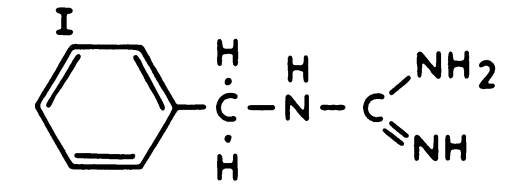
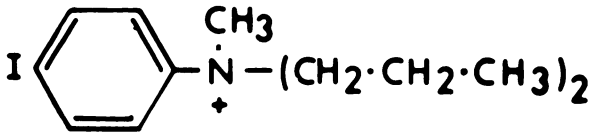
Problem with Mouse Neuroblastoma (C 1300) as a Model for Iodine-131 MIBG Uptake

TO THE EDITOR: The assumption, in utilizing an animal model, is that its behavior resembles that of the human counterpart. There are multiple reports in the literature that some human neuroblastomas accumulate the adrenal-localizing agent metaiodobenzylguanidine MIBG (*1*, *2*). We have found, however, that the mouse neuroblastoma C 1300 (National Cancer Institute) did not concentrate two radioiodonated compounds which localized in the adrenals.

Iodine-131 MIBG (Fig. 1) was supplied by Dr. William Beierwaltes of the University of Michigan. The compound *N,N*-dipropyl-4-(I-131)iodophenyl-*N*-methyl ammonium iodide, was prepared in two steps to produce a specific activity of 1,200 Ci/mmol. A precursor, *N,N*-dipropylaniline was iodinated and the resulting compound purified by high pressure liquid chromatography, followed by methylation. Using microcurie amounts, biologic distribution was followed in male mice after injection into a tail vein (CD-1, AJ, and AJ mice with neuroblastoma transplanted in the flank). The C 1300 neuroblastoma was in its thirtieth transplant and the flank tumors weighed 1–1.6 g at the time of study. Animals were killed at various times and the whole adrenals plus other tissues were removed, weighed, and counted for radioactivity in comparison with standards. Results (three mice per time interval) are shown as mean values in Table 1.



Meta-iodobenzylguanidine (MIBG)



N,N-dipropyl-4-iodophenyl-N-methylammonium (DIM)

FIGURE 1
Structural formulae of two compounds

TABLE 1
Results in Terms of Percent Injected Dose/g Tissue. Tissue Distribution of Two Radioiodinated Compounds

	^{131}I-DIM					
	(CD-1 mice)			AJ mice		Using ^{131}I-MIBG (AJ mice)
	5 min	1 hr	24 hr	1 hr	24 hr	24 hr
Blood	3.85	2.78	0.03	1.94	0.06	0.15
Adrenal	5.10	4.04	2.88	7.14	2.09	10.73
Neuroblastoma	—	—	—	0.30	0.05	0.26

These two compounds, which concentrate in the mouse adrenal gland, did not accumulate in the mouse C 1300 neuroblastoma. This raises concern about the biochemical similarity of the mouse neuroblastoma to the human tumor, since at least a portion of human tumors concentrate metaiodobenzylguanidine. Still unexplained are reasons for the heterogeneity of uptake by human neuroblastomas (whether dependent upon a characteristic of the tumor or the stage of development). In addition, since the mouse tumor was in its thirtieth transplant, changing affinity with the passage of time must be considered.

ACKNOWLEDGMENT

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References

1. Kimmig B, Brandeis WE, Eisenheit M, et al: Scintigraphy of a neuroblastoma with I-131-metaiodobenzylguanidine. *J Nucl Med* 25:773–775, 1984
2. Geatti O, Shapiro B, Sisson JC, et al: Iodine-I-131-metaiodobenzylguanidine scintigraphy for localization of neuroblastoma: preliminary experience in ten cases. *J Nucl Med* 26:736–742, 1985

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Pulmonary Sequestration or Tumor on Radionuclide Angiography?

TO THE EDITOR: We were intrigued by the case report, "Radionuclide Angiography in Pulmonary Sequestration" by Kobayashi et al. (*1*). They demonstrated the systemic arterial blood supply to the left lower lung lesion in a 7-yr-old male and concluded that it was a pulmonary sequestration, though it was suspected to be a mediastinal tumor radiographically. We wish to caution that the systemic blood supply to a pulmonary lesion does not necessarily indicate pulmonary sequestration, but also raises the possibility of a tumor. The following case report validates this statement.

