Exposure to ionizing radiation and pregnancy

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Abstract

The exposure of pregnant women to ionizing radiation is often a source of concern and provokes many questions. This anxiety is often unjustified and the questions are asked too late. Ignorance of the subject is likely to harm the woman who requires investigative imaging or lead to inappropriate attitudes to offer a medical termination of pregnancy after low-level exposure to ionizing radiation.

Any approach should look at both maternal and fetal safety. Therefore, it is important to review the key elements of the effects of ionizing radiation on the embryo, the doses received during diagnostic investigations and the attitude to adopt in the main clinical situations.

Keywords: pregnancy; ionizing radiation

There is a big concern in performing radiologic examinations in pregnant women. When a diagnostic test is medically intended for the wellbeing of the mother or the fetus, there is no reason not to be executed during pregnancy. The undetected diagnosis and delayed treatment may sometimes pose a greater risk to the patient and the pregnancy than the potential risk associated with exposure to ionizing radiation.

Biological effects of ionizing radiation to the fetus

Damage by ionizing radiation is caused by deposition of energy to tissue. The absorbed energy in tissue as a result of radiation is expressed as gray (Gy), and when also the kind of radiation is taken into account, this is expressed in Sievert (Sv). There are some more radiosensitive organs than other ones. According to the law of Bergonie and Tribondeau, cells are more radiosensitive if they have a high divi-

sion rate and low differentiation level, circumstances that match fetal tissue[1]. Radiation - induced biological effects are directly related to the stage of gestation: earlier in stage, the more detrimental the expected effects (Table 1).

Both the deterministic (non stochastic) and the stochastic effects should be discussed. As regards the former, the main risk is teratogenicity, while concerning the latter it is the risk of cancer in a child even before birth.

Risk of teratogenicity

Teratogenesis occurs only when a certain threshold of ionizing radiation is exceeded. It is concerned among early effects of ionizing radiation and will always be observed once a certain threshold is exceeded. Typical examples of these effects are fetal death, microcephaly, mental retardation and physical deformities which occur by a high radiation dose to the undifferentiated and rapid dividing fetal tis-

Table 1. Possible effects of radiation in relation to gestational age (Pavlidis 2002)[2]		
Stage	**Period**	**Adverse effects**
Pre-implantation/immediate post - implantation	From conception to 9 - 10 day	Lethal; if not lethal the fetus will recover completely
Early organogenesis	2 - 6 weeks	Teratogenesis, growth retardation
Late organogenesis/early fetal period	12 - 16 weeks	Mental and growth retardation, microcephaly
Late fetal stage	From 20 - 25 weeks to birth	Sterility, malignancies, genetic defects

Table 2. Radiation dose effect on fetal life (Pavlidis 2002)[2]	
Dose (mGy)	**Effects on fetus**
<100	No deterministic effects, only minor risk of stochastic effects
100-150	Increased risk of teratogenicity
2,500	Malformations in most cases
>30,000	Abortion

sue[3]. The magnitude of the effect increases with dose (Table 2). However, thresholds at which these effects occur are much higher than those delivered to the fetus from the majority of diagnostic procedures. There is different sensitivity of fetal tissues to the expose of radiation during pregnancy. During the first week after conception, the effects follow the rule of "all or nothing", because at this stage the cells are undifferentiated and multipotent. Whether most of cells die and the fetus is aborted, or only a few cells are damaged and the embryo develops normally[4].

During organogenesis, which occurs on the 9th day until the 9th week postconceptionally, the destruction of cells that are undergoing differentiation does not lead to the termination of pregnancy but interferes with the development of an organ or limb[5]. The threshold is set at 100mGy. After the ninth week, the risk of malformations is gradually reduced, since most tissues are already differentiated. The most sensitive organ is the brain, since the neuronal migration continues until the 15th week. Disruption of this process can result in defects or mental retardation[6]. The threshold of mental retardation is 200mGy. The contribution of ionizing radiation exposure on central nervous system malformations and mental retardation is in practice difficult to measure, since the rate of spontaneous malformations is high, estimated at 3% of all pregnancies[7].

