

Chapter 2

Chlorine

2.1. Background

2.1.1 Basic chemical information

37. Chlorine (Cl₂) is a greenish-yellow gas with a very pungent odour, which is readily detectable at low concentrations in the air. It is 2.47-times denser than air.

Conversion factors at 25°C:

$$1 \text{ ppm} = 2.90 \text{ mg/m}^3; 1 \text{ mg/m}^3 = 0.34 \text{ ppm}$$

2.1.2 Sources

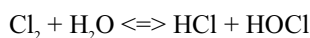
38. Releases of chlorine to air are not estimated by the National Atmospheric Emission Inventory and reporting is only required by the Environment Agency where the release is greater than one tonne per annum or as a specific permit condition. From the limited information available, the major source is the chemical industry, with a small amount arising from the metals industry.

2.1.3 Ambient levels

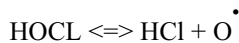
39. There are no reported air quality data for chlorine with which to assess population exposures.

2.2. Health effects

40. The mechanism of action of chlorine lies in two different free radical pathways. The first of these involves the action of the chlorine atom, which is itself a free radical; when released it reacts with other molecules to oxidise them. The second pathway is via the indirect generation of reactive oxygen species. On entering the respiratory (breathing) tract, chlorine reacts with water forming hydrochloric acid (HCl) and hypochlorous acid (HOCl).



Hypochlorous acid is a strong oxidising agent and on dissolution it releases hydrochloric acid and reactive oxygen species.



These react with the surrounding tissue components causing oxidative changes that lead to the generation of pro-inflammatory signals and the initiation of an inflammatory response in the airways. The hydrochloric acid then acts as a secondary irritant (Wolf *et al.*, 1995).

2.2.1 Animal studies

41. Chlorine is acutely toxic with LC_{50}^2 values of 700 ppm (2030 mg/m^3) in rats and 500 ppm (1450 mg/m^3) in mice for a 30-minute exposure (Zwart and Woutersen, 1988). A two-year inhalation exposure study of female and male mice and rats found chlorine-induced changes in the cells lining the nasal passages (hyperplasia) in all sex and species groups, including those exposed to the lowest concentration at 0.4 ppm (1.16 mg/m^3). This figure may be regarded as a lowest observed adverse effects level (LOAEL) for upper respiratory tract irritation, but it is not known whether this value is directly applicable to human subpopulations exposed for short periods.

2.2.2 Acute and subacute effects in humans

42. The most important consequence of exposure to chlorine gas relates to its strong irritant action when in contact with the moist mucous membranes (linings) of the respiratory tract and, to a lesser extent, the eyes and the skin. As it is only moderately soluble in water, following inhalation the gas is incompletely extracted in the nose and upper respiratory tract and so can exert a direct toxic effect on the lungs. At high concentrations – as may be encountered in accidental inhalation exposures in industry or when the gas was used in chemical warfare in World War I – a potentially lethal chemical-induced lung injury, toxic pneumonitis (inflammation of the lungs), can occur. As a bulk commercial chemical, chlorine is the commonest toxic gas for which emergency planning is required under major accident hazard regulations (Baxter *et al.*, 1989; COMAH, 1999). Between 1989 and 2003, 228 occupational inhalation accidents involving chlorine were reported to the SWORD database in the United Kingdom and of these 69 (16%) were estimated to have led to reactive airways dysfunction syndrome (RADS), a form of irritant-induced asthma (see Appendix 2). The exposures involved, however, are far higher than those encountered in ordinary ambient conditions.
43. Minimal and rapidly reversible changes in a range of lung function parameters were observed in a study of eight healthy volunteers who were exposed to 1 ppm (2.9 mg/m^3) of chlorine gas for up to eight hours (Rotman *et al.*, 1983). Symptoms of itchy eyes, runny nose and mild burning of the throat were also found. An 8-hour exposure to 0.5 ppm

² LC_{50} is that concentration lethal to 50% of those exposed of the stated time.

