with regard to blueness of the sclerae, many doctors seem to be looking for a deep Oxford blue and fail to notice the duck egg blue shimmer in an affected child.

I agree with Dr Taitz that osteogenesis imperfecta is not common and that it is not a frequent cause of infantile fractures. However, whenever there exists the possibility of osteogenesis imperfecta parents should be able to have their child examined by someone with experience of the condition, so that they do not become victims of the probability trap.

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SIR,—Dr L S Taitz (31 October, p 1082) has attempted to use statistical data to show that the differential diagnosis between non-accidental injury and osteogenesis imperfecta is not a realistic problem when explaining the presence of multiple unexplained fractures in infants.

He seems to concede that there might be one case in each large city every 100 to 300 years or so that might be wrongly diagnosed. (This would be one every 10 to 30 years nationally.)

I am at a loss to understand on what basis such children were ever diagnosed as having osteogenesis imperfecta (type IV or any other type), when there was no clinical, radiological, familial, or progressive history. How are these children differentiated from other children who present with a radiological diagnosis of multiple unexplained fractures? Often it is only the radiological evidence of fractures and absence of reasonable explanation alone that leads to the accusation and conviction of parents of child abuse.

Of course, it is possible that there are no such cases of occult osteogenesis imperfecta and the statistical 0.6 of 5% are really missed cases of child abuse. On the other hand, some of the 15 cases of fractures caused by child abuse a year in an average city might indeed be occult bone disease (osteogenesis imperfecta or any other type). Even if just 1% of these "non-accidental injuries" are genuine bone disease that would make 15 cases a year nationally in which parents are wrongly convicted of cruelty—15 cases a year where families are broken up and parents imprisoned unjustly. I am afraid that I have not that much faith in our present knowledge of bone disease or indeed that criminal courts are the best auditoriums for complex medical discussion.

Of course we must prosecute vigorously the abusers, but the article by Dr Taitz suggests that we are desperately short of data and research and we are still in the very early days of our knowledge on such matters. My 1% estimate of wrongly convicted parents seems to me to be based on just as strong (or weak) evidence as that presented in the leading article.

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AUTHOR'S REPLY.—My leading article was not primarily concerned with the presentation of evidence to criminal courts but for wardship hearings or care proceedings. In these settings it is the principle of "balance of probability" that prevails rather than that of "reasonable doubt." This is rightly so because less stringent criteria for the consideration of evidence should prevail where the protection of children is concerned.

Dr Acland suggests that about 1% of children diagnosed as having non-accidental fractures could have some form of bone disease. This seems a

reasonable margin and I wonder how many other pieces of forensic evidence are as accurate as this? In fact I doubt whether as many as 1% of cases do have undiagnosed bone diseases, which are very rare even as a group. None of the children I have seen over 15 years have subsequently been found to have such disorders.

I think too that Dr Acland is underestimating the reliability of diagnostic procedures for osteogenesis imperfecta. The great majority of cases are either type I or II and by general consent should produce no difficulty in diagnosis. The problem is that of type IV, particularly so called type IVA, and I agree with Dr Acland that many of these cases may in fact be children with non-accidental injuries who have been misdiagnosed. I do not in fact believe as strongly as Dr Acland does that we should "prosecute vigorously the abusers." I am much more concerned that children should be protected from further damage. Whether action in criminal courts is always desirable is open to question. The misdiagnosis of non-accidental injury where it has not occurred is, of course, serious, but far more serious would be the failure to recognise non-accidental injury and the possible catastrophic consequences to the child that might result.

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Effect of calcitonin in patients with malignant metastatic islet cell tumours

SIR,—Dr Alessandro Antonelli and colleagues describe a patient with the carcinoid syndrome who symptomatically responded to subcutaneous salmon calcitonin with a concomitant fall in urinary excretion of 5 hydroxyindoleacetic acid (17 October, p 961).

We have tested subcutaneous human calcitonin in doses of up to 2 mg thrice daily for two weeks in four patients with malignant metastatic islet cell tumours (see table for details of patients and hormone values before and after treatment).

