observations of Burns and Farinacci(13). Additional studies are in progress to establish whether the serological relationships observed in the complement fixation test can be more effectively demonstrated by other immunologic technics.

Summary. A virus recently isolated from the salivary glands of Mexican free-tailed bats (*Tadarida mexicana*) appears to be a new member of the JE-WN-SLE-MVE group of viruses. On the basis of the results of complement fixation tests it appears that the salivary gland virus of bats is more closely related to the West Nile virus than to other members of the group.

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Choline Antimetabolites. Studies with Intestinal Muscle. (22670)

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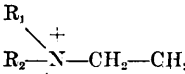
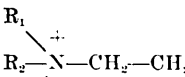
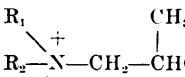
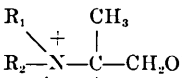
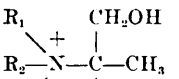
The report of Keston and Wortis(1) that frog muscle contracts in response to choline and that this contraction is inhibited by triethylcholine was of interest to us in our studies of compounds structurally similar to choline. Triethylcholine is only a very weak inhibitor of choline oxidation by choline dehydrogenase(2) and has usually been found to have choline-like activity (*Neurospora crassa* growth(3); lipotropic(4); antihemorrhagic (5)). In view of this anomalous behavior of triethylcholine with muscle we have extended our studies to include the effects of choline and related compounds on muscle contraction.

In this study segments of rabbit ileum were used instead of frog muscle. This acetylcholine sensitive tissue contracts in response to choline. We found that the response to choline was inhibited competitively by triethylcholine, β-methyltriethylcholine and α-methyl-α-hydroxymethylcholine. Triethylcholine was not, however, an inhibitor of acetylcholine. Methyldiethylcholine, triethylhomocholine, and α-methyl-α-hydroxymethyltrie-

TABLE I. Effect of Choline Analogues on Rabbit Ileum Muscle.

Compounds tested	R_1	R_2	R_3	Choline-like (relative activity, choline = 1.0)	Anticholine
	H	H	H	.3*	
	E	E	H	.1	
	M	M	E	4.0	
	M	E	E	.0	—
	E	E	E	.0	+
Ethanolamine					
	H	H	H	.2	
	E	E	H	.1*	
	E	E	E	.0	—
	M	E	E	.1	
3-Aminopropanol-1					
	E	E	H	.1*	
	M	E	E	.1*	
	M	M	M	.5	
	E	E	E	.0	+
1-Aminopropanol-2					
	H	H	H	.1*	
	M	M	M	.2	
	E	E	E	.1	
2-Amino-2-methylpropanol-1					
	H	H	H	.1*	
	M	M	M	.0	+
	E	E	E	.0	—
2-Amino-2-methylpropanediol-1,3					
Thiocholine chloride				3.1	

* Transient response. M = Methyl; E = Ethyl.

thylcholine were inactive at the concentrations tested while the remaining compounds studied possessed various degrees of choline-like activity.

Methods and materials. The choline analogues were prepared by methods previously described(2). Rabbit ileum was obtained soon after sacrifice of the animal, washed with Tyrode solution and then immersed in this medium at 5°C until used. A small segment was suspended in 100 ml of Tyrode solution at 37°, through which was bubbled a mixture of 95% O_2 + 5% CO_2, and its contractions recorded with a frontal writing lever on a kymograph.

When the spontaneous contractions had become constant, 2 mg of choline chloride were added and the increased contractions recorded. The bathing medium was then removed; the segment was washed 3 times with 50 ml of fresh Tyrode solution (37°), and resuspended in Tyrode solution as above. These operations could be repeated several times with essentially the same response to choline; the response to choline chloride was proportional to the dose up to a level of 6 mg.

The effects of the choline analogues on the segments of ileum were determined by adding the former to the bathing medium 2 mg at a time until 6 mg had been used. The testing of each compound was preceded by a test with choline, which was then washed out as above, and the segment was discarded when its response to choline was appreciably decreased.

Those compounds which failed to cause an increase in the contraction of the segment were tested for anticholine activity. Two mg of choline chloride were added to the bathing medium, and after the increase in contraction was established, 6 mg of the test compound were added. If no change in the contractions was produced, the test compound was considered to have neither choline-like nor anticholine activity.

Results. The activities of the compounds tested are presented in Table I. Fourteen of the compounds produced a response like that given by choline; the potencies were usually less than 0.5 that of choline on a weight basis with the exception of dimethylethylcholine and thiocholine which were 4.0 and 3.1 times as active as choline respectively. Diethylmethylcholine, triethylhomocholine and α-methyl- α-hydroxymethyltriethylcholine were inactive at the concentrations tested while triethylcholine, β-methyltriethylcholine and α-methyl- α-hydroxymethylcholine possessed anticholine activities.

