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Bacillus welchii as an agent in experimental anemia.

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By one or two intramuscular injections of rabbits with 0.5 to 1.0 cc. of whole culture of B. welchii it has been possible to produce a severe toxic anemia within five days. The blood picture has been that of a secondary anemia, in which the hemoglobin is reduced to 50 or even to 25 per cent of the normal, and the red blood corpuscles are reduced to 2,380,000 or even 840,000 per cu. mm., accompanied by a leucocytosis of 20,000 to 43,000 per cu. mm. Marked anisocytosis and poikilocytosis were observed at the height of the disturbance. Erythroblasts were observed, from 642 to 4,352 per cu. mm.; among them normoblasts, microblasts and macroblasts. Monocytes or clasmatocytes in the peripheral blood containing ingested red blood cells were present, numbering from 186 to 868 per cu. mm. The maximum loss of weight varied from 9 to 23.9 per cent. Histologic examination of the spleen of these rabbits showed a marked increase of erythrophagocytosis.

Repeated intramuscular injections of 0.1 to 1.0 cc. of whole culture or of toxic filtrates of *B. welchii* into rabbits produced chronic intoxication with accompanying secondary anemia. Those animals treated with whole culture showed decrease in hemoglobin from 56 to 53 per cent of the normal in periods varying from 5 to 19 days. A leucocytosis of 13,000 to 29,400 was present. Anisocytosis, poikilocytosis and polychromatophilia were marked from the third to the fifteenth day of treatment and remained to a slight degree as long as the injections were continued, covering in most instances, a period of 25 to 40 days. Nucleated red cells were present in numbers varying from 148 to 270 per cu. mm. Erythrophagocytosis in the blood stream was not observed. The final loss of weight varied between 8.3 and 8.5 per cent.

Animals treated with toxic filtrates of *B. welchii* revealed a blood picture somewhat less abnormal. The hemoglobin dropped

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only to from 82 to 77 per cent of normal and the red blood corpuscles to 3,220,000 to 3,800,000 per cu. mm. Leucocytosis was mild, varying from 10,000 to 21,400. Anisocytosis and polychromatophilia were most marked from the fourth to the tenth day of treatment, diminishing as the injections were continued over long periods. Little or no poikilocytosis appeared except with the use of toxin from one strain of *B. welchii*, in which case this change was marked from the 4th to the 11th day. Erythroblasts and erythrophages were not observed.

Bacteria of two other species common in chronic intestinal disease, namely, *B. bifermentans* and *B. sporogenes*, have been used by us in experimental infection by the same procedure. A mild anemia was produced with *B. bifermentans*, in which the hemoglobin was reduced to from 76 to 73 per cent, the red blood cells to 3,360,000 to 5,880,000 together with a leucocytosis of 17,600 to 19,000. Moderate anisocytosis and slight poikilocytosis appeared. Erythroblasts were seen in the blood of some of these animals, reaching 352 per cu. mm. at one time. No erythrophages could be demonstrated in preparations of peripheral blood. The loss of weight at the height of the infection varied from 17.9 to 44 per cent.

When infection was produced with *B. sporogenes* the hemoglobin showed a slight rise of 3 per cent and the red corpuscles, after an initial loss of 500,000 per cu. mm., rose again to 6,500,000. The leucocyte count reached 15,200. A moderate anisocytosis and polychromatophilia were observed but no erythroblasts nor erythrophages could be demonstrated by the usual technic. There was no appreciable change in weight.

Since butyric acid is a product of *B. welchii*, a one per cent solution of it has been administered by intramuscular injection, seventeen such injections being given over a period of 44 days. Hemoglobin diminished to 56 per cent of the normal and the red cells decreased to 2,760,000. Marked anisocytosis and poi-kilocytosis were present over half the period covered by the treatment. Nucleated red blood cells appeared on the thirtieth day, numbering 64 per cu. mm. The loss of weight was 18 per cent.

Sterile distilled water was also used as a hemolytic agent, injections being given intravenously for 19 days. The red cell counts, made approximately 30 minutes after each injection, showed a minimum count of 2,644,000. This destruction was compensated, however, in a considerable measure before the next injection, the lowest count observed immediately before injection being 3,220,000. Anisocytosis and polychromatophilia became marked on the 17th day. Erythroblasts appeared on the 12th day, numbering 124 per cu. mm. The loss of weight was 36 per cent.

The production of more or less severe experimental anemia in animals by injections of bacterial toxin only verifies generally accepted clinical experience on human beings that such poisons play a very important part in the more chronic types of anemia of man, but it is evident that further observations will be required before one can justly designate such experimental anemias, even when they are very severe or fatal, as presenting the counterpart of so called pernicious anemia in man.^{1, 2}

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Lactic acid and inorganic phosphorus of normals and diabetics after glucose, with and without insulin.

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Briggs, Koechig, Doisy and Weber¹ have observed a decrease in sugar, inorganic phosphorus, and potassium of the blood of normal dogs after insulin. There was a parallel increase in the lactic acid apparently formed from the glucose under the influence of insulin. The animals were not anesthetized, but the authors believe that the increased muscular activity played no part in the observed production of lactic acid. Best and Ridout² state that the blood lactic acid of dogs does not significantly increase during

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¹ Cornell, Beaumont S., J. Infect. Dis., 1925, vi, 508.

² Kahn and Torrey, PRoc. Soc. Exp. BIOL. AND MED., 1925, xxii, 8-13.

¹ Briggs, A. P., Koechig, I., Doisy, C. A., and Weber, C. J., J. Biol. Chem., 1924, Iviii, 721.

² Best, C. H., and Ridout, J. H., J. Biol. Chem., 1925, lxiii, 197.