nerves showed that regenerated nerve fibers had traversed the line of suture.

Conclusions. Clinical, electrical and microscopic studies demonstrated functional continuity after ulnar-femoral nerve anastomosis in a paraplegic rhesus monkey.

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Non-Utilization of Intravenously Administered Acetyl-*dl*-tryptophane.

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Albanese, Frankston, and Irby,[1] reporting on the fate of acetyl-*dl*-tryptophane given by mouth to human subjects, conclude "that, with the exception of a 5% urinary loss, all of the acetyl-*dl*-tryptophane may be available to man."

We have had occasion recently to investigate the fate of acetyl-*dl*-tryptophane administered intravenously to human subjects. Since the conclusions resulting from our investigation differ from those of Albanese *et al.*, publication of our findings is indicated: the difference in routes of administration must, of course, be emphasized.

Acetyl-*dl*-tryptophane (Merck) was used throughout. Two colorimetric methods for analysis of urine samples were employed. In the first of these the urine was diluted 100 fold. Portions of 1.0 cc were rendered strongly alkaline with 4.0 cc of 0.5 N NaOH and treated finally with 1.0 cc of the Folin-Ciocalteu phenol reagent.[2] The constituents were thoroughly and rapidly mixed and the resultant color read in a Klett-Summerson colorimeter after 2 minutes. The galvanometer deflections obtained were referred to a standard rectilinear reference plot of the corresponding readings obtained for varying quantities of 0.001 M acetyl-*dl*-tryptophane similarly treated with alkali and phenol reagent.

In the second method *p*-dimethylaminobenzaldehyde, as used by May and Rose[3] for tryptophane determination, was the reagent employed. Sodium nitrate, as proposed by Bates,[4] was used to accelerate the color development. Again the urine was diluted 100 fold. Portions of 0.25 or 0.50 cc, further diluted with water to 1.0 cc, were treated with 1.0 cc of sodium nitrate solution (1 mg per cc) and 5.0 cc of 0.05% *p*-dimethylaminobenzaldehyde in 12 N HCl. Readings were made on a Klett-Summerson colorimeter after 55 minutes and were corrected for the color given by normal urine. The reference curve, based on the use of 0.0 to 1.0 cc portions of 0.0005 M acetyltryptophane was rectilinear.

Recovery experiments on urine which was 0.0010 M to 0.0016 M with respect to added acetyltryptophane yielded a 96 to 101% recovery by either method. The correction for the color obtained with normal urine with the aldehyde reagent was, however, substantially lower than that obtained with the phenol reagent.

Three adult male subjects were used. In the first experiment each received intravenously 50 cc of 0.30 M acetyltryptophane adjusted to pH 7.2 with sodium hydroxide, passed through a sterilizing asbestos filter, and briefly heat-sterilized before use. The urine was collected in 3 post-injection periods of 6, 6 and 12 hours respectively, except in the third

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TABLE I.
Excretion of Acetyl-*dl*-tryptophane After Intravenous Administration.

Subject	Dose of acetyltryptophane	Acetyltryptophane excreted in 24 hrs in percentage of amount given*	
		Phenol method†	Aldehyde method
B	50 cc 0.3 M	80	79
L	"	83	83
H	"	74	78
B	50 cc 0.08 M		70
L	"		78

* Corrected for "apparent" tryptophane in pre-injection samples.

† Any tryptophane or tyrosine, and possibly other similar substances, in normal urine also give a blue color with the Folin-Ciocalteu reagent. However, the amount of color obtained under the above conditions with normal urine samples was small, and all values obtained were corrected for the colorimetric reading obtained with a normal 24-hour urine sample from the same subject. Both methods yield color with either tryptophane or acetyltryptophane. That the substance excreted by the experimental subjects was acetyltryptophane was evident since the amount present in the urines far exceeded the solubility of tryptophane, and in addition, acetyltryptophane could be readily isolated from the experimental urine samples.

subject where the collection periods were 3, 3 and 18 hours. Pre-injection 24-hour samples were analyzed for comparison.

