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A Comparison of ^{197} Mercury and ^{203}Mercury Chlormerodrin in Clinical Brain Scanning

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Although many agents have been employed in scintillation scanning of brain lesions, the most popular during the last four years has been radiomercury chlormerodrin. Bender and Blau introduced ^{203}Hg chlormerodrin for brain tumor scanning (1) and many reports have confirmed the advantages of this material (2-8). The main disadvantage to ^{203}Hg chlormerodrin has been the high radiation dose to the kidney. Blau and Bender reported that a dose of stable mercurial diuretic given before the radioactive material reduced the retention of radioactivity in the kidney (1). However, this added injection did not entirely eliminate the problem and was often an inconvenience, so another method of reducing radiation exposure was sought. In response to this need, ^{197}Hg chlormerodrin has been proposed as a more satisfactory agent for the performance of brain scans (9). Because of its short physical half-life of 65 hours, ^{197}Hg chlormerodrin delivers a radiation dose to the kidney of about one-eighth that of the longer lived ^{203}Hg. This radio accounts for a 2.5 per cent ^{203}Hg contamination. For ^{197}Hg, the values of Σ E and Γ have been taken as .082 mev and .35 γ/mchr at 1 cm, respectively (11).

Radiomercury brain scans have been used in the clinical evaluation of patients with brain lesions at the University of Texas Medical Center since June, 1962. A previous report from this institution documented the first year's experience with 152 patients (6). At the end of the second year's experience there were 658 patients in the series. Beginning in July, 1963, ^{197}Hg chlormerodrin was introduced in our institution, and on the basis of early comparative studies, was used almost exclusively after September, 1963. This report compares the clinical results of ^{197}Hg chlormerodrin with ^{203}Hg.

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MATERIALS AND METHODS

Patients: The majority of patients were referred from the clinical services of the University of Texas Medical Branch Hospitals. A few patients were referred from the USPHS Hospital in Galveston.

Preparation: Prior to performing ^{203}Hg chlormerodrin brain scans, 1 cc of stable mercurydrin was administered intramuscularly. Following the introduction of ^{197}Hg chlormerodrin, this procedure was no longer felt necessary and was abandoned.

Radiopharmaceuticals: ^{203}Hg chlormerodrin and ^{197}Hg chlormerodrin have been obtained in sterile, pre-calibrated solution for injection from commercial radiopharmaceutical suppliers.[2]

Dosage: ^{203}Hg chlormerodrin was given intravenously in a dose of 10 μc per kg, but not over 700 μc was given. ^{197}Hg Neohydrin was given in a dose of 700 μc for adults and 500 μc for children.

Instrumentation: A commercial photoscanning device[3] has been used throughout this experience. It is equipped with a 3 inch D X 2 inch NaI crystal and a 19-hole lead collimator. Simultaneous teledeltos dot scans and photoscans were recorded.

Technique: All brain scans were performed on consultation basis. The chart was reviewed by the physician in the nuclear medicine service to determine the indications for the study and the most likely location of suspected lesions. The patient was then interviewed and informed as to details of the procedure. The dose was administered intravenously in an antecubital vein and the scanning procedure was begun three to five hours later. Two views were selected as the ones most likely to cover the area of the suspected lesion, anterior or posterior and right or left lateral. Where there were no lateralizing signs, an anterior or posterior scan was usually done first and then a right or left lateral was performed as suggested by uptake on the first scan.

Settings: Scanning speed was 12 cm/minute for ^{203}Hg scans, and 18 cm per minute with ^{197}Hg. With the spectrometer set at 220 to 330 kev for ^{203}Hg and 60 to 90 kev for ^{197}Hg with a time constant of ⅛ second, the probe was moved by hand over the cranium until areas of maximum and minimum activity were located. The ratemeter time constant was then changed to five second and the maximum and minimum count rate obtained. With 700μc of ^{203}Hg the maximum count rate was usually 300-600 counts per minute (cpm) over the areas of normal concentration, (usually the nasal area) and brain tumors had count rate increases of up to 12 cpm. With ^{197}Hg maximum, concentration normally varied from 800 to 1200 cpm, and brain tumors showed count rates of up to 2500 cpm. With

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[2]E. R. Squibb & Sons, New Brunswick, New Jersey & Iso/Serve, Inc. Cambridge, Massachusetts.

