4 Too much to swallow: PCE contamination of mains water

David Ozonoff

PCE (perchlorethylene, also known as 'perc' or tetrachloroethylene), was used in the production of plastic linings for drinking water distribution pipes in the late 1960s and 1970s. This new and relatively untested type of distribution pipe was used in over 700 miles of New England's water distribution systems. Not until 1976 was it discovered that PCE had been leaching into the water from the pipe lining, causing widespread contamination of water supplies that still today require continuous remediation.

Before the pipes were put into production there was a substantial amount of scientific information available about the potential hazards of PCE. This did not include current concerns about PCE's carcinogenicity, teratogenicity and other health consequences of relatively low-level exposure upper most among today's concerns, but many early warnings suggested the need for caution in introducing PCE-based mains pipe linings.

PCE had been used to treat hookworm and data on side effects were in the literature, while later a variety of occupational users were studied, including aircraft workers, small companies in countries where biological monitoring was required, and dry-cleaning firms. Several environmental studies were also conducted to see if drinking water contaminated with PCE or its close relative, TCE (trichloroethylene), was associated with cancer. Results were mixed and the chemical industry consistently denied that PCE was a human carcinogen.

This case study explores the early (pre 1970) history researching the toxicity of the chemical. It also focuses on the failure of one manufacturer, Johns-Manville Corporation, to recognise the warning signals about using a suspected toxic substance. It examines why a new product was deployed without thought to the public health consequences and why evidence of the potential hazard was ignored.

The science has not been hidden. It has been ineffective in guiding and catalysing action. Whether the problem is a failed duty of care or a lack of clarity about what evidence will trigger action, the contemporary argument over how to interpret the scientific evidence is irresolvable within science itself. There are no overarching criteria from the philosophy of science that can dictate a solution.

This chapter also includes two supplementary texts. A panel that analyses the differences between the conclusions of risk assessments based on the same data, focusing in particular on assessments of PCE and TCE. A further panel describes the opportunities to switch to wet-cleaning technologies to reduce the current use of PCE in dry cleaning.

Institutions, large and small, make decisions every day where a conscious application of foresight could prevent a later hazard. Yet such foresight — based on existing information — is often absent.

The present chapter illustrates this with a case study on the use of a now ubiquitous chlorinated ethylene, PCE (perchlorethylene, also known as 'perc' or tetrachloroethylene), to produce plastic linings for drinking water distribution pipes in the late 1960s and early 1970s. Those years represented a strategic and historical turning point in awareness of the importance of environmental carcinogens and teratogens (substances causing embryo malformations).

Some public water supplies are still today contaminated with PCE and require continuous remediation. The use of PCE to apply plastic lining to water pipes occurred when there was already considerable scientific information about the potential hazards it posed. Admittedly, this understanding did not include current concerns about PCE's carcinogenicity, teratogenicity, and other health consequences of exposure to relatively low levels of PCE via various exposure routes, including water mains, whose public health implications remain unresolved. Nevertheless, certain clear early warnings suggested the need for caution in introducing PCE-lined drinking water pipe linings. And the lessons from this early period remain applicable to the situation today.

4.1 PCE linings in water mains

A new and relatively untested type of distribution pipe, installed in the years 1969–1979, is now known to have caused widespread PCE contamination of water supplies in the US state of Massachusetts (Demond, 1982; MDEE, 1982; Larsen et al., 1983).

Efforts to develop and market the new pipe began in the early 1960s when Providence, Rhode Island, Water Supply Board officials sought to replace cast iron mains in low-flow areas that were troubled with colour and taste problems. The Johns-Manville Corporation, a manufacturer of asbestos cement water mains, experimented with clear plastic linings of various kinds. To apply the lining, the plastic was dissolved in PCE and the resulting slurry used to paint the inside of the pipe. The first trial of plastic-lined pipes in 1966 produced water with a slight chemical taste and odour, whose origin was not revealed by routine water quality tests like pH, alkalinity and hardness. In early 1968 Johns-Manville delivered a pipe with the new type of clear lining to the Providence Water Supply Board for testing. It was immediately apparent that air trapped in the pipe took on a chemical odour of slight to moderate intensity, described as similar to chloroform and strongly resembling a commercial dry-cleaning fluid used at a local cleaning plant. Conventional water tests revealed no taste or odour, although the air in the pipe still had a chloroform-like smell.

Further testing showed that under static conditions the lining material continued to contribute a very slight odour even after substantial volumes of water had run through the pipe. Consequently a Johns-Manville representative visited the Providence Water Supply Board, accompanied by two representatives of the company, and they were shown first hand that the water retained a slight odour of chloroform. At a subsequent visit to inspect water samples at a 277-foot pipe with an eight-inch diameter that had been installed the previous month, neither the company representatives nor the water supply chemist detected a similar odour. Explaining the discrepancy, company representatives argued that the pipe with the odour had been kept covered in brown paper and therefore not 'cured' completely.

There is no indication that the taste and odour incident prompted Johns-Manville to investigate the curing process to evaluate whether PCE remained in the liner and potentially contaminated drinking water. Nor is there any record that tests other than routine water quality measures, which did not indicate the nature or amount of organic contaminants, were ever done on samples from the newly developed lined pipe. Not until 1976, when over 700 miles of this pipe had been installed in New England water distribution systems, was it accidentally discovered that PCE had been leaching from the pipe lining into the water.

4.2 Foreseeable harm?

The use of PCE in water mains is a classic case of deploying a new product without considering the public health consequences. In the ensuing battle over who should pay for the damage, Johns-Manville Corporation argued that it did not and could not have known that PCE was a chemical of public health concern, whose presence in drinking water was certainly inappropriate and probably harmful. Much work after 1970 has revealed potential adverse effects from environmental and occupational exposure to PCE, including various cancers, birth defects and autoimmune disease. But could this have been foreseen? If

it was unforeseeable, what factors made it so? Alternatively, if it was foreseeable, what factors prevented adequate foresight?

4.2.1 An insight from the early history of PCE

Before examining these questions, the early history of chlorinated hydrocarbons provides at least one lesson involving PCE. Michael Faraday, now best known for his work on electricity but also a great chemist (Williams, 1965) created hexachloroethane, C_2Cl_6, the first chlorinated hydrocarbon to be synthesised. Heating the mixture produced another gas, perchloroethylene, C_2Cl_4 (PCE).

Faraday was attracted to chlorine chemistry because of a philosophical dispute between his mentor, Sir Humphrey Davy, and Antoine Lavoisier, centred on reconciling the mechanical character of Newtonian mechanics with the notion of free will. Davy and Faraday were Kantians and deeply religious, and the philosophical stakes were extremely high. This resulted in intense disputes with other founders of modern chemistry, including Jöns Jacob Berzelius and John Dalton (Sharlin, 1966).

For the purposes of the present study, the key point to note from this early period in PCE's history is the way that non-scientific concerns can distort scientific disputes. Ideology can make it impossible for protagonists to reverse a course of action or alter a position. But other interests, such as money, market share and reputation, can have similar effects.

PCE's infancy was thus characterised by dispute and doubt. Of course, disputes and doubts are normal in science, particularly when the consequences matter. But this has two corollaries. The first is that a scientific finding may become the subject of dispute and doubt (whether real or manufactured to prevent action) because the outcome matters to someone with the means to challenge the finding and delay action. Conversely, the second corollary is that, if nobody cares or nobody with means cares, there will be little pressure to challenge a scientific finding or explore an issue in greater detail. Results of potentially great significance in other contexts may fail to influence the public health landscape.

