Administered Radionuclides in Pregnancy

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ABSTRACT
Radiopharmaceuticals are occasionally administered to pregnant patients either out of clinical necessity or by accident. In recognition of the latter, the Society of Nuclear Medicine recommends pregnancy testing before any procedure that will expose the fetus to >50 mGy. When pregnancy is known, the dose of radionuclide to be employed is kept as low as possible without sacrificing radiographic information. The commonly administered radiopharmaceuticals used for lung, gallbladder, kidney, bone, and bleeding scans are labeled with technetium-99m: all deliver whole fetal doses of ≤5 mGy. These doses are lower than those known to produce deterministic effects, and are likely to be very conservative, since radionuclide exposure delivers protracted irradiation exposures to the embryo and fetus. The actual deterministic risks will decrease with the magnitude of the protraction as compared with the acute effects of irradiating the embryo and fetus. The probability of late effects is considered sufficiently low not to contraindicate the use of these radiopharmaceuticals when medically required or to raise undue concern when they are accidentally administered. Teratology 59:236–239, 1999.

ESTIMATING THE RISK
Although there is virtually no human and limited animal data concerning the potential hazards of radiopharmaceutical exposure even at high doses, it is not unreasonable to assume that the risk is proportional to absorbed dose and that with some rare exceptions the proportionality is the same as with external photons. The estimates are likely to be very conservative, since radionuclide exposure delivers protracted irradiation exposures to the embryo and fetus (Brent, '71; Brizzee, '72). The actual deterministic risks will decrease with the magnitude of the protraction as compared with the acute effects of irradiating the embryo and fetus. This is particularly the case when the embryo or fetus is irradiated by radioactivity in maternal tissues and the placenta, somewhat more of an approximation when self-irradiated from embryonic or fetal tissues and, in the latter situation, very much dependent on the spatial distribution of absorbed energy. Thus, it is generally assumed that the risks at the low doses provided by radiopharmaceuticals are similar in magnitude to those from external photons, subject to the same estimates, uncertainties, and thresholds that have been discussed in earlier presentations. I will, in general, confine my discussion to diagnostic radiopharmaceuticals and doses as, by and large, therapeutic ones are not employed during pregnancy.

DOSIMETRY
Estimating doses to the embryo and fetus, particularly the latter, is a formidable task. Calculating the dosimetry is a dynamic exercise for a number of reasons. First, because there are several and changing sources: maternal tissues, the uterus for example, change in size and position during gestation; the placenta evolves as do its transport qualities; fetal tissues are formed, become functional, and grow. The fetal thyroid does not concentrate iodine until the 10th to

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13th week and uptake increases sharply through the 20th week, tailing slowly thereafter (Watson, '92b). Bone scanning agents, which cross the placental barrier with increasing facility as pregnancy progresses, do not appear to concentrate in bone until after the 18th week, although endochondral calcification begins at the eighth week. By the 30th week, the fetal skeleton can be visualized on scintigrams.

Not only are the sources changing, but the targets as well. Distances between maternal sources and the embryo or fetus are constantly varying; so are the size and shape of the fetal organs. Models of these changes for dosimetric purposes are shown in Figure 1 (Sikov and Hui, '96). Given the complex and different scenarios for scheduled proliferation of various cell groups, it is assumed that tissue sensitivities are changing as well, with some being most sensitive during embryogenesis and organogenesis. Fortunately, the radionuclides employed in diagnostic studies have short physical half-lives (of hours to days) and, thus, are not subject to organ growth and rearrangements during their period of active residence.

All of this creates a great challenge to the conscientious dosimetrist who must take into account not only new compartments but also varying rate constants in building his or her kinetic model. Consequently, not only must a changing geometry be considered during pregnancy, but increased complexity is often added to the compartmental model required for kinetic analysis. Figure 2 shows an example (created for radiogallium by Evelyn Watson), which in addition to the maternal compartments of bone, blood, liver, feces, kidney, and urine, includes placenta and fetus, although the latter is not subdivided into organs and excreta. In the practical calculations used for dosimetry, some of the kinetic constants in this schema, being unavailable for humans, were based on extrapolation from animal studies (Watson, '92a).

On the basis of this model, the dosimetry for gallium-67 with the usual clinical dose of 185 MBq is given in Figure 3. Although all doses are <30 mGy, this radionuclide is rarely, if ever, any longer used during pregnancy. For example, the yearly gallium-67 follow-up study requested for patients with Hodgkin's disease treated at our cancer center is routinely deferred until the pregnancy is over.

More frequent are scans performed with technetium-99m-labeled radiopharmaceuticals when life- and health-threatening diseases are suspected during pregnancy. The dosimetry for some of these is shown in Figure 4, taken from the master's thesis of Joy Russell (published in Sikov and Hui, '96). The calculations are based on the MIRD formulation and its pregnant female phantom, aided by MIRDose 3 computer software. Note that the doses are presented in mGy rather than mSv, given the great uncertainty in fetal organ uptake in those instances where the radionuclide crosses.
Because they are environmental contaminants as well as medical pharmaceuticals, much effort has gone into the dosimetry of radioiodines in pregnancy. In actual practice, radioiodine is rarely administered to pregnant patients, and then, almost entirely, by accident in early pregnancy. The current scanning agent of choice is iodine-123, which, when administered before 10 weeks of gestation, provides a whole fetal dose of only 148 μGy at the usual administered dose of 7.4 MBq, while the thyroid dose is negligible, given that the gland is not functional through that date (Watson, 92b). On the other hand, iodine-131 is almost universally no longer used in pregnancy, and thyrotoxicosis is managed by medical means. High doses are received by the fetal thyroid when it is functional, and depressed or absent thyroid function has been observed at birth in these instances (Stabin et al., 91). For this reason, before iodine-131 treatment is initiated, it is common practice to perform pregnancy tests on patients in the child-bearing age group to ascertain that they are not pregnant. In several jurisdictions, including the Commonwealth of Massachusetts, before treatment is administered, it is required that women in the child-bearing age group be informed that radiation can be hazardous to an unborn child.

With the increasing use of positron emitters as radiolabels in medical practice, one might imagine the potential for their administration in pregnant patients. 5-[18F]fluoro-2-deoxyglucose has recently been approved for the staging of lung tumors. It is known to cross the placenta and concentrate in fetal tissues. In the usual scanning dose of 370 MBq, it is estimated to deliver a maximum fetal dose of 6.3 mGy at 3 months. Were it to be used during pregnancy, 185 MBq would probably be sufficient, especially if coincident counting SPECT gamma cameras were employed.

**CONCLUSION**

Radiopharmaceuticals are occasionally administered to pregnant patients either out of clinical necessity or by accident. In recognition of the latter, the Society of Nuclear Medicine recommends pregnancy testing before any procedure that will expose the fetus to >50 mGy (Parker et al., 96).

When pregnancy is known, the dose of radionuclide to be employed is kept as low as possible without sacrificing radiographic information. The commonly administered radiopharmaceuticals used for lung, gallbladder, kidney, bone, and bleeding scans are labeled with technetium-99m: all deliver whole fetal doses of <5 mGy. These doses are below those known to produce deterministic effects, and the probability of late effects is considered sufficiently low not to contraindicate the use of these radiopharmaceuticals when medically required or to raise undue concern when they are accidentally administered.
LITERATURE CITED


