The Journal of Laryngology and Otology
November 1999, Vol. **113,** pp. 1004–1007

Carcinoma of the ear: a case report of a possible association with chlorinated disinfectants

S. A. MONEM, F.R.C.S.*, D. A. MOFFAT, F.R.C.S.*, M. C. FRAMPTON, F.R.C.S.†

Abstract
In this report we present a case of squamous cell carcinoma developing in a mastoid cavity after prolonged exposure to the chemical disinfectant, Eusol. The efficacy and safety of Eusol and other chloric acid (hypochlorous acid) derivatives in clinical use is debated.

Key words: Ear; Temporal bone; Carcinoma; Hypochorite; Disinfectants; Carcinogens

Introduction

Primary squamous cell carinoma of the temporal bone is a rare disease, however, it is the most common malignancy occurring in this region. It has a female to male ratio of 1.2:1, and an incidence of 1 and 0.8 per million per year respectively.

The aetiology of squamous cell carcinoma of the external ear, middle ear, and the temporal bone is unknown. A distinct relationship seems to exist between chronic suppurative otitis media and otorrohea of many years' duration and the development of the disease (Moffat *et al.*, in press). More than half the cases studied in large series (Conley and Novack, 1960; Lewis, 1975) supported this view. The latent period between the onset of suppuration and the appearance of the neoplasia has also been studied (Bizgalis *et al.*, 1992). Cholesteatoma is estimated to coexist in 25 per cent of cases (Michaels and Wells, 1980; Bizgalis *et al.*, 1992). Other authors (Coachman, 1951) concluded that progressive tumour growth results in secondary infection of the middle ear via the eustachian tube and the external auditory canal, and that the otorrhoea is more likely to be a result of, rather than a cause of, the carcinoma. Direct exposure to radium paint (Beal *et al.*, 1965) and previous history of head and neck irradiation (Applebaum, 1979; Ruben *et al.*, 1997) are believed to have a direct aetiological role in the development of this condition. Actinic ultraviolet rays have been incriminated as a causal factor in external ear neoplasms but their aetiological role in deep-seated tumours is doubtful (Shaheen, 1997). Chronic irritation as in cases of lupus vulgaris is said to play a role in producing the carcinoma and it may be that the prolonged repetitive use of an irritant disinfectant can also induce a squamous cell carcinoma.

Sodium hypochlorite has gained attention in recent toxicology literature since it was found to have mutagenic activity in *in vitro* studies (Kawachi *et al.*, 1980; Environmental Protection Agency DPIM report, 1983) and has a teratogenic effect on the developing rat foetus (Hasegawa *et al.*, 1986).

Case report

A 64-year-old Caucasian male who had had a left radical mastoidectomy 40 years previously, presented to the ENT department in 1995 complaining of blockage of his left ear with intermittent discharge. After the original surgery he failed to attend for follow-up and had since that time consistently irrigated the cavity with the disinfectant Eusol.

On examination at the time the cavity was full of benign-looking granulation tissue over the facial ridge which regressed with conservative treatment, of combined steroid-antibiotic ear drops. The patient then failed to

FIG. 1

Axial CT (in bone window) showing extensive bony erosion of the lateral one half of left temporal bone involving the middle ear, mastoid and sigmoid plate with extensive destruction of the external auditory canal. There is no invasion of the otic capsule.

From the Department of Neuro-otology and Skull Base Surgery*, Addenbrooke's Hospital, Cambridge and the Department of Otolaryngology/Head and Neck Surgery†, Bedford Hospital, Bedford, UK.
Accepted for publication: 20 July 1999.

