

## Absorption of hexachlorophane from dusting powder on newborn infants' skin

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### SUMMARY

In a maternity hospital in which the umbilicus and trunk of healthy newborn infants were treated with 0.33% hexachlorophane dusting powder, the hexachlorophane content of blood was measured in mothers before delivery, in infants' umbilical samples at birth, and at 8 days of age in capillary blood samples. One mother and her baby had rather high blood concentrations of hexachlorophane, probably derived from a toilet preparation used before admission to hospital. Hexachlorophane was absent or barely detectable in the other mothers' blood and in the infants' umbilical blood. The hexachlorophane concentrations in the blood of 8-day-old infants ranged from nil to 0.166  $\mu\text{g./ml.}$  (mean 0.066  $\mu\text{g./ml.}$ ). These were much less than the concentrations reported to be toxic in animals.

In a previous trial now reported here, a dusting powder containing chlorhexidine instead of hexachlorophane was found to delay the separation of the umbilical cord.

### INTRODUCTION

In a preliminary study (Alder, Burman, Corner & Gillespie 1972) small amounts of hexachlorophane were found in blood samples of infants whose skin was treated with 'Ster-Zac' dusting powder (containing 0.33% hexachlorophane) to prevent staphylococcal infection. The blood concentrations of hexachlorophane were less than those reported to be toxic in animals (Curley *et al.* 1971). It was evident, however, that blood obtained from the umbilical cord and by heel prick were liable to contamination by hexachlorophane on the skin and elsewhere, derived from powder used on infants in the nurseries and on infants and some mothers in the labour room. Hexachlorophane might also reach infants' blood from toilet preparations used by mothers before admission to hospital. Hence it seemed likely that hexachlorophane absorption through the skin was still less than that indicated by the blood analyses, with an even greater margin of safety. This would be consistent with the absence of reported damage to any of the many thousands of infants treated with 'Ster-Zac' powder, in many hospitals, since the method was introduced in Bristol about 18 years ago (Gillespie, Simpson & Tozer, 1958; Baber *et al.* 1967).

We report here a further study of hexachlorophane in infants' blood carried out

in the Bristol Maternity Hospital in 1973, with more stringent precautions to avoid contamination of the samples. Despite the opinion of Plueckhahn (1973) that capillary blood is necessarily unreliable because of contamination, heel-prick samples (also used for Guthrie tests) were again employed. We did not think it justifiable to take venous blood from newborn infants for experimental purposes. The mothers' blood was also analysed to detect hexachlorophane derived from toilet preparations.

The possibility, however remote, that hexachlorophane, even when correctly used, might have toxic effects, makes it relevant to consider other disinfectants as substitutes. One of these, chlorhexidine ('Hibitane') was investigated in Bristol about 13 years ago, but the trial was discontinued because of delay in the separation of the umbilical cords. These results, previously unpublished, are recorded here.

#### MATERIALS AND METHODS

The routine care of umbilicus and skin was as previously described (Alder *et al.* 1972) except that no hexachlorophane preparations were used by members of staff nor by mothers at any time after admission, and no hexachlorophane was used on infants in the labour room. The umbilical stump was sealed with 'Octaflex' in the labour room but 'Ster-Zac' powder was not applied to the umbilicus and flexures until the infant reached the nursery, within an hour or two of birth.

Three heparinized blood specimens were taken from each mother and her baby: (i) a venous sample from the mother, just before delivery, to detect hexachlorophane derived from toilet preparations used before admission to hospital, (ii) an umbilical cord sample collected in the labour room and (iii) more than 0.5 ml. of capillary blood by heel prick (also used for the Guthrie test), from the infant on the 8th day; before pricking the skin an assistant held the limb free from the bedding while it was thoroughly washed with 70% alcohol containing 0.4% ammonia and dried with cotton-wool.

Hexachlorophane in blood was measured as before, by gas/liquid chromatography at the Huntingdon Research Centre (Alder *et al.* 1972). The blank value was between 0.00 and 0.02  $\mu\text{g}$ . per ml. but no adjustment was made for this in the results.

#### RESULTS

Twenty-two mothers and their babies were investigated. Two babies left hospital before the 8th day, and the capillary blood samples from another three were insufficient. Among those remaining in the investigation, one mother (No. 21) had a high hexachlorophane concentration in her venous sample (0.211  $\mu\text{g}$  per ml.); her baby also had high concentrations in umbilical and heel-prick samples (0.158  $\mu\text{g}$ . per ml. and 0.307  $\mu\text{g}$ . per ml. respectively). These results could not be attributed to the use of hexachlorophane in hospital. The most likely explanation was the presence of hexachlorophane in one of several toilet preparations which this lady admitted to using before admission to hospital. Subsequent enquiry revealed only one that might have been responsible, a 'body mist deodorant'. This preparation was no longer manufactured and was not available for analysis. A blood sample from this

