too old animals, did not extend to second generations, or covered too short periods within one to overcome caries-resisting properties of the species, strain, or teeth in question.

An over-all analysis has been made of the trend of dental caries in about 800,000 children (*2*) surveyed by various workers in 11 European countries during the last 50 years. Following drastic reductions in consumption of refined carbohydrates at the beginning of the two World Wars, a marked caries reduction can be demonstrated. But the time relationship between the decrease in sugar consumption and the reduction in caries cannot be explained on the basis of a rapid mechanism in the oral environment. There is a delay of several years in the initial effect and a lag of many years in the terminal "effect

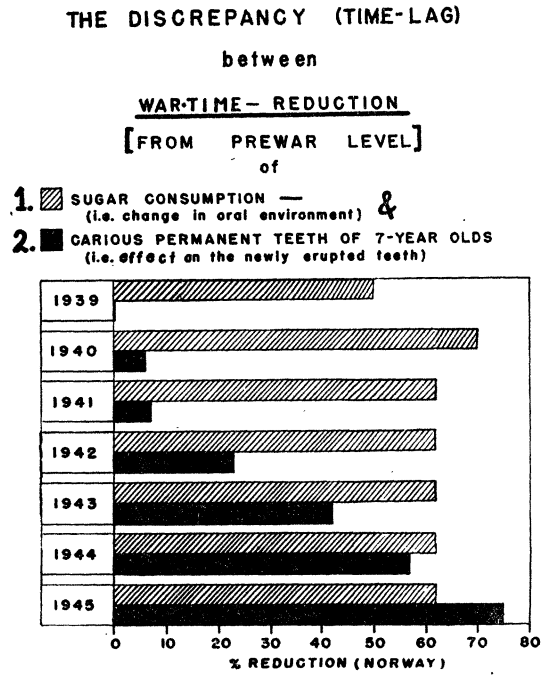

FIG. 2. A comparison of groups of 7-year-old children during each year of the war. Their permanent teeth *after eruption* were exposed to a similar sugar concentration in the oral environment. Significant caries reduction is seen in the teeth of those groups (1943/45) whose teeth had the longest "exposure" to the wartime diet *before eruption, i.e.* during development and final maturation.

of the wars" upon the caries reduction. This time factor can best be explained by an accumulative favorable effect before the teeth erupted into the oral environment (Fig. 2).

The mechanism of this beneficial influence upon the teeth developing during the war is not known. It cannot be attributed to any obvious, over-all uniform increase in the consumption of any previously demonstrated caries-inhibiting food or food factor, but may be related to the fact that the bulk of the caloric intake during the wars was in the form of natural foods. The large caloric loss resulting from the sugar and fat rationing primarily seems to have been compensated for by an increased consumption of nonpurified carbohydrates, potatoes, cabbage, and wartime bread (containing 80–95 per cent of the grain).

In view of these experimental and clinical observations, it is possible that the long-suspected relationship between dental caries and the excessive consumption of refined carbohydrates may be in the nature of an unrecognized indirect influence upon the quality of the offspring and its developing teeth, and that the effect may be accumulated through generations.

The hypothesis of an accumulative depletion of a nutritional factor or combination of factors favorable to the developing teeth is being tested.

References

1. SHAW, J. H., SCHWEIGERT, B. S., MCINTIRE, J. M., ELVEHJEM, C. A., and PHILLIPS, P. H. *J. Nutrition*, 1944, 28, 333.
2. SOGNNAES, R. F. An analysis of a war-time reduction of dental caries in European children; with special regard to observations from Norway. (To be published.)
3. SOGNNAES, R. F. The caries-conducive effective of a high intake of refined carbohydrates during tooth development. (To be published.)

