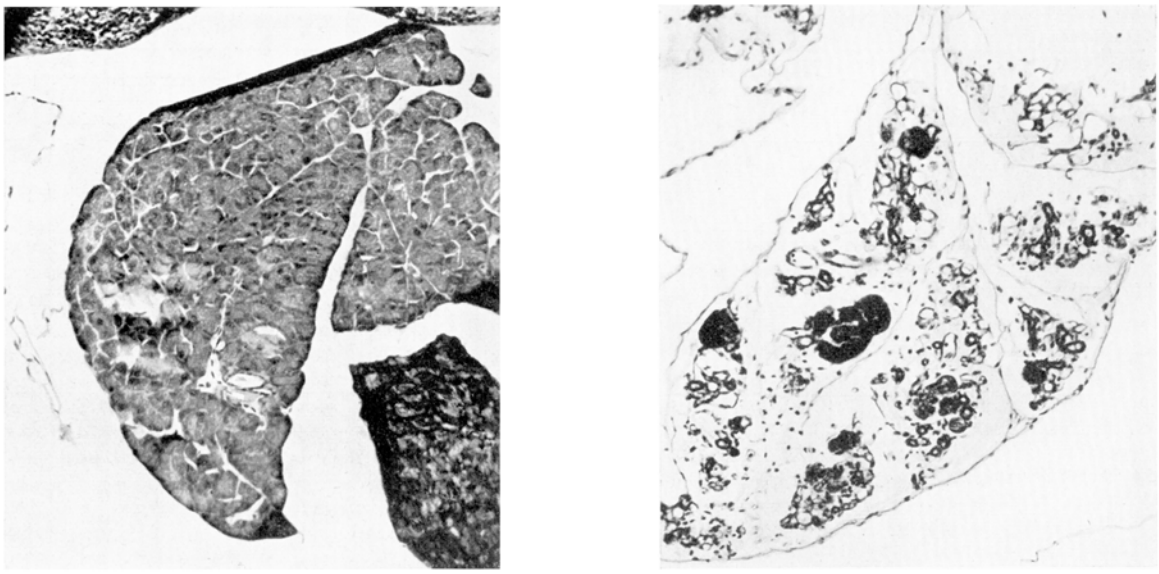

Fig. 2. Pancreatic atrophy. Left: control; right: after 80 days on the basal diet. Paraffin, H. E.

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National Institutes of Health, U. S. Public Health Service, Bethesda (Maryland), May 21, 1957.

Zusammenfassung

Bei der Maus wird durch eine Diät eine tödliche Mangelkrankheit, sogenannte multiple, nekrotische Degeneration, erzeugt. Diese Diät ist arm an Cystin und frei von Faktor 3 und Vitamin E. Nekrosen des Herzmuskels stehen im Vordergrund, ausserdem kommt es zu Degeneration von Leber, Nieren und Muskulatur. Pankreas und Testes zeigen Atrophie bei gestörtem Wachstum. Die Krankheit wird entweder durch den Faktor 3 oder durch Vitamin E verhütet. Der Faktor 3, der vor kurzem als eine organische Selenium-Verbindung identifiziert wurde, ist durch Selenit-Selenium ersetzbar.

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The Effects of Secretin on Urinary Volume and Electrolytes in Normal Subjects and Patients with Chronic Pancreatic Disease

It is well established that intravenous injection of secretin into normal subjects stimulates the release of a large volume of alkaline pancreatic juice containing a high concentration of sodium bicarbonate, whereas in chronic pancreatic disease, this response is altered[1]. The Secretin Test, based on these observations, involves duodenal intubation[2]. In an attempt to avoid the difficulties of intubation, we have investigated changes in *urinary* excretion of sodium and alkali following secretin injection, in normal subjects and patients with chronic pancreatic disease. Patients were included only if the diagnosis was supported by the most critical clinical and biochemical evidence.

The following experiments were performed:

(a) *13 Normal Subjects:* control injection of normal saline, followed within a week by secretin injection.

(b) *19 Normal Subjects:* secretin injection only.

(c) *7 Patients with severe chronic pancreatic disease:* secretin injection.

Most of the normal subjects were medical students.

Procedure: *Day before test:* adequate fluid intake (2–3 l).

