ren's mothers when questioned will give a history of acute overnight onset. Dr. Brooke's observation of the rapid drop in temperature of the sleeping malnourished child no doubt provides the explanation for these cases.—We are, etc.,

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The Pill and the Pituitary

SIR,—Your leading article of three months ago (27 November, p. 510) states that "none of the patients had an obvious endocrinological cause . . . of the [post-pill] amenorrhoea, such as pituitary tumour. . . ."

A 30-year-old nullipara with a pre-pill regular menstrual habit of 5/30 was referred because of 21 months' amenorrhoea since discontinuing oral contraception after four years of use. Her general condition was good and she had no other symptoms but milk was freely expressed from her breasts. The vulva and vagina were not atrophic but the uterus was small. X-ray of the pituitary fossa was reported as negative. Two courses of clomiphene were ineffective.

Inquisitive as to whether any anterior pituitary depressant action of the pill was confined to gonadotrophin production, I referred the patient to the Liverpool Endocrine Clinic. Dr. J. C. Davis found no evidence of other deficiency but tomographs indicated a small pituitary tumour. Hypophysectomy was performed by Mr. C. B. Sedzimir at Walton Hospital, Liverpool. Subsequently the patient had an episode of C.S.F. rhinorrhoea and meningitis but made a good recovery after which there was evidence of poor adrenocortical function, hypothyroidism, mild diabetes insipidus, and absent gonadotrophin production. She moved to Hull from where, 18 months after operation, Mr. A. N. Guthkelch's department reported that she was well on cortisone and thyroxine. Her galactorrhoea had gradually disappeared but her amenorrhoea of course persists. Fortunately she is not concerned about fertility.—I am, etc.,

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Enzyme Induction and Folate Deficiency

SIR,—The role of the liver in normal and abnormal folate metabolism has received insufficient attention. As the major anti-convulsant drugs, especially phenytoin and phenobarbitone, are powerful inducers of liver enzymes, and are ingested in high dosage for many years, it seems likely that they will disturb the metabolism of many substances, both exogenous and endogenous. It was for this reason that Dr. A. H. Waters and I suggested to the British Pharmacological Society last year¹ that enzyme induction may be an aetiological factor in anticonvulsant-induced folate deficiency. We presented evidence on the acute effect of phenytoin on serum folate concentration, showing that a progressive fall occurred in normal subjects taking 1,600 mg of the drug orally over four days. Six days after the subjects stopped taking the drug the serum folate concentration had returned almost to normal. We considered that the time course of this effect could be explained by a drug-induced change in liver enzyme activity,

although it by no means ruled out other effects, such as impaired absorption of dietary folate. Dr. J. D. Maxwell and others (29 January, p. 297) have now shown an inverse correlation between serum folate concentration and urinary D-glucuric acid excretion. As pointed out previously² in relationship to vitamin D metabolism a correlation between measures of two drug-induced abnormalities is to be expected, for both will show a dose relationship with the drug in question. There remains the possibility that folic acid deficiency is produced by some other dose-related effect than enzyme induction. So, although the observation provides supporting evidence, too great an emphasis should not be placed upon it, especially as the position which urinary D-glucuric acid holds as a measure of liver enzyme induction still requires evaluation.³ However, as Dr. Maxwell and others discuss, evidence is accumulating that altered liver enzyme activity is important in the production of osteomalacia in epileptic patients,² and, in addition, it can lead to an increase in the turnover of cortisol, oestrogens, and androgens,⁴ and explains a number of anti-convulsant drug interactions.⁵

In view of the disappointing results of many studies on the aetiology of anti-convulsant-induced folate deficiency liver enzyme induction should be looked upon as the most promising current hypothesis to explain the abnormality, but a great deal more work will be required before the question is resolved.—I am, etc.,

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¹ Richens, A., and Waters, A. H., *British Journal of Pharmacology*, 1971, 41, 414P.

² Richens, A., and Rowe, D. J. F., *British Medical Journal*, 1971, 4, 684.

