Review Paper

Prenatal X-ray Exposure and the Risk of Developing Pediatric Cancer—A Systematic Review of Risk Markers and a Comparison of International Guidelines

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Abstract—**Since the first Oxford Survey of Childhood Cancer's results were published, people have become more aware of the risks associated with prenatal exposure from diagnostic x rays. As a result, it has since been the subject of many studies. In this review, the results of recent epidemiological studies are summarized. The current international guidelines for diagnostic x-ray examinations were compared to the review. All epidemiological studies starting from 2007 and all relevant international guidelines were included. Apart from one study that involved rhabdomyosarcoma, no statistically significant associations were found between prenatal exposure to x rays and the development of cancer during 2007–2020. Most of the studies were constrained in their design due to too small a cohort or number of cases, minimal x-ray exposure, and/or data obtained from the exposed mothers instead of medical reports. In one of the studies, computed tomography exposure was also included, and this requires more and longer follow-up in successive studies. Most international guidelines are comparable, provide risk coefficients that are quite conservative, and discourage abdominal examinations of pregnant women. Health Phys. 121(3):225–233; 2021**

Key words: health effects; exposure, radiation; pregnancy; x rays

INTRODUCTION

Trauma is the leading cause of non-obstetric mortality in pregnant women worldwide. In countries with access to quality healthcare, the leading cause is venous thromboembolism (VTE) (Tirada et al. 2015). Both trauma and VTE require diagnostic radiographic examinations, mainly computed tomography (CT) and x rays, to diagnose. In these cases, it is justified to risk exposing a fetus to ionizing radiation, as these conditions can be fatal to the mother. In other cases where the situation is less acute and not life threatening, the risks associated with exposing a fetus to ionizing radiation must be taken into consideration when determining the diagnostic process. Accurate communication incorporating up-to-date, evidence-based information is essential when informing the parents of the risks to their unborn child.

The purpose of this review is to study recently published literature describing the risks to the fetus due to prenatal radiographic examinations. A patient's radiation dose received from a diagnostic x-ray examination is low (well below 50 mSv), meaning the only possible risks for the exposed fetus are stochastic effects. These describe an increased risk of inducing malignancy due to prenatal radiation exposure. Other harmful effects such as mental retardation or teratogenesis are not expected to occur below 50 mSv (ICRP 2000, 2003; Tirada et al. 2015) and are therefore excluded from this review.

When this study protocol was defined, the choice was made to follow the same approach as in the Schulze-Rath et al. (2008) review, which includes publications from 1996 through 2006. This review includes publications written since 2007. Schulze-Rath et al. (2008) constrained their review to publications discussing the risks of prenatal and postnatal exposure to diagnostic x rays. This review describes the carcinogenic risks of prenatal exposure to diagnostic x rays and compares current international guidelines on radiodiagnostic examinations on pregnant patients.

MATERIALS AND METHODS

This review has two parts: (1) a review describing recent risk levels for prenatal exposure to diagnostic x rays as found in scientific literature and (2) a comparison of current international guidelines. Both the review and the comparison are described separately in the following paragraphs.

Risks of prenatal exposure to diagnostic x-ray procedures

The inclusion and exclusion criteria are based on the Schulze-Rath et al. (2008) review and are shown in Table 1. The literature search was conducted using Pubmed and Google Scholar. The search question has been constrained to between January 2007 and September 2018 since Schulze-Rath et al. (2008) ended in December 2006.

The authors declare no conflicts of interest.

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Table 1. Inclusion and exclusion criteria based on the Schulze-Rath et al. (2008) review.

Inclusion	Exclusion
Cohort or case control studies	Reviews or comments
Only diagnostic exposure to x ray	Every other way of exposure to radiation (industry, background, accidents)
Publication between January 2007 and September 2018	Publication before January 2007
The study population exists of children, young adults and pregnant women	
Association with leukemia, lymphoma, CNS-tumors, and solid tumors	
If the same results are published in several different publications, the most detailed is used	

This review also compares the results found with the result of the Wakeford (2008) review. Unfortunately, keywords were not published in the Wakeford (2008) review, so this review's keywords are based only on Schulze-Rath et al. (2008). Also, this review limits itself to prenatal exposure, while Schulze-Rath et al. (2008) also studied postnatal exposure. As a result, it was necessary to adjust the selected keywords. Finally, the following keywords were selected: "prenatal or in utero" and "tumor or malignancy or childhood cancer or leukemia" and "x-ray or radiodiagnostic." Synonyms such as tumor, pediatric/pediatric, pregnant, antenatal, and so forth were all used; however, this did not provide additional results. These keywords were first used in Pubmed and then also in Google Scholar, but the latter search did not provide any new search results.