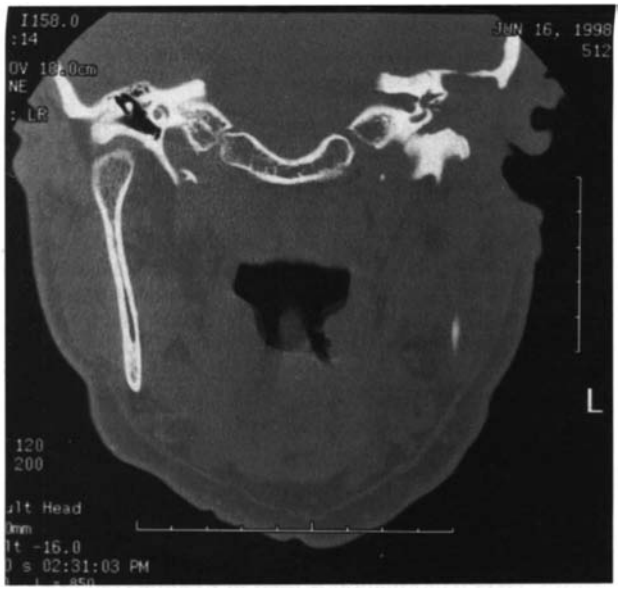

FIG. 2

Coronal CT view showing possible tegmental defect with extensive temporal bone erosion laterally and the tumour extending down the eustachian tube.

attend for review until he returned to the clinic, in 1998, complaining of otalgia, blockage of the ear and recurrence of the otorrhoea which recently had become blood-stained. On examination, on this occasion the mastoid cavity was filled with a granular firm and tender polypoid lesion, which bled easily to touch. The coexistence of an ipsilateral 2 × 2 cm firm and non-tender neck mass, level II neck nodes, was noted. His cranial nerve function including the facial nerve was normal. Pure tone audiometric assessment showed a left-sided conductive hearing loss of 75 dB average across the frequency spectrum and in the contralateral right ear he had a 35 dB high frequency sensorineural loss. A nip biopsy was taken from the polypoid lesion and histopathological examination revealed a well-differentiated squamous cell carcinoma. A high resolution axial and coronal computed tomography (CT) of the temporal bones revealed a soft tissue mass in the mastoid cavity extending into, and involving, the left petrous apex with minor erosion of the inferior aspect of

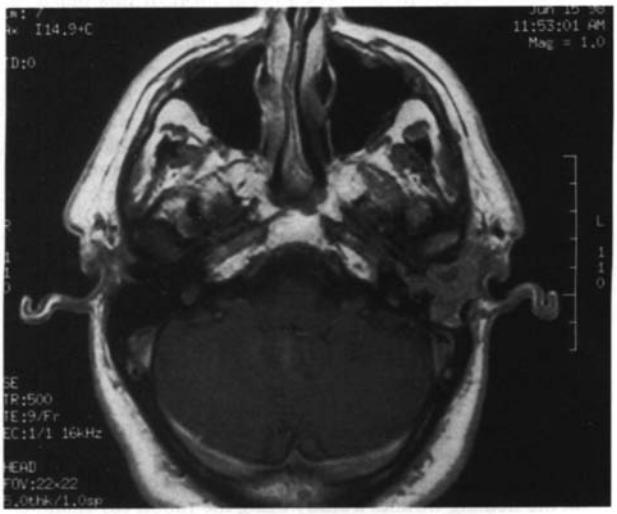

FIG. 3

T1-weighted axial MR image showing soft tissue mass replacing the lateral one half of the left temporal bone.

