

jections with vitaminized or non-vitaminized horse serum. In all cases stimulation of precipitin-production was noted, the contrast being practically identical with those recorded in Fig. 1.

In other groups the method of injection was varied by injecting the horse serum and ascorbic acid separately, such as at different times in the same ear vein, or in different veins, or by giving horse serum intravenously and vitamin C intraabdominally. Stimulation of specific-precipitin production was noted by all of these technics, confirming the conclusions of Burky⁶ and of Swift and Schultz⁷ in their studies of the immuno-"synergic"[‡] effects of staphylococcal toxin. The antibody-stimulation, however, was less pronounced in these separate injections than those previously obtained by mixing the horse serum and ascorbic acid before injection.

The relative efficiency of ascorbic acid and its sodium salt was also compared in small groups of animals. Sodium ascorbate prepared by Sollmann's technic⁹ was found to be but about half as effective as unneutralized ascorbic acid. Sodium ascorbate, however, is apparently unstable, a commercial preparation tested on a small group of rabbits being without demonstrable antibody-stimulating effect.

9589 P

Treatment of Human Pellagra with Nicotinic Acid.

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Pellagrins can be cured while on a maize diet by the oral administration of a filtrate of liver which contains the so-called "filtrate factor" but which is free from riboflavin and rat antidermatitis factor.¹

⁶ Burky, E. L., *J. Allergy*, 1934, **5**, 466.

⁷ Swift, H. F., and Schultz, M. P., *J. Exp. Med.*, 1936, **63**, 703, 725.

[‡] On presentation of this paper before the Pacific Coast Branch, Oct. 16, 1937, Dr. Swift's use of the word "synergic" was criticized by Dr. Tainter and other attending pharmacologists. In their opinion some variant of the word "potentiation" would be more nearly in accord with accepted usage.⁸

⁸ Sollmann, T., *A Manual of Pharmacology*, W. B. Saunders Co., 5th Ed., 1936, p. 80.

⁹ Sollmann, T., *ibid.*, p. 115.

¹ Fouts, P. J., Lepkovsky, S., Helmer, O. M., and Jukes, T. H., *Proc. Soc. Exp. Biol. and Med.*, 1936, **35**, 245.

The work of Jukes and Lepkovsky² indicates that the filtrate factor and the pellagra-preventing factor are probably not identical. Elvehjem, Madden, Worley, and Strong³ have recently isolated nicotinic acid amide from a liver concentrate which cures canine black-tongue. Both the material from the liver concentrate and a commercial preparation of nicotinic acid cured blacktongue in dogs. Lepkovsky and Jukes,⁴ however, have been unable to substitute nicotinic acid for either the filtrate factor or the rat antidermatitis factor in their studies on chicks and rats. Helmer and Fouts⁵ likewise in studies on rats have not been able to replace the filtrate factor with nicotinic acid. These studies, therefore, indicate that the liver filtrate used in previous studies contains at least 2 active components.

It is the purpose of this paper to record the results of feeding nicotinic acid to 4 pellagrins. On admission to the hospital the patients were placed on a maize diet similar to the one described by Spies.⁶ During the 3 or more days of the control period their condition either remained stationary or became worse. After this period one patient received one gram of nicotinic acid daily while the others received 500 mg.*

All patients showed distinct improvement in general condition and mental attitude within 48 hours of onset of therapy. The stomatitis of one patient showed beginning regression within 24 hours while in the others healing of the stomatitis was definite within 48 hours. Stomatitis was completely healed within 4 days in 3 patients and 5 days in the fourth. Excessive salivation which was present in only one patient decreased within 72 hours and had completely disappeared in 13 days. Severe diarrhea was present in 2 patients. The stools were less frequent and of more normal consistency within 24 hours in one and within 48 hours in the other. The stools were normal within 72 hours in one and by the fifth day in the other. The dermatitis increased during the first 24 hours in one patient but healing was initiated during the succeeding 24 hours. There was distinct abatement in the dermatitis within 48 hours in 2 of the other patients and within 4 days in the fourth. The dermatitis of the 4

² Jukes, T. H., and Lepkovsky, S., *J. Biol. Chem.*, 1936, **114**, 117.

³ Elvehjem, C. A., Madden, R. J., Worley, D. W., and Strong, F. M., *J. Am. Chem. Soc.*, 1937, **59**, 1767.

⁴ Lepkovsky, S., and Jukes, T. H., unpublished data.

⁵ Helmer, O. M., and Fouts, P. J., unpublished data.

⁶ Spies, T. D., *J. Clin. Invest.*, 1934, **13**, 807.

* The nicotinic acid was supplied in part by Mr. George B. Walden of Eli Lilly and Company.

patients had disappeared by the sixth, fourteenth, twenty-second and twenty-fifth days on therapy. Two of the patients developed neuritic pains in the lower extremities while the symptoms of pellagra were improving. All patients noted sensation of heat and tingling of skin within 10 minutes after ingesting nicotinic acid. These sensations lasted for 10 to 20 minutes. During this time there was distinct dilatation of peripheral blood vessels but only slight temporary fall in blood pressure.

Summary. Improvement in 4 patients with pellagra following administration of nicotinic acid was as satisfactory as that following administration of liver filtrate except for an increase in time required for complete disappearance of dermatitis.

9590 P

Hypoglycemic Action of Alloxan.

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The study of the physiological regulation of blood-sugar concentration embraces a complexity of independently variable factors whose individual influences are still incompletely understood. Many experimental substances and conditions will cause hyperglycemia, but none besides insulin are known which will cause hypoglycemia.

Alloxan will produce hypoglycemia in normal rabbits in a very characteristic fashion. If upwards of 70 mg. of alloxan monohydrate per kg. of body weight is injected intravenously the blood sugar level of the animal will fall below the normal value (less than 70 mg. %) in about 3-4 hours, and will continue to fall steadily during the next 2-4 hours until the convulsive level (less than 35 mg. %) is reached. It will keep falling further during the convulsive stage until the animal expires, and very low (less than 15 mg. %) values may be observed terminally. All normal rabbits respond in the same way, although some delay in the time of onset of convulsions is observed if the animals have not fasted for 12-24 hours before the experiment. The larger dosages of alloxan (150-200 mg./kg.) will not hasten the appearance of convulsions, but will very definitely cause the recurrence of convulsions after remissions induced by glucose.

Both the convulsions and the hypoglycemia are promptly relieved