Effect of Tetraethylammonium Chloride in Experimental Gastric Ulceration in the Rat

J. MAXWELL LITTLE, BEN C. OGLE, JOHN D. YEAGLEY, and DAVID CAYER[1]

Departments of Physiology and Pharmacology and *Internal Medicine, The Bowman Gray School of Medicine, Wake Forest College, Winston-Salem, North Carolina*

Recently a method has been described for the uniform production of gastric ulceration in the rat (*4*). This method, or a modification of it, has been used to test the effectiveness of antiulcer factors (*5*). Harkins has reported (*2*) the complete prevention of gastric ulceration in rats by transabdominal vagotomy, using this method.

It has been shown (*1*) that the tetraethylammonium ion blocks the transmission of impulses at autonomic ganglia. In view of the reported effectiveness of vagotomy in preventing gastric ulceration in the rat and the widespread use of vagotomy in the clinical treatment of peptic ulcers, it was thought that the tetraethylammonium ion might prove useful in the therapy of this condition. Therefore, the effectiveness of this compound in preventing gastric ulceration in the rat has been studied.

Eighteen female rats weighing 80–100 grams were fasted for 72 hours. The rats were kept separated in cages with a wide wire-mesh bottom and were given water throughout the fasting and experimental period. They were anesthetized with ether. A short midline incision extending downward from the xiphoid process was made and the pylorus carefully exposed and ligated. The incision was closed with sutures, and the wound was covered with a thin coating of flexible collodion.

Alternate rats were injected intramuscularly with 1 mg. of tetraethylammonium chloride (Etamon chloride,[2] 1 ml. of saline solution) just prior to the pyloric ligation and at hourly intervals thereafter until death or until the animal was sacrificed.

The results are summarized in Table 1. Rat #1 died as a result of anesthetization, and rat #9, a control, has been omitted from the series because it was found dead 2.5 hours after pyloric ligation and showed no lesions at autopsy. It

[1] The authors gratefully acknowledge the assistance of Woodrow Batten and J. I. Bumgarner in some of the experimental work.

[2] The Etamon chloride was generously supplied by E. C. Vonder Heide, of Parke, Davis & Company, Detroit, Michigan.

will be seen that all 7 of the controls died in less than 8 hours, with an average survival time of 6.7 hours. At autopsy, 6 of the 7 control rats showed perforation of the stomach. Of the 9 rats receiving Etamon chloride only 4 died; the shortest survival time was 7.1 hours, and only one of these 4 showed perforation. The remaining 5 experimental rats were sacrificed no sooner than 9.7 hours postoperatively, so that the shortest postpyloric ligation time was 1 hour longer than the longest control survival.

The stomachs were examined microscopically for ulceration. The results of this examination have been tabulated on the basis of an arbitrary division into two groups: (a) stomachs having ulcers in which one axis was at least 3 mm. long, and (b) stomachs having ulcers in which the longest axis was less than 3 mm. It will be seen that 6 of the 7 control rats were in

TABLE 1

Rat No.	Weight (gram)	TEAC* (mg.)	Survival (hr.)	Perforation	No. of ulcers					
					3 mm. or greater			Less than 3 mm.		
					Rumen	Body	Antrum	Rumen	Body	Antrum
Control series										
3	90	0	4.8	+	1	0	0	5	0	0
5	95	0	4.6	+	5	0	0	0	1	0
7	90	0	6.8	0	1	0	0	1	0	0
11	82	0	8.7	+	0	0	0	11	0	0
13	90	0	6.7	+	1	0	0	1	0	0
15	100	0	7.4	+	3	0	0	17	0	1
17	100	0	7.8	+	2	0	0	9	0	0
Total			46.8		13			44	1	1
Average			6.7		1.9			6.3		
Experimental series										
2	95	13	12.8†	0	1	0	0	0	0	0
4	90	10	9.8	0	0	0	0	0	0	0
6	90	11	9.9	+	1	0	0	9	0	0
8	95	12	11.5†	0	0	0	0	8	0	0
10	90	11	11.2†	0	1	0	0	1	0	0
12	80	8	7.1	0	0	0	0	0	0	0
14	100	10	10.4†	0	0	0	0	0	0	0
16	88	8	7.8	0	1	0	0	0	0	0
18	95	10	9.7†	0	1	0	0	4	0	0
Total					5			22		
Average					0.6			2.4		

* Tetraethylammonium chloride.

