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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D. N. BARON, FREDA NEWMAN*, and ANN WARRICK*

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.

F. PANIZON e G. PUJATTI

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.

Vom Material der Universitätskinderklinik Sassari ausgehend, habe ich 100 Familien anamnestisch auf Fabismus untersucht und dabei folgende Tatsachen festgestellt:

1. Das starke Überwiegen des männlichen Geschlechtes, das man am klinischen Material antrifft, ist nur an die grössere Schwere der Erkrankung bei den Knaben gebunden.

2. Die grösste Zahl der Fälle manifestiert sich binnen der ersten fünf Lebensjahre.

3. Bei 77% der Fälle sind beide Eltern normal, bei 21% eines und bei 2% beide gegen die Bohnen überempfindlich.

4. Die gefundenen Frequenzen der befallenen Kinder stimmen gut mit den nach BERNSTEIN berechneten überein, und zwar sind von den Kindern gesunder Eltern ¼, von denen eines kranken ½ und von denen beider kranken Eltern alle befallen.

Daraus möchte ich schliessen, dass der Fabismus als ein rezessives Erbleiden anzusehen ist, mit hoher Penetranz und beim männlichen Geschlecht stärkerer Expressivität. Der gefundene Erbgang entspricht nicht dem für die Allergie von anderer Seite vorgeschlagenen.

E. SARTORI

Kinderklinik der Universität Sassari (Italien), 10. August 1957.

Summary

Analysis of 100 families with at last one affected offspring seems conclusive for the assumption that favism is an inherited condition and that the responsible gene is a recessive one. The penetrance of the gene seems to be high and the expression stronger in males.

Antimalarials in Rheumatoid Arthritis

During the last few years a number of authors have described the use of antimalarials in the treatment of rheumatic disorders[1].

[1] Lancet *1957*/I, 414. – J. ESCARPENTIER-ORIOL, A. CARRERAS-BAYÉS, and M. SARIOLS-GOMEZ, Medizinische *1955*, 1083. – J. FORESTIER and A. CERTONCINY, Rev. Rhum. *21*, 395 (1954). – A. FREEDMAN, Ann. Rheum. Dis. *15*, 251 (1956). – A. FREEDMAN and F. BACH, Lancet *1952*/II, 321. – CH. GRUPPER, Bull. Soc. franç. Derm. *5*, 423 (1954). – G. G. HAYDU, Amer. J. med. Sci. *225*, 71 (1953). – W. HULL and L. PARR, VIIIe Congrès International du Rhumatisme, Genève 1953. – J. LACAPÈRE, H. MONIER, and G. VIAL, Rev. Rhum. *21*, 389 (1954). – X. VILANOVA, Klin. Wschr. *32*, 905 (1954).

Recent pharmacological investigations on animals throw some light upon these clinical results. We described previously[2] experiments in which mepacrine, proguanil and primaquine were examined in regard to their action on the formaline-arthritis of rats; the results obtained indicated that these antimalarials possess an intensive unspecific antiinflammatory action. We believe that this quality is in question when rheumatic disorders, lupus erythematosus, etc., are treated with antimalarials. Our earlier animal experiments were carried out under anesthesia (100 mg/kg subcutaneously of Numal 'Roche'). We have now investigated the effects of mepacrine and chloroquine on unanesthetized animals. For each substance 10 or 20 animals were used. Mepacrine or chloroquine were given by mouth, and, exactly 30 min later, inflammation was induced by the subcutaneous injection of 0·1 ml of 3% formalin into a hind paw. Exactly 135 min after the injection, the animals were killed; the paw and its uninflamed fellow were immediately amputated and their volumes determined. The difference of these volumes gave the volume of swelling caused by the irritant. The anti-inflammatory efficacy of the antimalarials tested was estimated by comparison of the volume of swelling in these animals with that similarly produced in control animals which had not received any anti-inflammatory treatment.

The results are summarized in the Table. They indicate, that the unspecific inhibition of inflammation by antimalarials as well in unanesthetized as in anesthetized animals corresponds to the anti-inflammatory intensity of cortisone under the same conditions.

R. DOMENJOZ and W. THEOBALD

Pharmacological Laboratories, J. R. Geigy, Basle, September 16, 1957.

Zusammenfassung

Mit Malariamitteln konnte am Formalinödem der Ratte in einer Dosis von 50 mg/kg *per os* sowohl bei narkotisierten als auch bei nichtnarkotisierten Tieren eine unspezifische entzündungshemmende Komponente nachgewiesen werden. Die Intensität der inhibitorischen Wirkung entsprach dabei der Entzündungshemmung von 2 × 50 mg/kg Cortison. Unserer Ansicht nach dürfte dieser unspezifische antiphlogistische Effekt bei der Behandlung rheumatischer Affektionen, des Lupus erythematodes usw. mit Malariamitteln zur Geltung kommen.

[2] R. DOMENJOZ, Sem. Hôp. Paris *31*, 2703 (1955). – W. THEOBALD and R. DOMENJOZ, Dtsch. med. J. *6*, 53 (1955).

'Formaline oedema' of rats

Substances	Under anesthesia				Without anesthesia		
	Cortisone	Mepacrine	Chlorguanid	Primaquine	Cortisone	Mepacrine	Chloroquine
Doses in mg/kg orally		50	50	50		50	50
Subcutaneously	2 × 50				2 × 50		
Number of animals	20	20	20	20	20	10	20
Volume of swelling in mm^3	124	115	116	123	191	216	211
$\sigma \pm$	78·28	48·69	47·88	55·40	81·68	68·95	61·94
$\varepsilon \pm$	17·50	10·89	10·71	12·38	18·26	21·81	13·85
Significant Difference	6·32	8·44	8·44	7·60	3·85	6·1	4·63
Inhibition in % in comparison to untreated controls	54	57	57	54	33	38	37