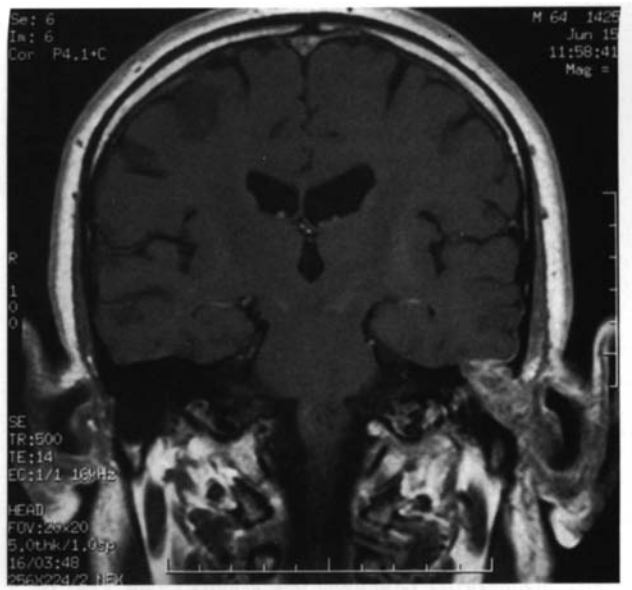

FIG. 4

Coronal MR image, with gadolinium, demonstrating that the tumour has eroded superiorly through the tegmen and superior surface of temporal bone to involve the dura in the middle cranial fossa and temporal lobe of the brain.

the cochlea (Figure 1) and the floor of the middle cranial fossa (Figure 2). Magnetic resonance (MR) imaging, dual echo axial and coronal, before and after gadolinium-DTPA, showed enhancement of the lesion in the lateral two thirds of the left petrous bone (Figure 3) and meningeal enhancement at the lateral portion of the temporal lobe (Figure 4). The patient underwent an extended left temporal bone resection which included a Crile's radical neck dissection with primary reconstruction (Moffat *et al.*, 1997). Six weeks post-operatively he received a full course of radiotherapy consisted of 64 Gy in 32 fractions over 6.5 weeks. The patient tolerated the treatment remarkably well and showed complete recovery. He is currently under surveillance in our combined Oncology clinic.

Discussion

The development of squamous cell carcinoma in long-standing mastoid cavities has been well documented (Coachman, 1951; Issing *et al.*, 1995) but the precise aetiology is not known. Disinfectants have been used empirically since 800 BC. Early reports of their use came into light in the Greek classic, *The Odyssey*, where sulphur dioxide was said to have been used. Chlorine was discovered by the Swedish chemist Scheele in 1774 (Rutala and Weber, 1997) and was later introduced for general sanitation by the Frenchman Labarraque. In France, in 1825, Parisian surgeons used diluted solutions of hypochlorites in managing wounds, gangrene and ulcers (Block, 1991) and reported great success. Chlorinated solutions have been used as disinfectants for the last 200 years (Morgan, 1989). They were widely used in various forms during the First World War when introduced by Lorrain-Smith (Lorrain-Smith *et al.*, 1915). Many microbiologists (Block, 1991) have questioned the efficacy of hypochlorites as disinfectants. They have a wide spectrum of antimicrobial activity; ranging from human immune-deficiency virus (HIV) (Resnick *et al.*, 1986), through bacterial spores (Sykes, 1970), protozoan species (Cursons *et al.*, 1980) to fungal pathogens (Whitmore and Denny, 1992).

https://doi.org/10.1017/S0022215100145839 Published online by Cambridge University Press

Chlorinated solutions are bleaching agents that have proved to be powerful skin and mucous membrane irritants (Dakin, 1915) due to the production of free oxygen radicals as a by-product of their reaction with organic material and water (Sax and Lewis, 1989). They are said to be effective in cleansing wounds but delay healing (Centers for Disease Control (CDC), 1982). Laboratory studies (CDC, 1982) and Martindale's Pharmacopoeia (Martindale, 1996) recommend that these solutions should not be used in clinical circumstances, and if Eusol is used to irrigate a wound the skin around the wound should be protected with soft paraffin. Their use as wound desloughers has been discouraged as they cause superficial tissue damage (Dakin, 1915). It has been suggested that their irritant effect on healing tissues may be sufficient to preclude their clinical use (Brennan and Leaper, 1985).