³ Aarts, E. M., *Lancet*, 1971, 1, 859.

⁴ Kuntzman, R., *Annual Review of Pharmacology*, 1969, 9, 21.

⁵ Hansen, J. M., Sjersboek-Nielsen, K., and Skovsted, L., *Clinical Pharmacology and Therapeutics*, 1971, 12, 539.

Haemophilus Epiglottitis

SIR,—The recent paper about "Haemophilus Epiglottitis" by Dr. M. G. Addy and others (1 January, p. 40) and subsequent letters prompt us briefly to record our experience in the last two months.

Though aware of the condition as a serious clinical entity for many years we do not remember sudden deaths from croup during the last nine years at this hospital, and can recall requiring a tracheostomy to be performed on only three children with "croup" during that time. This winter croup has shown a different pattern, and four children with haemophilus epiglottitis have been admitted to our hospitals.

Only the last patient (aged 5) was correctly diagnosed on arrival. He was in asystole and visualization of the epiglottis was necessary immediately for intubation. Though successfully resuscitated (after an estimated 15 minutes' cardiac arrest) the patient died a few hours later. The first two patients admitted by different doctors were diagnosed as laryngitis but were given hydrocortisone with ampicillin by injection. Both were considered not to have sufficient respiratory obstruction to require interference but were treated with moist atmosphere and sedation. Both deteriorated

suddenly after two hours. The first, aged 13 months, developed respiratory arrest and coma. Intubation proved impossible because of the size of the epiglottis but oxygenation was well maintained by Ambubag until tracheostomy. He recovered, but the attendant who attempted intubation as an emergency procedure, without donning a mask, developed haemophilus pneumonia (which did not respond to ampicillin, though the organism was sensitive to this). The second patient, aged four, became unconscious and had cardiac arrest as he was moved from his pillows to prepare for tracheostomy. He did not respond to resuscitation. Intubation through the cords was easily possible post mortem, suggesting that death was from toxemia rather than anoxia.

Since this tragic death all cases of croup are designated epiglottitis until proved otherwise. They all receive chloramphenicol and hydrocortisone on admission and the consultant is informed. The tracheostomy trolley is laid up beside the cot and all requisites for resuscitation are arranged on a second trolley. No attempt is made to do immediate laryngoscopy.

Despite this, the diagnosis on the third patient, aged 20 months, was not recognized at once, and he showed gradual improvement over the first six or seven hours and then suddenly, without further provocation, developed cardiac arrest. An endotracheal tube was passed and resuscitation was successful but voluntary respiration was associated with intercostal and subcostal recession in part due to airway obstruction and in part to pneumonia.

In view of the temporary nature of the swelling of the epiglottis a decision was made to leave the tube in situ and not to perform a tracheostomy. However, a further cardiac arrest ensued, and on the way to theatre for tracheostomy the heart stopped again. Tracheostomy was complicated by bilateral pneumothorax, which responded quickly to treatment. The tube could be removed after five days, but the child became febrile and ill again, convulsed, and stopped breathing 12 hours after its removal. The tube was reinserted for the purpose of artificial ventilation over the next 36 hours, after which the fever subsided and a rubella rash developed. There was severe hypotonia and atethosis but no detectable intellectual impairment. Gradual recovery is occurring.

These cases obviously underline the fulminating nature of this condition and the difficulty in diagnosis when the doctor has had no previous experience of it. They also demonstrate a hazard not mentioned in the other communications—that of cross infection to the attendant medical and nursing staff—and suggest endotracheal intubation as a method of maintaining the airway is undesirable if it does not completely relieve the obstruction in a patient likely to develop cardiac arrest. In our opinion a tracheostomy is easier to manage and causes less irritation to the patient. The scars are minimal and a small price to pay for survival.—We are, etc.,

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Lead Poisoning Scandal

SIR,—In the *Sunday Times* (30 January) and also on television (28 January, Dr. R. Murray) it was stated that the Factory Inspectorate doctor involved was also the company doctor. The integrity of the doctor