Day of test. Subject fasting, *7.30 a.m.* drinks 100 ml water. Continues to drink this volume at half-hourly intervals throughout the test.

8.30 a.m. Subject at rest in a chair.

9.00 a.m. Subject empties bladder. This specimen is discarded. Test begins: Bladder emptied at *9.20 a.m.*, *9.40 a.m.*, *9.50 a.m.* and *10.00 a.m.* and specimens kept separately under toluene.

10.01 a.m. Injection of test material. Bladder emptied at *10.10 a.m.*, *10.20 a.m.* and *10.30 a.m.*

The injection material was *either* Secretin (Lilly) at a dose of 1 clinical unit/kg body weight, in normal saline, at a concentration of 5 units per ml, *or* an equal volume of normal saline. Both injections were intravenous, and given over 2 min.

The principal measurements made on the specimens were:

(1) *Volume.*

(2) *Sodium* – by external standard flame photometry.

(3) *Titratable Acidity and Bicarbonate.* Separate estimation of these factors was avoided by using the method of DAWSON *et al.*[3], which measures, in a single

[1] G. ÅGREN and H. LAGERLÖF, Acta med. scand. *90*, 1 (1936). – D. A. DREILING and H. D. JANOWITZ, Gastroenterology *30*, 382 (1956).

[2] D. A. DREILING, Gastroenterology *24*, 540 (1953).

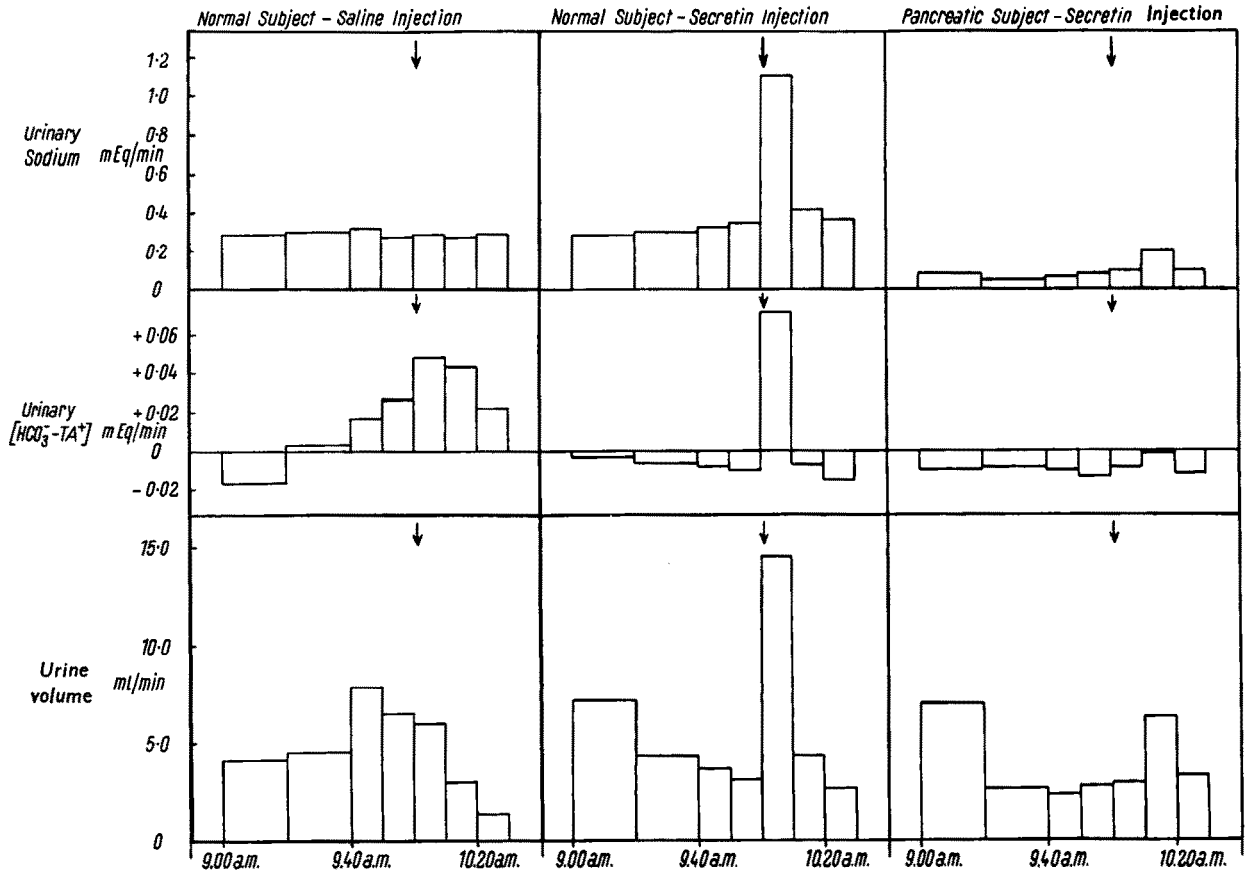
[3] J. DAWSON, E. DEMPSEY, F. BARTTER, A. LEAF, and F. ALBRIGHT, Metabolism *2*, 225 (1953).