The relevance of the publications was determined using the criteria shown in Table 1. Also, the impact markers and citations quota of the publications were determined. Articles excluded were either reviews or described exposure prior to conception. All characteristics of the included studies are shown in Table 2, which is identical in set up to the table in the Schulze-Rath et al. (2008) review.

Table 3 shows for which factors the different studies have been adjusted, providing insight into the comparability of the different studies. The studies are corrected for such a wide variety of factors that a meta-analysis most likely would not provide an unambiguous result that can be interpreted.

Guidelines

To collect data on current guidelines on radiodiagnostic examinations on pregnant patients, Google Scholar and Pubmed were used. The following keywords were selected "pregnant women or patients or clients," "radiodiagnostic or radiology or x-ray or CT exam" and "guidelines/directives." The search quickly revealed an article by Austin and Frush (2011), which contains a compendium of all (inter)national guidelines used in the United States (Austin and Frush 2011).

This article was used as a starting point for collecting the guidelines, whereby most guidelines were found due to the snowball effect. The Austin and Frush article was published in 2011, which meant several cited guidelines were no longer accessible or had been updated. Where possible, the most recent version of the guideline was used. Some guidelines are the result of collaboration between organizations that also have individual guidelines. If the contents of these guidelines were identical, the most recent directive was used. Guidelines other than those described in the Austin and Frush (2011) article, which are current and relevant, have also been included in this review.

RESULTS

Fetal risks due to prenatal exposure to diagnostic x rays

Only Rajaraman et al. (2011) provides separate risk markers for leukemia, but the other studies divide leukemia into acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) subtypes. ALL was examined in the Rajaraman et al. (2011), Bailey et al. (2010), and Bartley et al. (2010) studies. All three studies were case control studies and used interviews to collect data. Rajaraman et al. (2011) also uses medical records in addition to the interviews. Bailey et al. (2010) is the smallest study with 389 cases (4 exposed), Bartley et al. (2010) has 827 cases (39 exposed), and Rajaraman et al. (2011) 2,690 cases. All three studies take the sex of the child into account at the adjusted odds ratio (OR). Bartley et al. (2010) and Rajaraman et al. (2011) take the age at the time of diagnosis, the age of the mother at the birth, and the State/region in which the children live into account. Both Bartley et al. (2010) and Rajaraman et al. (2011) also examined AML, but this also did not produce significant results.

The only cohort study is the Ray et al. (2010) study, which investigates 1,835,517 mother and child pairs from Ontario, Canada. Of these pairs, 5,590 mothers were exposed to diagnostic radiographic examinations during their pregnancy, of which 4,088 underwent a CT scan. Interestingly, in this study, a hazard ratio (HR) of 0.68 with a 95% confidence interval (CI) of 0.25–1.80 is found. The adjusted HR takes the sex of the child and the age of the mother into account, but other factors are mainly socioeconomic.

In the case-controlled Grufferman et al. (2009) study, the association between the rhabdomyosarcoma and exposure to diagnostic x rays is examined. According to the author, this is the only study that has examined this specific connection. Data are available from the Children's Oncology Group Intergroup Rhabdomyosarcoma Study and were collected using standardized interviews with the children's

parents. There were 319 cases and matched controls in this study, taking sex, age, ethnicity, and pregnancy characteristics into account. Several significant outcomes are found in this study, including a 1.9 OR with a 95% CI of 1.1–3.4 when exposed to an x-ray examination at any point of the pregnancy. This study adjusted the results for eight factors; apart from the Stalberg et al. (2007) study, this is the highest number of factors corrected for.

The Goel et al. (2009) study, also from the Children's Oncology Group, examined the risk of a Wilms tumor due to prenatal x-ray exposure. This case-controlled study did not produce significant results with an OR of 0.9 with a 95% CI of 0.7–1.3.

