Gallium-67 Thoracic Scan and Pleural Disease in Asbestos Workers

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We have recently reported that ^{67}Ga scanning in asbestos workers can document excessive uptake of the marker among workers without sufficient criteria for asbestosis, but in our initial report we could not exclude definitely that ^{67}Ga uptake could be related to pleural disease. To further test this hypothesis, we analyzed the ^{67}Ga thoracic scan in relation to profusion scores of pleural disease on chest roentgenogram and CT scan of the thorax in 171 asbestos workers. We found no significant correlation between the ^{67}Ga lung uptake and the radiographic scores of pleural disease. We concluded that pleural plaques are not an active site of ^{67}Ga accumulation and do not contribute significantly to the thoracic uptake of the marker.

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The pulmonary uptake of gallium-67 (^{67}Ga) in the interstitial lung diseases is considered an index of inflammatory activity, which can be quantitated (*1–3*) and which correlates with histopathological and bronchoalveolar lavage cellularity (*4–8*).

In the evaluation of disease activity in long-term asbestos workers, we have previously demonstrated that the ^{67}Ga lung scan may provide a sensitive indicator of the alveolitis of asbestosis (*9*). In that earlier study, several long-term workers did not meet the criteria for asbestosis (*10*), but had significant increase in ^{67}Ga lung uptake and 85% of them also had increased rigidity of the lung pressure-volume curve. These changes in lung scan and pulmonary function were associated with evidence of macrophagic alveolitis as demonstrated by lung biopsy and bronchoalveolar lavage (BAL) on several of the workers (*9,11*). Similarly, in our sheep model of the disease, we have documented that the initial asbestos-induced alveolitis is associated with enhanced ^{67}Ga lung uptake and decreased lung compliance (*9,12–14*). In these studies, the possibility that increased ^{67}Ga thoracic uptake could be related to pleural disease was not completely ruled out.

To further study the relationship of pleuropulmonary disease and ^{67}Ga thoracic scan, we analyzed thoracic ^{67}Ga scan in relation to radiographic parameters of pleural disease in 171 newly enrolled asbestos workers, 69 of whom also had computed tomogram of the thorax [computed tomographic (CT) scan].

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MATERIALS AND METHODS

Asbestos workers

The 171 newly evaluated asbestos workers in this study were of average age 59 ± 3 yr (s.e.m.) (range 40–72) and had been exposed to Canadian chrysotile asbestos only in the mines and mills of the Eastern Townships of Quebec for an average 29 ± 3 yr (range 7–42) and had no history of other previous pulmonary disease.

Clinical evaluation

All patients had a history and complete physical examination with emphasis on the detection of abnormalities suggestive of pneumoconiosis. Asbestos exposure index was obtained as previously reported (*9*).

Chest roentgenogram and CT scan

Standard high kilovoltage postero-anterior, lateral, oblique, and CT scan films were obtained at maximal inspiration. The lung parenchyma was graded for profusion of small opacities as previously reported (*15,16*). Pleural changes were graded in terms of site, width, and extent of pleural thickening according to the International Labor Organization classification. For each of the

six sites of pleural thickening (chest walls, diaphragms, and costophrenic angles), the width category a, b, or c was converted numerically to 1, 2, or 3 and multiplied by the extent score 1, 2, or 3. Pleural calcifications were also recorded in terms of site and added to the pleural thickening score for each film.

Pulmonary function tests

The pulmonary function tests were measured according to standard methods (*17*) as previously applied in our laboratory (*9,18,19*).

Gallium-67 lung uptake

Fifty microcuries per kilogram body weight of [^{67}Ga] citrate* were injected i.v. into each patient. Forty-eight hours later, anterior and posterior scans from neck to pelvis were recorded.† Software for acquisition and processing of the data was developed in our institution. Grading of the ^{67}Ga pulmonary uptake was done as recently reported (*3,9*).

Diagnosis of asbestosis

The diagnosis of asbestosis was established on the basis of criteria recommended by the Canadian Task Force on occupational respiratory disease (*10*) as previously reported by us (*9,11,16*). Gallium-67 lung scans were not used in the clinical diagnostic decision.

Statistical analysis

All results are expressed as mean ± s.e.m. The data were tested for differences between groups by the Student t-test or the Mann-Whitney U-test when appropriate. The Spearman's correlation procedure was used to correlate ^{67}Ga thoracic scan scores with pleural plaque scores (*20,21*).

RESULTS

Asbestos workers

Four groups were formed.

Group A was composed of 47 workers who did not meet the diagnostic criteria for asbestosis and had normal lung pressure-volume curve and normal ^{67}Ga lung uptake (*9,11*).

Group B consisted of 31 workers who did not meet the diagnostic criteria for asbestosis but had increased ^{67}Ga lung uptake and/or a rigid lung pressure-volume curve (27/31 had both), six of these had lung biopsy proven alveolitis.