4.3 PCE and the chlorinated ethylenes

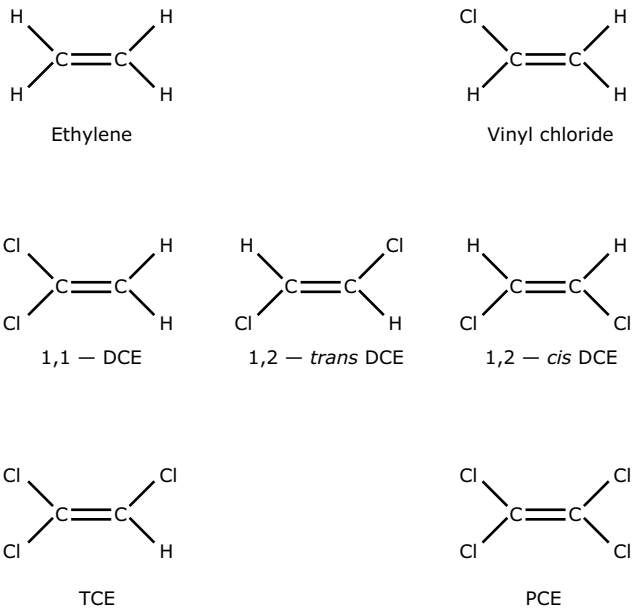
PCE is one of a closely related group of chemicals called chlorinated ethylenes. All the chlorinated ethylenes are built on a common chemical backbone, which consists of two carbon atoms connected by a double-bond. This leaves room or 'slots' for four more atoms, two on each carbon atom. When all slots are occupied by hydrogen atoms, we have the parent hydrocarbon, ethylene. As shown in Figure 4.1, successively replacing each hydrogen atom with a chlorine atom generates vinyl chloride (a known human carcinogen), dichloroethylene (DCE), trichloroethylene (TCE) and tetrachloroethylene (PCE).

All of these chemicals are used by the chemical industry as 'feedstocks' (i.e. the basic ingredients) for plastics or other chemicals. Several are commonly used as solvents for degreasing (i.e. cleaning) metal parts or in the dry-cleaning industry.

The chlorinated ethylenes trichloroethylene (TCE) and perchloroethylene (PCE) were among the highest production volume chlorinated solvents in the twentieth century, used for everything from dry cleaning, metal degreasing and printing to medical applications such as anaesthetics (TCE) or to kill parasitic worms (PCE). These medical and pharmaceutical uses date back almost a century. The familiarity and benefits of these substances should have alerted us to the fact that exposure to these chemicals has biological effects that could also be harmful.

Using PCE to apply plastic resin to the interior of water mains is thus just one of many applications.

Figure 4.1 Chemical structure of chlorinated ethylenes



But the use of PCE in close connection with drinking water occurred at a time when problems could have been foreseen. The early warnings are outlined briefly below.

4.4 Discovery of PCE's toxic effects

Despite PCE's current importance, for more than a hundred years after its discovery by Faraday it saw no significant commercial use. There was little literature about PCE or knowledge of its toxic effects until the 1920s when it was proposed as a treatment for hookworm — parasites of the small intestine that cause severe anaemia. In the nineteenth and early twentieth centuries, hookworm disease affected the health and vitality of millions of rural poor in the United States and elsewhere, stunting children's growth and robbing communities of productivity. Resulting economic losses were substantial (Rosenau, 1935). In the first decade of the twentieth century the Rockefeller Foundation undertook a massive campaign against hookworm disease in the southern regions of the United States using the relatively toxic medicine, thymol. Because thymol had frequent side effects, there was a continuing search for a better agent. One of the first shown to be effective was carbon tetrachloride (CCl_4), but this was less than ideal, leading to the trial of other similar compounds, including PCE.

The introduction of PCE as an anthelmintic (anti-parasite medication) by Hall and Shillinger in 1925 began a process of toxicological evaluation of PCE that has continued to the present day. As new uses for PCE were found in 1934 (dry cleaning) and 1939 (degreasing metals), further studies were undertaken to investigate the effects of PCE on those exposed to the chemical in these new applications.

This pre-carcinogen literature can conveniently be divided into two phases: in the first, from 1925 until approximately 1940, the main interest was in assessing the side effects of a medicine taken by mouth for hookworm disease. In the second phase, from 1940 to 1970 up to the point where PCE-lined pipes were installed, the effects of inhaling PCE from use as a dry-cleaning fluid or degreasing agent were the principal focus of concern.

4.4.1 Phase I: 1925–1940 (PCE use in treating hookworm disease)

When Hall and Shillinger introduced PCE as a treatment for hookworm disease in 1925 they first tested the substance on dogs: 'The question as to the safety of the drug is naturally one of major importance …' (Hall and Shillinger, 1925). Three of the 55 dogs tested died, even though they had received what were believed to be therapeutic doses. None of the dogs that died received the largest doses and as a result Hall and Shillinger became the first of many to comment on potentially significant differences in individual susceptibility.

To test PCE's effects on humans, one of the researchers took a 1 cc (one fifth of a teaspoon) capsule of PCE after breakfast. That night he experienced prompt and complete relaxation of the muscles with slight cerebral discomfort. He had an unusual dream involving levitation, which he believed was due to the effects of the drug.

The dog experiments, self-medication and PCE's chemical structure suggested to Hall and Shillinger that the drug's safety was comparable to carbon tetrachloride (useful in addressing hookworm disease but with known toxicity to the liver), causing lesions similar to those of chloroform. They recommended that PCE be tested under hospital conditions to ascertain its possible value in treating hookworm patients, with due attention to contraindications such as acute or chronic alcoholism, liver disease, infections or other debilitating diseases.

From this modest beginning the use of PCE for hookworm disease gradually increased. Additional studies suggested that PCE, even in relatively small quantities, could have harmful effects on animals and people. But because of its effectiveness as an anthelmintic, PCE's popularity continued to grow and was the subject of several articles (Manson, 1934; AMA Council on Pharmacy and Chemistry, 1936; Wright et al., 1937; Fernando et al., 1939). Thus, while PCE became a commonly used drug, it was not a completely safe one and untoward side effects continued to be reported. These included a paper by Sandground (1941) on two cases of unconsciousness following a normal therapeutic dose. He concluded that:

> 'While for want of a better drug [these cases] should not discourage the use of tetrachlorethylene [PCE], they illustrate the truth of a remark which the late Dr Maurice Hall made to me, to the effect that one cannot assume that any anthelmintic is entirely safe for human use until there are reliable reports on at least a million treatments without any untoward effects.'

The number of other severe side effects from using PCE as a drug is difficult to estimate, although the

question was being considered at the time that the PCE-lined pipes were installed (Bwibo, 1969).

Throughout its use over several decades, PCE tended to produce serious detrimental effects on a small percentage of those treated. As with the earlier dog experiments, the effects were not necessarily related to the dosage. The toxicological picture that emerges from this early literature is evidence of pathologic changes in animals at therapeutic doses, together with reported side-effects in humans, some of which were extremely serious or fatal at doses as small as half a teaspoon (2–3 cc). PCE's potentially lethal side-effects were tolerated because hookworm disease was a major public health problem. There remained uncertainties about the degree of absorption of the drug in humans and the individual variation in susceptibility to its effects. But there was a balance to be struck in terms of achieving public health goals — a balance not found in newer uses.

