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The toxicity of trimethylarsine: an urban myth†

1. Introduction

In environmental terms, the 19th century was the age of arsenic.[1,2] The uses of this element are almost too numerous to mention—embalming, cosmetics, glass and gunshot manufacture, pyrotechnics, taxidermy, weed and rodent control, and particularly in medicine, both by prescription and self-medication. Arsenic was characterized as a "therapeutic mule".[3] For centuries, it was used for murder being known in France as "poudre de succession" (inheritance powder); the name arsenic is essentially synonymous with poison. However, in areas such as the Austrian province of Styria, arsenic was eaten, as the oxide or sulfide, to give freshness and beauty to the skin, to enhance sexual potency and to improve breathing and stamina in mountain climbing.[4,5]

In 1775, Scheele discovered copper arsenite, $CuHAsO_3$, a green pigment, known eponymously as Scheele's Green. A related compound, copper acetoarsenite, $Cu(CH_3COO)_2 \cdot 3Cu(AsO_2)_2$, acquired a variety of names—Schweinfurt Green, Mitis Green, Vienna Green, *etc*. These pigments found extensive use for coloring wallpapers, cloth and tapestries, various wrappings, children's toys and even for foodstuffs (*e.g*, confectionery, blancmange).[1] Europeans, and to a lesser extent Americans, in the 19th century were living in a green environment, provided by green pigments based on arsenic, but in no way related to modern concepts for the adjective, green.

Early in the 19th century, it appeared that there was a connection between ill health, possibly death, and habitation in rooms containing arsenic-coated wall coverings, especially if the rooms were damp. In a newspaper letter of 1839, the famous chemist, Leopold Gmelin, strongly warned against the dangers of arsenical pigments on wallpapers.[6] He had observed an adverse, mouse-like odor in rooms containing them, especially those facing to the North, which he attributed to a volatile arsenic compound, "alkorsin"—it is probable that he intended alkarsin, dimethylarsinoxide, $(CH_3)_2As–O–As(CH_3)_2$. Other authors reported the odor as leek-like. An alternative possibility was that arsenic-containing particles were flaked from the walls as a poisonous dust. Over the years an extensive dust/gas controversy developed: was the poisoning due to formation of a toxic gas or to inhalation of dust particles? The early literature has been reviewed.[7–9] Some of the reported events were truly bizarre. For example, in the USA, a family slept in a house where the bedrooms had been cleaned with a solution of arsenic mixed with naphtha and turpentine.[10] Perhaps it is not surprising that they were seized the next day with symptoms of acute arsenic poisoning. One wonders where arsenic obtained a reputation as a cleaner, and what happened to whoever did the cleaning.

This article is concerned with the possible toxicity of an arsenical gas. However, the dust theory played a role in rather more recent times. The USA ambassador to Italy, Clare Booth Luce, had to resign her position in 1956 on account of arsenic poisoning. She had slept at the Embassy in a room with a ceiling decorated with arsenic-laden materials. A washing machine on the floor immediately above caused vibrations and lead arsenate particles fell as a "gray dust". A certain irony has been noted: she and her husband, Henry Luce, had been dubbed "Arsenic and Old Luce".[11,12]

2. The work of Bartolomeo Gosio and arsenic fungi

Although there were early suggestions that an arsenical gas, possibly arsine, AsH_3, could be formed from arsenical wallpaper, paste, *etc*., by microbial action, it was not until 1892 that the Italian physician, Bartolomeo Gosio, demonstrated that certain fungi do indeed convert a variety of arsenic compounds to a volatile form.[13,14] One particularly active organism was isolated from a piece of carrot exposed to air. It is now known as *Scopulariopsis brevicaulis*, but was then identified as *Penicillium* (*sic*) *brevicaule*. Growth of this, and some other fungi, on arsenic compounds, including the commercially-used "greens", led to the formation of a garlic-odored gas, often termed Gosio Gas. Early chemical analysis suggested that the gas was diethylarsine. Re-examination in 1933, however, conclusively proved that Gosio Gas was trimethylarsine (see later).

