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A SURVEY OF THE LONG-TERM EFFECTS OF TALC AND KAOLIN PLEURODESIS

RESEARCH COMMITTEE OF THE BRITISH THORACIC ASSOCIATION AND THE MEDICAL RESEARCH COUNCIL PNEUMOCONIOSIS UNIT*

Summary

Of 210 patients who underwent pleurodesis with iodized talc or kaolin 14 to 40 years previously, all but 11 were traced. There was no increased incidence of lung cancer and no case of mesothelioma.

INTRODUCTION

Exposure to high concentrations of talc dust in mining and processing in the USA has been shown to cause pulmonary fibrosis and a four-fold increase in the incidence of malignant tumours of the lung and pleura (Kleinfeld et al. 1967). However, this dust contained other silicates including tremolite and anthophyllite and the incidence of these malignant tumours fell and approached the expected mortality when dust levels were reduced (Kleinfeld et al. 1974). In a controlled study of Italian talc miners and millers exposed to a very pure type of talc Rubino et al. (1976) were able to show a lower than expected incidence of lung cancer, although the mortality rate amongst the miners exceeded the norm because of the high incidence of pneumoconiosis (silicosis) with or without tuberculosis. In Great Britain Henderson et al. (1971) described talc particles in association with carcinoma of the ovary and cervix, confirmed later by analytical electron microscopy (Henderson & Griffiths 1975). Jackson and Bennett (1973) reported a chest wall tumour of adenocarcinomatous type developing within three years of iodized talc pleurodesis for recurrent spontaneous pneumothorax but it is unlikely that the talc played any causative role in the development of this tumour. Animal studies using inhalation and intrapleural injection of an Italian cosmetic talc have failed to demonstrate a carcinogenic effect (Wagner et al. 1977).

Talc, which is mainly a hydrated magnesium silicate, is marketed in different grades, the higher grade being used for cosmetic and pharmaceutical purposes and the others in industry (Hildick-Smith 1976). Cosmetic talc consists of flake-like particles and is largely free of the long thin fibres of asbestos-like minerals (such as tremolite, actinolite and anthophyllite) which are closely related to it in the natural state. These contaminate some industrial talcs, however, and are possibly responsible for the fibrogenic and carcinogenic effects already referred to. In Britain talc has been used by intrapleural poudrage since 1935 to induce pleurodesis, usually for treatment of recurrent spontaneous pneumothorax. A follow-up of such patients should reveal any possible carcinogenic effects of talc and a subcommittee was set up by the British Thoracic Association and Medical Research Council Pneumoconiosis Unit to organize a survey.

* Members of the subcommittee were A. G. Chappell (chairman), A. Johnson (coordinator), J. Charles, J. C. Wagner, R. M. E. Seal, G. Berry and D. Nicholson.

Methods

In order to obtain a large number of index cases 11 thoracic centres were approached but only three were able to participate: Sully, Brompton and Harefield Hospitals. At each centre medical record indexes and surgical registers were reviewed and the notes scrutinized to identify patients who had received pleurodesis with talc or a like mineral such as kaolin (china clay, hydrated aluminium silicate) before January 1961 so that a minimum observation period of 14 years was possible. Tracing the patients proved a difficult and lengthy task. Methods used included direct written approaches to patients and general practitioners, family practitioner committees, the Office of Population Censuses and Surveys (OPCS) and foreign embassies. A large number of patients would have remained untraced without further assistance from two 'field' workers with experience of epidemiological studies who cross-checked information for accuracy and made visits to discover the present state of index cases not traced by letter.

The results were assessed by comparing the number of observed deaths with the number expected by the subject-years method (Case & Lea 1955) multiplying years of risk by death rates. The death rates for England and Wales were taken from tables compiled for studies of this kind (Institute of Cancer Research 1976). These tables give age-specific death rates with age in five-year groups and also calendar year in five-year groups up to 1966–70. The study extends beyond 1970 and the rates for 1966–70 were used for the later years. Deaths from all causes and also from cancer of the lung and pleura have been considered. Excess mortality has been tested by treating the observed number as a Poisson variable with expectation equal to the expected number.

Results

Two hundred and ten cases were collected from the three centres (Table I). The Sully patients, many of whom had chronic lung disease such as chronic bronchitis, emphysema and pneumoconiosis, received intrapleural kaolin as treatment for spontaneous pneumothorax between 1956 and 1960. All the Brompton and Harefield patients received intrapleural talc over half having been treated before 1945. In 22 Brompton and 70 Harefield patients iodized talc was used to produce pleurodesis in patients with bronchiectasis and other non-malignant disorders before lung resections.

Table I. Outcome of the study

Hospital	*No. of patients (males)*	*Contacted, alive and well*	*Untraced but believed alive*	*Emigrated and untraced*	*Dead (lung cancer in parentheses)*
Sully	63 (50)	45	—	—	18
Brompton	43 (24)	26	—	3	14 (1)
Harefield	104 (54)	81	2	6	15 (2)
	210 (128)	152	2	9	47 (3)

One hundred and fifty-two patients have been contacted and are well whilst a further two are thought to be alive (OPCS) but have not been traced (Table I). Follow-up data are available on nine emigrants for periods ranging from 14 months to 24 years but attempts to locate them have failed.

