flicting opinions regarding the influence of serum on the lysis of pneumococci by bile salts.[11, 15, 16]

Summary. Turbidity and flocculation developed in 2% horse serum broth containing concentrations of sodium desoxycholate between 1.2 and 2.4 mg per ml at a pH of 7.3 and cleared on the addition of an excess of sodium desoxycholate. Apparent failures of lysis of serum broth cultures of pneumococci were due to the occurrence of such turbidity because no bacteria were found in these mixtures.

11505

Influence of Arsenicals, Bismuth and Iron on the Plasma Ascorbic Acid Level.

CHESTER J. FARMER, ARTHUR F. ABT AND HANS C. S. ARON.
From the Departments of Chemistry and Pediatrics, Northwestern University Medical School, Chicago, the U. S. Public Health Service, and the Department of Health, Chicago.

Several reports indicate that the poisonous effects of a number of drugs like benzene, lead,[1] phenylcinchoninic acid,[2] and glycerol[3] and especially the arsenicals[1] may be counteracted successfully by giving suitable doses of ascorbic acid.

From examination of the urine Dainow[4] concluded that patients who showed symptoms of intolerance to arsenicals were in a state of hypovitaminosis C. By administration of ascorbic acid, these hypersensitive patients became able to tolerate neoarsphenamine. Other investigators[5–11] reporting similar observations, emphasize

15 Boecker, E., and Kauffmann, F., *Bakteriologische Diagnostik*, 1st Ed., 1931, Berlin, J. Springer, p. 71.

16 Park, W. H., and Williams, A., *Pathogenic Microörganisms*, 10th Ed., 1933, Lea and Febiger, Phila., p. 353.

1 Abt, A. F., and Farmer, Chester J., *The Vitamins*, Chapter XXII, American Medical Association, Chicago, 1939.

2 Bertellotti, L., *Minerva, Medic.*, 1939, **30**, 254.

3 Pfeiffer, C., and Arnove, T., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 467.

4 Dainbow, T., *Presse méd.*, 1937, **45**, 1670; *Annal. Dermat. et Syphil.*, 1939, **10**, 139.

5 Landfisch, S., *Polska gas. lek.*, 1937, **16**, 575; *J. A. M. A.*, 1937, **109**, 834.

6 Cormia, F. E., *Canad. Med. Assn. J.*, 1937, **36**, 392.

7 Montesano quoted by Bertellotti.[2]

8 Biss quoted by Dainow.[4]

9 Tibor, S., *Orvosi Hetilap*, 1939, **83**, 811.

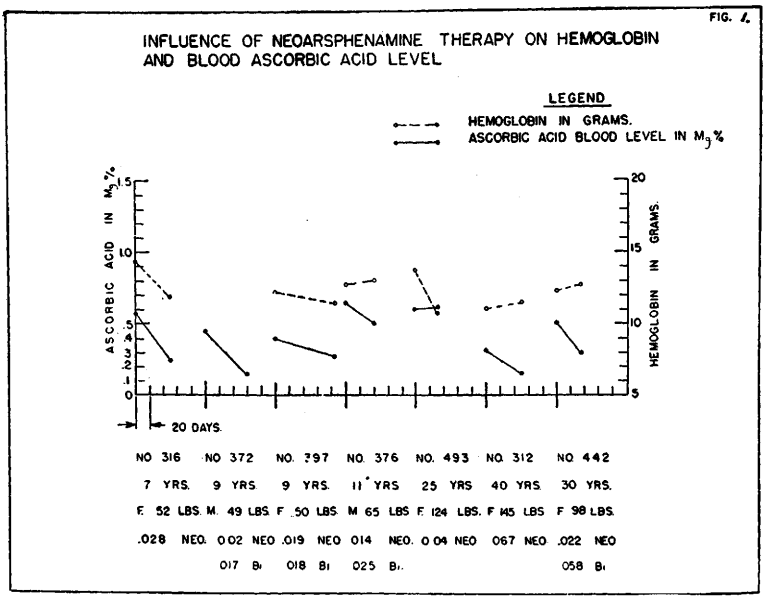
10 Santiago, A., *Zbl. Haut und Geschl. Krkh.*, 1938, **60**, 74.

11 Takahashi quoted by Bertellotti.[2]

the fact that in certain hypersensitive cases ascorbic acid gave favorable results after other methods of detoxification such as the administration of glucose, invert sugar, and calcium or sodium thiosulfate had failed.