Gosio apparently assumed that the arsenical gas was toxic, but his studies were minimal. He contributed a communication ("communicazione preventiva") titled "Action of Microphytes on Solid Compounds of Arsenic: A Recapitulation", to a Congress of Hygiene in London in 1891.[15] This paper briefly reviewed the gas/dust controversy and described the volatilization of arsenic from compounds and pigments by certain fungi (*e.g*., *Mucor* (*sic*) *mucedo*). He claimed that "experience has repeatedly demonstrated the serious evils that may arise from their use" (*i.e*., Scheele's and Schweinfurt Greens), and stated that "in given conditions... arsenical gases may be given off from hangings colored with Scheele's and Schweinfurth's green through the vegetation of the mucor... hence the dangers to those who live in such an atmosphere."

In 1892, he described in more detail the isolation of what he termed arsenic-fungi ("arsenio-muffe"), conditions for production of the garlic-odored arsenical gas, and the development of a microbiological test for small amounts of arsenic based on odor production. It again appears that toxicity was assumed; he referred to "transformazione del veleno solido in veleno gassoso" (*i.e*., to the transformation from poisonous solid arsenic compounds to a poisonous gas).[13]

One year later he re-emphasized the activity of *S. brevicaulis* towards arsenic compounds, stating that it developed "avec une notable intensité le gaz

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arsenical, et il est dangereux de s'en approcher'' (dangerous to approach it). Moreover, ''Un rat qu'on expose à ces sortes d'émanations tombe rapidement dans des convulsions mortelles''[16] (a rat exposed to the gas fell down with mortal convulsions). He also stated that individuals exposed to the garlic odor for too long experienced ''troubles''; he himself had this experience on occasion.[17]

Gosio described the lethal action of the gas to a mouse as follows: ''Denn setzt man eine kleine Maus (*Mus musculus*) in ein Gefäss, in welchen der Schimmelpilz in gegenwart von Arsenik reichlich entwickelt ist, so stirbt dieselbe häufig nach wenigen Secunden''[18] (a small mouse, placed in a vessel with abundant fungal growth in presence of arsenic, frequently dies in a few seconds). This report was the basis of the statement in *Science* that the volatile substance formed by *Penicillium* (*sic*) *brevicaule* was ''instantly fatal to a mouse''.[19]

In other work, rabbits exposed to an abundant growth of *S. brevicaulis* developed a form of pneumonia, ''polmonile penicillare''.[20] This was regarded as a direct toxicity from a massive amount of fungal spores in contrast to the indirect pathogenicity produced by ''un gaz toxique'' in the presence of arsenic. Gosio again reported his own ''troubles'' from contact with the gas and reported that this was confirmed by others (see later).

In 1901, Gosio indicated that animal experiments had not given very satisfactory results.[20] Rats placed in a flask (''ballon'') with the gas quickly died; other authors attributed these deaths to CO_2, rather than to the ''arsine''. There was a rapid consumption of O_2 and the creation of ''une véritable *grotte du chien*.'' However, Gosio claimed that death also resulted when CO_2 was removed by KOH and that the symptoms were similar to those observed with control animals using arsine itself (''l'hydrogène arsenical''). The colorful phrase, *grotte du chien* (english, Dog's Cave; italian, La Grotta del Cane) refers to certain caves, *e.g.*, in Royat, Clermont-Ferrand, France and near Naples, Italy, where gases such as CO_2 form a layer on the cave floor that is toxic to a certain height. Hence, a small animal such as a dog has trouble breathing and can die if it is not removed quickly. The upper layers of air are safe to breathe, so that an individual, presumably an adult, has no problem. Rather than harming or sacrificing a dog, the effect can be demonstrated with a candle.