† Rats were sacrificed after this survival time.

the group having large ulcers in the rumen, while this was true of only 5 of 9 experimental rats. Furthermore, 3 of the 6 control rats had more than one large ulcer. Six of the 7 control rats were in the group having small ulcers in the rumen, and in 4 of these the ulcers were multiple. Four of the 9 experimental rats had small ulcers in the rumen, and in 3 of these the ulcers were multiple. One control rat each had a small ulcer in the body and in the antrum of the stomach. Three of the experimental rats showed no gastric ulceration, while all of the control rats showed ulceration.

A comparison of the effect of Etamon chloride on gastric fluid volume and acidity was impossible due to the high incidence of perforation in the control series.

Although Etamon chloride did not completely prevent gastric ulceration in this series, on the basis of survival time, perforation, and incidence of ulceration it appears that it was definitely beneficial. When one considers the possibility that the difference between the two series might have been more striking had all remaining animals been sacrificed and examined after 7 hours (approximately the average survival time of the control rats), the probable clinical usefulness of Etamon chloride is enhanced.

Lyons, *et al.* (*3*) reported that in one hypertensive patient, who also had a duodenal ulcer, a single intramuscular injection of 1.2 gram of Etamon chloride resulted in the cessation of gastrointestinal motility, relief of the ulcer pain, and a decrease in the acidity and volume of the gastric juice. As the effects of the drug diminished, pain returned, at about 7 hours, and peristalsis was believed to be more rapid. We have studied the effect of Etamon chloride in two human patients who had active duodenal ulcers as well as in patients with other gastrointestinal disorders, with suggestive beneficial results. The clinical studies are being continued and will be reported elsewhere.

References

1. Acheson, G. H., and Moe, G. K. *J. Pharm. exp. Therap.*, 1946, **87**, 220; Acheson, G. H., and Pereira, S. *J. Pharm. exp. Therap.*, 1946, **87**, 273.
2. Harkins, H. N. *Bull. Johns Hopk. Hosp.*, 1947, **80**, 174.
3. Lyons, R. H., Moe, G. K., Nelich, R. B., Hoobler, S. W., Campbell, K. M., Berry, R. L., and Rennick, B. R. *Amer. J. med. Sci.*, 1947, **213**, 315.
4. Shay, H., Komarov, S. A., Fels, S. S., Meranze, D., Gruenstein, M., and Siplet, H. *Gastroenterology*, 1945, **5**, 43.
5. Wick, A. N., Irish, A. J., Pauls, F., and MacKay, E. M. *Proc. Soc. exp. Biol. Med.*, 1947, **64**, 40; Morris, C. R., Grossman, M. I., and Ivy, A. C. *Amer. J. Physiol.*, 1947, **148**, 382; Pauls, F., Wick, A. N., and MacKay, E. M. *Gastroenterology*, 1947, **8**, 774.

A Method for Screening Antimalarial Compounds in the Mosquito Host

Levon A. Terzian

Naval Medical Research Institute, National Naval Medical Center, Bethesda, Maryland

Although methods of antimalarial drug screening have been improved and refined during the past several years, there has, nevertheless, been need for new screening technics, principally because it has not been possible to establish consistent or predictable relations between drug activity in experimental animal malarias and that in human malaria. For example, whereas sodium sulfadiazine and other sulfonamide derivatives have a kind of prophylactic effect against sporozoite-induced *Plasmodium gallinaceum* infections in chicks, these drugs are ineffective as prophylactic agents against human malarial infections. The present study was undertaken to devise a method of drug screening which would permit of more direct screening for certain drug qualities against a specific malarial parasite, or which would permit of screening of compounds for prophylactic effect against the human malarial parasite without the need for infecting undue numbers of human hosts.

In these experiments, laboratory strains of *Aëdes aegypti* were infected with a strain of *P. gallinaceum* designated as the 8A strain. Quinine hydrochloride, quinacrine hydrochloride,