The most recent research in this review is the Tettamanti et al. (2017) study. This is a multi-center case-controlled study conducted in Denmark, Norway, Sweden, and Switzerland. This study sought to find possible causes for the emergence of brain tumors in children and adolescents. Data were collected using databases from several different countries. A total of 352 cases are matched to 646 controls. The results are adjusted for age and the parents' level of education at the birth. The results show no significant connection with a 95% CI of 0.54–1.68 and a OR of 0.96 (Tettamanti et al. 2017).

The studies of Tettamanti et al. (2017), Milne et al. (2014), Rajaraman et al. (2011), and Stalberg et al. (2007) examine whether the risk of developing a brain tumor in childhood is due to prenatal (ionizing radiation) exposure. The Stalberg et al. (2007) study is the largest, with 503 cases and 52 controls. In addition, this study distinguishes the various types of brain tumors in contrast to the other three studies. The results are adjusted for 10 factors, mainly related to pregnancy or childbirth. Again, this is in contrast with the other two studies that mainly examine socioeconomic factors. The results of the Stalberg et al. (2007) study, as with the three other studies on brain tumors, are not significant. The results found with regard to Primitive Neuro-Ectodermal Tumor (PNET) are striking; despite not being significant, the OR is much higher than in other studies.

In comparison to the Schulze-Rath et al. (2008) review, he Golding et al. (1992) and Shu et al. (1994, 2002) studies are of special interest. Golding et al. (1992) finds an OR of 1.8 (95% CI 1.16–2.8) for Non-Hodgkin's lymphoma, where Rajaraman et al. (2011) finds an OR of 1.48 (95% CI 0.66–3.32). Shu et al. (1994, 2002) finds an OR of 1.3 (95% CI 1–1.7) for "a malignancy in children," where Rajaraman et al. (2011) finds an OR of 1.14 (95% CI 0.90–1.45) and Ray et al. (2010) a HR of 0.68 (95% CI 0.25–1.80), respectively.

The largest overlap in results is found for leukemia. This is the only type of pediatric cancer for which a significant association with prenatal exposure to diagnostic radiology is found in multiple studies. Fig. 1 shows the results found for leukemia in the various studies, including studies from Schulze-Rath et al. (2008) and Wakeford (2008).

Guidelines

In the Netherlands, the Dutch Standard Safety Radiation Protection Norm (Bbs) "Article 8.11: Medical exposure of women who are pregnant or breastfeeding" is to be consulted when performing radiodiagnostic examinations on pregnant women. In practice, the guidelines herein can be complemented with practical standards, which have been drawn up by professional groups for specific situations such as appendicitis (Heij 2010). This is very concise when compared with the international guidelines. An appendix summarizing the guidelines may be requested from the author.

Various risk coefficients are being used in the guidelines. Tirada et al. (2015), the American College of Obstetricians and Gynecologists (Committee on Adolescent Health Care 2018), and McCollough et al. (2007) define their risk coefficient as a twice higher risk for developing a malignancy at 50 mGy. The Austrian Ministerium Frauen Gesundheit (Arrouas and Ditto 2017) has set their coefficient for the same risk at 30 mGy. In addition, ICRP 84: *Pregnancy and Medical Radiation* (IRCP 2000) and the Ministerium Frauen Gesundheit (Arrouas and Ditto 2017) also define the chances of an exposed fetus not being affected by exposure to ionizing radiation. These chances can be found in Fig. 2.

The guidelines state that an x ray may be performed as an alternative if an ultrasound is not an option. The Ministerium Frauen Gesundheit (Arrouas and Ditto 2017) and the International Atomic Energy Agency (IAEA 2018) state that the risk is negligible when the mother's abdomen is not included in the field of view (FOV).

All guidelines state that a CT scan may only be performed in acute or life-threatening situations such as trauma or when a pulmonary embolism is suspected. In case of acute appendicitis, the Dutch guideline advises an ultrasound instead of a CT scan (Heij 2010).

