DOMINANT CONGENITAL COXA VARA

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In 1970 a family with congenital coxa vara observed in three generations was reported (Say, Tunçbilek, Pirnar and Tokgözoglu 1971). During further questioning it was learned that there were many similar cases in the Turkish village called Gonyeli in Cyprus whence the family came. This paper reports the results of two field trips arranged for further study of these people.

MATERIALS AND METHODS

On arrival in the village, the purpose of the study was explained to the village elders and, through their cooperation, those villagers who accepted our invitation were seen. In this way ninety-four patients with congenital coxa vara and twenty-five unaffected relatives were

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Fig. 1
A partial pedigree.
examined clinically and radiologically. Clinical studies included, in addition to the routine physical examination of every subject, measurement of standing and sitting heights in fifty-seven affected and thirteen normal people. A pedigree covering thirteen generations was made from information given by the local populace. A partial pedigree with affected individuals in four generations is shown in Figure 1.

### TABLE I
**CORRELATION BETWEEN THE FEMORAL NECK-SHAFT ANGLE AND THE SEX**

<table>
<thead>
<tr>
<th>Neck shaft angle in degrees</th>
<th>&lt;80</th>
<th>81–100</th>
<th>101–110</th>
<th>111–115</th>
<th>116–120</th>
<th>121–124</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female patients</td>
<td>—</td>
<td>6</td>
<td>7</td>
<td>14</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Male patients</td>
<td>3</td>
<td>2</td>
<td>15</td>
<td>18</td>
<td>13</td>
<td>7</td>
</tr>
</tbody>
</table>

### TABLE II
**DISTRIBUTION OF THE PATIENTS ACCORDING TO FEMORAL NECK-SHAFT ANGLES**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Per cent of patients affected</td>
<td>2.2</td>
<td>1.1</td>
<td>1.1</td>
<td>1.1</td>
<td>1.0</td>
<td>6.0</td>
<td>3.2</td>
<td>4.6</td>
</tr>
</tbody>
</table>

### TABLE III
**DISTRIBUTION OF THE FEMORAL NECK-SHAFT ANGLES ACCORDING TO THE AGE OF PATIENTS**

<table>
<thead>
<tr>
<th>Age in years</th>
<th>&lt;80</th>
<th>81–100</th>
<th>101–110</th>
<th>111–115</th>
<th>116–120</th>
<th>121–124</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4</td>
<td>—</td>
<td>—</td>
<td>1</td>
<td>2</td>
<td>—</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>5–10</td>
<td>—</td>
<td>—</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>11–15</td>
<td>—</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>16–20</td>
<td>—</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>21–30</td>
<td>1</td>
<td>—</td>
<td>1</td>
<td>4</td>
<td>8</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>31–40</td>
<td>—</td>
<td>—</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td>—</td>
<td>10</td>
</tr>
<tr>
<td>&gt;40</td>
<td>2</td>
<td>1</td>
<td>7</td>
<td>6</td>
<td>7</td>
<td>1</td>
<td>24</td>
</tr>
<tr>
<td>Total</td>
<td>3</td>
<td>3</td>
<td>20</td>
<td>24</td>
<td>30</td>
<td>14</td>
<td>94</td>
</tr>
</tbody>
</table>

Radiographs of the hips of all the affected patients, together with complete skeletal surveys in some, were obtained. Any individual with a femoral neck-shaft angle smaller than 125 degrees was considered to have coxa vara. In a few patients chromosome studies, immunoelectrophoresis, serum calcium, phosphorus and alkaline phosphatase determinations, blood and urine amino acid chromatographs as well as routine blood counts and urine analyses were done by conventional methods. Dermatoglyphic analyses using the Faurot Inkless method were done in nineteen affected and eighty control subjects.

