ELECTROCARDIOGRAPHIC CHANGES CAUSED BY INDUCED ANOXEMIA IN NORMAL PERSONS AND IN PATIENTS WITH DISEASE OF THE CORONARY ARTERIES.*

(Abstract.)

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A method has been described for inducing generalized anoxemia without rebreathing, employing an apparatus which enables the subject to inhale a mixture of 10 per cent oxygen and 90 per cent nitrogen at the normal rate of pulmonary ventilation.

Changes in the form of the electrocardiogram have been analyzed following the induction of anoxemia in 105 persons, comprising 66 normals, 23 with disease of the coronary arteries, 11 in whom coronary disease was suspected but doubtful, and 5 with severe anemia.

The following criteria for normal and abnormal responses have been evolved:

NORMAL.

1. The RS-T junction is not displaced more than 1 mm. in any lead.

2. The T-waves tend to decrease in amplitude.

3. Partial or complete reversal of the direction of T in Lead I, in the absence of any RS-T displacement in this lead, is of uncertain significance. It was observed in 2 of 66 supposedly normal persons.

4. Partial or complete reversal of the direction of T in Lead II or Lead III, or both, even though associated with RS-T displacement of less than 1 mm., is of no significance. It was observed in 22 of 66 supposedly normal persons.

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ABNORMAL.

1. A change in the level of the RS-T junction of more than 1 mm. in any lead, even though unassociated with changes in the T-waves, is abnormal. Its importance is increased if combined with partial or complete reversal in the direction of T in Leads I or IVF, or both.

2. Partial or complete reversal in the direction of T in Lead I is abnormal when associated with any displacement of the RS-T junction in this lead. Such displacement may be as little as 0.5 mm.

3. Complete reversal in the direction of T in Lead IVF is always abnormal.

4. Partial reversal of the direction of T in Lead IVF, associated with any displacement of the RS-T junction in this lead, is abnormal. Such RS-T displacement may be as little as 0.5 mm.

It is recognized that the material is relatively small and that the criteria must be regarded as tentative. It has not been possible, thus far, to correlate the clinical diagnoses with the anatomical lesions.

Changes regarded as abnormal have occurred in patients with clinical symptoms and signs of coronary insufficiency. Similar alterations have been observed in those with anemia but without signs of cardiac disease.

There have been no serious untoward effects. Because of two unpleasant reactions, it is suggested that the test should not be given to patients with cardiac insufficiency and should not be repeated in the same patient, within twenty-four hours.

Changes in the form of the electrocardiogram caused by induced anoxemia may be used as a clinical test for insufficiency of the coronary circulation, whether this be manifest or latent. An index is afforded of the adequacy of the "coronary reserve." It should be of value in distinguishing pain of coronary origin from pain in the chest due to other causes, as well as from pain referred from the abdomen. It is possible that it can be employed also to study, in man, the effect of drugs and of various surgical procedures on the efficiency of the coronary blood flow. Such studies are in progress.

DISCUSSION.

DR. ENSER (Milwaukee, Wis.): I am very much interested in the use of oxygen in these cases. We have conducted two series of experiments which parallel Dr. Levy's report.

We use two methods: One, the process of reduction of oxygen in a closed circuit by the patient himself, over a period of half an hour's respiration, and the other, a subjection of the patient to 10 per cent oxygen and nitrogen, not for as long a period as Dr. Levy uses, however, because we were dealing with older individuals.

We have examined about one hundred and fifty individuals between the ages of forty and sixty-five, in all of whom there was an entire absence of evidence of coronary pain. In one case there was pain in the lower extremity, very rapid hypertension and marked arteriosclerosis, which substantiates Dr. Levy's report.

Concerning electrocardiograms, we made electrocardiograms at five-minute intervals and failed to detect any changes which we could regard as indicative of coronary insufficiency.

DR. C. C. WOLFERTH (Philadelphia, Pa.): Some seven or eight years ago, following the observations of Feil and Siegel on electrocardiographic changes during an attack of angina pectoris, Wood and I studied the electrocardiographic changes following angina produced by exercise.

It immediately became apparent that if such a study was to be made, it was necessary to observe the effects of exercise on the electrocardiogram of normals. We found that inversion of T-2 and T-3 occurred not uncommonly following exercise, although not immediately afterward, as a rule. The T-waves were usually larger immediately after exercise. A few minutes later, inversion might occur and then in ten or fifteen minutes or more the tracing would again become normal.

We found three general types of changes in cases of angina pectoris during pain that we did not find in normal cases. One was a type shown by Dr. Levy today, in which there was an inversion of T-1 often with RS-T interval deviation; sometimes inversion of T-2 and T-3 occurred with RS-T interval elevation; in the third type there were RS-T interval depressions in leads 1 and 2 which we later came to believe are due to involvement of the lateral wall of the left ventricle.