Not all guidelines consider it necessary to confirm pregnancy status prior to a radiographic examination. The Ministerium Frauen Gesundheit (Arrouas and Ditto 2017), Tirada et al. (2015), and the Belgian Federal Agency for Nuclear Control (FANC 2018) only require this if the fetus is located in the primary beam.

Information prior to and after a radiodiagnostic examination (with regard to possible fetal exposure) is a requirement in all guidelines. The guidelines that go into this in more detail indicate that it is important to explain risk markers in combination with the baseline risk of childhood cancer. In addition, calculating and mentioning the exact dose to the fetus is strongly recommended.

In all guidelines, it is specified that there is no justification for an abortion when the dose to the fetus is under 100 mGy, and abortion is not necessary up to a total dose of 500 mGy. The guidelines that discuss shielding state that extra shielding is not required when the abdomen is not in the

Table 2. Characteristics of the included studies.

Primary author (year)	Risk marker and disease	Place	Study population	Time period study	Exposure assessment	Definition of x-ray procedure	Exposure setting	Target organ(s)	Risk estimate	adjusted risk	95% CI
Stalberg (2007)	X rays and brain tumor during adolescence	Sweden	503 cases 0–15 y, 512 controls 0–15 y	1975– 1984	Hospital records and medical birth register	X ray yes vs. no	Prenatal	Abdominal (A) or non-abdominal (NA)	All brain tumors (A)(NA) Astrocytoma low grade (A)(NA) Astrocytoma high grade (A)(NA) PNET (A)(NA) Ependymoma (A) (*crude risk*) (NA) (*crude risk*)	1.02[a] 0.78[a] 0.72[a] 0.96[a] 1.06[a] 0.36[a] 1.88[a] 0.81[a] 1.01[a] 1.16[a]	0.64–1.62 0.25–1.17 0.36–1.42 0.57–1.62 0.39–2.86 0.12–1.08 0.92–3.83 0.83–1.69 0.34–2.98 0.47–2.87
Goel (2009)	X rays and Wilms tumor	USA	512 cases, 509 controls	1999–2002	Telephone interviews	X ray yes vs. no	Prenatal	All (non-specified)	Wilms tumor	0.9[a]	0.7–1.3
Grufferman (2009)	X rays and rhabdomyosarcoma	USA	319 cases 0–20 y, 319 controls 0–20 y	April 1982–July 1988	Standardised interviews of the parents	X ray yes vs. no	Prenatal	Abdomen/pelvis or thoracic area	Rhabdomyosarcoma	1.9[a]	1.1–3.4
Bartley (2010)	X rays and leukemia	USA, California	827 cases 0–14 y, 1107 controls 0–14 y	1995–2008	Standardised interviews of the parents	X ray yes vs. no	Prenatal	All (non-specified)	AML ALL	0.85[a] 1.20[a]	0.26–2.78 0.71–2.04
Bailey (2010)	X rays and leukemia	Australia	389 cases 0–15 y, 876 controls 0–15 y	July 2003–December 2006	Parent questionnaires	No of x rays	Prenatal	Abdomen or lower lumbar region, pelvis or hips	ALL	0.46[a]	0.15–1.40
Ray (2010)	X rays and childhood cancer	Canada, Ontario	1,835,517 mother-child pairs 5,590 of whom had prenatal X-rays, children 0–15 y	April 1991–March 2008	Different databases	CT or NM during pregnancy till day before birth	Prenatal	All (non-specified)	All tumor types	0.68[b]	0.25–1.80

Rajaraman (2011)	X rays and childhood cancer	England and Wales	2,690 cases <15 y, 4,858 controls 0–15 y	1992–1996	Hospital records, interviews	X ray yes vs. no (incl CT)	Prenatal	All (non-specified)	Leukemia overall	1.36[a]	0.91–2.02
									ALL	1.2[a]	
									AML	2.44[a]	
									any pediatric malignancy	1.14[a]	
									non-Hodgkin	1.48[a]	
									brain/CNS	1.06[a]	
									Sarcoma	1.13[a]	
									peripheral neural tumors	1.00[a]	
									renal	1.64[a]	
0.76–1.88											
0.95–6.33											
0.90–1.45											
0.66–3.32											
0.64–1.77											
0.49–2.61											
0.37–2.67											
0.48–5.59											
Milne (2014)	X rays and brain tumors	Australia	8 cases, 14 controls	2005–2010	Parent questionnaires	Radiological procedure	Prenatal	pelvis, hips, lower back, abdomen or kidneys	Childhood brain tumors (CBT)	1.71[a]	0.69–4.23
Tettamanti (2017)	X rays and brain tumors	Denmark, Norway, Sweden and Switzerland	352 cases 7–19 y, 646 controls 7–19 y	January 2004–31 August 2008	Different databases	No of x rays	Prenatal	Any or abdomen	Brain tumor	0.96[a]	0.54–1.68

