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The Scintigraphic Sign for Detection of Right-to-Left Shunts

TO THE EDITOR: In a recent paper in the *Journal*, Dogan et al. reported on lung scintigraphies in patients with right-to-left shunts (*1*). They found a new scintigraphic pattern in extrapulmonary distribution after intravenous injection of ^{99m}Tc-labeled macroaggregated albumin in 18 of 49 patients with proven cardiac right-to-left shunt, a so-called "quantum mottling" pattern, visible in kidneys and brain. Dogan et al. argued that this phenomenon is caused by too few particles, which where 50,000 to 100,000 in each patient. The size of the shunt was >10%. Dogan et al. concluded that the quantum mottling pattern allows a reliable proof of a cardiac right-to-left shunt.

Between 1978 and 1991 we carried out more than 500 investigations in 150 children with tetralogy of Fallot and pulmonary atresia with ventricular septal defect. We injected 2 MBq/kg body weight (minimum activity, 15 MBq) of ^{99m}Tc-labeled macroaggregated albumin intravenously in the supine position (Solco^{R} MAA, Sorin Biomedica, Italy; in more than 95%, the particle size ranged between 5–40 μm, the number of particles comes to 2,000/MBq according to the producer). If there was a perceptible extrapulmonary activity in the perfusion scintigraphies, we proceeded on the assumption that the right-to-left shunt was measurable. That was the case in 71 children. The scintigraphic right-to-left shunt varied between 7% and 63%, the average was 27.5%. A preoperative cardiac catheterization was also performed and determined a ventricular septal defect in all children. Due to the fact that the whole extrapulmonary activity was not measurable at the same time, we used the accumulation of the radioactive tracer in the kidneys as a reference to the extrapulmonary activity. Assuming that the kidneys receive about 25% of the heart-time volume, we multiplied the activity in the kidneys by a factor of 4:

$$\text{Formula 1: } \frac{\text{Activity}_{(\text{kidneys})} * 4 * 100\%}{\text{Activity}_{(\text{kidneys})} * 4 + \text{Activity}_{(\text{Lungs})}}.$$

However, we found a homogeneous pattern of activity over the kidneys and brain in all children. Depending on the size of the shunt volume, there was a corresponding strong accumulation over the kidneys and brain, which was always homogeneous. There was no evidence of a quantum mottling pattern described by Dogan et al. (*1*). Also, Gates et al. who reported on 36 children with various congenital heart defects, could not find this phenomenon in their scintigraphies (*2*). The number of particles in our study was between 30,000 and 60,000 which is comparable to Dogan et al. Thus, the small number of particles does not sufficiently explain the quantum mottling. Possibly, the activity has not been shaken up immediately before the injection causing several macroaggregates to be linked together. This might have led to a larger size of the conglomerated particles and to a decrease in the total quantity. Although in children the absolute number of particles is smaller than in adults, the specific number of particles per volume is higher. Consequently, the scintigraphy in children might be more homogeneous, on the other hand there is no significant difference in perfusion concerning the homogeneity of brain and kidneys between children and adults. Also, a smaller shunt volume is not a sufficient explanation for the quantum mottling because even in children with a small shunt (10%–20%) there was no evidence for that phenomenon. Even though Palevsky et al. mentioned quantum mottling of the brain in two adults with a right-to-left shunt, many other authors did not find this phenomenon (*3*). However, in our opinion, a quantum mottling pattern in children does not exist as illustrated in Figure 1.

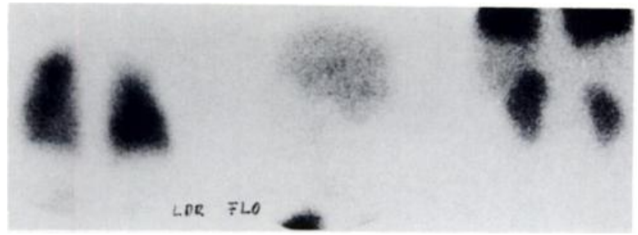

FIGURE 1. An 8-yr-old girl with a calculated right-to-left shunt of 25% shows a homogeneous distribution of activity over the brain and kidneys. Lack of activity in the thyroid demonstrates the absence of pertechnetate. For comparison of the relative distribution of radioactivity, the dorsal lung image is given. Activity used was 35 MBq with 70,000 particles.

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REPLY: We read with great interest the letter submitted to the *Journal* by Meins et al. regarding our recent article on the scintigraphic findings in patients with right-to-left shunts. We were surprised to hear that our colleagues from Hannover did not observe a quantum mottle (QM) pattern on ^{99m}Tc-MAA images obtained in patients with documented right-to-left shunts, and we were even more surprised by their suggestion that our reported finding was due to imaging artifacts or poor radiopharmaceutical preparation technique. Accepting the observations of our German colleagues, we decided to search for an explanation for the two discordant reports.

The question of imaging artifact or inappropriate radiopharmaceutical preparation was easily dismissed. In our department, all radiopharmaceutical preparations and evaluations are done under the close supervision of a board-certified radiopharmacist. Right-to-left shunt studies are done only with fresh preparations of ^{99m}Tc-MAA, and the contents of each newly prepared kit undergo meticulous quality assurance testing, including thin-layer chromatography and evaluation of particle size with a microscope and hemocytometer. Any preparation that does not meet all of our quality assurance standards is discarded and replaced by a new preparation. The vial and syringe are well shaken during labeling and prior to tracer injection. Our technologists (all registry-certified) are very aware of the need to keep blood from entering the syringe containing the tracer, and most of our tracer injections are done through previously placed scalp vein needles. Finally, our image data are at variance with the possibility of poor tracer preparation, or inadvertent labeling of blood clots, or excess statistical noise from inadequate image data collection. Our images rarely show more than minimal pertechnetate activity in the stomach or thyroid; none of our studies show hot spots (QM) in the lungs—the principal scintigraphic manifestation of radiotracer trapped in blood clots; and contrary to what is expected of statistical noise, the QM findings were present only in individuals with shunts and absent in the images of patients without shunts.