4.4.2 Phase II: 1940–1970 (PCE in degreasing operations and other industrial uses)

The initial information on PCE's adverse effects came from its therapeutic uses and was sufficient to arouse concern. Subsequent modes of PCE exposure were primarily by inhalation and skin absorption rather than ingestion. Investigators soon began to look more closely at inhalation in particular and for the next three decades much of the study of PCE toxicology involved exposure of human volunteers and animals to PCE via the air. Chronic exposure now joined acute effects as a concern. It is significant that the discipline of epidemiology — the systematic evaluation of the incidence, distribution and possible control of diseases and other factors relating to health — was still primitive and did not enter into most decisions.

In a general review of dangerous gases and vapours, Zernik (1933) noted that Lamson et al. (1929) had produced an optimistic assessment of PCE's risks but contrasted a report by Beyer and Gerbis (1932) of stomach and liver disease ending in death after chronic inhalation of a solution containing PCE as the main ingredient. The extent to which other ingredients might have been responsible for this fatal case was not clear but the potential hazard of PCE exposure appeared evident to the authors.

Dr Alice Hamilton, an industrial health pioneer, was among the first to focus on the new uses of PCE. Writing in *The New England Journal of Medicine* in 1936, Hamilton cautioned that data on PCE's effects on animals might be difficult to apply to human exposures. Humans tended to have more liver damage and less kidney damage than animals exposed to the same substances, she observed. Hamilton also emphasised the differences between acute clinical poisonings and chronic industrial exposures, citing lead and benzene as striking examples of the greater damage that can be caused by low, chronic exposures compared to large, acute ones.

In the discussion that followed her paper, a Massachusetts physician bemoaned the fact that manufacturers were marketing products under trade names, with little information for physicians about the effects of the chemicals. On this point, Hamilton (1936) had observed that:

> 'This, in my opinion, is a problem for the general practitioner since the use of these solvents in industry is increasing by leaps and bounds each day. I have seen many individuals, both male and female, who in my opinion were suffering from conditions brought about by prolonged exposure or exposure under definite circumstances to some of these solvents.'

The importance of low-level chronic exposures was emphasised again in a general review of the pathology of exposure to new volatile solvents, published the following year (St George, 1937). St George noted that slow, chronic intoxications were difficult to recognise and he suggested that chemicals could be broken down into other compounds or retained in the body. Outlining the available information on the toxicity of PCE, he described it as a 'relatively new solvent' and listed its symptoms on inhalation as nausea, giddiness and vomiting with mucous membrane irritation, headache and drowsiness. Echoing the Massachusetts physician, St George (1937) made a special point about warnings:

> 'The danger of these solvents should be explained to every worker and they should be instructed in the preventive measures that have been instituted. When these products are marketed for household use under trade names etc., detailed instructions should be stated on each container, and it is especially important to state that the product must only be employed in a room with at least one window wide open.'

One of the first to turn his attention directly to PCE as an industrial poison was Carpenter (1937).

He exposed albino rats and human volunteers to PCE vapours at a variety of concentrations. In the rat experiments no pathology was evident at 70 parts per million (ppm) over a 10-week period, but at the next highest level, 230 ppm, there was evidence of congestion, light granular swelling of the kidneys and minimal changes in the liver. Carpenter also exposed himself and his colleagues to PCE concentrations of 500, 1 000, 2 000 and 5 000 ppm. All of them could smell PCE at 50 ppm in air and this odour threshold was reported by many subsequent studies, citing Carpenter. After some hours of exposure, subjects noticed increased salivation, irritation of the eyes, and tightness in the frontal sinuses. One became slightly nauseated at an exposure of 500 ppm for two hours, while higher levels caused more marked effects of central nervous system depression and mucous membrane irritation. At the highest levels, exposure could only be endured for a few minutes. Carpenter concluded that a safe concentration for continuous daily exposure probably lay somewhere between 100 ppm and 500 ppm, but he stated a more precise statement would require additional human experience with exposures within this range.

In the 1940s, despite much discussion about the hazards of chlorinated solvent use, little original work was done, perhaps because of the war effort and the pressures of industrial production. However, several general reviews (e.g. Lehmann and Flury, 1943; Sappington, 1943) recounted information regarding the use of PCE as a drug and the findings of Carpenter (1937) and Barrett et al. (1939).

Morse and Goldberg (1943) affirmed that:

> 'Nevertheless, both solvents are regarded as toxic. There is only one published medical research with which we are familiar [Carpenter] … This investigation by no means clarified the toxicity of perchlorethylene. It stated that 50 ppm produced a definite odour and concluded that a concentration between 100 to 500 ppm is considered safe for daily exposures not in excess of 40 hours per week. This range of 100 to 500 ppm is in need of extensive study'.

They concluded that complaints of headache, nausea and dizziness were common among degreaser operators even when concentrations were well within the generally accepted toxic limit.

Many writers were alarmed by the lack of hard data and the misperception that PCE was non-toxic based on its therapeutic use. For example, in his 1949 textbook on industrial toxicology Fairhall noted that PCE should not be regarded as harmless; indeed, that under certain conditions it was even more toxic than carbon tetrachloride, which was recognised as a serious industrial hazard. Like other authors before him Fairhall called attention to the phenomenon of varying individual susceptibility.

In 1952 a major manufacturer of PCE for degreasing use, the Dow Chemical Company, began to publish reports on the chemical's toxicity. Rowe et al. (1952) assessed the toxicity of PCE vapour to laboratory animals and its effects on human volunteers, with attention primarily focusing on acute effects. Based on this analysis, Rowe et al. argued that exposure should be limited to an average of 100 ppm and should not exceed 200 ppm. They identified irritation of the eyes and central nervous system depression as the prime toxic effects, and considered serious organic injury to be unlikely.

The following year, however, Coler and Rosmiller (1953) reported the effects of PCE exposure and toxicity at a small pump-manufacturing company where parts covered with grease were cleaned with a solvent that consisted of 99 % PCE. A physician who examined a 35-year-old worker with severe stomach bleeding found that he also suffered from severe cirrhosis of the liver and ruptured oesophageal varicose veins. Two of the patient's co-workers complained of malaise, dizziness, light-headedness, headache and irritation of the nose. All three had been exposed to PCE. Worksite exposure measurements showed levels of 200–400 ppm. Subsequent interviews with other workers revealed similar complaints, including tiredness, and feelings of intoxication and hangovers. A few workers reported passing out after exposure but said that they recovered quickly. One worker reported that his eyes 'did not coordinate'. Staggering, stomach aches and slowed ability to think and remember were among the many complaints. Three of seven workers tested had abnormal liver function. The authors concluded that the liver toxicity of PCE should be investigated more thoroughly rather than disregarded. Thus, contemporary clinical observations contradicted the Dow studies.

Coler and Rossmiller's concern was echoed by Lob (1957) in an article entitled, 'The dangers of perchlorethylene'. Lob noted that a toxic industrial chemical is often considered harmless until experience shows the opposite. He then reviewed the animal literature on PCE, remarking that experience was meagre and that the conditions in which investigations had been conducted were

quite varied, meaning that definitive conclusions could not be drawn. He also cited the example of TCE as evidence that the results from animal experimentation could not always be transferred easily to humans.

Lob reviewed clinical experience with PCE, pointing out that it was also scant but identifying ten additional cases of PCE poisoning. One was a fatal case, two more were cases of severe chronic poisoning with damage to the autonomic nervous system, and seven cases were less serious, involving symptoms of fatigue, dizziness, vertigo, headache, nausea and vomiting, anorexia, insomnia, irritability and light cough. The latter symptoms disappeared when the workers were removed from exposure.