Eusol (*E*dinburgh *S*olution of *L*ime) is a well-known hospital disinfectant. The official chemical formula for Eusol (BNF, 1998) is: 1.25 per cent chlorinated lime and 1.25 per cent boric acid mixed in purified water, freshly prepared and cooled. It is one of the most commonly used hypochloric acid derivatives with a minimum amount of available chlorine of 0.25 per cent. There are no data supporting the theory that hypochlorites may act as carcinogens but data linking hypochloric acid to genetic mutation (Kawachi *et al.*, 1980; Environmental Protection Agency DPIM report, 1983) do exist. Sodium hypochlorite in particular has been the focus of attention since it was revealed to have mutagenic activity in *in vitro* tests, notably producing chromosomal aberrations in Chinese hamster cells (Kawachi *et al.*, 1980). Similar tests using human embryo fibroblasts showed aberration in sister chromatid exchange tests. Interaction of halogenated compounds and nucleic acids (Olivieri *et al.*, 1978) and teratogenesis in the developing rat foetus (Abdel-Rahman *et al.*, 1982) have been reported. Short-term and long-term bioassay studies on the carcinogenicity of sodium hypochlorite in F344 rats (Hasegawa *et al.*, 1986) demonstrated an increasing incidence in both benign and malignant neoplasia. Interestingly there was an increased incidence of benign tumours in the rat ear duct system (Zymbal's gland). A definite causal relationship with carcinoma was not established. However, a potential synergistic carcinogenic effect was observed when fibrosarcomas and squamous cell carcinoma developed after topical application of combined 10 per cent sodium hypochlorite with 4-nitroquinolone I-oxide to the skin of the mouse (Hayatsu *et al.*, 1979); neither of these chemicals proved to produce malignancy when applied alone. Hypochlorite agents have been shown to cause overgranulation, local oedema, burn and reduced capillary blood flow (Dakin, 1915). In concentrations of 0.5 per cent and above intense cell toxicity can occur (Martindale, 1996). Respiratory tract irritation by released chlorine is a documented side-effect of their usage. Furthermore, halogenated by-products have been reported as a causal factor in gastrointestinal tract cancer in several animal models (IARC working group, 1979; NIOSH, 1985). Ingestion of concentrated hypochlorite solutions leads to chronic toxicity and the development of active hepatic hyperplastic nodules and hepatocellular carcinoma (Kurokawq *et al.*, 1986).

Boric acid, the other component of Eusol, is a potent skin and mucous membrane irritant (Martindale, 1996) but, despite this, it has been used as the preferred antifungal treatment in certain conditions in the past. Boric acid has no known carcinogenic or mutagenic effect on human or animal tissues. It is known to be a potent respiratory tract irritant.

Both the ingredients of Eusol have toxic effects when ingested (Martindale, 1996) and fatalities have been reported.

We hypothesize that the continuous use of the irritant disinfectant Eusol in the mastoid cavity of this patient may be the aetiological factor in the development of his squamous cell carcinoma. It is possible that the long-term Eusol irrigation caused a mutagenic effect in the basal layers of the epithelium or altered the growth rate of the cells. Research into the efficacy of hospital and wound disinfectants and their safety continues to evolve, but there are no long-term studies of their effects on human tissues. In many hospitals, the use of Eusol has been discontinued because of its chemical instability, short shelf life, time-consuming preparation and its cost. However, in view of their recently revealed role in carcinogenesis, all oxidant chemicals should be used cautiously. Diluted concentrations of these compounds are still in common usage. Current clinical applications include decontamination of environmental spills of potentially infectious material and chlorination of water distribution systems in haemodialysis centres. Hyperchlorination is used in treating colonization with *Legionella* species. The emergence of new groups of compounds and their relative safety, and lower cost has reduced the usage of chlorinated disinfectants.

Conclusion

This report highlights the controversy surrounding the use of chlorinated disinfectants on human tissues. However, it has to be clear that there is no epidemiological data suggestive of a carcinogenic effect of these compounds. Many reports showed that chlorinated disinfectants can be very irritant to the skin and mucous membranes (Dakin, 1915; Brennan and Leaper, 1985), others showed a mutagenic effect on animal tissues (Kawachi *et al.*, 1980) and teratogenesis (Abdel-Rahman *et al.*, 1982). Nevertheless, one has to recall that the above studies have all employed high concentrations of these compounds far beyond the safety limits allowed for human usage, and for relatively short periods of time.

