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Malignant Mesothelioma in the Rotterdam Area, 1987–1989

Ronald A.M. Damhuis and Teun van Gelder

Malignant mesothelioma is commonly regarded as a rare disease. This, however, does not apply to the Rotterdam area. Registry data show an age-standardised incidence rate (per 100 000 per year, world standard population) of pleural cancer in men of 6.2 for the period 1987–1989. This is substantially higher than thus far reported by other cancer registries. Similar observations may be expected in other areas with shipbuilding or asbestos industries.
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INTRODUCTION

THE RELATION between asbestos exposure and the occurrence of malignant mesothelioma is well-known. After the original publication by Wagner *et al.* in 1960 [1], numerous researchers have confirmed the carcinogenic potential of this 'magic mineral'. As a consequence many governments have issued regulations to prevent or diminish exposure to asbestos. In contrast with the U.K., where the Asbestos Regulations date from 1969, legal measures were not taken in The Netherlands until 1977. The use of crocidolite (blue asbestos) was forbidden while the use of chrysotile (white asbestos) was restricted. However, taking into consideration the long latency period between exposure and diagnosis, effects of these measures may not be expected before the end of this century.

Studies reporting an increase of the incidence of mesothelioma initially came from countries with asbestos mines, like Australia and South Africa [2]. Later reports mentioned a high risk for specific occupational groups using asbestos products, such as insulators, pipe fitters and shipyard workers.

For The Netherlands an increase of the mortality of pleural cancer has been reported by Meijers *et al.* [3]. As a consequence of the increased use of asbestos after World War II, mortality appeared to have tripled. Most cases were found in coastal areas with shipbuilding and other heavy industries. This report deals with the incidence of pleural cancer and malignant mesothelioma in one of those areas.

PATIENTS AND METHODS

In this report we present data from the Rotterdam Cancer Registry for the period 1987–1989. The current registry started in 1982 and covers the southwestern part of The Netherlands, an area known for its industrial activities and shipping industry. Data on newly diagnosed cancer patients are collected from hospital and pathology records by specially trained registrars. From 1987 registration is complete in the central part of the region with about 1.5 million inhabitants. For this part of the region, age-standardised incidence rates (to the world standard population) were calculated using population data provided by the Central Bureau of Statistics.

RESULTS

The incidence rates of pleural cancer are shown in Table 1. To represent the impact of possible misclassification of other primary cancers the number of histologically or cytologically verified cases of mesothelioma is also given. For men the incidence rates correspond to a cumulative rate over 0–74 years, being an approximation of the life-time risk, of 0.7%. Apart from pleural mesothelioma 19 cases of peritoneal mesothelioma were registered, 17 in men, 2 in women.

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Table 1. Incidence of pleural cancer, Rotterdam area 1987–1989

Men	1987	1988	1989	(*n*)*
Incidence of pleural cancer†	6.1	6.1	6.5	(189)
Histological or cytological verification (%)	90%	87%	86%	(166)
Pathology-based diagnosis of mesothelioma (%)	83%	81%	80%	(153)

Women	1987–1989	(*n*)*
Incidence of pleural cancer†	0.3	(13)

* Number of cases 1987–1989. † Age-standardised to the world standard population.

DISCUSSION

The incidence of pleural cancer in the Rotterdam area is considerably higher than thus far reported by other cancer registries [4]. For the period 1978–1982 the highest rates were those from Western Australia (2.8) and Sweden (2.3). This comparison, however, may not be appropriate due to variation in time periods. Considering the fact that diagnosis of mesothelioma was pathology-based in more than 80% of all patients, misclassification of other primary cancers cannot account for the high incidence.

The high male to female ratio points to an occupational risk factor, in this case presumably crocidolite. Closer study revealed that the incidence of mesothelioma was focused in cities with shipbuilding industry, where crocidolite had been used for insulation purposes. Detailed information on occupational background of the patients is, however, lacking, implying that an effect of chrysotile, the principal type of asbestos used in The Netherlands, cannot be excluded. In view of the fact that the role of chrysotile and other factors is still subject to debate [5, 6], further epidemiological studies regarding the aetiology of mesothelioma should be considered.

Malignant mesothelioma has become an important health problem in the Rotterdam area. At the moment it constitutes almost 1% of overall mortality in men. It is unlikely that the incidence will decrease before the end of this century. Similar clusters of mesothelioma may become apparent in other regions with major shipbuilding or asbestos industries.

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24-Hour Plasma Etoposide Profile After Oral and Intravenous Administration in Children

C.R. Pinkerton, G. Dick and G.W. Aherne

Pharmacokinetic profiles of oral and intravenous etoposide have been compared in 9 children receiving the drug either as a single agent or in combination chemotherapy. The plasma etoposide levels were estimated using a competitive coated antigen ELISA technique. The median bioavailability was 48% and beyond 30 min after either oral or intravenous injection there was little difference in the plasma profile. The duration of plasma concentrations above 1, 5 and 10 μg/ml following either route were compared. It is concluded that unless the height of initial peak concentration is of therapeutic value the oral route should be comparable in children provided that twice the intravenous dose is administered. The short elimination half-life results in low plasma levels beyond 12 h and suggests that a twice daily regimen may be preferable.
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INTRODUCTION

Over the past decade etoposide has found an established role in the management of several childhood cancers. Despite the inconvenience of parenteral administration in almost all paediatric schedules the intravenous (i.v.) route is used. Capsules are difficult for smaller children to tolerate and only recently has the use of oral administration of the i.v. ampoule mixed with a suitable masking agent been adopted. One of the first treatment regimens to use the oral route was the VEEP regimen for Hodgkin's disease, developed by McElwain *et al.* In this regimen 4–5 days of oral etoposide (100 mg/m²/daily) is given. A pilot study showed this method to be feasible in the majority of children [1].

There has recently been particular interest in the oral schedule