MEASUREMENT OF CARDIAC SHUNTING WITH TECHNETIUM-LABELED ALBUMIN AGGREGATES

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The estimation of right-to-left heart shunting is usually derived from measurements made at cardiac catheterization. This procedure, however, carries some risk in cyanotic infants and children. A simple method for detecting and quantitating the amount of right-to-left cardiac shunting with macroaggregated albumin (MAA) tagged with ^{99m}Tc is described. The procedure is also used to measure the distribution of pulmonary blood flow between the two lungs.

METHOD

Technetium-99m-MAA is prepared according to the method described by Yamada, MacDonald, and Taplin (*1*). Each batch is examined microscopically to assure that particles are in the 10–50-micron size range. The amount of albumin per test dose does not exceed 0.2 mg. After intravenous injection, two or more scintigrams, each of 2-min duration, are taken with a gamma camera to produce a whole-body image. The data are stored on video tape for later playback. "Counts" from the separate scintigrams are summed to obtain a total-body count. Any extravasated radioactivity is measured. The estimation of MAA shunted from the pulmonary to the systemic circulation is calculated from Eq. 1.

$$\frac{\text{total-body count} - \text{total lung count}}{\text{total-body count}} \times 100 = \%\ \text{right-to-left shunt} \quad (1)$$

The distribution of pulmonary arterial blood flow between the two lungs is calculated using Eqs. 2 and 3.

$$\frac{\text{right lung count}}{\text{total lung count}} \times 100 = \%\ \text{pulmonary flow to right lung} \quad (2)$$

$$100\% - \%\ \text{pulmonary flow to right lung} = \%\ \text{pulmonary flow to left lung} \quad (3)$$

The degree of right-to-left shunting as measured by the radionuclide method was compared with that obtained at cardiac catheterization by the Fick oxygen method (*2*) as in Eqs. 4–6.

$$\text{right-to-left shunt} = \text{QAS} - \text{QIS} \quad (4)$$

$$\text{QAS} = \text{actual systemic flow (liters/min)} = \frac{VO_2}{SAO_2 - MVO_2} \quad (5)$$

$$\text{QIS} = \text{ideal systemic flow (liters/min)} = \frac{VO_2}{PVO_2 - MVO_2} \quad (6)$$

VO_2 = oxygen consumption (ml/min)

PVO_2 = pulmonary venous (left atrial) oxygen content (ml/liters)

MVO_2 = mixed venous oxygen content (ml/liters)

SAO_2 = systemic arterial oxygen content (ml/liters)

CASE MATERIAL

Three patients with tetralogy of Fallot were studied.

Case 1. A six-year-old cyanotic female with a 50% shunt by the Fick oxygen method was shown at cineangiography to have a left patent ductus arteriosus associated with *decreased* blood flow to the left lung. Four hundred microcuries of ^{99m}Tc-MAA were injected intravenously, and a 51% pulmonic-to-systemic shunt was determined by whole-body imaging (Fig. 1A). Thirty-nine percent of lung activity was found in the left and 61% in the right lung (Fig. 2A).

Case 2. A four-month-old cyanotic male had a systemic-to-pulmonic shunt surgically created be-