With the discovery of Gosio Gas, the dust/gas argument appeared to be largely settled in the latter's favor. Perhaps the idea of a silent poison gas surrounding individuals in their everyday lives was persuasive. However, although there is substantial literature concerning health problems allegedly associated with exposure to arsenic, especially wallpapers and tapestries, a careful analysis indicates that there is almost no solid evidence.[21] Analysis for arsenic in urine, an indicator of exposure, in the 19th century was neither easy nor exact and required large volumes; attempts to detect arsenic in air samples were inconclusive.

3. The work of Challenger and the Leeds school

In the early 1930s, Frederick Challenger and his colleagues at the University of Leeds restudied the fungal volatilization of arsenic. In May, 1932, they demonstrated that Gosio Gas was trimethylarsine, $(CH_3)_3As$, TMAs, and not, as Gosio had believed, diethylarsine.[22] Challenger pioneered the study of biological methylation reactions, publishing in 1945 a comprehensive and authoritative review, ''Biological Methylation''.[7] At the beginning of this review, he noted the use of arsenical pigments for decoration, stating that as long ago as 1815 ''more or less severe cases of arsenical poisoning occurred in Germany and were ascribed to the use of domestic wall-papers the pigments on which were shown to contain arsenic.'' In his second paragraph, he is unequivocal in favor of the toxic gas hypothesis: ''It may be stated at once that the toxic compound has been shown to be trimethylarsine and that moulds growing on the damp wall-paper are responsible for its production.''

Challenger was apparently influenced by reports of a mysterious illness that in 1931 had affected a family in the Forest of Dean—an area in Gloucestershire with ancient traditions and customs. Two children, a boy and a girl, had died and two other children and the parents were sickened. At an inquest in Cinderford, January 19, 1932, it was noted that the walls of their house were moldy and covered with wallpaper. The boy's death was attributed by an expert witness to pneumonia and blood poisoning; the jury found no evidence for a role for arsenic and returned a verdict of death from natural causes. At the inquest on the girl, the County Analyst, Mr R. H. Ellis, presented data on the arsenic level of the wallpaper and plaster. A roll of unused wallpaper contained 4.4 ppm arsenic, wallpaper on damp moldy areas, 2.3 ppm, and that on dry areas, 8.3 ppm. A much higher level was found in the plaster—91 ppm. It was hypothesized that moisture came through the wall, dissolved arsenic from the plaster, and deposited it on the wallpaper. Mold growth then liberated a toxic gas. It was stated that four of the six family members had traces of arsenic (unspecified amounts) in their systems. At the inquest, Mr Ellis had stated that he had ''found definite traces of arsenic being given off in gaseous form from the wall that was affected by mould...''. In a later statement to the Editor and Publication Committee of *The Analyst*, he noted that he had exposed filter papers (size and number not specified), saturated with silver nitrate, on the walls of the house for 7 and 9 d.[23] Subsequent analysis of these papers by the electrolytic Marsh test had yielded ''small mirrors of arsenic''. The jury ruled that the girl had died from dysentery and ''to exposure to arsenic, which was generated in the house in a gaseous form''. Clearly there was more to it than the jury's official conclusion—they added a rider that ''the house was not fit for human habitation in its present condition''. A major factor in the decision was the unlikely finding that the amount of arsenic in the lungs was greater than in any other part of the body except for the large intestine.

Despite the inadequate evidence, Challenger quoted this case at length in his review. He was probably influenced by media publicity since he cites ''Daily Press, January 19–20, 1932''. He is again unequivocal about this case: ''definite traces of arsenic (were) being given off in gaseous form from the wall that was affected by mould...''. Perhaps the weakest feature in this and other cases, is that the characteristic symptoms of arsenic poisoning were not recorded.