Hormone values before and after treatment with calcitonin in four patients with malignant islet cell tumours

Case No	Hormones secreted	Pretreatment hormonal value (pmol/l)	Hormonal value after treatment (pmol/l)
1	Pancreatic glucagon	3570	3430
	Pancreatic polypeptide	5159	5470
	Gastrin	76	69
2	VIP	264	285
	Pancreatic glucagon	905	1030
	Neurotensin	820	801
3	VIP	338	320
	VIP	276	301
4	Pancreatic glucagon	222	250

VIP=Vasoactive intestinal polypeptide.

Unlike the long acting somatostatin analogue SMS 201-995 (octreotide), human calcitonin did not suppress levels of vasoactive intestinal polypeptide (VIP), pancreatic glucagon, gastrin, or pancreatic polypeptide acutely. No clinical response was noted in terms of reduction in stool volume and frequency of bowel motion in the patients with vipomas; nor was increased resolution of the rash observed in the patients with glucagonomas.

Profound falls in the circulating plasma concentrations of gastrin, insulin, and pancreatic glucagon have been reported in 10 volunteers 40

minutes after a single subcutaneous injection of human calcitonin.¹

The unresponsiveness of the tumours to human calcitonin presumably represents loss of normal feedback control mechanisms, with autonomous hormone secretion, as is frequently observed in such islet cell tumours (for example, omeprazole does not further increase gastrin secretion from gastrinomas, and insulin does not decrease pancreatic glucagon secretion from glucagonomas). We conclude that human calcitonin has little value as a therapeutic agent in the general palliation of patients with metastatic pancreatic endocrine tumours.

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1 Stevenson JC, Adrian TE, Christofides ND, Bloom SR. Effect of calcitonin on gastrointestinal regulatory peptides in man. *Clin Endocrinol* 1985;22:655-60.

Psychological problems associated with lymphomas

SIR,—In discussing the physical and psychological side effects of treatment for lymphomas Dr J Devlen and colleagues (17 October, p 953) do not give exact details of the chemotherapy protocols that were used. This is important since the side effects of any drug are not only a function of the chemical properties of the compound itself but also of the way in which it is given.

It is unscientific to make generalisations about the side effects of drugs without stating how they were given and what steps were taken to minimise such effects. The side effects of most cancer chemotherapy protocols, for example, can be significantly reduced by admitting patients to hospital, giving them high doses of combined antiemetics as a premedication, and administering the drugs in full doses over 24 hours instead of over several days. About 80% of patients treated in this way will have no vomiting or diarrhoea, only rarely experience nausea, and lead a virtually normal life between treatment cycles. The validity of this method has been extensively tested over the past 15 years¹⁻³ and confirmed by several different groups.⁴ We are all concerned about the side effects of anticancer drugs, but failure to realise that these can now be given much more safely and with far fewer side effects than in the past is dangerous for two reasons. Firstly, many patients receiving chemotherapy are suffering from side effects which could largely be prevented and, secondly, the constant emphasis on only the negative aspects of the drug treatment of cancer means that certain patients in Britain are being deprived of the benefits of chemotherapy—for example, those with high risk breast cancer.

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1 Price LA, Hill BT. An experimentally-based safe method of administering intensive cancer chemotherapy: prospects for increased survival in patients with "solid" tumours in the next decade. *S Afr Med J* 1983;64:987-94.

2 Price LA, Hill BT, Marks P, et al. Twenty-four hour combination chemotherapy: a feasibility study with implications for improved adjuvant treatment of breast cancer. *Eur J Cancer Clin Oncol* 1983;19:1-4.

3 Price LA, Hill BT. Safer cancer chemotherapy using a kinetically-based experimental approach. *Mt Sinai J Med (NY)* 1985;52:452-59.

4 Price LA, Hill BT, Ghilchik M, eds. *Safer cancer chemotherapy*. London: Baillière Tindall, 1981.

SIR,—I do not want to belittle the efforts made by Dr Jennifer Devlen and her colleagues (17 October,