

port inferred that muscle fasciculations result from a direct action of the blood on the muscle fibers.

Under the conditions of these experiments, it is evident that the fasciculations and tonic spasms occasioned by alkalosis and hypocalcemia can occur as the result of spontaneous iterative discharges arising in peripheral motor nerve fibers or their terminations in the motor end plates. These results cannot, of course, preclude the possibility of the participation of neurons within the central nervous system, or of sensory neurons in spinal and perhaps even supraspinal reflex arcs. In fact, there is considerable evidence that sensory fibers also are irritated and discharge repetitively in human tetany(2). However, our results strongly suggest that activation of peripheral motor nerve fibers or terminations account for the motor manifestations of tetany whether caused by an elevation in blood pH or a reduction in ionized blood calcium. This view is supported by Kugelberg's(15) finding in one human subject with inveterate hypocalcemic tetany that impulses occurring in the fourth interosseous muscle of the hand and recorded electromyographically continued unaltered after apparently effective procaine block of the ulnar nerve at the elbow.

Summary. 1. Tetany was produced acutely in eleven cats and one dog with solutions of sodium bicarbonate, sodium carbonate and a phosphate buffer administered by venoclysis. Fasciculations and tonic spasms involving especially the head and forelimb musculature characterized this form of tetany. Clonic spasms were not seen in anesthetized ani-

mals. 2. Section of the hypoglossal nerve did not significantly influence the fasciculations of the tongue musculature. Section of the brachial plexus did not significantly influence the fasciculations or tonic spasms of the forelimb musculature. 3. Paralytic doses of d-tubocurarine blocked all motor manifestations of tetany. 4. It was concluded that all of the motor phenomena characterizing alkalotic and hypocalcemic tetany could result from the spontaneous iterative discharges occurring in peripheral motor nerve fibers or their terminations.

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Some Factors Influencing Production of Ulcers in the Shay Rat. (19368)

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In our experience, the incidence of ulcers in the Shay rat varied from 100% to 25%. There are no apparent reasons for this variation, and some of the complicating, but significant, observations are recorded in this

paper. Recently, Madden *et al.*(1) in a critical study of the Shay procedure concluded that the method is valuable for the study of gastric secretion and of less value for the study of the ulceration mechanism. We have used

TABLE I. Effect of Hematuria and Pigmented Urine on Production of Ulcers.

	No. of animals	Rating					Ulcer index
		0	1	2	3	4	
Hematuria	119	69	31	14	2	3	65
Pigmented urine	55	25	19	6	4	1	85
Negative urine	864	159	140	117	86	362	241

The rating and the calculation of the Ulcer Index were as follows: 0, no visible changes; 1, incipient ulcerations, few punctate ulcers; 2, many small or one large ulcer; 3, deep ulcers with necrosis; 4, perforations of gastric wall or esophagus perforation and death before 8 hr, massive ulcerations without perforation. The Ulcer Index is the sum of each rating times 100, divided by the number of animals. Maximum index, therefore, is 400.

the method extensively and recently summarized our observations(2) on a possible role of the metabolism of certain salts on the etiology of Shay rat ulcers.

The present paper is based on 4 years experience and the use of many thousands of Shay rats. We wish to record here data concerning the incidence of ulcerations, perforations, volume of gastric contents, acidity, etc., obtained from 1038 animals. The incidence of other complications, *i.e.*, hematuria and pigmented urines, suggesting further very interesting studies is noted.

Methods. Male Wistar rats of 130-150 g weight were starved for 70 hours, with access to water, and treated using the original Shay technic(3). They were sacrificed after 8 hours, a number of them dying before that time. The system of rating and calculation of the ulcer index is given at the bottom of Table II. In most cases, analysis of the stomach juice in relation to the ulcer rating was also made.

Results and discussion. Out of 1038 Shay rats, 119 showed hematuria, 55 had pigmented urine. The effect of the development of these conditions on production of ulcers is shown in Table I.

As an indication of the frequency of esophagus ulcerations and perforations, of 200 consecutive animals which did not develop hematuria, a clear esophagus was found in 120, ulcerations in 35, and perforations in 45 animals. Data on gastric acidity and volume of stomach liquid are tabulated in Table II. With higher ulcerations the tissue debris partly buffered the acidity, but on the whole, the greater degree of ulceration was accompanied by lower pH values.

