insufficiency in those individuals in whom
It was necessary to terminate the test because of pain. In the series of 45 patients with coronary sclerosis, 17 showed a positive reaction within the first ten minutes; 6 of these occurred in five minutes or less. Of these, 13 experienced pain, so that the test had to be discontinued. Four patients had a complete test with the electrocardiogram showing a positive result in the final ten minutes, but without the occurrence of pain. While there were 24 subjects in whom the reaction to the test was negative, in 9 of these pain was experienced, so that the test had to be discontinued before the end of the standard twenty-minute period.

**Table 5.—Result of Test in Forty-five Patients with Coronary Sclerosis**

<table>
<thead>
<tr>
<th>Result</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete test—negative reaction</td>
<td>15</td>
</tr>
<tr>
<td>Incomplete test—negative reaction</td>
<td>9</td>
</tr>
<tr>
<td>Test discontinued (time in minutes): 5, 5, 7, 9, 10, 14, 15, 15</td>
<td>8</td>
</tr>
<tr>
<td>Complete test—positive reaction</td>
<td>13</td>
</tr>
<tr>
<td>First noted positive (time in minutes): 10, 10, 10, 10, 15, 20, 20</td>
<td>13</td>
</tr>
<tr>
<td>Incomplete test—positive reaction</td>
<td>13</td>
</tr>
<tr>
<td>First noted positive (time in minutes): 2, 3, 4, 4, 5, 5, 8, 9, 10, 10, 10, 10</td>
<td>13</td>
</tr>
<tr>
<td>Test discontinued (time in minutes): 2, 3, 4, 4, 5, 5, 8, 9, 10, 10, 10, 13, 15</td>
<td>13</td>
</tr>
</tbody>
</table>

It is apparent in table 5 that 23 subjects (51 per cent) were able to complete the twenty-minute test. If the test had been terminated at ten minutes, 32 of the 45 (or 71 per cent) would have been able to complete it. Although only 51 per cent completed the twenty-minute test, the outcome is unknown in only those 9 who still showed a negative result when the test was discontinued before the end of the twenty minutes. So, for 36 of the 45 subjects (80 per cent) the outcome in terms of a complete, or at least a positive, reaction was known. At ten minutes the comparable figure is somewhat larger, namely 89 per cent. Against the advantage of running the test for only ten minutes in order to reduce the number of tests not completed must be balanced the disadvantage of failing to detect as positive those in which diagnostic changes in the electrocardiogram occur after ten minutes. In this series there are 4 such individuals. We may speak of the “yield” of the test in picking up positives as 17 out of 45, or 38 per cent, by ten minutes, and 47 per cent by twenty minutes.

It is thus readily seen that the majority of the changes in the electrocardiogram occur early in the test during the period of most rapid fall in oxygen saturation and before compensatory mechanisms, which level off the curve, become operative. Nevertheless, changes do occur in the last half of the test, especially in the final five minutes, so that it appears worth while to continue the period of anoxemia for the full twenty minutes. In the individuals who show a positive result and experience pain, it is usually necessary to terminate the test, because of discomfort, in the course of the first ten minutes.

**Comment**

It was suggested by Houston and by Dripps and Comroe that clinical applications of induced anoxia should be based upon arterial oxygen saturation or arterial oxygen tension attained rather than upon a specific percentage of inspired oxygen. Penneys and Thomas carried out studies at three fixed levels, 85 per cent, 80 per cent, and 75 per cent. By using this maneuver in performing the anoxemia test, it was thought that a sufficient degree of anoxia would be assured to decrease the number of negative reactions in patients with mild degrees of coronary insufficiency. At the same time, according to these authors, it would lessen the number of so-called false positives which might result from higher grades of anoxia and would tend to prevent unpleasant reactions in the patient.

We have not been impressed, in the routine use of the test, by the frequent occurrence of false positives; in fact, a follow-up study of 150 patients in whom the test was performed during a ten-year period has not revealed any instance in which a positive reaction occurred in a patient subsequently found to be free of coronary heart disease. By observing the precautions repeatedly outlined dangerous reactions can be entirely avoided and unpleasant symptoms largely eliminated.
It seems doubtful whether such a procedure would increase the incidence of positive reactions in patients in whom the degree of coronary insufficiency is relatively slight. In the apprehensive individual it would produce a greater sense of suffocation and could well result in a more marked degree of hyperventilation. Adequate control of the saturation at the desired level then would be practically impossible; frequent fine adjustments of the oxygen flow are necessary in any case.\(^{13}\) Varying the oxygen content of the inspired gas mixture might prove to be of some value in certain well conditioned subjects; in the routine use of the test, however, few of these are encountered.

Three of our 16 patients who hyperventilated showed an oxygen saturation curve which remained throughout above 80 per cent. The reaction was negative and was repeated on another day. A more normal type of respiratory response resulted in an oxygen curve at a lower level but the result was again negative.

**Summary and Conclusions**

1. In a group of 97 individuals, including normal persons and patients with manifest and suspected coronary disease, 109 anoxemia tests were performed in the standard manner. Oximeter readings, observations of heart rate and blood pressure, and the usual series of electrocardiograms were made.

2. The level of anoxemia induced varied widely in the individual and in different individuals. No optimal range of oxygen saturation could be defined which caused electrocardiographic changes characteristic of a positive reaction to the test. The determining factor appeared to be the degree of impairment in the functional capacity of the coronary circulation.

3. The heart rate rose in response to anoxemia. The curve was the inverse of that for the oximeter readings.

4. The blood pressure failed to show any significant increase or decrease during anoxemia.

5. Changes in the form of the electrocardiogram occurred over a wide range of levels of anoxemia. The highest percentage of positive results was obtained during the first ten minutes of the test but a significant percentage was observed also during the final ten minutes. For this reason, unless the patient experiences pain or other discomfort, it is desirable to continue the period of anoxemia for the full twenty minutes.

6. Lowering the oxygen saturation in the apprehensive subject to a level below that which the body attempts to maintain may produce unpleasant reactions and is unlikely to increase significantly the number of positive results.

**References**


(b) ---, Patterson, J. E., Clark, T. W., and Bruenn, H. G.: The “anoxemia test” as an index of coronary reserve. Serial observations on one hundred and thirty-seven patients with their application to the detection and clinical course of coronary insufficiency. J.A.M.A. **117**: 2113, 1941.


(m) Stewart, H. J., Horger, E. L., and Soren-
OBSERVATIONS DURING ANOXEMIA TEST


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