Discussion

Oral hydrocortisone is rapidly and almost completely absorbed. Urinary 17-hydroxycorticosteroid excretion in adrenalectomized patients receiving oral cortisone acetate amounts to about 36% of the dose in mg. (Moxham and Nabarro, 1956). Results with patients given hydrocortisone are comparable. From these figures it is possible to assess the approximate absorption of steroid administered per rectum. If, however, treatment is given to patients with intact adrenals there may be no increase in urinary steroid excretion because of suppression of endogenous steroid secretion. The short periods of treatment used in Cases 3, 4, and 5 minimize this difficulty, and the increase of urinary total 17-hydroxycorticosteroid output over the control figure may be taken as approximately one-third of the steroid absorbed. There was no evidence of absorption of hydrocortisone when given as a suspension of the acetate. Up to 30% of the free alcohol was absorbed from a suspension or suppositories. Hydrocortisone absorption from the skin lotion was considerable in Cases 2 and 3 (83% and 66% respectively), but much less in the other three (16%, 30%, and up to 36% in Cases 4, 5, and 1 respectively).

The fact that significant absorption of the steroid can occur raises a number of problems. It is important to ascertain whether the hydrocortisone is absorbed in a physiologically active state or whether it is reduced to inactive metabolites prior to absorption; in the latter case a high urinary steroid figure might still be obtained. Case 3 showed marked sodium retention and potassium diuresis with the free alcohol suspension, solution, and suppositories, and corresponding changes on stopping them. Similar alterations of electrolyte excretion were noted when Case 4 was given solution and suppositories and when Case 5 was given the free alcohol solution. There seems, therefore, to be little doubt that hydrocortisone is physiologically active when absorbed from the rectum. The greatly increased 17-ketosteroid excretion in Case 5 may be the result of bacterial modification of the hydrocortisone in the colon.

The hydrocortisone that is absorbed may produce undesirable side-effects. An important possibility is adrenal cortical suppression with

FIG. 4.—Case 1, urinary steroid excretion at the end of treatment; prior to this, 200 mg. rectal hydrocortisone had been given daily for 14 days.

absorbed in a physiologically active state, and it also means that there are potential dangers in prolonged pre-operative preparation with rectal steroid therapy.

Summary

The absorption of hydrocortisone administered by retention enema in ulcerative colitis has been studied in five cases.

There was no evidence that hydrocortisone was absorbed from a suspension of the acetate. Absorption occurred when hydrocortisone (free alcohol) was given

as a suspension or in suppositories, and to a slight extent with an aqueous solution of hydrocortisone hemisuccinate. Significant absorption was found when hydrocortisone skin lotion was used; in one patient it was estimated as 80%. One of the patients had a considerable increase of urinary 17-ketosteroid excretion while receiving rectal hydrocortisone.

Rectal steroid therapy may suppress the patient's adrenal glands and, if used pre-operatively, result in acute adrenal insufficiency in the immediate post-operative period.

We are indebted to Dr. A. E. Gremaux, of Roussel Laboratories Ltd., for the preparation of hydrocortisone acetate and alcohol suspensions given to Cases 3 and 4, and for information about the solvent used for the hydrocortisone alcohol solution. We are grateful to Glaxo Laboratories Ltd. for supplying the hydrocortisone hemisuccinate, and to Mr. G. Bryan, chief pharmacist to the Middlesex Hospital, for preparing the suppositories. We wish to thank the Clinical Research Committee for laboratory facilities in the Institute of Clinical Research of the Middlesex Hospital Medical School, and for a personal research grant to one of us (J.D.N.N.). The figures were prepared by Mr. V. K. Asta.

REFERENCES

- Appleby, J. I., Gibson, G., Norymberski, J. K., and Stubbs, R. D. (1955). *Biochem. J.*, **60**, 453.
 Liddle, G. W. (1956). *J. clin. Endocr.*, **16**, 557.
 Moxham, A., and Nabarro, J. D. N. (1956). *J. clin. Path.*, **9**, 351.
 Park, D. (1955). *British Medical Journal*, **2**, 1386.
 Truelove, S. C. (1956). *Ibid.*, **2**, 1267.
 — and Witts, L. J. (1955). *Ibid.*, **2**, 1041.

FINGERPRINT SWEAT TEST IN FIBROCYSTIC DISEASE OF PANCREAS

PRELIMINARY COMMUNICATION

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The diagnosis of fibrocystic disease of the pancreas is rapidly becoming more frequent as a result of the more general appreciation of the clinical picture and greater reliability of the laboratory tests confirming it. Recent reports seem to indicate that estimation of the sweat electrolytes is the most reliable of the many tests employed by the laboratory. The performance of this test offers few technical difficulties, but there is concern about its possible dangers, especially when applied to small infants. Many infants do not develop the ability to sweat perceptibly until the age of 6 weeks to 3 months, and, since the test implies wrapping up the infant in a plastic bag and, if necessary, applying external warmth, it can produce a dangerous rise in the body temperature. We have noticed that some small babies, especially where there is severe pulmonary involvement, rapidly become tachypnoeic and pyrexial. Careful supervision is necessary, and, since no untoward effects are produced in the vast majority of cases, this care is too easily relaxed. To our knowledge two infants have died as a result of the test.

Shwachman and Gahm (1956) reported a simple application of the basic principles of the sweat test, incorporating chemicals in an agar base to assess the salt content of the sweat in the fingerprint. They suggest this variation of the test may produce positive results as early as the third week of life. This preliminary communication records our experiences with this ingenious method which entails no risk.

