

Executive Summary

Introduction

The term Cot Death was coined in 1954 to describe sudden unexpected infant deaths that occur for no obvious reason. Such deaths have occurred throughout the ages but have become the major cause of postneonatal infant mortality as other causes of infant death have declined. In 1969 the term Sudden Infant Death Syndrome (SIDS) was proposed to describe those which remain unexplained after a postmortem examination. The terms are often used interchangeably and were gradually adopted after they were accepted as a registrable cause of natural death by the Coroners' Society and the Registrar General in England and Wales in autumn 1970. Because Sudden Infant Deaths were only identifiable in published national statistics from 1971 onwards and there was gradual diagnostic transfer to the new terminology, the combined rate for deaths certified by a coroner as a Sudden Respiratory Death occurring at home (SRDh) or as a Sudden Infant Death (SID) gives the most accurate measure of the scale of the cot death problem in the 1970s and '80s.

The toxic gas hypothesis originated when Mr BA Richardson, a materials consultant, and Mr PR Mitchell, an associate, postulated that a mould (*Scopulariopsis brevicaulis*) could degrade chemicals present in cot mattress fillings and covers with the subsequent release of toxic gases such as phosphine, arsine or stibine, and that poisoning by these toxic gases might be a cause of SIDS. Richardson's hypothesis was publicised with his recommendations through the media in June 1989 and later published, with his experimental observations, in a letter to the *Lancet* in March 1990.

The Chief Medical Officer (CMO) at the Department of Health in March 1990 appointed an Expert Working Group, chaired by the late Professor Paul Turner, to investigate the hypothesis. The Turner Committee's Report of May 1991 concluded "that the hypothesis relating SIDS with microbial infestation and gas generation from antimony or phosphorus based additives present in cot furnishings was unfounded."

Renewed publicity was given to the hypothesis when the ITV Cook Report programme on 17 November 1994 demonstrated Mr Richardson's original experimental work, which he believed produced evidence for his hypothesis, and provided new data on concentrations of antimony in infants which were claimed to substantiate it further. Publicity for a second programme, shown on 1 December 1994, claimed that the antimony concentrations in children's hair were higher than those in their mothers' and that they correlated with concentrations in their mattresses. It postulated that the source of the antimony in infants was the toxic gas stibine.

In response to great public concern, the CMO, on 30 November 1994, announced the setting up of an Expert Group to investigate Cot Death Theories (Expert Group) to be chaired by Lady Limerick. The terms of reference were to review the findings of the report 'Sudden Infant Death Syndrome' (the Turner Report, 1991) and any subsequent data on hypotheses linking antimony with unexplained deaths in infants; and to advise the CMO on what further studies should be undertaken to investigate postulated causal relationships between chemicals and cot deaths. The twelve member Expert Group met first on 16 December 1994 and on a further 23 occasions.

The sudden unexpected death of a baby is a devastating tragedy for the bereaved family. The aim of the Expert Group has been the protection of the health of infants. We agreed that if anything was found to indicate any risk to infants, we would bring it urgently to the attention of those responsible for their care.

The Expert Group began by considering the contents of the Turner Report, Richardson's publications and, in particular, his Report entitled Cot Mattress Biodeterioration and Toxic Gas Generation: a possible cause of Sudden Infant Death Syndrome, which he submitted to the Expert Group in December 1994. The Group also studied the content of the two ITV Cook Report programmes and examined reports of experimental work by other researchers since 1991. Richardson and other scientists were invited to present their work to the Expert Group in person and other specialists were consulted on particular aspects.

Richardson's toxic gas hypothesis, as updated in 1994, proposed that the primary cause of sudden infant death syndrome (SIDS) is poisoning by gaseous phosphines, arsines and stibines generated by the fungus *S. brevicaulis* from phosphorus, arsenic and antimony compounds in fire retardant or plasticiser in PVC mattresses. His postulated mechanism of poisoning in SIDS is by an anticholinesterase action causing cardiac inhibition and vasodilation in infants through progressive accumulation of acetylcholine.

As evidence for his hypothesis, Richardson cited his original experimental work, which reported that mattress samples generated the toxic gases, and his finding that all cot mattresses were naturally infected by *S. brevicaulis* which he suggested put all infants lying prone on PVC mattresses at risk of poisoning. He also cited the Cook Report evidence that some infants have high concentrations of antimony in their blood, liver and hair, and the claim that these correlated with antimony concentrations in their mattresses. Richardson also claimed the incidence of SIDS increased in the 1950s owing to the use of PVC covered mattresses from 1953 onwards, and that the rate further increased in 1986 to 1988 owing to the implementation of Furniture and Furnishings (Fire) (Safety) Regulations 1988 which resulted in the use of antimony trioxide (which might also contain arsenic impurities) as a fire retardant in PVC. He claimed the reduction in SIDS from 1989 was due to the publicity given to his hypothesis by the media from June 1989 onwards and to his recommendations that new mattresses should be provided for all new babies or that old mattresses should be covered with polythene to isolate the babies from mattress materials.

