gland products (ovarian, thyroid, pituitary). The following case may be quoted in illustration of these conditions.

A primipara, aged 28, since the birth of a child two years previously, which was nursed for seven months, had never felt well. There was complete amenorrhoea, and she complained of leucorrhoea. She gained nearly 3 st. in weight. The skin was dry, and the hair falling out. On examination she was found to have marked cervical infection; otherwise there was nothing abnormal in the pelvis. The cervix was treated, and half a grain of thyroid extract administered night and morning. Within two months the weight was reduced by 1 st. and menstruation resumed.

A still further cause of loss of health following child-bearing is found in the dregs remaining behind after pregnancy pyelitis and toxæmia. In the production of pyelitis, stasis in the ureter due to the pregnant state is an important predisposing cause, and there is usually a rapid recovery from the symptoms after delivery, but, on occasion, active infection of the urinary tract may remain, causing pain and tenderness in the kidney area and abdomen, frequency of micturition and dysuria, recurring pyrexia, and pyuria. In some cases the condition first reveals itself in the puerperium. It is important in all such cases to make a careful search for areas of focal sepsis, as this factor is known to play an important part in the initiation and perpetuation of infection of the urinary tract. Another lesion of the urinary tract, to which Hunner has recently directed special attention, is *stricture of the lower end of the ureter* with dilatation of its upper section and of the renal pelvis. Whilst predisposed to by child-bearing, it occurs not infrequently in childless women. In some cases it is associated with infection. Its chief symptoms are backache high up in the flanks, pain and tenderness over the corresponding side of the abdomen, and frequency and pain on micturition. The urine may be normal, or may reveal nothing but an occasional red blood cell or leucocyte. The pain, especially at first, may be definitely menstrual in its timing, and if situated, as it commonly is, in the iliac region, it may suggest a gynaecological source. In other cases the occurrence of nausea and sickness may lead to an erroneous diagnosis of appendix, gastro-intestinal, or gall-bladder disease. Such errors may lead to faulty treatment and to futile operations. In other cases the stricture of the ureter is combined with gynaecological or other disease. The condition is revealed by the existence of an obstruction to the passage of a bougie and by a pyelographic examination following the injection of an opaque fluid. The treatment consists in dilatation of the stricture in one or both ureters by means of a bulbous ureteral bougie. At the same time any local pelvic lesion that may be contributing to its production—for example, cervicitis or cellulitis—should be dealt with. According to Hunner a not uncommon causal factor is focal sepsis in the teeth or tonsils, and this, if found, must receive attention.

Pregnancy toxæmia, like pyelitis, is usually recovered from quickly after the birth of the child. In some cases, however, especially in women who have had a recurrent series of toxic pregnancies, the acute kidney lesion may pass over into chronic kidney disease. In such women chronic cardio-vascular lesions, as manifested by persisting hypertension, arterio-sclerosis, and hypertrophy and dilatation of the heart, are commonly present as well. In a recent communication¹ I have shown that in about 50 per cent. of cases pregnancy toxæmia (eclampsia, albuminuria) recurs in succeeding gestations, and that in women with this taint the risk of permanent cardio-renal lesions increases with each succeeding pregnancy. For this reason women who have had two toxic pregnancies should be instructed to avoid further pregnancies, whilst, in the event of conception again occurring, they must become the subject of very strict ante-natal supervision.

I must not take leave of our subject without a reference to the influence of child-bearing on *gall-bladder disease*, which constitutes a fertile source of chronic invalidism in women, especially in the middle and later periods of life. It is well known that gall-stones are two or three times commoner in women than in men, and that the main factor behind this high female incidence is multiparity. In attempting to explain the bearing of pregnancy on this tendency to cholelithiasis we have three possible factors to consider, which may operate singly or in combination.

The first is the high cholesterol content of the blood in pregnancy, and which in the last months is about twice the normal (Moynihan).² The second is the tendency to the occurrence of stasis in the biliary ducts during pregnancy. The third is the frequency with which women who have borne children suffer from focal sepsis in the pelvic, urinary, and other regions. There is reason for the belief that infection of the gall-bladder usually precedes the deposition of stones, and that this infection may reach the gall-bladder from some such distant source. Gall-bladder disease is notorious for the frequent obscurity of its symptomatology. Where it is associated with local pain and tenderness, recurring biliary colic, and jaundice its recognition is easy. Often, however, these cardinal features are absent, and its presence will be missed unless it is brought under suspicion in all cases of parous women, especially those tending to obesity, who suffer from chronic ill health, dyspepsia, and vague abdominal symptoms. It is a common accompaniment of chronic gynaecological disease.

CONCLUSION.