Changes in urinary volume, (HCO_3^-–TA^+) and sodium content in the three groups of experiments. Results are expressed as the *difference* between amounts excreted in the 10 min *before* and the 10 min *after* injection. A 'positive' result indicates that the amount excreted in the 10 min following injection was *greater* than the amount excreted in the 10 min before injection.

Subjects	Urine Excretion – 10 min changes					
	Volume ml		(HCO_3^-–TA^+) mEq.		Sodium mEq.	
	Mean ± S.D.	Range	Mean ± S.D.	Range	Mean ± S.D.	Range
Normal Control saline injection .	− 2 ± 31	− 63 to + 43	− 0·03 ± 0·19	− 0·45 to + 0.21	+ 0·13 ± 0.42	− 0·37 to + 0·80
	13 subjects		13 subjects		7 subjects	
Normals Secretin injection . . .	+ 58 ± 35	− 8 to + 113	+ 0·51 ± 0·37	0·00 to + 1.42	+ 3·24 ± 1·98	+ 0·50 to + 6·50
	32 subjects		32 subjects		25 subjects	
Chronic pancreatics Secretin injection . . .	+ 17 ± 40	− 56 to + 60	− 0·07 ± 0·20	− 0·33 to + 0.13	+ 1·24 ± 1·07	− 0·12 to + 2·80
	7 subjects		7 subjects		7 subjects	

operation, titratable acidity minus bicarbonate (TA^+–HCO_3^-). We have used this measurement, as (HCO_3^-–TA^+), to express urinary acid-base balance. Ammonia should, theoretically, be included in this balance, but we found in early experiments that urinary ammonia levels showed very little variation, despite significant changes in (HCO_3^-–TA^+) and sodium. Using this method, a 'positive' result for (HCO_3^-–TA^+) infers an alkaline urine, whereas a 'negative' figure infers acidity. Thus, if, before injection (HCO_3^-–TA^+) = − 0·1 mEq., and after injection = + 0·4 mEq., the injection has caused an increase in *alkali* excretion of 0·5 mEq.

(4) pH. No consistant changes were found in early experiments, and this measurement was, therefore, discontinued.



Histograms of typical rates of urinary volume, sodium and (HCO_3^-–TA^+) excretion in (1) normal subjects given (*a*) saline and (*b*) secretin; and (2) patients with severe pancreatic disease given secretin. Arrows mark the times at which the injections were given.

Results.—The Figure represents the typical response curves of (1) normal subject given saline, (2) normal subject given secretin and (3) patient with pancreatic disease given secretin. The histograms show that the normal response to secretin is an increase in the urinary volume sodium and alkali excretion, the maximal rates of excretion occurring in the first 10 min following injection. There is a rapid return to normal. The patient with pancreatic disease shows a smaller and delayed volume sodium and alkali excretion, which is maximal in the second or third 10 min period following injection.

The Table summarises the results obtained in the 52 experiments performed. These results are recorded as the *differences* between the quantities excreted in the 10 min period immediately *before* the injection, and the 10 min period immediately *following* the injection .

Normal subjects show a statistically significant difference between control and secretin response with regard to volume, alkali and sodium excretion. The mean increase in the 10 min excretion following secretin is 58 ml urine volume, 0·5 mEq. of alkali and 3·2 mEq. of sodium. Patients with pancreatic disease show significantly less response to secretin with regard to urine volume, alkali and sodium.