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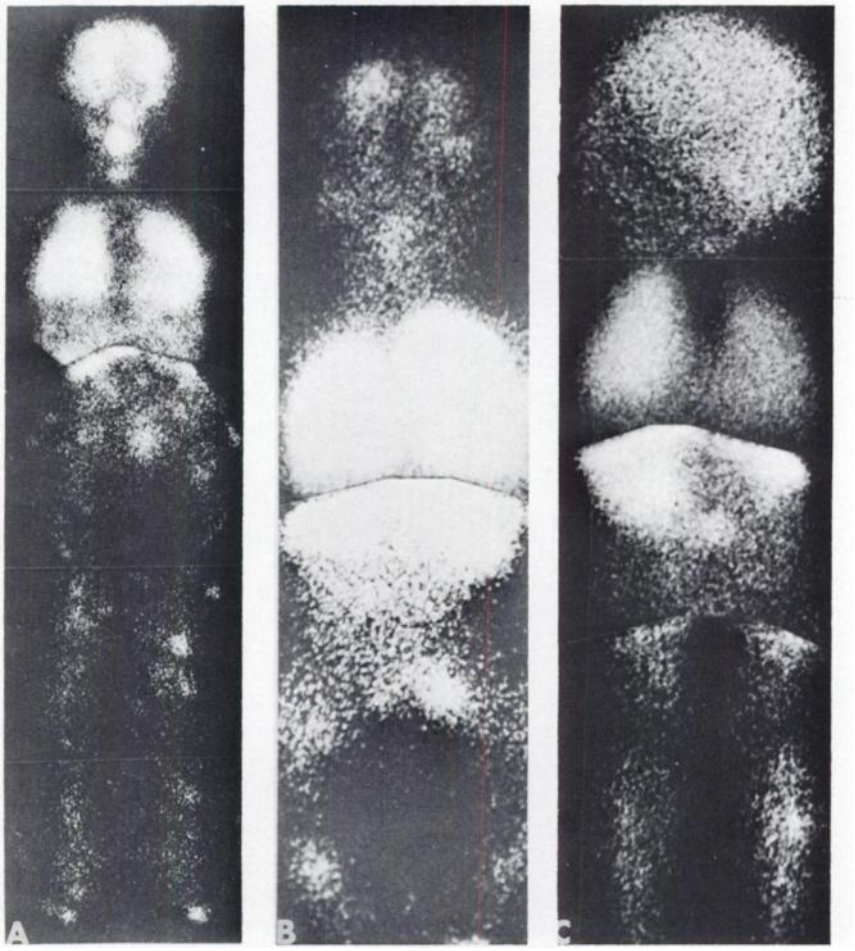

FIG. 1. Total-body scintigrams. A shows 6-year-old with 51% right-to-left shunt. B shows 4-month-old with 25% shunt. C shows 2-year-old with 53% shunt. Child's head is turned to right.

tween the aorta and the right pulmonary artery. Arterial oxygen saturation increased from 67 to 92% after surgery. A postoperative chest radiogram suggested an abnormal increase in right lung vascular markings. Two hundred fifty microcuries of ^{99m}Tc-MAA were injected. By the radionuclide method a 25% pulmonic-to-systemic shunt was calculated (Fig. 1B) which was in agreement with the clinical estimation of the remaining shunt. Forty-six percent of the MAA delivered to the lungs went to the right side (Fig. 2B). Followup chest radiograms showed similar vascular markings in both lungs.

Case 3. A two-year-old female was calculated to have a 20% shunt by the Fick oxygen method. The child was not cyanotic *at rest* nor during cardiac catheterization. Later when 300 μCi of ^{99m}Tc-MAA was injected she cried, strained, and became cyanotic. A whole-body scintigram showed a 53% right-to-left shunt (Fig. 1C). The right lung received 56% of the total MAA delivered to the lungs (Fig. 2C). The increased shunting is attributed to crying and straining. The development of cyanosis at that time supports this explanation.

DISCUSSION AND CONCLUSIONS

For years investigators have attempted to demonstrate right-to-left transcardiac shunts by radionuclide techniques. Recent methods depend upon 10–50-micron MAA particles reaching the systemic circulation where they are trapped in distal capillary beds. Because microembolization of the brain must occur, it was important to establish cerebral toxicity levels so that the number of particles injected remains far below the toxic threshold. The amount of albumin required to produce only a rare microinfarct in the brain of monkeys was determined by Kennady, Taplin, et al (*3,4*) to be 6.0 mg/100 gm brain tissue. The 0.2-mg dose used in patients with a 1-kg brain (proportionately reduced with smaller brains) and a 50% right-to-left shunt delivers about 1 μg/100 gm brain substance which gives a safety factor by extrapolation of approximately 6,000. Brain weight for these children was estimated from the tables of Stowens (*5*).

