strains of *Bordetella pertussis*.[2] One of the liquid-medium vaccines (coded V15) was made at the Lister Institute; the other liquid-medium vaccine was coded V14 and the solid-medium vaccine V12. In this field trial the Lister vaccine, V15, performed consistently better than V14, V12 being intermediate in efficacy. In laboratory tests V15 was significantly more potent than both V14 and V12. But having made this point I should not think of using it to suggest that any one method of manufacture is "better" than any other; another trial with different batches of vaccine would possibly give somewhat different results.

(4) Telephone calls to these laboratories following the appearance of Dr Griffith's paper and your leading article indicate that the impression has been created among some that pertussis vaccines other than Wellcome's may be less potent or more toxic. Practitioners should be aware that all such vaccines made in Britain have to meet identical statutory specifications and that no batch of vaccine containing an adsorbed pertussis component may be distributed until a sample has been submitted to the National Institute of Biological Standards and Control for examination before release.

(5) On the question of toxicity, the Wellcome method of growing vaccine on medium containing charcoal may indeed absorb out "bacterial toxins" (p 811); but the association of these putative toxins with adverse reactions in children is, as I am sure Dr Griffith would agree, a very moot point. In this connection—and in any consideration of reactions to pertussis vaccine—it is important to be clear as to what is meant by "toxicity." *B pertussis* can induce a remarkable range of responses in small animals; some of them appear to be associated with specific components of the organism, but none has as yet been unequivocally linked with reactions in children, which fall into two main groups: first, the sort of local inflammatory response, with or without transient fever and malaise, that can be caused by any bacterial vaccine, including the diphtheria and tetanus toxoids contained in the triple preparation; and second, the more serious reactions such as collapse, persistent screaming, convulsions, and encephalopathy. There is evidence[3] that toxicity tests in animals are of some use in predicting the liability of a given batch of vaccine to induce reactions in the first category; but—for the moment begging the question of a cause-and-effect relationship between pertussis vaccine and central nervous system (CNS) reactions—there is at present simply no evidence that the reactions in the second category are determined by the strains of *B pertussis* used, method of manufacture, or performance in any laboratory test. The comparative rarity of these serious reactions bedevils any attempt to relate them to such variables in pertussis vaccine—if indeed such a relationship exists; in addition to the possibility, referred to by Dr Griffith, that some reactions may be purely coincidental, susceptibility to convulsions or other CNS complications could be determined by factors pertaining to a particular child rather than to a particular vaccine. Again, such reactions might not be specific to pertussis; were it customary to inject large numbers of infants with vaccines made from other Gram-negative organisms such as cholera or typhoid, might not similar accidents occur from time to time?[4]

I share Dr Griffith's concern about the difficulty of obtaining reports of untoward reactions and about the poor quality of some of the information that is received. In view of the low incidence of major adverse reactions to pertussis vaccine every case is potentially valuable as a source of information and should be adequately recorded by a central agency; and means should be found of making such records available to manufacturers. For their part, manufacturers should obtain and record as much information as is practicable about the vaccines they distribute. It is the collation of the data from the field with those from the laboratory that provides the major challenge; this is an outstanding example of a problem in which the ability to pose the right questions at the outset will determine the validity of the answers.

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[1] Public Health Laboratory Service Whooping Cough Committee and Working Party, *British Medical Journal*, 1973, **1**, 259.
[2] Report of the MRC Whooping-Cough Committee, *British Medical Journal*, 1959, **1**, 994.
[3] Perkins, F T, *et al*, *Symposia Series in Immunobiological Standardization*, 1970, **13**, 141.
[4] Cameron, J, *Advances in Applied Microbiology*, 1976, **20**, 57.

"Human Growth and its Disorders"

SIR,—May I draw your readers' attention to an unfortunate error in my book "Human Growth and its Disorders" published by Academic Press? On p 166 the text states that testosterone oenanthate should be given intravenously. It should, of course, be given intramuscularly. Intravenous injection would be highly dangerous.

Sales of the book have been discontinued pending the insertion of errata and every effort is being made to contact those who have already purchased copies. I should be grateful if any readers who possess copies of the book but have not received correction slips would contact me.

