The incidence of Down’s syndrome over a 19-year period with special reference to maternal age

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SUMMARY  The incidence of Down’s syndrome in the Liverpool and Bootle areas from 1961 to 1979 was investigated. A total of 319 liveborn cases was ascertained over this period. Using 3-year moving averages, the incidence of the condition fell gradually from 1.62 per 1000 livebirths for 1961 to 1963 to 1.09 per 1000 livebirths for 1977 to 1979. This trend is significant at the 0.1% level. Over the same period the mean maternal age of Down’s syndrome births fell gradually from 36.7 years in 1961 to 29.0 years in 1979. This trend is significant at the 1% level. There was a contemporaneous decrease in the proportion of total births to women over 35 years in the study area.

Cytogenetic analysis was performed on 175 out of the 319 index cases (54.9%). Of these, there were 161 trisomies (92%), 11 translocations (6.3%), and three mosaics (1.7%). Between 1969 and 1979 four terminations of pregnancy for Down’s syndrome were performed, all for trisomy.

Quinquennial age specific incidences for Down’s syndrome were calculated for the years 1960 to 1964, 1965 to 1969, 1970 to 1974, and 1975 to 1979. There have been no statistically significant changes over this time. It is suggested that the fall in incidence of Down’s syndrome can be explained by the fall in mean maternal age.

Chromosomal abnormalities account for 3 to 5% of all congenital malformations. Down’s syndrome is the commonest and most important of these, having an incidence usually quoted as 1.5 per 1000 livebirths. Several recent reports have noted a decline in incidence of this condition and have suggested possible causes for this. The Liverpool Congenital Malformations Registry has been in existence since 1960 and it was decided to investigate the epidemiology of Down’s syndrome over this period, with special reference to the effect of maternal age and termination of pregnancy on the incidence.

Methods

Babies born with congenital malformations in the study area of Liverpool and Bootle are notified to the Registry by the paediatric registrars of the hospitals in which the births occurred. Secondary searches are made in the Supraregional Paediatric Cardiology Unit and Regional Neonatal Surgical Unit to improve ascertainment. In this study Down’s syndrome was investigated for the years 1961 to 1979 by the withdrawal of data from computer based records held in the Registry.

Total live and stillbirths for Liverpool and Bootle were obtained from the Liverpool and Sefton Area Health Authorities respectively. Quinquennial maternal age specific births for Liverpool for 1963 to 1979 were obtained from OPCS, London. Bootle births were assumed to have the same maternal age distribution. Quinquennial groups are not available for Liverpool County Borough before 1963 but are published for the Merseyside conurbation. In calculating quinquennial age specific births for 1961 to 1962 the distribution for Liverpool and Bootle is assumed to be similar to Merseyside as a whole.

Information regarding chromosomal analysis was obtained from the Regional Cytogenetics Unit, Royal Liverpool Hospital. All amniocentesis material obtained in the Liverpool and Bootle areas because of advanced maternal age is referred to this Unit and a record is kept of results of chromosomal analysis and the outcome of pregnancies. Data on terminations of pregnancy from Down’s syndrome were obtained from this source.

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Results

Over the years 1961 to 1979 there were 233 251 live and stillbirths in the Liverpool and Bootle areas. During this period 7575 congenital malformations were notified to the Liverpool Registry, giving a malformations rate of 3.25%. A total of 319 liveborn cases of Down’s syndrome was ascertained, an incidence of 1.39 per 1000 livebirths.

Of the 319 index cases, 175 were verified cytogenetically (54.9%, table 1). The figures for 1961 to 1969 and 1970 to 1979 are 47.7% and 81.5% respectively. Of the 175 cases, 161 (92%) were trisomies, 11 (6.3%) were translocations, and 3 (1.7%) were mosaics. Between 1969 and 1979 four terminations of pregnancy were performed for Down’s syndrome. All of these were trisomies.

During the years of the study, the incidence of Down’s syndrome has fallen steadily from a mean of 1.69/1000 livebirths for the period 1961 to 1964 to 1.07/1000 livebirths for 1975 to 1979 (table 2). When the incidence is plotted using 3-year moving averages this trend is significant at the 0.1% level (fig 1). Over this time there has been a very considerable fall in annual livebirths and birth rate, from 18 663 in 1961 to a low of 6962 in 1977, and from 22.0/1000 to 11.8/1000, respectively (table 3).

Mean maternal age of Down’s syndrome livebirths has also fallen steadily, from 36-7 years in 1961 to 29-0 years in 1979 (fig 2). This trend is significant at the 1% level. The proportion of all births in mothers aged 35 years and over in Liverpool has shown a gradual decline from 13.1% in 1961 to a low of 5.6% in 1978 (fig 3). There has been a decline in Down’s syndrome births in these older mothers since the early 1970s.

