EFFECTS OF ARSPHENAMIN ON RENAL FUNCTION IN SYPHILITIC PATIENTS *

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A short time after arsphenamin came into prominence, renal impairment following its administration was noted in a small percentage of cases. During the first year of its use, Ehrlich¹ called attention to the fact that it should be given judiciously to patients suffering from nephropathies other than syphilitic nephritis. In 1911,² Mohr reported three cases of serious renal complications following its use. Two years later, Schlasberg³ reported twenty-seven cases in all of which albumin and casts developed in the urine. This he attributed to the drug. In order to prove his contention, he injected a number of rabbits and produced in them an experimental nephritis. Other cases have been reported by Geronne, Jadassohn, Scholtz,⁴ Wechselmann⁵ and others. Wechselmann called particular attention to the deleterious effects on pregnant women and advised Schlayer's lactose test as a precautionary measure in all such cases before administering treatments.

No doubt the drug is more perfect today than it was at that time, and therefore it is less toxic. Perhaps the technic employed then may have been a contributing factor. With our present-day technic and with the perfection of the drug, there are still some patients who develop nephritis after the administration of arsphenamin. The number of such cases cannot be ascertained from the meager literature on the subject. Their occurrence, however, is frequent enough to warrant periodic urine examinations in every patient receiving arsphenamin. As stated by Schlasberg, the microscopic examination should not be omitted since albumin may or may not be present, whereas any marked damage will be detected by the appearance of casts in the sediment. Guy⁶ has recently reported observations on 3,000 soldiers who received

* From the Crowell Urological Clinic.

1. Ehrlich, quoted by Mohr, R.: *Med. Klin.* **7**:596, 1911.

2. Mohr, R.: *Med. Klin.* **7**:613, 1911; abstr. *J. A. M. A.* **56**:1517 (May 20) 1911.

3. Schlasberg: *Nord. med. Ark.* **45**:1844, 1913; abstr. *J. A. M. A.* **61**:910 (Sept. 13) 1913.

4. Quoted by Mohr (Footnote 2).

5. Wechselmann, W.: *München. med. Wehnschr.* **51**:1845 (Aug. 25) 1914; abstr. *J. A. M. A.* **63**:1431 (Oct. 17) 1914.

6. Guy, W. H.: *Reactions Following the Administration of Arsphenamin: Report of Reaction in a Series of Twenty-Five Thousand Injections*, *J. A. M. A.* **73**:901 (Sept. 20) 1919.

25,000 arsphenamin injections. He saw one death from nephritis, and thirty patients developed transient albuminuria, three of whom had numerous red blood cells and large granular casts in the urine. All of these cases developed after treatments had been administered on a day when all patients reacted. He does not attribute this to the drug but to impurities contained in the water. He draws his conclusions from the fact that he was able to use a drug of the same serial number on other occasions without reactions. Stokes and Busman⁷ offer the explanation that the group of reactions reported by Guy might have been due to the rubber tubing. Their cases simulated those described by Guy with the exception that they did not observe any signs of renal complications.

It cannot be denied that in a certain percentage of cases there is some renal damage produced by arsphenamin as shown by Pearce and Brown.⁸ Whether these cases of nephritis are caused by arsphenamin or whether they are latent and are only lighted up by the drug, are questions of mere speculation. In order to determine whether all patients might not show some renal functional disturbances following arsphenamin treatments, we picked a number of young men whose average age was 25 years and who so far as we were able to determine had no renal disturbance whatever before treatments were instituted.

TESTS AND RESULTS

As indicators of the influence that arsphenamin might have on renal function, determinations were made of the urea content of the blood by the Van Slyke and Cullen⁹ modification of Marshall's urease method and of phenolsulphonephthalein excretion by way of the kidneys by means of the method of Rountree and Geraghty.¹⁰ It was believed that these two tests performed both before and after treatment, together with a careful urinalysis made at the same time, would point out any definite alteration in renal function if such were produced. All tests in order to be comparable were performed by the same method in detail, under the same circumstances as far as possible, and read by the same observer. The phenolsulphonephthalein was administered by the intramuscular route. The initial function test was made the day before or on the day of the first treatment; the final test was made the day following the last injection of the course.

7. Stokes, J. H., and Busman, G. J.: Tubing as a Cause of Reaction to Intravenous Injection, Especially of Arsphenamin: Preliminary Report, *J. A. M. A.* **74**:1013 (April 10) 1920.