Not only did Challenger popularize the toxic gas hypothesis but, inexplicably, he described the odor detected by Gmelin as that of garlic. The 1933 paper[22] characterizing trimethylarsine, began as follows: ''GMELIN (Karlsruher Ztg., November, 1839) ascribed certain cases of poisoning to a volatile arsenic compound liberated from mouldy wall-paper in damp rooms and mentioned the garlic odor observed under such conditions.'' As mentioned above, a recent translation reveals that Gmelin described a mouse-like odor; moreover, at about the same time, other writers described a leek-like odor. Since Challenger was fluent in German, writing his PhD thesis in that language, it seems that the only explanation for this error is that he had not actually seen the newspaper article. He was very familiar with the characteristic garlic odor of TMAs and apparently assumed that this was what Gmelin had detected.

There is little doubt that Challenger's opinions were influential in promoting a

rather general belief in the "wallpaper hazardous to health" scenario. For more than 50 years following his identification of TMAs, the toxic gas theory held sway although there was little or no further research on it. Challenger (1887–1983) maintained an interest in organometallic and organometalloid compounds to the end of his very long life.[24] In 1978, at age 91, he contributed a keynote paper to an American Chemical Society Symposium, "Organometals and Organometalloids. Occurrence and Fate in the Environment", dedicated to him and his work.[25] Although he discussed the work on TMAs, he did not comment on the toxic gas hypothesis. However, the general possibility apparently was still of interest to him since he mentioned a case of chronic antimony poisoning in a house where silk curtains had been mordanted with an antimony compound. Although formation of a volatile antimony compound was a prime suspect, attempts to demonstrate microbial volatilization of antimony at the time (1913) were negative. Later experiments by Challenger's group were inconclusive, but biomethylation of antimony is now well established.[9]

Arsenic and its compounds have from ancient times been associated with poisoning. To some extent, this categorization influenced the attention given to the toxic, arsenical gas scenario. Much as Gosio had expressed it the usual, solid arsenic compounds were well known as poisons, so by inference, this condition was confidently applied to gaseous forms. Cullen and Reimer pointed out in 1989 that the "general public, and often even the scientific community, tends to associate arsenic with poison without regard to the widely different properties of arsenic compounds."[8] In part, this attitude persisted because only recently has it become possible to speciate arsenic at the trace levels frequently found in samples ranging from bacteria to man.

4. TMAs has low toxicity

In 1935, Challenger noted that at the time of the Forest of Dean case (1931) the chemical nature of Gosio gas was unknown although his work was already in progress.[26] However, he stated that there could be "little doubt that trimethylarsine was responsible". Paradoxically, he also stated that "published statements concerning this substance vary, but it appears that as would be expected it is less poisonous than hydrogen arsenide". He quoted specifically from one of three citations that indicated survival and reproduction of mice living above cultures producing the arsenical gas.[27] The two other papers had, in fact, described other animal studies. Thus in 1914, Huss (writing from the Bacteriology Laboratory of the Pharmaceutical Institute in Stockholm) made a detailed study of many microorganisms for arsenic volatilization, using many possible substrates.[28] His results were generally similar to those of Gosio and some other investigators with one exception. In tests, with guinea pigs, rabbits and mice, he found little if any toxicity for the arsenical gas. In addition, he noted that he himself had for 6 months been working in a laboratory with an atmosphere usually with an arsenical odor (Kakodylgeruch) without illness. He concluded that the arsenic-containing gas produced by fungi had comparatively little toxicity (Die von den Pilzen erzeugten arsenhaltigen Gase scheinen eine verhältnis mässig geringe Giftigkeit zu besitzen).

Similarly, Abel and Buttenberg in Germany had found little or no problems for mice exposed to the gas for 5 h.[29] One of these investigators had experienced some disturbances (dizziness, sickness) when working with the fungal cultures, as did Gosio, but other collaborators did not. These early toxicological studies were obviously imprecise since it was difficult to separate out the actions of the arsenical gas and carbon dioxide. Moreover, there were no assays for the amount of gas to which the animals were exposed; the only indication was the intensity of the garlic odor. Nevertheless, all of these three groups of investigators failed to observe strongly toxic effects. There was a single fatality—one guinea pig was bitten to death by another.

