Rhinology, 23, 118-120, 1985

Nasal mucosa changes after exposure to dicumylperoxide

Björn Petruson and Hans-Arne Hansson, Göteborg, Sweden

Dicumylperoxide is an organic peroxide which is used as a very strong oxidative agent in the production of polyethylene plastics. During oxidation free radicals are released. When skin or mucosal membranes were exposed to different peroxides severe inflammatory reactions have been observed (Oloffs, 1966). In some studies on occupational exposure to different irritants it has been noted that nosebleeds occur frequently. Among woolspinners 18% had occasional nosebleeds (Hussarek, 1968). Dust from gentian violet in applepacking paper caused nasal bleeding within a week in almost everyone exposed (Quinly, 1968).

Workers at a Swedish chemical plant complained of nosebleeds when handling dicumylperoxide (Petruson and Järvholm, 1982). When they were examined it was found that half of them had visible blood vessels in the mucosa on the anterior part of the nasal septum. During and after exposure to dicumylperoxide 11 out of 24 workers complained of having blood threads in their nasal secretion, only occasionally large nasal bleedings were observed. In order to make sure that the formation of blood vessels was initiated by the exposure to the peroxide 11 workers were examined before employment. In 6 of them visible vessels were observed after an exposure time of 1 to 16 weeks.
In an experimental study on animals rabbits were exposed to dicumylperoxide for up to one month. After one week an increased number of visible blood vessels were observed both on the lateral and medial wall of the nose. After one month still more vessels were visible. When the mucosa was examined with electronmicroscopy blood vessels with thick, non-fenestrated endothelium were observed (Hansson and Petruson, to be published).

During the last decade an increasing interest has been given to free radicals as mediators of tissue damage. Dicumylperoxide releases upon oxidation free radicals to the tissue, it is also possible that it can activate inflammatory cells. It is known that activated leucocytes release free radicals (Maestro et al., 1980). Pol-

Paper presented at the 10th Congress of the European Rhinologic Society and 4th ISIAN, Nancy (France), August 1984.

verini et al. (1980) noted that activated macrophages induced vascular proliferation when injected into the corneal stroma.

When endothelium is exposed to free radicals it has been observed that characteristic endothelial craters occur and that the endothelial cells are loosened and thickened (Demopoulos et al., 1980) and the permeability of the vessels is increased (Maestro et al., 1980).

It is probable that the formation of new blood vessels in the nose of the workers and the rabbits may start due to injuries of the endothelium caused by dicumylperoxide. However, another alternative is that the induced inflammatory reaction is of importance and that peroxides formed by activated leucocytes could initiate the neoangiogenesis. It is likely that the increased transvascular leakage observed in the workers as blood threads is due to the exposure to dicumylperoxide. Leakage from postcapillary venules has been shown in the hamster cheek pouch exposed to free radicals (Maestro et al., 1980).

Airborne pollutants can cause hypertrophy of the nasal mucosa. It is known that dust from coal and sand can cause chronic rhinitis (Manz, 1977). In 45% of the workers exposed to dicumylperoxide were noted signs of irritation and hypertrophy of the nasal mucosa. When rabbits were exposed to dicumylperoxide an increased amount of mucus was observed within one hour. Erythrocytes were also seen in the mucous membrane. After a week still more mucus was found. After one hour many cilia became club-shaped. After one month exposure many of the ciliated cells were distorted and irregular in contour, only a few disshaped cilia were found. Goblet cells normally not seen were observed after five days and increased frequency of adenocarcinoma. That this type of carcinoma developes caused by either the dicumylperoxide *per se* or possibly by substances released from the inflammatory cells resulting from the irritation.

Many irritating substances may induce an increase in the number of goblet cells in the airways (Jones et al., 1978). In patients with many infections in the nose (Karlsson et al., 1984) or after occupational exposure to wood dust (Wilhelmsson and Lundh, 1984) these changes in the nasal epithelium has been observed. It is likely that the increased frequency of goblet cells is related to stimulation of T-lymphocytes (Karlsson et al., 1984). The increased amount of debris, reflecting excessive mucus formation can be regarded as a non-specific protective adaption of the nasal mucosa to the irritation caused by dicumylperoxide or other irritants. After long time exposure to irritants like wood dust there has been observed an increased frequency of adenocarcinoma. That this type of carcinoma developes and not squamous cell carcinoma hypothetically may depend on the increased number of goblet cells observed after exposure to this kind of irritants.

REFERENCES

1. Demoupoulos HB, Flamm ES,Pietronigro DD, Seligman ML. The free radical pathology and the microcirculation in the major central nervous system disorders. Acta Physiol Scand 1980; Suppl. 492:91–119.
2. Hansson HA, Petruson B. Nasal mucosa changes after acute and long-term exposure to dicumylperoxide – An experimental study on animals. Acta Otolaryng (Stockh). Accepted for publication.
3. Hussarek M. Berufskrankheiten der Nase bei Arbeitern in Schafwollspinnereien. Mschr Ohrenheilk Lar-Rhinol 1968; 102:19.
4. Jones RM, Phil M, Reid L. Secretory cell hyperplasia and modification of intracellular glycoprotein in rat airways induced by short periods of exposure to tobacco smoke and the effect of phenyl-metyl-oxadiazole 1978; Lab Invest 1978; 39:41.
5. Karlsson G, Hansson H-A, Hansson G, Petruson B, Björkander J, Hansson L-A. Goblet cells in the nasal mucosa. Variations related to cell mediated immunity in selective IgA deficiency and hypogammaglobulinemia. Int Arch Allergy Appl Immunol. Accepted for publication.
6. Maestro del RF, Thaw HH, Björk J, Planker M, Arfors K-E. Free radicals as mediators of tissue injury. Acta Physical Scand 1980; Suppl 492:43–57.
7. Manz A. Gewerbliche Schäden der oberen Atemwege. In: Hals-Nasen-Ohrenheilkunde in Praxis und Klinik. Berendes J von, Link R, Zöllner F. eds. Stuttgart, Georg Thieme Verlag, 1977.
8. Oloffs J. Gesundheitsschäden durch die zur Kunststoffhärtung verwendeten organischen Peroxide. Zentbl ArbMed 1966; 16:25–8.
9. Petruson B, Järvholm B. Formation of new blood vessels in the nose after exposure to dicumylperoxide at a chemical plant. Acta Otolaryngol (Stockh) 1983; 95:333–9.
10. Polverini PJ, Cotran RS, Gimbrone MA Jr, Unanue ER. Activated macrophages induce vascular proliferation. Nature 1977; 269:804–6.
11. Quinby GE. Gentian violet as a cause of epidemic occupational nosebleeds. Arch Environ Health 1968; 16:485.
12. Wilhelmsson B, Lundh B. Nasal epithelium in wood-workers in the furniture industry. A histological and cytological study. Acta Otolaryngol (Stockh) 1984; 98:321–34.

B. Petruson, M.D.
ENT-Department
Sahlgrens Hospital
S-413 4 Göteborg
Sweden