The pharmaceutical industry may be very useful here. Of course, it helps if the research fellow works in a specialty in which there is a lot of industry interest. In our view this is a legitimate activity, although some will disagree. Make initial approaches through the relevant local representatives as chances of obtaining funding are often enhanced if the representative is pushing the case. Turn down the offer to discuss this or that product over lunch but tactfully suggest that help towards the travel costs of the next European meeting would be a more worthwhile way to spend the budget.

Make the most of the money raised

Advance programmes for many international scientific meetings provide the facility for booking convenient hotel accommodation beforehand. Furthermore, members of particular specialty associations receive, unsolicited, details of "package" deals to attend forthcoming major meetings. We have never availed ourselves of these opportunities, believing that good, cheaper alternatives are often possible. This does not apply to national meetings when adequate and cheaper accommodation is to be had in university halls of residence. The traditional "bucket shops" which deal in the "unsold stocks" of airline tickets have been heavily criticised because of financial losses and non-arrival of tickets. But some of these outlets are good and efficient: the difficulty lies in knowing which fall into this category. If you want to deliver your talk to

your colleagues at the meeting rather than to other stranded passengers at the airport it is best to use travel agents bonded to the Association of British Travel Agents (ABTA) or the International Air Transport Association (IATA) whenever possible.

Planning ahead is the most important consideration in obtaining the best deals. Cheaper excursion flights (stay includes a compulsory Saturday night) have to be booked at least two weeks ahead for most European flights and three weeks for those further afield. Consider charter flights and accommodation packages, such as City Breaks, which can be very good value, especially if you share a room with a colleague. Choosing an unpopular flight time (early morning, late night) may enable cheaper tickets to be obtained. For Europe it is worth considering rail travel, and for a small group travelling together driving may prove much cheaper. We know of some colleagues who actually camped out near one European city and travelled in daily for the meeting. For those not so hardy there are now plenty of available guides which detail cheap and clean basic accommodation in most cities.

Conclusions

It is well worth the challenge to raise money to attend the major meetings in your relevant specialty. An ex-chief known to us refused to give any financial help to his research fellows for travel. His parsimony led to an excellent training in raising money.

Lesson of the Week

Osteogenesis imperfecta in the differential diagnosis of child abuse

Colin R Paterson, Susan J McAllion

Osteogenesis imperfecta may lead to a mistaken diagnosis of child abuse

In children with unexplained fractures the differential diagnosis rightly includes non-accidental injury, but it also includes several bone disorders. One of the most important of these is osteogenesis imperfecta. This condition is not uncommon, but there may be little or no abnormality in the radiological appearances of the bone at the time of the first fracture.¹⁻⁴ The frequency with which diagnostic difficulties may arise is not known. On the basis of the known prevalence of osteogenesis imperfecta it has been suggested that errors of diagnosis should rarely occur.⁴

This study was based on a continuing large survey of patients with osteogenesis imperfecta in the British Isles, some of the results of which have been reported.⁵⁻⁷ The study includes 802 cases from the United Kingdom in which the diagnosis was not in doubt. This paper reports the extent to which these children were initially thought to have sustained non-accidental injury.

Subjects and methods

Our register includes clinical details of cases referred after the diagnosis of osteogenesis imperfecta had been made by local paediatricians or orthopaedic surgeons or as a result of a family study. A detailed questionnaire was completed for each patient, and in about two thirds of cases the patient was also examined by one of us. In classifying the patients we used the scheme of Silience and colleagues (table I)^{8,9} and had no difficulty in allocating to a Silience type all but 53 patients. In as

many cases as possible the original radiographs were reviewed.

We divided our patients into three groups in relation to the extent to which suggestions were made that the fractures were caused by child abuse. In 691 cases there was no problem in this respect, the diagnosis being made with confidence either at birth or at the time of the first fractures. In 96 cases the parents were accused of non-accidental injury on at least one occasion, but the period over which the difficulties continued was less than one week. In a group of 15 children parents had to contend with formal case conferences, care proceedings, and repeated interviews from social workers and police; in one case parents were prosecuted but acquitted.

