Determination of Gastric Acidity without Intubation by Use of Cation Exchange Indicator Compounds.* (17859)

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(Introduced by William S. McCann)

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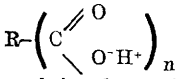
The present study is concerned with the use of cation exchange resins to produce cation exchange resin indicator compounds, which will permit the determination of gastric acidity without subjecting the individual to intubation.

The specific compound employed was prepared from Amberlite IRC-50 or Amberlite XE-96†. This type of synthetic cation exchange resin has the general formula of



When prepared in the sodium salt form, its sodium cations can be displaced by the hydrogen cations of a dilute hydrochloric acid solution or by those present in gastric juice. If a special cation is first combined with the cation exchange resin and this cation is displaceable only or mainly by hydrogen cations, is readily absorbed from the stomach or small intestine, is non-toxic and easily detectable in the blood, the urine, and/or the saliva, a test will be available for determining the presence of hydrochloric acid in gastric juice without subjecting the individual to intubation. If the special cation is displaceable to any extent by the cations of the secretions of the small intestine, the relationship between the time of oral administration of the indicator compound and the appearance of the indicator cation in the blood or urine, etc. must be taken into account. The indicator cation might be a dye, a radioactive material, or any other easily detectable substance.

Methods and results. The indicator compound called *quininium resin indicator compound* (IEC-QH)‡ was prepared as follows: A batch of the cation exchange resin used was conditioned in the acid form. It was then allowed to react with an aqueous solution of quinine hydrochloride so that one g of the resin took up the quinine cations present in 20 mg of quinine hydrochloride.

A. *In vitro* studies. The following technic was used to test the efficacy of the hydrogen cations in dilute hydrochloric acid solutions and in gastric juice, as well as the cations in 0.7% solutions of sodium, potassium, calcium, and magnesium chloride in displacing the quininium cation from the quininium resin indicator compound: To 0.1 g of the IEC-QH in a test tube were added 10 ml of the solution to be tested. The temperature was kept constant at 37.5°C and the mixture was stirred with a slow stream of air. The presence of the quininium cation resulting from the displacement of this cation from the indicator compound was demonstrated approximately by the intensity of the fluorescence observed when the solution was exposed to ultraviolet rays. The quininium cation was displaced from the cation exchange resin indicator compound only when the pH of the dilute hydrochloric acid solution was 2.9 or less. It was displaced by the hydrogen ions of gastric juice below pH 3.01-3.20. Sodium, potassium, and calcium cations displaced the quininium cation only faintly while magnesium cations had more avidity in desorbing the quininium cation.

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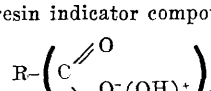
† The authors are grateful to the Rohm & Haas Co. of Philadelphia, Pa., for the generous supply of these Amberlites and other types of resin used in this study.

‡ IEC-QH will be used to designate the quininium cation resin indicator compound:



B. *In vivo* experiments. *In vivo* experiments were performed by administering the IEC-QH orally in 2 g doses with 50 cc of 7% alcohol, as the gastric stimulant, in patients in whom the gastric secretory response to alcohol had been determined previously by the usual intubation technic on a day other than that of the resin indicator test. About one-third of the liberated quininium cations will be excreted in the urine (1). Urine was collected before and one, 2, and 3 hours after the oral administration of the quininium indicator compound. From each sample the quinine was extracted by the ether-sulphuric acid technic described by Kelsey and Geiling(2). The cation indicator compound was administered orally to 63 individuals. In 34 of 38 patients with free gastric hydrochloric acid, quinine, as determined by the fluorescent (qualitative) technic was found in the urine excreted in the first hour after the administration of this compound, as well as in the second and third hours. With this same fluorescent technic none of the 25 achlorhydric patients showed the quinine in the first hour of urine excretion and 20 also failed to excrete it in the second hour.

Table I demonstrates the value of the quantitative photofluorometric technic in those patients in whom the qualitative fluorescent technic revealed quinine in the second and third hour and not in the first hour of urine excretion. Patients with no free gastric hydrochloric acid showed a very low photofluorometric reading in the second hour urine extract. Individuals with free gastric hydrochloric acid in whom the quinine did not appear in the first hour, but only in the second and third hours, revealed a high photofluorometric reading.

The data obtained in the studies *in vivo* show that it is now possible to divide proper subjects into 3 groups of gastric secretory response by examining the urine after the

TABLE I.