Macroaggregates of albumin are initially trapped in the nutrient arterioles of the brain which range

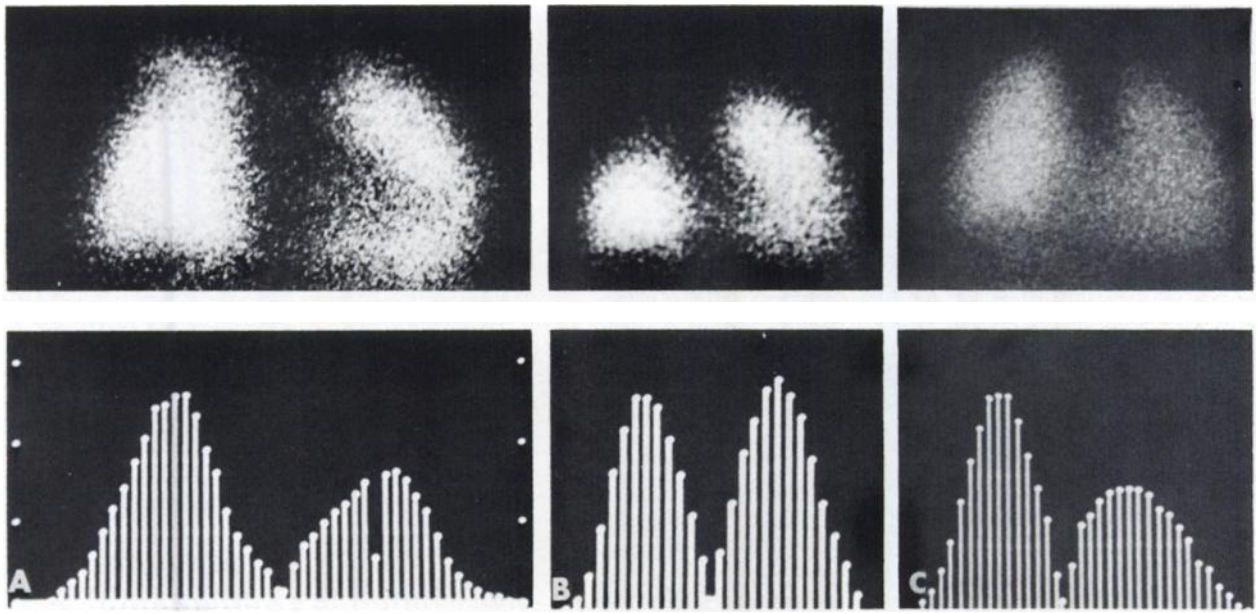

FIG. 2. Lung scan with graphic quantitation. A is patient in Fig. 1A with 61% of radioactivity in right lung. B is patient in Fig. 1B with 46% of radioactivity in right lung. C is patient in Fig. 1C with 56% of radioactivity in right lung.

from 15 to 50 microns in diameter. Although it might be expected that this temporary occlusion would lead to distal areas of ischemic necrosis, no such lesions were found in the histological examinations made by Kennady and Taplin (*3*). They speculated that the event of microembolization did not remain complete at any one location for more than a few minutes, but that the ongoing process of fragmentation moved the particles down the vascular tree. Later studies (*6*) by the same investigators, using labeled MAA and plastic microspheres, demonstrated strong evidence for collateral circulation within the cerebral micro-circulation of the monkey in that relatively few 35-micron spheres produced microinfarcts in view of the large number (80,000) injected.

Other investigators have performed lung scans in cyanotic children. Haroutunian et al (*7*) reported the scan findings in 20 cases of congenital right-to-left shunts with ^{131}I-MAA and ^{113m}In-ferric hydroxide particles. Particles crossed over into the systemic circulation where they were seen in liver and kidneys. Quantitation of the shunt was not reported. Several investigators (*8–10*) using scintiangiocardiography have shown right-to-left shunts by using ^{99m}Tc-sodium pertechnetate. However, the magnitude of the shunt was not calculated. Strauss et al (*11*) reported a method for calculation of shunting in a series of patients which included three with tetralogy. Their procedure involved an initial injection of ^{99m}Tc-sodium pertechnetate into an antecubital vein with a detector over the head recording the arrival of the nuclide. Shunting was calculated by comparing the cranial activity of subsequently injected ^{99m}Tc-labeled albumin microspheres to the cranial activity of the initially administered free pertechnetate.

SUMMARY

Right-to-left cardiac shunting was detected and quantitated in three children with tetralogy of Fallot after intravenous injection of ^{99m}Tc-tagged MAA. The test is performed rapidly, and the patient does not require heavy sedation. The method is calculated to have at least a 6,000-fold factor of safety. The only precaution required is that a particle size measurement of each MAA suspension be made before injection. We are impressed with the preliminary results and believe the procedure deserves further investigation.

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