INHERITANCE AND SPONDYLOLISTHESIS
A RADIOGRAPHIC FAMILY SURVEY

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A radiographic survey has been carried out of 147 first-degree relatives of forty-seven patients treated in Edinburgh for spondylolisthesis of the fifth lumbar vertebra; twelve patients had the dysplastic (congenital) type and thirty-five an isthmic defect. The survey identified 19 per cent of relatives with spondylolysis, and index patients with each type of spondylolisthesis had relatives with the opposite type. Index patients with the dysplastic form had a higher proportion of affected relatives (33 per cent) than had those with the isthmic type (15 per cent), but both figures were significantly in excess of the estimated frequency for the general population of under 1 per cent and 5 per cent respectively.

Spina bifida occulta at the fifth lumbar or first sacral level or both, and lumbosacral segmental defects were commoner amongst all individuals with spondylolysis than amongst unaffected relatives (dysplastic form 94 per cent, isthmic type 32 per cent, unaffected relatives 7 per cent). However, there was no single instance of a neural tube defect (anecephaly, spina bifida with or without meningocele, other generalised vertebral anomalies or spinal dysraphism) amongst 826 first-, second- or third-degree relatives. It is concluded that the developmental defects of the vertebrae associated with spondylolysis are not aetiologically related to the neural tube defects. The one in three risk of spondylolysis to near relatives of patients with the dysplastic form of spondylolisthesis is emphasised in order that the deformity in their sibs and children can be recognised at any early age.

Over the past forty years there have been numerous reports of families with spondylolysis and spondylolisthesis (Friberg 1939; Wiltse 1957; Laurent 1958; King 1966; Amuso and Mankin 1967; Turner and Bianco 1971; Haukipuro et al. 1978). More significantly, there have been some prospective family surveys with radiographic examination of unselected members (Baker and McHollick 1956; Wiltse 1960, 1962; Wiltse and Hutchinson 1965; Yano 1967) and the results have been remarkably consistent with a frequency of the same disorder in near relatives of about 27 per cent, a considerable increase over the estimated frequency of 4 to 8 per cent of most general populations studied (Roche and Rowe 1952; Barr 1955; Baker and McHollick 1956; Nathan 1959; Yano 1967; Krenz and Troup 1973). An exception to this was established by Stewart (1953), who found an unusually high frequency amongst Alaskan Eskimos. He, Rowe and Roche (1953) and Kettelkamp and Wright (1971) all noted that there was no defect at the outset of postnatal life, though some 5 per cent of children were affected by the age of six years and over 20 per cent by the age of thirty-five. The high frequency in this race was thought possibly to be due to unusual mechanical stresses and fatigue fractures of the pars interarticularis.

Many writers have noted a high proportion of spina bifida occulta at the fifth lumbar or first sacral level among patients with spondylolysis (Friberg 1939; Roche and Rowe 1952; Wiltse 1962). Blackburne and Velikas (1977) found that the risk of a progressive vertebral slip was greater in patients with a midline lumbosacral defect than in those without such a defect. An additional or missing lumbar vertebra or transitional vertebrae at the lumbosacral level has also been noted as being more frequent in spondylolytic patients than in the general population (Friberg 1939; Roche and Rowe 1952).

Newman (1955, 1963) described five types of spondylolisthesis, including a congenital Type I associated with sacral spina bifida and deficient development of the superior sacral facets, and Type II "spondylolytic spondylolisthesis" with an elongation or break in the pars interarticularis. Wiltse, Newman and Macnab (1976) have more recently reclassified these two groups as the dysplastic and isthmic forms of spondylolisthesis (Figs. 1 to 4).

The aim of the current survey was to take an unselected group of patients, all of whom had presented with dysplastic or isthmic spondylolisthesis of the fifth lumbar vertebra, and to carry out a radiographic review...
of their first-degree relatives (parents, sibs and children) looking for a similar defect. It was hoped to identify the mode of inheritance, distinguishing between the dysplastic and isthmic types and, in view of the known association with spina bifida occulta and vertebral anomalies at the lumbosacral level, to establish whether spondylolisthesis was aetio logically related to the neural tube defects of anencephaly, spina bifida with or without meningocele, multiple segmental anomalies of the vertebrae and spinal dysraphism.

