CLEFT LIPS AND PALATES
IN NORTHUMBERLAND AND DURHAM

BY

GEORGE KNOX and FENTON BRAITHWAITE
From the Departments of Child Health and Surgery, King's College, University of Durham, Newcastle upon Tyne

(RECEIVED FOR PUBLICATION JULY 27, 1962)

Under present-day conditions, and particularly because of the statutory examination of all children of school age through the School Health Service, we can be certain that almost all cases of cleft lip and palate in Great Britain come to notice and are referred for surgical treatment. The exceptions are those infants who are stillborn or who die before being referred, but even of the latter a considerable proportion will find their way into hospital index systems. In this region surgical care is concentrated in a few specialized units, making possible the ascertainment of all cases from a defined population over a defined period of time and affording an opportunity of measuring the incidence.

The object of this study is the measurement of the incidence of the various types of cleft lips and palates in the counties of Northumberland and Durham in the 10 years 1949 to 1958.

Methods and Material

The method of measurement was the systematic perusal of the hospital index systems, waiting lists and admission notes at the Newcastle General Hospital, The Royal Victoria Infirmary, Newcastle, the Babies' Hospital, Newcastle, the Hospital for Sick Children, Newcastle, and the Children's Hospital, Stockton, for the years 1949 to 1960. In order to be sure about the more remote areas of Northumberland and particularly with respect to the possibility that some patients may have gone to Edinburgh for treatment, further supplementary inquiries were made. This was done through the School Medical Service, the Maternity and Child Welfare Service, and through the health visitors for the area. A further search was made at Edinburgh; fortunately a study of cleft lip and palate is being carried out there too and the results of this were made available to us. So far as we know, all patients referred for surgical treatment are thus covered. We inquired at all other hospitals in the area, which regularly admit children, and have failed to find any other cases. Children dying at home at a very early age or stillborn, for example those with multiple malformations, are the only ones likely to have escaped.

Cases accepted for analysis were defined as any born within the time limits January 1, 1949, to December 31, 1958, a total of 10 years, and giving an address within the geographical limits of Northumberland and Durham. Care was taken to avoid duplication of records when children were admitted more than once or to more than one hospital, and we accepted addresses given at the time they were referred for a primary opinion or operation. Since we were unlikely to find any affected infants who might have moved away from the area before being referred to hospital, we excluded them as a matter of policy, but accepted any born outside the area who had moved into it by the time of their first operation. This is irrespective of the place of operation and we found two who were treated at Edinburgh. Children who had already had a first operation outside our area at the time of moving into it, were excluded. The problem of children referred or treated relatively late was met in large part by continuing the scrutiny for two years after the last date of birth acceptable for inclusion in this survey, and by including a search of the waiting lists. In practice we found that for children born in the early years almost all were referred before 18 months of age, and the only exceptions were a few referred later from speech therapists for nasal speech and sub-mucous clefts. The numbers affected by these various details were very small.

The limits of the area chosen are the sea to the East, the Scottish Border and the river Tweed to the North, the sparsely-populated Cheviot Hills and Pennines to the West, and the river Tees in the South. Except in the South, where the administrative border divides the populous area of Tees-side, these are natural divisions of population and there is a considerable degree of isolation from other densely-populated areas.

Newcastle upon Tyne on the North bank of the River Tyne is the largest city with a population of 292,000, and forms part of the conurbation of Tyneside with a total population of 835,000; two-thirds of this population is on the north (Northumberland) bank of the river. Outside the conurbation, however, Durham is relatively populous compared with Northumberland and contains the towns of Sunderland, Darlington, Hartlepool, West Hartlepool and Stockton. The total population of the two counties is 2,175,000, and the maximum North-South and East-West dimensions of the study area are about 90 and 45 miles respectively.
Results

We collected records of 574 clefts of lip and palate. There were registered during the same period 404,124 live births, giving a ratio of 1.42 per 1,000 live births (S.E. 0.06).

The regional distribution is given in Table 1. The estimates are reasonably constant in different districts of the North East except that Newcastle has a rather high incidence, significant formally at the 5% level. None of the other deviations approaches statistical significance. More detailed scrutiny of the distribution within Northumberland showed a surprising deficiency in the northern part of the county. There were 8,051 live births in the 10 years in the area covered by the Urban District of Alnwick, Berwick M.B., and the Rural Districts of Alnmouth, Belford, Glendale and Norham, but only two children with clefts against a proportionate expected number of 11.4. It was because of this deficiency that we made special efforts to check the completeness of our study in this part of the region. Since the survey ended we have records of three more affected infants from the area, and the apparent deficiency may eventually prove not to be a consistent one, but the detection of other very low incidence areas elsewhere would be of special interest.