Meanwhile, experimental toxicology continued to address PCE (Friberg et al., 1953) but new techniques in animal experimentation were beginning to show inconsistent effects. An investigation attempting to rank chlorinated hydrocarbons according to their liver-damaging potential (Plaa et al., 1958) revealed no correlation between the dose that caused liver damage and the lethal dose in acute exposure experiments.

These concerns spurred further activity in the 1960s on the part of the manufacturer, Dow Chemical Company. In a series of reports, researchers from Dow studied the absorption and excretion of PCE in the body (Stewart et al., 1961a and 1961b; Irish, 1962; Rowe et al., 1963; Stewart et al., 1963; Stewart and Dodd, 1964; Stewart et al., 1965; Stewart and Erley, 1965; Gehring, 1968; Stewart, 1969). Using gas chromatography with infrared spectroscopy or electron capture detection, these researchers discovered that excretion of PCE from the body took an extended time, suggesting that PCE accumulated with chronic exposure. The Dow researchers noted that acute exposure to PCE might, in fact, be a chronic exposure from the body's standpoint because of the slow excretion rate. In studying an accidental over-exposure, they discovered that liver function tests may not become abnormal until two to three weeks after exposure.

The Dow researchers also noted that the mistaken perception that PCE was relatively non-toxic encouraged careless use, which could result in poisoning (Irish, 1962). The Dow reports culminated in a human exposure experiment (Stewart et al., 1970), which found an unexpected prevalence of light-headedness and abnormal neurological results (based on a modified Romberg test) at the lowest exposure levels. The Dow authors could not interpret this unanticipated finding.

Finally, Smyth and his colleagues (1969) added a new and disturbing dimension when they investigated the toxicity of 27 industrial chemicals given to rats in all possible pairs. Using death as the endpoint, they found that most combinations showed no tendency to produce lethal effects in excess of what would be expected from the additive effects of each component separately. Of the nine combinations that did deviate significantly from this pattern, four of them contained PCE, making it the chemical most often associated with causing a net effect greater than the sum of the effects of its separate components. This strongly suggested that PCE could have a potentiating effect on the toxicity of other chemicals (and vice versa).

4.4.3 The view from 1970

The 1960s closed with continued reports of poisoning from PCE at the workplace, usually involving central nervous system depression and concomitant liver damage. There was uncertainty as to the threshold at which such damage first occurred, with some writers considering PCE to be more dangerous than conventionally believed. During that decade there were significant advances in the measurement of PCE and one of its leading manufacturers, Dow Chemical, performed in-house research that was published in the open scientific literature. It was known that individual susceptibility to the effects of PCE varied widely and that the chemical was excreted very slowly from the body, often concentrating there and resulting in a chronic, low-level internal exposure. The suspicion was also raised that PCE could act together with other chemicals to produce a synergistic effect of unknown magnitude.

4.5 Implications for PCE use in water supply infrastructure

What did all the evidence imply for water suppliers contemplating using a product containing PCE?

Leaving aside the acute and chronic effects, there was a potential aesthetic concern. In 1968 the United States Public Health Service Drinking Water Standards stipulated that 'drinking water should contain no impurity which would cause offence to the sense of sight, taste, or smell'. This was done to prevent consumers from seeking alternative but less safe sources of water. Public health experts might have worried that the new pipes could cause a health problem on that basis alone, as a chemical odour was an initial concern.

A review of the medical literature would have added to their unease. It showed that there was considerable individual variation in responses to the chemical, both in the therapeutic environment and in the workplace. Some variation was thought to be inherent and some due to wide variation in the health, diets and exposures of the general population. All these factors were known to affect the potential toxicity. The fact that extremely serious and sometimes fatal side effects were tolerated in mass treatment of a population for a serious disease such as hookworm would probably have been of little relevance to water managers who had no interest in purveying an anthelmintic drug through the water mains.

Experimental work and occupational experience had already shown PCE to be excreted from the body very slowly. Like a bathtub in which the amount flowing from the tap is greater than that draining out, it was plausible that PCE could accumulate from constant daily exposure until it reached the point where it caused toxic effects in some consumers. Using data from Stewart et al. (1965) an elimination rate constant of approximately 25 % (through the lungs) per day can be estimated. Regardless of the level of exposure, after about two weeks (four to five half-lives of 2.5 days each) the level of PCE in the body would have built up to the point where the amount eliminated from the body would be roughly equal to the amount ingested. The final level of PCE would depend on the amount ingested each day.

The maximum level of PCE in water is 100–150 ppm, as determined by its solubility. No measurements of PCE appear to have been made at the time the pipes were installed but assuming a worst case concentration of 125 ppm and the ingestion of 2 litres of water per day implies a constant body burden of approximately 1 gram of PCE. That is close to the dose used to treat hookworm, which had caused serious side effects in some people. For lower exposure, there could plausibly be concern about an 'internal' exposure to levels which would be about four times the daily ingested dose. Concern about such chronic exposures runs through the literature on chlorinated hydrocarbon solvents from Hamilton's 1936 paper onwards.

Public health experts might have been troubled by the emerging literature on the inconsistencies between the animal and human data, as well as inconsistencies in the animal data itself. They might also have been concerned about the possibility that exposures to other chemicals might heighten the toxicity of PCE synergistically.

Public health experts would have been unlikely to view the presence of any PCE in their water favourably unless it was unavoidable. This is not merely a statement based on hindsight. Public health and water managers of that era had been concerned for some time with contamination of groundwater from surface disposal of hazardous wastes like PCE, and the unusual mode of contamination in this case was irrelevant. The environmental historian Craig Colten (1991) has shown that by the early 1950s, 'governmental agencies, professional organisations and industry-trade associations, drawing on three decades of experience, all publicly recognised the hazards posed by the surface disposal of liquid wastes... By the 1940s, it had become apparent that simply protecting a well was insufficient. Public-health officials began to take stronger action to alter industrial waste-disposal practices and thereby prevent the introduction of contaminants into the ground.'

Other historians of waste disposal have come to the same conclusion: the propensity of wastes, including chlorinated solvents, to contaminate groundwater was generally understood in the 1940s–1960s and measures were advocated to prevent it. Put another way, it was understood that contamination of drinking water with chlorinated solvents was a threat to the quality of the water (Amter and Ross, 2001). The fact that in this case the solvent entered the water from the pipe lining rather than land disposal was irrelevant.

4.5.1 Why did Johns-Manville fail to foresee the potential harm?

Johns-Manville Corporation (the pipe manufacturer) may only have recognised the potential harm of PCE with the benefit of 'hindsight'. But the question remains as to why the risks were not recognised earlier.

In the best interpretation, it could be argued that Johns-Manville was never aware of the problem of PCE contamination. Yet, while it is possible that no one in this large industrial concern bothered to think about or investigate the medical literature on PCE, it is quite clear they could have done so. At that point they would have had several options, including redesigning the product, alerting water managers to the potential for contamination from an insufficiently 'cured' product, or continuing to act as if it was not a problem. The company did not even consider or worry about the possibility of insufficient curing, and once the problem was detected, it denied that there

were any health hazards — a necessary position if it were to avoid paying damages for a faulty product.