### RESULTS
Of the ninety-four affected patients fifty-eight were male and thirty-six were female. The youngest patient was eighteen months of age and the oldest eighty-two years. Approximately one-third of the patients were under the age of sixteen. The femoral neck-shaft angles are
TABLE IV
DISTRIBUTION OF THE FEMORAL NECK-SHAFT ANGLES IN FEMALES ACCORDING TO AGE

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Angle in degrees and percentage of patients affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-9</td>
<td>2-3</td>
</tr>
<tr>
<td>10-17</td>
<td>2-3</td>
</tr>
<tr>
<td>18-25</td>
<td>2-3</td>
</tr>
<tr>
<td>26-33</td>
<td>2-3</td>
</tr>
<tr>
<td>34-41</td>
<td>2-3</td>
</tr>
<tr>
<td>42-49</td>
<td>2-3</td>
</tr>
<tr>
<td>50-57</td>
<td>2-3</td>
</tr>
<tr>
<td>58-65</td>
<td>2-3</td>
</tr>
<tr>
<td>66-73</td>
<td>2-3</td>
</tr>
</tbody>
</table>

TABLE V
DISTRIBUTION OF THE FEMORAL NECK-SHAFT ANGLES IN MALES ACCORDING TO AGE

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Angle in degrees and percentage of patients affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-10</td>
<td>1-8</td>
</tr>
<tr>
<td>11-20</td>
<td>1-8</td>
</tr>
<tr>
<td>21-30</td>
<td>1-8</td>
</tr>
<tr>
<td>31-40</td>
<td>1-8</td>
</tr>
<tr>
<td>41-50</td>
<td>1-8</td>
</tr>
<tr>
<td>51-60</td>
<td>1-8</td>
</tr>
<tr>
<td>61-70</td>
<td>1-8</td>
</tr>
<tr>
<td>71-80</td>
<td>1-8</td>
</tr>
<tr>
<td>81-90</td>
<td>1-8</td>
</tr>
</tbody>
</table>

TABLE VI
STATISTICAL RELATIONSHIP OF THE FEMORAL ANGLES IN DEGREES AND THE SEX OF THE PATIENTS

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\bar{x}$</td>
<td>115.777</td>
<td>110.709</td>
</tr>
<tr>
<td>$S$</td>
<td>6.544</td>
<td>12.950</td>
</tr>
<tr>
<td>$S_x$</td>
<td>1.091</td>
<td>1.715</td>
</tr>
<tr>
<td>$D$</td>
<td>5.068</td>
<td></td>
</tr>
<tr>
<td>$S_D$</td>
<td>2.364</td>
<td></td>
</tr>
<tr>
<td>$t$</td>
<td>2.143</td>
<td></td>
</tr>
<tr>
<td>$P$</td>
<td>&lt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

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shown in Tables I and II. In every case except one, coxa vara was bilateral. Twenty-seven patients had severe coxa vara with neck-shaft angles under 110 degrees. The distribution of the angles according to the age of the patients is shown in Tables III to V. Although there

\[
\text{TABLE VII}
\]

\begin{center}
\textbf{HEIGHTS OF THE PATIENTS}
\end{center}

\begin{center}
\textit{(Percentile)}
\end{center}

\begin{center}
\begin{tabular}{ |c|c|c|c|c|c|c|c| } 
\hline
\textbf{Age in years} & \textbf{< 3} & \textbf{3-10} & \textbf{11-25} & \textbf{26-50} & \textbf{51-75} & \textbf{76-97} & \textbf{> 97} \\
\hline
\textbf{Female} & 15 & 6 & -- & -- & 1 & -- & -- \\
\textbf{Male} & 20 & 12 & 3 & -- & -- & -- & -- \\
\hline
\textbf{Total} & 35 & 18 & 3 & -- & 1 & -- & -- \\
\hline
\end{tabular}
\end{center}

\[
\text{TABLE VIII}
\]

\begin{center}
\textbf{RATIO OF THE LENGTH OF THE ARM TO THE LEG IN NINETEEN PATIENTS}
\end{center}