Table 1. *Hexachlorophane ( $\mu\text{g./ml.}$ ) in mothers' and infants' blood*

|  |       | Mothers' venous<br>blood (A) | Infants' blood   |                          |  |
|--|-------|------------------------------|------------------|--------------------------|--|
|  |       |                              | Umbilical<br>(B) | 8th day<br>capillary (C) |  |
| Present series<br>(excluding No. 21 –<br>see text) | Mean  | 0.030 (21)                   | 0.032 (21)       | 0.066 (16)               |  |
|  | Range | 0.000–0.100                  | 0.000–0.104      | 0.000–0.166              |  |
| Previous series<br>(Alder <i>et al.</i> 1972)      | Mean  | Not tested                   | 0.044 (15)       | 0.180 (15)               |  |
|  | Range | Not tested                   | 0.010–0.120      | 0.040–0.500              |  |

(The figures in brackets are the numbers of samples.)

Table 2. *Effect of dusting powders on dates of separation of umbilical cord in Nursery 2, Bristol Maternity Hospital*

| Date<br>(1962)           | Powder                                   | No.<br>of<br>babies | Day of separation of cord |   |    |    |    |    |    |    |                 |
|--------------------------|--|---------------------|---------------------------|---|----|----|----|----|----|----|-----------------|
|                          |  |                     | 4                         | 5 | 6  | 7  | 8  | 9  | 10 | 11 | 12 and<br>above |
| A 8–28 May               | 'Ster-zac'<br>hexachlorophane            | 32                  | 0                         | 4 | 4  | 8  | 13 | 3  | 0  | 0  | 0               |
| B 29 May–<br>10 July     | 0.2% chlorhexidine                       | 37                  | 0                         | 1 | 3  | 5  | 7  | 14 | 5  | 1  | 1               |
| C 31 July–<br>31 October | 'Ster-zac' base.<br>(No hexachlorophane) | 132                 | 6                         | 9 | 27 | 42 | 31 | 12 | 4  | 1  | 0               |

Comparisons of separation at 9 days or later.

A and C,  $\chi^2 = 0.059$ , Df = 1. Not significant.

B and C,  $\chi^2 = 29.455$ , Df = 1. Highly significant  $P < 0.001$ .

A and B,  $\chi^2 = 14.958$ , Df = 1. Highly significant  $P < 0.001$ .

mother 16 weeks after delivery contained only 0.02  $\mu\text{g.}$  hexachlorophane per ml., little more than the 'blank' value.

The results for the remaining mothers and babies are summarized in Table 1, with the results of our previous series for comparison. The hexachlorophane concentrations in umbilical blood and maternal blood were little more than the blank value. The values in the 8th day blood samples were slightly higher, but distinctly less than the 8th day values in our previous series. Evidently the precautions to reduce contamination had succeeded and justified the use of capillary blood. It is interesting to note that our results were rather similar to the venous concentrations reported by Plueckhahn (1973) in infants who were washed with hexachlorophane emulsion, although allowance must be made for differences between analytical methods.

#### *Chlorhexidine dusting powder*

In 1962 an investigation of dusting powder containing 0.2% chlorhexidine was begun in order to compare its efficiency in preventing staphylococcal sepsis with that of hexachlorophane (K. Simpson, R. C. Tozer and W. A. Gillespie, unpublished). Chlorhexidine powder undoubtedly diminished staphylococcal colonization

of the umbilicus and skin but, unexpectedly, it also caused delay in separation of the umbilical cord stump (Table 2). This effect could perhaps be explained by the wider range of organisms susceptible to chlorhexidine than to hexachlorophane, so preventing bacterial action that may assist the cord to separate. Because the effect sometimes caused inconvenience and delay in patients leaving hospital, the investigation of chlorhexidine powder was discontinued.

#### DISCUSSION

When investigating the concentration of hexachlorophane in infants' blood it is essential to minimize contamination of the samples by contact with skin or by placental transfer from mothers' blood (Plueckhahn, 1973). The importance of these precautions was well shown by the high concentration of hexachlorophane in the blood of one mother and her baby in our series, probably derived from a toilet preparation used outside hospital; and also by the lower concentrations in infants' blood samples when greater care was taken to avoid contamination than in the previous series.