The woman suffering from chronic ill health dating from childbirth is frequently the subject of multiple lesions. Failure to carry out a comprehensive investigation of the various systems may lead to an imperfect diagnosis, resulting in operations and other forms of treatment that bring little relief.

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¹ *British Medical Journal*, January 19th, 1929, p. 91. ² *Ibid.*, February 28th, 1925, p. 393.

THE DIAGNOSTIC VALUE OF THE PLANTAR RESPONSE IN INSULIN COMA.

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RECORDS of the plantar reflexes in insulin hypoglycaemia are rare. Emmons¹ was apparently the first to report an extensor response in a case of insulin coma during the period preceding recovery. Elliott and Walshe,² in comment on Emmons's case, suggested that the state of the plantar reflexes might be of great value in distinguishing between ordinary diabetic coma and that due to hypoglycaemia, but they could not supply the necessary clinical evidence. Pemberton³ then reported a fatal case of insulin coma, in which an extensor response was obtained, persisting up to within a few minutes of death. On the other hand, a flexor response was recorded by Graham⁴ in a case of temporary hemiplegia without coma, the result of insulin overdosage.

In the two cases of insulin hypoglycaemia described in this paper an extensor response was observed while the patients were comatose. As consciousness returned the extensor response faded, the plantar reflexes becoming flexor in one case and inexcitable in the other.

It seems to us that these cases now suffice to provide the evidence required to establish the clinical value of this physical sign as a means of distinguishing between the two states of coma in diabetics.

CASE I.

The patient, a man aged 70, was admitted to the Royal Northern Hospital on November 24th, 1928, suffering from severe diabetes of at least three years' duration. Two years previously he had been taken to an infirmary in insulin coma, but there had been no recurrence of this complication.

On admission his general condition was good, in spite of loss of weight. The urine contained sugar and acetone bodies in considerable amount. He was given a generous diet with 10 units of insulin morning and evening. On November 27th the blood sugar three hours after insulin and breakfast was 0.24 per cent., and accordingly the dose of insulin was increased.

At 11.30 a.m. on December 2nd the patient rose as usual for his bath, but on getting out of bed felt giddy, and fell against his locker. He was put back to bed. At 12.40 p.m. he collapsed, becoming breathless, cold, and clammy. He was able, however, to drink 7 ounces of 5 per cent. glucose, while 10 minims of

adrenaline 1 in 1,000 were given intramuscularly. In spite of these measures he passed, half an hour later (1.10 p.m.), without fits, into a state of complete coma. The pulse was slow and irregular, and the breathing stertorous. No acetone could be detected in the breath. The pupils reacted to light, and were not dilated. The knee-jerks were brisk, and the plantar response of both feet was definitely extensor. A catheter was passed, and the urine found to be free of sugar.

He was given 50 c.cm. of 25 per cent. glucose intravenously. This led to rapid recovery, the patient changing in five minutes from a condition of coma to complete consciousness and intelligence. Examined half an hour later the plantar reflexes were equivocal, the definite extensor response being no longer obtained.

During the night of December 4th the patient had a second attack of insulin coma. As before, this was heralded by shivering and a feeling of coldness. He was easily revived by rectal glucose, followed by a drink of tea with sugar.

Examined on December 14th, the knee-jerks were brisk, ankle-jerks slight, and the plantar response was absent in both feet.

No further attempt to lower the blood sugar to the accepted normal value was deemed advisable at this stage, and the patient was discharged on December 18th with instructions to attend the out-patient department. The dose of insulin was then 15 units morning and evening. This was increased later, and when last examined on February 6th, 1929, he was taking 25 units morning and evening; the blood sugar was 0.16 per cent., and the urine was sugar-free.

CASE II.

The patient, a woman aged 66, was admitted to University College Hospital on February 20th, 1929, suffering from severe diabetes. Emaciation was extreme, her weight being only $4\frac{1}{2}$ st., and the urine contained a large amount of sugar and acetone bodies. The knee-jerks were absent and the plantar reflexes flexor. She was given a diet of 1,000 calories with 20 units of insulin twice daily. With this dosage of insulin the glycosuria persisted, and the blood sugar was 0.23 per cent.; in consequence the dose was increased, together with the diet, until she was taking 100 units a day on a diet of 1,500 calories. The urine then became sugar-free.

Shortly after midnight on March 5th the patient had what appeared to be a hypoglycaemic attack. It lasted twenty-five minutes, during which she was unconscious and restless, throwing her limbs about, and foaming at the mouth. The pupils were inactive to light, and there was incontinence of urine and faeces. The condition was relieved by adrenaline and glucose.

The next day, at 1.45 p.m., the patient was noticed to be flushed, restless, and confused. Glucose was given by the mouth, but in spite of this she became more and more drowsy, and when examined at 3 p.m. was completely comatose, the swallowing reflex, however, remaining. Slight stiffening of both arms was noted, but no convulsions were observed. The left plantar reflex was definitely extensor, the right being doubtful on account of the deformity of hallux valgus.