Acknowledgements

Our thanks go to Dr Mark Farrington, Consultant Microbiologist, and Drug Information Pharmacists Ms Emma Chignell and Ms Julia Fletcher, Addenbrookes Hospital, for their help in the preparation of this paper.

References

Abdel-Rahman, M. S., Berardi, M. R., Bull, R. J. (1982) Effect of chlorine and monochloramine in drinking water on the developing rat foetus. *Journal of Applied Toxicology* **2:** 156.

Applebaum, E. L. (1979) Radiation-induced carcinoma of the temporal bone. *Otolaryngology – Head and Neck Surgery* **87(5):** 604–609.

Beal, D. D., Lindsay, J. R., Ward, P. H. (1965) Radiation-induced carcinoma of the mastoid. *Archives of Otolaryngology – Head and Neck Surgery* **81:** 9–16.

Bizgalis, A. R., Keith, A. O., Farrington, W. T. (1992) Radiotherapy in the treatment of middle ear and mastoid carcinoma. *Clinical Otolaryngology and Allied Sciences* **17(2):** 113–116.

Block, S. S. (1991) Historical review. In *Disinfection, Sterilization and Preservation* 4th Edition (Block, S. S., ed.) Lea and Febiger, Philadelphia, USA, p 3–17.

Brennan, S. S., Leaper, D. J. (1985) The effect of antiseptics on the healing wound: a study using the rabbit ear chamber. *British Journal of Surgery* **72:** 780–782.

British National Formulary (1998) Disinfectants and cleansers. British Medical Association and the Royal Pharmaceutical Society, London, In no 34, section 13: 11(4), p 504.

Center for Disease Control (1982) Acquired immune deficiency syndrome (AIDS): precautions for clinical and laboratory staffs. *Morbidity and Mortality Weekly Report* **31:** 577–580.

Coachman, E. H. (1951) Squamous cell carcinoma secondary to cholesteatoma. *Archives of Otolaryngology – Head and Neck Surgery* **54:** 187.

Conley, J. J., Novack, A. J. (1960) The surgical treatment of malignant tumours of the ear and temporal bone. *Archives of Otolaryngology - Head and Neck Surgery* **71:** 635–652.

Cursons, R. T. M., Brown, T. J., Keys, E. A. (1980) Effect of disinfectants on pathogenic free-living amoebae: in axenic conditions. *Applied Environmental Microbiology* **40:** 62–66.

Dakin, H. D. (1915) On the use of certain antiseptic substances in the treatment of infected wounds. *British Medical Journal* **2:** 318–320.

Environmental Protection Agency Genetic Toxicology Programme (1983) Vol. 1, No. 8 and Vol. 3, No. 6 DPIM report.

Hasegawa, R., Takahashi, T., Kokubo, F., Furukawa, K., Toyoda, K., Sato, H., Kurokawa, Y., Hayashi, Y. (1986) Carcinogenicity study of sodium hypochlorite in F344 rats. *Food and Chemicals Toxicology* **24(12):** 1295–1302.

Hayatsu, H., Hoshino, H., Kawazoe, Y. (1979) Potential carcinogenicity of sodium hypochlorite. *Nature* **233:** 495.

International Agency for Research on Cancer Working Group (1979) Some halogenated hydrocarbons. *Monographs on the Evaluation of the Carcincogenic Risk of Chemicals to Humans*. Vol. 20. International Agency for Research on Cancer, Lyon.

Issing, P. R., Kempf, H. G., Schonermark, M., Lenarz, T. (1995) Das Felsenbeinkarzinom-Aktuellediagostche and therapeutische Aspekte. *Laryngo-Rhino-Otologie* **74(11):** 666–672.

Kawachi, T., Komatsu, T., Kada, T., Ishidate, M., Sasaki, M., Sugiyama, T., Tajima, Y. (1980) Results of recent studies on the relevance of various short-term screening tests in Japan. In *The Predictive Value of Short-term Screening Tests in Carcinogenicity Evaluation*. (Williams, G. M., Waaijers, H. W., van de Poll, K. W., eds.) Elsevier, Amsterdam, p 253.

