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Preliminary note on chemical changes in the blood of syphilitics under arsphenamin treatment.[1]

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Among the very few recent publications on the subject of the chemistry of the blood in syphilis before or during arsphenamin therapy, the first is that of Rappleye.[2] He determined the urea of the blood and the phenol-sulphon-phthalein elimination in the urine of a series of twenty paretic cases before, and at intervals of one half, three and twenty-four hours after intravenous administration of *diarsenol*[3] (0.5 to 0.6 gm.), and also of a series of ten patients who had been under treatment for a long time. He observed fairly normal values (8 to 20 mg. of urea nitrogen per 100 c.c. of blood) in all cases both *before* and *after* treatment.

Elliott and Todd[4] made similar studies before and after a course of six weekly intravenous injections of 0.5 gm. of arsphenamin in a series of twenty syphilitic young men without evident renal disturbance. They found the average urea content of the blood to be 30.7 mg. before and 34.4 mg. per 100 c.c. of blood after treatment. One case showed an increase of 19 mg. In another series of nine cases to whom injections were given *twice* a week with the same total dosage, the average blood urea was 33.7 mg. before and 35.3 mg. after treatment. Five of the nine cases showed increases of from 4 to 5 mg. of urea nitrogen per 100 c.c. of blood.

It is important to note that although these authors had selected cases which clinically or by the albumin test showed no signs of renal disturbance, their values for blood urea nitrogen *before injection* are more or less pathological and range from 27 to 43 mg. with an average value of 33.7 mg. per 100 c.c. of blood.

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[1] Investigation aided by funds accruing from the preparation of arsphenamin.

[2] Rappleye, W. C. Notes on the Effect of Intravenous Diarsenol. *Jour. Lab. and Clin. Med.*, 1919, iv.

[3] This is the Canadian brand of arsphenamin (salvarsan).

[4] Elliott, J. A. and Todd, L. C. Effects of Arsphenamin on Renal Function in Syphilitic Patients. *Archives Der. and Syph.*, 1920, ii, 699–702.

Bailey and MacKay[1] in a study of 25 cases of syphilis that had developed toxic jaundice during arsphenamin treatment, found values for blood sugar fairly normal, cholesterol very high whenever there were any signs of liver disturbance, and in the greatest majority of cases, values for urea nitrogen ranging from 22 to 49 mg. per 100 c.c. of blood, twelve out of the twenty-five showing figures above 30 mg. They observed similar increases in the uric acid and creatinin of the blood. It is important to note that although none of these cases showed any proteinurea before or during treatment, they were distinctly nephritic, as proven by these pathological figures and by the fact that they became debilitated when placed on a high protein diet.

The importance of studying the kidney function of syphilitics before and during arsphenamin treatment has not been recognized by syphilographers in general. Wechselmann,[2] early in the history of arsphenamin therapy, emphasized the importance of kidney insufficiency in syphilitics, and ascribed most of the fatalities to this defect. Kolmer and Lucké,[3] in a recent histopathological study, showed that even small (therapeutic) doses of arsphenamin and neo-arsphenamin when injected repeatedly into the veins of rabbits produced vascular and tubular changes in the kidneys, characterized as "nephrosis." "Focal areas cf cellular degenerations and necroses were frequently well marked, particularly in the heart and liver."

Scope and Method of Investigation.—The patients studied were two cases of tertiary syphilis with optic atrophy. They were kept in a ward on a hospital diet, low in proteins and fats and fairly uniform from day to day. Their water intake was also controlled. The blood specimens were always obtained three hours after a special, constant breakfast. The analytical methods used were those of Folin and Wu.[4]

[1] Bailey, C. V. and MacKay, A. Toxic Jaundice in Patients under Antisyphilitic Treatment. *Archiv. Int. Med.*, 1920, xxv, 628–647.

[2] Wechselmann, W. Uber die Pathogenese der Salvarsantodesfalle. Berlin, 1913. Urban and Schwarzenberg.

[3] Kolmer, J. A., and Lucké, B. Summary of Experimental Studies on the Histopathologic Changes Produced by Arsphenamin and Neo-arsphenamin. *Archiv. Der. and Syph.*, 1920, ii, 289–291; *ibid.*, 1921, iii, 483–580.

