Environmental and lifestyle factors affecting cancer risk in children and young people – epidemiology and mechanistic understanding

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Recent years have seen remarkable advances in understanding the role of environmental and lifestyle factors affecting the risk of childhood leukaemia and possibly brain tumours, partly driven by increasing incidence rates that cannot be explained by improvements in diagnosis or registration alone. At the same time, the aetiology of other individual cancers in children and young adults (0–24 years) remains largely unknown and under-researched.

Perhaps half of childhood cancers initiate *in utero*. Acute lymphoblastic leukaemia, or common ALL is frequently associated with a chromosomal translocation creating the *ETV6-RUNX1 (TEL-AML1)* fusion gene present at birth, but only a small proportion (perhaps 1 in 100) of children born with this defect contract leukaemia, suggesting that the disease is at least a two-hit process. Brain tumours may also originate *in utero*, but whether this occurs in cancers arising postnatally in persistent embryonal cells, such as Wilm's tumour and Neuroblastoma, is questionable.

The rarity of these cancers creates severe challenges for the design of epidemiological studies. Adequate statistical power is often only achieved with pooled analyses of international studies. A particular difficulty is how to quantify exposure to putative causal agents be they radiation, chemical or infectious. Retrospective exposure involving historic cases is often crudely based on surrogate measurements or self-reported questionnaires. Increasingly, studies are using biomarkers of exposure, providing specific indicators of DNA damage from carcinogens notably in air pollution and diet. It may be that information on environmental exposures and lifestyle factors could be usefully gained at the point of diagnosis of childhood cancer.

Overall, epidemiologists and laboratory scientists need to work far more closely together to determine relevant exposure metrics and how they can be incorporated in epidemiological studies.

Medical science, however, will never give us true 100% proof of cause. Instead, cause is a matter of consensus. The International Agency for Research on Cancer, IARC, for example, uses highly structured procedures to determine carcinogenicity or otherwise, drawing on the findings of epidemiological and animal studies as well as mechanistic understanding.

For childhood cancer, Tables 1 & 2 testify to the multi-factorial nature of environmental and lifestyle factors associated with both increased and decreased risk. The strength of evidence varies widely. Ionising radiation is an established cause of childhood leukaemia. An association with pesticides is acknowledged but an association with air pollution though less well-known is strongly supported mechanistically. An association with power frequency magnetic fields is robust with increasing mechanistic understanding, but the effects of melatonin and circadian rhythm disruption has received less attention. Reports of protective factors are encouraging, not least because of the apparent magnitude of the effect.

Understanding these risks may lead to steps to reduce exposure to harmful agents and at the same time inform public health messages of lifestyle changes that may result in reduced risk of cancer in children. Potential causal factors for cancer in young people (age 15–24) have received much less attention and here much more research is needed.

Table 1. Environmental exposures and lifestyle factors associated with childhood cancer risk

Agent/activity	Which cancers?*	Overall link**	IARC category
Air pollution, notably from vehicle exhausts [this symposium]	All cancers as a group; leukaemia, brain & neuroblastoma in some studies	~30% with childhood ALL.	Group 1, including Group 1 chemicals
Pesticides & solvents in childhood, pregnancy; occupational paternal pre-conceptional exposure	Leukaemia & brain tumours	No quantitative estimate	Mainly Group 2A or B, some Group 1, and some Group 3
Mother's diet in pregnancy Child's diet	EU NewGeneris - cord blood DNA damage from dietary carcinogens. Brain tumours	No quantitative estimate	Acrylamide & glycidamide, Group 2A
Light-at-night (LAN), melatonin and circadian rhythm disruption	Potential effect on risk but research in its early stages	No quantitative estimate	Group 2A
Paternal pre- & peri-natal smoking	Leukaemia	No quantitative estimate	Group 1 for adult smoking
Background ionising radiation including radon gas	Leukaemia	15-20%, includes 5% from radon	Group 1
Paediatric X-rays & particularly CT scans	Leukaemia and high-grade glioma (brain tumour)	Unknown, but CT X-ray doses very high	Group 1
Magnetic fields associated with the electricity supply	Leukaemia	5% based on WHO estimate	Group 2B
Mobile phones & modern communication devices	Brain tumours	Unquantified, but suspected association	Group 2B
Maternal diabetes & obesity	ALL & Wilms' tumour (diabetes); leukaemia (obesity)	No quantitative estimate	–

Table 2. Potential protective factors for childhood cancer risk

Agent/activity	Which cancers?*	Reduced risk?**	Actionable?
Attendance at day-care in infancy – an assumed surrogate for early exposure to everyday infections which boost the immune system	Leukaemia	20% or more?	Yes, but costly
Healthy diet: both mother's diet in pregnancy and in early childhood	Leukaemia	20% or more?	Low cost, implementation a matter of education
Breast feeding (>6 months)	Leukaemia & lymphoma	20%	Breastfeeding rates are low in the UK
Pet ownership; Regular contact with farm animals in infancy	Leukaemia	Up to 50%?	Yes, but may be impractical
Socio-economic status	Inverse ALL relationship with SE status	20%	

*Reflects those cancers for which research has been carried out. **Refers to overall effect on UK incidence. Estimates are likely subject to wide margins of error.