Maternal age specific incidence for Down’s syndrome was calculated for each 5-year age group for the years 1961 to 1964, 1965 to 1969, 1970 to 1974, and 1975 to 1979 (table 2). Although these figures show an apparent decline in age specific incidence

![Incidence of Down's syndrome in Liverpool and Bootle, 1961-1963 to 1977-1979: 3-year moving averages](http://jmg.bmj.com/)

**FIG 1** Incidence of Down's syndrome in Liverpool and Bootle, 1961-1963 to 1977-1979: 3-year moving averages (p = <0.001).

**TABLE 1** Cytogenetics: chromosomal analysis.

<table>
<thead>
<tr>
<th>Chromosomal analysis</th>
<th>No</th>
<th>Percentage of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trisomy 21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Livebirths</td>
<td>161</td>
<td>92</td>
</tr>
<tr>
<td>Terminations</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Translocations</td>
<td>11</td>
<td>6.3</td>
</tr>
<tr>
<td>Mosaics</td>
<td>3</td>
<td>1.7</td>
</tr>
<tr>
<td>Total (excluding terminations)</td>
<td>175</td>
<td>100</td>
</tr>
</tbody>
</table>

**TABLE 2** Maternal age specific incidence of Down’s syndrome per 1000 livebirths.

<table>
<thead>
<tr>
<th>Maternal age group</th>
<th>Total</th>
<th>&lt;20</th>
<th>20-24</th>
<th>25-29</th>
<th>30-34</th>
<th>35-39</th>
<th>40-44</th>
</tr>
</thead>
<tbody>
<tr>
<td>1961-64</td>
<td>1.69</td>
<td>1.00</td>
<td>0.65</td>
<td>0.81</td>
<td>1.39</td>
<td>3.79</td>
<td>17.58</td>
</tr>
<tr>
<td>1965-69</td>
<td>1.46</td>
<td>0.50</td>
<td>0.36</td>
<td>0.73</td>
<td>1.56</td>
<td>4.61</td>
<td>15.71</td>
</tr>
<tr>
<td>1970-74</td>
<td>1.10</td>
<td>0.44</td>
<td>0.60</td>
<td>0.68</td>
<td>0.77</td>
<td>4.06</td>
<td>13.36</td>
</tr>
<tr>
<td>1975-79</td>
<td>1.07</td>
<td>0.80</td>
<td>0.47</td>
<td>1.04</td>
<td>0.97</td>
<td>5.20</td>
<td>6.96</td>
</tr>
</tbody>
</table>

*Figures not yet available.

**TABLE 3** Annual livebirths, birth rate, and Down’s cases ascertained in the Liverpool and Bootle areas 1961-1979.

<table>
<thead>
<tr>
<th>Year</th>
<th>Livebirths</th>
<th>Birth rate/1000 population (Liverpool only)</th>
<th>No of Down’s cases ascertained</th>
</tr>
</thead>
<tbody>
<tr>
<td>1961</td>
<td>18 663</td>
<td>22-0</td>
<td>26</td>
</tr>
<tr>
<td>1962</td>
<td>18 165</td>
<td>22-0</td>
<td>28</td>
</tr>
<tr>
<td>1963</td>
<td>17 626</td>
<td>21-5</td>
<td>34</td>
</tr>
<tr>
<td>1964</td>
<td>17 866</td>
<td>21-7</td>
<td>34</td>
</tr>
<tr>
<td>1965</td>
<td>16 217</td>
<td>20-5</td>
<td>27</td>
</tr>
<tr>
<td>1966</td>
<td>15 099</td>
<td>19-0</td>
<td>27</td>
</tr>
<tr>
<td>1967</td>
<td>13 970</td>
<td>18-0</td>
<td>21</td>
</tr>
<tr>
<td>1968</td>
<td>13 289</td>
<td>17-4</td>
<td>12</td>
</tr>
<tr>
<td>1969</td>
<td>12 662</td>
<td>16-8</td>
<td>17</td>
</tr>
<tr>
<td>1970</td>
<td>12 055</td>
<td>16-0</td>
<td>10</td>
</tr>
<tr>
<td>1971</td>
<td>10 791</td>
<td>15-8</td>
<td>18</td>
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<tr>
<td>1972</td>
<td>9 696</td>
<td>14-5</td>
<td>13</td>
</tr>
<tr>
<td>1973</td>
<td>8 652</td>
<td>13-0</td>
<td>9</td>
</tr>
<tr>
<td>1974</td>
<td>7 987</td>
<td>12-1</td>
<td>4</td>
</tr>
<tr>
<td>1975</td>
<td>7 394</td>
<td>11-8</td>
<td>8</td>
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<tr>
<td>1976</td>
<td>7 241</td>
<td>11-4</td>
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<tr>
<td>1977</td>
<td>6 962</td>
<td>11-8</td>
<td>13</td>
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<tr>
<td>1978</td>
<td>7 161</td>
<td>12-4</td>
<td>5</td>
</tr>
<tr>
<td>1979</td>
<td>7 836</td>
<td>11-8</td>
<td>6</td>
</tr>
</tbody>
</table>