Group C was composed of 70 workers with asbestosis and increased ^{67}Ga lung uptake.

Group D consisted of 23 workers with asbestosis and normal ^{67}Ga lung uptake.

The clinical and radiographic data of these four groups of asbestos workers are presented in Fig. 1. Briefly, the four groups did not differ significantly in terms of age, cigarette smoking habits, and asbestos exposure. Groups C and D, workers with asbestosis, had more parenchymal and pleural changes ($p < 0.01$).

In the workers without asbestosis (Groups A and B), there were no significant differences between pleural disease scores on chest roentgenogram and individual scores of radiographic pleural disease did not correlate with ^{67}Ga lung uptake index. In the workers with asbestosis (Groups C and D), radiographic scores of pleural disease were significantly higher than in the workers without asbestosis ($p < 0.01$). In these workers with asbestosis, radiographic scores of pleural disease did not differ between the Groups C and D and individual scores of radiographic pleural disease did not correlate with ^{67}Ga lung uptake index.

Among all asbestos workers, we found only eight patients with increased uptake in the periphery of the thoracic scan. They composed subset 1 of Table 1 and were matched for age with a subset of workers in the same Group C among the workers without enhanced peripheral uptake (subset 2 of Table 1). The two subsets were comparable in terms of cigarette smoking index, asbestos exposure index, ^{67}Ga lung uptake score, radiographic parenchymal opacity, or pleural plaque scores.

DISCUSSION

Gallium-67 thoracic scanning has been increasingly used in recent years as an index of inflammatory activity in the lung (*1–4*) and we have recently documented that enhanced uptake of the marker which occurs in the thoracic area may precede clinical or radiographic evidence of interstitial lung disease (*9,11*). Pleural plaques often occur in the absence of interstitial lung disease and often precede the development of asbestosis in asbestos workers. It is, therefore, quite legitimate to consider the possibility of a relationship between enhanced thoracic uptake of ^{67}Ga and pleural plaques. To evaluate this possible relationship, we have scored independently the ^{67}Ga thoracic scans and the pleuropulmonary changes on chest radiograph in 171 long-term asbestos workers and on CT scan in 69. We did not find significant correlation between ^{67}Ga thoracic uptake and radiographic scores of pleural changes.

Furthermore, we observed in eight workers an accentuated uptake of the marker in the periphery of the scan. When compared to a matched group of workers with asbestosis without enhanced peripheral ^{67}Ga thoracic uptake, we found no significant correlation of this peripheral uptake with radiographic pleural scores.

The mechanisms implicated in the excessive accumulation of ^{67}Ga in thoracic diseases have been elucidated only recently and well reviewed in this journal (*22*). In asbestos workers and in the sheep model of as-

