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.

BY

FREDERICK S. HAMMETT.

(The Research Institute of the Lankenau Hospital, Philadelphia.)

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).

The A values, therefore, represent the recovery response from the treatment accorded the B series.

The growth increment values by themselves hardly justify a conclusion, since the time interval was unavoidably longer in the A than in the B series. On the other hand, the differences may be valid, since I have noted, but not recorded, the fact that roots left in Pb-culture solutions for more than a day hardly increase in length over that which obtains at the end of the first twenty-four hours. The marked superiority in mitotic index values, however, indicating as it does a far greater cell proliferation activity, is striking proof that growth recovery after Pb-retardation is possible.

Particular note should be made of the fact that roots subjected to a Pb-ion concentration of 5 mg. per litre showed some seven times as many mitoses per 100 nuclei after transference to Pb-free culture solutions as roots subjected to only half the concentration (2.5 mg.), but not subsequently removed from the Pb environment. In view of this, and since root growth in length is to a great degree dependent upon the rate of cell division in the meristematic region, it is probable that the greater growth increment of the A series does in part at least represent a real renewal of length growth.

The results of these experiments show conclusively that the retardative influence of Pb on growth by increase in cell number is not a permanent affair in roots. This is no proof that a like recovery of cell proliferative activity would occur in animal forms under either normal or pathological conditions with cessation of Pb administration. Yet the biological hint afforded should serve as a warning against too high expectations from the use of Pb, or indeed any other metallic element, in the treatment of malignant growths.

In concluding I might state that the details of technique used in this investigation are to be found in the papers cited. They have not been repeated here, in order to save space.

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PROGRESS IN ANAESTHESIA FROM THE SURGEON'S STANDPOINT.

BY

BASIL HUGHES, D.S.O., M.A., M.B., B.Ch.CAMB.,
B.Sc.LOND., F.R.C.S.,

SURGEON TO BRADFORD MUNICIPAL GENERAL HOSPITAL; HONORARY
SURGEON TO BRADFORD CHILDREN'S HOSPITAL.

SINCE the great war, and no doubt as a result of experiences gained from it, the science of anaesthesia has been advanced in certain clinics in this country and on the Continent. Unfortunately, however, the advance at present is slow, and it may be said that, in so far as many clinics to-day adopt inhalation narcosis for practically all operations, irrespective of their magnitude or the condition of the patient, surgical anaesthesia has not kept pace with the requirements of modern surgery. Shock following a severe operation is generally attributed to the manipulations of the surgeon—perhaps a justifiable charge if rough usage of the tissues has occurred. But even the surgeon who handles the tissues with deliberate, gentle, and dexterous movements has his quota of failures in severe and prolonged operations when inhalation narcosis with ether or chloroform has been employed.

In operations demanding complete muscular relaxation inhalation narcosis may necessitate administration of large doses of the narcotic, with the production of serious toxic effects upon the myocardium, the liver, the suprarenal glands, the central nervous system, and, indeed, the tissues generally. Furthermore, the employment of this type of anaesthesia necessitates pre-operative preparation of the intestinal tract. The patient enters the theatre with an empty gut, and often three or four days pass before he is

able to take solid food. Four or five days' starvation takes its toll even of a healthy individual; how much greater must be the effect upon a patient who has undergone a severe operation! Add to this the pain and exhaustion resulting from post-anaesthetic vomiting, and it may be conceded that neither the surgeon nor the anaesthetist may be responsible for failures which follow prolonged anaesthesia by inhalation narcosis, but that it is the anaesthetic which is at fault.

On February 25th, at the Medical Society of London, Professor A. H. Burgess of Manchester, opening a discussion on acute intestinal obstruction,¹ stated that, excluding cases of strangulated hernia and intussusception, the mortality resulting from operations for the relief of this condition during the period 1920 to 1924 in seven leading hospitals was 37.9 per cent. No mention was made of the anaesthetic used, but I hope I am not wrong in assuming that it was some form or other of inhalation anaesthesia, as in a series of fifty similar cases operated upon by me during the period 1926-28, using spinal and block anaesthesia, the mortality was only 13.6 per cent. In view of the very different results obtained in these two series of cases I propose as briefly as possible to describe the procedure as regards surgical anaesthesia at the Bradford Municipal General Hospital.

Rectal Ether.

For operations on the head, neck, mouth, and thorax, including trephining for cerebral tumours, trigeminal neuralgia, extirpation of goitre (especially toxic goitre), total laryngectomy, and radical excision of the breast, rectal ether, and more recently avertin (tribromethyl-alcohol), are the anaesthetics of choice. After trying several mixtures the following formula for rectal ether has been adopted for some time as giving uniformly good results.

Magnesium sulphate	...	...	...	2 oz.
Glucose	...	...	...	1½ oz.
Olive oil	...	...	...	1 fl. oz.
Acacia	...	...	...	5½ dr.
Ether	...	...	...	4 fl. oz.
Paraldehyde	...	...	...	4 fl. dr.
Morphine sulphate	...	...	...	1/4 grain
Water	...	...	...	to 12½ fl. oz. (approx.)

Rub the acacia with olive oil in a dry mortar, dissolve the magnesium sulphate and glucose in 7 oz. of water, then add 1 fl. oz. of this solution to the acacia and olive oil; gradually add the remainder. Transfer to bottle of 16 oz. capacity and add the morphine sulphate, previously dissolved in water. Dissolve the paraldehyde in ether and add gradually, shaking well. Make up to 12½ fl. oz. (approximately). Secure the cork with string and keep in a cool place.

The anaesthetic solution should be made up the evening before operation, securely corked, and kept in a cool place. It is not safe to use a solution that is thirty-six hours old.

The solution is introduced high up into the bowel by means of a rubber catheter, and the procedure is best carried out in a dark room. The introduction requires twenty minutes for its completion, and during this period there may be, though very rarely, an interval of excitement. The onset of anaesthesia varies; it may follow immediately after the anaesthetic has been completely introduced into the bowel, but more often it occurs from ten to twenty minutes later than this. A smell of paraldehyde is readily, and of ether faintly, detected in the patient's breath. It has been suggested, I think with some reason, that in making up the mixture the ether is converted into ethyl sulphate and absorbed as such. This anaesthetic is ideal for operations on the head and neck, and has the following added advantages:

1. There is no anaesthetist's apparatus to hamper the surgeon.
2. The patient's respiration is quiet and uniform, resembling that of normal sleep.
3. The patient's colour is perfect throughout.
4. There are no toxic after-effects, and vomiting does not occur.
5. Following the operation the patient has a refreshing sleep, lasting three to four hours, after which he is able to take nourishment.
6. According to our experience the anaesthetic is absolutely safe, and has no harmful effects upon the bowel.

As a routine the bowel is washed out when the patient returns to the ward.