Work of the Expert Group

While recognising the need to report findings as rapidly as possible, the Expert Group felt it imperative to complete a programme of work to determine definitively whether toxic gases can be generated from the fire retardant chemicals in cot mattress materials and, if so, whether these are the primary cause of SIDS or a danger to infants. We decided also to investigate the source and significance to health, if any, of tissue and hair antimony concentrations reported in the Cook Reports. We recognised that it might be necessary to determine whether and in what conditions antimony and phosphorus can be biovolatilised in order to ascertain whether such volatilisation could occur in the cot environment. We also reviewed the toxicity of the gases and considered possible pathophysiological mechanisms and examined the epidemiological evidence which Richardson postulated supported his hypothesis.

Review of the Turner Report and Subsequent Events 1990-94 (Chapter 4)

The Turner Committee had commissioned the Laboratory of the Government Chemist (LGC) and the International Mycological Institute to replicate Richardson's experiments, using his techniques supplemented by analysis of the test papers and more sophisticated quantitative techniques to

detect any gases evolved. They concluded that there was no evidence to substantiate the claims that microorganisms on cot mattress material produce toxic gases from antimony or phosphorus compounds present in mattresses fillings or covers even though very sensitive and specific detection methods were used. Drs A Donavan and C Simpson (University College London and Birkbeck College) reached the same conclusion.

The Turner Committee made two key recommendations:-

The need for chemical additives (as fire retardants) in cot furnishings should be carefully considered, and only grades of antimony trioxide containing the lowest possible levels of arsenic should be used in the treatment of cot furnishing. The Expert Group reviewed these: the British Standard for Domestic Bedding: BS 1877: Part 10: 1982 specified maximum levels of soluble arsenic (100µg/g) and antimony (250µg/g). The standard was revised in 1997, and, as a result of improvements in detection methods, the permitted concentration has been reduced to 25ppm (25µg/g) of soluble arsenic and 60ppm (60µg/g) of soluble antimony.

The Turner Committee also recommended investigation of the microbial infestation of cot mattresses and their covers to determine the significance of the more pathogenic microorganisms, especially fungi, and the possible development of a British Standard relating to microbial resistance. This area was investigated by the Expert Group (Chapter 5).

The Expert Group reviewed the new data received from the Cook Report and decided that further investigation was needed to determine whether antimony levels in SIDS were different from those in other infants and whether there was any correlation with antimony concentrations in their mattresses.

Repetition and Extension of Richardson's Experiments on Microbial Gas Generation (Chapter 5)

The Expert Group felt it was crucial to replicate Richardson's experiments with his collaboration, and to extend them. This was arranged at the Public Health Laboratory in Bristol, and the results were analysed in an independent laboratory, the Trace Element Analysis Unit at Southampton General Hospital. Richardson accepted the Group's invitation to help draw up the experimental

protocol, took part in selecting the mattress samples to be tested and observed the experiments at the crucial stages. In addition the protocol was approved by an expert analytical chemist, independent of the Group, and critical stages of experimentation were monitored by an independent observer from the University of Bristol. Richardson agreed that the experiments followed his procedures.

Small samples of mattress PVC from SIDS cases were incubated on malt soya flour nutrient medium in plates. When microbial growth was established, indicator papers were added to the plates so that any gas production could be detected by the appearance of a colour change and by subsequent chemical analysis.

The organisms that grew on the PVC mattress samples were, according to Richardson, the same, when examined by eye, as those he had seen. When examined under a microscope, however, these organisms were found to be bacteria and not the fungus *S. brevicaulis*, as earlier stated by Richardson. They were subsequently identified as *Bacillus* species commonly found in the normal domestic environment. It was noted that the colour changes on the indicator papers occurred in the presence of bacterial growth whether or not there was any mattress material present. Analysis of the indicator papers showed that the colour changes were due not to deposits of phosphorus, arsenic or antimony but to sulphur-containing gases arising from bacterial growth on the medium.

The Expert Group concluded that Richardson's interpretation of the colour changes on his test papers was mistaken. There was no evidence from his experiments to support the hypothesis that chemicals in PVC cot mattresses are converted into toxic gases by the growth of *S. brevicaulis* or microorganisms isolated from cot mattresses.

These findings were published in the *Lancet* and also in the Expert Group's Interim Report in December 1995 which concluded that thus far the Expert Group had found no evidence of risk to infants.

Subsequent investigations carried out on behalf of the Expert Group at Royal Holloway University of London, by Professor Pridham and Dr Gates, have identified the sulphur-containing substances as dimethylsulphide and dimethyldisulphide, which are ubiquitous in the environment.

It is central to Richardson's hypothesis that all mattress covers from SIDS infants are contaminated with the mould, *S. brevicaulis*. At the request of the Expert Group, cover and mattress filling of 56 cot mattresses on which SIDS babies had died and 296 used control mattresses from live infants were subjected to mycological investigation; this was part of supplementary studies carried out in the last year (1995-6) of the Confidential Enquiry into Stillbirths and Deaths in Infancy/Sudden Unexpected Deaths in Infancy (CESDI/SUDI). Although mould contamination was found on most mattresses, the nature and extent of mould contamination on SIDS mattress covers was similar to that found on control covers. *S. brevicaulis* was not found on any of the covers belonging to SIDS infants but was found on a small proportion of control covers from live infants. *S. brevicaulis* was found in only one filling and this was from a control case.

