

The gelation is accelerated and intensified: (a) by increasing the concentration of the alcohol; (b) by raising the temperature of the mixture; (c) by inactivation of the serum (that is by heating $\frac{1}{2}$ hour at 55-56° C); (d) by aging the serum.

Experiments on about 1500 sera of various origins were made, and the results, which will be reported in more detail in a later publication, are as follows:

1. The complete gelation in normal sera takes place after several hours. In certain cases however it does not occur even after days.
2. It is noticeable that positive Wassermann sera react like normal sera.
3. In most cases the value of the gelation was correlated with the sedimentation rate and only to a certain degree did the 2 reactions run parallel. Apart from normal sera there was no parallelism between the rate of the gelation and the sedimentation time.
4. Other serum reactions were also used for comparison. Takata-Staub positive sera in several cases showed a corresponding positive result to the gelation test.
5. At the first reading (after 5 min. at room temperature) the gelation was strong to complete in many cases of the following diseases: pulmonary tuberculosis, pleurisy, lobar pneumonia, Hodgkin's disease, cirrhosis of the liver, carcinoma.

The phenomenon described is a non-specific serum reaction which is striking in certain diseases. Its value as a differential diagnostic test remains to be determined by further studies.

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Failure of Nicotinic Acid to Prevent Nutritional Cytopenia in the Monkey.*

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Day, Langston and Shukers¹ demonstrated that when monkeys (*Macaca mulatta*) were given a diet "deficient in vitamin G (B₂) and possibly deficient in less well-known organic substances which may be essential . . ." they developed a rapidly progressive blood

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¹ Day, Paul L., Langston, W. C., and Shukers, C. F., *J. Nutrition*, 1935, **9**, 637.

dyscrasia characterized by anemia, leukopenia, loss of weight and death, and, in some cases, ulceration of the gums, anorexia and diarrhea. It was later shown² that when the diet was supplemented with yeast or a liver-stomach preparation the blood picture remained normal. Unpublished experiments have demonstrated that riboflavin did not appreciably alter the course of the disease.

Funk and Funk³ reported that nicotinic acid possessed vitamin activity. Recent experiments have shown that this substance is effective in the treatment of black-tongue in dogs^{4,5} and pellagra in man.^{6,7} György⁸ has reported that it prevented nutritional panmyelophthisis in rats.⁹ The effectiveness of nicotinic acid in these nutritional disorders suggested its use in experimental anemia and leukopenia in the monkey.

In the experiments here reported the original monkey diet¹ was modified by the substitution of 0.01 g of ascorbic acid (Merck) daily for the orange juice, and the use of a more complete salt mixture.¹⁰ Nicotinic acid (Eastman) was added in the form of a standard aqueous solution, which was mixed with the individual portions of the diet immediately before feeding. Detailed data on 2 of the monkeys are presented in Table I. Similar data were obtained in one other animal which also received 10 mg of nicotinic acid, and in 2 monkeys which received 50 mg daily. All 5 of the monkeys developed the characteristic syndrome of leukopenia and anemia and the condition terminated fatally in periods of time similar to the survival of monkeys receiving the deficient diet only. The blood picture of normal animals in our colony is presented elsewhere.¹¹ It is evident that the nicotinic acid was ineffective in pre-

² Day, Paul L., Langston, W. C., and Shukers, C. F., *J. Biol. Chem.*, 1936, **114**, xxv.

³ Funk, C., and Funk, I. C., *J. Biol. Chem.*, 1937, **119**, xxxv.

⁴ Elvehjem, C. A., Madden, R. J., Strong, F. M., and Woolley, D. W., *J. Am. Chem. Soc.*, 1937, **59**, 1767; *J. Biol. Chem.*, 1938, **123**, 137.

⁵ Smith, D. T., Ruffin, J. M., and Smith, S. G., *J. A. M. A.*, 1937, **109**, 2054.

⁶ Spies, T. D., Cooper, C., and Blankenhorn, M. A., *J. A. M. A.*, 1938, **110**, 622, 766.

⁷ Fouts, P. J., Helmer, O. M., Lepkovsky, S., and Jukes, T. H., *Proc. Soc. Exp. Biol. and Med.*, 1937, **37**, 405.

