

COMMERCIAL IN CONFIDENCE  
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ARVI/86/1st Meeting

ARVI/86/3

COMMITTEE ON SAFETY OF MEDICINES  
JOINT COMMITTEE ON VACCINATION AND IMMUNISATION

JOINT SUB-COMMITTEE ON ADVERSE REACTIONS TO VACCINES AND IMMUNOLOGICAL PRODUCTS

THE UNIVERSITY OF NOTTINGHAM



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*Received  
30/12/85  
D.Z.*

13 December 1985

Dr D Zutshi  
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Dear *Senk*

I showed the Tabled Paper 1, (Appendix to ARVI/85/34) to Richard Madeley and he kindly prepared the enclosed observations. I agree with everything that he has said. As you know, at the meeting I had grave misgivings about the exercise and of the assumptions that were made. It was very interesting to me when I discussed it with Richard, that his first response was that he did not think a numbering exercise of this nature would resolve the problem, but rather the reverse.

I am sorry the response is not more positive.

Yours sincerely

Enc

UNIVERSITY OF NOTTINGHAM

MEMORANDUM

12th December 19 85

FROM.....  
DEPT. Community Medicine & Epidemiology  
EXTENSION..... 3552

TO.....  
DEPT. Child Health

RE: NOTE ON THE ESTIMATION OF SUDDEN INFANT DEATHS EXPECTED  
TO OCCUR BY CHANCE AFTER IMMUNISATION

1. Thank you for asking me to comment on this.
2. My note is divided into two sets of comments:-
  - a) relating to the hypothesis that immunisation may cause SIDS, and how the DHSS should react to it, and
  - b) relating to the statement prepared by the Statistics Division of the DHSS.
3. The hypothesis that immunisation may cause SIDS
  - a) The hypothesis, appearing in 1985, is surprising. Despite 30 years of intensive research in many countries, it has never before been suggested. An important research method used has been that of interviews with the parents of the dead child to try to evaluate possible pre-disposing factors. This has led to a number of fruitful areas of research, but many more which have been fruitless or even far-fetched. The problem is that the distraught parents will remember every little thing that happened that might conceivably have been related to SIDS. In view of this, it is almost beyond belief that something as dramatic as death immediately following vaccination would not have been volunteered by such parents long ago.
  - b) There is some already existing data which casts doubt on the hypothesis. Infants who do not attend child health clinics have higher mortality rates from all causes than those who do<sup>1</sup>.
  - c) Most deaths from SIDS occur before the age of four months<sup>2</sup>, when the first immunisation takes place.
  - d) There is no foolproof method of discrediting the hypothesis by statistical or epidemiological methods. On the contrary, there is a danger of getting drawn into a lengthy argument about numbers which neither side could win, thus giving more credibility to the hypothesis than it deserves.
  - e) This is particularly so if the statements prepared by the DHSS is in any way flawed, which I think is the case.

4. The statement prepared by the Statistics Division of DHSS

- A) Page 1, section entitled "Data Used". This section states that "the note uses data for England and Wales for 1983, which were readily available when the work was done" and "OPCS publishes statistics of sudden infant deaths". Both of these statements are true, but the problem is that two recent studies<sup>3,4</sup> undertaken by the OPCS itself have demonstrated that the published incidence of SIDS in official statistics is not an accurate reflection of the true incidence, because of the different habits of coroners and pathologists in different parts of the country. It is always essential to combine the published figures for SIDS with those for deaths from respiratory infections before any meaningful conclusions can be drawn.
- B) The list of "Assumptions Made" on Page 2 contains a number of factual inaccuracies, and other statements which seem unlikely to be true but are in any case irrelevant. The author states as a final conclusion on Page 4 that "the assumptions are unrealistic".
- i) Births are not evenly distributed throughout the year, according to OPCS statistics<sup>5</sup>. In 1983, the year mentioned, there was a difference of 8.1% between the highest and lowest quarter.
- ii) SIDS is not uniformly distributed throughout the year. Fedrick<sup>6</sup>, using data from the Oxford Record Linkage Study, writes of two distinct types of cot-death. Those which occur before 12 weeks have little variation, whereas those after 12 weeks have a marked seasonal variation.
- Carpenter and Gardner<sup>2</sup>, and Emery<sup>7</sup>, also distinguish between the "genuine cot-death as understood by the general public", i.e. one where a perfectly well child is put to bed and found dead subsequently, and other "cot-deaths" where symptoms of some sort have been present beforehand. The former type have little seasonal variation, though they seem to occur more often at weekends, but the second type are much more common in the winter. The important point is that both groups will be coded as SIDS in the official data on which the DHSS memorandum is based. Postneonatal deaths in general are much more common in the winter. This is particularly so for deaths from respiratory tract infections.
- iii) The statement that "children who die suddenly are as likely to be immunised as those who do not" seems unlikely to be true. Most SIDS deaths occur before the date of the first immunisation (a fact which casts doubt on the hypothesis), but infants who attend clinics before or after four months, have a lower risk of death, not higher.
- iv) Assumptions iii) and iv) use the word "all" and therefore by definition are unlikely to be correct.
- v) I know from personal experience with my own children that immunisations are not necessarily given at the recommended age, e.g. because of intercurrent illness.

- C) On the section "Variation in Assumptions", commencing at the bottom of Page 2, nothing needs to be added to the author's own conclusion on the top of Page 4 that "the lack of data means that the statements obtained using alternative assumptions can be little better than guesses". I think this is true for every single variation considered.

#### Final Comments and Conclusion

For those reasons, I think it would be extremely unwise for the DHSS to get involved in any type of epidemiological work on this hypothesis. The hypothesis seems most unlikely on grounds of basic scientific reasoning, and such evidence as already exists points in the opposite direction.

To go ahead in these circumstances would endow upon the hypothesis a respectability which it does not deserve. It is impossible to disprove through numbers. To try to do so, using flawed assumptions, as in the memorandum of the DHSS Statistics Division, weakens the position.

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## References

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4. Gardner, A., (1982), "An attempt to identify cases of the sudden infant death syndrome, from death certificates and hence determine the incidence", In Studies in the Sudden Infant Death Syndrome, Studies in Medical and Population Subjects No.45, pp.33-38, HMSO London.
5. OPCS Monitor (1984), "Live births during 1983", Ref. FMI, 84/1, OPCS London.
6. Fedrick, J., (1973), "Sudden unexpected death in the Oxford Record Linkage Area: an analysis with respect to time and place", Brit.J.Prex.Soc.Med, 27, 217-224.
7. Emery, J.L., (1976), In "Recent Advances in Paediatrics", ed. D. Hull, pp.208-9, Churchill Livingstone.