The Expert Group concluded that fungal infestation of SIDS and non-SIDS mattresses was similar and that contamination with the fungus *S. brevicaulis* is rare both in mattress materials from SIDS infants and in other used mattresses.

Laboratory Investigations of the Ability of Microorganisms to Produce Volatile Products from Antimony and Phosphorus Compounds (Chapter 6)

Richardson's hypothesis, quoting Gosio's work on arsenic in 1892, suggested that the trihydrides of phosphorus, arsenic and antimony were produced by the fungus *S. brevicaulis*. The volatile gas biogenerated from arsenic compounds was identified by Challenger in 1932 as trimethylarsenic, $(\text{CH}_3)_3\text{As}$, not arsine (arsenic trihydride, AsH_3), as stated by Richardson. In 1947 Barnard, a student of Challenger, had observed that an aerobic fungus, *Penicillium notatum*, when incubated with an inorganic antimony compound, released a volatile but unidentified product; attempts to reproduce the findings with *S. brevicaulis* had been unsuccessful.

Recently several scientists, however, have reported the anaerobic generation of methylated antimony products and phosphine, assumed to arise by microbiological activity, in environmental samples including those from natural waters, waste tips, sewage, and river sediments. In 1996 Dodds and colleagues detected methylantimony compounds in extracts of pondweed from a polluted lake and in 1997 Gurleyuk, Chasteen and colleague found inorganic antimony salts could be biomethylated by unidentified organisms in soil samples.

Two other research groups had attempted to confirm Richardson's hypothesis using inorganic compounds as a source of antimony. Pearce and colleagues (University of Birmingham) in 1995, using a method shown to biovolatilise arsenic trioxide, found no evidence of antimony biovolatilisation by *S. brevicaulis* and only equivocal evidence of the biovolatilisation of antimony compounds by *Phaeolus schweinitzii*, a wood decay fungus. Gates and colleagues (1995) were unable to demonstrate volatilisation of antimony under conditions which allowed arsenic biovolatilisation to produce trimethylarsenic.

The Expert Group felt it essential that further research be undertaken first to establish whether there were laboratory conditions in which biovolatilisation of antimony and phosphorus compounds could be achieved by *S. brevicaulis*, and, if so, to identify the gases formed, and second to investigate whether cot mattress samples tested in the same conditions would react in a similar way. We would also consider the relevance of the findings to the conditions in an infant's cot. Research was commissioned on behalf of the Expert Group to investigate these aspects.

Gates, Pridham and colleagues (1997) investigated the ability of a range of microorganisms (bacteria and fungi) including those from ponds, soil and cot mattresses to generate gaseous hydrides and methylated compounds from antimony compounds. Unidentified microorganisms, present in soil and cultured anaerobically, generated trimethylantimony ($(\text{CH}_3)_3\text{Sb}$) but not stibine (antimony trihydride SbH_3). They found no evidence for the production in culture of methylated antimony gases from antimony compounds by either aerobic microorganisms (*S. brevicaulis* or *Bacillus* species) or by anaerobes from cot mattress materials.

Jenkins, Craig and colleagues (De Montfort University, Leicester 1997) have identified laboratory conditions, remote from those in a cot, in which antimony can be volatilised from potassium antimonyl tartrate (PAT) and less easily from antimony trioxide (used as fire retardant) and even less from antimony pentoxide, by strains of *S. brevicaulis* when grown in liquid medium. The volatile gas was identified as trimethylantimony. No stibine was found. No evidence of antimony volatilisation was found, however, when PVC mattress samples were incubated with *S. brevicaulis* in either liquid or solid media, even in the presence of 10% carbon dioxide at 33°C (conditions which are known to increase the biovolatilisation of arsenic).

Further experiments were conducted to test whether antimony, incorporated in PVC mattress samples, could be solubilised. When PVC mattress samples with antimony contents up to 3.1% were agitated with acidic, neutral and alkaline solutions at 25°C for 5 days, or with urine or saliva or detergents at 25°C or 35°C for up to 8 days, some antimony was leached. The availability of the antimony, leached by the most effective treatments i.e. high or low pH, detergents and urine, for volatilisation by *S. brevicaulis*, was not established because these laboratory treatments decreased or inhibited the germination or growth of *S. brevicaulis*. Mattress foam filling does not contain added antimony fire retardant. The Expert Group considered, however, the possibility that leached antimony, which may theoretically permeate the foam filling, might be volatilised by microorganisms present in the foam. We concluded that, since the process would require a large number of anaerobic organisms to be active for a prolonged period in conditions devoid of oxygen to prevent oxidation of any gases formed, this was most unlikely to occur. Even if volatilisation could occur in such circumstances, the Expert Group has found no evidence to suggest it would pose a risk to infants.

Antimony was also extracted by heating mattress samples to very high temperatures, 80°C for 3 days, or 110°C for ten minutes in an autoclave, conditions which would destroy *S. brevicaulis* and most microorganisms normally present on cot mattresses. When the very high temperature samples were later incubated with added *S. brevicaulis* in liquid culture, some evidence of antimony volatilisation was found, but the amount volatilised was about 1 part in 300,000 of the original amount of antimony trioxide present in PVC and less than a fifth of the amount volatilised from an equivalent amount of antimony trioxide.

