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.

6 Schnitzer, R. J., Foster, R. H. K., Ercoli, N., Soo-Hoo, G., Mangieri, C. N., and Roe, M. D., *J. Pharm. and Exp. Therap.*, 1946, **88**, 47.

7 Sarnoff, S. J., Freedman, M. A., and Hyman, A. A., *J. Urol.*, 1946, **55**, 417.

8 Haines, W. H., and Micali, S., *Pennsylvania Med. J.*, 1947, **50**, 1328.

9 Narins, L., *J. Urol.*, 1948, **59**, 92.

10 Rodgers, R. S., and Colby, F. H., *J. Urol.*, 1948, **59**, 659.

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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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1 Edkins, J. S., *J. Physiol.*, 1906, **34**, 133.

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

TABLE I.
Effect of Antrum Resection on Average 24 hr Secretion of Pavlov Pouch Dogs.

	Before resection				After resection			
Dog No.	No. of days	Vol. in cc	Free acid in clinical units	HCl in m.eq.	No. of days	Vol. in cc	Free acid in clinical units	HCl in m.eq.
D-928	17	733	120	83.8	21	246	70	17.4
D-939	25	539	124	67.1	29	79	7	0.6
D-944	16	989	122	122.7	20	439	99	43.7
D-879	29	863	129	112.0	24	157	36	6.1

response to chemical stimulation by food stuffs.

Ivy and Whitlow,[3] using Pavlov pouch dogs with an isolated antral pouch, obtained no acid secretion after stimulation of the antral mucosa with food substances. Therefore, Ivy concluded from this and other studies[4] that the substance causing the chemical or hormonal phase of gastric secretion was for the most part elaborated by the upper small intestine. Smidt,[5] working with Pavlov pouch dogs, reported marked reduction in the secretion of acid after antrum resection. Portis and Portis,[6] Shapiro and Berg,[7] and Thompson,[8] found little or no change in acid secretion in Pavlov pouch dogs after antrectomy.

For the most part, all of the above work was qualitative rather than quantitative, the conclusions being based upon the concentration of free acid in fractional samples. For this reason, it was decided to re-investigate the importance of the antrum in the chemical phase of gastric secretion using the quantitative methods of Dragstedt, Haymond, and Ellis.[9]

In 4 dogs, large Pavlov pouches were constructed which were drained by gold-plated brass cannulas. The 24 hour pouch secretion was collected in a detachable rubber bladder, and volume, free acidity, and hydrochloric acid content determined. The animals were fed a standard diet supplemented by oral sodium chloride. After a period of observation, the entire antrum was resected, and following recovery, comparable data collected.

Results and conclusions. In all animals, antrum resection was followed by a pronounced reduction in pouch secretion (Table I). The average reduction in the 24 volume was 73%, and in free acidity, 57%. The reductions in average 24 hour hydrochloric acid output were 79, 99, 64, and 95% respectively, averaging 84%. These data indicate that the antrum is important in the chemical or hormonal phase of gastric secretion, and supports Edkins' hypothesis.

[3] Ivy, A. C., and Whitlow, J. E., *Am. J. Physiol.*, 1922, **60**, 578.

[4] Lim, R. K. S., Ivy, A. C., and McCarthy, J. E., *Quart. J. Exp. Physiol.*, 1925, **15**, 13.

[5] Smidt, H., *Arch. v. Klin. Chirurg.*, 1923, **125**, 26.

[6] Portis, S., and Portis, B., *J. A. M. A.*, 1926, **86**, 836.

[7] Shapiro, P. F., and Berg, B. N., PROC. SOC. EXP. BIOL. AND MED., 1932, **39**, 743.

[8] Thompson, H. L., *Calif. and West. Med.*, 1932, **36**, No. 6.

[9] Dragstedt, L. R., Haymond, H. E., and Ellis, J. C., *S. G. O.*, 1933, **56**, 799.