

6 hours, the distillate being extracted with ether and the ether removed *in vacuo*. A third extract, C, was made as in the first extract, A, except the thawed bile was slightly acidified (pH 4.0) with phosphoric acid.

That amount of extract equivalent to 6 cc of the fresh bile was injected slowly intravenously.

Results. The liver glycogen content of 10 control rabbits, which were fasted, treated with 2 g of glucose per kilo but were not given the bile extracts, averaged 1.37%, range 0.11 to 2.93%. The liver glycogen content of 5 rabbits which received bile extract A averaged 1.16%, range 0.29 to 1.78%; of 6 rabbits which received extract B averaged 1.22%, range 0.15 to 1.99%; of 10 rabbits which received extract C averaged 1.44%, range 0.13 to 2.03%. None of these differences are significant. The average liver glycogen of the 21 rabbits receiving the bile extracts was 1.31%, which compares very favorably with the average of 1.37% for the controls.

Using extract C on 11 rabbits which were given 4 g of glucose per kilo instead of 2 g, the average liver glycogen found was 2.01%, range 0.96 to 2.97%. The average liver glycogen of 8 control rabbits receiving the same amount of glucose was 3.0%, range 1.6 to 3.6%. This difference is statistically significant, indicating that the extract interfered with the deposition of glycogen; however, we doubt its physiologic significance. In 5 rabbits the ether extract of dried but otherwise unmodified cattle bile had no effect on glycogen deposition.

We were, therefore, unable to confirm the report that bile contains a substance which favors glycogen deposition in the liver.

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Effect of Inhalation of High Oxygen Concentrations, With and Without Carbon Dioxide, on the Electrocardiogram.

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In another communication¹ it was shown that the addition of 2 to 3% carbon dioxide to low oxygen mixture reversed the electrocardiographic changes of induced anoxemia in the majority of patients with

¹ Barach, A. L., and Steiner, A., to be published.

heart disease and in some normal individuals. The physiological basis for the trial of carbon dioxide was the existence of alkalosis at the termination of a 20-minute period of oxygen want. Since it had been recognized that alkalosis stimulates contraction of smooth muscle and constriction of the capillary bed, and that administration of carbon dioxide has an opposite influence, the hypothesis was presented that these factors might play a rôle in the regulation of the coronary circulation. It was also recognized that breathing even small percentages of carbon dioxide increased the arterial oxygen saturation and facilitates the unloading of oxygen into the tissues, factors which will be presented in a fuller report.

In this study the effect on the electrocardiogram of inhalation of 100% oxygen and of 97 to 96% oxygen with 3 to 4% carbon dioxide is presented. Observations were made on 26 patients in whom primary heart disease was present, or in whom cardiac function was affected by pulmonary or other disease. In addition, 6 normal and 2 patients with chronic arthritis were similarly studied.

Methods. The method of administration of the gas employed has been previously described.² After the control electrocardiogram was obtained the patient was given 100% oxygen for 20 minutes; after a rest period of 10 minutes, oxygen with carbon dioxide was given for a similar period. In the second test of case 1, oxygen was administered for one hour.