Very many thousands of normal infants have been treated with 3% hexachlorophane in emulsion or 0.33% in dusting powder, in many hospitals, with no evidence of harm. Toxic effects, sometimes fatal, have been associated with topical application of the emulsion to burned or excoriated skin (Plueckhahn, 1973). Our results and those of Plueckhahn in healthy infants treated in hospital for the first week or so of life with either of these preparations, showed that blood hexachlorophane concentrations were much below the minimum of about 1  $\mu\text{g}$ -per ml. that was found to be toxic when maintained in rats or monkeys for many weeks (Curley & Hawk, 1971; Hart, 1971). Hexachlorophane undoubtedly has prevented much staphylococcal sepsis in infants (Simpson, Tozer & Gillespie, 1960; Gluck & Wood, 1961; Plueckhahn & Banks, 1963; Baber *et al.* 1967). The incidence of breast abscess in mothers was also reduced (Corner, Crowther & Eades, 1960; Plueckhahn & Banks, 1964). Several authors have recently reported increases in staphylococcal sepsis when hexachlorophane prophylaxis was withdrawn (Ayliffe, Brightwell, Ball & Derrington, 1972; Alexander & Pitkewicz, 1973; Dixon, Kaslow, Mallison & Bennett, 1973). It would be wrong, therefore, to discard hexachlorophane unless an effective and safer substitute is found. One possible substitute, chlorhexidine, had the undesirable effect of delaying separation of the umbilical cord.

Although all evidence shows that hexachlorophane treatment of normal infants' skin is safe when correctly performed it should be realized that hexachlorophane, like other disinfectants, is toxic if misused. Its use therefore should generally be confined to the first 7-10 days of life, in hospital and under medical supervision. Hexachlorophane should not be used on infants with burnt or excoriated skin. Special caution is advised in treating low birth weight babies (Plueckhahn, 1973); but the protection of these babies from staphylococcal sepsis is particularly important and the use of hexachlorophane should be investigated further before deciding upon its safety.

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## REFERENCES

- ALDER, V. G., BURMAN, D., CORNER, B. D. & GILLESPIE, W. A. (1972). Absorption of hexachlorophane from infants' skin. *Lancet* ii, 384.
- ALEXANDER, G. M. C. & PITKEWICZ, J. S. (1973). The incidence of infections in nurseries since the discontinuance of hexachlorophane bathing. *Pediatrics* 51, 360.
- AYLIFFE, G. A. J., BRIGHTWELL, K. M., BALL, P. M. & DERRINGTON, M. M. (1972). Staphylococcal infection in cervical glands of infants. *Lancet* ii, 479.
- BABER, K. G., CORNER, B. D., DUNCAN, E. H. L., EADES, S. M., GILLESPIE, W. A. & WALKER, S. C. B. (1967). A prospective study of staphylococcal infection and its prevention among infants and mothers after childbirth in hospital and at home. *Journal of Hygiene* 65, 381.
- CORNER, B. D., CROWTHER, S. T. & EADES, S. M. (1960). Control of staphylococcal infection in a maternity hospital. Clinical survey of the prophylactic use of hexachlorophane. *British Medical Journal* i, 1927.
- CURLEY, A., HAWK, R. E., KIMBROUGH, R. D., NATHENSON, G. & FINBERG, L. (1971). Dermal absorption of hexachlorophane in infants. *Lancet* ii, 296.
- CURLEY, A. & HAWK, R. E. (1971). Hexachlorophene I. Analysis in body fluids and tissues of experimental animals, paper read at 161st National Meeting of the American Chemical Society, Los Angeles. March 28 to April 2. (Cited by Pleuckhahn, 1973.)
- DIXON, R. E., KASLOW, R. A., MALLISON, G. F. & BENNETT, J. V. (1973). Staphylococcal disease outbreaks in hospital nurseries in the United States - December 1971 through March 1972. *Pediatrics* 51, 413.
- GILLESPIE, W. A., SIMPSON, K. & TOZER, R. C. (1958). Staphylococcal infection in a maternity hospital. Epidemiology and control. *Lancet* ii, 1075.
- GLUCK, L. & WOOD, H. F. (1961). Effect of an antiseptic skin-care regimen in reducing staphylococcal colonization in newborn infants. *New England Journal of Medicine* 265, 1177.
- HART, E. R. (1971). Toxicity of pHisoHex on 90-day skin applications to infant rhesus monkeys, report submitted to Sterling-Winthrop Research Institute by Bionetics Research Laboratories, December 3. (Cited by Pleuckhahn, 1973.)
- PLEUCKHAHN, V. D. (1973). Infant antiseptic skin care and hexachlorophane. *Medical Journal of Australia* i, 93.
- PLEUCKHAHN, V. D. & BANKS, J. (1963). Antisepsis and staphylococcal disease in the new-born child. *Medical Journal of Australia* ii, 519.
- PLEUCKHAHN, V. D. & BANKS, J. (1964). Breast abscess and staphylococcal disease in a maternity hospital. *British Medical Journal* ii, 414.
- SIMPSON, K., TOZER, R. C. & GILLESPIE, W. A. (1960). Prevention of staphylococcal sepsis in a maternity hospital by means of hexachlorophane. *British Medical Journal* i, 315.