Correspondence

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The incidence of Down's syndrome over a 19-year period

SIR,

Owens *et al*¹ recently reported on the incidence of Down's syndrome in the Liverpool and Bootle areas for the years 1961 to 1979 inclusive. Cases were primarily identified from the Liverpool Congenital Malformations Registry. The overall incidence of Down's syndrome declined from 1.69/1000 livebirths for the years 1961 to 1964 to 1.07/1000 livebirths for 1975 to 1979.

Owens *et al*¹ attributed part, if not all, of the observed decrease in the incidence of Down's syndrome to a decline in the mean age of women having babies. While it is well recognised that women of 35 and over have an increased risk for delivering a child with Down's syndrome,² the fertility rate for this group is low. In British Columbia (BC), only 4% of livebirths are to women of 35 and over.³ Therefore, the overall contribution by these mothers to the total population of Down's syndrome livebirths is relatively low despite the increased risk for these women on an individual basis. In BC, only 20% of Down's syndrome livebirths are to women aged 35 and over.³ Therefore, a decrease in the mean maternal age of women having children would not necessarily dramatically decrease the incidence of Down's syndrome.

Another factor which may be responsible for the apparent decline is that less time for ascertainment has elapsed for the more recently born part of the cohort. The time before a person with a mental or physical handicap or both comes to attention is often appreciable and this 'lagtime' must be taken into account. It has been observed in BC that, even for a condition as well recognised as Down's syndrome, case identification increases for a given birth cohort with time.⁴ Data from the population based BC Health Surveillance Registry⁵ on the same birth cohort, analysed in 1963, 1967, and 1975, showed incidence rates per 1000 livebirths for Down's syndrome to be 0.83,⁶ 1.25,⁷ and 1.32,⁴ respectively. Increased case identification can therefore be expected for children born in 1961 to 1964 compared with those born in 1975 to 1979 as a result of the longer 'lagtime'.

In conclusion, we question whether the overall decline in the incidence of Down's syndrome observed for the Liverpool and Bootle areas can

entirely be attributed to a decrease in the mean maternal age of mothers. Other factors, such as less complete ascertainment for the more recently born part of the cohort, must also be considered.

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This letter was shown to Dr Owens *et al*, who reply as follows.

Professor Baird and Dr Sadovnick make three main comments in their letter:

- (1) *The fertility rate of women aged 35 years and over is low and only accounts for 4% of livebirths in British Columbia.* By reference to fig 3 of our paper it can be seen that fertility for this group in the late 1970s was very similar in Liverpool and Bootle, being 5.6% of total (livebirths + stillbirths) births for Liverpool AHA in 1978. However, this has not always been the case, the figure for 1961 being

13.1% with a gradual decrease in fertility over the two ensuing decades. We conclude that it is this trend which has accounted for the fall in incidence of Down's syndrome which we describe.

(2) *The overall contribution of Down's syndrome babies born to mothers aged 35 years and over is small, being only 20% of Down's syndrome livebirths in British Columbia.* Again, our fig 3 shows that the proportion of Down's syndrome livebirths born to this maternal age group has fallen over the two decades. Despite this, the proportion is not as small as in British Columbia, being 57.1% for 1961 to 1969 and 40.9% for 1970 to 1979.

(3) *Ascertainment for the latter years of the study may have been incomplete.* While not claiming total ascertainment we do not feel that many cases have been missed for several reasons. Firstly, since our paper was drafted 2 years ago we have only picked up two extra cases for the years 1975 to 1979. Secondly, nearly all Liverpool and Bootle births occur in hospital in a health area where the neonatal services are excellent. Thus, we do not find that there are many cases of Down's syndrome which are not recognised in the neonatal period. Finally, assuming that Lindsjo's¹ figures for the maternal age specific incidence of Down's syndrome apply universally, and knowing the annual total births for quinquennial maternal age groups for Liverpool over the period of study, an estimate of the number of cases of Down's syndrome which should have been born can be made. One finds that the estimated incidence falls gradually from 1.69 per 1000 livebirths in 1963 to a trough of 1.16 in 1977. This compares with an observed incidence of 1.62 per 1000 for 1961 to 1963 (using 3-year moving averages) to 1.09 for 1977 to 1979. Using the same calculated figures the degree of ascertainment can be estimated (observed cases of Down's syndrome ÷ estimated cases × 100%). This is 98.8% for 1963 to 1969 and 83.1% for 1970 to 1979. Thus, while we acknowledge that the lower ascertainment may have contributed slightly to the fall in incidence of Down's syndrome, we still believe that by far the major factor has been the decrease in mean maternal age in Liverpool and Bootle over the last two decades.

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Neural tube defects in sibs of children with tracheo-oesophageal dysraphism

SIR,

David and O'Callaghan¹ and Warren *et al*² reported an increased frequency of neural tube defects (NTD) in sibs of children with oesophageal atresia with or without tracheo-oesophageal fistula. They found NTD in nine of 495 sibs ($1.8 \pm 0.60\%$). At the same time, in the series by Chen *et al*,³ only one of 358 sibs had NTD and Fraser and Nussbaum⁴ found NTD in one of 141 sibs. Baird and MacDonald⁵ found no cases of NTD among sibs of 167 infants with tracheo-oesophageal dysraphism. Unfortunately, they gave no total number of sibs in their series. As the mean ratio affected:sibs is 1:1.8 in most American series,^{3,4} we can approximately evaluate the total number of sibs in the series of Baird and MacDonald⁵ as 300.

In our series, 105 cases (64 males and 41 females) with tracheo-oesophageal dysraphism were analysed. Additional anomalies were found in 56 cases, of which two had anencephaly and spina bifida. There were 81 sibs, none of whom had NTD, though in one case hydrocephalus was present. Other congenital malformations and genetic disorders were observed in eight sibs, including two with adreno-genital syndrome (in one family), two with inguinal hernia, and one each with thoracopagus, duodenal atresia, cleft lip/palate, and rib malformations.

It is well known that the frequency of NTD varies significantly in different populations. In England, and especially in Ireland and Wales, it reaches 5:1000, whereas in Canada or the USA it is nearer to 1:1500.^{6,7} In the USSR it is slightly lower than 1:1000.⁸ Therefore we divided the data on NTD frequency in sibs into two groups, according to the incidence of NTD in the population (table).

This shows that there is no evidence for an increased risk of NTD for the sibs of patients with

TABLE NTD in sibs of patients with tracheo-oesophageal dysraphism.

Population	No of sibs	NTD
A. High incidence of NTD		
David and O'Callaghan ¹ (England)	365	6
Warren <i>et al</i> ² (England)	130	3
Total	495	9 ($1.8 \pm 0.60\%$)
B. Low incidence of NTD		
Chen <i>et al</i> ³ (USA)	358	1
Fraser and Nussbaum ⁴ (Canada)	141	1
Baird and MacDonald ⁵ (Canada)	300	0
Our data (USSR)	81	0
Total	880	2 ($0.23 \pm 0.16\%$)