The apparent excess in Newcastle seems to be limited entirely to cases of cleft lip. Of the 86 clefts in Newcastle, 25 were of this variety, giving a rate of 0.71 per 1,000 live births compared with 0.41 per 1,000 for the rest of the area ($\chi^2 = 8.34, p < 0.005$).

Type of Lesion. Of the 574 children, 181 (31.6%o) had only a lip lesion or a lip lesion with a notch of the gum; 188 (32.8%o) had only a palate lesion either of soft palate alone or of both hard and soft palate; the remaining 205 children (35.7%o) had combined lesions of lips and palates, the majority of them with complete clefts, either unilateral or bilateral.

Isolated cleft lip was usually pre-alveolar, only 16 having definite alveolar notches. Two cases also had bifid uvula, but are included here rather than with the combined lips and palates. Of those in which the side of the lesion was clearly recorded, 84 were on the left, 53 were on the right, 12 were bilateral and three were apparently median. It is appreciated, however, that an apparently median cleft may sometimes in fact be a bilateral cleft with a very small premaxilla. There were no evident differences between the sexes in terms of laterality, except that the three median clefts were all in girls.

Of the isolated cleft palates, six were purely submucous soft palate clefts and another two submucous with a bifid uvula; 49 involved only the soft palate; nine involved the soft palate with a minor cleft of the hard palate; 106 were complete or almost complete post-alveolar clefts; the remainder were not completely specified.

Of the combined lip and palate lesions, 56 were complete bilateral clefts, 81 were complete left clefts, and 33 were complete right clefts; another four children had a complete cleft on one side with a pre-alveolar cleft on the opposite side. As well as these last four there were 14 examples of bridged clefts, usually a lip cleft separated from a palate cleft by an intact alveolus or hard palate or both. Although one presented the unusual picture of an anterior cleft involving all structures as far back as the soft palate which was intact. Possible additions to the list of bridged lesions are the two cases of cleft lip with bifid uvula mentioned earlier. The remaining cases were incompletely specified, most of them being unilateral complete clefts with the side not recorded. There was no evidence of heterogeneity of sex ratio with respect to laterality or completeness of combined clefts.

Associated Malformations. The three children with median cleft lips are a special group. One also had a bifid nose and when admitted at a later date for an injury, was found to have an abnormal electroencephalogram. Another is known to be mentally retarded. The third has not been followed up.

Only three of the children with lateral cleft lips had other recorded malformations; one had a deformity of the spine, one had a short neck, an abnormal facial appearance and well-marked epicanthic folds, and another died with a tracheoesophageal fistula.

A larger proportion of children with cleft palate had other defects recorded. Five had a considerable degree of micrognathia (Pierre-Robin syndrome)
and one of them died. Another ten had skeletal defects of which cleft palate was a part. These included Marfan's syndrome, Madelung's deformity, absence of thumb and radius and a heart malformation, hydrocephalus, microcephaly with microphthalmos, teratoma of skull, craniostenosis, short humeri, severe talipes, and a widespread deformity that included dislocated knees. Visceral malformations were less frequent, but two further children had congenital heart disease, one with anal stenosis died, and another had hydronephrosis. Two children, including one with heart disease, were known to be mentally defective, another was deaf, and two, brother and sister, had a cerebromacular degeneration combined with cleft palate. One other child later developed pyloric stenosis.

Combined clefts of lip and palate were also sometimes part of a wider skeletal malformation. These included micrognathia, synderactyly, bifid thumb, a severe scoliosis, severe talipes, and one child had the curious combination of a deep pit in the midline of the lower lip and contractures of the legs. Visceral defects included three cases of congenital heart disease, one of imperforate anus and one of hydrocephalus. Three children were known to be mentally defective, one of them a mongol and another epileptic.

The proportions with associated defects were cleft lip, 2-8%; cleft lip with palate, 7-3%; cleft palate, 12-2%. The overall rate was 7-5%.

Sex Ratios of Different Lesions. One of Fogh-Andersen's (1942) reasons for postulating that isolated cleft palate differed from the other two main types of lesion was the difference he observed in the sex ratios. Our results are given in Table 2 and confirm that observation. The ratio for cleft lip is statistically indistinguishable from that for combined clefts of lip and palate, and their combined ratio is significantly different from the sex ratio of isolated cleft palate. This finding has also been confirmed by MacMahon and McKeown (1953), by Gylling and Soivio (1962), and by others.