Cancer risk after ionizing radiation exposure
Cancer risk constitutes a theoretical, stochastic effect are associated with possible changes in DNA sequence, without contributing to cell death and is a late effect of ionizing radiation exposure[8]. The ef-

fects are not related to a certain threshold, but it is the probability of the effect that icreases with administered dose[9]. Even the lowest dose may provoke them but with a smaller possibility compared to a higher dose[10]. The prenatal carcinogenic effects of ionizing radiation is likely to be similar to those in children. The increase in the risk of cancer is estimated at 0.05% per 10mGy of radiation received in utero. This is comparable with the sporadic incidence of cancer in children <15 years old which is estimated at 0.25%. In studies in populations with increased exposure to radiation in utero, as in Hiroshima and Nagasaki, no increase in the incidence of cancer was found. Data from the literature are contradictory. An increased risk of cancer by 40% after exposure to ionizing radiation was revealed in a meta - analysis[11]. In contrast, in another meta - analysis, there was no increase in the incidence of leukemia or cancer associated with exposure to ionizing radiation during prenatal screening[12]. Because of the fact that it is difficult to distinguish the risk of sporadic cancer from the risk of that contributed by ionizing radiation, most clinicians have the impression that the risk of carcinogenesis is much greater than it really is[13].

Therefore, because of scientific uncertainty in this subject, a consensus has been applied, according to which we must proceed in examinations absolutely necessary when there is exposure to ionizing radiation, while simultaneously we have to give special attention to technological improvement, so we can have the highest possible quality of diagnostic tests with the lowest dose of ionizing radiation. The fact that these effects are not threshold - related, forms the basis for one of the major principles in radioprotection, the ALARA principle (as low as reasonably achievable). This means that the administered radiation dose should be kept as low as possible (for the patient, the fetus and the environment), without impairement of the diagnostic value.

A fetal exposure of less than 100mSv is considered to provoke no deterministic effects and has an associated risk of stochastical effects <1%, a fact that does not justify pregnancy termination, according to the recommendations of the ICRP (International Commision on Radiological Protection)[14,15]. Hence, termination of pregnancy for diagnostic radiation exposure is never indicated.

Nuclear medicine examinations

Nuclear medicine studies use a radionuclide bound to a chemical agent, which has the role of a tracer to reveal the underlying lesion. The effect of these agents on the fetus depends upon the placental permeability, tissue affinity, half - life, dose and type of radiation emitted.

The main fraction of fetal exposure evokes from proximity to radionuclides excreted into the maternal bladder. The radionuclide has an augmented concentration into the bladder and so maternal hydration and frequent voiding can reduce the exposure. In certain circumstances, as in a scan with prolonged immobilization or when the radiopharmaceutical follows renal excretion, a folley catheter may be useful[16].

The administered dose of the radiopharmaceutical can often be reduced compared to the standard dose, but it is possible that a prolonged acquisition time is needed to preserve the image quality. This option should be discussed between the pregnant woman and the medical physician.

Spiral CT and ventilation perfusion scan for pulmonary embolism are among the most common nuclear medicine studies during pregnancy. By limiting the administered activity to 80 MBq Tc[99m] - MA, we can limit radiation dose to a 6 month old fetus to 0,4mSv. Estimated risk of fatal pediatric cancer in this dose is less than 1/100,000, compared with a normal background incidence of 80/100,000[17]. The risk of undiagnosed pulmonary embolism for the mother and the fetus is higher. Spiral CT has a lower fetal dose but has an increased risk of maternal breast cancer due to much higher radiation dose to breast tissue[18].

Bone scanning demands a higher dose of the radiopharmaceutical 740 MBq Tc[99m]-MDP, leading to an estimated fetal dose of about 2mSv. Since this technique is used in the standard work up of patients

Table 3. Approximate fetal doses from most common radiological procedures (adapted from Sharp et al)[23]		
Examination	Mean (mGy)	Maximum (mGy)
X-ray		
Abdomen	1.4	4.2
Chest	<0.01	<0.01
IV urogram	1.7	10
Lumbar spine	1.7	10
Pelvis	1.1	4
Skull	<0.01	<0.01
Thoracic spine	<0.01	<0.01
Fluoroscopy		
Barium meal	1.1	5.8
Barium enema	6.8	24
Computed tomography		
Abdomen	8	49
Cheast	0.06	0.96
Head	<0.005	<0.005
Lumbar spine	2.4	8.6
Pelvis	25	79

with a low pre - test probability for bone metastasis, and a change in patient management is unlikely to happen, this exposure has to be judged against the clinical benefit although this dose is still limited in terms of risk estimates. Magnetic resonance imaging (MRI) is an alternative option.