[a]OR [b]HR

FOV. When the abdomen is in the FOV, the ALARA principle (As Low As Reasonably Achievable) must be adhered to, meaning the dose must be optimized.

DISCUSSION

The main issue when researching an increased risk of a form of pediatric cancer is the low incidence of pediatric cancer. The overall incidence for all types of cancer in children together is 2 to 3 per 1,000 children (Kaatsch 2010; Arrouas and Ditto 2017). As a result, even large cohort studies such as Ray et al. (2010) find it almost impossible to locate a large enough group of prenatally exposed children to determine a significant risk increase. Therefore, most of the studies use a case control design. In addition, as it will take many years for cancer to develop, a very long follow-up is required, making case control studies generally unsuitable. So far, only the Life Span Study (LSS) and the Oxford Survey of Childhood Cancer (OSCC) have completed such a long term follow up period.

Recent studies based on the LSS do find a significant risk, for example in the Preston et al. (2008) study. In this study, an excess relative risk (ERR) of 1.0 per Sv, 95% CI = 0.2–2.3 per Sv at age 50 y is found. Most of the current guidelines are based on the numbers found in the LSS and OSCC. These have the largest cohorts and longest follow-up. However, the exposure in these studies is much higher than in many of the recent studies based on exposure due to diagnostic x-ray examinations.

Another issue is that most studies have obtained the data by means of interviews with the parents. The problem here is the so-called recall bias. How reliable is the data that parents provide? Do they still know exactly what kind of examination it was, when it occurred, and if shielding and/or a reduced dose was applied? The studies using hospital data such as Ray et al. (2010), Tettamanti et al. (2017), and Rajaraman et al. (2011) are more reliable in that aspect. Nevertheless, these studies also do not have access to the exact fetal dose, which makes it impossible for these studies to provide exact risk numbers.

Another question that has not been clarified is the association between prenatal exposure and the type of cancer. The association between leukemia and prenatal exposure has been demonstrated in multiple studies, as shown in Fig. 1 with both significant results and non-significant results. The Wakeford (2008) review only displays results for leukemia in general. To be able to compare these results correctly with later studies, further division into subtypes is necessary.

The Grufferman et al. (2009) study shows a significant association between prenatal exposure and rhabdomyosarcoma. However, this is the only study that has

Table 3. Rendition of adjusting factors.

	Study								
Adjusted for	Stalberg (2007)	Goel (2009)	Grufferman (2009)	Bartley (2010)	Bailey (2010)	Ray (2010)	Rajaraman (2011)	Milne (2014)	Tettamanti (2017)
Gender child			x	x	x	x	x	x	
Ethnicity child			x	x					
Age		x	x		x			x	
Age in years at moment of diagnosis				x			x	x	
State (VS)/region		x			x		x	x	
Birth order	x				x			x	
Education level parents								x	x
Education level mother		x			x				
Age father at birth									x
Age mother at birth	x				x	x	x		x
Income		x				x		x	
Urban residence						x		x	
Mother diagnosed with cancer during pregnancy or within 6 months after delivery						x			
Chromosomal or congenital anomalies						x		x	
Any major radiodiagnostic examination exposure after birth						x		x	
Length of pregnancy	x		x					x	
Type of delivery	x		x						
Spotting during pregnancy			x						
Cramping during pregnancy			x						
Abnormal vaginal bleeding during pregnancy			x						
Birth weight	x						x		
Ethnicity mother	x							x	
Birth location	x								
High blood pressure during pregnancy	x								
Breech position	x								
Head circumference	x								
Maternal alcohol use during pregnancy								x	
Maternal alcohol use 12 months before pregnancy								x	
Maternal folic acid supplementation 1 mo before pregnancy								x	

examined this association, leaving no other that can confirm this connection.

