are affected, as is quantification in human studies that rely on lumped constants obtained using this assumption in nonprimate studies. For example, a value of 0.67 for the lumped constant has been widely used for estimation of myocardial glucose utilization in human studies, based on the study in dogs by Ratib et al. (*5*). That study made the assumption that glucose and FDG freely crossed the erythrocyte membrane, and myocardial glucose utilization was calculated by the Fick principle from the product of myocardial blood flow and the arteriovenous plasma glucose difference. However, because the canine erythrocyte glucose concentration is much lower than that in plasma and transport across the membrane is very slow (*2–4*), the correct value is given by the product of myocardial plasma flow and the arteriovenous plasma glucose difference, equivalent to the product of myocardial blood flow and the arteriovenous whole-blood glucose difference. As a result, myocardial glucose utilization will be overestimated by a factor of 1/(1 − Hct), with a resultant reciprocal underestimation of the lumped constant. Assuming a hematocrit of 50%, this would lead to a lumped constant of 0.67/0.5 or 1.34.

In summary, both animal model and age should be taken into account when making the assumption of rapid equilibration of glucose and FDG across the erythrocyte membrane, because this assumption is unlikely to be valid except in primates and in neonatal nonprimate mammals.

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REPLY: In our study (*1*), we showed that an ^{18}F-fluorodeoxyglucose (FDG) PET image-based time-activity curve can be used to estimate the sampled whole-blood time-activity curve. We used fitting of the macroparameter K as a reference with which to compare the image and sampled blood-derived time-activity curves. Although the area under the curve could also be used, the use of K allows for measurement of the relative impact of any given estimate of the blood time-activity curve on a macroparameter estimate. If the FDG does not equilibrate rapidly enough across the erythrocyte membrane in mice so that the sample time-activity curve does not represent the plasma time-activity curve, then the values for K we obtained would be inaccurate; however, the validity of the relative comparison of the image time-activity curve versus the sample time-activity curve would still stand.

From the PET images themselves, one can never isolate the plasma from the whole-blood activity. We have shown that the liver image time-activity curve can be used as an approximation to the sampled whole-blood time-activity curve. We agree that to rigorously validate using these blood time-activity curves for obtaining meaningful estimates of K, plasma and whole-blood concentrations should be compared experimentally for a given species, strain and age. Because of the limited blood volume of the mouse, this could not be done accurately in our study because several blood samples, therefore of small volume, were needed to observe the full duration of the blood time-activity curve. In our experience, a total of 285 μL blood can be withdrawn successfully from a C3H/HeN mouse and plasma can be separated from whole blood in samples as small as 60–70 μL. To properly compare whole-blood and plasma concentrations of FDG, one could obtain fewer samples (one to four) with larger volume (at least 60–70 μL) from a group of mice at different times.

We agree that there is a need for such experiments across all species for which FDG studies are used. We also agree that the lumped constant used in the FDG model may be affected by the hematocrit. Furthermore, we would add that the literature results cited for glucose transport into erythrocytes may not hold for FDG because of transport differences between the two substrates. The definitive solution is to measure the plasma and whole-blood time-activity curves for FDG and directly determine the differences, if any.

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Dopamine D_2 Receptor Brain Imaging in the Neonatal Period Using ^{123}I-IBZM SPECT

TO THE EDITOR: Kapucu et al. (*1*) recently reported the ability of dopamine D_2 receptor imaging to assess the severity of hypoxic-ischemic brain injury in young infants (7.8 ± 2.3 mo). As they emphasized, these results have to be verified by further studies earlier in the neonatal period.

After obtaining informed parental consent, we performed ^{123}I-iodobenzamide (IBZM) SPECT studies 1 wk after birth in seven neonates with hypoxic-ischemic events. Images were acquired with a Ceraspect gamma camera (Digital Scintigraphics Instruments, Waltham, MA) 1 h after an intravenous injection of 37 MBq ^{123}I-IBZM. The preliminary results confirmed that these studies can be performed without adverse events. The basal ganglia were fully detected in all neonates, showing the biochemical maturation of D_2 receptors. Relative uptake of ^{123}I-IBZM determined by calculating ratios between the mean uptake in the basal ganglia and that in the cerebellum was between 1.38 and 2.6, indicating some differences in the uptake of ^{123}I-IBZM, with lower uptake according to the severity of the hypoxic-ischemic injury as quantified by Sarnat and Sarnat score (*2*). Brain MRI performed on the same day to detect cortical and subcortical lesions was negative in all of the neonates.

These results are in agreement with the results reached by Zouakia et al. (*3*) in a previous ex vivo autoradiographic neonatal rat study, with a 40% decrease in striatal binding of D_2 receptors both on the side ipsilateral to the carotid ligation and on the

contralateral side even when there was no macroscopic evidence of brain ischemia.