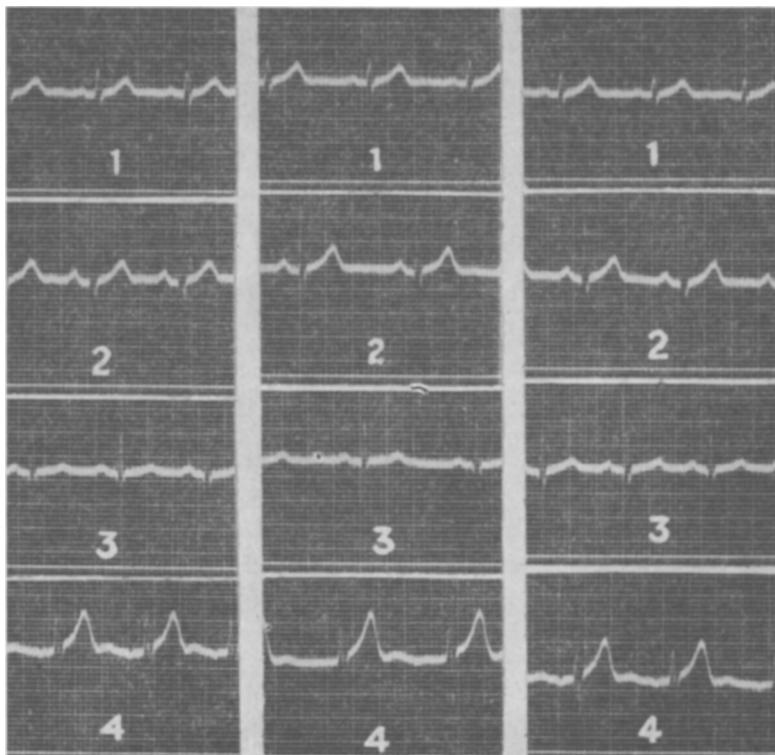
Results. Of the 26 cases in the cardiac group, 20 responded to inhalation of either 100% oxygen, or 97% to 96% oxygen and 3 to 4% carbon dioxide, with elevation of the T wave, in one or more of the 4 leads, less inversion of the T wave, or a T wave previously diphasic becoming upright. In 4 cases there was no change after inhalation of either oxygen or oxygen with carbon dioxide. In one case T_1 was very slightly lower after both tests and in another T_3 was very slightly lower after oxygen and very slightly higher after oxygen with carbon dioxide.

Of 20 cases in which the electrocardiographic changes due to 100% oxygen were compared with those due to oxygen plus carbon dioxide, there were 7 in which the T wave elevation was higher with 100% oxygen, one in which the oxygen plus carbon dioxide mixture was very slightly higher, and 12 in which the result was approximately the same. In the 12 instances in which the elevation of the T wave was noted as being equal after the two tests, the impression was frequently gained that there was very slight lowering of the T wave when carbon dioxide was added to the oxygen mixture, as con-

² Levy, R. L., Barach, A. L., and Bruenn, H. G., *Am. Heart J.*, 1938, **15**, 187.

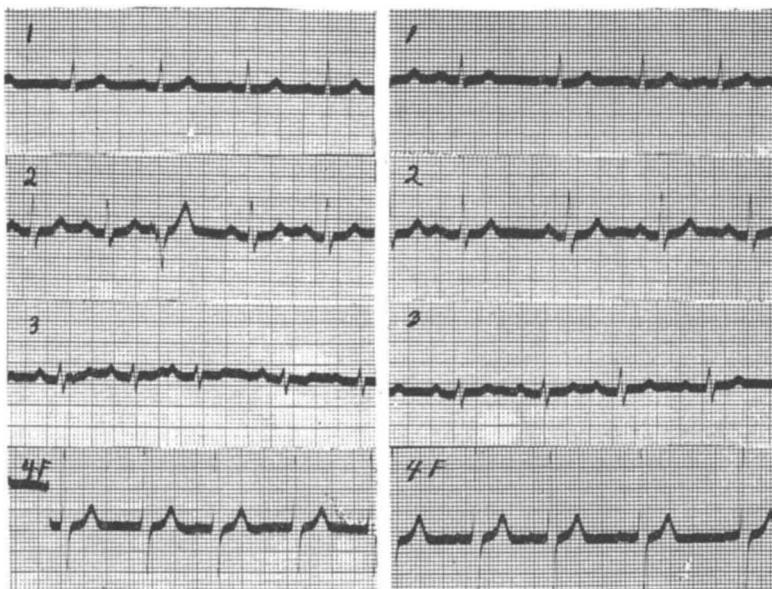
trasted to the effect of 100% oxygen; it was believed, however, that changes of a magnitude of 0.25 mm were too small to be considered significant. The increase in height of the T wave ranged from 0.5 to 2.0 mm; occurring more often in lead 4 than in the other leads.