It is difficult to understand why Challenger's belief hardened in the face of contrary evidence. In his extensive 1945 review,[7] the papers by Huss[28] and Abel and Buttenberg[29] are cited only as literature summaries and that by Hausmann,[27] featured in the 1935 paper, is not given. In promoting the toxic gas hypothesis, particularly after the Forest of Dean case, it appears that Challenger was uncharacteristically devious. For many decades, his pre-eminent role in biomethylation studies influenced other writers to indicate toxicity for TMAs.

It seems to be the case that when something is dignified as a fact, or natural law, people can be browbeaten into ignoring obvious facts that disagree with it. For instance, an account of the microbial methylation of metalloids (arsenic, antimony, and bismuth) emphasized the toxic gas theory but did note an apparently paradoxical situation.[9] A 1990 paper reported that when TMAs was dissolved in olive oil and administered *per os* to mice it had a very low acute toxicity; the 50% lethal dose was 7.87 g kg^{-1} body weight.[30] It was shown that the orally administered TMAs was rapidly and largely excreted in the urine as trimethylarsine oxide, indicating that TMAs was actually absorbed by this route. With high doses, a mild, transient hemolysis was observed in hamsters. Since hemolysis is a characteristic of arsine poisoning, it was possible that high levels of TMAs exhibited arsine-like toxicity. Although it seemed possible that the result might be different for inhalation, it is now apparent that this 1990 paper was the tip of an iceberg.

As the industrial use of arsines including TMAs increased,[31] particularly for the preparation of compounds such as the semiconductor, GaAs, *via* metalorganic chemical vapor deposition (MOCVD) the toxicity question, particularly for inhalation, had to be addressed. It appears that much research on TMAs toxicity was done by industrial groups and tended to be discussed at various meetings, rather than published in the open literature. These results are relatively inaccessible. Thus, in July 2004, a query to PubMed for "trimethylarsine toxicity" gave 16 responses that were generally not very informative. The paper on oral administration[30] was included but there were no papers dealing with toxicity on inhalation. For acute inhalation toxicity, the LC_{50} value for TMAs (4 h exposure) is now regarded as $>20\,000$ ppm:[32,33] comparable values for dimethylarsine and arsine are, respectively, 130 and 5–45 ppm. The OHS Material Safety Data Sheet (revised September 18, 2001) gives the following data for TMAs:[34]

20 000 ppm inhalation—mouse LC_{50} (Bioresearch laboratories)

20 500 ppm/4 h inhalation—mouse LC_{50} (no citation)

7870 mg kg^{-1} oral-mouse LD_{50} (clearly the data of Yamauchi *et al.*, ref. 30) Q3

This Data Sheet also notes that the main inhalation hazard for TMAs is associated with "arsenic oxide fumes" on account of a pyrophoric property. The latter might also lead to thermal burns. More recent work in Belgium indicates that 3 month-old male rats sustain a 1 h exposure to air mixed with gases emanating from a mixture of trimethylarsine oxide, TMAsO, and $NaBH_4$ in 2 M HCl (*i.e.*, a generating system for TMAs). Measured TMAs concentrations were from 21–70 ppm.[35]

Unlike TMAs, arsine itself is very toxic. The present guidelines for arsine exposure vary among jurisdictions but the USA Federal Standard (TLV, Threshold Limit Value) is 0.05 ppm (0.2

mg m^{-3}). Toxicity depends on both the arsine concentration and the length of exposure. Thus 3–10 ppm (60–200 mg m^{-3}) may cause slight symptoms in several hours, 10–60 ppm may be dangerous in 30–60 min, and 250 ppm may be fatal after 30 min exposure.[36] Only 4 decades ago it was confidently asserted that "Arsine is unique among the industrially toxic arsenic compounds, being of no economic importance and seldom manufactured outside the laboratory...".[37] This interesting comment vividly indicates how rapidly a technology such as MOCVD can develop.