Moreover, Zouakia et al. (*3*) confirmed the effect of early hypoxic-ischemic injury on D_2 receptor status, as proposed by Kapucu et al. (*1*), even when no brain lesion was detected on MRI. This result suggests a long-term deleterious effect of hypoxic-ischemic injury on D_2 receptors, still detectable up to 8 mo old, and could guide the therapeutic approach (drugs, physiotherapy, and others) as early as the critical neonatal period.

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REPLY: In their letter, Tranquart et al. report the results of their dopamine D_2 receptor imaging study that was performed on seven 1-wk-old neonates with hypoxic-ischemic brain injury. These neonates had no brain lesions detected on MRI. ^{123}I-iodobenzamide (IBZM) scintigraphy revealed lower uptake in basal ganglia as the severity of injury increased according to Sarnat and Sarnat score.

In a previous study that was performed on older infants (7.8 ± 2.3 mo) with hypoxic-ischemic brain injury, we had shown that striatal D_2 receptor density was inversely related to the degree of brain injury (*1*). We had also shown that striatal D_2 receptor density was higher in infants who had recovered without neurologic deficit compared with those who had neurologic sequelae. Therefore, the results of Tranquart et al. are in accordance with and complementary to our findings.

The two studies highlight the importance of ^{123}I-IBZM brain SPECT in detecting the deleterious effects of hypoxic-ischemic brain injury when no brain lesion is detected on conventional MRI studies.

A follow-up study on these newborns would be interesting to see if any of them eventually show signs of neurologic recovery. It may be expected that neurologic recovery will be associated with a higher D_2 receptor density in the basal ganglia. If this happens to be the case, D_2 receptor imaging can be useful as a prognostic indicator and a guidance to therapeutic approach.

To minimize the radioactivity received by these infants, we would suggest that a lower dose (11 MBq) of ^{123}I-IBZM be used, which would still allow for good quality imaging.

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Direct and Indirect Radionuclide Cystography: Dosimetry in Children

TO THE EDITOR: We believe that the nuclear medicine community welcomes useful guidelines for radionuclide investigations that have been published in the *Journal of Nuclear Medicine* and also as a manual (*1*). We would like to comment on the topic of radiation dosimetry in the guideline for direct radionuclide cystography (DRC) and indirect (IRC) radionuclide cystography in children (*2*).

We wish to note that in Table 1 of the article by Mandell et al. (*2*), second column, the unit for the administered activity of radiopharmaceuticals for DRC is erroneously given as MBq/kg (mCi/kg); it should be MBq (mCi).

The value of 0.0024 mSv/MBq from ^{99m}Tc-pertechnetate for a 5-y-old child in Table 1 (*2*) is denoted as the effective dose but, in fact, it is the effective dose equivalent as taken from Stabin's book chapter (*3*). The effective dose from ^{99m}Tc-pertechnetate for DRC recently calculated by Stabin and Gelfand (*4*) is 0.002 mSv/MBq, which is about 15% lower than the value given in Table 1. Similar and even larger differences between effective dose and effective dose equivalent are typical for most radiopharmaceuticals. Confusion between the terms "effective dose" and "effective dose equivalent" can be found in other radiation dosimetry tables, including those in the *Procedure Guidelines* manual (*1*).

Stabin's calculation (*3*) of the urinary bladder wall dose of 0.028 mGy/MBq from DRC in Table 1 is based on the static urinary bladder model with a volume of 65 mL and the assumption of a 15-min residence time of the radiopharmaceutical in this organ. The application of the formula (age in years + 2) × 30 mL (*2*) gives a bladder volume of 210 mL in a 5-y-old child. The residence time, as well as electron and photon doses to the wall of the bladder with a volume of 210 mL, can be expected to be lower than that for a bladder volume of 65 mL. According to Stabin and Gelfand's estimate (*4*), reduction by a factor of 2 for the total dose might be a reasonable approximation; in Table 1 the urinary bladder wall dose should be about 0.014 mGy/MBq instead of 0.028 mGy/MBq. The effective dose from DRC of 0.002 mSv/MBq should be reduced in approximately the same proportion to 0.001 mSv/MBq.

Dimitriou et al. (*5*) estimated a somewhat lower urinary bladder wall dose from DRC of 0.0094 mGy/MBq, calculated for a 7-min bladder filling time in 5-y-old child. They assumed that all of the activity injected into the catheter was situated in the bladder during the entire filling phase. A delay time of 0.5 min between initiation of saline flow and radionuclide injection was also assumed.

Stabin's data on radiation burden from DRC, modified as shown above, are in relatively good agreement with those of Dimitriou et al. (*5*), in spite of the fact that different methods were used for the calculation.