This research showed that under optimised laboratory conditions, *S. brevicaulis* can volatilise antimony compounds to produce trimethylantimony. Stibine, the hypothesised toxic gas, was not detected. Biovolatilisation of antimony compounds encapsulated in cot mattress covers was not achieved under any laboratory conditions, except when the antimony constituents had first been extracted at very high temperatures from PVC. These high temperature conditions are inconceivable in the cot environment.

Antimony compounds used as fire retardants may be contaminated with low levels of arsenic. The arsenic content of the mattress samples was negligible and there was no evidence of arsenic volatilisation from PVC samples under any conditions.

Phosphorus is ubiquitous in the environment and it is known that biogenic phosphine can be generated in landfills, compost, and in animal and human faeces. Gates and Pridham, Jenkins and Craig collaborated in testing whether phosphine could be generated from PVC. Neither phosphine nor trimethylphosphorus was generated by *S. brevicaulis* from cot mattress samples, even when other phosphate compounds were added to or were present in the culture medium.

In 1997, W R Cullen (University of British Columbia, Canada) in a talk described one experiment in which *S. brevicaulis* was grown with added soluble PAT under totally aerobic conditions in which after 11 days he detected trace amounts of antimony gases including 10 picograms of stibine (a picogram is one millionth of a microgram). Cullen considered that impurities in the medium could account for the trace amounts found and concluded that the finding was irrelevant in the context of cot death. This explanation is consistent with the extensive studies of Jenkins and Craig who found no stibine using PAT. Cullen did not detect any volatile antimony compound when *S. brevicaulis* was grown with antimony trioxide, the compound used as a fire retardant.

The Expert Group conclude that the substantial new scientific data generated by these experiments demonstrate that biovolatilisation of antimony compounds can be achieved under optimised laboratory conditions to produce trimethylantimony but not stibine. These conditions could not occur in an infant's cot. No research group has found any evidence for volatilisation from antimony trioxide encapsulated in PVC mattress cover samples under any conditions. No evidence of arsenic volatilisation from PVC materials has been found even under optimal laboratory conditions. There was no evidence of phosphine production by *S. brevicaulis* under any conditions.

Toxins and Sudden Infant Death Syndrome (Chapter 7)

According to the toxic gas hypothesis, phosphine and stibine have the same lethal mode of action as arsine, and would cause SIDS by inhibiting cholinesterases. (The function of one cholinesterase, acetylcholinesterase (AChE) is to break down acetylcholine, a chemical which is of critical importance for the normal functioning of the nervous system.) Richardson claimed that the anticholinesterase effect would result in increased levels of acetylcholine in the blood and lead to cardiac failure and hypoxia in infants.

The features of SIDS, however, are not compatible with those of acute poisoning with anticholinesterases such as organophosphate or carbamate pesticides, and there is no evidence of reduction in mean brain AChE activity in the brains of SIDS infants which have been examined. Hussain and colleagues (Bristol University) recently found that antimony, either as a soluble salt or as stibine gas, did not inhibit plasma or red cell cholinesterase.

The Expert Group reviewed further published data on the toxicity and mode of action of the gases. While it is agreed that phosphine, arsine and stibine all have high overall toxicity, their modes of action are not identical. Poisoning with arsine and stibine is characterised by haemolysis of red blood cells. SIDS babies do not show postmortem evidence of haemolysis, and, therefore, these gases cannot be the cause. Trimethylarsenic does not cause haemolysis in animals and its overall toxicity is much lower than arsine. Similarly the available data indicate that trimethylantimony is of very low toxicity and is unlikely to cause death even at very high exposures. Phosphine has not been associated with haemolysis in cases of human poisoning but causes pulmonary oedema of a severity not found in SIDS.

The Expert Group conclude that there is no toxicological evidence that SIDS is due to an anticholinesterase action or to poisoning by the toxic gases phosphine, arsine or stibine, or their trimethyl derivatives.

The Expert Group also considered the wider question of whether chemicals in cot mattresses pose any risk to infants. We have reviewed the toxicity of antimony- and phosphorus-containing fire retardants used in PVC and other cot mattress material, and have found no reason to believe that they present any risk to the health of infants.

Pathology of SIDS, Normal Infant Development Physiology and Insights into Possible Pathophysiological Mechanisms (Chapter 8)

Sudden deaths of unknown cause are reported in England and Wales to the Coroner (in Scotland to the Procurator Fiscal), who arranges a postmortem examination. The Expert Group considered the characteristic postmortem findings in SIDS for evidence of poisoning by phosphine, arsine or stibine. Poisoning by arsine or stibine would be apparent as significant haemolysis - yellow staining of blood vessels and deep discolouration of blood serum or plasma and urine - which has not been

seen in SIDS postmortems. Nor is there in SIDS any postmortem evidence of gross pulmonary oedema characteristic of phosphine poisoning.

The Group also reviewed the developmental physiological features of sleep, temperature and metabolic rate which Richardson proposed put infants at especial risk, and examined what is known about the modes of death in SIDS babies to see if they provided support for the toxic gas hypothesis.