Method and Results

The medium is prepared by adding to 500 ml. of normal agar base 4.2 g. of silver nitrate and 2.4 g. of potassium chromate, both chemicals being thoroughly mixed on addition. Plates are poured, and storage at 4° C. appears to preserve the medium for periods of up to a few weeks. The salt in the sweat produces bleaching of the suspended chromate, and the result can be read, as was suggested by Shwachman and Gahm, as +, ++, or ++++. By testing a known case of fibrocystic disease and a series of normal children, these differentiations are readily learned. A fingerprint from the unwashed hand is taken as a "baseline" and further prints are made 5, 10, 15, and 20 minutes after thoroughly rinsing the hands in warm running water to remove any accumulated salt, care being taken to avoid excessive handling by the fingers during the waiting period. A different finger should be used for each impression. No attempt to control the temperature of the room seems to be necessary: it is sufficient that the room be reasonably warm.

To date, 54 cases of known fibrocystic disease have been tested by this method. All gave a +++ reaction in the unwashed print. After washing, 15 showed a similar reaction in 5 minutes, 45 in 10 minutes, 51 in 15 minutes, while all 54 gave a +++ reaction only after a full 20 minutes. Of the number tested one infant was 4 weeks of age, 6 more were less than 6 months, while 14 others were less than 1 year. The result of the fingerprint test has been confirmed in 46 cases so far tested by finding raised electrolyte levels in the sweat obtained from the full sweat technique; 8 of the 54 remain to be tested. These preliminary results are in complete agreement with the larger series investigated by Shwachman and Gahm and reported in their article. Of their 140 cases, all but two gave a +++ reaction, while in one of the two giving a ++ reaction the full sweat test showed normal sweat electrolytes, the other giving the elevated figures normally found in fibrocystic disease. In a series of nearly 200 "normal" children of the same age group tested as controls no false positives have been encountered.

It is thought, therefore, that this fingerprint method offers a simple and probably very reliable screening test for cases of fibrocystic disease. A negative test, however, in the first few weeks of life does not necessarily exclude the diagnosis. The larger-scale investigations at present being undertaken may show the full sweat test to be unnecessary, and, it is hoped, prove the almost complete specificity of the test. At the least, it seems to obviate the necessity of performing the sweat test in full in small babies.

REFERENCE

Shwachman, H., and Gahm, N. (1956). *New Engl. J. Med.*, 255, 999.

The Scientific Film Association, in collaboration with the London University Institute of Education, has recently issued a catalogue of films on psychology and psychiatry. This catalogue is a revised edition of the S.F.A. catalogue of films on psychology (1953), and includes films made available since that date. The size and duration of each film are given, together with a brief description of its content and the type of audience for which it is thought suitable. The catalogue (price 5s. net) is obtainable from the Scientific Film Association, 164, Shaftesbury Avenue, London, W.C.2.

A LONG-ACTING INHIBITOR OF GASTRIC SECRETION

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This is a preliminary report on (1-methyl-2-pyrrolidyl) methyl benzilate methyl methosulphate (IS 499), a substance having atropine-like properties, which promises to be useful in reducing the gastric secretion of acid in patients with peptic ulcer. Chemical and pharmacological details will be published shortly (Doyle *et al.*, 1957; Acred *et al.*, 1957).

Present Investigation

Twenty-four oral doses of IS 499 varying between 5 and 20 mg. were given to five normal subjects, and the salivary flow was measured from collections with a dental aspirator. Doses of 10 mg. taken by mouth partly inhibited salivary flow after a latent period of two hours, but the maximal effect was not reached until about four hours after taking the drug. The reduction in salivary flow lasted from seven to nine hours. With doses of 15 to 20 mg. the only other effects were tachycardia and slight difficulty in micturition. The unusually long duration of action of IS 499 was an encouraging feature which made it worth while to test the effect of the drug on gastric secretion.

Seven normal subjects were given a total of 98 test meals lasting 30 minutes by a technique which allows the amounts of acid secreted in response to the meal to be calculated. The tests also gave information about the volume of meal remaining in the stomach after 30 minutes (Hunt, 1954). For each subject the response to the meal without any drug was determined several times during the period of the tests. Doses of the drug varying between 1 and 20 mg. were given either at 11 p.m. or at 5 a.m., before the tests were made at 8 a.m., so that two dose-response curves were made for each person. It was found that doses of 1 or 2 mg. given at 5 a.m. or 2.5 mg. at 11 p.m. reduced the secretion of acid in response to the test meal. The Table shows the results of tests in the seven normal subjects and in five patients with peptic ulcer. In 8 out of 12 persons the

Percentage Inhibition of Secretion of Acid at 8 a.m. by Doses of IS 499 Given at 11 p.m. or 5 a.m.

Subject	Diagnosis	Percentage Inhibition		No. of Tests	Control Secretion of Acid (ml. 0.16 N HCl)/30 min.
		5 mg. at 5 a.m.	10 mg. at 11 p.m.		
P	Normal	60	50	16	40
H	"	40	10	24	24
W	"	—	50	10	34
L	"	5	30	8	14
M	"	40	10	6	128
Q	"	40	40	20	76
T	"	60	60	14	77
H	Prepyloric ulcer	—60	—30	3	36
C	Duodenal "	20	—10	4	39
		8 mg. at 11 p.m.			
B	Duodenal ulcer	60	60	3	91
R	Gastric "	50	50	3	37
G	Duodenal "	50	30	3	139