8. Pearce, Louise, and Brown, W. H.: *J. Exper. M.* **22**:517, 1915.

9. Van Slyke and Cullen: *J. Biol. Chem.* **19**:211, 1914.

10. Rountree, L. G., and Geraghty, T. J.: *J. Pharmacol. and Exper. Therap.* **2**:579, 1910.

For obvious reasons four nephritics with syphilis coming under observation at this time were not included in the group. The case of one of these patients will be reported separately as a case of acute syphilitic nephritis; another was a case of chronic nephritis in a man past middle age; and the other two were in young men who were discovered to have a definite nephritis after having had some treatment and who may have had a pre-existing nephropathy. Owing to the fact that our patients were not hospitalized it was difficult to obtain complete data on all cases and therefore a portion of our work had to be discarded.

In twenty patients on whom phenolsulphonephthalein determinations were made both before and after a course of six arsphenamin injections with a total dosage of 2.7 gm., the average phenolsulphonephthalein excretion before treatment was 51.9 per cent. for two hours as compared with 47.7 per cent. excretion after completing treatment. Five, or 25 per cent., showed a reduction of from 10 to 17 per cent. each, while the other fifteen, or 75 per cent., remained the same at both determinations or showed only a slight reduction after treatment. Only one patient showed a higher phenolsulphonephthalein excretion. The urea content of the blood in twenty cases showed an average of 30.7 mg. per 100 c.c. before treatment, and 34.4 mg. after treatment, while one showed an increase of 19 mg. Four cases, or 20 per cent., remained the same, while three, or 15 per cent., showed a decrease of 1 to 3 mg. each. On the whole the changes in 75 per cent. were not significant.

In forty-four cases in which only the first phenolsulphonephthalein was secured the average excretion for two hours was 53.1 per cent.—closely comparable to the 51.9 per cent. in the twenty cases mentioned. In twenty-eight cases in which the phenolsulphonephthalein test was not performed until the treatment was completed, the average excretion was 49 per cent., closely resembling the final phenolsulphonephthalein excretion of 47.7 per cent. in the group previously mentioned.

The question as to whether those patients receiving two arsphenamin injections a week would show a definite variation from the results obtained with the patient receiving injections at weekly intervals, led us to separate a group of patients treated twice a week with the same total dosage. The results in this group were outlined in the accompanying table.

It is noteworthy that the resulting figures in this table do not vary greatly from those obtained in the cases less intensively treated. These nine patients showed an average phenolsulphonephthalein excretion treatment of 50.4 per cent. and an excretion of 44 per cent. after treatment. The blood urea figures are 33.7 mg. and 35.3 mg., respectively. Three, or 33⅓ per cent. of the cases showed a phenolsulphone-

phthalein reduction of from 10 to 17 per cent. each, although there was no other clinical or laboratory evidence of impaired renal function. The blood ureas showed very little change, but there was a tendency to be higher after treatment.

RESULTS IN A GROUP OF PATIENTS TREATED TWICE A WEEK

Patient	Age	Diagnosis Syphilis	Wasser-mann Reaction	Phenolsulphone-phthalein Excretion		Blood Urea	
				Before	After	Before	After
1. P. B. S.	27	Primary	++++	42 - 10 52	29 - 12 41	32	36
2. Sch.	31	Primary	++++	33 - 18 51	38 - 12 50	36	40
3. E. L. C.	50	Primary	Negative	27 - 20 47	25 - 17 42	36	34
4. W. W. B.	25	Secondary	++++	25 - 16 41	15 - 25 40	32	37
5. H. H.	20	Primary	Negative; dark-field, positive	31 - 16 47	22 - 10 32	27	31
6. J. Q. H.	16	Primary	Negative; dark-field, positive	38 - 20 58	29 - 12 41	32	31.2
7. B. F. R.	30	Tertiary	++++	34 - 17 51	37 - 14 51	34	37.2
8. P. T.	24	Primary	++++	34 - 19 53	23 - 25 48	43	43
9. W. S.	40	Primary	++++	39 - 15 54	34 - 16 50	31.2	28.2
Average 9 cases.....				50.4	44	33.7	35.3

The patient with acute syphilitic nephritis, previously mentioned, who was under observation at this time, showed an initial high blood urea reading which rapidly declined under arsphenamin treatment, illustrating presumably the beneficial effect of arsphenamin on this type of nephritis. On the other hand, the phenolsulphonephthalein excretion, which was rather high to begin with, declined somewhat during the treatment in spite of the obvious renal improvement as evidenced by the decline in the blood urea content and the disappearance of the albumin. These findings suggest that the admitted inadequacy of the phenolsulphonephthalein test to detect acute nephritides applies also to syphilitic nephritis.

Recently, we have supplemented the other test with blood creatinin determinations. Since we do not have parallel determinations with this test, our results so far do not permit of comparisons and the report of our findings must be withheld until a later date.