[4] Folin, O. and Wu, H. A System of Blood Analysis. *Jour. Biol. Chem.*, 1919. xxxviii, 81–109; and *ibid.*, 1920, xli, 367–375.

After a preliminary period of observation of about one week, 0.6 gm. of arsphenamin (using ampules of the same lot number and produced at the Dermatological Research Institute) was injected intravenously in 120 c.c. of distilled water by means of a gravity apparatus. Details of the analyses are given in Table I.

TABLE I.

SHOWING CHEMICAL CHANGES IN THE BLOOD OF SYPHILITICS DURING ARSPHENAMIN TREATMENT.

Patient I: T. M., Male, Age 38—Optic Atrophy.

Date.	Total Non-Protein Nitrogen.	Urea Nitrogen.	Sugar.	Remarks.
10–25–20	24.2	11.1	85.1	
10–26–20	30.0	13.2	100.0	[2]
10–26–20	32.9	13.2	123.8	V[3]
10–27–20	36.8	20.6	130.2	V
10–29–20	31.4	17.2	133.8	
11– 2–20	39.5	14.3	115.6	
11– 4–20	33.4	14.9	103.9	
11– 8–20	34.3	22.4	131.6	
11– 9–20	23.2	8.1	133.3	[2]
11– 9–20	28.4	9.4	129.9	D[3]
11–10–20	44.3	14.8	121.2	
11–13–20	34.5	11.3	137.9	
11–16–20	32.6	12.6	137.9	
11–18–20	31.0	12.4	139.9	
11–22–20	32.4	18.1	121.6	
11–23–20	34.8	16.9	116.3	V[2]
11–24–20	38.2	18.3	117.6	
11–26–20	30.3	13.5	108.1	

Patient II: M. J., Male, Age 28—Optic Atrophy.

1–19–21	33.5	11.4	93.5	
1–20–21	32.1	11.4	88.3	
1–21–21	32.6	11.7	111.4	
1–25–21	30.7	12.2	75.5	[2]
1–25–21	32.8	15.5	153.8	V[3]
1–27–21	31.5	11.3	113.0	
1–28–21	31.5	12.6	89.9	
1–31–21	30.7	14.2	137.9	
2– 2–21	38.8	18.6	96.4	G
2– 4–21	35.8	17.5	119.0	
2– 7–21	30.9	14.3	107.5	

[1] All figures are given in milligrams per 100 c.c. of blood.

[2] Injection immediately *after* sample was drawn.

[3] Patient received an intravenous injection of 0.6 g. arsphenamin 3 hours *before* this sample of blood was drawn.

V = "reaction"—patient vomited.

D = severe reaction with vomiting, diarrhea and pain in the legs.

G = gastric crisis. C = slight reaction—chills.

Summary of Results.—During the period of observation preceding the injections the values for urea nitrogen, sugar, and total non-protein nitrogen of the blood were within the upper normal limits given by Myers.[1] Three hours after the intravenous injection of 6 decigram doses of arsphenamin, a slight rise in the total non-protein nitrogen of the blood (2 or 3 mg.) was observed in each of the two cases studied. This rise became more pronounced one week later, reaching a value of about 38.0 mg. per 100 c.c. of blood, and then gradually declined. The injections were repeated two weeks later. A more pronounced rise (up to 44 mg. per 100 c.c. of blood) was observed twenty-four hours later—the immediate increase (three hours after injection) being similar to that seen after the first injections. The changes in the blood-urea nitrogen were, in general, parallel to the curves of the total non-protein nitrogen. The individual values of the former occasionally reached as high as 23 mg. per 100 c.c. of blood and often constituted more than 60 per cent. of the latter. Marked increases in the blood sugar were seen three hours or within three to seven days after the injections. In one case the blood sugar was more than doubled three hours after the injection. In no case, however, did the blood sugar reach much above the upper normal limit,—the value in the last case referred to being 153 mg. per 100 c.c. of blood.

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Chemical stimulation of the annelid nerve cord.

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According to Maxwell's[2] classification, based on work with mammals, there are two classes of excitants for nervous tissue, viz: (1) those which act only upon the medullated fibers, such as the

[1] Myers, V. C. Chemical Changes in the Blood in Disease. *Jour. Lab. and Clinic. Med.*, 1920, v, 344.

[2] Maxwell, S. S., *Am. J. Physiol.*, 1918, xlvii, 283.