[3]Picker Magnascanner I, Picker X-Ray Corporation, White Plains, New York.

this count rate information available, the photoscanning and dot scanning controls were set accordingly, the time constant was changed back to ⅛ second, landmarks were marked on the teledeltos paper and the scan begun.

Interpretation: When the photoscan was developed, skull films were used, when available, to trace the outline of the skull onto the scans. Photocopies were made to additionally enhance contrast (12) and served as a copy to be sent to the patient's chart. The scans were interpreted by visual inspection of the dot scan, photoscan and photo copy. Scans were classified as positive, negative or equivocal. The report was immediately dictated and sent to the patient's chart.

Review of Materials: One of us (M.CO) received carbon copies of all reports. Positive and equivocal reports were followed carefully to determine the most likely cause for the abnormality. Negative reports were routinely screened for possible false-negatives and repeated if necessary.

RESULTS

Patient Experience: Between June, 1962 and June, 1964, there were 658 patients studied. Table I illustrates the results in all cases studied during the period covered by this report. Thirty-two patients were not included in this analysis because complete information was not available concerning final clinical impression. This included four ^{203}Hg scans and 28 ^{197}Hg scans. Ten patients (4 ^{203}Hg and 6 ^{197}Hg) were excluded from this study because their scans were judged technically unsatisfactory, usually because of lack of patient cooperation. The remaining 616 patients constitute the subject of this analysis and include 93 per cent of scans performed. They consist of 108 positive scans, 491 negative scans and 17 equivocal scans. The comparison of ^{203}Hg and ^{197}Hg reveals a higher

TABLE I

TOTAL PATIENT EXPERIENCE, June, 1962–June, 1964
Results of Scans

	^{203}Hg		^{197}Hg		
	Number of Patients	%	*Number of Patients*	%	*Number Patients—% Total*
Positive	55	25	53	12	108— 17%
Negative	163	69	328	77	491— 74%
Equivocal	8	3	9	2	17— 2%
Technically Unsatisfactory	4	1.5	6	2	10— 2%
Incomplete	4	1.5	28	7	32— 5%
TOTAL	234	100%	424	100%	658—100%

percentage of positive scans using ^{203}Hg (25%) compared to ^{197}Hg (12%). This primarily reflects the more liberal usage of the brain scan as a screening test since the introduction of ^{197}Hg. The percentage of equivocal or indeterminate scans was not significantly different between the two groups.

Clinical Correlations: Table II correlates the clinical diagnosis with results of brain scans. Patients with neoplasms are divided into four groups; meningiomas (24 paitents), gliomas (35 patients), metastatic carcinoma (23 patients) and miscellaneous neoplasms (18 patients). The table shows that overall results in neoplastic lesions are comparable between ^{203}Hg scans (82% positive) and ^{197}Hg scans (88% positive). ^{197}Hg appeared somewhat less effective than ^{203}Hg in the glioma group, but more than made up for this difference in the other groups. Among the 62 patients with nonneoplastic lesions, cerebral infarcts were by far the most common (34 patients). A detailed analysis of nonneoplastic lesions is being presented as a separate report.

In nonneoplastic lesions, a higher percentage of positive scans was encountered using ^{197}Hg (75%) than with ^{203}Hg (50%). This was principally true in patients with cerebral infarcts, A-V malformations and aneurysms. Most of the positive scans in cerebral infarcts were performed shortly after the onset of symptoms and follow-up scans usually revealed gradual loss of uptake. For the most part, nonneoplastic lesions did not concentrate as much radioactivity as did the neoplastic lesions, but there were some exceptions to this rule (13).

