ings are taken with a photoelectric colorimeter after the solutions have stood for 20 minutes in the dark. The zero is set with 10 cc of 3% trichloroacetic acid to which the reagents have been added (6 N hydrochloric acid, nitrite, sulfamate and coupler).

Recovery. For a 1:50 dilution of whole blood, the average recovery of added p-aminosalicylic acid was 90% (86-95); for a 1:50 dilution of plasma, the average recovery was 95% (91-97); and for a 1:20 dilution of plasma, the average recovery was 93% (89-96).

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Distribution of 3,4-Dimethyl-5-sulfanilamidoisoxazole in the Body.*

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Sulfanilamide has been found to be distributed in all tissues and fluids of the body in approximately equal concentration.[1] Since the apparent volume of distribution of sulfanilamide is 87 to 98% of the body weight, which is somewhat in excess of the water content of the body (about 65%), it must be localized to a slight degree in tissue.[2] Sulfapyridine is distributed in a manner similar to that of sulfanilamide.[3,4] Sulfathiazole, sulfadiazine, sulfapyrazine and sulfamerazine are distributed in a volume corresponding to 45 to 55% of the body weight,[4] indicating that they penetrate tissues but to a lesser extent.† The data to be presented indicate that 3,4 dimethyl-5-sulfanilamidoisoxazole is distributed differently from any of the sulfonamides in clinical use; it appears to be confined to the extracellular water, with a volume of distribution of the order of magnitude of 25-30% of the body weight.

Methods. Determinations of the distribution of the drug were done on 3 dogs and 4 patients. The drug was injected intravenously; in the dog the sodium salt was used and in man, the lithium salt. About 50 mg per kilo were given in each case. Blood samples were taken at 0.5, 1, 1.5, 2 and 2.5 hours and urine was collected for the first hour after injection. The drug was determined in plasma and urine by the usual sulfonamide method.[5] In man both free and total sulfonamide were estimated; in the dog, no conjugated drug was found. The amount of conjugated drug in either the plasma or urine taken at 1 hour was 3% or less in 3 of the individuals and was about 10% in the other. All calculations have been based on the figures for free sulfonamide. No great error is involved.

Results. The apparent volume of distribution in per cent of body weight was calculated from the data obtained in two ways. The logarithms of plasma concentrations were

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† In addition to data given in the literature for distribution of these drugs, I have unpublished experiments showing that in the dog sulfanilamide is distributed in 87% and sulfadiazine and sulfapyrazine in 48% of the body weight.

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TABLE I.
Apparent Volume of Distribution of 3,4-dimethyl-5-sulfanilamidoisoxazole in % of body weight.

Dog	Calculated from Zero time	Calculated from 1 hr
1	33	
2	26	30
3	33	29
Patient		
H.W.	25	24
L.H.	24	23
G.B.	28	29
C	22	22

plotted against time, and the resulting straight line extrapolated to zero time. The value obtained, together with the dose given per kg, allowed a calculation of the distribution in per cent of body weight. The other method used was to calculate the distribution from the concentration in the plasma at 1 hour assuming that the amount of drug excreted in the urine during this hour represents the total amount disappearing from the body in that time. The results of these calculations are given in Table I.

Discussion. 3,4 dimethyl-5-sulfanilamidoisoxazole has been studied experimentally by Schnitzer *et al.*[6] Both the drug and its acetyl derivative are much more soluble in water than the sulfonamides in clinical use; in this respect, it resembles sulfanilamide. One would, therefore not anticipate any renal toxicity due to precipitation of the drug in the urinary tract. It is also stated to be quite effective against bacteria susceptible to the sulfonamides. The drug has been used to a limited extent clinically.[7-10] The observation that the drug is apparently distributed in extracellular water only has two important implications for its clinical use. These are 1) the same amount of drug in the body will give a concentration in the plasma 3 times that for sulfanilamide and about twice that for sulfadiazine and sulfamerazine, and 2) its apparent failure to penetrate cells should make it less toxic than sulfonamides which readily enter the tissues.

Summary. The distribution of 3,4 dimethyl-5-sulfanilamidoisoxazole has been studied in the dog and in man. Its apparent volume of distribution in per cent of the body weight indicates that it is contained only in extracellular water.

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Quantitative Study of Effect of Antrum Resection on Gastric Secretion in Pavlov Pouch Dogs.*

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In 1906, Edkins[1] found that extracts of antral mucosa stimulated gastric secretion when administered intravenously. Three years later, Edkins and Tweedy[2] reported that secretion of acid by the fundus could be produced by introducing various food substances into the antrum separated from the fundus by a diaphragm. Edkins postulated from these studies that this fundic secretion was due to a hormone, which he named gastrin, and which was produced by the antral mucosa in

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2 Edkins, J. S., and Tweedy, J. M., *J. Physiol.*, 1909, **38**, 263.