Further evidence of heterogeneity by sex ratio is given in Table 3 where complete post-alveolar cleft is compared with lesser degrees of cleft palate. The high female/male ratio characteristic of cleft palate is seen to be limited to complete post-alveolar cleft. Fogh-Andersen (1942) made similar observations.

Table 2: Sex and Type of Lesion

<table>
<thead>
<tr>
<th>Cleft Type</th>
<th>Male</th>
<th>Female</th>
<th>Male</th>
<th>Female</th>
<th>Male</th>
<th>Female</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cleft Lip</td>
<td>113</td>
<td>68</td>
<td>139</td>
<td>66</td>
<td>77</td>
<td>111</td>
<td>329</td>
<td>245</td>
</tr>
<tr>
<td>Cleft Lip and Palate</td>
<td>181</td>
<td>205</td>
<td>188</td>
<td>574</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$\chi^2 = 5.64, p < 0.025$

* Extent of cleft not specified in remainder.

Table 3: Cleft Palate: Extent and Sex

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Female</th>
<th>Male</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete post-alveolar cleft</td>
<td>72</td>
<td>34</td>
<td>106</td>
</tr>
<tr>
<td>Submucous, soft palate, soft palate and minor hard palate defect</td>
<td>104</td>
<td>68</td>
<td>172</td>
</tr>
</tbody>
</table>

Distribution by Season and by Year. The seasonal distribution of the three types of lesion over the 10 years is given in Table 4. There is no evidence of a seasonal variation.

Year by year variations are given in similar fashion in Table 5. Neither cleft palate nor cleft lip with palate show any convincing variation by year, but cleft lip shows a greater fluctuation. By calculating expected annual figures according to the annual number of live births $\chi^2$ for cleft lip is 18-4, which is significant at the 5% level. 1950 and 1958 were particularly bad years and produced

Table 4: Clefts of Lip and Palate, 1949 to 1958: Seasonal Distribution

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cleft lip</td>
<td>14</td>
<td>16</td>
<td>16</td>
<td>18</td>
<td>16</td>
<td>14</td>
<td>12</td>
<td>15</td>
<td>19</td>
<td>13</td>
<td>13</td>
<td>10</td>
<td>176</td>
</tr>
<tr>
<td>Cleft lip with palate</td>
<td>13</td>
<td>19</td>
<td>24</td>
<td>16</td>
<td>18</td>
<td>20</td>
<td>11</td>
<td>15</td>
<td>6</td>
<td>17</td>
<td>19</td>
<td>23</td>
<td>201</td>
</tr>
<tr>
<td>Cleft palate</td>
<td>14</td>
<td>11</td>
<td>16</td>
<td>14</td>
<td>18</td>
<td>15</td>
<td>17</td>
<td>21</td>
<td>22</td>
<td>7</td>
<td>14</td>
<td>19</td>
<td>188</td>
</tr>
</tbody>
</table>

41  46  56  48  52  49  40  51  47  37  46  52  565*

* Exact month not recorded in nine cases.
more cases of cleft lip than the four years 1951 to 1954.

Discussion

The regional incidence of all clefts of lip and palate, 1.42 per 1,000, is comparable with other estimates. Gylling and Soivio (1962) quote 18 studies, including their own in Finland, with a range of 0.57 to 1.83 per 1,000 births. Five other studies not quoted by them are (i) the only recent large British study by MacMahon and McKeown (1953), with an incidence of 1.30 per 1,000 total births in Birmingham; (ii) a study by Bulatovskaya (1959), giving an incidence of 0.80 per 1,000 births in the Sverdlovsk region of the Urals; (iii) a Canadian study (Curtis, Fraser and Warburton, 1961), giving a combined incidence, in Ontario and Montreal, of 1.07 per 1,000 births; (iv) Pleydell (1957) found an incidence of 1.57 per 1,000 in Northamptonshire, and (v) Rank and Thomson (1960) found an incidence of 1.66 per 1,000 live births in Tasmania. The 10 studies which were based upon more than 100 cases range in their estimates between 0.66 and 1.66 per 1,000 births.

It is difficult to make positive comments upon the consistency of these different estimates since ascertainment clearly varies both in intended method and in reliability of execution, and the definitions of the included malformations are not always precise. Nevertheless, there is an apparent range such that the highest estimates are more than twice the lowest, and although each estimate individually (including the present one) may be considered to be in reasonable general agreement with the others there are sufficient now to suggest a considerable degree of variation among them.