All studies containing adjusted risks identified different confounding factors. As shown in Table 2, the overlap is almost nil. It will require research to determine which factors really are of influence so that the results found can be adjusted and compared. The influence of birth weight, among others, is complex. A low birth weight has an underlying cause and will require diagnostic x-ray examinations at a young age. Both the examinations as well as the underlying cause increase the risk of developing a malignancy. Babies with a higher birth weight, however, also have an increased risk of developing childhood malignancy, as is evidenced by the Wakeford and Bithell study (2015).

The mother's exposure during pregnancy to other agents such as tobacco and pesticides is not taken into consideration in these studies, and so these can act as confounding factors.

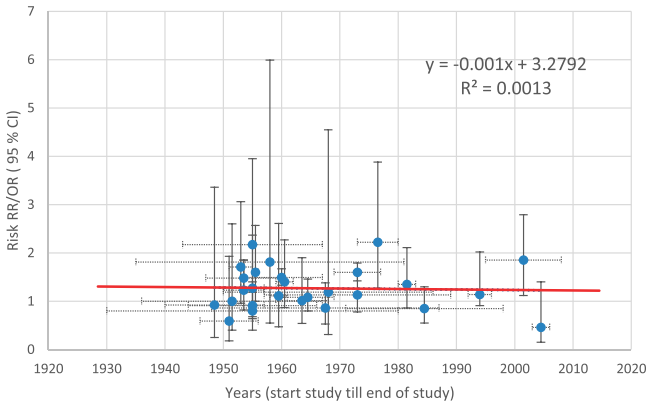

Fig. 1. Risk markers for leukemia from the studies described in the publications of Schulze-Rath et al. (2008), Wakeford (2008), and the present study (Stewart et al. 1956; Bartley et al. 2010; Tettamanti et al. 2017; Golding et al. 1992). The expectation was that recent studies would cause a downward trend due to improved equipment, or an upward trend would be visible through the advent of CT; however, both are not visible.

None of the studies in this review provide a risk coefficient per mSv, which is necessary for an accurate risk assessment. This is due to the fact that the studies only looked at whether or not exposure occurred and, if possible, the frequency of exposure. More exact information is not available when using interviews, and hospital data in these studies was insufficient to determine this. When the risk per Sievert is known, studies with different fetal doses can be (accurately) compared.

Fig. 1 shows that over the years, there is no downward trend line visible in the found risk relating to leukemia. Despite the reduced dose, due to the use of improved techniques and newer equipment, it does not show a visible result in the form of a declining risk. The International Agency for Research on Cancer (IARC 2012) gives prenatal exposure to x rays as a risk marker for developing cancer. With this conclusion, they rely in particular on older studies such as those performed by the OSCC. Improved and new techniques, and techniques with higher doses such as CT scans, cannot be compared to those older studies. The guidelines provide risk coefficients, but there is no consensus; the numbers are also based on older studies.

The question whether a fetus is more or less radiosensitive than a child has been around for many decades (Brent 2015). With an equal radiosensitivity, the results of postnatal studies can be used to determine the risk to the fetus. Several studies find a significantly increased risk of developing a malignancy with postnatal exposure (Bartley et al. 2010; Pearce et al. 2012; Mathews et al. 2013; Kutanzi et al., 2016; Meulepas et al. 2016).

The Nakano et al. (2014) study, however, shows that mice irradiated in utero have genetically less DNA translocations in peripheral T-irradiated blood cells, spleen cells, and bone marrow cells when compared to mice that were irradiated postnatally. The frequency of these translocations was 0.8% vs. 5% for prenatal irradiation versus postnatal radiation. Nakano et al. (2014) suggests that in the fetus, the abnormal cells with translocations were replaced by stem cells.

If this repair mechanism also exists in humans, it can be concluded that a fetus is less radiosensitive than a child, which is fitting with the limited significant evidence for an increased risk of malignancy due to prenatal irradiation in this review. In this respect, the Rajaraman et al. (2011) results with regard to exposure of a child of less than 100 d old, which show no increased risk in malignancies, are interesting for follow-up research.

