Correspondence

Drugs, infections, and congenital anomalies

Sir,

In his annotation under this title (Archives, 1978, 53, 93) Smithells states that all evidence to suggest a teratogenic role for sex hormones has been 'derived from retrospective studies, whereas all prospective studies published show no such effect'. This is incorrect. In a follow-up study of 50,282 pregnancies we reported an approximate doubling of the cardiovascular malformation rate in 1042 children exposed in utero to female hormones during the first 4 lunar months of pregnancy (Heinonen et al., 1977).

Under a causal hypothesis, an association should be evident and relatively invariant regardless of whether the results are derived from prospective (or more precisely, cohort) studies, or from retrospective (case-control) studies. In fact, when different research strategies support each other, a causal inference is strengthened. The classical work of Lenz (1962) in documenting a connection between limb-reduction deformities and in utero exposure to thalidomide was a case-control study.

References


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Professor R. W. Smithells comments:

I am grateful to Drs Slone and Shapiro for calling my attention to their excellent study. It was perhaps foolish of me to attempt to summarise the evidence regarding teratogenicity of sex hormones in one sentence. Their findings (that the relative risk of congenital heart disease in infants exposed to combined oestrogen/progestogen was significantly increased [P<0.05], and in infants exposed to oestrogens or progestogens was increased, but not significantly), considered in conjunction with other prospective studies which have shown no increase in malformation rates among exposed infants, lead me to believe that my classification of sex hormones as 'possible' rather than 'probable' teratogens is justifiable at present.

I certainly did not intend to disparage retrospective studies. Nearly all known human teratogens have been initially identified or suspected this way. I accept that when case-control and cohort studies agree they strengthen each other. If I may rephrase my offending sentence, I think it is fair to say that 'the suggestions of teratogenicity (of sex hormones) mainly derive from retrospective studies, whereas most prospective studies published show no such effect'.

English law insists that the prisoner is innocent until proved guilty. Scottish law allows a verdict of 'not proven', which may be appropriate until further studies have been completed.

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The first feed of low birthweight infants: changing attitudes in the twentieth century

Sir,

I read the review article under this title by D. P. Davies (Archives, 1978, 53, 187) with particular interest, as I had just completed a brief comparison of outcome at early school age in very low birthweight (LBW) infants born 1953-55 and 1966-70, with the results shown in the Table.

Table  Outcome, IQ, and type of school attended in low birthweight infants at early school age by year of birth

<table>
<thead>
<tr>
<th>Birthweight (g) and no. of cases</th>
<th>Born 1953-55 (n = 117)</th>
<th>Born 1966-70 (n = 264)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤1367</td>
<td>≤1367</td>
</tr>
<tr>
<td></td>
<td>1368-1500</td>
<td>1368-1500</td>
</tr>
<tr>
<td></td>
<td>(22) %</td>
<td>(29) %</td>
</tr>
<tr>
<td></td>
<td>1501-2000</td>
<td>1501-2000</td>
</tr>
<tr>
<td></td>
<td>(29) %</td>
<td>(181) %</td>
</tr>
<tr>
<td>IQ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥110</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>90-109</td>
<td>18</td>
<td>22</td>
</tr>
<tr>
<td>80-89</td>
<td>24</td>
<td>25</td>
</tr>
<tr>
<td>70-79</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>69</td>
<td>43</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>MH/PH*</td>
<td>50 (22)</td>
<td>6 (16)</td>
</tr>
</tbody>
</table>

*Attending schools for mentally or physically handicapped. Numbers of cases in parentheses.

Severe restriction of fluid and calorie intake, particularly in 1953-54, was routine practice for all infants of 3 lb (1367 g) or less; earlier feeding was generally attempted above that weight. The Table demonstrates a striking improvement by date of birth only in those who were 3 lb or less at birth. In view of the fact that all 1966-70...
Drugs, infections, and congenital anomalies.

D Slone and S Shapiro

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doi: 10.1136/adc.53.7.604

Updated information and services can be found at:
http://adc.bmj.com/content/53/7/604.1.citation

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