its testoid action. The experiments suggest, furthermore, that by combining moderate doses of testosterone with a non-testoid compound such as pregnenolone, therapeutic doses of testosterone may be given in cases of eunuchoidism without the danger of producing testis atrophy.

13523 P

Comparative Distribution and Retention of Crystalloid and Colloid Fraction of Arsphenamine and Neoarsphenamine.

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Wright, *et al.*,[1] have separated both arsphenamine and neoarsphenamine, by dialysis in an inert atmosphere, into a crystalloid and a colloid fraction. The crystalloid fraction is less toxic and more curative for trypanosomiasis in rats than either the whole drug or colloid fraction. Death from toxic doses of either the crystalloid fraction or whole drug was due to delayed arsenical poisoning. The colloid fraction produced acute toxic symptoms, such as extreme respiratory embarrassment and death from respiratory failure.

We have investigated the comparative distribution and retention of the whole drug and the crystalloid and colloid fractions of arsphenamine and neoarsphenamine in the tissues of the rat following their intravenous administration.

The drugs were injected intravenously in a dose of 15 mg/kg and the animals were sacrificed at intervals of ½, 2, 6, 12, 24, 168, and 336 hours, at which times blood, skin, muscle (skeletal), bone, liver, kidneys, spleen, brain, stomach, small intestine and colon were taken for analysis. The arsenic content was determined by the Gutzeit method of the A.O.A.C.[2] A total of 308 rats was employed

* Accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at the University of Minnesota.

1 Wright, H. N., Biederman, A., Hanssen, E., and Cooper, C. I., *J. Pharm. Exp. Therap.*, 1941, **73**, 12.

2 Methods of Analysis, Official and Tentative, of the Association of Official Agricultural Chemists, 4th edition, 1935.

and 2034 analyses of tissue arsenic were made. The results obtained with arsphenamine showed the following:

Blood. The amount of arsenic present in the blood stream in the case of the colloid fraction was at all times greater than that of the crystalloid fraction. This was particularly marked in the later time intervals.

Skin, Muscle, Bone, Spleen and Kidneys. With respect to the retention of arsenic in these tissues it was found that the retention of the colloid fraction was greater than that of the crystalloid fraction, both as to quantity and duration of retention. The crystalloid fraction showed a high initial penetration into these tissues, followed by a rapid lowering of the arsenic content. In contrast, the colloid fraction showed an appreciable concentration in these tissues at all time intervals. The whole drug showed retention of amounts of arsenic intermediate to those of the two fractions.

Liver. The liver showed a decided affinity for arsphenamine, 39.70% of the injected arsenic being found in this organ ½ hour after the injection of the whole drug, 35.05% of the crystalloid and 32.93% of the colloid fraction. The concentration of the crystalloid arsenic dropped more rapidly than either the whole drug or colloid fraction, both of which are long retained and eliminated slowly and incompletely over 14 days.

Brain. The amount of arsenic retained by the brain is small, only a fraction of a percent for any of the preparations studied. Somewhat greater penetration and retention was found for the whole drug and colloid fraction than for the crystalloid fraction.

Gastrointestinal Tract. The retention of arsenic in the stomach following the injection of these three drugs is small (approximately 1%) and little was found after 24 hours. The intestine, thoroughly washed free of contents, showed the high retention of 33.70%, 33.73%, and 29.85% for the whole drug, crystalloid and colloid fractions respectively at the ½-hour time interval. This had fallen to a small percent by the end of 24 hours. The colon retained only a small percent of arsenic with the exception of the 6-hour time interval at which time 7.40%, 13.69%, and 6.69% of the whole drug, crystalloid and colloid fractions respectively were recovered.

Total Recovery and Tissue Retention. The summation of the arsenic recoveries for all tissues shows that at the ½-hour time interval total recoveries of 108.7% for the crystalloid fraction, 116.2% for the colloid fraction and 109.2% for the whole drug were obtained. The amount of arsenic localized in the tissues, exclusive of blood, at the end of ½ hour, was found to be 90.82%, 89.46%, and

83.59% for the whole drug, crystalloid and colloid fractions respectively. Subsequent time intervals showed that the crystalloid fraction was eliminated more rapidly than the colloid fraction, which was long retained, the recoveries for the respective preparations at 2, 6, 12, and 24 hours being 49.81, 28.91, 7.43, and 6.06% for the crystalloid fraction and 53.79, 41.13, 28.79, and 33.45% for the colloid fraction. After 14 days less than 4% of the crystalloid fraction was recovered while in the case of the colloid fraction 36.92% was found to be still present in the body. The retention by the tissues of the whole drug was intermediate to that of the two fractions.

Neoarsphenamine. The results obtained in a similar study with neoarsphenamine were quantitatively different but identical in principle with those obtained for arsphenamine.

Conclusion. The separated colloid fraction of either arsphenamine or neoarsphenamine is retained long in the body in comparison with the crystalloid fraction which is rapidly eliminated.

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Prevention of Perosis by Biotin.*

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Perosis was reported[1] to be a symptom accompanying the egg white syndrome in chicks. In the present investigation, single-comb White Leghorn chicks were placed on the following diet at hatching: Yellow corn meal, 55 g; wheat middlings, 20; dried skim milk, 10; commercial casein, 10; ground limestone, 2; steamed bonemeal, 2; alfalfa meal, 1; choline chloride, 0.1; NaCl, 0.5; $MnSO_4$, 0.05; fresh raw egg white, 30 cc. The wet mixture was spread in thin layers and dried at 45°C, after which 0.3 g of fish oil blend (3000-A, 400-D) was added. In addition to dermatitis,[2] symptoms of perosis developed in from 50 to 70% of the chicks at the age of 3 to 5 weeks. If egg white was omitted from the diet, or if cooked egg white re-

* Aided by a grant from the Williams-Waterman Fund of the Research Corporation, New York, N.Y.

1 McElroy, L. W., and Jukes, T. H., PROC. SOC. EXP. BIOL. AND MED., 1940, **45**, 296.

2 Ringrose, A. T., Norris, L. C., and Heuser, G. F., *Poultry Sci.*, 1930-31, **10**, 166.