MATERIAL AND METHOD

A survey was made of forty-seven patients with spondylolisthesis, all living within the Edinburgh area and attending one orthopaedic clinic (JHSS). Their ages ranged from five to sixty-six years with a mean of thirty-two years. Twelve had the dysplastic (congenital) type of spondylolisthesis and thirty-five the isthmic type. Patients with generalised skeletal disease, degenerative spondylolisthesis or that clearly due to acute injury were excluded.

For the genetic survey, the patients were initially visited in their homes and the pedigree obtained. A history of developmental defects was taken and, where necessary, confirmed from medical records. Epidemiological information was collected in relation to social and birth histories, parental age and parity. Subsequently all first-degree relatives willing to help with the survey attended hospital for further examination and radiography. The forty-seven index patients had a total of 300 first-degree relatives, but only 195 were still alive, over five years of age and available in the district. Of these, 147 (75.4 per cent) attended for radiography. Anteroposterior and lateral views of the lumbar spine were taken routinely and oblique views in addition when the diagnosis could not be made on the first two radiographs.

RESULTS

Sex ratio. In the dysplastic group there were seven males and five females (sex ratio 1.4), and in the isthmic group twenty-five males and ten females (sex ratio 2.5), these ratios being similar to findings in other surveys.

Affected relatives. Only six of the 147 relatives (4 per
cent) gave a history of symptoms suggestive of spondylolysis; but on radiography twenty-eight of them were shown to be affected (19 per cent, or nearly five times as many as suspected on the history alone). This 19 per cent included 22 per cent of parents, 14 per cent of sibs and 24 per cent of children of the adult index patients (Table I). Their ages ranged from five to seventy years; six were under the age of twenty, eleven were between the ages of twenty and thirty-nine, and eleven were forty years and over. There was a higher proportion of affected relatives of patients with the dysplastic type compared with the isthmic group (33 and 15 per cent respectively). Both these figures are significantly in excess of the expected frequency for the general population of approximately 5 per cent (estimated at under 1 per cent for the dysplastic form and 4 to 5 per cent for the isthmic form). Each group of index patients, dysplastic and isthmic, had relatives with the opposite type of defect, the dysplastic form always being less common. Of the eleven affected relatives of the dysplastic group of patients, ten had an isthmic and only one a dysplastic defect. In the isthmic group, fourteen of the seventeen affected relatives had an isthmic lesion and only three a dysplastic defect (Fig. 5).

Table I. Proportions of first-degree relatives with spondylolysis or spondylolisthesis

<table>
<thead>
<tr>
<th>Patients</th>
<th>Parents</th>
<th>Sibs</th>
<th>Children</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>(12) Dysplastic type</td>
<td>6 of 18</td>
<td>2 of 12</td>
<td>3 of 3</td>
<td>11 of 33 (33.0%)</td>
</tr>
<tr>
<td>(35) Isthmic type</td>
<td>5 of 32</td>
<td>7 of 51</td>
<td>5 of 31</td>
<td>17 of 114 (14.9%)</td>
</tr>
<tr>
<td>(47) Total</td>
<td>11 of 50 (22.0%)</td>
<td>9 of 63 (14.3%)</td>
<td>8 of 34 (23.5%)</td>
<td>28 of 147 (19.0%)</td>
</tr>
</tbody>
</table>

Figure 3—In the less common dysplastic form of spondylolisthesis the anteroposterior view frequently shows spina bifida occulta or transitional lumbosacral vertebrae or both. Figure 4—In this lateral view there is a break in the pars interarticularis, but this need not be present. The most important difference between this and the isthmic type is the line of the superior sacral facet joint, which here approaches the horizontal.
There was one instance of consanguinity among the isthmic group, the patient's parents being first cousins, but neither they nor a brother had a lesion. There was one pair of (dizygous) twins in the survey, only one affected with the isthmic lesion.

**Back symptoms in relatives.** Only six of the twenty-eight relatives (21 per cent) with a proven spondylolytic lesion had any symptoms; this was little above the figure of 16 per cent of the remaining relatives who complained of backache but did not have a defect (twenty of 119 individuals). Nevertheless, backache could be of value in diagnosing spondylolysis under the age of twenty years since all these younger relatives did have a lesion.