That the compounds having anticholine activities were actually competitive inhibitors of choline was established by determining response of the segments of ileum to choline in the presence of 15 mg of the inhibitory compounds. The results are plotted in Fig. 1. In each case the response curve was roughly parallel to that obtained with choline alone and displaced toward higher choline concentrations. Under the same conditions, however, these compounds were found to have choline-like activities with segments of jejunum.

Discussion. The ability of choline to cause contraction of intestinal muscle may be (a) an inherent property of the compound or such activity may result from (b) its conversion to acetylcholine or (c) its being an inhibitor of

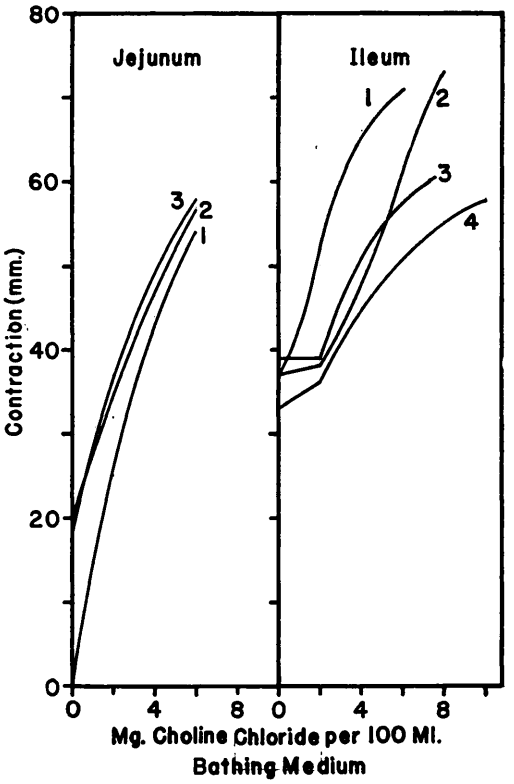


FIG. 1. Curve 1, choline alone; curve 2, choline plus 15 mg triethylcholine chloride; curve 3, choline plus 15 mg β-methyltriethylcholine chloride; curve 4, choline plus 15 mg α-methyl-α-hydroxymethylcholine chloride. In the segments of jejunum the contraction recorded was largely due to a change in tone. The contractions plotted for both tissues represent the sum of actual contraction and increased tone. Curves plotted are avg obtained with the same intestinal segment. Pieces of intestine from other animals gave similar results.

choline esterase. Whatever the mechanism of action is, it is reasonable to assume that the remaining compounds having choline-like activity would exert their activities by a similar means. That choline is a competitive inhibitor of choline esterase has been demonstrated (6,7). However, this does not seem to be the mechanism involved here since the anticholine effects of triethylcholine, β-methyltriethylcholine and α-methyl- α-hydroxymethylcholine would not then be explicable.

An unequivocal differentiation between the first two possible modes of action cannot be made from the experiments done in this study. However, there is some evidence against the second interpretation. First, we ob-

served that the contractions of the ileum began almost immediately on the addition of the choline and were constant after a relatively few contractions. If it were necessary to acetylate the choline in order for it to be active one might expect a delay followed by a relatively long period of increasing contractions. Second, by analogy to studies of the action of choline and related compounds on the heart of *Venus mercenaria*(8. 9) it seems also that the first possibility is more likely. It thus appears that our results are best explained by assuming that choline and certain other compounds related to it are capable *per se* of stimulating intestinal muscle. The mechanism of this action may be similar to the coenzyme theory proposed by Welsh(10) to explain the mode of action of acetylcholine. Accordingly, triethylcholine, β-methyltriethylcholine and α-methyl- α-hydroxymethylcholine have anticholine activity because they compete with choline for active sites on the apoenzyme.

Summary. Choline-like and anticholine activities of a series of compounds structurally related to choline have been determined using segments of rabbit ileum. Triethylcholine, β-methyltriethylcholine and α-methyl- α-hydroxymethylcholine were competitive inhibitors of choline in this tissue but had choline-like activity on segments of jejunum.

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Effect of Aspirin Administration on Serum Glutamic Oxaloacetic and Glutamic Pyruvic Transaminases in Children.* (22671)

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Elevations of the serum glutamic oxaloacetic transaminase (SGO-T) activity during the course of rheumatic fever in children have been noted previously(1). Despite the irregular pattern of these elevations and the absence of parallel alterations in the indices of inflammation commonly used (erythrocyte sedimentation rate, white blood cell count and C-reactive protein) and in the clinical course of the patients, it was suggested that the alterations of SGO-T were the result of myocardial necrosis during the course of rheumatic carditis. This enzyme is known to be present in the heart in high concentration(2) and elevation of its activity in the serum following myocardial infarction in man(3) and in dogs (4) has been described. Elevations of SGO-T also occur in human(5) and murine(6) hepatic diseases, but no clinical evidence of hepatic disease was present in the rheumatic fever patients studied and their liver function tests were normal(1). Drugs such as digitalis and mercurial diuretics which are often used in the treatment of patients with rheumatic fever were shown to have no effect on

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