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Gallium-67 scintigraphy in lung diseases

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There is some disagreement in the literature about the tumour affinity and tumour specificity of gallium-67 (^{67}Ga). The present investigation showed good uptake of ^{67}Ga in most cases of bronchial carcinoma, but some uptake of ^{67}Ga was also found in 30% of those with non-malignant lung lesions. There was no relationship between the uptake of ^{67}Ga and the histological type of bronchial carcinoma. After radiotherapy, a transient uptake of ^{67}Ga in the irradiated field was seen. In five patients who were studied again two months after the end of radiation treatment, uptake of ^{67}Ga was no longer demonstrable at the original site of the tumour. ^{67}Ga appears to be an isotope with a high affinity for bronchial carcinoma but it is not tumour specific. However, our experience indicates that a negative ^{67}Ga scintigram of the lung in a case of suspected malignancy calls for reconsideration of the clinical diagnosis.

Edwards and Hayes (1971) reported that gallium-67 (^{67}Ga) was taken up by bronchial carcinoma but that this uptake was much more striking in cases of squamous-cell carcinoma than in other histological types. We have studied the tumour specificity of ^{67}Ga citrate in lung lesions, the influence of radiotherapy, and the uptake of ^{67}Ga in relation to the histological type of carcinoma.

METHODS

Our scans were taken two to three days after the intravenous administration of 2 mCi ^{67}Ga (as carrier-free gallium citrate) when normally a high activity was found over the liver. We used a Picker Magnascanner V with a spectrometer window setting of 160 to 320 KeV and an 85-hole collimator. The maximum count rate was 4,000–6,000 counts/min, the ratemeter range 6 K, the count range differential 40%, and the scanning speed about 40 cm/min. We graded the uptake in the lung lesions by comparing the ^{67}Ga count rate over the lesion with that over the liver and with the corresponding area of supposedly normal contralateral lung. We graded ++ when the count rate over the lung lesion was as high as or higher than that over the liver (Figs. 1 and 2), + when the count rate over the lesion was lower than that over the liver, and — when there was no uptake seen in the lesion.

MATERIAL

^{67}Ga scintigraphy was performed in 79 patients with lung diseases. In 53 cases the clinical diagnosis was bronchial carcinoma, confirmed by either histological or cytological methods in 41 cases (Table I).

RESULTS

No less than 40 of the 41 proved cases of bronchial carcinoma showed a positive ^{67}Ga scan; in 11 of these cases the diagnosis was only confirmed after operation or necropsy. The only proved case with a negative ^{67}Ga scan was that of a woman, 60 years old, with an excavated anaplastic large-cell carcinoma in the right lower lobe. Microscopical examination after lobectomy showed that only a shallow shell of living tumour tissue remained. In the 12 unproved cases of bronchial carcinoma, 10 showed a positive scan; 26 cases of non-malignant lung disease were also studied. The diagnoses in these patients and grades of ^{67}Ga uptake can be seen in Table II.

Of the 26 cases of non-malignant lung diseases two patients with pulmonary tuberculosis are interesting. The first patient, a man aged 27 years, had primary tuberculosis of the left lung confirmed by a positive culture of the

TABLE I

PATIENTS WITH A CLINICAL DIAGNOSIS OF BRONCHIAL CARCINOMA

No. of Patients	Microscopic Confirmation		^{67}Ga Uptake		
	With	Without	++	+	—
53	41		16	24	1
		12	4	6	2
			20	30	3

