The Foundation for the Study of Infant Deaths
35 Belgrave Square London SW1X 8QB
Telephone: 071-235 1721 / 071-235 0965 / 071-823 2216 (Appeals)
Fax: 071-823 1986

Patron: Her Royal Highness The Duchess of Gloucester

COT DEATH RESEARCH AND SUPPORT

13th March 1990

STATEMENT TO ALL FSID STAFF FOR INFORMATION

"Sir Donald Acheson, the Chief Medical Officer, announced today (9th March 1990) that he has asked a group of independent experts to investigate the claim that the emission of toxic gases from fungal growth on some cot mattresses is a cause of sudden infant death.

The group will be chaired by Professor Paul Turner who is Chairman of the Government's independent expert advisory committee on toxicity and will include experts in toxicology, neonatal pathology, mycology, epidemiology and analytical chemistry.

Announcing the review, Sir Donald said that the sudden infant death syndrome was almost certainly due to many causes and these are little understood. Any new hypothesis therefore warranted careful consideration. The hypothesis - put forward by Mr B A Richardson, Director of Penarth Research International and Mr P R Mitchell, Director of Mitchell Marquees - is that due to the action of certain fungi, soiled cot mattresses may emit toxic gases.

Sir Donald went on: "The death of an infant is a shattering blow to parents. We have a duty to investigate possible causes. But this needs to be done in a way which, on the one hand avoids alarming parents unnecessarily before claims can be properly assessed and on the other, raising hopes that a 'preventable cause' of sudden infant death has been found".

"Mr Richardson's and Mr Mitchell's work which has not been published in the scientific literature, and therefore has not been subject to the usual scrutiny and discussion, is already being assessed by the Laboratory of the Government Chemist. The independent experts will be examining the laboratory findings as well as the work done by Mr Richardson and Mr Mitchell. I have asked the group to report as soon as possible and will make public their recommendations".

In the meantime, Sir Donald has taken advice from a range of experts including neonatal pathologists and paediatricians. He has been advised that no case of cot death in this country due to the toxic gases arsine, stibine and phosphine has been reported. Nor is there any need for parents to take any special action in respect of cot mattresses. Nevertheless, as a matter of prudence he has invited an independent assessment of the evidence".

The above extract is taken from a Department of Health press release, and follows articles in the Daily Express in February 1990. These articles stated that "startling evidence by government scientists has confirmed a possible new link between cot death syndrome and fire resistant mattresses", that "Ministers begin a series of crisis meetings in Whitehall", that "Health Secretary Kenneth Clarke (has) ordered an immediate enquiry into the possible link between cot deaths and fireproof mattresses" and that "Mr Clarke is prepared to order tens of thousands of baby mattresses to be withdrawn from sale if Government scientists confirm a possible link".

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The articles correspond to a theory of a cause of sudden infant death syndrome (SIDS) that was widely reported on television, radio and in the press at the beginning of June 1989. Laboratory work by a chemical analyst, Mr Barry Richardson, suggested that toxic gases were being released when biocides (substances acting against infecting organisms) and fire retardants contained in cot mattress coverings of plasticised polyvinyl chloride (PVC) were acted on by a normal household fungus. He believed that the gases might be a significant cause of SIDS and informed both the Foundation for the Study of Infant Deaths and the Department of Health of his views.

Mr Richardson told a meeting of the Scientific Advisory Committee of the Foundation for the Study of Infant Deaths about his work, and was questioned about it by members. After careful consideration, the Committee formed the view that this was an unproven hypothesis for which no direct evidence existed and that this was unlikely to be a major cause of SIDS.

The infant mortality rate (all first year deaths) has continued to fall since plasticised polyvinyl chloride (PVC) was introduced while the SIDS rate has stayed relatively constant.

However, the toxic gas theory was widely publicised on radio and television and in the press before any scientific confirmation of the laboratory work had been undertaken. The Foundation was concerned that any possible such link with SIDS should be quickly and appropriately investigated and for that reason is at present funding a project in London (£10,000 over 6 months) to undertake suitable tests.

Advice to parents:

The Foundation for the Study of Infant Deaths advises parents that they need not feel that they should take any special action following these claims, and warns them NOT to endanger their baby by wrapping polythene around the mattress as has been suggested by Mr Richardson.

