of cooperation as a process which has a measurable improvement and objective criteria of success and perfection. The preliminary practice level eliminates the individual learning phase. Each subject is equally necessary to the solution of the problem, and each is equally rewarded. Competition between subjects is eliminated, although the usual factors of the cooperative relationship, such as dominance, submissiveness, and initiative, are also allowed to operate. The level of cooperation can be measured in at least three ways: (1) by the number or proportion of responses in unison per trial; (2) by the number or proportion of the same levers pulled simultaneously; and (3) by the time gap between patients' pulls. The first two of these clearly tend to increase with practice.

With this method, it was found that extremely regressed schizophrenics, at least those who have previously been brought individually to a high practice level at multiple-choice learning, can learn to cooperate with one another. Qualitative features of their interaction behavior are also evident and tend to point up a fixed pattern for each individual's cooperative behavior. These features are observed and tallied on a specially prepared trait sheet during the experimental sitting. They include watching the levers pulled by partner, telling him which levers to pull, holding back a lever until partner pulls the same, and actually telling the other patient the principle of the solution. It is possible to wire together more than two of the multiple-choice boxes, thus permitting the study of cooperation in a group of several individuals.

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The Potential Value of Sulfaguanidine in Urology[1]

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Following a review on absorption and excretion of sulfaguanidine, a new therapeutic rationale for the use of sulfaguanidine is suggested.

Since 1940, texts have generally stated that sulfaguanidine is slowly and/or poorly absorbed from the gastrointestinal tract. Dosages of approximately 20 g in a day have been used for thousands of persons with bacillary dysentery, and as much as 60 g in a day have been given (*1*). The facts that blood levels remain relatively low (*2–5*) and that toxic manifestations occur infrequently (*2–10*) have probably contributed toward false impressions about the actual situation in regard to absorption of sulfaguanidine.

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[2] Appreciation is expressed for aid from Horace W. Stunkard, and advice from Charles Willey, Harold Fay, Harry Bergman, and Benjamin Slivko.

TABLE 1. Excretion of sulfaguanidine by five persons.

Experimental individual	Oral dose (g)	Av. conc. free drug in urine during stated time interval following administration	Yield of dose in urine during stated time
Ingalls	4	107 mg % at 3–6 hr	15.0% in 8 hr
Pearl	2	126 mg % at 1–3½ hr	11.5% in 3½ hr
Parker	2	168 mg % at 1¾–6½ hr	13.5% in 6½ hr
Greenberg	3	176 mg % at 1¾–3 hr	6.0% in 3 hr
Slivko	3	210 mg % at 4½–13 hr	42.0% in 13 hr

There is considerable literature dealing with the absorption and excretion of sulfaguanidine. Beling and Abel (*11*) found concentrations of sulfaguanidine in the urine varied from 25 to 200 mg %, while concentrations of the drug in the blood remained within the narrow limits of 1.5 to 1.8 mg %. Anderson and Cruickshank (*2*) found concentrations in urine as high as 240 mg %; and in blood, 3 mg %. Jamieson, Brodie, and Stiven (*8*) found as much as 154 mg % in urine. Fairley and Boyd (*12*) mentioned that sulfaguanidine is absorbed to a large extent when very small doses are given, but to a small extent when larger doses are given. Hawking (*13*) considered the possibility that sulfaguanidine appears to be poorly absorbed because it is in fact first absorbed from the intestine and then excreted from the blood back into the intestine, but he demonstrated that this hypothesis was not valid. Hubbard, Butsch, and Aaron (*14*) thought that the apparent failure of absorption of sulfaguanidine might be due to removal of the drug from the blood stream by the liver and its return to the intestine in the bile. They proved this is not the case. Rose and Spinks (*15*) postulated that poor absorption of sulfaguanidine might be accounted for on the basis of its molecular structure. They failed to find direct evidence to substantiate this idea.

Investigations, into excretion in 45 normal healthy young men, indicate that sulfaguanidine is often well absorbed and rapidly absorbed. The combined effect of absorption from the gastrointestinal tract and excretion into the urinary tract is such that higher titers of

TABLE 2. Rapidity with which drug appears in urine.