The remaining 454 patients had a variety of miscellaneous neurological and psychiatric diseases. All of these scanned negative. Among the neurological disorders are patients with idiopathic epilepsy (65), cerebrovascular insufficiency (41), cephalalgia (34), organic brain syndrome (31), cerberal atrophy (13), pseudotumor cerebri (10), basal ganglia disorders (11), demyeliating disease (15), toxic delirium states (7), and CNS lues (5).

False-Negative Scans: In view of the suggestion (14) that deep seated lesions might be missed with ^{197}Hg because of its relatively weak gamma ray, an analysis of those patients with neoplasms in which the scan was normal has been of particular interest. These patients are listed along with data regarding histology, location and size in Table III. The size, as given in this table, is based on observation as the inherent nature of removing tumor tissue at surgery forecludes direct measurement; thus only approximate sizes can be established. The main cause for missed lesions appears to be size ($<$3 cm), location (sellar, sphenoid ridge and posterior fossa), and differential uptake. There did not appear to be any marked difference between ^{203}Hg and ^{197}Hg in this analysis. Two gliomas in the frontal area were missed with ^{197}Hg Neohydrin, but it is by no means certain that they would have been detected using ^{203}Hg. Although we have observed some attenuation of the softer gamma of ^{197}Hg (Fig. 1), it does not follow from this study that this significantly affects the diagnostic accuracy of the procedure.

False-Positive Scans: We have encountered only one patient with a positive scan

TABLE II

CORRELATION OF CLINICAL DIAGNOSIS WITH SCAN FINDINGS IN 616 PATIENTS

	^{203}Hg			^{197}Hg				
	Total Pts	*Positive or equivocal scans*	*Negative scans*	*Total Pts*	*Positive or equivocal scans*	*Negative scans*	^{203}Hg	^{197}Hg
MENINGIOMAS		15	1		8	0	94%	100%
GLIOMAS		15	1		16	3	94%	84%
Astrocytomas								
grade III & IV		(10)	(1)		(9)	(1)		
grade I & II		(3)	(0)		(2)	(0)		
Other Gliomas		(2)	(0)		(5)	(2)		
METASTATIC CARCINOMA		12	2		9	0	86%	100%
MISCELLANEOUS NEOPLASM		5	6		4	3	40%	57%
craniopharyngiomas		(1)	(2)		(2)	(1)		
pituitary adenomas		(0)	(3)		(0)	(1)		
pinealoma		(1)	(0)		(0)	(0)		
epidermoid cyst		(0)	(1)		(0)	(0)		
acoustic neuroma		(2)	(0)		(1)	(0)		
neuroblastoma		(0)	(0)		(1)	(0)		
maxillary sinus carcinoma		(1)	(0)		(0)	(0)		
unvarified		(0)	(0)		(0)	(1)		
TOTAL (NEOPLASMS)	57	47	10	43	37	6	82%	88%

TABLE II—*Cont d*

	Total Pts	^{203}Hg *Positive or equivocal scans*	*Negative scans*	*Total Pts*	^{197}Hg *Positive or equivocal scans*	*Negative scans*	^{203}Hg	^{197}Hg
NON NEOPLASTIC (Focal)	30	15	15	32	24	8	50%	75%
cerebral infarct (active)		(6)	(6)		(10)	(8)		
intracerebral clot		(3)	(0)		(2)	(0)		
A-V malformation		(1)	(5)		(5)	(0)		
aneurysm		(2)	(3)		(2)	(0)		
brain abscess		(1)	(1)		(2)	(0)		
cerebral contusion		(1)	(0)		(1)	(0)		
subdural hematoma		(1)	(0)		(0)	(0)		
subgaleal hematoma		(0)	(0)		(1)	(0)		
inflammatory orbital tumor		(0)	(0)		(1)	(0)		
NON-NEOPLASTIC (Misc)	139	1	138	315	1	314	0.7%	0.3%
TOTALS	226	63	163	390	62	328		

in which there was no lesion found to explain the abnormal concentraton. This patient also had an abnormal EEG and arteriogram, but craniotomy failed to reveal the cause of these abnormalities.