For further information please contact:

Erica De'Ath (Chief Executive) or
Tracy Lamb (Research and Information Officer)
The Foundation for the Study of Infant Deaths
35 Belgrave Square
London
SW1X 8QB
Phone: 01-235 0965/1721. Fax: 01-823 1986

(ENDS)

PENARTH RESEARCH INTERNATIONAL LIMITED
Consulting and Research Scientists
Castle Emplacement, P.O. Box 142 St. Peter Port, Guernsey, C.I. Tel: 0481-28559

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Cot mattress biodeterioration and sudden infant death

1. Introduction

1.01 PRIL research in 1988 included an investigation into deterioration of reinforced polyvinyl chloride (PVC) fabric used as tentage. The fabric was found to be infected by various fungi which were utilising the plasticisers as nutrient, particularly *Aspergillus niger* which causes grey staining along the reinforcement fibres and *Streptomyces rubrireticuli* which causes patches of pink staining, despite the presence of the arsenical biocide 10,10'-oxybisphenoxyarsine (OBPA). The clients sponsoring the research were warned by the project director B A Richardson that other fungi might develop such as *Scopulariopsis brevicaulis* which could convert the OBPA biocide into toxic arsine gas, and that accumulations of this gas might occur in folded tentage in winter storage. One of the clients, P R Mitchell of Mitchell Marquees, enquired whether similar infections might occur on PVC cot mattress coverings and whether generated arsine might be the cause of unexplained sudden infant death.

1.02 The fungus *Scopulariopsis brevicaulis* is commonly found infecting protein substrates such as meat, milk and cheese, as well as damp wool, leather and silk (1,2). It has been known since about 1890 that this fungus is able to convert arsenic compounds into arsine (arsenic trihydride) and related alkyl compounds (1-17). Gosio and Sanger reported that some mystery illnesses and deaths were due to arsine generation through this fungus infecting wallpaper printed with the arsenical pigments Paris green and Scheele's green, although another source of arsine on papered walls was horse-hoof size which often contained white arsenic (arsenious oxide) as a rodent repellent. In the United Kingdom the last deaths from these causes were reported in 1932 (12).

1.03 Investigations on PVC cot mattress coverings show that all used mattresses are naturally infected by the fungus *Scopulariopsis brevicaulis* in the area affected by the warmth and perspiration of the sleeping infant. Arsine generation is not usually identified as OBPA biocide is not generally used in PVC cot mattress coverings. However, phosphine (phosphorus trihydride) and particularly stibine (antimony trihydride) and related alkyl compounds are frequently identified, originating from the phosphate plasticisers and antimony trioxide that are used to improve fire retardency. Exposed foam mattresses are infected by a wide range of micro-organisms where they are affected by dribble and vomit, including *Scopulariopsis brevicaulis* which generates phosphine if phosphate fire retardents are present.

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2. Research observations

2.01 All used cot mattress coverings are infected by a wide range of the micro-organisms that are commonly found in the domestic environment.

2.02 PVC cot mattress coverings are generally affected by surface soilage infections but *Scopulariopsis brevicaulis* always develops on the area affected by the warmth and perspiration of the sleeping infant. This infection, which is apparently prompted by the nitrogen content in the perspiration, develops in the plasticiser within the PVC sheet and is invisible, the only evidence being progressive loss of plasticity and the development of brittleness and splits. Phosphine, arsine and stibine or related alkyl gaseous compounds are usually detected when samples are incubated. Stibine, originating from the antimony trioxide fire retardent component in the PVC, is most often detected. Phosphine from fire retardent phosphate plasticisers is also often detected. Arsine from the arsenical biocide OBPA is rarely detected but traces of arsine are sometimes detected which are attributable to arsenical impurities in antimony trioxide. Fungal activity and gas generation vary with temperature, the rate of generation at 40°C being about 100 times that at 20°C. Phenolic compounds, released when aryl phosphate plasticisers are degraded by the infection, sometimes cause pink staining in the shape of the sleeping infant.

2.03 Exposed foam mattresses, that is mattresses which comprise foam alone, or covered with net, or partly covered with PVC, are usually infected by a wide range of infections, including many fungi which produce spores or support mites which can prompt allergic respiratory reactions such as asthma. *Scopulariopsis brevicaulis* infections on foams are usually associated with phosphate fire retardents and phosphine generation.

2.04 Unexplained sudden infant deaths or cot deaths usually involve infants in the prone or face down position with generous coverings. Death usually occurs after the infant has remained undisturbed for six hours or more. Death is usually attributed to sudden infant death syndrome or SIDS. The prone position and heavy coverings maximises exposure to any gas generation from the mattress, and hyperthermia in the infant caused by the heavy coverings also increases the rate of gas generation through both the higher temperature and the increased perspiration.