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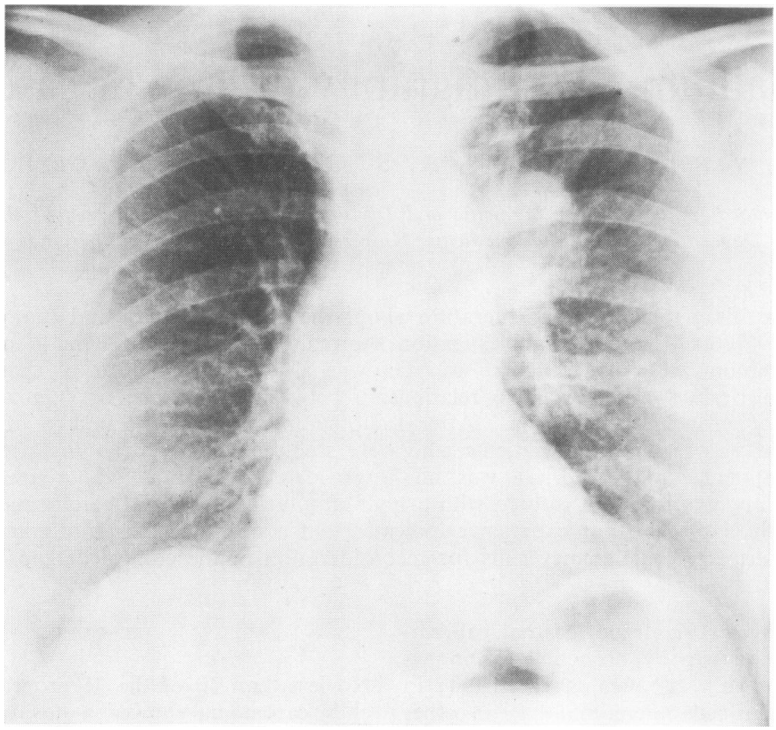

FIG. 1. *Chest radiograph of a 66-year-old man showing a bronchial carcinoma in the apicoposterior segment of the left upper lobe.*

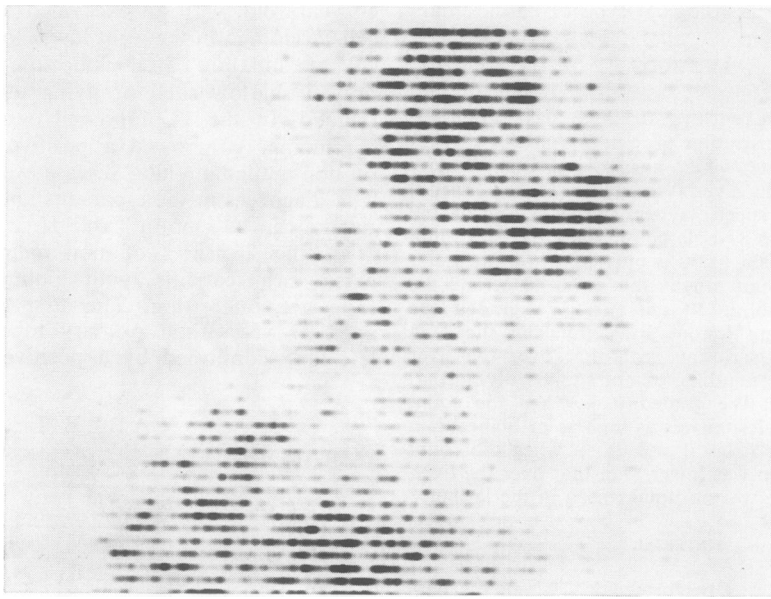

FIG. 2. *Same patient as in Fig. 1. Frontal scan made three days after injection of 2 mCi gallium-67 citrate. The ^{67}Ga-accumulation in the tumour is graded ++.*