\begin{center}
\begin{tabular}{ |c|c|c|c|c|c|c| } 
\hline
\textbf{Age in years} & \textbf{Sex} & \textbf{Height (centimetres)} & \textbf{Lower segment (centimetres)} & \textbf{Arm/leg ratio} & \textbf{Found} & \textbf{Expected*} \\
\hline
6 & Female & 106 & 47.5 & 1.23 & 1.00 \\
10 & Female & 118 & 53 & 1.22 & 1.00 \\
39 & Female & 143.8 & 60.8 & 1.36 & 1.01 \\
50 & Female & 145 & 55 & 1.63 & 1.01 \\
71 & Female & 148.5 & 75.5 & 0.96 & 1.01 \\
18 & Male & 162 & 71 & 1.28 & 0.99 \\
6 & Male & 115 & 51 & 1.25 & 1.12 \\
5 & Male & 96 & 41.5 & 1.31 & 1.19 \\
2 & Male & 82 & 32 & 1.56 & 1.42 \\
11 & Male & 125 & 54.8 & 1.29 & 0.98 \\
27 & Male & 160 & 72 & 1.22 & 0.99 \\
44 & Male & 157 & 71 & 1.21 & 0.99 \\
45 & Male & 152.5 & 68 & 1.24 & 0.99 \\
31 & Male & 153 & 61 & 1.50 & 0.99 \\
24 & Male & 154 & 68 & 1.22 & 0.99 \\
31 & Male & 163 & 72 & 1.29 & 0.99 \\
29 & Male & 148 & 60 & 1.45 & 0.99 \\
63 & Male & 159.2 & 71.2 & 1.23 & 0.99 \\
63 & Male & 148 & 63 & 1.34 & 0.99 \\
\hline
\end{tabular}
\end{center}

\[
t = 6.288. \quad P < 0.001.\]

* Wilkins 1960.

was no case with an angle smaller than 80 degrees among patients under the age of twenty and none of the patients over the age of thirty-one had an angle greater than 120 degrees, statistical analyses failed to show significant correlation between the age of the patients and
the degree of neck-shaft angle (correlation coefficient was $r = -0.22$ for females and $r=0.21$ for males; $p>0.05$ for each group). Mean values for femoral neck-shaft angles were found to be significantly lower in the males compared to females ($p<0.05$ in Table VI).

The heights of the fifty-seven patients (thirty-five males and twenty-two females) are shown in Table VII. In twenty males and fifteen females the heights were under the third percentile for their respective ages. The ratio between the lengths of the arm and the leg in nineteen patients studied revealed that the legs were relatively shorter than the arms (Wilkins 1957): details are shown in Table VIII, in which $p<0.001$. A typical case of congenital coxa vara with marked short stature and bowing of the legs is shown in Figure 2.

The results of the serum calcium, phosphorus, alkaline phosphatase, immunoelectrophoresis, chromosome analyses, blood and urine amino acid chromatographs, routine blood counts and urinalyses were all normal in the few cases studied. Dermatoglyphic studies also showed no deviation from the normal when compared with a sample of the local population.

The pedigree, comprising over 300 subjects, showed classical autosomal dominant inheritance.

**Radiological findings**—The main radiological abnormality was coxa vara (Figs. 3 to 8). However, there were other radiological findings which can be divided into two groups: 1) nonspecific degenerative changes, usually in the hip and knee, apparently secondary to the coxa vara deformity; 2) idiopathic pathological changes in the rest of the pelvis developing at the same time as the coxa vara and possibly with the same etiology.

The first group included degenerative osteoarthritic changes with narrowing of the articular space, irregularity of the subchondral osseous margins, sclerosis interspersed with areas of cystic rarefaction and marginal hyperostotic spur formation (Fig. 9). The changes increased with the age of the patient and the severity of the coxa vara. Abnormal distribution of the weight-bearing load because of the coxa vara is the probable cause. Most of the patients with coxa vara also showed bowing of the femora.