While it now appears certain that TMAs has very low toxicity on inhalation or by oral administration, it is a potent genotoxin *in vitro*.[38] Thus supercoiled DNA (pBR32 or ϕX174) on cellulose nitrate filter paper was exposed to monomethyl arsine, MMAs, dimethylarsine, DMAs, and TMAs. Both DMAs and TMAs damaged DNA in less than 30 min and these materials were 100 times more potent than dimethylarsinous acid (the most potent genotoxic arsenical then known). DNA nicking was also pronounced with DMAs and TMAs in solution. More recently, stibine and trimethylstibine were also shown to be genotoxic.[39] In earlier work, TMAs was examined for embryolethal and embryotoxic effects with rat embryos.[40] Small amounts of pure TMAs (7.5, 15 or 30 μl) were added to 15 ml portions of culture medium; acute toxicity began to be observed with 9 mM TMAs. This concentration was much higher than for other environmental toxicants and TMAs was not classified as very embryotoxic.

5. Public health considerations for arsenic in the 19th century

It is clear that in the 19th century, certain habitations had an atmosphere whose odor (mouse-like, leek-like) may have suggested a volatile arsenic compound. In a very few cases, a garlic odor was reported, generally by those having prior experience with the odor of TMAs. It is, therefore, remotely possible that some volatile arsenic compound may have been present as required by the toxic gas hypothesis. It must be asserted, however, that it is now very clear that illness could not have been due to TMAs, for the following reasons:

1. There is no good evidence that TMAs had actually been formed in any room coated with arsenical-containing wallpaper.

2. Gas production on wallpaper is unlikely. Although *S. brevicaulis* is said to be abundant in nature, the fungal process is inefficient, the organisms do not grow well at high arsenic concentrations, and are easily crowded out by more robust species.

3. The amount of TMAs produced is very small even under optimal growth conditions.

4. All of the above reasons pale into insignificance in view of the very low toxicity of TMAs by inhalation or by mouth, as just described.

R.B. hereby renounces previous convictions.[9] It appears to us most likely that TMAs is not and never was a silent poison or killer.

This being so, what exactly was happening in the latter part of the 19th century? Why were there so many reports of illness in rooms papered with arsenic-containing materials, not only in those that were damp and airless but also in houses owned by apparently well-to-do individuals and kept in good condition?

It has to be remembered that 19th century living conditions were far from ideal and public health standards left much to be desired. In 1861, Queen Victoria's consort, Prince Albert, had died from typhoid; a little earlier, a cholera epidemic in London had been traced to a contaminated public well. Moreover, it was only in 1851 that the sale of arsenic was regulated in England; and only in the 1860s had a Children's Employment Commission investigated several industries leading to the Factories and Workshops Act of 1867 and further subsequent legislation.[2,41] Illness attributed to arsenical wallpapers could have had many other causes. By about 1860 it had been realized that there were serious problems with the widespread uses of arsenic and a reaction set in—arsenophobia ran wild in 19th century Europe and especially in Victorian England.[1] An unseen and unknown poison gas, related to arsenic, could be used as a convenient excuse or scapegoat for mysterious, poorly understood illness. It was also generally ignored that many microorganisms produce odorous compounds, some with unpleasant smells. For example, geosmin, produced by some *Streptomyces*, has a somewhat unpleasant, earthy odor.

6. The "sick building" phenomenon: then (?) and now

In a strange turn of the wheel, the "sick building" phenomenon has become prominent in today's world. In some cases, no obvious causes can be found for mysterious illnesses in particular buildings. In others, however, growth of fungi, in particular, *Stachybotrys chartarum*, is clearly indicated.[42] By an even stranger turn of fate, *S. chartarum* was first isolated in 1837 from wallpaper (!) in a house in Prague. This organism prefers damp conditions for growth and favors surfaces such as paper and wallboard. A number of changes in building technology have made mold damage in housing, schools, *etc.* more frequent than 40 years ago. Insurance losses for mold damage have risen sharply from US $700 million in 2000 to US $3 billion in 2003 for property alone.[43] An extreme case is the 25 story Kalia Tower hotel in Waikiki that had cost US $95 million to build. A year after opening in 2001 it had to be closed on account of a persistent mold problem; a 13 month clean up operation cost a further US $55 million.

