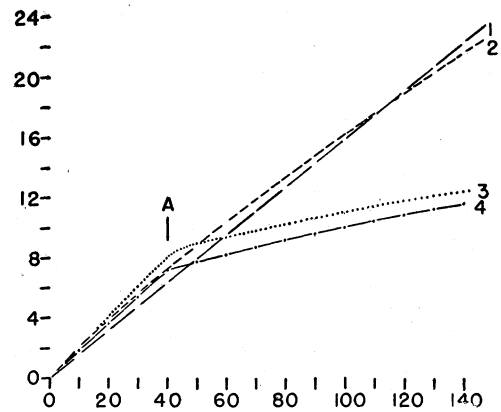

FIG. 2. The action of *n*-amyl carbamate. Solutions same as in FIG. 1, except for *n*-amyl carbamate (0.009 molar). Curve 1, glucose control; 2, glutamate control; 3, glucose with amyl carbamate added at 40 min (*A*); 4, glutamate with amyl carbamate added at 40 min (*A*).

That this cannot be done is illustrated in Fig. 3. Histamine dihydrochloride (pH adjusted to 7.35) at a concentration of 0.03 molar did not influence the rate of oxygen consumption of brain slices respiring in glutamate (Curve 2). Neither did histamine dihydrochloride prevent the inhibition of respiration by benadryl hydrochloride (Curve 4).

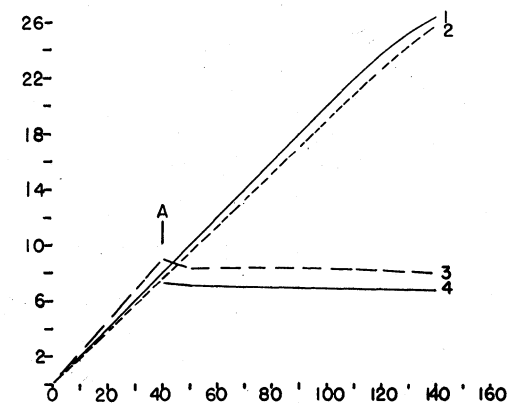

FIG. 3. Failure of histamine dihydrochloride to reverse benadryl effect. Solutions and conditions same as Fig. 1 except for histamine dihydrochloride (0.03 molar). Curve 1, glutamate control; 2, glutamate and histamine dihydrochloride; 3, glutamate with benadryl hydrochloride added at 40 min (*A*); 4, glutamate and histamine dihydrochloride with benadryl hydrochloride added at 40 min (*A*).

An analysis of the mechanism by which benadryl produces this selective inhibition of respiration will have to await the outcome of experiments now in progress. Obviously, selective alterations in permeability produced by the benadryl must be considered as a possible mode of action. The inhibition of respiration in experiments with *l*-glutamate and without added substrate makes the permeability concept unlikely, but experiments with brain homogenates, now in progress, should settle this point. If permeability is ruled out, the possibility exists that some metabolic step in the oxidation of *l*-glutamate is interfered with. Experiments with various metabolites linked to glutamic acid should prove useful in elucidating this point. All these matters will be discussed in a later report after the results of current experiments become available.

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Ammoniated Dentifrices and Hamster Caries: The Effect of Ingestion

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Experimental dental caries has been studied extensively in the Syrian hamster. Arnold (*1*) and Shafer (*6*) have shown that this animal is susceptible to dental caries when placed on a high-carbohydrate diet. Keyes (*4*) believes the carious process in hamsters is fundamentally the same as that observed in human beings.

Recently, ammoniated products have been proposed as an aid in controlling dental caries. Studies *in vitro* seem to indicate that an inhibitory effect on dental caries is possible. There has been very little actual testing of the effect of these products on caries in persons or in animals. Kesel (*2*) reported encouraging results from the use of a dentifrice and mouth rinse containing ammonia, but stated that further studies are necessary for conclusive results. Stephan (*7*) has shown that the application of urea in 40%–50% concentrations overcomes the effect of carbohydrate in lowering the pH of the dental plaque material. Keyes (*5*) studied the effect of weekly topical applications of a 50% urea solution on hamster teeth and found no apparent beneficial results.

It was thought desirable to devise an experiment in which the effect of the ammoniated compounds would be evaluated in regard to caries activity in the hamster. The effect of daily brushing with nonammoniated and ammoniated dentifrices, as well as the effect of ingestion, was studied. This report considers solely the effect of ingestion of dibasic ammonium phosphate and urea on caries incidence in the Syrian hamster.

The hamsters used were from an inbred colony. The animals were weaned at 21 days and placed on a diet of Purina Fox Checkers (with a weekly supplement of fresh carrots and hamburger meat), until they were approximately 30 days of age. The animals were separated into the experimental groups by sex and littermates.

