and 1024, respectively, and the sera at dilutions of 1024, 512, and 512, respectively. The findings will be published *in extenso* elsewhere.

7308 P

Experimental Hemosiderosis.*

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Many pathologists have assumed that hemosiderin is a product in the partial degradation of hemoglobin. It is recognized mostly as phagocyted material of a yellowish-brown color within mononuclear phagocytes, liver cells, or cells of the kidney tubules. It yields a Prussian blue reaction when tissues containing it are treated with acidified potassium ferrocyanide. The substance is therefore iron-containing in distinction to hematoidin. Brown[1] pointed out a number of years ago that hemosiderin-like products can be obtained experimentally by the injection of hematin derivatives. These substances he termed *hemosideroid,* for he found that they were soluble in hydrogen peroxide or in potassium hydrate. True hemosiderin was found to be insoluble when treated with these agents. Sprunt[2] and more recently Whipple[3] have pointed out the possibility that hemosiderin may be the result of a change in the fundamental pigment metabolism of the organism rather than a product in the partial degradation of hemoglobin.

For the past few years the writer[4, 5, 6, 7] has demonstrated, in studies on inflammation and tuberculosis, that following intravenous injections of ferric chloride, the iron salt accumulates at the site of an acutely inflamed area; and in tuberculous rabbits, within the tubercles themselves, when the injections are given repeatedly. Concomitantly with this accumulation the life span of experimental rab-

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1 Brown, W. H., *J. Exp. Med.*, 1911, **14**, 612.

2 Sprunt, T. P., *Arch. Int. Med.*, 1911, **8**, 75.

3 Whipple, G. H., and Bradford, W. L., *Am. J. Dis. Child.*, 1932, **44**, 336.

4 Menkin, V., *J. Exp. Med.*, 1930, **51**, 879

5 Menkin, V., and Menkin, M. F., *J. Exp. Med.*, 1931, **53**, 919.

6 Menkin, V., *J. Exp. Med.*, 1932, **55**, 101.

7 Menkin, V., *Am. J. Med. Sci.*, 1933, **185**, 40.

bits is prolonged and the course of their disease is protracted. The ferric chloride when injected in the circulation forms a ferric proteinate precipitate which, in the concentration of the salt employed (0.25%), immediately redissolves. The writer[6] pointed out that hemosiderin-like granules were frequently found in the spleen, liver, bone marrow, and at times in the kidney tubules of rabbits repeatedly injected with ferric chloride.

A summary of further studies on the production and distribution of hemosiderin is here presented. Twenty-eight tuberculous rabbits that had received no ferric chloride were studied for the distribution of hemosiderin in the spleen, liver, and bone marrow. The spleens of 9 animals in this group showed small amounts of a brownish iron-staining material within mononuclear phagocytes. The spleen of the remaining 19 rabbits showed absolutely no sign of hemosiderosis. There was no trace of hemosiderin in either the liver or bone marrow in any of the rabbits. On the other hand 28 rabbits that had received repeated intravenous injections of 0.25% ferric chloride for a number of weeks yielded some interesting information in regard to the production and distribution of material indistinguishable from hemosiderin. In the spleens of 26 rabbits out of a total of 27 studied, massive deposits of this pigment were found. Mononuclear cells both in sinuses and reticular cords of the spleen were loaded with this yellowish-brown material. Upon treatment with potassium ferrocyanide the pigment yielded a strong positive reaction for iron. When the microchemical tests with 3% and 30% hydrogen peroxide or with diluted potassium hydrate solution, as described by Brown, were applied, the pigment failed to dissolve, acting thus in a manner identical to true hemosiderin. The pigment was found deposited in all sections of bone marrow and in about half of the livers studied. In the latter the pigment was located for the most part within the Kupffer cells, while in the former, yellow, iron-containing granules were seen in the reticular cells of the bone marrow. Identical results were obtained when ferric chloride was injected in non-tuberculous rabbits. Accompanying the hemosiderin deposits in the spleen, variable degrees of fibrosis replacing in part the peripheral portions of the Malpighian follicles were noted.

These observations reveal the fact that repeated injections of diluted ferric chloride solution in the circulating blood are followed by the deposition, largely within the cells of the reticulo-endothelial system, of a pigment which by known criteria is indistinguishable from true hemosiderin. The conclusion is warranted that a typical state of hemosiderosis has been experimentally reproduced by re-

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.

7309 C

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.