There is a close link between the embryological development of the musculoskeletal system and all other main organ systems. We report a prospective series of 202 patients with congenital vertebral abnormalities and document the associated abnormalities in other systems. There were 100 boys and 102 girls. In 153 there were 460 associated abnormalities, a mean of 2.27 abnormalities for each patient. Intravenous pyelography was carried out on 173 patients (85.6%) and ultrasonography on the remaining 29 (14.4%). Patients with genitourinary anomalies were more likely to have musculoskeletal (p = 0.002), gastrointestinal (p = 0.02) and cardiac abnormalities (p = 0.008) than those without genitourinary involvement. A total of 54 (26.7%) had at least one genitourinary abnormality, the most frequent being unilateral renal agenesis. There was urinary obstruction in six (3%). There was no association between genitourinary abnormality and the place of birth, parental age, birth order, level of spinal curvature, or the number, type and side of spinal anomaly. There was, however, a statistically significant association (p = 0.04) between costal and genitourinary abnormalities. The incidence of genitourinary abnormalities (26.7%) was similar to that of previously reported series. The diagnosis of a congenital vertebral abnormality should alert the clinician to a wide spectrum of possible associated anomalies most of which are of clinical importance.

The genitourinary and musculoskeletal systems are both of mesodermal origin and develop at the same time in the embryo. As a result, any genetic defect or other insult acting at a crucial stage of organogenesis which results in a congenital vertebral abnormality, may also lead to a congenital genitourinary malformation. There is also the possibility that other developing organ systems will be affected. Thus, a cluster of disparate congenital abnormalities may occur.

In 1976, MacEwen, Winter and Hardy drew attention to the frequent occurrence of congenital genitourinary abnormalities in patients with congenital scoliosis. Other authors, principally from North America, have since recorded similar observations. Our aim was to document the coexistence of congenital malformations of the vertebral axis and the genitourinary tract in an Australian population. This has not been previously investigated. We also describe concomitant congenital malformations in other systems.

Patients and Methods

We studied 202 children with congenital vertebral abnormalities who had been managed by one of us (TKFT) between 1970 and 1999, and who had undergone routine investigation of the genitourinary tract. Children with myelomeningocele were not included, but three patients had a small meningocele without an accompanying neurological defect. All had had prospective clinical documentation and had undergone physical examination.

There were 100 boys and 102 girls. The mean maternal and paternal ages at birth were 27.6 (17 to 49) and 30.8 (19 to 49) years, respectively. A history of consanguinity was present in three parents (1.5%). Five patients (2.5%) had siblings with congenital vertebral anomalies.

Intravenous pyelography (IVP) was carried out on 173 children (85.6%) and ultrasonography on the remaining 29 (14.4%). Table I gives the classification of genitourinary abnormalities which was designed by one of us (GHH) and Table II the classification of abnormalities in other systems. The spinal radiographs of patients with multiple congenital abnormalities were difficult to interpret particularly when there is severe deformity and a simplified classification has therefore been used. Abnormalities were...
classified as either a failure of segmentation (congenital fusion) or of formation (hemivertebra, etc.). Both frequently occur in the same vertebral column. The numbers and spinal levels of the abnormalities were documented. The changes in the costal elements were similarly classified as either absence or fusion of ribs. Rib abnormalities were detected in 87 patients (43%).

No attempt was made to categorise the spinal abnormalities by syndrome for a number of reasons. There were no radiological features of the vertebral abnormalities which distinguished those in one syndrome from another or when they occurred in isolation such as in a solitary hemivertebra. Similarly, Barnes and Smith reported that there was no specific type of oesophageal atresia, tracheo-oesophageal fistula or imperforate anus in subjects with the VATER association and that these lesions were indistinguishable in type and complications from those which occurred when associated anomalies were not present. Also, pure syndromes of congenital abnormalities are the exception rather than the rule. For example, Goldenhar’s syndrome has an incidence of 60% of concomitant congenital spinal abnormalities. The diagnosis of a syndrome does not, in itself, have any particular clinical or prognostic merit unless it has a known inheritable basis. An association, a term which warrants wider application in this field, implies a greater-than-random tendency for anomalies to occur together. The literature on congenital vertebral abnormalities, in itself, is quite confusing and misleading terminology has been applied. For example, the term ‘costovertebral dysplasia’ is a misnomer because there is neither radiological nor histological evidence of an intrinsic disorder of enchondral ossification such as in achondroplasia and spondyloepiphyseal dysplasia. In these conditions, the dysplasia presents as irregularity of the endplates of vertebral cartilage and this is not seen in congenital vertebral abnormalities.