It is apparent from Table I that the occur-

TABLE II.

Rating	No. of animals	Median pH	No. of animals	Median vol of gastric liquid (ml)
0	92	3	91	6
1	98	2.5	96	8
2	76	2	74	9
3	42	2.5	36	8.5
4	72	2.5	18	6.5

TABLE III. Effect of Pre-Operative Diet.

	No. of animals	% 0 rating	% hematuria
No APF added	347	34.6	18.3
APF* added	474	15.8	9.3

* Aureofac, Lederle.

rence of hematuria or pigmented urine greatly reduces the degree of ulceration. It appears plausible that the greater number of rats with 0 rating is due perhaps to an incipient pigment disturbance, not discerned by us. The incidence of both these disturbances varied greatly with the batch of animals received. Sometimes, almost 50% of the animals on test developed these disturbances; at other times, there were none, and the ulcer index reached the maximum of 400. Most likely the pre-operative diet plays a major role, for when APF was added to the preoperative diet, the incidence of hematuria and pigmented urines were reduced with a corresponding increase in the ulcer index.

In the hematuric animals the presence of blood was plainly visible, often with congestion of the kidneys. The benzidine reaction and the presence of erythrocytes were demonstrated. The pigmented urines (we could not yet determine the nature of the pigment) con-

tain some red cells, show a negative reaction for bile pigments, and a maximum absorption at 3700 Å, not shown by the normally colored urines. It is possible that hematuria and pigmented urine development are an expression of the same metabolic disturbance, which is responsible for the failure of these animals to develop ulcers. The role of the above pigments, or pigment derivatives is now under investigation.

Summary. The paper presents data on the degree of ulceration developed in a large number of rats treated according to the Shay technic, showing the incidence of esophageal changes, stomach acidity, and gastric liquid

volume. The incidence of hematuria and pigmented urines is emphasized in their possible relationship to the etiology of Shay rat ulcers, as is the effect of preoperative diet in reducing hematuria and pigmented urines and increasing the incidence of ulceration.

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Effect of Oral Neomycin on Normal Intestinal Flora of Dogs and Man. (19369)

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Neomycin,* an antibiotic isolated from *Streptomyces fradiae* by Waksman and Lechevalier(1), has been reported to be effective *in vitro* and *in vivo* against a wide variety of gram positive and gram negative bacteria, including species resistant to other antibiotics (2-5). As the nephrotoxic and ototoxic effects of the drug(6) preclude for the present its parenteral administration, only the action after oral administration was investigated. The drug is so poorly absorbed from the gut that it is recovered nearly quantitatively and unchanged in the feces(4). This report deals with cultural data on the fecal flora after oral administration to man and to dogs.

In vitro studies. Seventy strains (*E. coli*, 10; *A. aerogenes*, 10; *Pseudomonas aeruginosa*, 10; *B. proteus vulgaris*, 10; hemolytic *Staphylococcus aureus*, 10; beta hemolytic streptococcus, 10; enterococcus, 5; and *Clostridium welchii*, 5), freshly isolated from hu-

man feces, were tested for sensitivity *in vitro* by a twofold tube serial dilution method, the concentrations of neomycin ranged from 200.0 to 0.006 µg per cc of nutrient broth. Each tube was inoculated with a bacterial suspension of 5,000-10,000 bacteria obtained by diluting an 18-24 hour broth culture of the particular strain. The lowest concentration of neomycin in µg/cc that showed no visible growth after 48 hours incubation at 37°C and did not yield living organisms in subculture was considered to be the bactericidal titer. **Comment.** In reading after 24 or 48 hours of incubation a series of tubes containing diminishing concentrations of neomycin, the last clear tube is followed by a tube just as cloudy as the control tube. In plating out this last clear tube there is no growth in the subculture. This indicates that *in vitro* neomycin has no bacteriostatic range and that the action of the drug is bactericidal—in sharp contrast to aureomycin which has a broad bacteriostatic range(7).

* The neomycin was provided by Dr. Earl L. Burbidge of Upjohn Co., Kalamazoo, Mich.