There is considerable anecdotal evidence for human problems resulting from sick buildings but the question remains controversial. There is now a vast literature; a recent review, "Indoor Mold, Toxigenic Fungi, and *Stachybotrys chartarum*: Infectious Disease Perspective" lists more than 450 citations.[44] A book, "Damp Indoor Spaces and Health", being published by the National Academies Press (2004), states that "Exposure to various mold products including volatile and semi-volatile organic compounds and mycotoxins and components of and substances produced by bacteria that grow in damp environments has been implicated in a variety of biologic and health effects".[45] *S. chartarum* is one of several molds producing mycotoxins such as the tricothecenes (known to be responsible for acute cases of animal stachybotryotoxicosis). It is also clear that mold exposure in buildings is associated with exacerbation of asthma in mold-asthmatic patients, with increasing upper respiratory disease and with building-associated allergic disease. The symptoms experienced from working in a moldy environment include headaches, sore throat, general malaise, diarrhea and fatigue. Vomiting, hemorrhage, and skin lesions can be added for exposure to molds producing toxins such as tricothecene.

In 1893 Sanger reported the symptoms of over twenty individuals supposedly exposed to arsenic (he was unable to detect elevated concentrations of arsenic in urine samples).[46] The symptoms vary widely but are not unlike those noted above as resulting from mold exposure. While we have no medical expertise, it seems reasonable to conclude that the symptoms do not strongly match those briefly described as follows for arsenic poisoning:[47] "Throat constriction, dysphagia; burning GI pain, vomiting, diarrhea; dehydration; pulmonary edema; renal failure; liver failure."

It is a striking feature of today's sick building patients, that just as with those in the 19th century, removal to a

different environment (arsenic free? mold free?) leads to improvement in health. It has been noted that "While employees felt better after being relocated, there was no evidence that *Stachybotrys* was a causative agent...". Similarly, "... it is important to note that individuals get better with remediation efforts... although perhaps not always".[44] The sick building phenomenon including *Stachybotrys*, may well have accounted for some of the illness associated with residing in rooms containing arsenic-coated wallpaper. In any event, as previously noted, *Scopulariopsis brevicaulis* can be exonerated as causing illness. Interestingly, this organism does not appear in a list of 44 representative fungi found in dust and air samples from houses.[44]

7. Volatile metalloids and SIDS

It should be mentioned that Gosio Gas also came to attention in connection with Sudden Infant Death Syndrome (SIDS). It was suggested that materials such as arsenic, antimony or phosphorus, either present naturally or added as flame retardants or fungicides to crib mattresses or covers, might undergo microbial biomethylation forming toxic volatile compounds.[48] There has been much controversy with suggestions of a governmental cover up.[49] A website, http://www.criblife2000.com, incorrectly describes Gosio as a chemist and states, again incorrectly, that he had identified arsine as the volatile arsenic compound. In recent work, sheepskin bedding materials, one used by an infant perishing from SIDS, were examined for aerobic microorganisms forming methylarsenic species.[50] Three such fungi, *Fomitopsis pinicola*, *Penicillium gladioli* and *Scopulariopsis koningii*, were isolated; of these, only *P. gladioli* actually formed TMAs and in small amounts. This process required arsenic concentrations in liquid media higher than those available in the sheepskin bedding. In any event, the very low toxicity of TMAs appears to rule out arsenic (or antimony) biomethylation as a cause of SIDS.

8. Conclusion

In conclusion, it is doubtful that Gosio's name would be associated with a gas if the assumed association between human health and arsenic-laced molds had not achieved the status of fact by the early 20th century. It seems a pity that we should now have to abandon this fascinating urban legend. Gosio deserves recognition for showing the volatilization of arsenic by fungi and he will be remembered for other achievements such as the isolation of the very early antibiotic, mycophenolic acid.[51]

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