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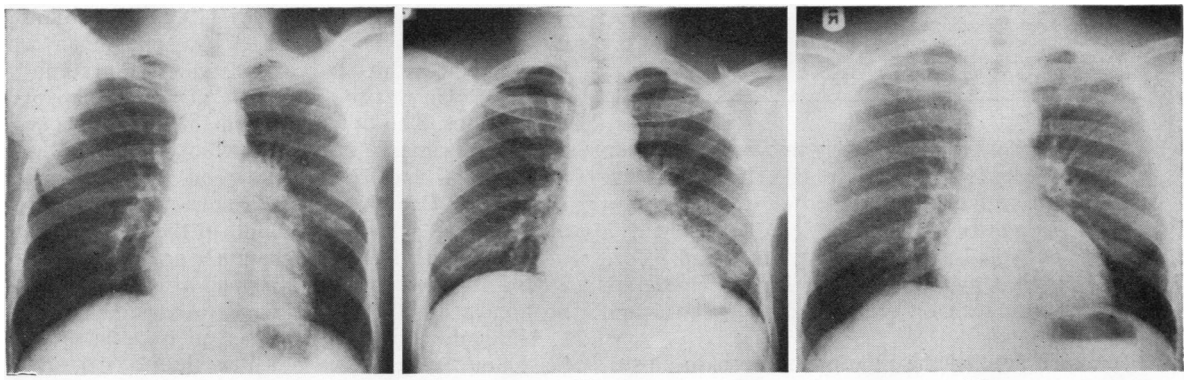
TABLE II

PATIENTS WITH NON-MALIGNANT LUNG DISEASES

No. of Patients	Diagnosis	^{67}Ga Uptake		
		++	+	−
7	Tuberculosis	1	1	5
7	Pneumonic infiltration		2	5
3	Sarcoidosis (inactive)			3
1	Cystic lung disease		1	
1	Adenoma (carcinoid)			1
1	Asbestosis			1
2	Lung fibrosis		1	1
1	Filariasis		1	
2	Pleural exudate		1	1
1	Pneumothorax			1
26		1	7	18

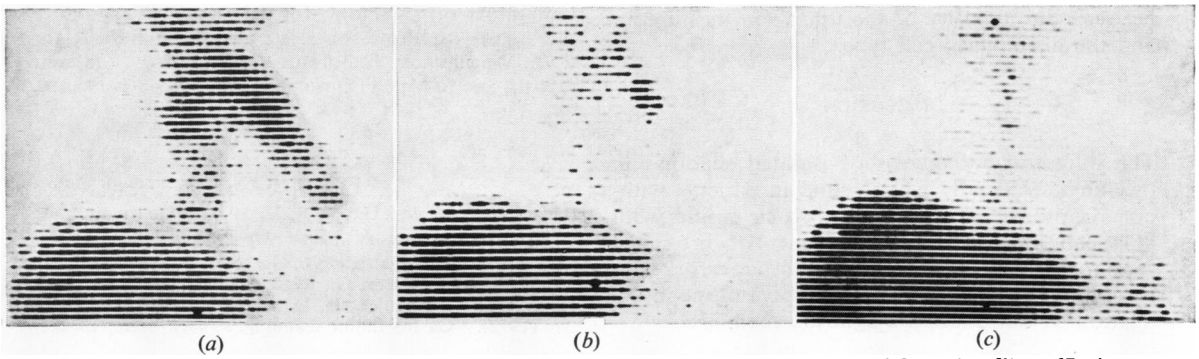
sputum. The enlarged hilar lymph nodes showed a high uptake of ^{67}Ga, which diminished and disappeared under treatment with tuberculostatics (Figs. 3 and 4). The radioactivity registered in the left lower lobe was probably due to an accumulation of ^{67}Ga in tomographically visualized enlarged intrapulmonary lymph nodes. The second patient, a man aged 45 years, had suffered from pulmonary tuberculosis in his youth but this had been quiescent for several years. A routine radiograph one month before admission showed a shadow in the apex of the lung in the area of the old tuberculous foci. This patient had been smoking 30 cigarettes a day for 30 years. The ^{67}Ga scan was negative and, although the clinical diagnosis was more inclined to tuberculosis than to bronchial carcinoma, a lobectomy was performed. Microscopy showed a tuberculoma. The four other cases with post primary lung tuberculosis also showed no uptake of ^{67}Ga at the site of the lesion.