⁸ György, P., *Proc. Soc. Exp. Biol. and Med.*, 1938, **37**, 732.

⁹ György, P., Goldblatt, H., Miller, F. R., and Fulton, R. P., *J. Exp. Med.*, 1937, **66**, 579.

¹⁰ Hubbell, R. B., Mendel, L. B., and Wakeman, A. J., *J. Nutrition*, 1937, **14**, 273.

¹¹ Shukers, C. F., Langston, W. C., and Day, Paul L., *Folia Hæmatol.*, 1938, in press.

TABLE I.
Blood Pictures of Monkeys Receiving Deficient Diet Supplemented with 10 mg of Nicotinic Acid Daily.

Date	No. of days on diet	Total white blood cells	Total lymphocytes	Total neutrophils	Total erythrocytes	Hemoglobin, g	Wt, g	Remarks
Monkey No. 37 ♂								
10-7		10,500	6,830	2,730	5,040,000	13.1	3455	
10-21		8,700	6,180	2,260	5,385,000	10.1	3465	On diet 10-22-37
11-4	13	10,775	5,820	4,310	6,015,000	13.5	3135	
11-18	27	11,975	5,510	5,630	5,265,000	10.2	3095	
12-2	41	8,250	3,550	4,370	4,280,000	10.4	3075	Gums slightly injected; bleed easily
12-7	46	4,550	2,180	2,180	3,760,000	9.16	2940	
12-9	48	5,000	2,100	2,750	4,215,000	10.3	2850	
12-16	55	4,225	1,820	1,900	4,095,000	8.54	2740	
12-23	62	6,900	2,550	4,000	4,310,000	9.64	2570	Weak
12-28	67	8,675	1,300	7,370	4,105,000	7.66	2505	Eating diet satisfac- torily
1-4	74	925	680	170	3,850,000	10.4	2280	Died
Monkey No. 43 ♂								
1-19		18,950	8,900	8,720	4,965,000	11.8	2145	
1-26		15,050	7,680	5,720	5,725,000	10.5	2200	On diet 2-12-38
3-3	19	10,325	7,020	3,100	4,405,000	8.8	1920	
3-19	35	12,925	8,530	3,620	3,825,000	8.42	1945	
3-25	41	11,600	6,030	5,220	3,820,000	9.09	1940	
4-7	54	10,200	6,630	3,060	3,805,000	7.80	1970	Gums bleed easily
4-20	67	7,525	2,100	5,420	3,650,000	7.22	1815	Gums necrotic along margin
4-24	71	2,160			4,375,000	8.21	1580	Died

venting the blood dyscrasia. In view of the rapid disappearance of oral lesions in pellagrins treated with nicotinic acid, it is interesting to note that the substance failed to prevent the gum ulceration in the monkeys.

These data clearly indicate that monkeys require some factor (contained in yeast and liver extract^{2,11}) in addition to those commonly recognized as components of the vitamin B complex. We do not interpret these results as showing that monkeys do not require nicotinic acid, but rather that this factor necessary to prevent nutritional cytopenia in the monkey is not identical with nicotinic acid. Furthermore, this syndrome in monkeys is not analogous to black-tongue in dogs or to that portion of the pellagra syndrome which is cured by nicotinic acid. Although Harris did not report blood findings in his experiments on the P-P requirement of the monkey,¹² the diet, weight curves, and the survival periods would suggest that his animals may also have been suffering from a partial deficiency of this hitherto undifferentiated factor. In view of the similarity of György's panmyelophthisis in rats and this nutritional cytopenia in monkeys, it is surprising that the one is prevented by nicotinic acid and that the other is not.

Summary. Five monkeys were given a diet which experience had shown would produce anemia, leukopenia and death. Three of the monkeys received daily supplements of 10 mg, and 2 received 50 mg of nicotinic acid. The nicotinic acid did not prevent the cytopenia or prolong life. It is evident that this syndrome in the monkey is not analogous to black-tongue in dogs or pellagra in man. We wish to propose the designation "vitamin M" for the hitherto undifferentiated factor which prevents this nutritional cytopenia in the monkey.

¹² Harris, L. J., *Biochem. J.*, 1937, **31**, 1414.