presence of glucose interferes with the oxidation of the amino acids. The quantitative differences in the effect on different organisms, as well as the variable influence of lactic acid, must be presumed to be due to the different capacity of each organism for aerobic oxidation of the hydrocarbons and amino acids. The stimulating effect of nicotinic acid in the amino acid medium without carbohydrates can also be explained on this basis. A more detailed study of the relation of vitamins to the metabolic activity of staphylococci (to be reported elsewhere) indicates that the oxidation of amino acids is similar to that of lactate and pyruvate.

Summary. When nicotinic acid is lacking in a substrate otherwise suitable for growth, the addition of glucose inhibits the growth of organisms capable of fermenting this sugar in the presence of nicotinic acid. The degree of inhibition is 5 to 1000 fold, and depends on the organism and the medium. With Proteus XK the inhibition was 5-10 fold; with dysentery organisms and with staphylococci 100-1000 fold.

14145 P

Effect of Glutamic Acid on the Central Action of the Ammonium Ion.

MILTON R. SAPIRSTEIN. (Introduced by G. B. Wallace.)

From the Department of Pharmacology, New York University College of Medicine.

In 1936, in a study of the effect of various stimulants and depressants of the central nervous system on the aftercontraction in humans, it was noted that small amounts of ammonium salts (.5 g ammonium), taken by mouth, caused a marked increase in this phenomenon. We have considered the aftercontraction a measure of the excitability of the human cerebral cortex.[1,2,3] It has been repeatedly affirmed in the literature that the concentration of ammonium ion increases in the brain tissue and cerebrospinal fluid in states of increased excitability of humans and animals. The fact that oral and parenteral administration of ammonium salts can produce convulsions in animals is well known.

Since ammonium convulsions so closely simulate spontaneous seizures, it seemed that any substance which would prevent these seizures, might be useful in other types of convulsive activity. The work of Krebs on the metabolism of amino acids in brain tissue slices offered an important clue.[4] Of many substances tested he found that glutamic acid specifically caused a marked reduction in the ammonium ion concentration present in the medium surrounding the tissue slices, due to the action of the enzyme glutaminase which synthesized glutamine from glutamic acid and ammonia. The enzyme system was reversible, was stimulated by the physiological *l* (+) glutamic acid and inhibited by *d* (—) glutamic acid. Under this concept, it should be possible to increase or decrease the ammonium ion concentration of the brain and thus control its convulsive activity. Experiments to test this hypothesis were begun in July, 1942.

In our studies on the role of ammonium ion in the convulsive state, we developed a uniform method of production of seizures in rabbits by the slow intravenous injection of 2½% ammonium chloride solution. One cc per kilo of this solution is administered every 5 minutes until a generalized convulsion results. All 12 of the rabbits (2 kg) used in these experiments had convulsions after 15-25 cc of the solution had been injected. The observations were

[1] Sapirstein, M. R., Herman, R. C., and Wallace, G. B., PROC. SOC. EXP. BIOL. AND MED., 1936, **35**, 163.

[2] Sapirstein, M. R., Herman, R. C., and Wallace, G. B., *Am. J. Physiol.*, 1937, **119**, 549.

[3] Sapirstein, M. R., Herman, R. C., and Wechsler, I. S., *Arch. Neurol. and Psychiat.*, 1938, **40**, 300.

[4] Krebs, H. A., *Biochem. J.*, 1935, **29**, 1951.

repeated at weekly intervals to check the thresholds.

We have employed the natural *l* (+) glutamic acid by intravenous injection in an attempt to prevent ammonium convulsions. In a series of preliminary experiments, we have found *l* (+) glutamic acid to give complete protection from the convulsant effects of the ammonium chloride solution. In 8 experiments 50 cc of *l* (+) glutamic acid (5% glutamic acid and 3% sodium bicarbonate) was given intravenously shortly before the injection of ammonium chloride (also dissolved in sodium glutamate solution) and no convulsion resulted in any instance even after 50 cc of the 2½% solution of ammonium chloride was injected. As a control, similar experiments with equimolar amounts of *l* aspartic were performed in the same rabbits. Aspartic acid fails to protect from the convulsant activity of ammonium chloride, indicating the specificity of the glutamic acid reaction.

If *l* (+) glutamic acid is capable of preventing ammonium convulsions, it should be effective in other types of convulsive activity, which are associated with disturbances in ammonium metabolism, perhaps including human epilepsy. We have injected intravenously as much as 500 cc of 5% *l* (+) sodium glutamate into humans within a few hours without any apparent toxic effects. We are now investigating its action in human epileptic seizures.

14146

Blood Histamine in Gastric Cancer and Peptic Ulcer.

MICHAEL B. SHIMKIN, LEO ZON, AND CATHERINE W. CRIGLER.

From the Research Laboratory, Tumor Clinic, Marine Hospital, Baltimore, Maryland, United States Public Health Service.

The production of peptic ulcers in experimental animals injected with histamine,[1] and the presence of a gastric secretory depressant in the extracts of achlorhydric cancerous stomachs and juices from such stomachs[2] suggested the investigation of the histamine content of the blood of patients with gastric carcinoma and with peptic ulcer. Histamine determinations in some cases of Hodgkin's disease, leukemia, and polycythemia vera are also reported.

Experimental Procedure. The blood samples were obtained from adult male patients. The diagnosis of gastric carcinoma or of gastric ulcer was established at subsequent operation and by microscopic examination of the tissue. The diagnosis of duodenal ulcer was made clinically on the basis of roentgenographic findings, and the cases of hemorrhagic and atrophic gastritis were studied roentgenographically and gastroscopically. Biopsy of the lymph nodes was made in all cases of Hodgkin's disease.

The histamine content of the whole blood was determined by the method of Barsoum and Gaddum,[3] as modified by Code.[4] The values are expressed as μg of free base per 100 cc of blood.

Results. As given in Table I, the blood histamine in patients with gastric carcinoma and with peptic ulcer was between 1.2 and 8.5 γ per 100 cc. There was no difference between the two groups, and the values did not deviate significantly from the normal range, reported to be between 1.8 and 7.8 γ (average 4.0 γ) in 173 normal individuals

1 Hay, L. J., Varco, R. L., Code, C. F., and Wangensteen, O. H., *Surg. Gyn. Obst.*, 1942, **75**, 170.

2 Brunschwig, A., Schmitz, R. L., and Rasmussen, R., *J. Nat. Cancer Inst.*, 1941, **1**, 481.

3 Barsoum, G. S., and Gaddum, J. H., *J. Physiol.*, 1935, **85**, 1.

4 Code, C. F., *J. Physiol.*, 1937, **89**, 257.