PET scan is another sensitive technique for the detection of tumoral lesions. This scan is usually performed in combination with CT scan. A standard F - FDG - PET scan examination results in a dose exposure of a 6 months fetus of 5 - 6mSv, which is still acceptable in many indications, considering the important information that PET can add on staging purpose of e.g. lymphomas[18]. Consultation of the nuclear medicine physician and medical physicist allows taking simple measures which limit the fetal exposure, including dose limitation, maternal hydration, and a bladder catheter[19].

Parturition is also an important period, because some radioagents will appear in breast milk. It is recommended to wait for 10 half - lives of the radionuclide before resuming nursing, after which no significant amount of the radionuclide would present. International Atomic Energy Agency stands that breastfeeding should not be discontinued after administration of Tc^{99m} - MDP or Tc^{99m} - MA[20].

X-ray imaging

There is great variability in dose exposure in radiological procedures. The estimated fetal exposure for some common imaging procedures are listed in Table 3.

Diagnostic studies remote from fetus (chest or extremities radiographs) can be safely performed at any time during pregnancy, with new generation radiological equipment. These examinations result in

very low doses of <1 mGy to the fetus. The risk of not making the diagnosis is greater than radiation risk involved. Nevertheless, when an examination is at the high - end of the diagnostic dose range and the fetus is near the radiation beam, it should be tailored to the clinical indication and the number of images should be reduced[21,22].

Some of the methods of minimizing the dose to the fetus include restricting the X - ray beam size, reduction of radiation, adapting the direction of the primary beam, and keeping the exposure time as low as possible. In cases of direct exposure, a lead shield might cover the area being imaged. If the fetus is not in the direct X - ray field, this has little effect because the radiation exposure to the fetus arises from the scattered radiation within the patient.

CT of the abdomen and pelvis are by far the examinations with the highest radiation exposure to the fetus, although a high variability is shown. When possible, it should be replaced by ultrasound and radiation exposure should be carefully balanced against the potential change of patient management and benefit.

Ultrasonography, MRI and contrast media

Despite the fact that MRI and ultrasound does not constitute sources of ionizing radiation, it would be useful to refer some of their effects to the ebryo. Contrast media, on the other hand, constitute an integral part of CT and MRI scans in the vast majority of instances.

No short- or long- term effects have been documented from B - mode ultrasound in pregnant women despite intensive use over the past 3 decades[24]. However, in utero exposure to high energy of Doppler ultrasound gives rise to increased apoptosis in animal models, and there is evidence of the effects of exposure to Doppler ultrasound persisting throughout life, with increased non - right - handedness observed in epidemiological studies. These effects may be mediated via thermal or mechanical disruption to the developing conceptus, giving rise to free radical damage[25].

Although there is no evidence that the use of MRI produces deleterious effects on human embryos, its safety during pregnancy has not been definitively proven. MRI is not recommended during the first trimester, because embryo is vulnerable to injury from various physical agents[26]. Possible biological effects at cellular level include the induction of local electric fields and currents from the static and time varying magnetic fields, and tissue and cellular heating due to radio - frequency radiation.

Both iodinated and gadolinium contrast agents may have effects that should be considered. They permeate through the placenta and enter the fetal blood and amniotic fluid, although no mutagenic or teratogenic effects have been described so far. Suppression of fetal thyroid function is the most significant harmful effect of iodinated agents[27]. A few cases of hypothyroidism have been reported after the use of lipid soluble contrast media. Newer water soluble contrast media contain small amount of free iodine and have not shown this effect. Regarding gadolinium, some early animal experiments have shown spontaneous abortion and teratogenic effects due to its long half - life, but no effect was confirmed on the fetus in the more recent studies.

