TABLE I.
Erythema and Wheal Reactions to the Intracutaneous Administration of Dimethylaminoethyl Benzhydryl Ether Hydrochloride.

No. subjects	Dosage (mg/daily)	Duration treatment (weeks)	Degree of Reaction (% of control)‡ Erythema 5 min.	Erythema 10 min.	Wheal 5 min.	Wheal 10 min.
10	0	—	100	100	100	100
5	150	0.6	105	63	63	75
5	300	2.0	4	37	3	7
3	400	2.3	24	33	4	8
6	—	0.5†	138	155	185	168
2*	—	1.0†	493	300	104	104

* Both of these patients had received treatment for more than 11 weeks, and at the 400 mg dosage level for not less than 2 weeks.
† Length of time since treatment was discontinued.
‡ Figures represent averages for the number of subjects indicated.

to develop, even on long continued administration, and the clinical results thus far attained,[4-10] warrant further extensive clinical trial of the drug in a wide variety of allergic conditions.

Summary. Dimethylaminoethylbenzhydryl ether hydrochloride orally administered in sufficient amounts is capable of completely suppressing the sensitivity of the skin to histamine, at least as expressed by the wheal and flare reaction. In limited trials, this effect appears to have widespread clinical application.

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The Reputed Antipyretic Action of Camphor.*

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Many current textbooks of pharmacology contain statements to the effect that camphor is antipyretic and useful in the symptomatic treatment of fevers. Thus for example, in Sollmann's treatise[1] we find, "Camphor Spirit is a household remedy in colds, bronchitis, etc. It is thought to be somewhat expectorant, diaphoretic and antipyretic (Binz, 1875 and 1877)." In older books, published 100 years or more ago, less cautious statements are made, for there the virtues of camphor as an antipyretic are panegyrised. Camphor was first used in China and brought to Europe by the Arabians.[2] Its introduction as an antipyretic seems to have been based upon at least two properties, first that it has some antidiarrheic activity and secondly that spirit of camphor, applied to the skin, has a cooling effect. There has been no recent work done to check these ancient conceptions of the antipyretic value of camphor.

In the work described in this report, some 500 animals, including albino rats, guinea pigs, rabbits and cats, were rendered febrile by the intramuscular injection of peptone (B.D.H.) in a dose of 1 g per kilo body

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1 Sollmann, T., *A Manual of Pharmacology*, 6th ed., Saunders, London, 1942.

2 Flückiger, F. A., and Hanbury, D., *Pharmacographia*, Macmillan, London, 1879.

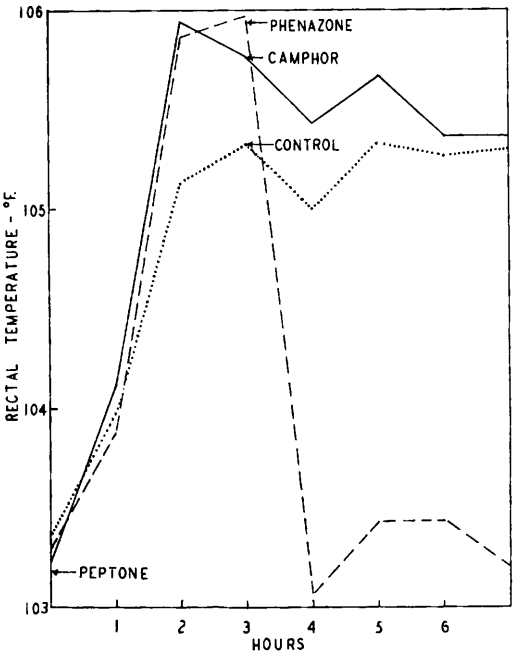

Fig. 1.

The effect of phenazone and of camphor upon peptone-induced fever in rabbits.

weight. In the first experiment, 66 rabbits were divided into 6 groups. Rabbits in 3 of the groups were injected with peptone while rabbits in the other 3 groups received no peptone. Rectal temperatures were taken before the injection of peptone and at hourly intervals thereafter, the latter in all groups of animals. Three hours after the injection of peptone, when fever was at its height, rabbits in one group were given an intramuscular injection of camphor in oil at a dose of 100 mg per kilo body weight; at the same time the second group of febrile rabbits received phenazone B.P., (antipyrine, U.S.P.) at a dose of 200 mg per kilo body weight; the third group of febrile rabbits received no further treatment and acted as controls. The remaining 3 groups of afebrile rabbits, which received no peptone, were treated in a corresponding manner at the end of the third hour of the experiment, *i.e.* one group received phenazone, the second camphor and the third no further treatment.