Results

Table II summarises our findings in relation to the clinical types of the disorder. Not surprisingly, children with the type IVA and type IVB variants figured prominently in the group with diagnostic difficulties. In most of the type IVB cases the difficulty arose before teeth erupted. There were, however, surprisingly large numbers of patients with type I disease, in whom the diagnosis should have been apparent at the time of presentation by virtue of the scleral abnormality. In most cases in which we reviewed the radiographs the skeletal appearances were normal at this stage and radiology was unhelpful. This group of patients included many whose osteogenesis imperfecta arose as a

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TABLE 1—Classification of osteogenesis imperfecta (Sillence types^a)

Sillence type	Clinical features	Inheritance
I*	Mild to moderate severity. Little impairment of growth. Blue sclerae at all ages	Autosomal dominant. New mutation occurs frequently
II	Very severe disease causing stillbirth or early neonatal death	Not known in most cases; autosomal recessive in some; new dominant mutation in some
III	Severe disease with antenatal fractures in most cases. Progressive deformity common. Severe impairment of growth. Blue sclerae in some but not all cases	Autosomal recessive in most cases
IV*	Mild to moderate severity. Impairment of growth may occur. White sclerae in older children and adults; pale blue sclerae in early childhood	Autosomal dominant. New mutation occurs frequently

*Subdivided into A (no dental abnormality) and B (dentinogenesis imperfecta present).

TABLE 11—Accusations of non-accidental injury in 802 cases of osteogenesis imperfecta in the United Kingdom

Sillence type	Total	Parents accused of non-accidental injury*	Case conferences or care proceedings
IA	361	44 (24)	3
IB	93	16 (11)	2
II	5	0	0
III	123	10	1
IVA	99	28 (6)	7
IVB	68	11 (4)	2
Not classified	53	2 (0)	0

*Figures in parentheses indicate numbers of subjects with clear evidence of osteogenesis imperfecta in one or other parent.

new mutation. When patients with types IA and IB disease were taken together, however, 35 of 60 were found to have a positive family history. The extent to which the family history may be ignored is illustrated by the following case.

A 2 year old boy tripped and fractured a femur. His father, grandmother, and great grandmother were all known to have osteogenesis imperfecta with blue sclerae, and he himself also had blue sclerae. At the hospital he was examined and radiographed, but when the fracture was found a second doctor repeatedly asked questions such as, "Did he really fall over?" He was admitted "for investigation." After a week his mother was told that he had osteogenesis imperfecta, which she knew already. After this she was more frightened of going to hospital than of missing a fracture because of the attitude of the staff. On several subsequent occasions doctors and nurses apparently implied that the child had been abused. The mother could contain her anger because of her familiarity with the condition in her husband's family and because the family was already aware that the child was affected.

The problem may be more serious and an inappropriate accusation more damaging when there is no family history.

A 5 month old boy was taken to hospital because his mother thought the leg was sore. A radiograph showed a spiral fracture of the femur, and the mother was repeatedly asked if he had been "naughty" or if there had been problems in the home. Doctors and social workers repeatedly asked how the fracture had happened and suggested that it could only have happened with a fall from a height. All this led to delay in treatment; it was six hours before he was put in traction. Two days later it was accepted that the sclerae were abnormal. The subsequent history was typical of osteogenesis imperfecta.

In some cases accusations were made in the casualty department despite a well established diagnosis having been made in the same hospital.

A girl was born with a fracture, but despite that on several subsequent occasions the parents were treated inappropriately in the casualty department. The paediatrician gave the family a letter explaining the disorder. When the next fracture occurred the letter was produced and put with the notes. After radiography a new doctor examining the x ray pictures asked the parents how the injury had happened. When he was told he replied, "Are you telling me that she received an injury of this degree by sitting in a chair?"