As a tentative explanation of these results, we suggest that the initial effect of secretin is the release of preformed alkaline pancreatic juice into the duodenum, where both the water and electrolytes are rapidly reabsorbed and then excreted in the urine, giving an 'alkaline tide'.

The validity of this explanation is being further investigated, with special regard to possible actions of secretin on gastric or intestinal secretion or renal tubular function.

The overlap of the ranges of the normal and abnormal response limits the possible application of this test in the diagnosis of pancreatic disease. However, it is likely that if a patient has a maximal normal response severe pancreatic disease can be excluded, whereas a negative response neither proves nor disproves the presence of pancreatic insufficiency. In differentiating between steatorrhea of pancreatic or intestinal origin, this test may, therefore, be helpful, but much further work is required to establish the response in patients with intestinal steatorrhea where the delayed absorption of water and electrolytes may affect the result of the secretin test. In one case of intestinal steatorrhea (non-tropical sprue) investigated so far, a normal response was obtained.

Further work on the physiological basis and possible clinical application of this test is in progress and will be reported at a later date.

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Department of Chemical Pathology, The Royal Free Hospital, London, October 3, 1957.

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Zusammenfassung

Injektion von Sekretin ruft bei normalen Versuchspersonen Diuresis und Vermehrung der Natrium- und Alkali-Ausscheidung hervor. Diese Wirkungen sind vermindert bei Patienten mit chronischer Pankreaserkrankung. Der mögliche Mechanismus und die praktische Bedeutung dieser Beobachtungen werden diskutiert.

Primi rilievi sulla presenza di corpi di Heinz durante la crisi emolitica da favismo

Il problema patogenetico della anemia emolitica da favismo è tuttora dibattuto; la maggior parte dei ricercatori dell'ultimo decennio, pur senza aver ottenuto finora dimostrazioni conclusive, si sforza di trovare argomenti in favore di una patogenesi allergica, ed in particolare autoanticorpale.

La dimostrazione da noi raggiunta della presenza di corpi di Heinz nelle emazie durante la crisi emolitica depone in via analogica contro questo modo di vedere. Infatti questi corpi sono stati finora osservati precipuamente in forme emolitiche di natura tossica (anemia da fenilidrazina e derivati, da sulfamidici, da primaquine ecc.).

Noi li abbiamo trovati in 14 su 17 fabici esaminati in fase emoglobinurica, in una percentuale di emazie variante dal 70% al 20% nelle prime 36 h dalla ingestione delle fave, e dal 25% al 0% nella giornata successiva. In 5 casi che al momento del ricovero non presentavano emoglobinuria, o perchè lievi, o perchè già alla fine della crisi, essi erano assenti. In alcuni casi, seguiti nel tempo, si è osservata la progressiva diminuzione e scomparsa dei corpi entro le 48–72 h. In un caso in cui si è potuto seguire il decorso spontaneo della malattia procrastinando la trasfusione di quasi 24 h, si è notato che la diminuzione in valore assoluto delle emazie con corpi di Heinz corrispondeva con sufficiente approssimazione alla quantità totale delle emazie distrutte. Ciò fa pensare che l'azione eritrolesiva delle fave avvenga in un solo tempo e sia quantitativamente determinata fin dall'inizio.

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Clinica Pediatrica dell'Università di Sassari, il 7 agosto 1957.

Zusammenfassung

Die Verfasser haben Spontaninnenkörper bei 14 von 17 daraufhin untersuchten, an Fabismus leidenden Kindern während des Anfalles gefunden, und zwar innerhalb der ersten 36 h *post ingestionem* der Bohnen in 70–20% der roten Blutkörperchen, am folgenden Tag nur in 25–0%. In einem Fall konnten sie den (durch Bluttransfusion) nicht beeinflussten Verlauf der Krankheit verfolgen und feststellen, dass die Anämie mit dem Schwinden der Innenkörper enthaltenden Blutkörperchen parallel geht. Sie sind daher der Auffassung, dass die blutschädigende Wirkung der Bohnen unmittelbar auftritt und von Anfang an quantitativ festliegt.

Zum Fabismus als Erbleiden

Der Fabismus ist geographisch streng umschrieben, wird aber trotzdem heute noch eher als eine allergische Erkrankung angesehen.