**Results**

Congenital scoliosis differs from idiopathic scoliosis in that the malalignment is often kyphoscoliotic and not lordoscoliotic. Pure deformities in the sagittal plane are less common. In 137 patients (67.8%) the deformity was primarily scoliotic (mean Cobb angle 40°), in 35 (17.3%) it was primarily kyphotic (mean Cobb angle 51°) and in 20 (14.9%) there was no significant deformity. Surgical correction of the deformity had been carried out in 76 patients (37.6%). Two patients are awaiting surgery and 124 (61.4%) have been managed non-operatively. All patients undergoing surgical correction had preoperative myelography or MRI, which became available in 1986.

**Genitourinary anomalies.** There were 460 associated
abnormalities in 153 of the 202 patients, 2.27 for each patient. Overall, 54 patients (26.7%) had at least one genitourinary abnormality (Table III). The most frequent was unilateral renal agenesis with an incidence of 11.9% (Table IV). This was followed by duplication of the ureter and renal ectopia, each with an incidence of 4.5%. There was renal fusion or a horseshoe kidney in 2.5%. Two patients (1%) had an obstructive pattern with a unilateral kidney. Four (2%) of the nine patients with reflux had evidence of hydronephrosis, but only three had required corrective surgery, two with ureteropelvic obstruction and one with obstruction of the ureterovesical junction.

There was no statistically significant association between the place of birth (urban or rural), parental age, birth order, the level of spinal curvature, or number, type and side of spinal anomaly, and genitourinary abnormality. There was, however, a statistically significant association (p = 0.04) between costal and genitourinary abnormalities.

### Anomalies in other systems

The distribution of gender in non-vertebral abnormalities is shown in Table V. The only association close to statistical significance was for ear, nose, and throat (ENT) abnormalities, which appeared to be more common in girls (p = 0.06). The most common system to be involved was the musculoskeletal, followed by the ENT, genitourinary, gastrointestinal, respiratory, central nervous and cardiac systems (Table V). Patients with genitourinary anomalies were more likely to have musculoskeletal (p = 0.002), gastrointestinal (p = 0.02) and cardiac abnormalities (p = 0.008) than those without genitourinary involvement (Table VI).

## Discussion

The incidence of genitourinary abnormalities (26.7%) in our series of patients with congenital vertebral abnormalities, is comparable with that previously described in North America. While these anomalies may remain asymptomatic, some can be associated with significant morbidity. Infection, obstruction and the formation of calculus are the main reported problems. A recent review by Argueso et al of 157 subjects with unilateral renal agenesis suggested that those with a normal solitary kidney...
Table VII. Abnormalities associated with congenital vertebral abnormalities in different series

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients studied</th>
<th>Patients with associated abnormalities (%)</th>
<th>Number of associated abnormalities</th>
<th>Number of associated abnormalities per patient in those with associated abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kahn and Hormell</td>
<td>165</td>
<td>Data not provided</td>
<td>156</td>
<td>Data not provided</td>
</tr>
<tr>
<td>Winter et al</td>
<td>234</td>
<td>73 (37)</td>
<td>115</td>
<td>1.6</td>
</tr>
<tr>
<td>Bernard et al</td>
<td>47</td>
<td>35 (62)</td>
<td>46</td>
<td>1.3</td>
</tr>
<tr>
<td>Beals et al</td>
<td>218</td>
<td>133 (61)</td>
<td>322</td>
<td>2.4</td>
</tr>
<tr>
<td>This study</td>
<td>202</td>
<td>153 (76)</td>
<td>460</td>
<td>2.3</td>
</tr>
</tbody>
</table>

are at increased risk of proteinuria, hypertension and renal insufficiency, and it is essential to have prolonged and careful follow-up. Horseshoe kidney is a common renal anomaly, and in a follow-up of 51 patients for ten years Glenn found that although 60% remained asymptomatic, 13% had persistent urinary infection or pain, and 17% developed recurrent calculi. Obstructive uropathy occurred in 3.0% of our series compared with 2.5% in the series of MacEwen et al. Two of the six patients with obstructive uropathy had a unilateral kidney and were asymptomatic, and the kidney could be saved after early diagnosis of obstruction. The remaining four patients had reflux and three required surgery.