Since the presence of imaging artifacts or improper radiopharmaceutical preparation do not appear to be plausible explanations for the discordant results in clinical studies done in Iowa City and Hannover, we refocused our attention on the image data. According to their communication, our German colleagues evaluate right-to-left shunts by using the images of the kidneys as a diagnostic and quantitation standard (instead of our practice of estimating extrapulmonary counts from images of the entire body), and they assume in patients with right-to-left shunts that the extrapulmonary activity would be four times the kidney activity. They obtain scintigrams of the brain in some or all cases, but apparently do not record scintigraphic images of the rest of the body. Could it be that the QM pattern we observed in our shunt patients rarely occurred on images of the kidneys? To evaluate this possibility, we retrieved the image data of the last 10 patients with proven right-to-left shunts and re-examined the images. Only 2 of the 10 studies showed a faint QM pattern on the kidney images (easily missed), even though all 10 showed unmistakable QM patterns in the soft tissues of the lower torso and extremities (see example in Fig. 1), and 9 showed a less noticeable QM pattern on images of the brain. In view of this, we can only speculate that Meins et al. may have missed seeing QM patterns in shunt patients, because they were not able to review images of the lower abdomen, pelvis and extremities.

One can theorize further on the implications of these observations. Patients with moderately large right-to-left shunts may deposit a sufficiently large number of MAA particles in the kidneys to avoid the nonuniform tissue distribution of particles that we believe to be the cause of the QM phenomenon. This explanation is consistent with the lack of any QM patterns in the lungs of our subjects. This argument also provides at least theoretical support to the hypothesis stated by Meins et al. that large shunts may obscure QM patterns in children due to their smaller volume of distribution for the shunted particles. Our own limited experience, however, indicates that the ratio (MAA particles)/(distribution volume) may not be sufficiently large in the peripheral tissues of even small children with large shunts, since we observed the QM pattern in three young children (ages 1 mo, 3 mo and 3 yr) with moderate-sized shunts (13%, 23% and 24%). Interestingly, none showed a QM pattern on the images of the kidneys, but two showed QM patterns on the brain images.

Whether our speculative explanation of the discordant findings at two reputable institutions is valid remains to be seen. As we stated in our original article, our observation is based on a relatively small number of patient studies. Since our "new scintigraphic sign" has the potential for considerable clinical value, it deserves evaluation and confirmation by other groups. We thank Meins et al. for their response to our article; and, once again, we invite other clinical centers, and especially our pediatric nuclear medicine colleagues, to test the value of our observation in larger sets of patients with right-to-left shunts.

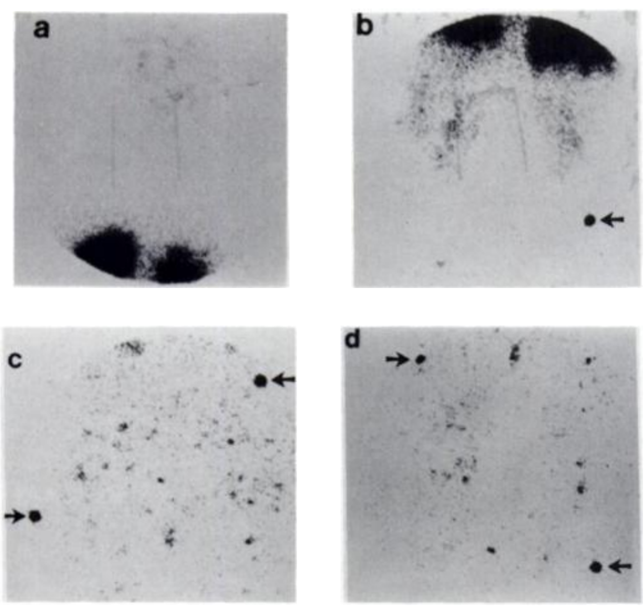

FIGURE 1. Scintigraphic images of ^{99m}Tc-MAA distribution in a 12-yr-old with an estimated 11% right-to-left shunt. The arrows indicate skin markers (cf. original article). A quantum mottle pattern is probably present in both brain (a) and kidneys (b), but is hard to identify with certainty, whereas it is very obvious on images of the pelvis (c) and thighs (d).

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Treating Hyperthyroidism with Radioiodine

TO THE EDITOR: I was particularly interested in Dr. Shapiro's editorial comments (*1*) on the article of Bockisch et al. (*2*) in the October issue of *JNM* concerning the treatment of hyperthyroidism with radioiodine.

Bockisch insists on the differences in thyroid pathology between the United States and Europe, a fact that I stress whenever I have the opportunity. This means that results of clinical studies cannot be extrapolated without caution when crossing the Atlantic Ocean. This is of course due to the differences in alimentary iodine, as he mentioned.

It is nevertheless unfortunate that he did not further discuss the consequences of this fact regarding the treatment of hyperthyroidism with radioiodine. In our experience, the amount of stable thyroidal iodine pool (ITI) plays a crucial role and should be put in front of the "fudge factors" he lists in his Table 2.

Using the x-ray fluorescence method to measure ITI, we showed that autonomy can be explained in toxic nodules, at least in part by the fact that they are still able to store iodide in contrast