Richardson suggested that leaving infants for long periods, especially at weekends, increased the danger of inhaling toxic gases. The observation that there is an increased risk of sudden unexplained infant death at weekends can be found in reports of deaths attributed to accidental suffocation dating back to the nineteenth century, long before PVC mattresses were available. Some recent studies, however, have not found a weekend excess of SIDS.

There is no evidence that temperatures as high as 42°C occur in the cot environment, as suggested by Richardson. Several studies of the range of skin temperatures in healthy babies and those with respiratory infections have shown that the body surface skin temperature range is normally 33° to 35°C and rarely exceeds 37°C.

Richardson has suggested that the reason for the excess of boys amongst infants dying as SIDS is that their metabolic rate (and thus heat production) is higher than that of girls. Several studies, however, have found no evidence of any difference in the metabolic rate between boys and girls during infancy.

The suggestion that apparent life-threatening events in infants are a result of partial anticholinesterase poisoning is not supported by the rapidity with which such infants recover consciousness when given resuscitation and the relative rarity of further major events within the following hours.

The features of those infant deaths which have occurred during the course of detailed physiological recordings are also different from the sequence of events which would be expected to occur during anticholinesterase poisoning where a decrease in heart rate is not usually observed. For example, recent (1994) evidence from infants who died suddenly and unexpectedly whilst undergoing cardiorespiratory monitoring showed that, in these cases at least, the first abnormal

event was a sudden severe, prolonged bradycardia (slowing of the heart rate), followed by cessation of breathing. The precise series of events which occurs during a sudden infant death is seldom known; nor is it known whether there is a single final common pathway or a number of pathophysiological pathways. The characteristic pathological findings have been interpreted as suggesting that respiratory failure is the final event in the majority of cases, perhaps preceded by one or more episodes of tissue hypoxia of variable severity.

Antimony and Infant Health (Chapter 9)

The detection of antimony in infants was used on the Cook Reports as key evidence in the support of the toxic gas hypothesis. In particular, the concentration of antimony in liver and in blood was reported to be higher than normal in SIDS infants and to correlate with the antimony content of their cot mattresses. Hair antimony concentrations in apparently healthy live infants were said to be higher than in their mothers and also to correlate with the antimony content in the infants' cot mattresses. It was argued that the antimony found in infants indicated exposure to stibine.

The Expert Group reviewed published data on antimony levels in human tissues and initiated research studies to investigate the range of antimony concentrations in healthy infants, in infants who had died from known causes and in SIDS. We also examined the relationship between antimony concentrations in infants and their cot mattresses.

Measurement of extremely low quantities of an element in body tissues and fluids is particularly susceptible to several technical difficulties which can influence the accuracy of values obtained. These include collection, processing and storage of samples, since, for example, antimony is present in formalin used prior to preservation of tissue samples in paraffin wax.

Antimony, usually as trivalent antimony trioxide, is present in the domestic environment and in human diet. When ingested, it is poorly absorbed. When inhaled there is long term accumulation in the lung and eventual redistribution to the liver. Measurement of antimony in the blood reflects recently absorbed antimony but, because of its uneven distribution between the red cells and the plasma or serum, measurements of the latter are unreliable.

The Expert Group reviewed the published data on antimony concentrations in adults and in infants, in order to establish the normal range in different tissues in fetal and stillborn infants and in infants dying from known causes. We also reviewed recent studies of antimony levels in the urine, serum and hair of live healthy infants.

This review demonstrated that antimony concentrations found in lung and liver of infants dying in utero and from known causes are similar to those in tissues obtained at postmortem examination in adults not occupationally exposed. The concentration of antimony found in fetal lung and liver, in stillborn tissue and in umbilical cord tissue, amniotic fluid, human placenta and in human breast milk falls within a similar range to each other and indicates prenatal or early postnatal assimilation, the most likely source being maternal diet.

Trace amounts of antimony were found in samples from the majority of healthy infants. There was wide individual variation and the range of concentration differed between different types of sample, with very small concentrations found in urine, serum and liver and lung tissues, and the highest in hair. This is similar to the pattern of distribution in adults. The distributions are skewed, the majority of cases having low concentration and a small number having high concentration, a pattern common to other non-essential trace elements. Two studies, undertaken before the introduction of antimony trioxide in cot mattresses and published in 1982 and 1985, found a similar range of antimony concentrations in the hair of healthy infants and in fetal liver, respectively.

The Expert Group investigated the distribution of antimony in SIDS. We examined the blood data presented on the Cook Report. This had used reference values derived years earlier on specimens collected and processed differently; hence no conclusions could be drawn. We also examined unpublished data from SIDS and non-SIDS sera provided by the Cook Report. Since the collection and storage methods were not known and because serum data are unreliable, interpretation of the results was not possible.

We investigated Taylor's (St Lukes Hospital, Guildford) finding of increased antimony in the liver of 20 out of 38 SIDS and only 1 out of 15 non-SIDS control infant livers, presented on the Cook Report. We examined further studies of liver and lung concentration in SIDS and in control infants who had died from known causes to establish whether higher concentrations of antimony are associated with SIDS. This focused on liver in three studies to replicate Taylor's work and on lung as a more direct marker of acute exposure to inhaled antimony.