*Figures not yet available.
Discussion

In a paper on babies with congenital malformations drawn from a Liverpool based hospital population of 13,964 between 1923 and 1932, Malpas reported 18 cases of Down's syndrome, an incidence of 1.29/1000 total births.\(^{7}\) Our more recent data show there has been a gradual decrease in the overall incidence of Down's syndrome in Liverpool and Bootle from 1.39/1000 livebirths in 1961 to 0.77/1000 livebirths in 1979. This has been accompanied by a concurrent decrease in maternal age, both for the general population and Down’s syndrome births. Over this period the maternal age specific incidence has not changed significantly from year to year. When the data for 1961 to 1979 are pooled (table 4) the age specific incidences are very similar to those for Sweden between 1968 and 1970.\(^{2}\)

Our results suggest that the decreasing incidence of Down’s syndrome in Liverpool and Bootle is due primarily, if not entirely, to the decrease in mean maternal age in the population. The commonest chromosomal abnormality in Down’s syndrome is trisomy 21\(^{2-6} 8-11\) (92% in our series) and the incidence of this is maternal age dependent. Thus a reduction in mean maternal age would inevitably lower the incidence.

An antenatal screening programme has been available in the Mersey Region since 1969 but between 1969 and 1974 only 2.37% of women over 35 years were given amniocentesis for cytogenetic investigation. Between 1975 and 1979 this rose to 16.37% (S Walker, unpublished data). Assuming the uptake in Liverpool and Bootle to be similar to the region as a whole, then during the period 1969 to 1979, approximately 471 women over 35 years were given an antenatal test for Down’s syndrome and four terminations for trisomy Down’s syndrome were performed. Using birth frequency figures over the same period, 3.09 cases of Down’s syndrome would have been expected as livebirths from this group of mothers over 35 years. Therefore, while the screening programme was effective, it had little effect on the overall incidence of Down’s syndrome because of the low percentage of women given antenatal diagnosis.

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</tr>
<tr>
<td>Sweden 1968–1970</td>
<td>0.59</td>
<td>0.74</td>
<td>0.88</td>
<td>1.46</td>
<td>3.74</td>
<td>17.74</td>
</tr>
</tbody>
</table>

Several other reports have shown a decline in the overall incidence of Down's syndrome, but this decline has not been universal. Some have also shown a variety of changes in the maternal age specific incidence, for example, a rise in the 20 to 29 year age group and the over 40 age group in Sweden, a rise in the 35 to 39 year group in Manitoba, a rise in the over 35 year group in New York State, and a rise in the 20 to 34 year group in Charleroi. Although these may represent real changes dependent on local environmental factors, it is perhaps more likely that they are the result of improved ascertainment as all of the changes reported have been increases rather than decreases. The role of the paternal age contribution has not yet been established in relation to changes in incidence.

In a recent paper we drew attention to a fall in the incidence of neural tube defects over the same period in the Liverpool and Bootle areas, which was almost unaffected by the number of terminations performed. The decline in incidence of Down's syndrome reported here has a more obvious cause, reduction in maternal age, but is similarly unaffected by the screening programme.

The proportion of mothers over 35 years giving birth has halved over the last decade. The cost-effectiveness of antenatal screening for Down's syndrome in this age group can be further enhanced by increasing considerably the take-up of the antenatal screening, which in 1980/1981 was 40% of women over 35 years (S Walker, unpublished data).

Lilienfeld and Benesch, in their monograph on the epidemiology of mongolism published in 1969, said “One finds that about 20% of mongol births would be born to mothers 40 years of age and over. This suggests that a relatively simple means of decreasing the number of mongols is available by limiting the number of pregnancies among older mothers. One would expect a decrease of between 20 to 45% in the frequency of mongolism if family limitation was practiced by mothers 35 to 40 years of age.”

This has been borne out by the fall in the number of pregnancies in older mothers with a commensurate fall in babies with Down's syndrome born to women in Liverpool and Bootle during the period of study.

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References


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