

Berkefeld filtrates of 4, 7 and 17 days' brain medium cultures were tested in rabbits for the elicitation of the Shwartzman phenomenon. 0.25 cc. undiluted filtrate was injected intradermally into rabbits and followed in 24 hours by a single intravenous injection of the same filtrate undiluted or in varying dilutions. Comparative studies of the brain culture filtrate with "chocolate agar" culture washings were made. The results may be described in brief as follows:

It was possible to elicit the phenomenon under discussion in prepared rabbits by an intravenous injection of the brain filtrate in dilutions ranging from 1:40 to 1:400 and recently 1:1500. The chocolate media culture filtrates in our hands could never be diluted higher than 1:5, and usually were active only undiluted. It is interesting to note that some of the brain media culture filtrates when retitrated 2-4 months after preparation showed a rise in effective titer of 5 to 20 fold. This was not observed with "chocolate agar" culture filtrates. The optimum incubation period for brain infusion cultures seemed to be about 17 days, while 4 and 7 day cultures yielded filtrates of lower potency. The H-ion concentration in the range employed had no effect. Neopeptone and proteose-peptone (Difco) appeared superior to Witte's peptone.

This report seems to be justified because of the ease with which *B. pertussis* filtrates in large quantities can be obtained for the elicitation of the Shwartzman phenomenon; and because of the considerable potency of these preparations, *i. e.*, 5-20 times higher than with preparations hitherto described.

Experiments on specific serum neutralizations are under way in order to determine the nature and antigenicity of the toxic substances described above.

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Blood Changes Following Gastrectomy in Monkeys.

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There has been considerable speculation as to whether the "pernicious anemia-like" blood picture following gastrectomy in man¹ is the result of the operation, or is an independent phenomenon. In-

investigators, working with dogs,² rats,³ and hogs,⁴ have attempted to produce a macrocytic anemia by removal of the stomach, but in all instances a "secondary anemia" developed. This paper reports the observations on hematopoiesis following total gastrectomy in the *Macacus rhesus* monkey.

Eight monkeys (2 females and 6 males) averaging 8 pounds in weight, were used. Exact data concerning their ages were not available. The animals were observed at least 2 weeks before operation and during this period normal blood findings were recorded.⁵ The first operation was performed on January 16, 1933, at which time the entire stomach was removed. The proximal end of the duodenum was sealed and the esophagus anastomosed with the jejunum. Similar operations were performed on 7 other monkeys.*

Six of the animals died within a period of 2 weeks after operation; 5 from aspiration pneumonia and atelectasis, and one from peritonitis. Of the 2 remaining monkeys, one (No. 2) lived for 10 weeks and the other (No. 4) lived for 23 weeks. Autopsies were performed on all animals immediately following death. In the animal living 10 weeks there was terminal circulatory failure with pulmonary congestion and edema, and necrosis at the cardiac end of stomach. In the animal living 23 weeks, a marked atrophic catarrhal enteritis was noted. One portion of the intestine showed extensive necrosis, diffuse phlegmon and early gangrene. There were small areas of diphtheritic colitis.

The monkeys were housed in the same environment before and after the operation. The diet was the same throughout, consisting primarily of green vegetables, fresh fruits, bread and sugarized milk. No anti-anemia therapy was instituted as it was desired to note the effect of gastrectomy on the functional activity of the hematopoietic system.

Three hours after the operation on Monkey No. 2 the red blood cell and white blood cell counts were markedly increased. This probably was due to dehydration and to contraction of the spleen. Within 72 hours a "secondary anemia" occurred, characterized

¹ Goldhamer, *Surg., Gynec. and Obst.*, 1933, **57**, 257.

² Ivy, Morgan and Farrell, *Surg., Gynec. and Obst.*, 1931, **53**, 2.

³ Jung, Maison and Highstone, *Proc. Inst. Med.*, Chicago, 1933, **9**, 389.

⁴ Maison and Ivy, *Proc. Soc. Exp. Biol. and Med.*, 1934, **31**, 554.

⁵ Hall, *Folia Haemat.*, 1929, **38**, 30. Scarborough, *Yale J. Biol. and Med.*, 1931, **4**, 199.

* All the operations were performed by Dr. Walter G. Maddock of the Department of Surgery, University of Michigan. The author wishes to express his gratitude to him for his assistance.

by a lower color index than normal, a moderate reduction in the red blood cells and a more pronounced reduction of the hemoglobin. During the 10-week period of life following the operation, the red blood cells fluctuated somewhat in number, reaching the lowest level on the day of death. The hemoglobin reached its lowest level 72 hours after the stomach was removed; it gradually increased for about 4 weeks, and then remained stationary. At no time did the hemoglobin return to a normal level. Red blood cell measurements at the time of death showed only a slight increase in the degree of dispersion and the average size of the red blood cells remained the same. The average uncorrected color index before the operation was 0.66. For about 8 weeks after the operation, the uncorrected color index was less, but gradually increased to this level. On the day of death the uncorrected color index and the increased dispersion in the red blood cell size were slightly suggestive that a macrocytic anemia might have developed if the animal had survived for a longer period of time but the evidence is very meager.

In animal No. 4, a "secondary anemia" occurred 24 hours after the operation and persisted. A study of the stained films of the blood of both monkeys revealed such signs of regeneration as nucleated red blood cells, polychromatophilia, basophilic stippling and an increase in the number of reticulocytes. This response is similar to that seen in "secondary anemias" in man.

Summary. Following total gastrectomy in monkeys, a "secondary" type of anemia occurred 72 hours after operation, and persisted. Evidence of regeneration (reticulocytosis, nucleated red blood cells, polychromatophilia and basophilic stippling) was noted. The specific blood picture of human pernicious anemia did not develop within the 6 month period of study, although there was a decrease in the number of red blood cells, a slight tendency for the color index to rise above the preoperative value, a leukopenia and a slightly increased degree in size dispersion of the red blood cells.