What is the lesson here? Although there is abundant evidence that Johns-Manville wilfully disregarded and concealed scientific evidence with respect to its principal asbestos products (Ozonoff, 1988), there is no such evidence in relation to PCE. Assuming that knowledge was not hidden, the proposition that Johns-Manville was merely indifferent to these dangers is a plausible explanation for its action; there are many similar examples involving other companies in this period.

The lack of epidemiological evidence would not have been a reason to delay action. Epidemiology was in its infancy and the requirement that even well accepted findings be reconfirmed with epidemiological studies was not yet the norm. The available evidence mainly circulated in the restricted arena of medical specialist literature and the ignorance of most treating physicians and workers about what materials they were being exposed to further served to keep the problem of solvent toxicity off the agenda. This also prevented workers, their unions and their advocates from entering into the conversation about solvent toxicity. If occupational exposures were not on the table, water contamination was also unlikely to be well recognised in this period.

1970 also marked a turning point in the US from minimal federal engagement in workplace and

Panel 4.1 Differences between risk assessments drawn from the same basic data

Christina Rudén

Trichloroethylene, TCE, a relative of PCE, is widely used as a raw material for chemical synthesis, as a solvent for cleaning metal parts and in dry cleaning. A review of 29 TCE carcinogenicity risk assessments conducted between 1973 and 1997 (Rudén, 2002) explored how differences in the selection, interpretation and weighting of primary data affected their differing conclusions.

Classification of TCE risk in risk assessment reports 1973 and 1997

Conclusions of risk assessments: carcinogenicity, epidemiology, human cancer risk				
	No evidence indicating carcinogenicity: *human risk not plausible*	Plausible evidence of carcinogenicity in animals: *human risk not plausible (animal data not considered relevant for humans)*	Plausible evidence of carcinogenicity in animals: *plausible human risk (based on animal data)*	Plausible evidence of carcinogenicity in animals and in epidemiology: *plausible human risk (based on a combination of animal and epidemiological data)*
Total number of assessments 1973–1997	6	10	9	4
Assessments conducted 1995–1996	1	1	1	3

Note: 'Plausible epidemiological evidence' means that people exposed to TCE have greater prevalence of cancer compared to unexposed people.
'Plausible evidence for carcinogenicity in animals' means that animals exposed to TCE in laboratory experiments have an increased incidence of cancer compared to unexposed animals.

Eight of the 10 evaluations that identified a risk for animals but not for humans were conducted by international organisations or industry. Contrastingly, eight of the nine assessments that concluded a human risk based on animal evidence were conducted by government or academic authors. Rudén (2002) observed that this may reflect more risk-averse assessment policies applied by government agencies and academia, and a tendency for industry to apply less precautionary criteria. These wide variations in conclusions continued even within a narrower period, such as 1995–1996, when the evaluating bodies were working from the same available body of knowledge.

Similarly, as shown in the table below, different risk assessors have reached varying conclusions about PCE.

Panel 4.1 Differences between risk assessments drawn from the same basic data (cont.)

Conclusions on the carcinogenicity of PCE

	ECETOC (1999)	IARC (1995b)	ACGIH (1993)	MAK (1992)
Conclusions on PCE carcinogenicity	Plausible evidence of carcinogenicity in animals: *human risk not plausible*	Plausible evidence of carcinogenicity in animals and in epidemiology: *plausible human risk (based on a combination of animal and epidemiological data)*	Plausible evidence of carcinogenicity in animals: *human risk not plausible (animal data not considered relevant for humans)*	Plausible evidence of carcinogenicity in animals: *plausible human risk (based on animal data)*

One important reason why risk assessors differ in their conclusions concerning the size and even the nature of risk is that scientific knowledge increases over time. As risk assessments are updated to include new data the conclusions may change. This is a time-dependent and natural part of the scientific and regulatory process. However, risk assessors may also select different sets of data to support their risk assessments and may interpret key studies in different ways.

An example of this is the interpretation of PCE epidemiology (Rudén, 2006). PCE epidemiology was considered positive in the risk assessment performed by IARC in 1995 and negative in the ECETOC assessment from 1999. The IARC conclusion on epidemiology is based on findings of elevated relative risk of non-Hodgkin's lymphoma (NHL) in three epidemiological studies: Blair et al. (1990), Spirtas et al. (1991) and Anttila et al. (1995). Contrastingly, ECETOC acknowledged the increased incidence of non-Hodgkin's lymphoma in Spirtas et al. (1991) but assigned little weight to the data since the study was initiated because of a priori concerns about lymphatic cancers. ECETOC described the excess of non-Hodgkin's lymphoma in the Anttila study as not statistically significant. Regarding the Blair study ECETOC stated that it did 'not provide results for NHL as a cause of death'. Furthermore, ECETOC concluded that there was 'no excess of deaths due to lymphosarcoma or reticulosarcoma in the Ruder study (1994) and no excess of deaths due to other lymphatic or hematopoietic cancers'. ECETOC concluded that 'available epidemiological studies were either negative or were not sufficient to provide evidence of a relationship between exposure to [tetra] and cancer in humans'. The varying interpretations in the ECETOC and IARC studies are set out in the table below, which is adapted from Rudén (2006).

Interpretation of four epidemiological studies regarding non-Hodgkin's lymphoma by ECETOC (1999) and IARC (1995b)

	ECETOC 1999	IARC 1995
Anttila et al., 1995	Negative (*)	Positive
Ruder et al., 1994	Negative	Data on non-Hodgkin's lymphoma not reported
Spirtas et al., 1991	Positive (**)	Positive
Blair et al., 1990	Negative	Positive

(*) ECETOC described this study as positive on p. 143 ('Anttila et al. reported an excess of NHL...'), and as negative on p.136 ('Increased risks...but none was significant').

(**) Not considered a key study by ECETOC since it was initiated due to a priori concerns about lymphatic cancers.

Various case studies in the first volume of *Late lessons from early warnings* (EEA, 2001) emphasise that such differences are not uncommon in risk assessments. Indeed, as EEA (2008) indicate, this variance in interpretations is attracting increasing attention from regulators and policymakers.

Evidently, evaluators must communicate better about the approach they use to evaluate the strength of evidence and scientific uncertainties. Different evaluators must also employ clear and consistent terminology. This will help minimise the concerns that arise among risk managers and stakeholders when different experts derive different conclusions from the 'same' body of scientific knowledge, or when conclusions and uncertainties are communicated using unclear or inconsistent terminology.

environmental concerns to a prominent role. With the new attention after 1970 came new concerns about contaminating water.

The scientific information on PCE never figured in the water mains product design. It was ignored or invisible. This suggests that the principal reason that Johns-Manville did not care enough to examine thoroughly the risks of using PCE was that nobody made them care. Industrial firms are not people but they nevertheless have interests and intentions, which are rarely related to public health and environmental concerns. The job of a company is to make money for its owners. For Johns-Manville, PCE water mains represented a means of generating profits, with the actual nature of the product having secondary importance. In order for public health concerns to be brought to the forefront, additional mechanisms are needed, most notably criminal and civil liability, both of which rely on state enforcement of legal rules. Other mechanisms are possible, such as moral pressure and voluntary industry standards, but they must all pass the acid test: are they sufficient to make the company care?

Photo: © istockphoto/Steve Jacobs

Once a problem has risen to the level where it can no longer be ignored (and the ability to ignore a problem depends on contextual factors such as the state of knowledge, power relations, economic considerations and political arrangements), much will depend upon a company's assessment of what is at stake. High stakes mean the deployment of considerable resources — resources more at the disposal of large corporations. In such circumstances, uncertainty favours the side of inaction.

