INFECTIOUS CAUSES OF CHILDHOOD CANCER

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It is estimated that at least 20% of the global burden of cancer is linked to infectious agents. Roughly one quarter of cancer deaths in developing countries, and almost 10% in developed nations, is associated with infections caused by viruses, bacteria or trematodes.

Identifying infectious causes of cancer is not straightforward. The latency period may last for decades, the infectious agents are not synthesised within cancer cells, most infections linked with cancer are universal with only a small proportion resulting in malignant transformation, while chemical and physical mutagens may also be required. Establishing disease-pathogen associations relies upon both epidemiological and molecular biology tools. Infectious agents can act directly by promoting or expressing oncogenes or inducing chromosomal instability within host cells. Alternatively, they may act indirectly by inducing mutations from oxidative stress secondary to chronic inflammation. Host factors, such as immune status, and environmental exposures to physical agents, including aflatoxins, alcohol or high concentrations of salt, can also play a role.

The five most common causes of cancer associated with infectious agents are the Epstein-Barr virus, hepatitis B + C, human papillomaviruses and *Helicobacter pylori*. Most infections caused by these ubiquitous pathogens begin in childhood or adolescence. Effective vaccines are available for hepatitis B and ‘high-risk’ human papillomavirus types 16 and 18. Already, within two decades of introducing universal hepatitis B vaccination there is evidence for reduced hepatocellular cancer rates amongst children from populations at increased risk of liver cancer.

Leukaemia is the most common childhood cancer. A two-step ‘hit’ hypothesis, not unlike that for asthma, has been proposed as an underlying mechanism for causing acute lymphoblastic leukaemia. This involves pre-leukaemic clones being formed ‘in-utero’, then an abnormal or delayed pattern of exposures to infectious agents resulting in dysregulated T-cell responses and malignant transformation of a pre-leukaemic clone.

Future studies may demonstrate additional links of infectious agents with the development of cancer, including studies helping to clarify the aetiology of childhood leukaemia. This information would likely have a profound effect upon the diagnosis, treatment and prevention of cancer in children as well as adults.