

of arsphenamine is 100 milligrams. Considering the arsenic contents of these two substances, 50 milligrams of arsenic in the form of neoarsphenamine is tolerated as compared to 30 milligrams in the form of arsphenamine. Here it is evident that a change in the amino group resulted in the reduction of the toxicity amounting to about 40 per cent. The minimum therapeutic dose, however, was increased from 23 milligrams to 40 milligrams or in terms of arsenic from 6.9 milligrams to 8.0 milligram, *i.e.*, the curative power decreased 16 per cent. In the 3, 5:3', 5'-tetraamino 4, 4'-dihydroxyarsenobenzene¹ we have a derivative which contains two more amino groups than arsphenamine. The maximum tolerated dose established by us is equal to seventy milligrams per kilo or in terms of arsenic 18.2 milligrams, an increase in toxicity of 39 per cent. The therapeutic effect remains as with arsphenamine. We also prepared 4, 4'-dihydroxyarsenobenzene—3, 3'-diaminoacetic acid, 4, 4'-dihydroxyarsenobenzene—3, 3'-alpha diaminopropionic acid, 4, 4'-dihydroxyarsenobenzene—3, 3' alpha diaminobutyric acid, 4, 4'-dihydroxyarsenobenzene—3, 3' alpha diaminovaleric acid. All of the above compounds are derivatives of arsphenamine in which both amino groups contain fatty acid substituents. In each case we observed a considerable reduction in the toxicity as well as therapeutic effect. We may conclude, therefore, that the toxicity as well as the curative power of organic arseno compounds is dependent to a considerable extent upon the fact as to whether the amino groups are free or substituted.

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Refractometric studies with the sera of syphilitic patients under arsphenamin and neo-arsphenamin treatment.By **KENCHI TOKUDA.**

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Refractometric studies were made by the writer upon thirty-two cases of *untreated* syphilis and the following observations were made:

¹ Raiziss, G. W., and Gavron, J. L., *Jour. Am. Chem. Soc.*

1. There is a marked increase in the refractive index of the serum and also in the globulins in Syphilis, *especially in active secondary cases*. This confirms the findings of Rowe.

2. The refractive index of the serum is highest in secondary cases, lowest in the congenital and is intermediate between these two in the tertiary cases. The figures for total proteins, albumins, globulins and the relative amount of globulin are somewhat higher in secondary than in tertiary syphilis, the figures for congenital syphilis being somewhat lower than those of the latter.

3. Considered in relation to the Wassermann reaction of the sera, before treatment, the strongly positive cases show values of total proteins, albumins, globulins and relative amount of globulins *higher*, and values of non-proteins correspondingly lower than the weakly positive cases.

4. During a course of fourteen intravenous injections of arsphenamine (0.4 to 0.6 gm.) and neoarsphenamine (0.9 gm.), each drug being given at weekly and semi-weekly intervals, the refractometric studies (made before each injection) show the following results:

5. Classified according to the Wassermann reaction of the sera *before treatment*, there are no sufficiently constant or striking differences to warrant differentiating between the strongly and weakly positive series.

6. Considered according to the *intervals* of injection the data have much significance. The refractive indices of the sera, when *neoarsphenamine* was given at seven-day intervals, show a more uniform and continuous decline during the fourteen weeks of treatment, than when arsphenamine was similarly injected. *The relative amounts of globulins*, on the other hand, show more rapid decline during weekly arsphenamin than neoarsphenamin injections.

During semi-weekly periods of administration the changes are very irregular. The relative amounts of globulins, however, behave as during the weekly periods.

7. Classified according to the *degree of resistance* of the patients to anti-syphilitic treatment (as indicated by repeated Wassermann tests) the following was observed:

When the Wassermann reaction remained persistently positive,

the refractive index, the percentage of total proteins and the relative amount of globulins of the sera showed little or no tendency to drop below their original values. When the Wassermann reaction, on the other hand, became very readily negative the curves fell progressively and fairly rapidly during the course of injections.

The writer is indebted to Dr. John A. Kolmer and Dr. Jay F. Schamberg for the laboratory and clinical facilities of the Dermatological Research Laboratories and the Polyclinic Hospital which they kindly placed at his disposal. Special acknowledgement is due to Dr. Charles Weiss of the D. R. Laboratories who compiled and interpreted the data and prepared this manuscript for publication.

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The analysis of factors which determine the life and growth of transplanted tissues.

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1. We may distinguish between two sets of factors determining the fate of transplants: (a) primary or constitutional; (b) secondary or extraneous factors. The former comprise the individuality and species differentials, and possibly organ specific factors; the latter include such factors as age, sex, pregnancy, infection and immunity. There are in addition general factors as oxygen supply, character of circulation and temperature; the latter we shall at present leave out of consideration.

If we take the subcutaneous transplantation of the thyroid gland as type, we find the following variables which may be influenced by the two sets of conditions: (a) the amount of surviving parenchyma and its growth energy; (b) the behavior of the connective tissue cells; (c) of blood and lymph vessels, and (d) of the lymphocytes of the host towards the transplant.

2. In a series of earlier papers we have analysed the effect of the individuality and species differentials on these four variables