generally recognized until they had been in use for several years." In their large series of cases Stokes and Nunn² do not report the effects on carbohydrate metabolism. So far, we have found no mention of unfavourable effects on carbohydrate metabolism in the literature.

In our study³ we noted that one of the patients experienced a diabetogenic effect during treatment with frusemide.

We treated with frusemide (0.08 g./day) for four weeks a 61-year-old female patient who had sclerotic congestive heart failure. The patient was also taking digoxin 0.25 mg./day. She had no family history of diabetes and was not obese, being 155 cm. tall and weighing 45 kg. Before the treatment with frusemide there was a normal oral glucose tolerance test (Fig. 1). After four weeks'

FIG. 1.—Results of glucose tolerance test of the patient on frusemide medication, before medication (continuous line), after 4 weeks' medication (broken line), and 2 months after discontinuation of medication (dotted line). ● = Occurrence of glucosuria.

administration of frusemide we noted a clearly pathological change in the glucose tolerance test and the occurrence of glycosuria. During the glucose tolerance test of 3½ hours there was glucose in the urine continuously; the total glucose excretion was 1.8 g. No hypokalaemia was noted. The value of serum potassium was 4.3 mEq/l. before and 4.4 mEq/l. after the treatment with frusemide.

To be sure about the diabetogenic effect of frusemide we repeated the glucose tolerance test two months after discontinuing the administration of the drug. We now observed that the glucose tolerance test was normal and the glycosuria had disappeared (Fig. 1).

According to the literature, frusemide probably belongs to a different group of diuretics than benzothiadiazine. However, in the article in the *B.M.J.*¹ attention was drawn to a basic similarity of the structures by comparing frusemide and hydrochlorothiazide with each other (Fig. 2). We think that our

HYDROCHLOROTHIAZINE

FRUSEMIDE

Fig. 2.—Hydrochlorothiazine (Frusemide).

primary observation concerning the diabetogenic effect of frusemide indicates that frusemide is an analogue of benzothiadiazines on this basis. However, the diabetogenic effect of frusemide seems to be weaker than that of benzothiadiazines.—We are, etc.,

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Coproporphyrin and Oral Contraceptives

SIR,—Dr. P. Koskela and others (12 March, p. 652) found no increase in total urinary coproporphyrin excretion in patients on oral contraceptives. They regarded an increased proportion of coproporphyrin I in the urine with a normal total urinary coproporphyrin excretion as a sign of relatively mild liver functional impairment. Lead also interferes with urinary coproporphyrin excretion, causing an increased output of coproporphyrin III and total coproporphyrin.

I have recently published¹ a study of the use of a urine coproporphyrin screening test in general practice. This was employed in the antenatal care of maternity patients exposed to an abnormal intake of lead because of the attack of soft-water supplies on lead water pipes. The simple test was described by Donath² and Zelhuys³ and compares the extracted coproporphyrin with a fluorescent colour scale under ultra-violet light. A number of variations of this test have been used in industry.⁴ More complicated methods giving increased sensitivity have been described⁵ but the comment has been made that increasing the complexity of the test destroys much of its value for large-scale screening.⁶

Nesbitt and Snell⁷ gave the following correlations between increased urine coproporphyrin and degrees of hepatic damage: mild, between 100 and 200 µg. coproporphyrin per 24 hours; moderate, between 200 and 300 µg./24 hours; severe, between 300 and 600 µg./24 hours.

The Donath coproporphyrin test has been used for over a year to screen patients in this practice who were taking oral contraceptives in an attempt to detect early evidence of hepatic dysfunction. In one case there was a rise in urinary coproporphyrin excretion to a level on the Donath scale corresponding to the coproporphyrin range 800–1,600 µg./l. This patient, aged 24, had been taking Anovlar for one year, and when this was discontinued her urinary coproporphyrin excretion fell to the 50–100 µg./l. range. She had a previous history of a marked urticarial reaction following a bereavement and had pruritus vulvae while taking Anovlar. There was no history of over-indulgence in alcohol. Urine contained neither glucose nor protein. The liver-function tests which were done showed no abnormality: thymol turbidity 1 unit, zinc sulphate turbidity 1 unit, bilirubin 0.2 mg./100 ml., alkaline phosphatase 3.5 K.A. units/100 ml., transaminases S.G.O.T. 12 i.u./l., S.G.P.T. 11 i.u./l. Haemoglobin 13.4 g./100 ml., E.S.R. 3 mm. in 1 hour

(Westergren). No punctate basophilia present. The highest urinary coproporphyrin result recorded in her previous pregnancy was in the 50–100 µg./l. range.

An increase in the total urinary coproporphyrin excretion does not differentiate between hepatic dysfunction, porphyria, and lead toxicity or any combination of these. A marked abnormality in this, however, developing in a patient taking oral contraceptives, appears to warrant the discontinuing of that drug.—I am, etc.,

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Reaction to Insect-bites

SIR,—We are interested to read the article of Drs. G. Sharan, R. K. Anand, and K. P. Sinha (12 March, p. 656), reminding us of the varieties of vascular reactions in the skin which may follow insect bites—a situation in which a number of potentially sensitizing physiological and pharmacological substances enter the body. We have seen¹ a case of erythema multiforme in a woman aged 51 that had developed following non-infected insect bites, but, unlike Dr. Sharan's case, while under observation she developed an acute nephritis.

We feel that whatever the cause of an abnormal vascular reaction in the skin, whether it be from drugs, infections, or other agents, it may be important to anticipate the possibility of a concurrent vasculitis affecting the kidneys.—We are, etc.,

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SIR,—The interesting report by Dr. G. Sharan and others of a case of Schönlein-Henoch syndrome following an insect-bite (12 March, p. 656) and its alleged rarity prompts me to report a similar case. In this instance there was renal involvement.

An 11-year-old girl was bitten by an unidentified insect on the left leg 2 in. above the internal malleolus on 20 September 1965. There was no history of sore throat or any other infection in the girl or her family.

Three days later the left ankle began to swell, and by the next day the foot and ankle were very swollen, and the mother records seeing a group of tiny red spots on both shins. When I saw her the following day the ankle swelling had practically subsided but she was vomiting repeatedly. The punctum of the bite was sealed by a hard blood clot and there was a narrow collar of surrounding erythema. The area was neither hot nor tender to pressure. She vomited off and on for two nights and a day and then seemed to recover completely.

Eleven days after the bite crops of petechiae appeared on both legs and the next day both