We conclude that the reported increase in liver antimony in SIDS infants compared to controls is unsupported by the subsequent studies. Antimony is detectable in the majority of postmortem liver and lung samples of infants irrespective of the cause of death. The concentrations of liver and lung antimony in SIDS infants are not significantly different from those found in infants who have died from known causes and are within the normal range.

The Expert Group examined the relationship between antimony in infants' tissue and the antimony trioxide content of their mattresses. The Cook Report supplied us with their data. Their evidence for a correlation was flawed since it relied upon one paired liver and mattress antimony value. We found that in their other two cases measurements were unreliable having been done on formalin-fixed liver samples embedded in paraffin wax. In a supplementary study, recommended by the Expert Group, no evidence was found for an association between liver or lung antimony in SIDS infants and the antimony content of their mattresses, in particular, liver and lung antimony concentrations were not increased in infants who slept on mattresses containing higher amounts of antimony.

The Expert Group also investigated the antimony concentration in adult and infant hair and the infant hair concentration in relation to the antimony content of cot mattresses. Detailed analysis of the Cook Report data and the chemical determinations confirmed that hair antimony was higher in infants than in their mothers, but did not show a correlation between the amount of antimony in the hair of an infant and the antimony trioxide content of the infant's mattress. New studies carried out on behalf of the Expert Group showed similar results.

The Expert Group conclude that the hair antimony concentration is higher in infant than in maternal hair but that there is no correlation between infants' hair antimony and the antimony trioxide content of their mattresses. Antimony is detected in the hair of the majority of live, apparently healthy infants which suggests the amounts found are not harmful.

Use of Flame Retardant Chemicals in Cot Mattress Materials and Environmental Sources of Antimony (Chapter 10)

The toxic gas hypothesis states that the source of the phosphorus and antimony compounds which supposedly generate phosphine and stibine is the phosphate plasticiser and antimony trioxide used as a fire retardant (FR) in cot mattress covers or fillings. Richardson attributes the problem of cot deaths to the introduction of PVC mattresses in about 1953, and the claimed increase in the 1980s, with a peak incidence 1986-88, to the increased concentration of fire retardants, especially in 1985-87 in preparation for the introduction of the Furniture and Furnishings (Fire) (Safety) Regulations 1988.

The Expert Group's enquiries have found that PVC was first used as a mattress covering material in the early 1960s. The cot mattress manufacturers purchase the foam fillings and PVC covering from a variety of different manufacturers. The Furniture Regulations promulgated in July 1988 required upholstered articles to have fire resistant fillings but were not mandatory immediately. The requirements were phased in over time, applying to polyurethane foam from November 1988 and to other fillings from March 1989, and were met by using melamine plus phosphate fire retardant in polyurethane foam used in cot mattress fillings. The Regulations did not specify fire resistance requirements for the cover fabric of mattresses. These materials come under the General Product Safety Regulations, which are complied with by conforming with a relevant standard for fire safety or ignition resistance, and which do not specify the use of particular fire retardants. Antimony trioxide was used in domestic PVC cot mattress covers from about 1988, and the alternative of using a phosphate fire retardant, which also has plasticising properties, increased in the 1990s.

The Expert Group recommended a further study to analyse the antimony content of cot mattresses and compare this with the family's recollection of date of purchase. This CESDI/SUDI supplementary study indicated that antimony fire retardant was first present in PVC cot mattress covers from 1988 onwards, was found at highest concentrations in mattresses purchased between 1989 and 1991 and the median level was still high in those purchased in the period 1992-4. The SID rate decreased over a period when the highest amounts of antimony fire retardant was present in mattresses. High levels of antimony were still present in 1992 when the steepest decline in SID rate occurred, immediately following the 'Reduce the Risk of Cot Death'/'Back to Sleep' campaign.

The Expert Group also investigated other sources of antimony and the possibility of transfer to infant tissues in a form other than as a gas. Several groups have identified antimony compounds in many products in common use, e.g. vehicle tyres and polyester fabrics, and hence it is present in household dust, and particles are available for inhalation and ingestion.

The LGC examined whether antimony could be transferred from the polyester net webbing used on some cot mattresses and from flame retardant push chair covering, and showed that transfer to human hair can occur when hair is rubbed against fabric materials containing this element. The quantity transferred was enhanced slightly by the presence of moisture and marginally increased by simulated stomach acid. Washing and drying of the hair removes the antimony.

The Expert Group conclude, therefore, that there does not appear to be any correlation between the concentration or use of antimony trioxide or phosphate based FR in cot mattresses and the SID rate, and that there are sources and routes by which antimony can be adsorbed onto human hair other than via a gas.

Trends and Epidemiology of Sudden Infant Death Syndrome in Relation to the Toxic Gas Hypothesis (Chapter 11)

Richardson claimed that the increased incidence of SIDS since the 1950s can be traced to the introduction in the early 1950s of PVC covered cot mattresses and to the addition of fire retardant chemicals from 1985-87. He compared the SIDS rates in countries using PVC mattresses with low rates in Japan, where infants sleep on cotton futons which reportedly do not contain phosphorus, arsenic and antimony compounds (but where few postmortems are held and hence the SIDS rate is unreliable). He also claimed that the epidemiological features of SIDS are consistent with the toxic gas hypothesis and suggest a single cause.

