peated administration of an iron salt. Rous and his collaborators[8] obtained the deposition of hemosiderin by the injections of hemoglobin. Evidences on hand, accumulated in collaboration with Mr. S. Talmadge, show that repeated injections of ferric chloride do not have any effect on the hemoglobin or red cell counts of rabbits that might thus indirectly account for the hemosiderosis obtained. Further studies on this phase will be reported subsequently. The observations obtained indicate that hemosiderin is not solely a product in the degradation of hemoglobin but may result from a release in the body fluids of iron (presumably in combination with proteins) from cells in general. This material, when ultimately phagocyted, appears in the familiar form of hemosiderin.

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Inversion of the P Wave in the Third Lead of Electrocardiograms with a Large Q-3 Wave.

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In the course of a study of electrocardiograms which show a large Q-3 deflection, we noted what appeared to be a relative frequency of inversion of the P deflection in the third lead of these tracings. This appeared to be consistent with the finding of Carr, Hamilton and Palmer[1] that inversion of P-3 is occasionally associated with the production of a large Q-3 wave in electrocardiograms taken from pregnant women.

We undertook to determine the frequency with which an inverted P-3 wave is found in an indifferent series of electrocardiographic tracings and in a series of electrocardiograms which contain a large Q-3 wave.

No attempt was made in this study to exclude or separate electrocardiograms showing auricular fibrillation, auricular flutter, paroxysmal auricular tachycardia or nodal rhythm. In tracings where extrasystoles were present these were ignored—the P-waves associated with the normal sinus rhythm alone were exam-

[8] Rous, P., and Oliver, J., *J. Exp. Med.*, 1918, **28**, 629.

[1] Carr, F. B., Hamilton, B. E., and Palmer, R. S., *Am. Heart J.*, 1933, **8**, 519.

ined. No attention was paid to diphasic P-waves or to isoelectric P-intervals. Only when the P-wave was wholly inverted was it included in this study. The large Q-3 waves were selected in accordance with Pardee's criteria[2]: 1—the Q was at least 25% as large as the largest deflection of Q-R-S; 2—there was no S-wave; 3—waves of the M and W types were omitted.

Analysis of 2500 consecutive electrocardiograms taken at the Jewish Hospital of Brooklyn revealed 73 with an inverted P-3 wave (3%); one with an inverted P-1 wave (0.04%); and one with an inverted P-2 wave (0.04%). Of the group of 73 with an inverted P-3 wave, 50 (68%) showed deviation of the ventricular electrical axis to the left; 20 (27%) showed normal direction of the ventricular electrical axis, and 3 (5%) showed deviation of the ventricular electrical axis to the right. Eight of the group of 73 showed a large Q-3 wave. The single record with an inverted P-1 showed deviation of the ventricular electrical axis to the left. The single record with an inverted P-2 showed inversion of P-3 as well, and a normal direction of the ventricular electrical axis.

One hundred and twenty-nine electrocardiograms were found in

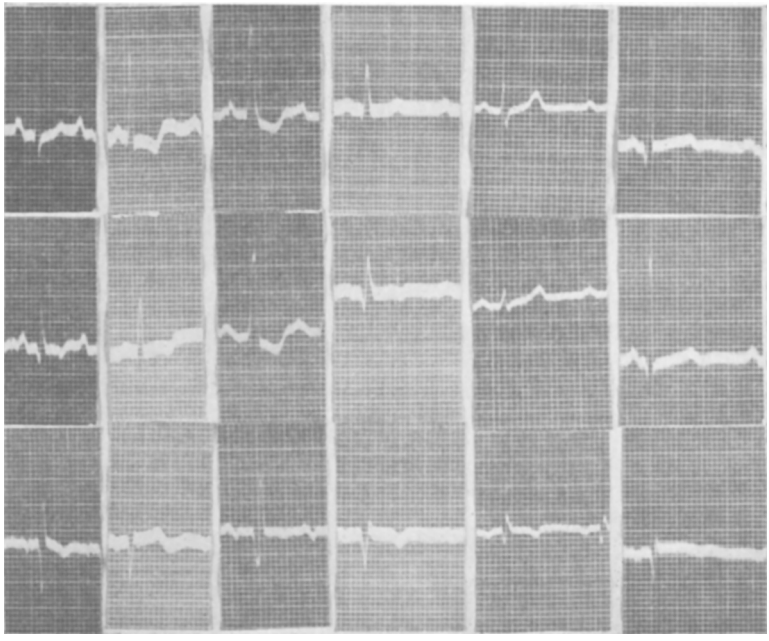

FIG. 1.
Examples of large Qs and inverted P-waves in the third lead.

[2] Pardee, H. E. B., *Arch. Int. Med.*, 1930, **46**, 470.

another series of 2500 consecutive records (not the same list reported above) which showed a large Q-3 wave according to Pardee's criteria (5%). Twenty-eight of the series of 129 records showed inversion of the P-wave in Lead III (22%). Inversion of P in Leads I and II was not found in this series.