In the group of 2 cases of chronic arthritis and 6 normal individuals there was no change due to inhalation of 100% oxygen in 6, and elevation of the T wave in 2. In 5 of this group there was no change due to inhalation of the oxygen-carbon dioxide mixture; in 4, there was elevation of the T wave in 1, and lowering in 2. The changes were less frequent in the control group, but in one instance illustrated in the text (Electrocardiographic Picture No. 1) there was definite elevation of the T wave in all 4 leads; these changes were slightly less marked with the oxygen-carbon dioxide mixture. An



ELECTROCARDIOGRAPHIC PICTURE No. 1.

- A. Electrocardiogram of normal individual breathing air.
- B. After breathing 100% oxygen for twenty minutes, T₁, T₂, T₃, T₄ higher.
- C. After breathing 96% oxygen and 4% CO₂ for twenty minutes, changes are similar to B, although slightly less marked.



ELECTROCARDIOGRAPHIC PICTURE NO. 2.

A. Electrocardiogram of patient with coronary sclerosis breathing air.

B. After inhalation of 97% oxygen and 3% carbon dioxide for twenty minutes, T_2 and T_4 are higher, and T_3 previously diphasic is upright.

illustration of the effect of 97% oxygen and 3% carbon dioxide is shown in the accompanying illustration (Electrocardiographic Picture No. 2). It will be observed that T_2 is higher, T_3 which was diphasic has become upright, and T_4 is higher.

According to Wilson, *et al.*,³ and MacLeod⁴ the T wave represents that part of the cardiac cycle in which heart muscle is in the main regressing from the active state, during which products of metabolic activity are being eliminated. According to MacLeod, when this recovery period is prolonged, the T wave is relatively lower; conversely, shortening of the recovery period is represented by a more elevated T wave. If we apply these concepts to our findings an explanation is seemingly afforded. The inhalation of low oxygen mixtures prolongs the recovery period and results in flattening of the T wave; inhalation of 100% oxygen shortens the recovery period in some cases and is followed by elevation of the T wave. When

³ Wilson, F. N., MacLeod, A. G., and Barker, P. S., *Currents of Action and of Injury*, Univ. of Michigan Studies, Scientific Series X, 1933.

⁴ MacLeod, A. G., *Am. Heart J.*, 1938, **15**, 165; *ibid.*, 1938, **15**, 402; also, personal communication.

alkalosis is induced by acute anoxia, the administration of small doses of carbon dioxide tends to counteract the T wave depression induced by acute anoxia; in the absence of alkalosis in the resting individual the addition of 3 to 4% carbon dioxide to a high oxygen mixture may result in less marked elevation of the T wave than that induced by 100% oxygen. This would suggest, according to MacLeod's studies, that increasing the CO₂ tension in the blood beyond that normally present may prolong the recovery period of the cardiac muscle. Additional studies will be made on the comparative effects of 1 to 2% carbon dioxide, with the remainder oxygen.

It is pertinent to mention that although 50% oxygen has been shown to relieve anginal pain,^{5, 6} more striking clearing of pain resulting from acute coronary occlusion has been recently reported as result of inhalation of 100% oxygen.⁷

Summary. Inhalation of 100% oxygen has been shown to result in the elevation of the T wave in the electrocardiogram in 20 of 26 cardiac cases, and in 2 of a group of 8 normal and miscellaneous cases. When 97 or 96% oxygen with 3 or 4% carbon dioxide was tested, similar electrocardiographic changes were observed although the degree of change was frequently less marked; thus, in 7 of 20 cardiac cases the T wave was distinctly more elevated after inhalation of 100% oxygen than after the oxygen-carbon dioxide mixture. The significance of these observations is discussed. It seems likely that inhalation of 100% oxygen shortens the recovery period of cardiac muscle.

⁵ Rizer, R. L., *Minnesota Med.*, 1929, **12**, 506.

⁶ Barach, A. L., *Ann. Int. Med.*, 1931, **5**, 428.

⁷ Boland, E. W., *J. A. M. A.*, 1940, **114**, 1512.