Our investigations have shown that Richardson's claims about sudden infant death rates before 1970 are unsubstantiated. There are no reliable data before 1971. Estimated rates for cot deaths quoted in special reviews in different localities in the UK over periods between 1948 and 1976 give rates ranging from 1.6 to 4.0 per 1000 live births. The general picture that emerges is of a national rate of about 1.6 in the late 1950s that increased, probably in association with an increased prevalence of prone sleeping in the 1960s, to a level up to 2.5 per 1000 live births in the late 1980s

and was followed by a sharp fall, particularly after the introduction of the ‘Reduce the Risk of Cot Death’/‘Back to Sleep’ campaign in Autumn 1991, to a level of 0.65 per 1000 live births in 1996.

We compared trends in SID rates with the use of antimony FR in cot mattresses introduced in 1988. The combined SRDh and SID rate is a more accurate reflection of the scale of the problem since 1971. This rate, with minor fluctuations, was relatively stable between 2.3 and 2.5 per 1000 live births until 1988. The rate began to fall in 1989 and 1990 but the steepest decline in the SID rate occurred in the year 1992 when the amount of antimony FR in cot mattress materials was still at a high level.

Although Richardson claims the decline in SIDS rates from 1989 was due to his precautionary advice that a new mattress should be used for every new child or old mattresses should be covered with a polythene sheet, the evidence from the CESDI/SUDI Study (June 1995-March 1996) was that very few, 9 out of 448, control infants (2.0%) were noted to be sleeping on cot mattresses wrapped in polythene sheeting, whilst 2 out of 82 (2.4%) SIDS infants died on mattresses wrapped this way. A third SIDS death, 1 out of 117 SIDS, had occurred on a polythene wrapped mattress in a previous period, February 1993-January 1995, when 14 out of 664 (2.1%) control infants had slept on polythene wrapped cot mattresses. Furthermore the decrease in SIDS rates following adoption of supine sleeping position, not only in Britain but also in countries reportedly not using fire retardants, is compelling evidence that the changes were related to sleeping position rather than to the use of fire retardants.

Richardson quoted high rates, above 5 per 1000 live births, for SIDS in army families, but misinterprets information when he claims this was due to the use of biocides and fire retardants in service issue mattresses. These rates were based on very small numbers and although such rates were apparent in some military districts in the 1970s and 1980s, the rates for British Forces in Germany 1987-89 and 1990-95 had fallen to 3.9 and 1.9 per 1000 live births respectively. The higher rates in Army families than in married civilians could reflect the socio-economic status and occupational life style of the military rather than the constituents of cot mattresses. The decrease in service family rates of SIDS is more likely to be due to intervention to reduce the risk and advice, in particular, on supine sleeping position. The Ministry of Defence informed us that service issue cot mattresses had not contained arsenical preparations and Richardson’s assumption that army mattresses before 1989 contained arsenical preservative OBPAis incorrect.

Epidemiological data from two published studies (CESDI/SUDI and the Scottish Cot Death Trust study) found no increased risk of SIDS for infants who slept on PVC cot mattresses.

The Expert Group reviewed the epidemiological features of SIDS in relation to sex, age, prematurity and birthweight, birth order, environmental conditions, socio-economic status and smoking and found many of Richardson's arguments to be either incorrect or to have other possible explanations. For example, although SIDS rates are higher in later born children in a family, it is incorrect to claim that this can only be because they are sleeping on previously used mattresses. Similar patterns of risk in relation to birth order are found in the epidemiology of infectious diseases.

The Expert Group concludes that changes in the SIDS rate are unrelated to the use of antimony-containing fire retardants, that the epidemiological features of sudden infant deaths can be explained without invoking the toxic gas hypothesis, and that some aspects of the epidemiology are at variance with the hypothesis. Richardson's assertions are not supported by incidence rates in Britain and in other countries, nor by the direct measurement of antimony fire retardant in cot mattresses in the late 1980s and early 1990s or the evidence of mattress manufacturers.

Conclusions (Chapter 12)

The Expert Group has investigated all aspects of Richardson's toxic gas hypothesis and accompanying evidence. Our conclusions are as follows:-

1. Cot mattress contamination with the fungus *S. brevicaulis* is rare, and no more common in SIDS mattresses than in other used mattresses. In his experiments, Richardson had mistaken bacteria for the fungus.
2. There is no evidence for biovolatilisation of phosphorus, arsenic and antimony from PVC cot mattress samples by *S. brevicaulis*, under conditions relevant to an infant's cot. We have, however, identified laboratory conditions, wholly unlike those that could occur in an infant's cot, in which added antimony is biovolatilised, but to trimethylantimony and not stibine.

