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Review article

Respiratory effects of trichloroethylene

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ABSTRACT

Trichloroethylene (TCE) is a chlorinated solvent that has been used widely around the world in the twentieth century for metal degreasing and dry cleaning. Although TCE displays general toxicity and is classified as a human carcinogen, the association between TCE exposure and respiratory disorders are conflicting. In this review we aimed to systematically evaluate the current evidence for the respiratory effects of TCE exposure and the implications for the practicing clinician.

There is limited evidence of an increased risk of lung cancer associated with TCE exposure based on animal and human data. However, the effect of other chlorinated solvents and mixed solvent exposure should be further investigated. Limited data are available to support an association between TCE exposure and respiratory tract disorders such as asthma, chronic bronchitis, or rhinitis. The most consistent data is the association of TCE with autoimmune and vascular diseases such as systemic sclerosis and pulmonary veno-occlusive disease.

Although recent data are reassuring regarding the absence of an increased lung cancer risk with TCE exposure, clinicians should be aware of other potential respiratory effects of TCE. In particular, occupational exposure to TCE has been linked to less common conditions such as systemic sclerosis and pulmonary veno-occlusive disease.

1. Introduction

Trichloroethylene (TCE) is a non-flammable, volatile, colourless and lipophilic liquid, belonging to the chlorinated aliphatic solvent family. Before the 1990s, TCE was used primarily as an industrial solvent for the cleaning and degreasing of metals. TCE was also widely used as a chemical intermediate and extractant in chemical, dry-cleaning and textile industries, and as a component of many consumer products such as paints, typewriter correction fluids, wood finishes, cleaners, polishes and lubricants [1]. Although there are consistent data to indicate that TCE has kidney and blood toxicity and TCE is currently classified as a human carcinogen by the International Agency for Research on Cancer [7], the association between TCE exposure and respiratory disorders remains unclear. We aimed to review the current knowledge on the adverse respiratory effects of TCE exposure (see Box 1).

2. Occupational exposure to TCE

This section briefly presents the main industries and occupations that are involved, or were involved in the past, with exposure to TCE. The major sources of occupational exposure to TCE are provided in Table 1.

A systematic literature review by Bakke et al. published in 2007 highlights the different occupational situations (industries and activities) that are associated with occupational exposure to TCE in the United States (US) and Europe [2]. In the 20th century, the major uses of TCE was degreasing, mainly for cleaning of metal parts but also for other products such as inorganic fibres, glass, and carbon fibres.

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Box 1
Search strategy for the epidemiologic literature.

Published studies were identified from PubMed using the key words “occupational AND trichloroethylene”, published from 1980 through December 2015. We made a critical selection of studies relevant for the topic (respiratory disorders). To identify potential studies not retrieved from the initial search, we performed additional searches on specific disorders (e.g., using keywords “asthma trichloroethylene”, “solvents occupational asthma”, or “chlorinated solvents asthma”; and similar searches replacing “asthma” by “respiratory”, “lung”, “pulmonary” or “COPD”). We also reviewed all selected papers for reference citations that had not been otherwise identified in the initial search.

Table 1
Major exposure sources of TCE.