Since there are usually no QRS changes of any importance in such tests, it has seemed to us that they may fail to reflect in a significant way disturbances in circulation involving the posterior or lateral wall of the left ventricle. Temporary depression of T-2 and T-3 is so apt to occur in normals after exercise that unless RS-T interval deviations are also present, the changes cannot be regarded as highly significant. Moreover, the lateral wall is almost a silent area. Thus, even if infarction occurs in this part of the heart, electrocardiographic changes are apt to be present for only a very short period of time. As a matter of fact, a very large infarction may be situated in this area and the electrocardiogram fail to reveal its presence. It is therefore quite probable that con-

siderable anoxemia might occur in this portion of the heart without being reflected in the electrocardiograms.

I think, therefore, that if Dr. Levy's patient, whose disability insurance was removed, dies some time in the near future, he may be found to have trouble on the lateral wall of the left ventricle.

DR. J. C. MEAKINS (Montreal, Quebec): If I may have the privilege of the floor, I would like to say a few words to recount some as yet unpublished observations which I made some years ago, at the time when arterial puncture was much more in vogue than at present, and many of us were the human guinea pigs.

We well remember how the radial artery was extremely sensitive and produced pain on puncture, whereas the brachial was less so, and the femoral not at all. We noted amongst those of us who were amenable to repeated radial puncture in the study of the effects of respiratory changes — that is, repeated practical experiments that Dr. Levy has reported — that on puncture of the radial artery, when the saturation of the arterial blood was below 85 per cent, the pain was much more easily produced and much more severe.

I have often wanted to follow up that observation which I experienced myself on many, many occasions, and I think that perhaps it is a straw to show the way the wind is blowing in regard to the correlation of anoxemia and muscular irritability.

DR. L. W. GORHAM (Albany, N. Y.): I think Dr. Levy has made a very important and a very interesting contribution. Criteria which would be definitely established to measure coronary insufficiency would be of great value. I think that this test is a superior one to the adrenalin test suggested by Dr. Levine.

In the case of anoxemia which can be immediately stopped and its effect counteracted by oxygen, I think that one has a much better reason for applying such a test to these patients.

One point I would like to make is that pain and anoxemia are not necessarily synonymous. There was one patient, the boy with the sickle cell anemia, who had no pain with his test, and yet his electrocardiogram showed definite signs of anoxemia.

In the work which I have been doing with my associate, Dr. S. J. Martin, during the past year, we have been able in dogs to produce pain without anoxemia by applying tension at three points in the arterial wall of the coronary vessel, and taking a controlled electrocardiogram before and after the application of the tension, so that I feel the question of cardiac pain is still an open one.

DR. S. J. MARTIN (Albany, N. Y.): In the laboratory at Albany we have been concerned with the same problem as reported by Dr. Levy. However, we use dogs instead of patients, and have found very much the same set of results. But in many instances we noted changes in rate and rhythm as well as in the height of the compression arc, depending upon the extent of the anoxemia.

I would like to know if Dr. Levy has made any determinations on the oxygen saturation and the difference at five, ten, or fifteen-minute intervals.

DR. THOMAS CLAYTOR (Washington, D. C.): I am interested in any method by which we can determine the presence of disease of the coronary arteries. I am particularly interested for this reason, that I am one of the visiting physicians on the Veterans Bureau Diagnostic Center in Washington, where we have many cases coming in complaining of pains which they claim are angina.

Now, we all know there is no method of determining the presence of angina except by the statements of the patients and it would certainly be a very easy matter for any ex-soldier to study up on the subject and come in and present himself as a typical case of angina pectoris. So if there is any method, any apparatus for determining disease of the coronary arteries, I think it is a most important thing to know.

DR. HENRY M. THOMAS, JR. (Baltimore): I would like to ask Dr. Levy one question, whether he has correlated the electrocardiographic results with the production of pain by induced anoxemia.

DR. ROBERT L. LEVY (Closing): We are, of course, glad to have confirmation from other sources.

With respect to Dr. Wolferth's comments, we have not had an opportunity, as yet, to correlate these findings with autopsy observation. Perhaps we will find that our so-called malingerer has coronary disease; but I do think that the most delicate index, according to our criteria so far, is deviation of the RS-T interval. That is, a change in any lead of more than one millimeter we have found significant, but I cannot speak about that with finality.

Dr. Gorham pointed out that pain and anoxemia are not always coincidental. They certainly are not, and a number of patients, as we indicated in a study finished last February, to whom 12 per cent oxygen was given, experienced no pain with the anoxemia, although they complained of spontaneous attacks, and we had evidence that they suffered from coronary disease.

We have made studies of the arterial oxygen saturation and have found that it varies considerably in different persons under apparently similar conditions. We have obtained values anywhere from 62 to 84 or 86 per cent in these individuals who, I may add, all became very cyanotic if they took the full twenty minutes of 10 per cent oxygen.

We have not been able to make any correlation between the appearance of pain and the level of oxygen saturation in the peripheral arterial blood.

I want to leave one idea with you, namely, that we realize that this is a preliminary communication; we have merely presented our results to date. The number of observations is not large, and it may well be that criteria which we have tentatively established will have to be materially modified.