A 75-yr-old woman presented with abrupt onset of right-sided chest pain. Physical examination showed decreased breath sounds in the right lower lung. Chest x-rays revealed a mass in right lower lung field (Fig. 1). CT scan duplicated the same finding but upper cuts of liver suggested hepatic involve-

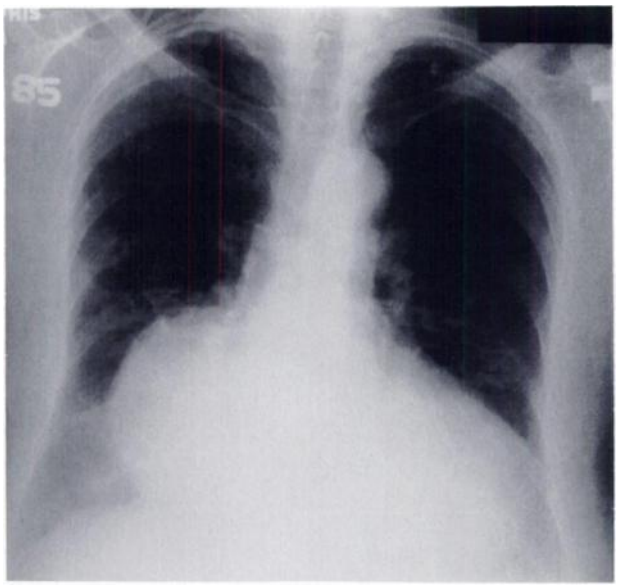

FIGURE 1
Chest x-ray showing mass in right lower lung field

ment. To verify this, a liver scan was requested. The flow study obtained with technetium-99m sulfur colloid 8 mCi i.v. showed photopenia in the mass lesion in the pulmonary arterial phase (Fig. 2A) but filled in during the aortic phase (Fig. 2B). These findings were compatible with systemic arterial blood supply to the lesion the differential diagnosis of which included a tumor. Liver scan was normal. At surgery, the mass was found to be supplied by internal mammary artery. Histologically the tumor was malignant fibrous histiocytoma. Another case was reported in the literature (*2*) wherein this tumor was supplied by bronchial arteries as demonstrated on bronchial arteriograms.

On the basis of our observation we conclude that the aortic blood supply of the pulmonary lesion should include the differential diagnosis of tumor and pulmonary sequestration and not the latter alone as reported by Kobayashi et al.

References

1. Kobayashi Y, Abe T, Sato A, et al: Radionuclide angiography in pulmonary sequestration. *J Nucl Med* 26:1035–1038, 1985
2. Case records of the massachusetts general hospital (Case 19-1985). *N Engl J Med* 312:1242–1252, 1985

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REPLY: While it is indeed possible that a tumor can be supplied by systemic blood supply, it is hard for us to agree with the main direction of the conclusion presented by Dr. Moinuddin concerning his extremely interesting case, i.e. that differential diagnosis of tumor and pulmonary sequestration is necessary, per se, when aortic blood supply of a pulmonary lesion is recognized. Only if the uptake increase of an abnormal mass in the aortic phase is unclear must both cases be considered. The reason for this is that it has been shown that the blood flow in sequestration is larger than that of tumor, because the feeding artery is thicker. This in turn results in a difference in radioisotope uptake between sequestration and tumor in radionuclide angiography. In fact, in Dr. Moinuddin's case there is little uptake by the tumor in the aortic phase and in this phase there is little difference between the tumor itself and the lung. On the other hand, in our case (*J Nucl Med* 26:1035–1038, 1985) uptake of sequestration increased on the aortic phase and we could clearly recognize the mass. Evidence suggests that there are few cases of sequestration with such poor blood supply that differential diagnosis from tumor would be necessary.

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Can a 24-Hour Image in Bone Scan Differentiate Osseous Metastasis From Benign Bone Disease?

TO THE EDITOR: In a recent report, Israel et al. (*1*) suggested that the ratio of lesion-to-nonlesion technetium-99m methylene diphosphonate ([^{99m}Tc]MDP) uptake at 4 and 24 hr might be a reliable method for separating metastatic lesions from degenerative changes in the vertebral column. On the other hand, Alazraki et al. (*2*) recently have commented on

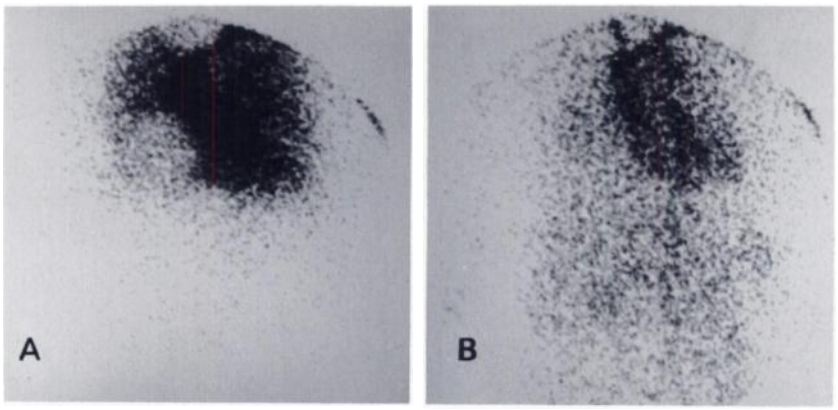

FIGURE 2
A: Dynamic flow study in pulmonary phase showing photopenia in mass. B: Aortic phase of flow study demonstrates systemic blood flow to mass