

Occupational nasal cancer caused by nickel and nickel compounds

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In 1761 John Hill claimed that tobacco used as snuff caused nasal cancer. This is probably the first paper that suggests a causal association between chemical irritants and nasal cancer, and published 14 years before Sir Percival Pott described carcinoma of scrotum in chimney sweepers induced by tar.

During the last decades progressively more chemical compounds applied in the industry have been associated with the development of nasal cancer in man. Thus, increased incidence of nasal and paranasal cancer have been reported in a number of industrial processes, such as: Nickel refining, chromate production, shoe manufacturing and furniture making, as well as exposure to certain chemicals (such as bischloromethyl ether, hexamethylphosphoramide, isopropyl oils, and mustard gas) (Acheson et al., 1968; 1970; Hadfield, 1970; Eckhardt, 1973; Sunderman et al., 1975; IARCH, 1975; NIOSH, 1977; Roush, 1979; Barton, 1980). Among these various chemicals Nickel and Nickel compounds take up a central position.

Nickel, on the one side being documented as an essential element to animals nutrition (Schnegg et al., 1975; 1976;), on the other hand represents a hazard to the same animal species by inducing malignant growths (Sunderman et al., 1975; 1977).

Figure 1 demonstrates the incidence rate for nasal cancer in various regions of Norway and indicates that this type of tumour is rare. It also distributes evenly

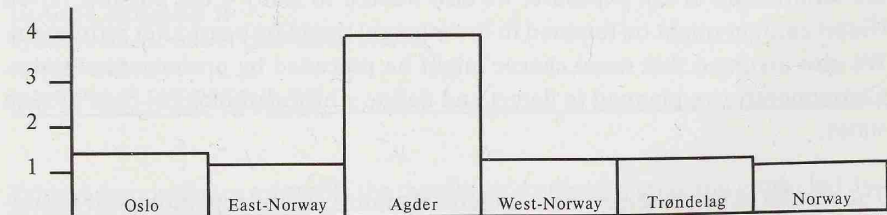


Figure 1. The incidence rate for nasal cancer in various regions of Norway (Cancer Registry of Norway, 1975).

over the country, with only one exception: In Vest-Agder County the incidence rate is some three times higher than in any region of Norway (Cancer Registry of Norway, 1975). This significant increase is mainly due to the high incidence of nickel-related nasal cancers demonstrated at a local Nickel plant in Kristiansand, the capital city of Vest-Agder County (Pedersen et al., 1973; Table 1). Pedersen and co-workers (1973) analyzed the incidence rate of respiratory tract cancers in 1916 men with at least three years employment at the plant before 1961 in the period between 1953 and 1971. They traced 14 men with nasal cancer. The ratio Observed (O) to Expected (E) number of cancers, O/E, was 28.0. The risk factor was even higher among process workers (Table 1).

Table 1. Nasal cancer at a Norwegian Nickel plant (Pedersen et al., 1973).

nickel work at the refinery (1953-1971)	no. of men	no. with nasal cancer		
		observed (O)	expected (E)	O/E
process work	1071	11	0.3	36.7
non-process work	845	3	0.2	15.0
all work	1916	14	0.5	28.0

Based on these epidemiological observations our main concern during the last decade has been to study the development of nasal cancer in workers at this local Nickel plant along different lines, applying epidemiological, histopathological, chemical, histochemical and clinical methods (Torjussen et al., 1978; 1979a; 1979b; 1979c; 1979d; Boysen et al., 1980).

We suspected a local carcinogenic effect of inhaled Nickel on the nasal mucosa. Accordingly, it seemed relevant to study the uptake and content of Nickel in the mucosal tissue.

Furthermore, as the nickel-related cancers frequently appear several years after the termination of the exposure, we also wanted to study if the possible raised Nickel content might be retained in the mucosal tissue for years after retirement. We also assumed that nasal cancer might be preceded by precancerous states. Consequently, we planned to detect and define a histopathological base of such states.

The results to be presented here include chemical and histopathological examination of biopsy specimens taken from the anterior tip of the middle turbinate in 318 randomized active nickel workers (i.e. 30 per cent of the entire staff), 57 age-matched non-exposed controls, and 15 retired nickel workers.

The tissue samples were analyzed for Nickel content by atomic absorption spectrometry in accordance with a method described by Torjussen et al. (1978). Table

Table 2. (Torjussen et al., 1979c).

category of subjects	no. of men	mean nickel concentration in nasal mucosa ($\mu\text{g}/100 \text{ g}$) wet weight \pm S.E.
nickel workers	318	273.9 + 23.1
retired nickel workers	15	114.4 \pm 46.0
controls	57	12.9 \pm 2.7

2 demonstrates the results of the Nickel analyses. Significantly raised Nickel was present in both active and retired nickel workers, as compared with the controls. The raised tissue Nickel in retired workers also confirmed the assumption that accumulated Nickel during active work has been stored in the mucous membrane for years after termination of Nickel inhalation. We estimated the half-life for the release of Nickel from the tissue to about 3 $\frac{1}{2}$ years (Torjussen et al., 1979c). Specimens were also prepared for detailed histopathological studies, applying both light-microscopic and electron-microscopic techniques (Torjussen et al., 1979b; Boysen et al., 1980). The various characteristics of the surface epithelium were given scores from 0 to 7 according to Table 3. All samples were examined simultaneously by two investigators without access to any informations on the specimens. The point scores were later used for statistical purposes in a stepwise, multivariate analysis, attempting to explain the histological scores by means of relevant variables (Torjussen et al., 1979 a + b). As we can see from the table, the most diverging changes from normal pseudostratified columnar epithelium were given the highest point scores.

Table 3. (Torjussen et al., 1979b).

histological characteristics of nasal epithelium	histologic score
pseudostratified columnar	0
stratified cuboidal	1
mixed cuboidal/squamous	2
stratified squamous I	3
stratified squamous II	4
hyperchromatic nuclei (additional score)	(1)
epithelial dysplasia	6
carcinoma or carcinoma <i>in situ</i>	7

Table 4 demonstrates primarily the distribution of carcinomas and epithelial dysplasias in the material. The prevalence of 0.6 per cent nasal carcinoma (i.e. 2 men among 318 investigated) was surprisingly high. Both men had been employed as process workers at the Nickel plant for 28 years, but had no symptoms when they met for the first examination. One of them had a squamous cell carcinoma and the second one an anaplastic carcinoma.