

ity before taking the blood samples or while measuring oxygen absorption.

In no case was there any significant change in lactic acid although thyroidectomy caused a 25% decrease in the basal metabolism, and thyroid feeding of the operated animals caused approximately 100% increase above the cretinoid level which existed before thyroid administration was begun.

<sup>1</sup> Meyerhof, O., *Pflug. Arch.*, 1921, clxxxviii, 112.

<sup>2</sup> Meyerhof, O., Lohmann, K., and Meier, R., *Biochem. Zeitschr.*, 1925, clvii, 473.

<sup>3</sup> Hill, A. V., Long, C. N. H., and Lupton, H., *Proc. Roy. Soc.*, 1924, 97B, 84 and 155.

<sup>4</sup> Meyerhof, O., *Biochem. Zeitschr.*, 1925, clxii, 43.

<sup>5</sup> Warburg, O., Posener, K., and Negelein, E., *Biochem. Zeitschr.*, 1924, clxx, 309.

<sup>6</sup> Clausen, S. W., *J. Biol. Chem.*, 1922, lii, 263.

<sup>7</sup> Brehme, Th., and Brahdly, B., *Biochem. Zeitschr.*, 1926, clxxv, 348.

<sup>8</sup> Foster, G. L., and Sundstroem, E. S., *J. Biol. Chem.*, 1926, lxxix, 565.

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#### General Tuberculin-like Reactions in Rheumatic Fever Patients Following Intravenous Injection of Streptococcus Vaccines or Nucleoproteins.

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Several years ago one of us<sup>1</sup> suggested that rheumatic fever had many points of similarity with tuberculosis. Since then we<sup>2, 3</sup> have shown that rabbits may be rendered hypersensitive to streptococci by the production of focal lesions with various types of non-hemolytic streptococci which have been isolated from patients with rheumatic fever and other diseases. As these streptococci have been shown<sup>4</sup> to belong to various immunological groups, we formulated the hypothesis that if they had any etiologic relationship with the disease it was because of a peculiar type of tissue reactivity acquired by the rheumatic patient. We have, therefore, tested the reactivity of a number of patients in the late stages of rheumatic fever to intravenous injection of streptococci or products derived from them. These test materials were heat killed suspensions, vaccines, prepared from both green and hemolytic streptococci and nucleoproteins made from hemolytic streptococci. In all instances the initial

dosage was very small and subsequently increased by slow degrees in order to avoid too severe reactions.

The type of febrile reaction has been uniform, and consisted, as a rule, of slowly rising temperature which usually did not begin until 6 to 8 hours after the injection, and often did not reach its maximum until from 16 to 30 hours. In a few instances the fever has persisted for 2 to 4 days, but as a rule it has disappeared by the end of 36 hours. There was an accompanying increase in pulse rate, often headache, dizziness and general malaise. Chills or chilly sensations have been rare. In some cases there has been moderate reactivation of previously quiescent arthritis, and symptoms pointing to activation of cardiac foci.

These reactions are strongly suggestive of the late reactions observed in tuberculous individuals after injections of tuberculin. They are distinctly different from the non-specific shock reactions we have observed in control cases and that others have reported in rheumatic patients following intravenous injection of typhoid vaccine. In the latter instance the reaction is usually ushered in by a chill within 1 to 4 hours after the injection; this is followed within 1 to 3 hours by the peak of the fever, which soon subsides. In our cases the reaction following typhoid vaccine was usually completed in 10 hours or less.

Small<sup>6</sup> has observed similar late general reactions 24 to 48 hours after subcutaneous injection of rheumatic fever patients with vaccines of *Streptococcus cardioarthritidis* described by him. At times these reactions were very severe. In their focal features they were strongly suggestive of tuberculin-like reactions.

In view of the rather widespread variety of streptococci with which it has been possible to induce this reaction in rheumatic fever patients, and also because of the peculiar character of the general and focal reaction which follows injection of these streptococci or their products—a reaction similar to that induced by tuberculin in tuberculous subjects—we feel justified in assuming that these patients have a tuberculin-like allergy (hyperergy) towards streptococci, and that probably this altered tissue reaction accounts for many of the peculiar characters of this disease.

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<sup>1</sup> Swift, Homer F., *Am. J. Med. Sc.*, 1925, clxx, 631.

<sup>2</sup> Andrewes, C. H., Derick, C. L., and Swift, Homer F., *J. Exp. Med.*, 1926, xlv, 35.

<sup>3</sup> Derick, C. L., and Swift, Homer F., *Proc. Soc. Exp. Biol. and Med.*, 1927, xxv, 222.

<sup>4</sup> Swift, Homer F., and Kinsella, R. A., *Arch. Int. Med.*, 1917, xix, 381.

<sup>6</sup> Small, J. C., personal communication, and paper read before Phil. Path. Soc., Dec. 8, 1927.