On the basis of this experience, it appears that ^{197}Hg chlormerodrin brain scans are comparable to ^{203}Hg chlormerodrin scans in the diagnosis of brain lesions. Since ^{197}Hg delivers a lower radiation dose to the patient, it would seem to be the preferable agent. There are, however, some objections to ^{197}Hg, both theoretical and practical, which need to be considered in arriving at this conclusion. The economic factor of cost must be taken into account. Because of the shorter physical half-life, more frequent shipments of material are necessary, and much material may be lost by radioactive decay during periods of inactivity. This creates a serious problem for small scanning programs. For the larger, more active laboratories, this should prove no problem. We have received bi-weekly ship of 7-9 mc ^{197}Hg Neohydrin per shipment for ten months, and have obtained 6-8 brain scans per shipment at a cost slightly below the comparable cost using ^{203}Hg Neohydrin. Second, all ^{197}Hg chlormerodrin contains detectable amounts of ^{203}Hg (usually less than 2.5%). As the material ages, the parentage ^{203}Hg increases so that arrangements must be made to use ^{197}Hg as soon after receipt as possible. Bi-weekly shipments are of great help in reducing this prob-

TABLE III

NEGATIVE SCANS IN PATIENTS WITH NEOPLASMS

Case No.	*Histology*	*Location*	*Size*
		^{203}Hg	
1.	Meningioma	Sphenoid Ridge	2–3 cm
2.	Glioma III–IV	Parietal	3–4 cm
3.	Metastatic Carcinoma	Cerebellum	2 cm
4.	Metastatic Carcinoma	Cerebellum	2 cm
5.	Craniopharyngioma	Suprasellar	2 cm
6.	Craniopharyngioma	Suprasellar	3 cm
7.	Pituitary Adenoma	Sella	2 cm
8.	Pituitary Adenoma	Sella	2–3 cm
9.	Pituitary Adenoma	Sella	2–3 cm
		^{197}Hg	
1.	Glioma III–IV	Frontal	2–3 cm
2.	Glioma, mixed	Frontal	3–4 cm
3.	Glioma	Pons	2–3 cm
4.	Craniopharyngioma	Suprasellar	2 cm
5.	Pituitary adenoma	Sella	3 cm
6.	Papilloma, Choroid Plexis	Right lateral ventricle	3–4 cm

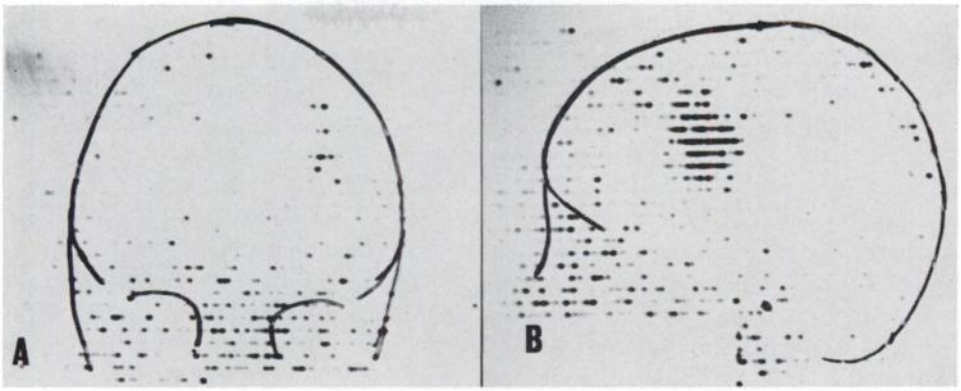

Fig. 1a. Frontal scan in the same patient showing diminution in activity partially due to the greater imposition of bone and tissue filtering the gamma ray of ^{197}Hg.