2.05 50 mattresses from 45 SID incidents have been examined, including 1 cotton covered, 26 PVC covered, 15 PVC covered with exposed foam at one or both ends, and 8 exposed foam; 2 mattresses were involved in 5 incidents. All the PVC and foam mattresses were infected by the fungus *Scopulariopsis brevicaulis* and, when samples were incubated, all generated phosphine, arsine or stibine gas. Mattresses had generally been used for a previous infant, the mattresses varying from apparently excellent clean condition to grubby surfaces with brittle and split PVC coverings or heavily stained foam. Five mattresses were involved which had not been used for previous infants. Two of the mattresses involved PVC coverings which were brittle, pink stained and generating phosphine; purchase dates are also known for some of the used mattresses, those generating phosphine and therefore containing phosphate plasticisers apparently deteriorating more rapidly than those containing other plasticisers. Another mattress was exposed foam, pink stained and generating phosphine from a phosphate fire retardent treatment. In all cases the infection and gas

generation were restricted to the area affected by the warmth and perspiration of the sleeping infant. Bed coverings were also sometimes examined. Cotton sheets covering the mattresses were always found to be saturated with perspiration if examined shortly after death.

3. Notes

3.01 Incubation of naturally infected samples of PVC and foam at high humidity is sufficient to cause phosphine, arsine or stibine gas generation. However, incubation of small samples on nutrient plates is necessary for the infection to spread from the samples so that it can be identified. Samples are therefore examined routinely by plating on agar plates containing 5% malt and 5% soya flour, the protein in the soya flour encouraging *Scopulariopsis brevicaulis* growth. Samples are incubated at 22 to 25°C in order to restrict activity and limit the rate of gas generation to avoid danger to staff; headaches are the first indication of excessive gas concentrations.

3.02 Silver nitrate and mercuric bromide (or chloride) papers are used for gas detection; gold compounds can also be used. With silver nitrate phosphine gives a yellow colour, whilst arsine gives a brown or mauve colour and stibine a pink or brown colour; high concentrations eventually cause darkening to grey or black with all three gases. With mercuric bromide phosphine and stibine cause no colour change as white complexes are formed but arsine gives a yellow colour, darkening to orange and red with high gas concentrations. These reactions are quantitative and sensitivity can be improved by the use of optimum loadings on the detection paper and by limiting the size of the paper strips; high humidity is also essential as the reactions do not occur if the papers are too dry. Routine studies involve placing small samples of PVC or foam on malt/soya agar plates in Petri dishes and incubating for several days at 22 to 25°C until active *Scopulariopsis brevicaulis* growth develops, either as beige coloured hyphal growth or the buff coloured slime form which develops under stress. With PVC the fungus develops only on the nutrient medium and the edge of the PVC. Small strips of detection paper about 5mm wide and 25mm long are then slipped over the edge of the dishes and secured with the lid, the colour generated after 1 to 3 hours identifying any phosphine, arsine or stibine generation. Hydrogen sulphide interference, which is indicated by early darkening of the silver nitrate, does not normally occur. Alkyl compounds are also generated by *Scopulariopsis brevicaulis* and account for the characteristic garlic odour associated with phosphine, arsine and stibine, but the silver, mercury and gold complexing method of detection is more sensitive to the trihydrides.

3.03 The increase in the rate of gas generation at higher temperatures can be observed by placing well established open plates in a desiccator in a water bath, conditioning to the required temperature for an hour or more, flushing with air, and determining the rate of gas generation by introducing test paper and observing the rate of development of the detection colour. Silver nitrate and mercuric bromide papers can be used but greater detection sensitivity can be achieved using paper treated with mercuric chloride and a pH indicator, the trihydride gases complexing with mercury forming hydrochloric acid.

3.04 The gases can also be detected using, for example, the termite *Reticulitermes santonensis*. Termites placed on well developed plates with PVC samples generating easily detectable arsine and stibine are generally killed within two hours but phosphine is distinctly less toxic. Did he do that?