Comparison Between Fluorescent and Photofluorometric Methods of Determining Amount of Quinine in Urine of Individuals With and Without Free Gastric Hydrochloric Acid.

Case	Diagnosis	Gastric acidity in M.Eq./L 30 min. after alcohol (Intubation technic)		Intensity of fluorescence Hr of urine collection			Photofluorometric readings* Hr of urine collection			
		Free acid	Total acid	0	1st	2nd	3rd	0	1st	2nd	3rd
S.	Duod. Ulcer	93	101	—	+	++	++	3.0	15.0	42.3	69.4
P.	" "										
	Diabetes mellitus	90	102	—	—	+	++	3.5	3.5	24.6	41.7
W.G.	Cholecystitis	0	8	—	—	—	+	3.6	3.7	3.9	†
H.G.	"Nervous indigestion"	0	12	—	—	tr	+	3.1	3.6	6.0	14.9
O.	"Achlorhydric diarrhea"	0	8	—	—	tr	tr	2.6	3.0	4.1	5.5

* These readings can be converted by appropriate tables to concentration values.
† No urine obtained.

1. Goodman, L., and Gilman, A., The Pharmacological Basis of Therapeutics, The Macmillan Co., 1941, 910.

2. Kelsey, F. E., and Geiling, E. M. K., *J. Pharm. and Exp. Therap.*, 1942, v75, 183.

administration of IEC-QH with the fluorescent qualitative technic described.

(1) The gastric secretion of the group in whom the quininium cations appear in the urine during the first 2 hours after the administration of the indicator compound will have free hydrochloric acid. (2) The gastric secretion of the group in whom the quininium cation does not appear in the urine until the third hour after the administration of the indicator compound will have no free hydrochloric acid. (3) The group in whom the quininium cation is not excreted in the first hour but appears in the second hour will require quantitative photofluorometric examination of the urine extracts to determine the presence or absence of free gastric hydrochloric acid.

The use of this cation exchange indicator compound should find an important place in both clinical diagnosis and in preventive medicine.

Summary. The preparation of a cation exchange indicator compound called quininium resin indicator compound has been described. The rationale and method of its use have been stated.

In vitro tests have demonstrated that the quininium cation present in this compound will be displaced by the hydrogen ions of dilute hydrochloric acid solutions and of the gastric juice.

In vivo experiments have shown that, by administering this cation exchange resin indicator compound orally and noting the time of appearance of the quininium cation in the urine, the presence or absence of free hydrochloric acid in the gastric juice can be determined without subjecting the individual to intubation.

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Transmission and Multiplication of Newcastle Disease Virus (NDV) in Brains of Suckling Mice. (17860)

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Adult mice have generally been found resistant to Newcastle disease. Brandly *et al.* (1) concluded that NDV failed to multiply on intracerebral inoculation of weanling mice. Recently Reagan *et al.*(2) report transmission of Newcastle disease to adult mice, using virus from the 203rd hamster passage. The results of present investigations indicate that 3-day-old mice are almost all susceptible to at least 2 strains of NDV and that this infection is readily transmissible to successively older mice.

Materials and methods. The California strain of NDV (No. 11,914) was obtained from Dr. Erwin Jungherr of Storrs, Conn. Dr. Alfred S. Evans kindly supplied an Australian strain of NDV. Suspensions of these viruses were prepared in amniotic and allantoic (AA) fluids as described elsewhere (3). The Newcastle disease immune hen serum used as a standard was kindly supplied by Dr. Clarence H. Thompson, Jr. of the Bureau of Animal Industry, U. S. Department of Agriculture. Hen erythrocytes were employed in antihemagglutination tests as elsewhere described(3).

Mouse passages. The Australian and California strains were passed in essentially the same manner in separate series of Swiss albino mice. Virus suspensions were diluted in buffered saline (pH 7.6) and inoculated intracerebrally in amounts of 0.03 ml. Infected brain tissue was ground without

1. Brandly, C. A., Moses, H. E., Jungherr, E. L., and Jones, E. E., *Am. J. Vet. Res.*, 1946, v7, 289.

2. Reagan, R. L., Lillie, M. G., and Brueckner, A. L., PROC. SOC. EXP. BIOL. AND MED., 1949, v70, 5.

3. Kilham, L., Jungherr, E., and Luginbuhl, R. E., *J. Immunol.*, 1949, v63, 37.