

30 days in medicine

Childhood leukaemia possibly preventable by early exposure to infections

Acute lymphoblastic leukaemia (ALL) is the most common childhood cancer in developed countries, affecting one in 2 000 children up to the age of 15 years, and is growing in incidence at 1% a year. Because of its epidemiology there has been a suspicion that infection, or an abnormal response to infection, plays a causal role. Now research has shown that the disease is caused by a two-stage process of genetic mutation and may be preventable.

It appears that two genetic changes, the first of which occurs in the womb, are responsible. The first change, found in 5% of newborns, makes the immune system more susceptible to react to routine infections after birth with a poorly regulated inflammatory response, causing a second genetic change, which in turn causes the disease. This second change only causes disease in children who have been raised in environments relatively free of bacteria. When these children are later faced with a pathogen such as the flu virus, the second change takes place, which leads to ALL. The absence of exposure to infections before the age of 1 year prevents the immune system from functioning correctly later, explaining why ALL is a disease of affluence and almost unknown in poorer countries, why it is usually seen in firstborns and why cases arise in clusters.

Greaves M. A causal mechanism for childhood acute lymphoblastic leukaemia. *Nat Rev Cancer* 2018 (epub 21 May 2018). <https://doi.org/10.1038/s41568-018-0015-6>

Seven in 10 women with breast cancer do not need chemotherapy

Most women with early-stage hormone receptor-positive breast cancer do not need chemotherapy as well as endocrine therapy after surgery if tests with a 21 tumour gene expression assay (Oncotype DX) are in the mid-range for risk of recurrence. This is the finding of a large randomised trial published recently in the *New England Journal of Medicine*.

The study, from the US National Cancer Institute, included 10 273 women with hormone receptor-positive, HER2-negative, axillary node-negative early-stage breast cancer. Of the 9 719 patients with follow-up information, >69% had a mid-range score when tested with

Oncotype DX. These women were randomised to treatment with chemotherapy plus endocrine therapy or to endocrine therapy alone. At 9 years, 83.3% of patients treated with endocrine therapy alone were free from breast cancer compared with 84.3% of those treated with chemotherapy and endocrine therapy. In addition, both groups had similar rates of freedom from distant site recurrence. Further analysis showed that women aged ≤ 50 years and with a risk score of 16 - 25 were more likely than others to benefit from the addition of chemotherapy.

Sparano JA, Gray RJ, Makower F, et al. Adjuvant chemotherapy guided by a 21-gene expression assay in breast cancer. *N Engl J Med* 2018 (epub 3 June 2018). <https://doi.org/10.1056/NEJMoa1804710>

Years of education linked to risk of myopia

The prevalence of myopia is increasing rapidly, and it is one of the leading causes of visual disability worldwide. Currently, 30 - 50% of adults in the USA and Europe are myopic, with levels of 80 - 90% reported in school leavers aged 17 or 18 years in Singapore, South Korea, China and other high-income Eastern and Southeast Asian countries. A recent study published in the *British Medical Journal* suggests that exposure to more years in education contributes to the rising prevalence of the condition.

Using a mendelian randomisation study, the researchers looked at 67 798 men and women from England, Scotland and Wales with the UK Biobank cohort, for whom information on years of completed education and refractive error was available. They found that every additional year of education was associated with a more myopic refractive error of -0.18 dioptres per year. The cumulative effect of more years in education on refractive error means that a university graduate in the UK with 17 years of education would, on average, be at least -1 dioptre more myopic than someone who left school at age 16 (with 12 years of education). This is enough to need glasses for driving.

Mountjoy E, Davies NM, Plotnikov D, et al. Education and myopia: Assessing the direction of causality by mendelian randomisation. *BMJ* 2018;361:k2022. <https://doi.org/10.1136/bmj.k2022>

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