After a suitable method for determining plasma ascorbic acid had been developed, studies were commenced in 1938 on syphilitic patients showing symptoms of intolerance to arsenicals. A more extended systematic study of this problem was recently made possible in connection with our Nutritional Survey of the syphilitic patients attending the Municipal Social Hygiene Clinic, Chicago.*

It was noted early in the work that patients hypersensitive to neoarsphenamine in whom treatment had to be discontinued because of severe reactions‡ required exceedingly large oral doses of ascorbic acid† to bring their plasma levels up to optimal values (1.0 mg %



These data demonstrate that neoarsphenamine (in contrast to bismuth) exerts a depressive action on the plasma ascorbic acid level. In 6 out of the 7 cases a distinct decrease in the plasma level occurs. The hemoglobin is but slightly affected.

* We are indebted to Dr. O. C. Wenger, Senior Surgeon, U. S. Public Health Service, and to Dr. Herman N. Bundesen, President of the Chicago Board of Health, for the facilities and opportunity of studying patients attending the Municipal Social Hygiene Clinic. We also wish to acknowledge the cooperative assistance of Dr. G. G. Taylor, Director of the Clinic.

‡ These reactions consisted of nausea, vomiting, fever, dermatitis, and in one case hepatitis.

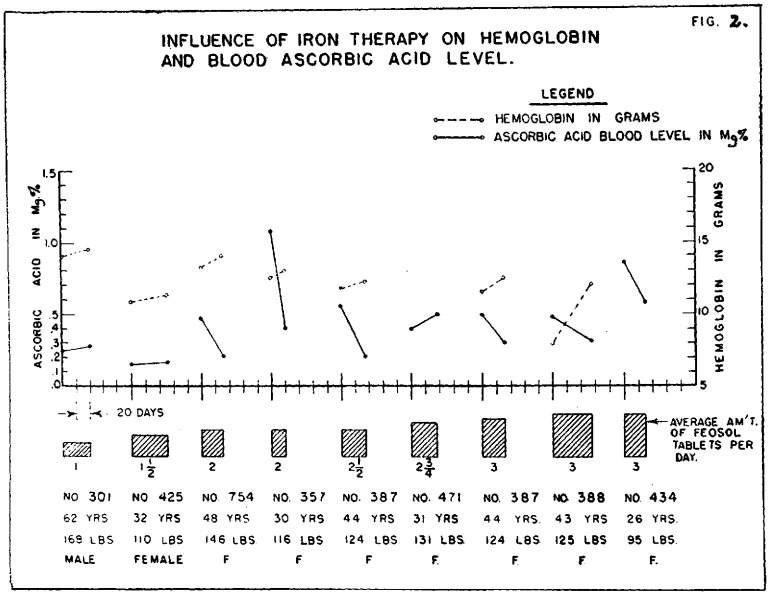
† We are indebted to Merck and Company, Inc., Rahway, N. J., for a generous supply of Cebione (ascorbic acid) used in this investigation.

or above). When showing severe symptoms of intolerance, a decline of the plasma level occurred in spite of the oral administration of ascorbic acid during treatment. It was frequently observed that a marked lowering of the plasma level followed the administration of neoarsphenamine in patients showing no intolerance to the drug (Fig. 1).

When bismuth was given in doses routinely used for antiluetic treatment, no appreciable effect was observed either on the plasma ascorbic acid or hemoglobin levels.

Striking effects were observed on the administration of ferrous sulphate (Feosol§). Doses smaller than 6 grains daily were ineffective. However, 6 grains or more caused a sharp drop in the plasma ascorbic acid level as will be seen from Fig. 2.

Exactly the same type of response was observed when ferrous sulphate was given to 12 patients receiving bismuth therapy. The greatest drop in plasma ascorbic acid level occurred in patients taking