In the second group a relatively hypoplastic appearance of the iliac bones in thirty-seven of the ninety-four patients was seen and caused the sacrum to appear disproportionately wide (Fig. 10). There was also a mild protrusio acetabuli in twenty-one patients (Fig. 11). Osteomalacia or other similar conditions having been excluded both radiologically and by blood chemistry, it is considered that this was probably related to the underlying primary disorder.

**DISCUSSION**

Although congenital coxa vara is not universally accepted as a familial condition, the occurrence of this deformity in parents and their children (Almond 1956) and in siblings (Francke 1906), especially in identical twins (Martin 1942), suggests that the condition is familial...
Selected radiological examples which show the coxa vara, with varying degrees of protrusio-acetabuli.
at least in certain instances. Jones and Lovett (1923) recorded this condition in mother and daughter, and more interestingly Almond (1956) reported a family in which a two-year-old girl, her father and his niece had coxa vara. We believe that our findings throw further light on this condition. The fact that the pathology could be traced back in both sexes for thirteen generations by history and four generations by radiology, indicates a dominantly inherited mutant gene located on an autosome. The observed change in the severity of the condition from patient to patient may merely indicate the variable expressivity of the mutant gene. The effect of environmental factors on expressivity has not, however, been thoroughly investigated.

It has been suggested that the basic pathology in congenital coxa vara consists of disturbance of ossification and growth of the subcapital epiphysial plate (Phylkkänen 1960). Because this leads to a weakness of the juxta-epiphysial bone of the femoral neck, the neck-shaft angle progressively decreases when the child begins to walk. Without being able to get permission for a bone biopsy we cannot comment on this hypothesis. However, in one patient, radiographs taken a year apart showed a significant decrease of the neck-shaft angles even in that short period. Also the worst cases were usually found in the older population, although statistical analyses failed to show any significant correlation between the age of the patient and the severity of coxa vara.

There were many findings suggesting that the pathology is not confined to the hip region only. The subjects were quite short in height and had other changes in the pelvic bones. Many had bowing of the legs. Shortness of stature was so marked that, out of ninety-four patients, there were only two whose heights were above the 25th percentile. More significantly,
in more than 30 per cent of the affected group the height was under the third percentile for their respective ages. It should also be noted that the latter patients were not confined to any particular age or sex. It is also interesting that shortness was more marked in the leg than in the arm, and only part of the increase in shortening can be the result of the coxa vara itself.

In general the patients enjoyed good health, many of them reaching advanced ages. However, eight out of seventeen in whom radiographs of the knees were obtained had bilateral degenerative arthritis which restricted their daily activities. Figure 9 shows the knees of a patient who was almost housebound because of pain. Many others complained of pain in the hip of variable severity, with consequent restriction of activity.

Pedigree analyses have shown that congenital coxa vara is a hereditary condition. An autosomal dominant inheritance is present because it has been found in four successive generations by radiographic studies and in thirteen generations by history. The ratio between affected and non-affected is close to 1:1 regardless of sex. Furthermore, certain unaffected family members have given birth to normal children. The variable expressivity of the condition among the patients studied may also be considered as evidence of the dominant nature of this particular mutant gene. The penetrance of the gene seems to be close to 100 per cent.

In conclusion, the condition seen in some of the people living in Gonyeli in Cyprus is a hitherto undescribed systemic entity. The cardinal findings of this syndrome include short stature, coxa vara and bowing of the legs. Additionally in some, relative iliac hypoplasia and protrusio acetabuli are seen. Pedigree analyses indicate that it is inherited as an autosomal dominant trait.

SUMMARY

1. Observations on ninety-four persons with congenital coxa vara living in a Turkish village named Gonyeli in Cyprus are presented.
2. Various clinical and laboratory studies showed, in addition to the congenital coxa vara of varying severity, marked short stature and bowing of the lower extremities in almost all affected individuals and relative iliac hypoplasia and protrusio acetabuli in some.
3. Pedigree analysis indicates that this hitherto undescribed condition is inherited as an autosomal dominant trait.

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REFERENCES