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Hexachlorophane Challenged

The Secretary of State's statement in the House of Commons[1] about the potential hazards of hexachlorophane inevitably aroused some public anxiety at a time of growing awareness of hazards from toxic chemicals, and it is important to get the facts into perspective. The Commons statement was both restrained and sensible, but lacked the evidence on which the Committee on Safety of Medicines had based its recommendations.

Hexachlorophane is a chlorinated phenol derivative. It has been used as a powerful bactericidal agent for over 20 years. Its toxicity on oral administration precludes its use systemically, but for topical application it has two principal advantages over related compounds: firstly, it is much less irritant to the skin than, for example, phenol, though sensitivity dermatitis has been reported;[2] and, secondly, it maintains its activity in the presence of soap.

The studies which doubtless prompted representations to the U.S. Food and Drug Administration in early January and to the Secretary of State by the Committee on Safety of Medicines in mid-February were published in August 1971.[3] Oral administration of hexachlorophane in a dosage of 25 mg/kg body weight per day for two weeks to adult rats or a single dose of 100 mg/kg given to weanling rats has been reported to cause paralysis, with vacuolation in cerebral white matter reminiscent of, but not identical with, "spongy degeneration" seen rarely in some human infants. In another series of experiments 5 mg/kg body weight given to rats for about 100 days caused brain damage and affected the survival of offspring.[3] The only published reports of human mishap[4-6] describe the effects of accidentally drinking 3% solutions. A 6-year-old girl died, and 10 hospital patients experienced acute gastrointestinal upset, in some cases leading to dehydration and peripheral circulatory failure. The main disadvantage of hexachlorophane apart from its potentially toxic effect is that it is relatively ineffective against Gram-negative organisms.[7 8] Dispensing bottles replenished from a stock bottle of 3% hexachlorophane provided a medium in which, for example, *Pseudomonas aeruginosa* could be easily cultured.

Concentrations of up to 3% have been included in soaps, washes, creams, and powders for use on infants in neonatal units to reduce staphylococcal sepsis, and there are numbers of reports of its value for this purpose.[9-12] But not all have been laudatory. For example, J. O. Forfar and his colleagues[13] observed that alongside a reduction in staphylococcal sepsis there was an increase in Gram-negative infections. Moreover, some doubt is cast on the wisdom of using hexachlorophane in this way by the detection of surprisingly high levels in cord blood and in venous samples from newborn babies.[3] Concentrations in cord blood varied from 0·003 to 0·182 μg/g (mean 0·022 μg/g), and in venous samples obtained 1-11 days later levels varied from 0·009 to 0·646 μg/g (mean 0·109 μg/g). At the hospital where the infants were studied they were bathed daily with a diluted 3% solution in detergent, and rinsing was haphazard. The infant with the highest blood level, which was two-thirds of the minimum level in the rat experiments mentioned earlier, had been bathed five times with hexachlorophane. In this investigation there was no correlation between numbers of washings and blood levels, but sampling intervals after bathing were not standardized. The authors urged that infants should be rinsed carefully to diminish parenteral absorption. On the other hand repeated washing with hexachlorophane in soap or water is needed if it is to accumulate in the skin and so maintain a bactericidal effect, reaching a maximum concentration in two to four days.[14] Careful rinsing reduces this concentration, and recolonization with normal bacterial flora may begin immediately after a single wash and rinse.

It is premature to conclude from present evidence that the spongy degeneration in the brains of infants dying from obscure neurological illnesses may be due to hexachlorophane, as these abnormalities were recognized before hexachlorophane came into use. Nor have any deaths or damage been attributed to this substance. But it is possible for a significant association to have been overlooked in newborn babies owing to the difficulty of detecting it.

Further studies of hexachlorophane toxicity proposed by the Secretary of State will be welcomed. The special characteristics of absorption of drugs and chemicals through the skin of infants also deserve more study.

[1] *British Medical Journal*, 1972, 1, 579.
[2] Baker, H., Ive, F. A., and Lloyd, M. J., *Archives of Dermatology*, 1969, 99, 693.
[3] Curley, A., Hawk, R. E., Kimbrough, R. D., Nathenson, G., and Fingberg, L., *Lancet*, 1971, 2, 296.
[4] Wear, J. B., *et al.*, *Journal of the American Medical Association*, 1962, 181, 587.
[5] Lustig, F. W., *Medical Journal of Australia*, 1963, 1, 737.
[6] "pHisohex" (Product Literature). Bayer Products Company, December 1968.
[7] Anderson, K., *Medical Journal of Australia*, 1962, 2, 643.
[8] Knights, H. T., and Harvey, J., *New Zealand Medical Journal*, 1964, 63, 653.
[9] Gillespie, W. A., *et al.*, *Lancet*, 1958, 2, 1075.
[10] Simpson, K., *British Medical Journal*, 1960, 1, 315.
[11] Corner, B. D., *et al.*, *British Medical Journal*, 1960, 1, 1927.
[12] Gezon, H. M., *et al.*, *New England Journal of Medicine*, 1964, 270, 379.
[13] Forfar, J. O., Gould, J. C., and Maccabe, A. F., *Lancet*, 1968, 2, 177.
[14] Shemano, I., and Nickerson, M., *Federal Proceedings*, 1954, 13, 404.