4.6 The view from 2013

The period before 1970 had revealed the outline of acute reactions to PCE, and established concern about chronic and delayed effects. Not long after the Massachusetts pipes were installed, an entirely new dimension of PCE toxicology became apparent, concerning carcinogenicity, teratogenicity and other health effects.

In the early 1970s it was discovered that the first member of the chlorinated ethylene series, vinyl chloride monomer, was a human carcinogen (see Chapter 8 on vinyl chloride). This immediately raised the question as to whether other high-volume chlorinated ethylenes, primarily trichloroethylene (TCE) and PCE, might also be carcinogens. By this time PCE was widely used in the dry-cleaning industry, exposing workers and patrons of dry cleaners, and often producing groundwater contamination from improper disposal of spent solvent from the numerous small firms using it.

Because of this heightened suspicion, both TCE and PCE were tested in animal bioassays for carcinogenicity beginning in the mid-1970s (for PCE see NCI, 1977; Mennear et al., 1986). Both were found to be animal carcinogens, although by this time the methodology and validity of animal bioassays had become a matter of dispute and no finding went unchallenged. Attempts at epidemiological verification of PCE's carcinogenicity were difficult because of the long latency for cancer, lack of exposure information and low statistical power of most studies.

A variety of occupational groups were studied, including aircraft workers, small companies in countries where biological monitoring was required, and dry-cleaning firms. Several environmental studies were also conducted to see if TCE/PCE-contaminated drinking water was associated with cancer. Results were mixed and

Panel 4.2 Wet cleaning technology eliminates PCE use in dry cleaning

Joy Onasch

Massachusetts has designated PCE as a higher hazard substance under the Toxics Use Reduction Act but further policy measures could help phase out the solvent, including by encouraging a shift away from dry cleaning to wet-cleaning technologies. This shift could be further supported by a more comprehensive assistance programme helping convert facilities to professional wet cleaning. As outlined below, the electricity and gas savings involved mean that partnerships with utility companies could help create a programme with additional depth.

Able to dissolve most organic materials, PCE is the most widely used dry-cleaning solvent in the US. The US Environmental Protection Agency estimates that some 85 % of cleaners use PCE as their primary solvent. PCE is also a major contributor to contamination at dry-cleaning facilities, mainly due to past unsafe handling practices. PCE is reported to be the chemical most widely found in groundwater contamination at Superfund sites (TURI, 2007), dry cleaning being one of the main sources.

The concept of wet cleaning in the professional garment care industry has existed for several decades. However, it is only in the last 10 years or so that technology has advanced such that 100 % of garments can be cleaned using the wet-cleaning system. In 1997, Keoleian et al. recommended in the *Journal of Cleaner Production* that larger cleaners could consider operating mixed mode facilities using both dry-cleaning and wet-cleaning equipment.

Today over 150 dedicated wet cleaners operate in California, a state where PCE is being phased out through regulations. California Air Resources Board amendments will over time phase out the use of PCE dry-cleaning machines and related equipment by 1 January 2023. Still, the shift to wet cleaning from solvent-based cleaning has been slow, especially where regulations phasing out solvent use do not exist. Sinsheimer et al. concluded in the *Journal of the Air and Waste Management Association* in 2007 that cleaners they studied in California that switched to professional wet cleaning were able to maintain their level of service and customer base while lowering operating costs. They also found that the cleaners were able to transition to professional wet cleaning without great difficulty and were highly satisfied with the new technology (Sinsheimer et al., 2007).

Onasch (2011) studied a dry cleaning shop in Bellingham, Massachusetts, showing that by becoming a dedicated wet cleaner electricity and natural gas use were reduced by as much as 20 % and even water use was reduced. For this facility, equipment costs were reduced by USD 500 over 12 months, performance costs (claims) were reduced by USD 1 000 over 12 months, operational costs (mainly due to costs of detergents) increased by USD 1 069 over 12 months and costs associated with resource use (calculated using normalised rates) were reduced by USD 2 318 over 12 months. Together, savings totalled USD 2 749 over the 12 months of the study. To replace its solvent machine, the facility spent approximately USD 12 000 (in actual costs, but not factoring in discounts and grant monies received). This implies that the firm would have realised a return on the investment in just under 4.5 years.

Photo: © istockphoto/Frances Twitty

With appropriate training and practice the personnel at this facility were able to master difficult garments and even boasted that wet cleaning resulted in 'whiter' whites and brighter colours than had been possible via dry cleaning.

Time spent cleaning garments was difficult to quantify but with proper training and practice total cleaning time could be reduced due to less pre-spotting, the ability to simultaneously wash and dry in separate machines (unlike the all-in-one traditional dry-cleaning machines) and mastery of the finishing equipment. Indirect benefits of improved air quality, reduced liability, elimination of regulatory oversight, and environmentally friendly niche marketing should all also factor into the analysis of the professional wet-cleaning system.

the chemical industry consistently denied that PCE was a human carcinogen. In each of the individual studies it was possible to find limitations or alternative explanations for positive results (and for negative ones). With each new iteration, new arguments were spun out, sometimes involving epidemiology, later involving sophisticated toxicological arguments as to why PCE could be a carcinogen in rodents but not a carcinogen in humans. In this setting it is not surprising that scientists could look at exactly the same set of data and come to opposing conclusions.

Christina Rudén's panel on inconsistencies between risk assessments of TCE and PCE drawn from the same basic data (Panel 4.1) explores these issues in more detail. Taken as a whole, however, the literature shows a clear and consistent progression towards increasing concern about the carcinogenic effects of PCE. According to Karstadt (1998):

> 'Trichloroethylene and tetrachloroethylene have been reviewed by IARC panels several times: three times (volumes 20, supplement 7, and volume 63) for tetrachloroethylene, four times (volumes 11, 20, supplement 7, and volume 63) for trichloroethylene. Until the consensus meeting that resulted in volume 63 (published 1995) animal evidence for the two chemicals was evaluated as limited and human evidence as inadequate; both evaluations were raised in volume 63, to sufficient in animals and limited in humans. The IARC reviews of those two chemicals clearly show the gradual accretion of human evidence over the years as well as the development of definitive animal data.'

Throughout this period PCE has been on the radar screen of the occupational health and environmental scientific communities, unlike the period before 1970. As a result, fairly strict community drinking water standards have been established, although occupational standards have lagged behind. This inconsistency may partly result from the combination of a weak labour movement and some highly publicised environmental cases involving childhood cancer (e.g. Lagakos et al., 1986).

The problem is no longer invisibility and neglect, but intense scrutiny. The chemical industry has been active and aggressive in countering new information through the strategy of artificially and purposefully creating doubt and uncertainty in the minds of decision-makers. With this chemical now on the cusp of being declared a confirmed human carcinogen in some major national markets, the industry is essentially buying extra time (and creating continuing exposure and disease) by this strategy. Thus 40 years after the hard lesson of the water mains in Massachusetts, a sound precautionary strategy for continued exposure to PCE has still not been initiated.

The means used to avoid or promote action today are different from those of 1970, employing many sophisticated means to create doubt and increase uncertainty about the true value of a regulatory action. The 1970 context was simpler. Evidence was available and not acted on for reasons not complicated by complex regulations, the potential of lawsuits or the activities of environmental or activist organisations. Information about effects and exposure was restricted or non-existent and available primarily to scientists. The industry felt no special need to consult it (although they had contributed to it) and apparently did not. It was of no interest to them.