Experimental individual	Oral dose (g)	Conc. of free drug in urine at time after administration
Slivko	3	101.0 mg % at 1¾ hr
Greenberg	3	71.5 mg % at 1¾ hr
Parker	2	59.0 mg % at 1¾ hr
Pearl	2	50.5 mg % at 1 hr
Ingalls	4	6.5 mg % at ¾ hr
Ingalls	2½	2.5 mg % at ½ hr

drug in the urine are obtained much more quickly following administration of sulfaguanidine than following administration, for example, of sulfadiazine. This was demonstrated in 90% of experiments with 40 students—using the method of Marshall, Emerson, and Cutting (*16*) as modified by Bratton and Marshall (*17*) and as described in the Department of the Army Technical Manual TM 8-227, except that smaller total quantities of sample and reagents were employed in a semimicrochemical method.

Excretion of sulfaguanidine by five other persons was further investigated. Free drug levels of sulfaguanidine in urine and percentage yields of the dose over short intervals after administration were determined (Table 1). The rapidity with which the drug appears in the urine was also studied (Table 2).

The amount of drug passed in the urine following administration of a single dose was measured. This varied from a low of 17.3% of the dose recovered as free drug to a high of 84.3% of the dose recovered as total drug (free sulfaguanidine plus acetylsulfaguanidine). In the last instance, a total of 2.53 g from a 3-g dose was excreted; 79% of this was in the free form and 21% acetylated.

The renal clearance for sulfaguanidine was calculated as the volume of blood which would contain the amount of material excreted in one minute. The renal clearance of sulfaguanidine often approached 120 ml/min. This figure indicates some tubular resorption, but less than occurs with urea. Thus the kidney can remove sulfaguanidine from the blood more effectively than it removes urea from the blood. Throughout these studies on renal excretion, blood levels remained at the expected low titers, usually below 1 mg % and never exceeding 2 mg %.

The literature gives ample evidence that sulfaguanidine is effective, especially in intestinal infections, but sulfaguanidine is being replaced to some extent by other drugs now used for intestinal infections. It therefore seems desirable to reevaluate the drug's therapeutic potential. In regard to the therapeutic potential for sulfaguanidine, there is an important piece of pure research in the literature by Clapper and Kurita (*18*). They found that urea and sulfaguanidine at concentrations of 10 mg % each are synergistic against *E. coli*. This is particularly interesting in view of such work as that of Gershenfeld and Sagin (*19*) who found that 220 mg % of sulfaguanidine did not inhibit *E. coli in vitro*.

Since a normal adult passes at least 25 g of urea and rarely passes more than 2500 ml of urine a day, the concentration of urea in urine will almost invariably exceed 1000 mg % or 100 times the concentration needed for a synergistic effect with 10 mg % of sulfaguanidine.

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Communications

Is the Black Widow Spider Invading New England?

DURING the middle nineteen-thirties a number of biologists were showing considerable interest in the distribution of the black widow spider, *Latrodectus mactans* (Fabricius), and from time to time short notes were published indicating an extension of its known range in the United States, particularly in the North. In early 1937 I showed that records had existed for some of the states for many years (*1*). Later that year the known records indicated that the spider had been collected in every state of the U.S.

This revival of interest occasioned numerous comments in the public press, and the impression received by many laymen was that black widow spiders were spreading northward. It appeared that this idea was particularly prevalent in New England, and at the request of the officials at the New England Museum of Natural History I prepared a short article about the spider for their *Bulletin* (*2*). In this paper were listed all the records then known for New England, which revealed that the black widow had been collected as far back as 1883 for Massachusetts, and 1884 for New Hampshire. It was also shown that although the species is not particularly common in New England, many records exist; and on occasion a large number of specimens has been picked up in a restricted locality.

In 1945 renewed publicity was given the spider after the appearance of a book (*3*) which includes a "Table of Reported Spider Bites by States." In this