THE PROGNOSIS FOR WALKING IN OSTEOGENESIS IMPERFECTA

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We report a postal survey of 59 families of children with osteogenesis imperfecta. From the 51 replies we collected data on developmental milestones and walking ability and related them to the Sillence and the Shapiro classifications of osteogenesis imperfecta. Twenty-four of the patients had been treated by intramedullary rodding.

Both classifications helped to predict eventual walking ability. We found that independent sitting by the age of ten months was a predictor for the use of walking as the main means of mobility with 76% attaining this. Of the patients who did not achieve sitting by ten months, walking became the main means of mobility in only 18%. The developmental pattern of mobility was similar in the rodded and non-rodded patients.

J Bone Joint Surg [Br] 1996;78-B:477-80.

Received 14 September 1995; Accepted after revision 22 January 1995

Osteogenesis imperfecta is usually classified by the methods of Sillence, Senn and Danks (1979) based on the patient's genotype and phenotype. Another classification, introduced by Shapiro in 1985, relates the outcome in terms of survival and motor ability to the time of initial fracture and the radiological appearances of the long bones and the ribs. We aimed to compare these two classifications in regard to the prognosis for walking and the general motor development of the child.

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0301-620X/96/31158 \$2.00

Table I. Developmental milestones (in months) for 'crawlers' and 'bottom shufflers' (Robson 1984)

Milestone	Crawler		Bottom shuffler	
	Mean	SD	Mean	SD
Sit	7.0	1.8	8.5	2.5
Crawl/shuffle	8.0	2.5	11.0	3.0
Stand	9.5	2.4	13.5	3.5
Walk	13.5	1.7	16.0	4.0

Table II. The classification of osteogenesis imperfecta by Shapiro (1985)

Class	
Congenita A	Fractures at birth Bones radiologically abnormal*
Congenita B	Fractures at birth Bones radiologically normal*
Tarda A	First fracture before or at walking stage Bones narrow and osteopenic
Tarda B	First fracture after walking Bones radiologically normal*

* as defined by Shapiro

PATIENTS AND METHODS

The families of 59 patients registered at the multidisciplinary osteogenesis imperfecta clinic at the Wolfson Centre in London were sent a postal questionnaire. Individuals who had been seen recently at the centre were chosen for study.

We asked specific questions on the age at which patients achieved certain developmental milestones. These were: rolling, sitting, crawling, pulling to standing, 'cruising' and walking. Patients were recorded as crawlers or 'bottom shufflers' and as having *delay* in development if the milestones were not passed before the mean age +2 standard deviations for each of the four groups shown in Table I (Robson 1984). Development was recorded as *abnormal* when milestones were not passed in the standard order and as *arrested* if they were never achieved. The parents were asked to state the main means of mobility, as independent walking, aided walking, shuffling/crawling, or the use of a wheelchair. Our definition of aided walking excluded the help provided by intramedullary rodding, as in the definition of 'ambulatory with assistance' given by Shapiro (1985).

Fig. 1

The relationship between the Sillence and Shapiro classifications.

Table III. The classification of osteogenesis imperfecta by Sillence et al (1979)

Class	
IA	Autosomal dominant Normal stature Blue sclerae
IB	As above plus DI*
II	Autosomal recessive Lethal perinatally, crumpled femora
IIIA	Autosomal recessive Multiple fractures at birth Progressively deforming Normal sclerae
IIIB	As above plus DI
IVA	Autosomal dominant Bone fragility White sclerae
IVB	As above plus DI

* dentinogenesis imperfecta

The patients were also classified according to both the Shapiro and Sillence classifications (Tables II and III).

Twenty-four patients (13 male, 11 female) had had intramedullary rodding of one or more long bones in the legs at a mean age of 4.6 years (2 to 8, mode 3) for the first procedure. Both expanding and non-expanding rods had been used and the surgery had been performed at several different hospitals.

RESULTS

There were 51 replies to the 59 questionnaires. Separate forms were returned for three siblings in one family (male twins and an older brother) but all other responses concerned unrelated children. There were 25 boys and 26 girls with a mean age of 7.4 years (3.5 to 16.3). Figure 1 shows the classification of these 51 patients according to the criteria of both Sillence and of Shapiro.