Fig. 1b. Lateral brain scan with ^{197}Hg chlormerodrin in a patient with a 3 cm, grade III glioma of the lateral portion of the left parietal lobe.

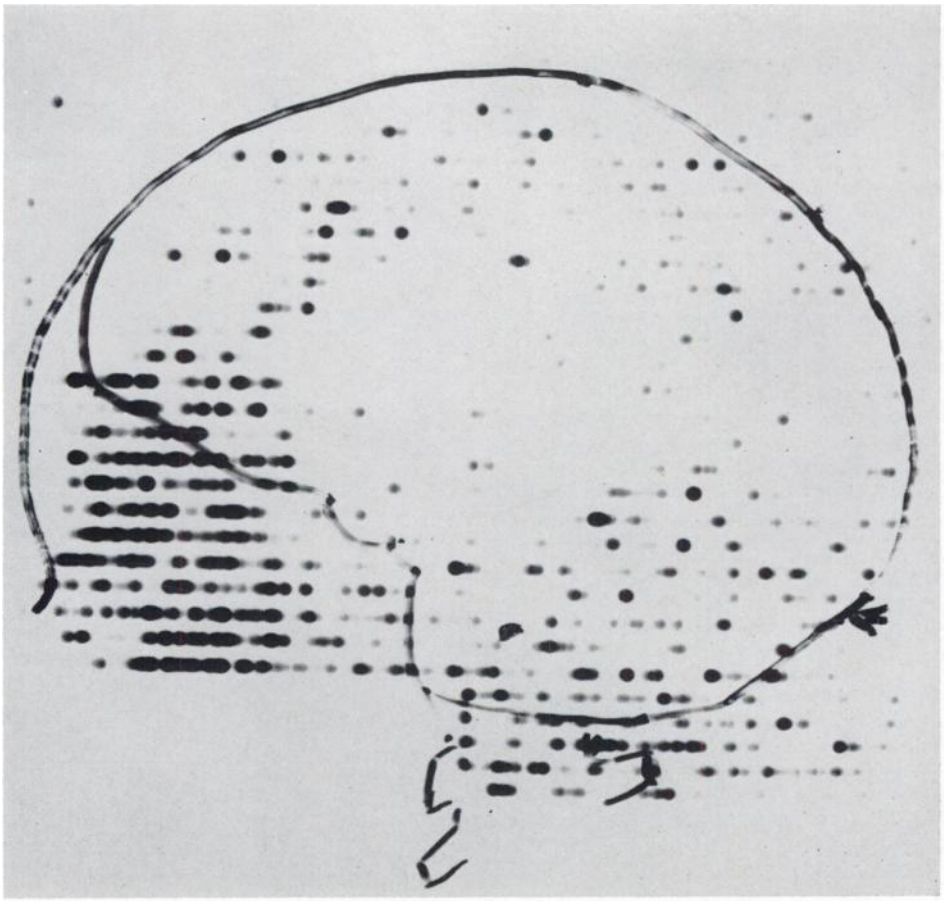

Fig. 2a. Lateral ^{203}Hg chlormerodrin brain scan in a patient with a 4 cm brain abscess in the tip of the left frontal lobe.

lem. Finally, the softer gamma of ^{197}Hg presents theoretical disadvantages which cannot be overcome. Although we have shown that clinical results are comparable, there still exists the possibility the deep midline lesions containing minimal activity might be missed due to attenuation of this gamma ray, which might be detected if the gamma ray had a greater penetrating energy. These difficulties have been recently discussed by Blau and Bender. (14,15) It has been suggested that a more convincing result would be obtained by using both ^{197}Hg and ^{203}Hg on the same patient. We are in the process of approaching the problem along a similar line using phantoms. We completely agree that the search should continue for a more ideal agent for brain scanning. Perhaps ^{99m}Tc under investigation now will be such an agent. For the present, ^{197}Hg offers results comparable to the best obtainable, without the high radiation dose of a longer lived isotope.