In eight patients receiving telecobalt therapy for lung cancer we studied ^{67}Ga uptake directly



(a) (b) (c)

FIG. 3. *Male patient aged 27 years. Primary tuberculosis of the lungs with enlarged left hilar lymph nodes: Chest radiographs* (a) *before treatment;* (b) *after two months' tuberculostatic treatment;* (c) *after seven months' tuberculostatic treatment.*



(a) (b) (c)

FIG. 4. *Same patient as in Fig.* 3. *Frontal scans made three days after injection of 2 mCi gallium-67 citrate: chest radiographs* (a) *before treatment;* (b) *after two months' tuberculostatic treatment;* (c) *after seven months' tuberculostatic treatment.*

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TABLE III

^{67}Ga UPTAKE IN 8 PATIENTS WITH BRONCHIAL CARCINOMA BEFORE AND AFTER IRRADIATION

Patient	Before Irradiation	Directly After Irradiation		6-12 Weeks Later	
	Tumour	Tumour	Irradiation Field	Tumour	Irradiation Field
1	+	+	+	−	−
2	+			−	−
3	++			−	−
4	+	+	−	−	−
5	++	+	+		
6	++	+	+	−	−
7	++	−	+		
8	+	−	+		

TABLE IV

TUMOUR CELL TYPE AND ^{67}Ga UPTAKE IN 41 PATIENTS

Cell Type	^{67}Ga Uptake		
	++	+	−
Squamous-cell carcinoma	8	9	0
Small-cell anaplastic carcinoma	2	3	0
Large-cell anaplastic carcinoma	0	0	1
Adenocarcinoma	2	5	0
Alveolar-cell carcinoma	0	1	0
Non-classified carcinoma	4	6	0

after the conclusion of therapy and again between 6 and 12 weeks later (Table III). In five of six patients examined directly after the radiation treatment we found in the irradiation field a diffuse, but small uptake of ^{67}Ga, not found before radiation therapy. This uptake in the irradiation field was not seen on scans made between 6 and 12 weeks later.

We also studied the relation between the histological type of tumour and the uptake of ^{67}Ga (Table IV) and found an uptake of ^{67}Ga in all our cases of small-cell anaplastic carcinoma (5), adenocarcinoma (7), and in a case of alveolar-cell carcinoma. We did not find a relationship between the intensity of the uptake in the tumour and the histological cell type.

DISCUSSION

The differential diagnosis of isolated shadows in the lungs, especially when found in patients without symptoms, remains difficult. Our results with ^{67}Ga scintigraphy in proved cases of bronchial carcinoma suggested that diagnostic errors can be diminished by the addition of this isotope investigation to our routine diagnostic methods.

Unfortunately, mediastinal localizations of tumour cannot always be recognized owing to the normal uptake of ^{67}Ga in the spine. The importance of such a possibility was illustrated by a patient with a proved bronchial carcinoma and a positive ^{67}Ga scan. Tomography did not demonstrate enlargement of mediastinal lymph nodes but on the ^{67}Ga scan a small uptake was noted next to the spinal activity. During surgery a lymph node in the carina of the upper lobe was found to contain carcinoma and pneumonectomy was performed instead of a lobectomy. We are investigating the possibilities of a subtraction technique for recognizing abnormal ^{67}Ga accumulation in the mediastinum. The uptake of ^{67}Ga in the irradiation field, seen shortly after the end of radiation treatment, was unexpected. A possible explanation may be the uptake of ^{67}Ga in the fast proliferating connective tissue cells, known to be present after radiation treatment.

Unlike Edwards and Hayes (1971), we found no relationship between the ^{67}Ga uptake in a tumour and its histological cell type. An accumulation of ^{67}Ga was found in 30% of non-malignant lung lesions. The uptake was small, except in one case of primary lung tuberculosis where the activity was localized in enlarged lymph nodes. With respect to this it is of interest that a high uptake of ^{67}Ga has been found in the hilar nodes of active sarcoidosis (Langhammer *et al.*, 1972). In a case of tuberculoma (confirmed after operation) no uptake of ^{67}Ga in the lesion was found.

Although ^{67}Ga evidently has no tumour specificity, our experience indicates that a negative ^{67}Ga scintigram of the lung in a case of suspected malignancy calls for reconsideration of the clinical diagnosis.

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