In general, however, in many of the cases in this group the difficulties could have been minimised by providing a letter for the parents to show to casualty

staff. Many casualty officers are not familiar with osteogenesis imperfecta and miss even obvious cases.

In the second group of patients (table III) the children were the subject of case conferences and often care proceedings. All the children in this group were seen personally by one or both of us. Within this group the difficulty in making a diagnosis, even in retrospect, varied greatly. The one patient with type III disease (case 6) had clearly abnormal radiographs at the time of the first fracture, but this fact was missed and it was only after a further fracture in hospital that the radiographs were reviewed. In most of the other cases the radiographs were correctly reported as normal at the time of the first fracture.

In some cases the diagnosis would not have been made when it was had the child not sustained a further fracture in hospital. A confident diagnosis of non-accidental injury had been made in cases 2 and 15 before further fractures at the hands of hospital staff led to a reconsideration. In two other cases (5 and 6) fractures in hospital contributed to the diagnosis. The subsequent fracture history was very variable. It is not always recognised that in types I and IV osteogenesis imperfecta the fracture rate may vary greatly within a family. In some of the cases in table III the subsequent history of fractures over the years was typical of osteogenesis imperfecta, but long periods without fractures are recognised in all forms of the disease. For example, in case 8 there were no further fractures for 18 months after the child had been taken into care. In four cases no further fractures were recognised during periods of follow up of between three and five years. An even more surprising difficulty occurred in case 1. After an entirely typical fracture history between 10 months and 3 years a paediatric registrar wrote of this patient, "It would seem that she does have a mild degree of osteogenesis imperfecta, but certainly not sufficient to account for six fractures. . . ."

Many patients in this group had no family history and the disorder was thought to have resulted from new mutations. Eight patients, however, had a family history of fractures in childhood in close relatives but this history had not been elicited at the time. In two cases (4 and 10) the family history was obvious and should not have been missed. In case 7 the family history was missed because the parents spoke no English and nobody had made appropriate inquiries.

Table III shows the fractures that had been noted before the case conferences and care proceedings. As in other cases of osteogenesis imperfecta, there was a preponderance of limb fractures. In two cases, however, rib fractures were detected incidentally when a skeletal survey was carried out because of a symptomatic fracture elsewhere. In neither of these cases were there any clinical signs to correspond with these fractures, but the rib fractures found "by accident" initially increased the suspicion that non-accidental injury was likely. In case 7 it was clear that most of the

FIG 2—Example of blue sclerae in a child with type IA osteogenesis imperfecta

FIG 1—Example of dentinogenesis imperfecta in a girl with osteogenesis imperfecta type IVB

fractures identified at the age of 3 weeks had occurred at or before birth. In case 2 it was likely that the rib fractures seen at 3 weeks had occurred at birth.

Overt dentinogenesis imperfecta (fig 1) was subsequently noted in five patients (cases 4, 5, 6, 14, 15), but in each case there were no teeth when the first fracture caused diagnostic difficulty. Surprisingly, five patients had consistently blue sclerae (fig 2) throughout the period of observation and were classified as having type I or type III disease.

Discussion

It is right that in children with unexplained fractures non-accidental injury should be considered. None the less it is also important that bone diseases should be considered. Even though our survey was large, we still cannot say how frequently osteogenesis imperfecta is misdiagnosed. Given the numbers of patients, however, ignorance of the clinical and radiological features of osteogenesis imperfecta seems to be worryingly common. The disorder is not particularly rare, affecting some one in 20 000 of the population in Western countries.

