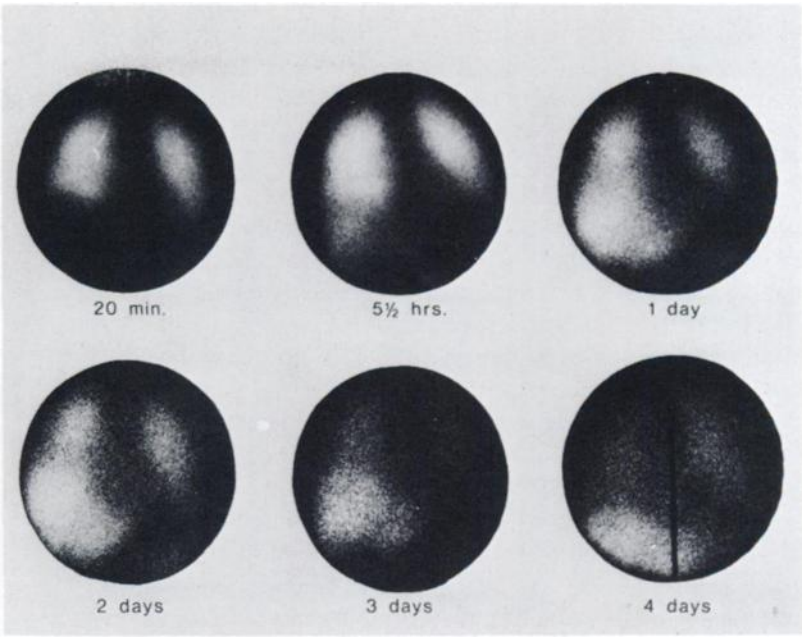

FIG. 2. Scintigrams showing removal of ^{113m}In-labeled ferric hydroxide particles from normal lungs.

toxic reactions. These were a transient flushing and tachycardia due to free iron in the preparation. We have essentially eliminated this reaction by the addition of a heating step as described by Gemmill et al (*5*) and have not observed it in the last 300 lung scans performed with this agent.

In summary, our observations indicate 80% of the ferric hydroxide particles are removed from the lungs within the first 2–3 days following intravenous injection in both mice and humans. The slow component of removal begins about Day 4 and comprises approximately 10% or about 30 μg of ferric hydroxide. Preliminary data suggest this is slowly excreted from the lung with a biological $T_{1/2}$ of between 40 and 80 days. Further research is required to accurately determine the biological half-life of this slow component. We feel that the advantages of the ferric hydroxide macroaggregates labeled with short-lived ^{113m}In for lung scanning greatly outweigh the hazards at the present time.

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COMMENTS BY THE AUTHORS

Since authors of earlier publications (*1–3*) on ^{113m}In-Fe(OH)$_3$ did not allude to long-term pulmonary retention of the iron carrier, we are pleased to learn of Dr. Goodwin's most recent results which confirm that a fraction of the carrier is cleared from the lungs very slowly. The fact that the size and half-time of this fraction in this study do not agree closely with our results (*4*) may be explained by (A) differences in particle-size distribution and particle "hardness," (B) differences in the quantity of ^{113m}In-^{59}Fe(OH)$_3$ administered (a possibility that cannot be evaluated since Dr. Goodwin did not specify the amount of ^{113m}In-^{59}Fe(OH)$_3$ administered in his study), or (C) changes in the preparation procedure made by Dr. Goodwin (*5*).

We have repeated (in abbreviated form) our study of the pulmonary clearance of ^{113m}In-^{59}Fe(OH)$_3$ prepared according to Stern et al (*3*). Approximately 30–35% of this preparation was present in the lungs of mice 42 days after injection compared with 40–45% for the preparation used in our earlier study (*4*). Also Colombetti, Goodwin, and Togami (*5*)

reported a pulmonary clearance curve for ^{68}Ga-$^{59}Fe(OH)_3$ that showed that 20% of the administered dose had a half-time of about 80 days. Thus it appears that the size and half-time of the long-term fraction may vary considerably from one preparation to another.

Although the quantity of $Fe(OH)_3$ normally administered for lung scanning is quite small (300 μg), we feel that the 30–150 μg (depending on the clearance data used for the estimate) associated with long-term retention should be regarded with suspicion until it has been proven safe. This approach would seem particularly prudent in view of the fact that ^{113m}In-$Fe(OH)_3$ particles have been indicated for use in serial studies using repeated injections at intervals as short as 24 hr (*2*).

We agree with Dr. Goodwin that more research is required for a more accurate estimate of the biological half-time of the slowly cleared fraction. In addition, we believe that extended pathological studies are necessary for the evaluation of the long-term safety of this type of preparation.

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