The incidence of congenital genitourinary abnormalities which was found in our patients greatly exceeds that found in routine postmortem studies. Campbell found an incidence of 0.2% for unilateral renal agenesis in 19,046 autopsies and of 0.7% for duplication of the renal pelvis in 51,880 similar examinations. Table VII gives the incidence of renal abnormalities associated with congenital vertebral anomalies in five different series. The proportions of the different types of abnormality of the renal tract in our series are similar to those reported by Drvaric et al who also used ultrasonography as a diagnostic technique. Historically, IVP has been the investigation of choice in the evaluation of the morphology of the urinary tract, but diagnostic ultrasonography has been shown to be an acceptable alternative method of screening. Some centres reserve IVP for confirmation in those patients in whom an abnormality has been identified ultrasonographically, or when the study is inconclusive. Ultrasound is non-invasive, less expensive and has a reduced exposure to radiation. This is relevant in patients in whom multiple anomalies have been identified and repeated imaging is required. In our series, which spans over 30 years, IVP was more commonly used than ultrasound (85.6% compared with 14.4%), but recently the trend has been for an initial ultrasonographic evaluation. This can be difficult in the overweight patient and in those with severe spinal deformity in whom the chest is abutting against the pelvis. In these circumstances IVP is recommended.

The embryological development of the mesodermally-derived vertebral column and genitourinary system is closely linked. Vertebral development is sensitive to genetic and environmental influences. All segmented animals have a definite sequence of genetically-controlled events which establish the basic aspects of somite formation. The regional specialisation of the individual segments is determined by the homeotic system of genes. Whatever the precise mechanism of action may be, it provides an early determination within the vertebral sclerotome.

It is tempting to speculate that the almost identical distribution of genitourinary abnormalities in our patients, and in those reported by Drvaric et al from North America (Table IV) reflects, in some way, the expression of these genes as does the comparable incidence of associated abnormalities recorded by Beals et al (Table VII).

Embryonic cell masses show a marked ‘position effect’ before any regional differentiation of the somites occurs. This has been demonstrated in the chick embryo, in which the transplantation of an early thoracic sclerotome into the cervical region resulted in a rib-bearing thoracic vertebra. This specific character development was not modified by its heterotopic location. Renal anomalies are non-hereditary which supports the suggested aetiology of an insult to the embryo between the fifth and seventh week. This period corresponds to the stage of organogenesis when the stem-cell population is being established for the primordial organs. These interactions are sensitive to insult from genetic and environmental influences.

In our series there is a significant association between costal and genitourinary abnormalities. Thus, if a plain radiograph shows a congenital vertebral abnormality with an associated rib anomaly (fusion or absence), it is more likely that imaging will reveal a genitourinary abnormality. The ribs develop from the costal processes of the primitive vertebral arches and in the thoracic region these grow laterally to form a series of precartilaginous ribs. It could be postulated that an insult here could also disturb the development of the lateral mesoderm, from which the kidney develops, and thus represents an extended morphogenetic field effect.

There were almost equal numbers of boys and girls with congenital vertebral abnormalities (male/female ratio 0.98) in our series. This is quite different from the populations reported in North America (male/female ratio 0.54) and in the UK (male/female ratio 0.31 for multiple vertebral anomalies and 0.68 for solitary vertebral anomalies). It suggests that congenital vertebral anomalies in Australia are sporadic in nature and carry no risk to subsequent...
siblings. Five of our patients, however, had siblings with vertebral abnormalities. Two of these children have spondylocostal dysostosis (Jarcho-Levin syndrome), a disorder which can be inherited in both an autosomal dominant and recessive manner.17,18

The mean age of Australian parents having their first child has risen steadily over the last 20 years.19,20 Between 1976 and 1996, the median age of married fathers increased by four years (to 32.7 years) and of mothers by three years and five months (to 29.2 years). Advanced maternal and paternal age has been suggested as a factor in the aetiology of congenital vertebral malformations,16 but this was not seen in our patients.

Four previous studies provide data on the frequency and type of abnormality associated with congenital vertebral anomalies4,6,21,22 (Table VII). There were 460 associated abnormalities in 153 of our 202 patients. With 76% of patients having associated abnormalities, an average of 2.27 per patient, this is higher than in previous reports. We believe that the higher incidence in this Australian population may be more accurate than previously reported, since it reflects the follow-up of our patients until skeletal maturity, during which time associated anomalies were detected.

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