There is further evidence of variation in the relative proportions of infants with different types of deformities. Hixon (1951) reports isolated cleft palate in 19% of cases, our own figure is 33%, while Gylling and Soivio (1962) reported 53%. On the other hand, Gylling and Soivio report 11.5% isolated cleft lips, MacMahon and McKeown (1953) report 23%, while Bulatovskaya, Hixon, Fogh-Andersen and the present authors found proportions in the range 30 to 33%. Absolute rates for different types of malformations are difficult to interpret because of small numbers, but the variations are considerable; for example, the Sverdlovsk data give an incidence for isolated cleft palate of 0.20 per 1,000, while the Helsinki data give 0.95 per 1,000.

It is of particular interest to compare our own results with those of MacMahon and McKeown, the only other large recent study in this country. For isolated cleft palate the respective incidences for Birmingham and Newcastle are 0.49 and 0.46 per 1,000; for cleft lip with palate 0.51 and 0.51 per 1,000; for isolated cleft lip 0.30 and 0.45 per 1,000. It is isolated cleft lip which accounts entirely for the difference in overall incidence. Because this particular component may vary so considerably between two essentially similar areas and two essentially similar populations at a distance of only 200 miles, and because of its local regional variations and its year-to-year variations in incidence, there is a strong suggestion of the existence of a labile determining factor and of heterogeneity of aetiology between some cases of cleft lip and other deformities.

The other much-quoted suggestion of heterogeneity is mainly based upon the sex ratios of the different malformations and suggests that isolated cleft palate is aetologically distinct. The finding has been confirmed several times. However, so far as we know this study supplies the first independent confirmation of Fogh-Andersen's (1942) original observation that the high female/male ratio is limited to complete post-alveolar clefts and does not apply to lesser degrees of cleft palate. This is of some importance because it corrects a discernible tendency towards an oversimplified view of the aetiology of the group of malformations as a whole. There are probably several aetiological mechanisms for each type of malformation and more than one possible consequence of each causal factor, and heterogeneity may be demonstrated at different levels by using different methods. The association with a wide variety of other malformations in a considerable proportion of cases, and the variation of the proportion between each of the main groups

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cleft lip</td>
<td>13</td>
<td>30</td>
<td>14</td>
<td>13</td>
<td>14</td>
<td>12</td>
<td>21</td>
<td>16</td>
<td>20</td>
<td>28</td>
<td>181</td>
</tr>
<tr>
<td>Cleft lip with palate</td>
<td>25</td>
<td>22</td>
<td>17</td>
<td>28</td>
<td>20</td>
<td>20</td>
<td>16</td>
<td>19</td>
<td>17</td>
<td>21</td>
<td>205</td>
</tr>
<tr>
<td>Cleft palate</td>
<td>18</td>
<td>24</td>
<td>19</td>
<td>21</td>
<td>19</td>
<td>21</td>
<td>17</td>
<td>14</td>
<td>15</td>
<td>20</td>
<td>188</td>
</tr>
<tr>
<td></td>
<td>56</td>
<td>76</td>
<td>50</td>
<td>62</td>
<td>53</td>
<td>53</td>
<td>54</td>
<td>49</td>
<td>52</td>
<td>69</td>
<td>574</td>
</tr>
</tbody>
</table>
in different studies, confirm the probable complexity of the pattern.

The present findings, and comparisons with those of Fogh-Andersen and of MacMahon and McKeown, suggest in particular that a component of cleft palate demonstrates the existence of an aetiological factor distinctively associated with a high female/male ratio, while a component of cleft lip seems to demonstrate the existence of a labile determinant. This seems to be a more correct formulation than a statement that one particular type of malformation is as a whole biologically distinct from the others.

Summary

The incidence of clefts of lip and palate is measured in Northumberland and Durham and found to be 1:42 per 1,000 live births.

Cleft lip in particular shows considerable local variations in incidence, considerable variations in incidence between years, and alone differs in incidence from the only other large recent study in this country. A labile determinant for this malformation is postulated.

Sex ratios suggest that complete post-alveolar cleft, but not lesser degrees of cleft palate, contains a distinctive aetiological group.

Variations between types of cleft in the rates of associated malformations confirm the probable complex aetiology of the group of malformations as a whole.

We are indebted to the Eugenics Society for a grant towards cost of this work, to Mr. J. Potter at the Stockton Children's Hospital for access to case notes, to Dr. T. T. S. Ingram of the Department of Child Life and Health, University of Edinburgh for information, to Dr. J. M. H. Hopper, Senior School Medical Officer for Northumberland for arranging inquiries in the northern rural areas, to Professor S. D. M. Court for advice and interest, and to many others for assistance.

References