We found five different patterns of development:

Table IV. The Shapiro classification related to developmental pattern and main level of mobility in 51 children

Class	Number	Development	Mobility
Congenita A	1	Delayed/arrested (1)	Wheelchair
Congenita B	31	Abnormal/arrested (6)	Wheelchair (all)
		Delayed/arrested (6)	Wheelchair (all)
		Normal/arrested (9)	Wheelchair (all)
		Delayed (9)	Wheelchair (6), independent walker (3)
		Normal (1)	Independent walker
Tarda A	15	Delayed/arrested (4)	Wheelchair (all)
		Normal/arrested (1)	Aided walker
		Delayed (3)	Independent walker
		Normal (7)	Independent (6), aided walker (1)
Tarda B	4	Normal (4)	Independent walker (4)

Table V. The Sillence classification related to developmental pattern and main level of mobility. Type II is the lethal perinatal form and does not appear in this table

Class	Number	Development	Mobility
IA	8	Normal/arrested (1) Delayed (3) Normal (4)	Aided walker Independent (all) Independent (all)
IB	7	Delayed (1) Normal (6)	Independent Independent (all)
III	29	Abnormal/arrested (6) Delayed/arrested (10) Normal/arrested (8) Delayed (5)	Wheelchair (all) Wheelchair (all) Wheelchair (all) Wheelchair (4), independent walker (1)
IVA	3	Normal/arrested (1) Delayed (2)	Wheelchair Wheelchair (1), independent walker (1)
IVB	4	Delayed/arrested (1) Delayed (1) Normal (2)	Wheelchair Wheelchair Independent (1), aided walker (1)

Table VI. Motor development in non-rodged and rodged patients

Main mobility	Development	Number	Age sitting in months	Age walking in months
Non-rodged				
Walkers	Normal/arrested	1	Unknown	Aided only
	Delayed	4	6, 10, 8, 6	17, 30, 18, 60
	Normal	8	6, 10, 6, 10, 7, 7, 8, 8	14, 18, 13, 17, 11, 9, 12, 14
	Abnormal/arrested	3	12, 24, 12	None
	Delayed/arrested	4	24, 48, 24, 18	None
Wheelchair	Normal/arrested	5	16, 6, 5, no, no	None
	Delayed	2	12, 18	26, 72
Rodged				
Walkers	Delayed	1	8	24
	Normal	4	9, 9, 10, 7	18, 18, 14, 15
Wheelchair	Abnormal/arrested	3	24, 11, 12	None
	Delayed/arrested	7	24, 54, 12, 36, 11, 24, 12	None
	Normal/arrested	4	12, 33, 7, 24	None
	Delayed	5	12, 6, 12, 18, 9	48, 24, 30, 60, 22

Abnormal/arrested. In these cases milestones were not passed in the defined order and development was arrested at the sitting, crawling or standing stages.

Delayed/arrested. In these the time of passing milestones was delayed from infancy, and like the first group, progress had been arrested at varying stages.

Normal/arrested. The initial milestones were achieved within normal age ranges, but further development was arrested, usually resulting in failure to walk independently.

Delayed. The age of achieving milestones was delayed but independent walking was achieved eventually.

Normal. The Shapiro classification of the patients, their developmental pattern and the main means of mobility are shown in Table IV. Of the 32 in Congenita groups A and B only four were classified as walkers. Three of these had delayed development, but had achieved independent sitting by the age of ten months; one had normal development. Of the 15 classified as Tarda A, four used a wheelchair and 11 were walkers (two aided). Of these 11 walkers, seven had normal, three had delayed and one had normal/arrested development. This last patient was studied at the age of ten years: he had pulled to stand at 9.5 months, then sustained

his first fracture. He never achieved independent walking although he regularly used crutches. The four patients classed as Tarda B all walked independently and showed normal development. All but one of the 15 walkers in both Tarda groups had normal motor development or only slight delay, in that sitting had been achieved before ten months.

The results according to the Sillence classification are shown in Table V. The eight children in classes IA and the seven in IB all used walking as their main means of mobility; only one required crutches. Development was only slightly delayed (all achieved sitting by ten months) or normal.