Because of the uncertainty about their use, the European society of urogenital radiology (ESUR) published recommendations on the use of contrast media during pregnancy and breastfeeding[28]. In circumstances where radiographic examination is essential, iodinated contrast media may be given to the mother. In this case, neonatal thyroid function should be checked during the first week after birth. When MRI is necessary, gadolinium may be used with no additional neonatal tests required.

What should we know and what to do

The prenatal doses of ionizing radiation for the majority of the diagnostic examinations, when these are performed under certain specifications, they do not increase the risk of stillbirth, perinatal death or growth abnormalities (including the risk of mental retardation and congenital malformations), compared with the baseline risk in the general population. The lifetime risk of developing cancer after

in utero exposure to ionizing radiation is the same to that during childhood. Higher radiation doses, in particular those used in radiotherapy, may cause developmental abnormalities. The ICRP has determined the rules to be observed in pregnancy [29].

When the exposure to ionizing radiation is concerning a woman of reproductive age, then both the physician requesting the examination as well as the one who performs it, should think about the possibility of pregnancy. If the woman is pregnant, in parturition, or pregnancy can't be ruled out, the performed examination should be absolutely justified. It is necessary to balance the urgency of the situation with the risk of radiation exposure for the woman and the unborn child. If the exposure in ionizing radiation is inevitable for a woman during pregnancy, parturition or in a woman that pregnancy can't be excluded, the examination should be performed with the best possible conditions[30].

During everyday practice, examinations should be performed when fully justified. In case of pregnancy, it is necessary that all examinations have absolute indication, not to be able to be delayed until after the pregnancy completion or be replaced by another test without radiation exposure. The examination should be carried out using the technique with the least possible radiation exposure that is necessary for a reliable diagnosis. If a test was performed on a pregnant woman without having knowledge of her situation, the radiologist or the nuclear medicine physician is responsible to discuss with the couple, providing them all the necessary informations. If the examination is outside the field of the abdomen, the situation is considered reassuring, since the exposure dose to the fetus is probably less than 100mGY and usually less than 1mGy[31]. Nevertheless, it is necessary to explain to the parents that there is physical exposure to ionizing radiation and spontaneous congenital defects due to this is approximately 3%. The random occurrence of mental retardation is also 2 - 3%[32].

Whenever the examination is on the abdomen, the exposure dose on the fetus is usually less than 10mGy. Calculating the dose of the exposure is not necessary. There is no increased risk of congenital defect, but only a small increase in cancer risk[33]. It should be noted that for every 1,000 neonates who were not exposed to ionizing radiation, 997 children will develop cancer by the age of 19 years. When there is in utero exposure of 10mGy dose, the corresponding figure is 996. This minor difference is very small and it cannot indicate the termination of the pregnancy.

When a CT or an examination using contrast media on the abdomen and the pelvis is performed, the dose of the exposure to the fetus by a single scan, is less than 50mGy. However, in this case the dose received by the fetus needs to be estimated by a medical physicist[34]. The risk of congenital malformations is not increased, and 994 out of 1,000 children will not develop cancer before 19 years old. The ICRP states that exposure dose to the fetus < 100mGy should not be considered a reason for pregnancy termination[30].

When performing a multiple CT scan of the pelvis, accurate dose calculation must be preceded, because the radiation received by the fetus could be more than 100mGy. Pregnancy termination due to exposure to ionizing radiation is a decision that many factors must be taken into account. Sufficient information should be provided to the pregnant woman in order to take the proper decision regarding the estimated dose of fetal exposure, the potential risk of defects, and the risk of cancer later in child's life[35].

Special provisions for pregnancy and parturition for women in working environment with exposure in ionizing radiation

The provisions relating to occupational radiation exposure define that exposure of an unborn fetus must be the lowest possible. The cumulative dose of exposure from the moment the pregnancy is confirmed until delivery should not overcome 1mSv. Furthermore, women who are breastfeeding must not be placed in a working position that has a risk of internal exposure[36].

Conclusion

In conclusion, the rules of good practice include the systematic question of women of childbearing age about the possibility of pregnancy, and the test should only be performed if there is an absolute indication, using the best method with the lowest exposure to ionizing radiation. The good knowledge of the effects of radiation allows health care providers to act professionally and with responsibility. It is our obligation to provide to the parents reliable counceling in this controversial subject. ◗

Conflict of interest

All authors declare no conflict of interest.

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