During both periods the lesson of this small but revealing case study seems clear. Mechanisms are needed to force the production, sharing and publication of information about exposure and effects; normative and legal requirements concerning the duty of care of employers and manufacturers are also required. Alternatives are available, as Joy Onasch's description of wet-cleaning technologies (Panel 4.2) illustrates.

Today, continued argument over how to interpret the scientific evidence is irresolvable within science itself because the same evidence can be interpreted differently and there are no overarching criteria from the philosophy of science that can force a solution.

Whether the problem is a failed duty of care or a lack of clarity about what evidence will trigger action, the history of PCE will continue in the future as it has in the past. The science has not been hidden. It has been ineffective in guiding and catalysing action.

Table 4.1 Early warnings and actions

1860	PCE synthesised
1920s–1960s	PCE used in the treatment of hookworm
1925	First toxicological evaluation of PCE
1925–1940	Clinical and toxicological evaluation of therapeutic use identified a variety of problems and recognised that the responses of different subjects varied
1940–1970	New uses prompt consideration of inhalation dangers; chronic effects studied (central nervous system depression) and new analytical methods brought into play (gas chromatography)
1970–present	Discovery that vinyl chloride is a carcinogen prompts controversy and large literature with competing accounts of PCE's carcinogenicity Environmental and occupational standards were promulgated, generating controversy couched in scientific terms. PCE figures in lawsuits
Today	PCE is regulated in the environmental and occupational environments but controversy continues over where to set standards and whether PCE has caused harm in many legal cases

References

ACGIH, 1993, *Tetrachloroethylene, Documentation of the TLVs*, seventh edition, American Conference of Government Industrial Hygienists.

AMA Council on Pharmacy and Chemistry, 1936, 'Preliminary Report: Report on the Present Status of Tetrachlorethylene', *JAMA*, (107/14) 1 132–1 133.

Amter, S. and Ross, B., 2001, 'Was contamination of souther-n California groundwater by chlorinated solvents foreseen?', *Environmental Forensics*, (2) 179–184.

Anttila, A., Pukkala, E., Sallmén, M., Hernberg, S. and Hemminki, K., 1995, 'Cancer incidence among Finnish workers exposed to halogenated hydrocarbons', *J. Occup. Environ. Med.*, (37) 797–806.

Baader, E.W., 1954, *Gewerbedrankheiten: Klinische Grundlagen der 40 meldepflichtigen Berufskrankheiten*, Urban & Schwarzenberg, Munich, pp. 159–161.

Barrett, H.M., Cunningham, J.G. and Johnston, J.H., 1939, 'A study of the fate inn the organism of some chlorinated hydrocarbons', *J Ind Hyg & Toxicol,* (21) 479–490.

Beyer, A. and Gerbis, H., 1932, 'Jahresberict ubeer die Tatigkeit der preussischen Gewerbemedizinalrate wahrend des Kalenderjahres', *Veroffentlichungen aus dem Gebiete der Medizinialverwaltung*, (39) 1–30.

Blair, A., Stewart, P.A., Tolbert, P.E., Grauman, D., Moran, F.X., Vaught, J., and Rayner, J., 1990, 'Cancer and other causes of death among a cohort of dry cleaners', *Br. J. Ind. Med.*, (47) 162–168.

Bwibo, N.O., 1969, 'Accidental poisoning in children in Uganda', *Br med J*, (4) 601–602.

Carpenter, C.P., 1937, 'The chronic toxicity of tetrachlorethylene', *J Ind Hyg & Toxicol*, (119) 323–336.

Coler, H.R. and Rossmiller, H.R., 1953, 'Tetrachlorethylene exosure in a small industry', *AMA Arch of Indust Hyg & Occ. Med*, (8) 227–233.

Colten, C., 1991, *Geographic Review,* (81) 215–228.

Demond, A.H., 1982, *A source of tetrachloroethylene in the drinking water of New England: an evaluation of the toxicity of tetrachloroethylene and the prediction of its leaching rates from vinyl-lined asbestos-cement pipe* (MS Thesis), Massachusetts Institute of Technology, Cambridge, MA.

ECETOC, 1999, *Tetrachloroethylene*, European Centre for Ecotoxicology and Toxicology of Chemicals, Joint Assessment of Commodity Chemicals, vol. 39.

EEA, 2001, *Late lessons from early warnings: the precautionary principle 1896–2000*, Environmental issue report No 22, European Environment Agency.

EEA, 2008, *Evaluating and Communicating Scientific Evidence on Environment and Health Issues*, report of the European Environment Agency workshop, Copenhagen, 28–29 May 2008.

Fairhall, L.T., 1949, *Industrial Toxicology*, Williams & Wilkins, Baltimore, p. 442–444.

Fernando, P.B., D'Silva, M. and Stork, G.K.B., 1939, 'Tetrachlorethylene in the treatment of hookworm

disease with special reference to toxicity', *Ind J Med Res*, (3) 759–783.

Friberg, L., Kylin, B. and Hystrom, A., 1953, 'Toxicities of trichloroethylene and tetrachlorethylene and Fujiwara's pyridine-alkali reaction', *Acta Pharmacol et Toxicol*, (9) 303–312.

Gehring, P.H., 1968, 'Hepatotoxic potency of various chlorinated hydrocarbon vapours relative to their narcotic and lethal potencies in mice', *Toxicol and Appl Pharmacol*, (13) 287–298.

Hall, M.C. and Shillinger, J.E., 1925, 'Tetrachlorethylene, a new anthelmintic', *Am J Trop Med*, (5) 229–237.

Hamilton, A., 1936, 'Some new and unfamiliar industrial poisons', *NEJM*, (2215) 425–532.

IARC, 1995a, 'Drycleaning, some Chlorinated Solvents and Other Industrial Chemicals', *IARC Monogr Eval Carcinog Risks Hum*, vol. 63.

IARC, 1995b, *Tetrachloroethene*, International Agency For Research On Cancer Monographs, vol. 63.

Irish, D.D., 1962, 'Common chlorinated aliphatic hydrocarbon solvents', *Arch Env Health*, (4) 110–116.

Karstadt, M., 1998, 'Availability of epidemiologic data for chemicals known to cause cancer in animals: an update,' *Am J Ind Med*, (34) 519–525.

Keoleian, G.A., Blackler, C.E., Denbow, R. and Polk, R., 1997, 'Comparative assessment of wet and dry garment cleaning', *Journal of Cleaner Production*, (5/4) 279–289 (and 1998, 6, 23–36).

Lagakos, S.W., Wesson, B. and Zelen, M., 1986, 'An analysis of contaminated well water and health effects in Woburn, Massachusetts', *Journal of American Statistics Association*, (81) 583–596.

Lamson, P.D., Robbins, B.H. and Ward, C.B., 1929, 'The pharmacology and toxicology of tetrachlorethylene', *Am. J. Epidemiol*., (9/2) 430–444.

Larsen, C.D.F., Love, T.O., Reynolds, G., 1983, 'Tetrachloroethylene leached from lined asbestos-cement pipe into drinking water', *J. Am Water Works Assoc*, 75L 184–188.

Lehmann, K.B. and Flury, F., 1943, *Toxicology and hygiene of industrial solvents*, Williams & Wilkins Co., Baltimore, pp. 184–186; 310–325.

Lob, M., 1957, 'Les dangers du perchlorethylene', *Archiv fur Gewerbepatholgie und Gewerbehygiene*, (16) 45–52.