A common misconception is that osteopenia is a usual feature of osteogenesis imperfecta. Some patients with types I and IV disease have abnormal radiographs at the time of the first fracture, but most do not. In these the abnormalities seen later largely reflect not the underlying disease but the fractures and the periods of immobilisation used in their treatment. Even in adult life normal appearances and normal figures for cortical thickness are usual in bones not previously fractured.^{7 10} It is not surprising that this is so, as the fundamental defect in all forms of osteogenesis imperfecta is thought

FIG 3—Example of gross excess of wormian bones in posterior part of skull of 4 month old boy with osteogenesis imperfecta

to be in collagen. The growing range of biochemical defects includes many in which defective cross linkage may be important for bone fragility. Even if osteopenia were common it cannot be recognised with any confidence with ordinary radiography unless the bone density is reduced by more than about half.¹¹

A positive family history is helpful in diagnosis but, as in other dominantly inherited disorders, new mutations are well recognised.¹² Though every effort should be made to obtain an adequate family history, its lack does not exclude the disorder.

Radiological evidence of excessive numbers of

TABLE III—Details of children with osteogenesis imperfecta who were subjects of case conferences and care proceedings

Case No	Sillence type	Year of birth	Age when first fracture recognised	Family history	Scleral colour	Dentinogenesis imperfecta	Wormian bones	Fracture(s)	Consequences	Follow up
1	IA	1974	10 Months	0	Blue	0	—	Left ulna	Case conferences. At risk register 3 years. Two admissions to hospital for observation	Continues to fracture
2	IA	1974	3 Weeks	0	Blue	0	>20	Ribs, right femur	Case conferences. Place of safety order	Fractured in hospital and continues to fracture
3	IA	1983	21 Months	0	Blue	0	>10	Right tibia, right humerus	Case conferences. At risk register for several years	Further regular fractures
4	IB	1986	4 Months	+	Blue	+	0	Left femur	Case conferences. Care proceedings. Prosecution proposed but dropped	No further fractures
5	IB	1986	6 Months	0	Blue	+	>20	Right femur, left tibia	Case conferences. Detention in hospital	Further fractures (one in hospital)
6	III	1976	4 Weeks	0	Blue	+	—	Right femur	Case conferences. Detention in hospital	Further fracture in hospital. Subsequent fractures
7	IVA	1985	3 Weeks	+	Pale blue	0	0	Ribs, clavicle, acromion, left radius, right radius	Case conferences. Interim care order. Later discharged at local authority's request	One further fracture
8	IVA	1973	10 Months	0	White	0	>20	Right humerus, right femur	Case conferences. Prosecution considered but dropped. Care order made. Adoption proposed	No fractures for 18 months, then further fractures in foster care
9	IVA	1974	6 Weeks	+	Pale blue*	0	4	Left humerus, left radius, skull, right femur, left radius and ulna	Case conferences. Parents prosecuted but acquitted. Care proceedings; twice taken into care	Further infrequent fractures until 1986
10	IVA	1976	2½ Years	+	White	0	—	Left tibia	Case conferences	20 Further fractures over 8 years
11	IVA	1982	15 Months	+	White	0	1	Left femur, left fibia	Case conferences. Police investigation, no prosecution. At risk register	No further fractures
12	IVA	1975	5 Months	0	White	0	6	Right femur (+ rib fractures found)	Case conference. Detention in hospital	Further fracture in hospital and many subsequent fractures
13	IVA	1985	11 Months	+	White	0	7	Right humerus, left humerus	Case conferences. Care proceedings. No order made	No subsequent fractures
14	IVB	1983	10 Months	0	Pale blue*	+	6	Right femur	Case conferences. At risk register. Police inquiries	Further regular fractures including skull fracture
15	IVB	1975	7 Weeks	0	Pale blue*	+	>10	Right femur	Case conferences. Police inquiries	Further fracture in hospital and many subsequent fractures

*Pale blue sclerae that became normal later in childhood.

wormian bones (fig 3), particularly if they are in a "mosaic" rather than linear distribution, provides strong evidence for osteogenesis imperfecta. Most or possibly all patients with type III disease show large numbers of wormian bones in skull films that include Towne's view. Our experience of type IV and type I disease (unpublished) is that as few as one third of patients have excessive numbers of wormian bones.