There were 47 deaths including three from lung cancer (Table II). Two patients with lung cancer had a tumour on the side opposite to the pleurodesis with intervals of 18 months and 19 years between pleurodesis and death. The third case was a 61-year-old

Table II. Observed and expected mortality

Hospital	*Sex*	*All causes**		*Lung cancer†*	
		Obs.	Exp.	Obs.	Exp.
Sully	Men	18	9.1	0	0.84
	Women	0	0.8	0	0.03
Brompton	Men	9	3.4	1	0.36
	Women	5	4.0	0	0.06
Harefield	Men	11	7.1	2	0.72
	Women	4	4.6	0	0.13
Total		47	29	3	2.14

* $P<0.01$.
† $P>0.3$.

man with an oat cell carcinoma who died 32 years after pleurodesis. The site of the carcinoma is not known and at autopsy no tumour was found, but he had received radiotherapy. Although lung cancer deaths were no greater than expected, there was a significant excess of observed over expected mortality for all causes (the two untraced patients were assumed to be alive for the purposes of this calculation).

Table III shows that although follow-up was longer than 15 years in the majority of patients, 36 deaths occurred within 15 years of pleurodesis. The observed deaths in these three quinquennia were significantly more than expected. The probable explanation is the already high incidence of respiratory disease in these patients at the time of pleurodesis for 21 of the deaths were due to respiratory causes.

Table III. Duration of follow-up after pleurodesis

Duration of follow-up (years)	*Deaths*	*Others*
0–4	16	4*
5–9	9	2*
10–14	11	5†
15–19	6	70
20–24	2	7
25–29	0	3
30–34	2	45
35–39	1	27
Total	47	163

* Emigrated.
† Includes one emigrant.

Discussion

This study was devised in 1974 because of the suggestion that talc might be carcinogenic. Later reports quoted in the introduction have not supported this view and asbestos-like contaminants were possibly responsible for the early reports of an increased incidence of carcinoma. Strict standards for the manufacture of cosmetic talc have been adopted only in recent years (Editorial, 1977). We have been able to ascertain that talc B.P.

was used at Brompton and Harefield Hospitals even before 1945. Indian Finex has been used extensively for this preparation in the past and is unlikely to have contained any fibrous amphiboles but we have no idea of the composition of other B.P. talcs over the past 40 years (Pooley 1978). It was decided to include patients treated with kaolin because of its chemical similarity to talc and its propensity for producing pulmonary fibrosis after prolonged and heavy exposure, even though no carcinogenic effect has been ascribed to the mineral. All the Sully patients received kaolin rather than talc for their pleurodesis, but even if they are excluded from the analysis of lung cancer deaths (Table II) the ratio of the observed to expected incidence is still not significant ($P=0.14$).

Tracing of patients proved very difficult, particularly those from Brompton and Harefield cases, over half of whom were treated prior to 1945. No attempt was made to examine or X-ray the patients, who were scattered throughout the country. It was felt that this would prolong the study and prove unrewarding as very few asymptomatic cases of mesothelioma would have been expected, for Elmes and Simpson (1976) in their study of 327 cases found a mean interval between onset of symptoms and arrival at hospital of only 3.4 months.

We have therefore found no increased incidence of lung cancer and no case of mesothelioma in the series of 210 patients, 88 of whom have been followed for between 15 and 30 years and 75 for 30–40 years after pleurodesis.

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References

Case, R. A. M. & Lea, A. J. (1955) Mustard gas poisoning, chronic bronchitis, and lung cancer. *Br. J. prev. soc. Med. 9*, 62.

Editorial (1977) Cosmetic talc powder. *Lancet 1*, 1348.

Elmes, P. C. & Simpson, M. J. C. (1976) The clinical aspects of mesothelioma. *Q. Jl Med. 45*, 427.

Henderson, W. J. & Griffiths, K. (1975) Identifications of particles in ovarian tissue. In *Gynaecological Malignancy: Clinical and Experimental Studies*, ed. M. G. Brush and R. W. Taylor, pp. 225–40. London: Baillière Tindall.

Henderson, W. J., Joslin, C. A., Turnbull, A. C. & Griffiths, K. J. (1971) Talc and carcinoma of the ovary, and cervix. *J. obstet. gynaec. Br. Commonw. 78*, 266.

Hildick-Smith, G. Y. (1976) The biology of talc. *Br. J. indust. Med. 33*, 217.

Institute of Cancer Research (1976) *Serial Mortality Tables—Neoplastic Diseases, Vol. 1. Deaths and Death Rates by Sex, Age, Site and Calendar Period.* London.

Jackson, J. W. & Bennett, M. H. (1973) Chest wall tumour following iodised talc pleurodesis. *Thorax 28*, 788.

Kleinfeld, M., Messite, J., Kooynar, O. & Zaki, M. H. (1967) Mortality among talc miners and millers in New York State. *Archs envir. Hlth 14*, 663.

Kleinfeld, M., Messite, J. & Zaki, M. H. (1974) Mortality experiences among talc workers: a follow-up study. *J. occup. Med. 16*, 345.

Pooley, F. D. (1978) Personal communication.

Rubino, G. F., Scansetti, G., Piolatto, G. & Romano, C. A. (1976) Mortality study of talc miners and millers. *J. occup. Med. 18*, 186.

Wagner, J. C., Berry, G., Cooke, T. J., Hill, R. J., Pooley, F. D. & Skidmore, J. W. (1977) Animal experiments with talc. In *Inhaled Particles IV*, ed. W. H. Walton, pp. 647–54. Oxford and New York: Pergamon.