My thanks are due to Dr A Stuart Mason for mentioning this error in your review columns (1 April, p 845).

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Beta-blockers and plasma triglycerides

SIR,—We have been conducting a trial comparing the effects of propranolol (160-240 mg), pindolol (15-30 mg), and atenolol (100 mg) given as a single daily dose for the control of hypertension. A randomised block design was used so that each patient received all of the treatments. We observed small but significant increases in fasting plasma triglyceride levels after four weeks of treatment with these drugs when compared with the placebo phases. These rises were not accompanied by changes in plasma cholesterol or blood glucose levels. Although the rise was greatest with atenolol, the changes were significant with all three drugs (see table). Subsequently we examined the effects of metoprolol in the same group of 17 patients. After a further period on placebo patients were given metoprolol 100 mg daily. Again a small but significant rise in fasting plasma triglyceride levels was observed.

While food and alcohol intake may well account for major fluctuations in triglyceride levels, the evidence from plasma glucose and insulin determinations, particularly in the latter experiment, indicates that all of the subjects were fasting at the time of blood sampling. From direct questioning and our knowledge of the patients only three are regular heavy alcohol users and the fluctuations in their plasma triglyceride levels observed during these studies did not correlate with periods of heavy alcohol intake.

Previous authors[1 3] have reported varying changes in plasma triglyceride levels in patients taking β-adrenoceptor antagonists. Most have reported the effect of a single drug and have not compared the effects of different drugs within a group of patients.

In view of the associations between hypertension, coronary artery disease, and blood lipids these findings may have important implications. If plasma triglyceride levels remain elevated during long-term treatment of hypertension with β-adrenoceptor antagonists, do the benefits outweigh the risks?

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[1] Barboriak, J P, and Friedberg, H D, *Atherosclerosis*, 1973, **17**, 31.
[2] Nilsson, A, Hansson, B-G, and Hökfelt, D, *British Medical Journal*, 1977, **2**, 126.
[3] Waal-Manning, H J, *Drugs*, 1976, **11**, suppl 1, p 121.

Price of survival in childhood leukaemia

SIR,—Your leading article (11 February, p 321) emphasises the need for long-term surveillance of children who have completed two or three years of intensive therapy for lymphoblastic leukaemia. This is already standard practice in children who appear to have been cured of solid tumours and there is now substantial evidence for clinically significant growth hormone deficiency in children who have received high-dose (5000-6000 R) irradiation for the treatment of intracranial tumours.[1] These children, however, have often had the associated problems of raised intracranial pressure and neurosurgical intervention.

The effects of leukaemia therapy on growth and the endocrine system is not so clear-cut and the results you quote from the Manchester group of Shalet *et al* have not as yet been substantiated by other centres. Shalet *et al*[2] have described a blunted growth hormone response to hypoglycaemia rather than growth hormone deficiency except in one girl who received more than the now conventional doses of radiation. The quoted cortisol responses[3] (not corticotrophin (ACTH) as suggested in your article) to hypoglycaemia are all within the normal limits and the

Mean fasting plasma triglyceride, plasma cholesterol, and blood glucose concentrations (± SEM) and fasting insulin levels in 17 patients during treatment with placebo and beta-blockers

	Placebo	Atenolol	Pindolol	Propranolol	Metoprolol
Triglycerides (mmol/l)	1·35 ± 0·11	2·19 ± 0·44*	1·73 ± 0·19*	1·85 ± 0·28*	1·79 ± 0·22*
Cholesterol (mmol/l)	5·5 ± 0·21	5·6 ± 0·33	5·8 ± 0·28	5·7 ± 0·27	5·6 ± 0·22
Glucose (mmol/l)	4·3 ± 0·21	4·1 ± 0·16	4·0 ± 0·11	4·1 ± 0·15	4·1 ± 0·15
Insulin (mU/l)	12·2	12·5	11·8	12·5	13·3

P<0·05 by paired *t* test
Conversion: SI to traditional units—Triglycerides: 1 mmol/l ≈ 88mg/100 ml. Cholesterol: 1 mmol/l ≈ 39 mg/100 ml. Glucose: 1 mmol/l ≈ 18 mg/100 ml.