There was no appreciable change, over the period of 7 hours of the experiment, in the mean rectal temperature of rabbits receiving no peptone, no camphor and no phenazone. Neither did phenazone nor camphor have any significant effect upon the mean rectal temperature of afebrile rabbits. There were distinct changes in rectal temperature of rabbits injected with peptone and the means of these have been plotted in Fig. 1. The control febrile rabbits developed a mean rectal temperature which varied between 105° F. and 106° F. The injection of phenazone rapidly reduced the febrile temperature to normal. The injection of camphor, however, had little effect upon febrile temperature.

This experiment demonstrated that camphor, in the dose used, was not antipyretic under conditions in which phenazone had a marked antipyretic effect. There was the possibility, however, that camphor might have been antipyretic in smaller or larger doses than that used. To investigate this, a second experiment was performed in which 6 groups of 12 rabbits each were given peptone and then respectively, 0, 1, 10, 50, 100, and 500 mg per kilo body weight of camphor dissolved in oil and injected intramuscularly. In this entire series of animals, camphor had no consistent effect upon the febrile temperature.

Thus far, our experiments proved that camphor was not antipyretic when injected into rabbits with a fever induced by injection of peptone. We next considered the possibility that camphor might be antipyretic in other species of animals. Accordingly, the technique used in the second experiment, just described, was applied to 72 albino rats, 66 guinea pigs and 80 cats, each divided into 6 groups, injected with peptone and the respective doses of camphor. The 500 mg per kilo dose of camphor produced convulsions in cats and was discontinued after 5 trials. In no instance was there any evidence that camphor had any appreciable antipyretic activity.

In these 3 experiments, camphor was not found to be antipyretic in animals with a fever induced by injecting peptone. There was the possibility that it might be antipyretic towards fever induced by pyrogens other than peptone. From time to time, we

had available animals with a natural fever due, usually, to infection and abscess formation at the point where peptone had been injected. This group of animals included 9 rabbits, 6 guinea pigs, 8 albino rats and 6 cats. We made no systematic study of these but injected them with various doses of camphor in oil. In the entire group of 29 animals, 24 or 83% showed no change or increased fever after injecting camphor, in 4 animals the temperature fell toward normal and 1 animal died.

Finally, we considered the possibility that camphor given by stomach tube in the form of Spirit of Camphor, B.P., might be antipyretic. Six groups of 13 rabbits each were injected with peptone and 3 hours later given respectively 0, 0.01, 0.1, 0.5, 1.0, and 5.0 ml of Spirit of Camphor by stomach tube, washed down with water. Again camphor failed to exhibit any antipyretic activity.

These 5 experiments convinced us that camphor has little or no antipyretic activity and that statements to the effect that the internal use of camphor is "supposed" or "considered" to have some antipyretic value should be deleted from textbooks, thus in some measure, even though small, lightening the burden of information which the medical student, physician and pharmacologist have to learn.

Summary. Camphor was administered parenterally and by stomach tube, in a wide range of doses, to some 500 animals, including albino rats, guinea pigs, rabbits and cats with a fever induced by previous injection of peptone and, in a few instances, fever from infection. Under these conditions, phenazone was found to be antipyretic in rabbits, but no evidence was obtained that camphor possessed antipyretic properties, at least to any marked degree.

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Blood Chemical Changes Following Intravenous Administration of a Casein Hydrolysate to Human Subjects.*

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To determine the criteria for the proper administration of Parenamine,‡ one of the commercially available casein hydrolysates which are used parenterally, and as a part of an investigation of its clinical effectiveness, a study was made of some of the blood chemical changes that occurred when this preparation was injected intravenously. The clinical studies have been reported elsewhere.[1]

Forty-five g of Parenamine (equivalent to 6 g of nitrogen) dissolved in 1000 cc of distilled water were injected intravenously into 30 hospital control subjects at a commonly used clinical speed of 300 to 350 cc per hour. The injections were made in the morning, breakfast having been withheld. Blood samples were drawn at the beginning, middle and end of injections and at 1 and 2 hours after the injection was completed. Plasma amino acid nitrogen concentrations were de-

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‡ Kindly furnished by Frederick Stearns and Company, Detroit, Mich. Parenamine is an acid hydrolysate of casein, fortified with 1% d, l-tryptophane. It is put up in 15% solutions in bottles containing 100 cc. The method of preparation of Parenamine is essentially that described by Sahyun.[7] An analysis of the distribution of the amino acids in the preparation has been reported by Block and Bolling.[8]

[1] Kozoll, Donald D., Hoffman, William S., and Meyer, Karl A., *Arch. Surg.*, 1945, **51**, 59.