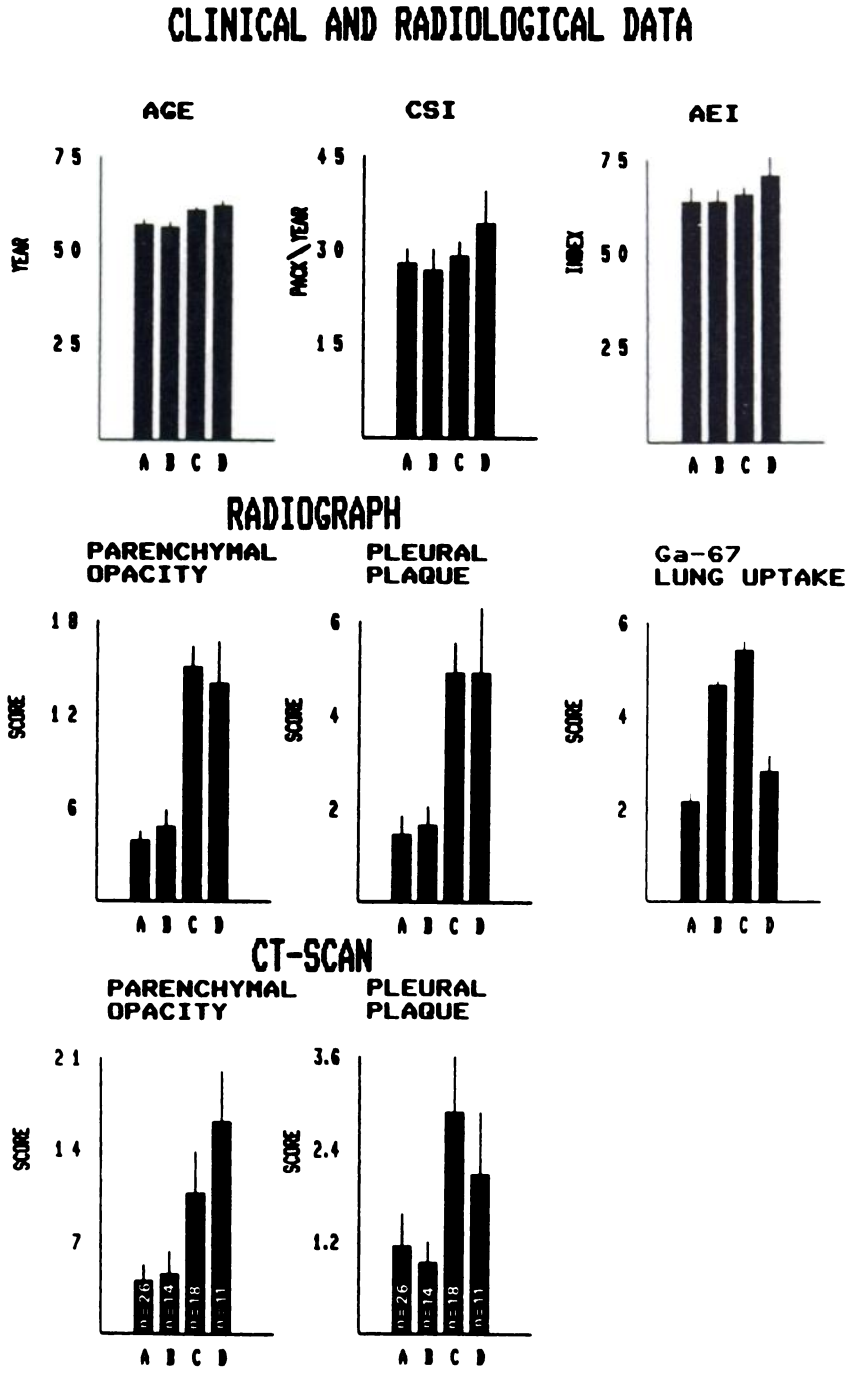

FIGURE 1
CSI: Cigarette smoking index; AEI: Asbestos exposure index (see text for details); Groups A, B, C, and D were determined on bases of + or − diagnosis of asbestosis along with normal or increased ^{67}Ga thoracic uptake (*3*) (see text for details). A: Asbestos workers without asbestosis, ^{67}Ga < 3.5, n = 47; B: Asbestos workers without asbestosis, ^{67}Ga > 3.5, n = 31; C: Asbestos workers with asbestosis, ^{67}Ga > 3.5, n = 70; D: Asbestos workers with asbestosis, ^{67}Ga < 3.5, n = 23

bestosis, we have documented that ^{67}Ga is localized in the lung through enhanced protein-bound leakage into the bronchoalveolar milieu and by accumulation in the macrophages at the disease sites (*7,9*). Similar mechanisms of ^{67}Ga accumulation in diseased lungs have also been reported in sarcoidosis (*5,6*). The accentuated accumulation of the marker in the periphery of the thoracic scan observed in some 5% of our scans likely reflects more active disease in the subpleural parenchyma as it has been previously reported in asbestosis (*23*).

Although the mechanisms implicated in the formation of pleural plaques in asbestos workers are ill defined, it is clear from pathological studies that they are composed of lamellar deposits of hyaline, sclerotic, collagenous, connective tissue fibers in a tissue that is poorly vascularized with a small cellular component (lymphocytes) and minimal local inflammatory activity (*24–26*). Thus, knowing the mechanisms of ^{67}Ga body localization, it is understandable that pleural plaques are not an active site of ^{67}Ga accumulation.

TABLE 1
Clinical and Radiographic Data

Subset	1*	2†
Age (yr)	60.75 ± 0.73	60.50 ± 1.50
Cigarette smoking index (pack-yr)	30.38 ± 4.95	26.63 ± 5.51
Asbestos exposure index	60.75 ± 5.67	54.74 ± 3.54
Parenchymal opacities score	14.25 ± 5.23	13.00 ± 4.05
Pleural plaques score	3.38 ± 1.15	4.00 ± 1.84
Gallium-67 lung uptake score	4.50 ± 0.50	4.56 ± 0.51

* Subset 1: eight asbestos workers (Group C) with accentuated peripheral ^{67}Ga uptake on thoracic scan.

† Subset 2: eight asbestos workers matched for age and categories (Group C) without accentuated peripheral ^{67}Ga uptake on thoracic scan.

In conclusion, this study of ^{67}Ga thoracic scans in a large population of patients with asbestos exposure documents that the radionuclide does not accumulate excessively at sites of pleural plaques.

FOOTNOTES

* New England Nuclear Corp., Billerica, MA.

† Dyna 4c/15-61 camera (Picker, Northford, CT) coupled with a Cromenco system 3 microprocessor (Cromenco, Mountainview, CA).

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