3.05 Although the fungus *Scopulariopsis brevicaulis* can survive on simple carbohydrate media such as malt agar, a source of nitrogen will greatly enhance activity and enable the fungus to compete strongly with other organisms. This fungus is often therefore the dominant species on substrates containing protein such as meat, milk and cheese, but substrates containing nitrogen sources such as ammonium compounds and urea are equally suitable. Extracellular enzymes are produced by invading hyphae which convert the nitrogen sources to ammonia (nitrogen trihydride) gas which is then absorbed by the hyphae and utilised for protein formation. However, the extracellular enzymes do not act on nitrogen sources alone but also on other Group V/Vb compounds, generating phosphine, arsine and stibine which are apparently liberated into the atmosphere as they cannot be absorbed by the hyphae. The fungus has an affinity for Group V/Vb compounds; if they are sprinkled on plain agar plates to form a distinctive pattern the fungus will follow the pattern. If the fungus is under stress, usually due to inadequate nitrogen in the substrate, the beige hyphal growth degenerates to a buff coloured slime, reverting when plated onto a more suitable medium. The infection is invisible in PVC fabric because it is in this structureless slime form and causes only slight distortion of the PVC; the infection does not spread over the surface of the PVC.

3.06 Phosphine, arsine and stibine poisoning cannot be readily detected on post mortem investigation. Normal lethal doses will cause increases in phosphorus, arsenic and antimony levels in blood and tissue but these increases are smaller than normal ambient variations and therefore undetectable.

3.07 Standard toxicological references indicate that chronic exposure to phosphine, arsine or stibine causes death by haemolytic anaemia in adults, although a headache is an early symptom of poisoning (32-36). It is suggested that these gases are accumulative but this is not strictly correct; chronic exposure simply causes the anaemia to become progressively more severe. However, SIDS is not normally associated with haemolytic anaemia, although colour changes in the lungs may result from local haemolysis in lung tissue. Infants are sometimes reported to be irritable in their cot several hours prior to death which may indicate headaches. Infants are sometimes provided with monitors which detect cessation of respiration but prompt attempts at resuscitation are apparently unsuccessful. These observations may indicate a poisoning action causing cessation of respiration, perhaps acting through the respiratory centre in the medulla, although the trihydrides are likely to degrade in the blood before reaching the brain, and respiration in young infants is controlled by the carotid sinus rather than the respiratory centre. Whilst the trihydrides may block the carotid sinus, the circumstances of sudden infant death are also consistent with damage to sensitive cells due to oxygen or blood sugar deprivation. The trihydrides are reducing agents and may obstruct oxygen transport by blocking the oxygen acceptor sites on erythrocyte haemoglobin. Alternatively phosphine, arsine and stibine may form phosphonium, arsonium and stibonium hydroxide which may condense onto blood sugar hydroxyl groups, preventing blood sugar utilisation by cells. Research by PRIL in 1968 showed that poisoning by organotin compounds, which caused numerous deaths and brain

injuries in France in the Stalinon affair, involves similar condensation on blood sugar hydroxyl groups (40-42).

4. Further information

4.01 This Research Note will be revised as this project progresses. Revised issues will be distributed only to bona fide research teams. Further information on this project is available from the director B A Richardson.

4.02 This project is not sponsored. PRIL has provided laboratory facilities for the microbiological and entomological work. The project consultants are B A Richardson, T R G Cox and J G Watt. The culture of *Scopulariopsis brevicaulis* involved in the initial work was provided by Dr D Allsopp of the International Mycological Institute at Kew; subsequent research involved cultures from naturally infected samples.

5. References

1. Smith G. *An introduction to Industrial Mycology.* London, Edward Arnold, 6th edition, 1969.
2. Morton F J & Smith G. The genera *Scopulariopsis* Bainer, *Microsacus* Zukal, and *Doratomyces* Corda. *Mycol Paper 86,* 1963
3. Thom C & Raper K B. The arsenic fungi of Gosio. *Science* 1932, 76, 548-550.
4. Gosio B. Azione di alcune muffe sui composti fissi d'arsenico. *Riv d'Igiene e San Publ* 1892, 3, 201-230, 261-273.
5. Gosio B. Action de quelques moisissures sur les composes fixes d'arsenic. *Arch Ital Biol* 1893, 18, 253-265.
6. Gosio B. Zur Frage, wodurch die Giftigkeit arsenhaltiger Tapeten bedingt wird. *Ber Deuts Chem Ges* 1897, 30, 1024-1026.
7. Schmidt H R. Uber verschimmelte Tapeten. *Diss Erlangen,* 1899
8. Bub-Bodmar F & Tilger B. *Die Konservierung des Holzes in Theorie und Praxis,* Berlin, 1922.
9. Richardson B A *Wood Preservation* London, Construction Press & Longmans, 1978.
10. Broese van Groenou H, Rischen H W L & van den Berge J. *Wood Preservation during the last 50 years.* Leiden, Sijthoffs, 1952.
11. Hamilton A. *Industrial Poisons in the United States* New York, 1925
12. Anon. Gaseous arsenic from wall-plaster, *The Analyst* 1932, 57, 163-164.
13. Sanger C R. On formation of volatile compounds of arsenical wall papers. *Proc Am Acad Arts & Sci* 1894, 21, 112-147.
14. Sanger C R. On chronic arsenical poisoning from wall papers and fabrics. *Proc Am Acad Arts & Sci* 1894, 21, 148-177.
15. Biginelli P. Composizione e costituzione chimica de gas arsenicale delle tappezerie. *Atti R Accad Lincei Rendic Cl Sc Fis Math e Nat* 1900, 9, 210-214, 242-249.
16. Maasen A. Die biologische Methode Gosio's zum Nachweis des Arsens und die Bildung organischer Arsen-, Selen- und Tellurverbindungen durch Schimmelpilze und Bakterien. *Arb a d kaiserl Gesundh ambt* 1902, 18, 475-489.
17. Huss H. Zur Kenutnis der biologischen Zersetzung von Arsenverbindungen. *Z f Hyg u Infekt krankh,* 1914, 76, 361-406.

