Are pre- or postnatal diagnostic X-rays a risk factor for childhood cancer: a systematic review

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CRD summary
This review of epidemiological research found no evidence of an increased risk of childhood cancer from low-level intrauterine and postnatal radiation exposure. This was a suitably cautious conclusion given the limitations of the study designs, but the review was limited by potential language bias and a lack of detail about the review methods.

Authors’ objectives
To evaluate whether exposure to ionising radiation from diagnostic X-rays during pregnancy or early childhood is a risk factor for childhood cancer.

Searching
PubMed was searched from January 1990 to December 2006. Search terms were reported. Also searched were Current Contents, The Cochrane Library, Scirus, MEDPILOT, Deutsches Medizin-Forum and kinderkrebsinfo.de. Reference lists and two key journals in the field were searched. Only studies published in English were included.

Study selection
Cohort and case control studies of children (less than 18 years) or pregnant women that investigated exposure to low doses of ionising radiation for diagnostic reasons were eligible for inclusion if the studies reported epidemiological risk estimates. Eligible outcomes were risk of all solid tumours, tumours of the central nervous system, lymphomas and leukaemia. Studies of treatment for non-malignant diseases such as haemangioma were not included.

X-ray exposure dates in the included studies ranged from 1920 to the 1990s. Recruitment periods ranged from 1936 to 1998. Studies assessed either prenatal and/or postnatal exposure to X-rays and the risk of one or more of leukaemia, non-Hodgkin lymphoma, solid or central nervous system tumours and unspecified childhood cancer. X-ray exposure was assessed by standardised parental interviews, hospital records and a cancer registry.

The authors did not report how many reviewers performed the study selection.

Assessment of study quality
Validity was assessed using the criteria: estimation of individual radiation dose; description of confounders; and reported study strengths and limitations.

The authors did not report how many reviewers performed the validity assessment.

Data extraction
Odds ratios (OR) and 95% confidence intervals (CI) were estimated for each case-control study. If only adjusted odds ratios were reported in the study, these were extracted. Results were extracted from the cohort studies as reported, because different measures were used: standardised incidence ratios (SIR); standardised mortality ratios (SMR); and relative risks (RR).

The authors stated neither how data were extracted for the review nor how many reviewers performed the extraction.

Methods of synthesis
Studies were grouped by pre- or postnatal exposure and by cancer type. If there were at least five studies in one of these groups, they were pooled using a random-effects model. Heterogeneity was assessed with a $X^2$ test ($p<0.05$ indicated statistical heterogeneity). Publication bias was assessed using funnel plots.
Results of the review
Nineteen case-control (n=17,725) and six cohort studies (n=approximately 49,000 with 134 diagnosed cancers) were included.

Case-control studies: Nine studies assessed the effect of prenatal X-rays on leukaemia and found no association (pooled OR 0.99, 95% CI 0.87 to 1.13) and little heterogeneity between studies ($I^2=0\%$). The funnel plot indicated some evidence of publication bias. There was no association observed between prenatal X-rays and solid tumours (three studies), central nervous system tumours (four studies) and non-Hodgkin lymphoma (three studies). Four studies reported inconsistent results for postnatal X-rays and leukaemia (two significantly increased odds, one significantly decreased and one no association). There was no association observed between postnatal X-rays and solid tumours (three studies), central nervous system tumours (four studies) and non-Hodgkin lymphoma (two studies).

Cohort studies: One study assessed prenatal X-rays and childhood cancer and found a significantly reduced risk (SIR 0.7, 95% CI 0.5 to 0.9). One study found no association between postnatal X-rays and cancer risk, but one reported an increase in risk over all cancer sites (SIR 2.3, 95% CI 1.2 to 4.1). Two studies found no association between postnatal use of diagnostic iodine-131 and risk of thyroid cancer. One large study found an increased risk of breast cancer after postnatal X-rays for scoliosis diagnostics in girls (SMR 1.7, 95% CI 1.3 to 2.1), but no association with leukaemia.

Authors' conclusions
There was no clear evidence for an increased cancer risk after low-level intrauterine and postnatal radiation exposure, but this did not mean that there was no risk and the results should be viewed alongside larger, earlier studies that indicated increased risk.

CRD commentary
This review had a clearly stated research question and specified the inclusion criteria for study design, population, exposure and outcomes. The search covered a number of databases, but only including studies published in English put the review at risk of language and publication biases. The authors concluded that publication bias was possible, but they highlighted the difficulties of searching for epidemiological literature. It was stated that validity was assessed; details for each individual study were not reported, but the authors highlighted the quality of the evidence as a limitation. The presentation of results grouped by study design and cancer type was clear. In the one case where a meta-analysis was performed the methods were appropriate. The main drawback of this review was the lack of reporting of the review methods; without information about how many reviewers undertook the study selection, data extraction and validity assessment it was unclear whether the authors took steps to minimise the risk of reviewer error or bias. The authors conclusions are suitably cautious based on the data presented, but this review is limited by the lack of detail about the review methods and potential language bias.

Implications of the review for practice and research
Practice: The authors stated that continued efforts were needed to reduce doses and the number of radiological investigations in childhood.

Research: The authors stated that future studies that assessed cancer risk with computed tomography were needed.

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