The probability of, after prenatal radiation exposure, a child being born without malformations and without severe mental retardation, or of a child not developing childhood (0-15 years) leukemia or cancer.		
Uterus dose (mGy or mSv)	Probability of a child being born without malformations and without severe mental retardation	Probability of a child not developing childhood (0-15 years) leukemia or cancer
0	96.5%*	99.75%**
1	96.5%	99.74%
5	96.5%	99.71%
10	96.5%	99.67%
20	96.5%	99.59%
30	96.5%	99.51%
50	96.5%	99.35%
100	96.5%	98.95%
* A rate of 3% was assumed for spontaneous malformations and 0.5% for severe mental retardation ** Spontaneous rates for leukemia and childhood cancers (0 to 15 years) were assumed to be 0.25%		

Fig. 2. Table translated from Schwangerschaft und Röntgenuntersuchungen (Arrouas and Ditto 2017). This indicates the probability that the exposed fetus receives no malformations, severe retardation, or leukemia or cancer through exposure compared to the natural incidence of such events.

In the Wakeford (2008) review, studies are included in which a similar dose is incurred through non-medical exposure. Schulze-Rath et al. (2008), however, did not include these exposures. Schuz et al. (2017) and Akleyev et al. (2016) published two studies on the effects of the in-utero dose received by mothers in the Urals who worked at the Mayak Production Facility or lived near the Techa river. Using different calculation models, this study calculated the dose in utero as closely as possible, dividing the mothers into dose groups of 1–4 mGy and higher. Both studies find no significant evidence for an increased risk of hematological or solid malignancies. Despite the lack of significant evidence, both studies conclude there is a weak connection and ascribe the lack of significance especially to the small number of cases included in the studies.

Despite that there are only a small number of studies that show significant evidence of an increased risk in developing a malignancy, all guidelines advise restraint in the use of radiodiagnostic procedures of the abdomen. Above all, CT scans are not recommended except in trauma situations and when there is a suspicion of pulmonary embolism. With regard to information to the patient, most guidelines only provide a risk coefficient.

Exceptions here include the Ministry for Frauen Gesundheit (Arrouas and Ditto 2017) and the ICRP 84 (IRCP 2000); in the table in Fig. 2, these show how likely it is that the child will have no effects due to the exposure. Information in which both the risk coefficient and the likelihood that the exposed fetus will not be affected by exposure are included should be available and mentioned in combination with the baseline risk of developing malignancy. By combining this information, patients can better understand the numbers that will make it easier for them to decide whether to undergo the exam or not.

CONCLUSION

The goal of this review was to provide insight into the most recent knowledge about the risks of prenatal exposure to diagnostic x-ray examinations and the international guidelines.

In comparison to the Wakeford (2008) and Schulze-Rath et al. (2008) studies, less statistically significant results are found in this review. Not a single study in this review has found significant results for the development of brain tumors as a result of prenatal exposure. Significant results for leukemia are found in several studies as shown in Fig. 1.

Grufferman et al. (2009) does show a significant risk for the development of rhabdomyosarcoma after prenatal exposure to x rays. A side note here is that the number of cases is very low.

The guidelines all use risk numbers from older studies; the highest risk coefficient used is that for developing a malignancy after prenatal exposure at 30 mGy, in which the risk is twice as high (Arrouas and Ditto 2017). All guidelines indicate that x rays outside the abdomen do not present a risk. Radiodiagnostic abdominal examinations are justified if there is no alternative and it is necessary and urgent. CT scans of (or in the neighborhood of) the abdomen are not recommended with the exception of trauma situations and suspected pulmonary embolism.

In the case of a radiodiagnostic examination of the abdomen, pregnancy should be confirmed with a pregnancy test when in doubt. All guidelines require the use of patient information, using extra attention to put the risk numbers into context by using the risk numbers for the baseline occurrence of malignancy in children.

It is important to realize that the results found in this and previous reviews result from up to three radiodiagnostic examinations, and likely the dose remained under the 50 mGy limit. This is the limit below which no detectable non-carcinogenic effects occur; the ICRP even uses a 100 mGy limit. In the case of repeat examinations, the dose may exceed the 50 mGy level, and it may be possible for non-carcinogenic effects to occur.

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