18. Lerrigo A F. The biological method for the detection of arsenic. *The Analyst* 1932, 57, 155-158.
19. Challenger F, Higginbottom C & Ellis L *J Chem Soc* 1933, 95.
20. Challenger F *Chem Rev* 1945, 36, 315.
21. Braman R S & Foreback C C *Science* 1973, 182, 1247.
22. Cullen W R & Reimer K J. Arsenic speciation in the environment. *Chen Rev* 1989, 89, 713-764.
23. Cox D P & Alexander M *Bull Environ Contam Toxicol* 1973, 9, 84.
24. Mahlke F & Troschel E. *Handbuch de\Holzkonservierung* Berlin, 1928
25. Berge J van den. Beoordeeling van de waarde van fungicide stoffen voor houtconserveering. *Diss Delft, 1934. (Testing the suitability of fungicides for wood preservation.* Publ Int Adv Off Wood Pres, The Hague).
26. Klausmeier R E. Results of the second interlaboratory experiemnt in biodeterioration of plastics. *Int Biodet Bull* 1972; 8(1): 3-7
27. Yeager C C. Pink staining in polyvinylchloride. *Plastics World* 1962; 20:14.
28. Yeager C C. Laboratory and service tests for PVC *Proc 1st Int Biodet Symp* 1968; 151-161.
29. Klausmeier R E & Jones W A. Microbial degradation of plasticizers. *Dev Ind Microbiol* 1961; 2:47-53.
30. Klausmeier R E. The effect of extraneous nutrients on the biodeterioration of plastics. *Monograph 23, Soc Chem Ind* 1966; 232-243.
31. Hollo J & Kollar-Volgyesi M. Resistance of plastics to microbiological corrosion. *Bioch Exp Biol* 1975; 11:163-173.
32. Plunkett E R *Handbook of Industrial Toxicology* 3rd edition, Edward Arnold, London 1987.
33. Dreisbach R H *Handbook of Poisoning* 11th edition, Lange, Los Altos, 1983.
34. Cooper P *Poisoning by Drugs and Chemicals* 3rd edition, Alchemist, London, 1974.
35. Polson C J, Green M A & Lee M R *Clinical Toxicology* 3rd edition, Pitman, London, 1983.
36. Kleinfeld M J. Arsine poisoning *J o M* 1980; 22:820.
37. Wilson R, Lovejoy F H, Jaeger R J & Landrigan P L. Acute phosphine poisoning aboard a grain freighter. *JAMA* 1980, 244, 148-150.
38. Nelson E A S, Taylor B J & Weatherall I L. Sleeping position and infant death bedding may predispose to hyperthermia and the Sudden Infant Death Syndrome. *Lancet* 1989;i:199-200.
39. Stanton A N, Scott D J & Downham M A P S. Is overheating a factor in some unexpected infant deaths? *Lancet* 1989;i:1054-7.
40. Richardson B A. Action mechanisms of some organometallic preservatives. *Proc 1st Int Biodet Sym* 1969,498-505.
41. Richardson B A. Tributyltin wood preservatives. *Rec Ann Conv BWPA* 1970.
42. Richardson B A. Organotin wood preservatives; activity and safety in relation to structure. *Proc AWPA* 1988.

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