Kurokawq, Y., Takayama, S., Konishi, Y., Hiasa, Y., Asahina, S., Takahashi, M., Maekawa, A., Hayashi, Y. (1986) Long-term *in vivo* carcinogenicity tests of potassium bromate, sodium hypochlorite and sodium chlorite conducted in Japan. *Environmental Health Perspectives* **69:** 221–235.

Lewis, J. S. (1975) Temporal bone resection. Review of 100 cases. *Archives of Otolaryngology – Head and Neck Surgery* **101:** 23–25.

Lorrain-Smith, J., Drennan, A. M., Rettie, T., Campbell, W. (1915) Antiseptic action of hypochlorous acid and its application to wound treatment. *British Medical Journal* **2:** 129–136.

Martindale (1996) *The Extra Pharmacopoeia*. 31st Edition. Royal Pharmaceutical Society Press, London, pp 1145 and 1680.

Michaels, L., Wells, M. (1980) Squamous cell carcinoma of the middle ear. *Clinical Otolaryngology* **5:** 235–248.

Moffat, D. A., Chiossone, J. A., de Cruz, M. Ear canal. In *Tumours of the Ear and Temporal Bone,* (Jackler, R., Driscoll, C. eds.) Lippincott–Raven, (in press).

Moffat, D. A., Grey, P., Ballagh, R. H., Hardy, D. G. (1997) Extended temporal bone resection for squamous carcinoma. *Otolaryngology – Head and Neck Surgery* **116(6 pt 1):** 617–623.

Morgan, D. A. (1989) Chlorinated solutions: (E) useful or (e) useless? *Pharmaceutical Journal* **243:** 219–220.

National Institute for Occupational Safety and Health (1985) *Registry of Toxic Effects of Chemical Substances* (Lewis Sr., R. L., Sweet, D. V., eds.) Vol. 2 Entry No. NH3486300, p. 1044, NIOSH, Cincinnati, OH.

Olivieri, V. P., Dennis, W. H., Snead, M. C., Richfield, D. T., Kruse, C. W. (1978) Reaction of chlorine and chloramines with nucleic acids under disinfection conditions in water chlorination. *Environmental Impact and Health Effects*. Vol. 3. Ann Arbor, MI.

Resnick, L., Venen, K., Salahuddin, S. Z., Tondreau, S., Markham, P. D. (1986) Stability and inactivation of HTLV-III/LAV under clinical and laboratory environment. *Journal of The American Medical Association* **255:** 1887–1891.

Ruben, R. J., Thaler, S. B., Holzer, N. (1997) Raidation-induced carcinoma of the temporal bone. *Laryngoscope* **87:** 1613–1621.

Rutala, W. A., Weber, D. J. (1997) Uses of inorganic hypochlorite (bleach) in health-care facilities. *Clinical Microbiology Reviews* **10(4):** 597–610.

Sax, N. I., Lewis, R. J. (1989) *Sax's Dangerous Properties of Industrial Materials*. (7th ed. Vol. 3) Van Nostrand Reinnold Company, New York, NY pp. 1971–2 and 3072.

Shaheen, O. H. (1997) Epithelial tumours of the external auditory meatus and the middle ear. In *Scott Brown's Otolaryngology*, Vol. 3. (Kerr, A. G., ed.) Butterworth-Heinemann, Bath, p. 1.

Sykes, G. (1970) The sporicidal properties of chemical disinfectants. *Journal of Applied Bacteriology* **33:** 147–156.

Whitmore, T. N., Denny, S. (1992) The effect of disinfectants on a geosmin-producing strain of *Streptomyces griesus*. *Journal of Applied Bacteriology* **72:** 160–165.

Address for correspondence:
Mr S. A. Monem,
Department of Neuro-otology/Skull Base Surgery,
Addenbrookes Hospital (Box 48),
Hills Road,
Cambridge CB2 2QQ.

Fax: +44 (0)1223 217559