Of the 29 children in Sillence class III only one was a walker, and none had normal motor development. Only three were able to sit by ten months. Three children were in Sillence class IVA: two used wheelchairs and one was a walker. The latter was sitting at the age of ten months but did not manage to walk until five years of age. Of the four children classified as IVB, two were wheelchair users, and the others had normal motor development and were walkers.

Of the whole group of 51, 25 patients had normal or slightly delayed motor development, gaining sitting by ten

months. Of these, 19 (76%) used independent walking as their main means of mobility.

Table VI shows motor development in the non-rodde and rodde patients. In the non-rodde group who were walkers, the mean age of sitting was 7.6 months (6 to 10); in the non-walkers this was 18.3 months (6 to 48). In the rodde group, the mean age of sitting was 8.6 months (7 to 10) in the walkers and 18 months (6 to 54) in the non-walkers.

Only seven of the 23 patients who used wheelchairs had ever been able to walk and this had usually been achieved late, at a mean age of 40 months (22 to 72). The mean age of achieving walking in those who used this method was 18 months (9 to 60).

DISCUSSION

Osteogenesis imperfecta affects much more than just bone. It is a heterogeneous group of conditions due to one of several genetic defects, which produces either a reduced quantity or an abnormality of type-I collagen. The most obvious result is an increased tendency to sustain fractures, but the primary defect causes abnormalities in other tissues containing type-I collagen, including skin, tendon and fibrocartilage. There is evidence that children with osteogenesis imperfecta may follow a delayed or abnormal pattern of development (Engelbert et al 1993). This appears to be related to the severity of the disease as judged by the degree of growth inhibition, other deformity (such as scoliosis) and the number of fractures.

Our study group is based on a very specialised clinic and therefore includes relatively more patients with severe disease. We have been able to show clear differences between the subgroups and consider that there are enough patients in the more common type I or Tarda groups to make valid comparisons. The inclusion of larger numbers of those with severe disease of types III or IV or Congenita as compared with other reported series strengthens the conclusions drawn about these patients.

In contrast to Porat et al (1991) we have found the Silience classification to be useful in predicting the likelihood of walking. The Shapiro classification uses different criteria but is also helpful. We have found that the age of achieving independent sitting is another useful predictor. A child who can sit by the age of ten months is likely to achieve independent or useful walking; in our series walking was the main means of mobility in 76% of this group, as against only 18% of those who were not able to sit by ten months. Independent sitting is easily defined and because it is an early event it is useful for providing a long-term prognosis for the assessment of different treatment programmes.

In our series, seven of the 23 patients who had become wheelchair-users (30%) had achieved walking at an earlier stage, although this was much later than in those who remained walking. This suggests that if walking is established very late it is unlikely that it will become the preferred means of mobility.

In our series no child who eventually used walking as the main means of mobility was older than 60 months when walking was first established. At the time of the study, seven children were under 60 months; four were walkers with a normal development and it is unlikely that any of these will cease to walk. One child of four years had ceased to progress developmentally after sitting at 18 months and the other two children had achieved crawling only by 48 months, after being independent sitters at 11 and 24 months. The last two may progress to useful walking, in the future, but this is unlikely and will not alter the overall conclusions of the study.

It has been claimed that the surgical management of osteogenesis imperfecta by intramedullary rodding may influence motor development (Engelbert et al 1993) and allow previously non-ambulatory children to walk, (Nicholas and James 1990). This assumes that the delay is mainly due to the tendency to fracture, rather than to associated joint laxity and other undefined factors. Our results suggest that intramedullary rodding has no major influence on motor development, but this is difficult to define since there are more severely affected patients in the rodde group as shown by the greater proportion of wheelchair users. We consider that delayed development should not be seen as a specific indication for rodding: this type of surgery is associated with high rates of reoperation and complications. It is important that surgical intervention is planned carefully within the context of the natural history of the condition.

Conclusions. Both the Silience and the Shapiro classifications of osteogenesis imperfecta are useful predictors of walking ability, but we have shown that sitting by the age of ten months is also a good prognostic sign. We have described several patterns of development of osteogenesis imperfecta.

Intramedullary rodding should not be advised for delay in motor development alone, but reserved for nonunion of a fracture of a single bone, recurrent fracture on attempting to walk, and disabling deformity.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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