The results given indicate that inversion of P-1 or of P-2 is relatively rare while inversion of P-3 is not uncommon. There is a definite association between inversion of P-3 and inversion of Q-R-S-3—about two-thirds of the records with an inverted P-3 showed deviation of the ventricular electrical axis to the left. This association suggests the possibility that the inverted P-3 might bear the same relation to a rotation of the auricular electrical axis (in a counter-clockwise direction) that the inverted Q-R-S-3 bears to a similar rotation of the ventricular electrical axis. Early investigations on inverted P-waves by Lewis,[3] Ritchie,[4] V. Hoesslin,[5] Einthoven, Fahr and de Waart[6] suggested that intrinsic auricular causes, such as change in the position of the pacemaker in the auricle (as, for example, that which follows vagal stimulation) could cause inversion of the P-wave. The last named authors suggested also rotation of the auricle as a whole as another possible cause for inversion of the P-wave. That this was possible was shown by Cohn[7] when he rotated chest leads in a clockwise manner, which simulated rotation of the heart to the left and upward, and produced inversion of P-3, of Q-R-S-3 and of T-3. Master and Oppenheimer[8] came to a similar conclusion after an electrocardiographic study of 97 obese patients in which left axis deviation of Q-R-S and inversion or flattening of P-3 appeared in three-quarters of the records. Their view that these changes were caused by elevation of the diaphragm and rotation of the heart appeared to be confirmed by the fact that 13 of 15 patients who subsequently lost weight showed a change of P-3 from flat or inverted to upright. Bland and White[9] made a study of complete inversion of Lead III in human electrocardiograms and they concluded that the inversion of P-3 as well as of Q-R-S-3 and T-3 in these tracings was caused by a rotation of the heart as a whole to the left.

Data presented in this paper show a definitely increased fre-

3 Lewis, T., *Heart*, 1910, **11**, 2.

4 Ritchie, W. F., *Quart. J. Med.*, 1912, **6**, 47.

5 von Hoesslin, H., *Deutsch. Arch. f. Klin. Med.*, 1914, **113**, 537.

6 Einthoven, Fahr, and deWaart, *Arch. f. d. ges. Physiol.*, 1913, **100**, 275.

7 Cohn, A. E., Heart, 1921-1922, **9**, 311.

8 Master, A. M., and Oppenheimer, E. T., *J. A. M. A.*, 1929, **92**, 652.

9 Bland, E. F., and White, P. D., *Am. Heart J.*, 1931, **6**, 333.

quency of inverted P-3 waves in electrocardiograms that also show a large Q-3 deflection—22% as compared with 3% in an indifferent series. In the light of the discussion given above, this finding could be explained by assumption of a counter-clockwise rotation of the auricular electrical axis in these cases. However, we recently presented evidence[10] for a belief that the large Q-3 wave is usually representative of a rotation of the ventricular electrical axis *about a longitudinal axis* to the left. In the light of this work it appears possible that the increased frequency of inverted P-3 waves in these records may partly be the result of a similar rotation of the auricular electrical axis about a longitudinal axis to the left. We have already mentioned the work of Carr, Hamilton and Palmer,[1] who found occasional inversion of P-3 associated with the production of a large Q-3 in electrocardiograms from pregnant women. Elevation of the diaphragm, as in pregnancy, can probably cause rotation of the heart as a whole in either a vertical or a horizontal plane or both, with the production of a large Q-3 or a deep S-3, associated with an inverted P-3.

Summary. 1. Three percent of 2500 consecutive electrocardiograms showed an inverted P-3 wave. 2. Of 73 electrocardiograms with an inverted P-3, 68% showed left axis deviation; 27% no deviation of the ventricular electrical axis; and 5% right axis deviation. 3. Of 129 electrocardiograms with a large Q-3 (taken from another series of 2500 records) 22% showed an inverted P-3 wave. 4. The association between inversion of P-3 and inversion of Q-R-S-3 can be explained by the assumption that counter-clockwise rotation of the ventricular electrical axis is not infrequently associated with counter-clockwise rotation of the auricular electrical axis. 5. The increased frequency of inverted P-3 waves in electrocardiograms with a large Q-3 may be due to rotation of both ventricular and auricular electrical axes about a longitudinal axis to the left. In all probability the electrical axes of the heart frequently shift with relation to both vertical and horizontal planes rather than in one alone. 6. Elevation of the diaphragm, as in pregnancy, can probably cause rotation of the heart as a whole in either a vertical or a horizontal plane or both, with the production of a large Q-3 or a deep S-3, associated with an inverted P-3.

[10] Shookhoff, C., and Douglas, A. H., PROC. SOC. EXP. BIOL. AND MED. 1933, **31**, 209.