In a second experiment, 2 of the above subjects received 50 cc portions of 0.08 M acetyltryptophane and urine was collected in 3 post-injection periods of 3 hours each. The purpose of this experiment was to determine whether the excretion of acetyltryptophane, observed in the first experiment to be a very high percentage of the amount given, was abundant only because of the comparatively large amount given. The results are presented in Table I.

Over 95% of the acetyltryptophane excreted was found to be voided within 6 hours of administration. Of this, the major portion was excreted within 3 hours.

Excretion of acetyltryptophane, in copious amounts, was confirmed by direct isolation. For this purpose the urine was acidified by addition of 1 cc of 6 N HCl per 10 cc of urine and allowed to stand at +1°C for 10 to 24 hours. The crystalline precipitate was centrifuged off and washed several times with cold water. It was dissolved in the minimum volume of hot ethyl alcohol, decolorized with charcoal and filtered. Four volumes of water were added to the filtrate and the solution placed in the cold room overnight for crystallization. The crystals were harvested again, decolorized, and twice recrystallized. From the urine of Subject B 1.7 g of final product were obtained, as compared with the 3.0 g estimated to be present on the basis of the colorimetric analysis. Since the isolation procedure was for qualitative rather than for quantitative purposes, it is clearly evident that the quantity of acetyltryptophane excreted must have been well in excess of the quantity of recrystallized product actually isolated. The substance possessed the chromogenic activity, crystal structure, and solubility of acetyltryptophane and was concluded to be such.

The rotation of a 10% solution of the substance was found to be +0.09°, that of the original acetyl-*dl*-tryptophane in 10% solution was +0.07°. The calculated rotation for a 10% solution of acetyl-*d*-tryptophane is —3.1°. We conclude, therefore, that acetyl-*dl*-tryptophane was excreted and no preferential utilization of acetyl-*l*-tryptophane is to be observed when the racemic compound is intravenously administered. We conclude further that acetyl-*dl*-tryptophane, given intravenously, is so rapidly excreted and so poorly utilized by the human subject that its incorporation in protein hydrolysates intended for intravenous alimentation is of little value. Likewise, the nutritive value of acetyl-*dl*-tryptophane in "stabilized" serum albumin appears to be negligible.

Summary. Acetyl-*dl*-tryptophane in aqueous solution was administered intravenously to

3 human subjects. Seventy to 83% of the administered substance was excreted unchanged, almost all within the first 6 hours after injection. The substance excreted was racemic: there was no preferential utilization or retention of acetyl-*l*-tryptophane.

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Effect of Quinacrine Hydrochloride (Atabrine) on Isolated Mammalian Heart.

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In laboratory animals (dog, cat, rabbit) the intravenous administration of atabrine causes a fall of blood pressure and, if the doses are large enough, disturbance of respiration.[1,2] As is the case with many substances, the toxicity is directly related to the rate of injection.[3] Studies on preparations of the isolated heart of the frog[4] as well as of mammals[1,5] suggest that atabrine has a negative inotropic action.

On the basis of the available clinical evidence[6-9] it appears possible that the negative inotropic action may play a rôle under certain clinical conditions when atabrine is injected intravenously in relatively large doses.

While the therapeutic levels, with the routine oral treatment now accepted, range between 25 and 75 μg per liter of plasma[10] and in total blood are of the order of 3 to 6 times these values;[9] in the experiments of Table VII in the paper of Shannon *et al.*, levels of the order of 1 mg per liter of whole blood and higher must have been present immediately after the rapid intravenous injection of the dose of 0.5 g.

Unna[2] ascribes the circulatory disturbance to action of atabrine upon the central nervous system. Before it is possible, however, to exclude the involvement of the heart in circulatory disturbances due to atabrine, it appears necessary to know at what atabrine blood level the heart begins to be affected. The following experiments on the heart-lung preparation of the dog were therefore undertaken to determine the minimum blood concentration of atabrine at which toxic effects are observed in the isolated mammalian heart.

It is fully appreciated that the atabrine concentration in whole blood does not represent the concentration in equilibrium with the body tissues because of the distribution of atabrine among the various components of the blood. It is our opinion, however, that our data are valid for the purpose of indicating the concentration range within which toxic effects upon the heart may be encountered, and that they apply to clinical

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