Industry	Type of exposure
Metal-working industries: manufacturing of primary metals	Solvent degreasing product: metal furniture, fabricated products, non-electric machinery, electric and transportation equipment's, instruments and clocks
Metal-working industries: maintenance and service operations	Solvent degreasing products: automotive repair, railroad transportation maintenance and aircraft maintenance (still used).
Dry cleaning et dyeing/other fabric cleaning	Solvent: Batch process cleaning large quantities of textiles or spot remover on individual pieces, with use of TCE between 1910 and early 1960s, very rare after
Textile Mill products and apparel	Solvents including TCE: Scouring, sizing or desiring textiles, removing foreign substances.
Leather and leather products	Removing fat from hides in the processing of leather (until the 1960s) and disinfecting hides and skins
Electronic components and accessories	Manufacturing of semiconductor substrates and integrated circuits/manufacturing of printed circuit boards. Use small in 1984.
Rubber and miscellaneous plastic products	Binding and cementing materials (treads, tire, and bead building) TCE still used in the 1970s but probably rarely.
Agricultural production and chemicals	Fumigant in grain storage and related industries and solvent for insecticides/component of fungicides/aerosolized insecticides from 1930s through 1970s at least
Food and kindred products	Extractant in two processes: decaffeination of coffee and spice oleoresins. Uses stopped in 1977 after banishment of TCE as a food additive by the Environmental Protection Agency (EPA)
Heath services	- Anesthetic (dental extractions, orthopedic manipulations, cystoscopy, obstetrics, burn dressing, and similar short surgical procedures). use decline in the 1970s - Analgesics, detergent for skin, veterinary medicine
Chemicals and allied products	- Extracting resin from wood and production of pulverized sulphur. - Dye manufacturing (use rare in the 1970s) - Vehicle in glues, adhesives, and cements in the shoe, foam, and rubber industries. Since the 1930s, rare in the 1970s
Paints, varnishes, lacquers, enamels, and allied products	Thinner for paints and varnishes
Transportation by air	Aircraft maintenance industry (including parachute cleaning). Introduction in 1955, use apparently ended before the 1980s.
Papers and allied products	Pulp and papermaking industry in impregnating cardboard and paper board boxes. use rare in the 1970s
Perfumes, cosmetics, and other toiletry preparations	Component in dry shampoo/cleaner for false eyelashes/perfumes. Use banned in the cosmetics by the Federal Drug Administration (FDA) in 1977.

Degreasing is the process of removing water insoluble substances such as grease or wax from a surface. TCE was first used as a degreaser in the 1910s and became the most common degreasing agent in the 1940s. In 1966, TCE was used for more than 90% of all vapor degreasing processes, and in the 1970s, approximately 12% of all industrial plants used TCE for their cleaning operations. However, in 1971, the U.S. Environmental Protection Agency issued a warning against the environmental impact of some chlorinated solvents, including TCE. Since then, the use of TCE has declined and by 1980, less than 2% of cold cleaning and only a third of all vapor degreasing continued to use TCE. Metal-working industries are the major users of solvent degreasing in the U.S. and in Europe. In the 1970s, the cleaning of metals accounted for the majority of industrial metal work, and 40–65% of plants used solvents for metal degreasing.

While the commercial use TCE began to decrease in the late 1970s in the US and Europe and is currently very limited, its use actually increased in many Asian countries concurrent with the rapid expansion of their industrial sectors. In South Korea, TCE was used commonly in the following industrial sectors (in descending order) [3]: manufacturers of motor vehicle and engine parts and accessories, machinery workers, manufacturers of electric components, computer, radio, television, and communication equipment, and primary metal workers and manufacturers of fabricated metal products. TCE was also used frequently in cleaning activities, with the highest level of TCE exposure reported by manufacturers of non-metallic mineral products, followed by manual cleaning for optic device production, degreasing for rubber good production, and cleaning for transport machineries and equipment production. Similarly, TCE use in China began to increase in the 1990s as its electronic, microelectronics, and telecommunications industries rapidly expanded and required efficient chemical degreasers. TCE use in China increased from 4 to 5 kilotons between 1980 and 1990 to 40 kilotons in 2000 and 165 kilotons in 2010 [4]. Finally, the highest means of TCE concentrations were found in textile dyeing and printing jobs, and laundry jobs. Other activities with high ambient concentration of TCE were the production of cultural, education, and sports articles, the plate makers, and the workers in surface treatment of metals.

3. TCE penetration and metabolism in human

TCE is a lipophilic solvent that can readily cross biological membranes. TCE is taken up by the inhalation, oral or cutaneous route. Metabolism of TCE occurs through two main irreversible pathways: the cytochrome P450 (CYP450)-dependent oxidative pathway and the glutathione (GSH)-conjugation pathway by glutathione S-transferases (GST) [5]. [6] [7].

CYP-dependent oxidative metabolism occurs predominantly in the liver, and to a lesser extent in the lung. The reaction between TCE and CYP450 produces three metabolites: TCE epoxide, chloral, and chloral hydrate. The first one, TCE epoxide, is chemically unstable and spontaneously generates directly oxalic acid or dichloroacetyl chloride