MAK, 1992, *Tetrachloroethylene, Toxikologisch-arbeidsmedizinische Begrundung von MAK-Werten*, Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area.

Manson, D., 1934, 'A comparative record of anthelmintic treatment with tetrachlorethylene and oil of chenopodium', *The Indian Med Gaz*, (69) 500–507.

MDEE, 1982, *Status Report on Tetrachloroethylene Contamination of Public Drinking water Supplies by Vinyl-lined Asbestos Cement Pipe*, Massachusetts Department of Environmental Engineering, Commonwealth of Massachusetts, Boston, MA.

Mennear, J., Maronpot, R., Boorman, G., Eustis, S., Huff, J., Haseman, J., McConnell, E., Ragan, H., Miller, R., 1986, 'Toxicologic and carcinogenic effects of inhaled tetrachloroethylene in rats and mice,' in: Chambers, P., Gehring, P. and Sakai, F., (eds), *New Concepts and Developments in Toxicology*, Elsevier Science Publishers, pp. 201–210.

Morse, K.M. and Goldberg, L., 1943, 'Chlorinated solvent exposures—at degreasing operations', *Ind Med*, (12) 706–713.

NCI, 1977, National Cancer Institute, *Bioassay of Tetrachloroethylene for Possible Carcinogenicity* (CAS No. 127-18-4) Tech. Rept. Ser. 13, Bethesda, MD.

Onasch, J., 2011, 'A feasibility and cost comparison of perchloroethylene dry cleaning to professional wet cleaning: case study of Silver Hanger Cleaners, Bellingham, Massachusetts', *Journal of Cleaner Production*, (19) 477–482.

Ozonoff, D., 1988, 'Failed Warnings: Asbestos Related Disease and Industrial Medicine' in: Bayer, R. (ed.), *The Health and Safety of Workers*, Oxford University Press, New York, pp. 139–218.

Plaa, G.L., Evans, E.A. and Hine, C.H., 1958, 'Relative hepatotoxicity of seven halogenated hydrocarbons', *J Pharmacol & Exp Therap* (123) 224–229.

Rosenau, M., 1935, *Preventive Medicine and Hygiene*, D. Appleton-Century Company.

Rowe, V.K., McCollister, D.D., Spencer, H.C., Adams, E.M. and Irish, D.D., 1952, 'Vapor toxicity

of tetrachloroethylene for laboratory animals and human subjects', *AMA Arch of Ind Hyg & Occ Med*, (5) 566–579.

Rowe, V.K., Wujowski, T., Wolf, M.A., Sadek, S.E. and Stewart, R.D., 1963, 'Toxicity of a solvent mixture of 1, 1, 1,-trichlorethane and tetrachloroethylene as determined by experiments on laboratory animals and human subjects', *Am Ind Hyg Assoc J*, (24) 541–554.

Rudén, C., 2002, 'The Use of Mechanistic Data and the Handling of Scientific Uncertainty in Carcinogen Risk Assessments: The Trichloroethylene Example', *Regulatory Toxicology and Pharmacology*, (35) 80–94.

Rudén, C., 2006, 'Science and policy in risk assessments of chlorinated ethenes', *Ann. N.Y. Acad: Sci.*, (1076) 191–206.

Ruder, A.M., Ward, E.M. and Brown, D.P., 1994, 'Cancer mortality in female and male dry-cleaning workers', *J. Occup. Med.*, (36) 867–874.

Sandground, J.H., 1941, 'Coma following medication with tetrachlorethylene', *JAMA*, (117) 440–441.

Sappington, C.O., 1943, *Essentials of Industrial Health*, JB Lippincott, Philadelphia, p. 249.

Sharlin, H.I., 1966, *The Convergent Century: The Unification of Science in the Nineteenth Century*, Abelard-Schuman.

Sinsheimera, P., Grouta, C., Namkoonga, A., Gottlieba, R. and Latif, A., 2007, 'The viability of professional wet cleaning as a pollution prevention alternative to perchloroethylene dry cleaning', *Journal of the Air and Waste Management Association*, (57) 172–178.

Smyth, H.F., Weil, C.S., West, J.S. and Carpenter, C.P., 1969, 'An exploration of joint toxic action: twenty-seven industrial chemicals intubated in rats in all possible pairs', *Toicol and Appl Pharmacol*, (14) 340–347.

Spirtas, R., Stewart, P.A., Lee, J.S., Marano, D.E., Forbes, C.D., Grauman, D.J., Pettigrew, H.M., Blair, A., Hoover, R.N. and Cohen, J.L., 1991, 'Retrospective cohort mortality study of workers at an aircraft maintenance facility I. Epidemiological results', *Br. J. Ind. Med.*, (48) 515–530.

St George, A.V., 1937, 'The pathology of the newer commercial solvents', *Am J Clin Path*, (7) 69–77.

Stewart, R.D. and Dodd, H.C., 1964, 'Absorption of carbon tetrachloride, trichlorethylene, tetrachloroethylene, methylene chloride, and 1,1,1-trichloroethane through the human skin', *Am Ind Hyg Assoc J*, (25) 439–446.

Stewart, R.D., Baretta, E.D., Dodd, H.C. and Torkelson, T.R., 1970, 'Experimental human exposure to tetrachlorethylene', *Arch Environ Health*, (20) 224–229.

Stewart, R.D., Dodd, H.C., Erley, D.S. and Holder, B.B., 1965, 'Diagnosis of solvent poisoning', *JAMA*, (193) 115–118.

Stewart, R.D. and Erley, D.S., 1965, 'Detection of volatile organic compounds and toxic gases in humans by rapid infrared techniques', *Prog Chem Toxicol*, (2) 183–220.

Stewart, R.D., Erley, D.S., Schaffer, A.W. and Gay, H.H., 1961a, 'Accidental vapor exposure to anesthetic concentrations of a solvent containing tetrachlorethylene', *Ind Med Surg*, (30) 327–330.

Stewart, R.D., Gay, H.H., Erley, D.S., Hake, C I. and Schaffer, A.W., 1961b, 'Human exposure to tetrachloroethylene vapor', *Arch Env Health*, (2) 40–46.

Stewart, R.D., Swank, J.D., Roberts C.B. and Dodd, H.C., 1963, 'Detection of halogenated hydrocarbons in the expired air of human beings using the electron capture detector', *Nature*, (198) 696–697.

Stewart, R.D., 1969, 'Acute tetrachloroethylene intoxication', *JAMA*, (208) 1 490–1 492.

TURI, 2007, *Massachusetts Chemical Fact Sheet, Perchloroethylene (PCE)*, Massachusetts Toxics Use Reduction Institute (http://www.turi.org/About/Library/TURI-Publications/Massachusetts_Chemical_Fact_Sheets/Perchloroethylene_PCE_Fact_Sheet/PCE_Details/PCE-Fact-Sheet-pdf) accessed 28 December 2011.

Williams, L.P., 1965, *Michael Faraday*, Da Capo Press.

Wright, W.H., Bozicevich, J. and Gordon, L.S., 1937, 'Studies on oxyuriasis, V. Therapy with single doses of tetrachlorethylene', *JAMA*, (109) 570–573.

Zernik, F., 1933, 'Neuere Erkenntnisse auf dem Begiete der schadlichen Gase und Dampfe', *Ergebnisse der Hygiene Bakeriologie Immunitatsforschung und Experimentellen Therapie*, (14) 139–141, 200–210.