One well known feature of osteogenesis imperfecta is the blue or grey appearance of the sclerae seen in type I disease and in some patients with type III disease. Surprisingly, even within the group of patients with the greatest diagnostic difficulties there were some with classic blue sclerae. Those unfamiliar with the disorder may not be aware of what to expect in scleral colour,¹³ but in some of our cases scleral colour was not even looked for. The preponderance of children with white sclerae and type IV disease was not surprising, though a history of abnormal scleral colour earlier in life was found in this group.⁷

The fracture history may vary greatly in undoubted osteogenesis imperfecta,⁷ and some children have few or even no fractures despite other obvious evidence of the disorder. Some cases are identified only in adult life as a result of family studies or after fractures in later life.¹⁴ There is no support for the view that there is a typical age of first fracture in the type I and type IV variants, nor can the lack of fractures in a particular period be construed as evidence against the diagnosis unless the earlier fractures were very numerous.

Though bruising with little or no obvious trauma is a well recognised feature of osteogenesis imperfecta,^{15 16} it is a paradoxical but frequent finding that fractures may not be accompanied by the superficial evidence of trauma that might be expected.

It is in only a small proportion of patients with osteogenesis imperfecta that the serious difficulties that we have outlined arise, and we suspect that the disorder underlies only a small proportion of fractures in childhood. Nevertheless, the damage done to the

families concerned as a result of a mistaken diagnosis of non-accidental injury must be recognised. Some of the parents were subjected to great pressure to "confess" to what had happened, usually with the implication that there would be no chance of rehabilitation without an "explanation." In some of our cases there was a striking failure to take an adequate history, sometimes rationalised by the claim that it was a job for the police. Though all the cases reported concluded with preservation of the family, long term support was sometimes needed.

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ANY QUESTIONS

A patient with asthma that is well controlled with a high inhaled dose of beclomethasone dipropionate has developed thrush on her vocal cords. What treatment is advised?

High doses of inhaled steroids are important in treating bronchial asthma and usually need to be taken for some months for their full therapeutic effects to take effect—including reduction in bronchial hyperreactivity. They are generally well tolerated with few important side effects. But all topical steroid preparations may lead to redness or soreness of the throat when inhaled and also cause troublesome hoarseness or dysphonia.

The reported incidence of oropharyngeal candidiasis varies from 0% to 77% in patients taking inhaled steroids.¹ Differences in diagnostic criteria may confuse interpretation. Candida is a usual inhabitant of the normal oropharynx, and most patients in whom throat swabs show candida will not develop any symptoms. Clinical evidence of faucial thrush is usually found in about 5-10% of adult patients, and the incidence probably increases with increasing daily dose, greater duration of treatment, and possibly poor inhaler technique and increased frequency of administration. Candidiasis probably relates to local deposition of steroid, and this may be reduced by using a large volume spacer device—for example, Volumatic for beclomethasone dipropionate and Nebuhaler for budesonide.

Dysphonia may occur in patients inhaling propellant alone but is commoner in patients taking inhaled steroids and may be related to the dose. It occurs independently of oropharyngeal candidiasis. It has been

reported in up to a half of patients treated. Voice strain is a possible contributing factor.^{2 3} On inspection of the larynx a characteristic abnormality has been described, and it is suggested that this reversible, bilateral adductor vocal cord myopathy is more often the cause of dysphonia than candidal infection. The incidence of this abnormality, however, is not known. Hoarseness is rare in patients taking oral corticosteroids and probably dysphonia relates to deposition of aerosol on or near the cords.

If inspection of the larynx shows clinical evidence of candida then antifungal treatment including amphotericin lozenges in combination with nystatin mouthwash is usually effective. If laryngoscopy is difficult to arrange then antifungals are probably worth a trial together with the other usual strategies, which include mouth rinsing and gargling with tap water or mouthwash, changing to a powder form of inhaled steroid, using a large volume spacer device, and reducing the dose. Only rarely is it necessary to stop the inhaled steroids. A short course of oral prednisolone may then be required. It may then be possible to reintroduce inhaled steroids in the same or a lower dose. — PHILIP W IND, consultant physician, London

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