[1] The authors are indebted to Jean M. Hartman, Department of Biostatistics, University of Minnesota, for aid in computing the statistics.

They were then placed on a caries-producing diet,[2] ad libitum, for 100 days, after which they were sacrificed and their caries scored and recorded by the method of Keyes (*3*). The control group (14 ♀ and 14 ♂) received the caries-producing diet only, and the ingestion group (13 ♀ and 12 ♂) received the same diet plus dibasic ammonium phosphate 1% and urea 0.6%—the ratio commonly found in ammoniated dentifrices.

TABLE 1

	Caries scores				
	No. of animals	Mean caries score	Standard deviation	t	p
Female					
control	14	26.4	40.0	2.11*	.05
ingestion	13	1.9	5.2		
Littermates					
control	7	36.8	46.6	1.93†	.10
ingestion					
Male					
control	14	57.5	76.3	2.03*	.05
ingestion	12	10.0	16.4		
Littermates					
control	9	66.1	83.4	2.24†	.06
ingestion					
Male and female groups combined					
control	28	42.0	62.9	2.77*	.006
ingestion	25	5.8	12.6		
Littermates					
control	16	53.3	71.2	2.90†	.011
ingestion					

$$* \; t = \frac{\bar{x} - \bar{y}}{SE_{\bar{x}-\bar{y}}} \qquad \text{where } SE_{\bar{y}-\bar{x}} = \sqrt{\frac{\hat{\sigma}^2}{N_x} + \frac{\hat{\sigma}^2}{N_y}}$$

$$\text{where } \hat{\sigma}^2 = \frac{N_x s_x^2 + N_y s_y^2}{N_x + N_y - 2}$$

$$\dagger \; t = \frac{\bar{d}}{\frac{s_d}{\sqrt{N-1}}}$$

From the mean caries score in Table 1, it appears that a striking inhibition of caries has occurred. The variation is considerable, however, and, in general, more than reported in other studies. It is possible that, if the animals had continued longer on the diet, the scores would have been higher and possibly more homogeneous. We are assuming a 1% level of significance when testing the difference between two means because of the small number of animals in the groups, and the relative infrequency of valid statistical evaluation of previously published experimental caries data. In addition, one must keep in mind the possibility that the effect of ingestion of these compounds by hamsters may not be comparable to the effect produced in human beings by these compounds.

Previous reports generally have indicated a sex difference in caries activity, if the animals are maintained for approximately 100 days on a caries-producing diet, although the difference is less striking when the animals are maintained for longer periods of time. It is of interest to combine the male and female animals in the control and ingestion groups. With more animals in each group, the difference between the mean caries scores seems more significant (i.e., below the .01 level). These data strongly indicate that the animals employed enjoyed a reduction in caries experience associated with the ingestion of the ammoniated products studied.

[2] Whole wheat flour, 30%; whole powdered milk, 30%; cornstarch, 20%; confectioners' sugar, 15%; alfalfa meal, 4%; and sodium chloride, 1%.

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Chloromycetin in the Treatment of "Red Leg"[1]

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The epidemic disease "red leg" has long been a source of difficulty to workers using any of the usual species of frogs as experimental animals. Control of the disease has always been unsatisfactory, as far as can be ascertained from the literature. It was therefore considered worth while to report the use of chloromycetin (chloramphenicol) in the successful treatment of the homologue of frog red leg in a toad, *Bufo marinus.*

The disease was apparently first described by Ernst (*6*), who isolated a bacterium, which he named *Bacillus ranicida,* from infected frogs. Sanarelli (*9*) studied an organism, which he isolated from frogs with red leg and named it *B. hydrophilus fuscus.* He reported the organism to be pathogenic for a variety of anurans and urodeles and briefly described some of the pathological findings in infected frogs. Russell (*8*) reported the pathology of the infection in more detail and described the experimental infectivity of the organism for some of the common laboratory mammals when injected intravenously; he also mentioned the production by the organism of at least two toxins that had pronounced effects upon frog cardiac and skeletal muscle and central nervous system. The nomenclature was revised to *Proteus hydrophilus* in the fifth edition of Bergey's *Manual* (*1*) in 1939. In the sixth edition (*3*) it was changed to *Pseudomonas hydrophila.* In 1942 Kulp and Borden (*7*) made an extensive study of the bacteriology of the disease, describing two distinct strains of the organism from different sources and reviewing the pathology in frogs. They indicated the existence of "carrier" frogs that harbor the organism in their gall bladders.

The disease in anurans is septicemic and is remarkable

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