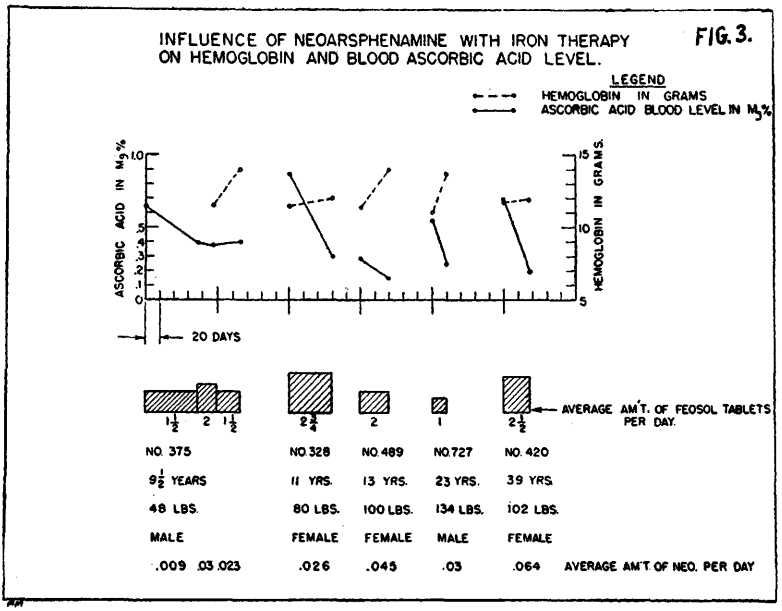


Patients who were at a rest period and did not receive antiluetic treatment were given iron orally in the form of ferrous sulphate ("Feosol" tablets, each containing 3 grains of ferrous sulphate). The hemoglobin rose in every case examined. However, when the dosage of "Feosol" *amounted to 2 or more tablets per day* there was a sharp drop in the plasma ascorbic acid level in 6 out of the 7 patients.

§ We are indebted to Smith, Klein and French Laboratories, Philadelphia, for a liberal supply of Feosol Tablets. Each tablet contains 3 grains of ferrous sulphate. The other ingredients are of no significance here.

ferrous sulphate while receiving neoarsphenamine. These data are presented in Fig. 3. It should be emphasized that in spite of this decline in plasma ascorbic acid level the hemoglobin rose in practically every case. This observation is in good accord with the findings of Moore, Bierman and Minnich,[12] who noted a definite decrease in plasma ascorbic acid following a rise in serum iron and hemoglobin after ingestion of large amounts of ferrous or ferric salts.

Our observations suggest 3 types of action of drugs containing heavy metals on plasma ascorbic acid. Bismuth is without influence. Iron causes a marked decrease, which may be of significance in rapid hemoglobin formation. Arsenic in drugs as neoarsphenamine, lowers plasma ascorbic acid, which in some cases may be an attempt on the part of the organism to detoxify the drug. As evidence of detoxification, patients previously hypersensitive to arsenicals have been permitted to resume treatment upon administration of suitable doses of ascorbic acid, when the optimal plasma level was attained. Repeated plasma analyses must be made to determine the amount



These data present the simultaneous action of neoarsphenamine and Feosol on plasma ascorbic acid level and hemoglobin. It will be seen that plasma ascorbic acid values dropped from fairly normal to decidedly low levels. The hemoglobin, on the other hand, rose more or less in every case.

12 Moore, C. V., Bierman, H., and Minnich, V., Centr. Soc. Clinic. Res., 12th Ann. Meet., 1939.

of ascorbic acid required for maintenance of the optimal plasma level during treatment. In conclusion our data indicate the necessity for a high ascorbic acid intake during certain types of medication with heavy metal compounds, to meet excessive requirements either for physiological demands, or for detoxification of drugs in certain cases before therapeutic levels can be attained.

We wish to acknowledge our indebtedness to H. J. Fagen and J. Meyer for much of the analytical data reported here.

11506 P

Respiratory Metabolism of Pigeons after Adrenalectomy and its Increase by Prolactin.

OSCAR RIDDLE AND GUINEVERE C. SMITH.

From the Carnegie Institution of Washington, Station for Experimental Evolution, Cold Spring Harbor, N. Y.

Recent experience in the maintenance of adrenalectomized animals in fair or good condition without use of cortical hormones gives new interest and value to measurement of the basal metabolism of such animals, and the adrenal-pituitary relationship is now the subject of much investigation. The pigeon has been found useful in such studies. It seems to survive complete adrenalectomy readily, though it is best to do the operation in two stages and to inject desoxycorticosterone just before the second operation; thereafter pigeons maintain themselves well without special nutritional or hormonal supplements. Repeated metabolism measurements have been made on 12 such pigeons of various races (both sexes) and on 4 of these birds the ability of prolactin to increase the B.M.R. was demonstrated.

Thirty measurements made at 30°C indicate that adrenal removal in pigeons has little effect on heat production; a decrease of 6% was found. Measured at 25°C this decrease was also 6%. Respiratory quotients obtained after a 24-hour fast were the same in operated (0.73) and intact pigeons. In 10 tests made on birds from which a single adrenal was removed no significant effect was observed. The effect of adrenalectomy on the metabolism of the bird is thus found to be less though similar in direction to that previously reported by others for certain mammals. Interpretation