![Figure 5](image)

**Diagrammatic illustration of the proportions of patients and their affected relatives with the dysplastic and isthmic forms of spondylolisthesis or spondylolysis.**

**Associated spina bifida occulta and segmental defects.** Eleven of the twelve patients with a dysplastic lesion had either spina bifida occulta or segmental defects in the lumbosacral area or both; all four relatives with a dysplastic lesion had an associated defect here. Of the patients with an isthmic lesion, eleven of the thirty-five had such a defect, as had eight of their twenty-four affected relatives. In contrast, only eight of 119 (6.7 per cent) unaffected relatives had a defect (Table II). Spina bifida occulta at the fifth lumbar or first sacral level is common in the general population, occurring in 25 per cent or more; other lumbosacral defects occur less frequently, probably in only 5 to 8 per cent of the population (Paterson 1893; le Double 1912; Friberg 1939; Friedman, Fischer and Van Demark 1946). Clearly these additional developmental defects are particularly associated with spondylolysis and spondylolisthesis, being almost invariable in the dysplastic type and present in one third of individuals with an isthmic lesion.

There were no other anomalies of note among the patients or their relatives, and in particular there was no single instance of a neural tube defect among 826 first-, second- or third-degree relatives. An accurate comparison can be made with the sibs of spondyloesthetic patients. If these two lesions were aetiologically related, the expected number of sibs with a neural tube defect (for the Edinburgh region) would be eleven, or 8 per cent of the total of 143 sibs (Wynne-Davies 1975).

**Epidemiological data.** There were no abnormal findings relating to the pregnancy or birth of these patients, where these histories were available. Length of gestation, presentation, birth weight, season of birth, social class, previous abortions or stillbirths were all within the expected range. The only finding of probable significance was a raised maternal age in patients with the isthmic type of lesion (28.39±1.03 years) compared with control figures of 26.04±0.22 years (0.05>P>0.025).

**CONCLUSIONS**

It is clear that a lumbosacral midline lesion or other segmental defect at this level is common amongst individuals with spondylolysis and spondylolisthesis, but since this is not associated with an increased family frequency of the neural tube defects we conclude that the two disorders are not aetiologically related. It seems likely that there is a genetic element to both the dysplastic and isthmic types of spondylolisthesis. Since each defect appears in the other's family in a higher proportion than expected for the general population, they are likely to be aetiologically related, but the dysplastic type presents a higher risk to near relatives (one in three affected) than the isthmic form (only one in seven affected). This high risk needs emphasising in order that affected sibs and children of these patients can be identified at an early age. The lower proportion of affected relatives among patients with an isthmic lesion could be due to the fact that it is not possible to isolate all those patients who have a simple traumatic (though not acute) lesion from those that have some genetic background in addition (Wiltse, Widell and Jackson 1975). The pattern of inheritance cannot be certainly identified on such a small survey as this but it probably lies between autosomal dominant inheritance with reduced penetrance and multifactorial inheritance. Our view is that there is likely to be a genetic predisposition to spondylolisthesis; if an associated lumbosacral spina bifida occulta or segmental defect is present, it raises the probability of a vertebral slip which may then be precipitated by quite minor injury.

**Table II. Proportions of index patients and relatives with lumbosacral midline or other segmental defects**

<table>
<thead>
<tr>
<th></th>
<th>Spina bifida occulta (L5 or S1)</th>
<th>Lumbosacral segmental defect</th>
<th>Total (individuals)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysplastic spondylolisthesis</td>
<td>10 of 16</td>
<td>6 of 16</td>
<td>15 of 16 (93.8%)</td>
</tr>
<tr>
<td>Isthmic spondylolisthesis</td>
<td>11 of 59</td>
<td>11 of 59</td>
<td>19 of 59 (32.2%)</td>
</tr>
<tr>
<td>Unaffected relatives</td>
<td>4 of 119</td>
<td>5 of 119</td>
<td>8 of 119 (6.7%)</td>
</tr>
</tbody>
</table>

who have some genetic background in addition (Wiltse, Widell and Jackson 1975). The pattern of inheritance cannot be certainly identified on such a small survey as this but it probably lies between autosomal dominant inheritance with reduced penetrance and multifactorial inheritance. Our view is that there is likely to be a genetic predisposition to spondylolisthesis; if an associated lumbosacral spina bifida occulta or segmental defect is present, it raises the probability of a vertebral slip which may then be precipitated by quite minor injury.
REFERENCES