Blood was taken for the estimation of sugar, which was found to be 0.05 per cent.; meantime the oral administration of glucose was continued, but in increased amount. During the succeeding half-hour consciousness returned, at first gradually, and then with rapid awakening; when examined at 3.45 p.m. she was completely conscious, and the plantar response was flexor in both feet.

A fortnight later, on examination, the knee-jerks were sluggish, ankle-jerks absent, and both plantar reflexes were flexor.

There was no arterial obstruction in the circulation through the feet in this case.

There is thus a certain amount of evidence to show that insulin hypoglycaemia, if severe enough to produce coma, is likely to be accompanied by an extensor plantar response during the stage of unconsciousness. In exhibiting this phenomenon insulin hypoglycaemia resembles a variety of other toxic states associated with coma, including cholaemia, eclampsia, and uraemia. While, however, in the latter two conditions epileptiform fits seem to be essential for the appearance of an extensor response (Elliott and Walshe²), this does not hold in insulin coma, for in Case i no convulsions were observed at any stage.

The character of the plantar reflexes in insulin coma is in striking contrast to that obtaining in ordinary diabetic coma, in which condition, unless there is some other associated organic disease affecting the pyramidal tract, an extensor response apparently never occurs. Allen and his co-workers³ give a detailed description of 17 cases of diabetic coma. They frequently found the tendon-jerks diminished or absent, but noted no other abnormality of the reflexes. Elliott and Walshe² failed to obtain an extensor plantar response in any of the cases observed by them, even after two days of coma, and within an hour of death. In examining the records of 53 cases of diabetic coma of all degrees of severity we have not found an

extensor response noted, except in one instance; this was a patient in whom coma had been precipitated by a cerebral abscess. A flexor response was definitely recorded in 21 of the other cases.

It is suggested, therefore, that the state of the plantar reflexes may prove to be of great assistance in quickly distinguishing ordinary diabetic coma from that due to insulin hypoglycaemia. Mild hypoglycaemic attacks without coma are not accompanied by an extensor response, and it is possible that even deep insulin coma may not show the extensor phenomenon. But inasmuch as diabetic coma, unless complicated by an organic pyramidal tract lesion, does not give an extensor response, it is plain that the occurrence of this physical sign in a comatose diabetic on insulin treatment should be accepted as evidence that the coma is due to excess of insulin, and consequently sugar (intravenous 10 per cent. by preference), together with subcutaneous adrenaline, should at once be given very freely. The state is dangerous when once an extensor response has appeared, and there is little time to be lost. The quick recovery of the patient, upon adequate treatment with sugar, is totally unlike the very slow emergence from diabetic coma.

We wish to express our thanks to Dr. E. G. B. Calvert and Professor T. R. Elliott for permission to publish these cases of insulin coma, and to the physicians of the Royal Northern Hospital, St. Mary's Hospital, and University College Hospital, who have allowed us to use the records of their cases of diabetic coma for comparison.

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GROWTH RECOVERY AFTER INHIBITION BY LEAD.

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In previous papers of this series (Studies in the Biology of Metals) results were reported demonstrating that growth in length of roots is retarded by Pb-ion,¹ and that this is due to inhibition of cell division.² These findings as they stand seem good evidence in favour of the lead treatment of malignant growths,³ particularly in view of the fact that the regions of most active growth by increase in cell number in the chick embryo are similarly affected.⁴ But the whole story is not told until we know what happens when the growing organisms are removed from the Pb environment. With this in mind I have first inhibited growth of roots of yellow corn (*Zea mays*) seedlings for twenty-four hours by Pb¹ and then transferred them to non-Pb-containing culture solutions, and after eighteen hours determined the mitotic index.

Comparing Growth and Mitotic Index of Pb-retarded Roots subsequently allowed to grow in Pb-free Culture Solutions (A) with Roots grown in Pb cultures only (B).

Pb-ion Concentration.	Growth Increment.		Mitotic Index.		
	A.	B.	A.	B.	Individual Counts.
mg.	Per cent.	Per cent.			
25.0	26.5	5.5	3.7	0.5	10 mg. Pb 0.5:0.6:0.3:0.4:0.5: 0.4:0.5:0.6
5.0	64.0		10.0		
5.0	81.3		9.4		
5.0	55.5		13.5		
5.0	64.3		15.2		
2.5	83.0	17.8	12.2	1.7	2.5 mg. Pb 1.6:1.7:1.9:1.6:1.8: 1.4:2.1:1.5

The results (A) given in the accompanying table are compared with those obtained from roots taken directly after growth in the Pb-containing culture solutions (B).