SUMMARY AND CONCLUSION

During the past two years, we have employed ^{203}Hg and ^{197}Hg chlormerodrin in an active brain scanning program. The results of this clinical experience have

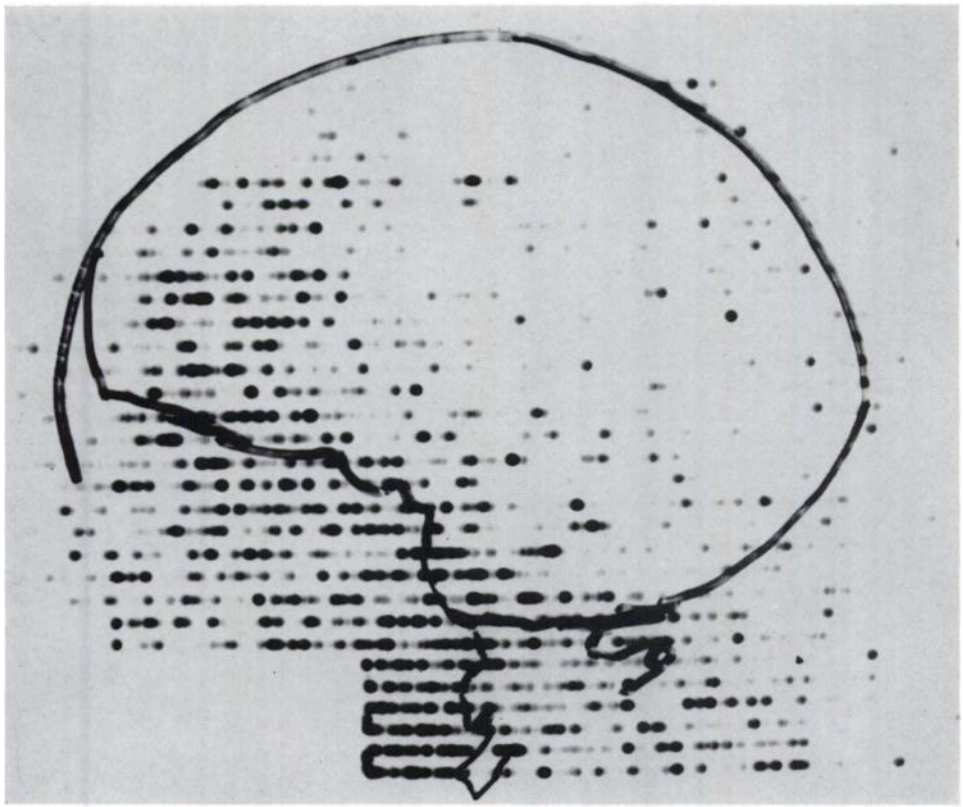

Fig. 2b. Lateral ^{197}Hg chlormerodrin brain scan in the same patient performed one week later. The intensity of activity appears less, but the lesion looks slightly larger.

been analyzed in an effort to determine if results are comparable between these two agents. The overall rate of correctly diagnosing as positive, neoplastic lesions revealed very little difference between ^{203}Hg (82%) and ^{197}Hg (88%). In non-neoplastic lesions, results with ^{197}Hg (75% positive) appeared superior to ^{203}Hg (50% positive) but the cause of this discrepancy is not clear at the present time. We have observed some attenuation of the softer gamma ray of ^{197}Hg in some instances where the tumor is distant from the detector, but have not found this to constitute a major problem in clinical practice. We would recommend that the opposite lateral views be performed when ^{197}Hg is utilized and a negative result is obtained on the original AP and lateral views.

We agree that the search for better and safer brain scanning agents should continue. Hopefully, new agents will offer practical as well as theoretical advantages. ^{197}Hg chlormerodrin in our experience clinically has given results comparable to those obtained in ^{203}Hg chlormerodrin with the advantage of a lower radiation dose to the patient.

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