- (1.45 mg/m³) produced no changes in lung function and no significant symptoms of sensory irritation (Rotman *et al.*, 1983). However, one sensitive volunteer in this study did suffer an asthmatic attack from exposure to 1 ppm (2.9 mg/m³) chlorine and left the exposure chamber after four hours.
44. A study at the TNO Nutrition and Food Research Institute of the nasal and respiratory effects of chlorine was undertaken with eight male volunteers exposed to 0, 0.1, 0.3 and 0.5 ppm (0, 0.29, 0.87 and 1.45 mg/m³) for six hours per day on three consecutive days to each of four exposure conditions spaced 11 days apart. Measurements were made of lung function and nasal lavage (nose washings) parameters. The results did not reveal an inflammatory effect in the nose nor did they show a consistent effect on respiratory function at repeated exposure up to 0.5 ppm (1.45 mg/m³) (Emmen *et al.*, 1997).
 45. It is clearly established that individuals with pre-existing non-specific airway hyper-responsiveness, with and without clinical asthma, can be more adversely affected by inhaled irritant substances such as sulphur dioxide. To determine the responses to chlorine in this susceptible group, D'Alessandro *et al.* (1996) exposed ten healthy volunteers to low levels of chlorine gas and the effect on their lung function was measured. Five volunteers had, and five did not have, baseline airway hyper-responsiveness as defined by baseline methacholine challenge testing (that is exaggerated constriction of the airways in response to stimuli, tested by inhaling methacholine). After exposure to 1 ppm of chlorine for 60 minutes both groups experienced a temporary fall in lung function (as FEV1 - forced expiratory volume in 1 second), which was greater in those with methacholine hyper-responsiveness. However, after exposure to 0.4 ppm (1.16 mg/m³) of chlorine there was no significant fall in lung function in either group (D'Alessandro *et al.*, 1996).
 46. In a nasal provocation study by Shusterman *et al.* (1998) involving eight volunteers in each of two groups that were either normal or had seasonal allergic rhinitis (hay fever), those with rhinitis had a greater increase in nasal airway resistance than the non-rhinitic subjects. The concentration of chlorine gas was 0.5 ppm (1.45 mg/m³) and exposure lasted for 15 minutes. Individuals identified as having asthma were excluded. There were no clinically significant changes in peak expiratory flow (exhalation), whereas both nasal irritation and nasal congestion were reported more frequently in the subjects with rhinitis.
 47. There have been no published studies undertaken on the effects of low levels of chlorine on people with asthma, but anecdotally such exposures are widely considered to acutely aggravate their condition.
 48. Few epidemiological studies have been undertaken in industry that can be used to correlate low-level exposures to chlorine with chronic (irreversible) lung disease developing at low-level industrial exposures. Wide variations in exposure, potential confounding effects of previous exposures to chlorine and/or other chemicals and lack of information on

smoking habits make it difficult to correlate exposure with potential effect (NIOSH, 1976).

49. Other acute accidental exposures can occur at home or inside buildings during domestic cleaning with chlorine-releasing agents. The concentrations of chlorine in the air to which individuals are exposed are usually unknown. However, a recent study (Medina-Ramón *et al.*, 2005) showed that cleaners with respiratory symptoms were more likely than those without to have used bleach regularly with a dose response relationship. Airborne chlorine levels during cleaning activities for ten of the cleaners ranged from unrecordable to 0.4ppm although shorter-lived peaks to 1.3 ppm (3.77 mg/m³) were recorded. Chlorine-releasing agents are also commonly used as disinfectants for swimming pools, but clinically significant levels of chlorine are unlikely to be present in the atmosphere. Asthmatic responses because of swimming pools are more likely to be due to chloramines (chemical compounds of chlorine and nitrogen), in particular NCl₃, that are produced by chlorine reacting rapidly with body secretions and excretions (Thickett *et al.*, 2002).
50. The Health and Safety Commission (HSE, 2002a,b) has set occupational exposure limits of 1 ppm (2.9 mg/m³) (as a 15-minute time-weighted average) and 0.5 ppm (1.5 mg/m³) (as an 8-hour time-weighted average) based on the lung function data of Rotman *et al.*, (1983) (HSE, 1993; 2002a,b). This evidence was considered to be more objective than the reports of 'irritation' described elsewhere.

2.2.3 Carcinogenicity and effects on reproductive outcome

51. Published studies give no evidence that chlorine vapour is carcinogenic in mice or rats (Wolf *et al.*, 1995). IARC (The International Agency for Research on Cancer) concluded that there was no substantive evidence for carcinogenicity of chlorine in drinking water in either humans or animals (group 3 unclassifiable IARC 1991). There is insufficient evidence available to determine whether there is an effect of chlorine vapour on reproductive outcomes.

2.3. Justification for the air quality guideline value

52. Chlorine has an acute irritant effect on the airways and as a consequence the Panel recommends a short averaging exposure time, similar to the approach taken for sulphur dioxide. The Panel considered that for irritant or potential inflammatory effects on the upper and lower respiratory tract, a concentration of 0.5 ppm (1.45 mg/m³) over 6 to 8 hours was acceptable as a no observed adverse effect level (NOAEL) in fit volunteers and in subjects with a degree of pre-existing airway hyper-responsiveness. To take into account the more susceptible members of the general population, in particular those with asthma who may be particularly sensitive to exposure to chlorine gas, a safety factor of 5 was chosen, which allows for the irritant effects on the upper and lower respiratory tract. This factor should also be protective in subjects

with seasonal allergic rhinitis who may also be particularly sensitive to the adverse effects of chlorine gas on the lining of the nasal passages.

53. The Panel considered that there were no grounds for regarding chlorine as a human carcinogen.

2.4. Recommendation

54. **The Panel recommends that a concentration of chlorine gas or mass equivalent aerosol not exceeding 0.1 ppm (0.29 mg/m³) over a 1-hour averaging period should protect against irritant and inflammatory effects on the skin, eye and breathing airways. Long-term effects at these low concentrations are considered most unlikely.**

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