3. There is no evidence that SIDS is due to poisoning by phosphine, arsine and stibine or their methylated derivatives. We note also the absence, in postmortem and pathological studies of SIDS infants, of the features normally associated with haemolysis or gross pulmonary oedema which would be compatible with arsine/stibine or phosphine poisoning respectively; nor is there any evidence of anticholinesterase poisoning

4. Low amounts of antimony can be detected in samples from the majority of live infants, and the concentrations in SIDS infants are not exceptional. The antimony tissue distribution in infants is typical of the pattern seen with other non-essential trace elements. The presence of antimony in fetal tissue and infant hair was reported before the introduction of antimony fire retardants in mattresses. There is no correlation between antimony concentrations in infants' tissues and their mattresses. The measurable amount of antimony in fetal liver, lung and umbilical cord tissue suggests maternal transfer during pregnancy. Antimony can also be transferred physically from child care articles to hair postnatally. We conclude that antimony concentrations in the tissues of SIDS infants are not excessive and that there are a number of sources of antimony other than the fire retardants used in cot mattress materials.

5. We have found no evidence that the changing rates of sudden infant death correspond to the introduction and removal of antimony- and phosphorus-containing fire retardants in cot mattresses. Although some features of the epidemiology of SIDS are compatible with the hypothesis, a detailed review of the data does not support it.

6. Overall, we conclude the toxic gas hypothesis is unsubstantiated. There is no evidence to suggest that antimony- and phosphorus-containing compounds used as fire retardants in PVC and other cot mattress materials are a cause of SIDS. In addition, we considered the wider question of whether chemicals used as fire retardants in cot mattress materials pose any other health risk to infants and found no reason to believe that they do.

Key Steps in Our Investigation of the Toxic Gas Hypothesis

Key Components of the Hypothesis	Expert Group Verdict	Reasons for the Verdict	Report Reference
1) A fungus, <i>Scopulariopsis brevicaulis</i> , grows on the mattresses of all SIDS infants.	Incorrect	<ul style="list-style-type: none"> • Mattress contamination with <i>S. brevicaulis</i> is rare and no more common on SIDS mattresses than on other used mattresses. • Replication of Richardson's experiments using microscopy showed bacteria had been mistaken for the fungus. 	Chapter 5 and Appendix III
2) The fungus acts on chemicals in cot mattresses to produce phosphine, arsine and stibine, and their lower alkyl derivatives.	Incorrect	<ul style="list-style-type: none"> • Replication of Richardson's experiments but with additional chemical analysis of papers found that the colouration, used as evidence of gas production, was not due to phosphorus, arsenic or antimony deposits, but to sulphur-containing gases. • <i>S. brevicaulis</i> has been shown to volatilise added antimony compounds to generate trimethylantimony, not stibine, in specific laboratory conditions wholly unlike those in a cot. PVC mattress samples incubated with the fungus did not produce volatile phosphorus, arsenic or antimony compounds when tested under these conditions. • A small proportion of the encapsulated antimony trioxide can be extracted from PVC by specific treatments. Very high temperature treatment of PVC (which could not occur in a cot) released just sufficient bioavailable antimony to enable volatilisation to occur when it was cultured with added <i>S. brevicaulis</i>. 	Chapters 5 and 6
3) Death from SIDS is due to anti-cholinesterase activity of the gases resulting in increased acetylcholine in the blood and subsequent cardiac failure in infants.	Incorrect	<ul style="list-style-type: none"> • Laboratory tests have shown that stibine at toxic concentrations does not inhibit plasma cholinesterase or acetylcholinesterase activity. • Acetylcholinesterase activity is not reduced in brain tissue from SIDS infants. • Pathological findings in SIDS are not consistent with anticholinesterase poisoning. Neither is there postmortem evidence of gross pulmonary oedema or haemolysis, effects characteristic of poisoning by phosphine and stibine, respectively. 	Chapters 7 and 8
4) Antimony in blood, serum, lung and liver of SIDS infants is higher than normal and reflects exposure to volatile stibine. Higher levels in infants' hair compared to their mothers' was evidence of infant exposure to stibine from cot mattresses since antimony is rare in the domestic environment.	Incorrect	<ul style="list-style-type: none"> • Technical difficulties make comparisons of SIDS and non-SIDS blood/serum antimony levels unreliable. • Antimony can be detected in the majority of fetal and infant tissues. Liver and lung antimony concentrations in SIDS and non-SIDS are similar and within the normal range. • Antimony in infant hair and fetal liver was reported before the use of antimony fire retardants in PVC. • Antimony in infants' tissues and hair is not related to the antimony content of cot mattresses. • Antimony is ubiquitous in the domestic environment and measurable amounts are found in adult diet and breast milk. In general, the antimony concentration in infant hair is higher than maternal hair. The source in infants may be prenatal and post-natal exposure, from diet and the environment. 	Chapters 9, 10 and Appendix III
5) Changes in SIDS rates correspond to the introduction and removal of antimony - and phosphorus - containing fire retardants and plasticisers in PVC cot mattresses.	Incorrect	<ul style="list-style-type: none"> • The introduction of these fire retardants was not associated with an increased incidence of SIDS. Antimony was not introduced in domestic cot mattresses until about 1988 and was used in many until 1994. This was a period during which the fall in the SIDS rate was the most rapid. The SIDS rate was high before the use of antimony as a fire retardant in PVC. • Changes in SIDS rates in other countries are not related to use of antimony-containing fire retardants in cot mattress material. 	Chapters 10, 11 and Appendix III