

associated with diarrhoea (0.72, 0.57 - 0.91). Vitamin A supplementation was associated with a reduced incidence of diarrhoea (0.85, 0.82 - 0.87) and measles (0.50, 0.37 - 0.67) and a reduced prevalence of vision problems, including night blindness (0.32, 0.21 - 0.50) and xerophthalmia (0.31, 0.22 - 0.45). Three trials reported an increased risk of vomiting within the first 48 hours of supplementation (2.75, 1.81 - 4.19).

They concluded that vitamin A supplementation is associated with large reductions in mortality, morbidity and vision problems in a range of settings, and these results cannot be explained by bias. Further placebo-controlled trials of vitamin A supplementation in children between 6 and 59 months of age are not required. However, there is a need for further studies comparing different doses and delivery mechanisms (for example, fortification). Until other sources are available, vitamin A supplements should be given to all children at risk of deficiency, particularly in low- and middle-income countries.

Mayo-Wilson E, et al. *BMJ* 2011;343:d5094.

Modern cigarettes linked with more bladder cancer

We've long known that smoking is the most important modifiable risk factor for bladder cancer. A new study quantifies the excess risks in contemporary populations. Nearly half a million US citizens in the National Institutes of Health Diet and Health Study cohort reported their smoking habits and were then followed up over 11 years. During that period new bladder cancer was recorded in about 4 500 participants.

Compared with people who had never smoked, those who had reported smoking regularly had a fourfold increased risk of bladder cancer, with a number needed to harm of 727. The risk was doubled in former smokers compared with never smokers; for every 1 250 former smokers, one extra bladder cancer was diagnosed.

About half of all bladder cancers could be avoided among both men and women if everyone stopped smoking. This contrasts with earlier studies, where the population attributable risk of bladder cancer for tobacco smoking was estimated at 50 - 65% in men and 20 -30% in women. As these studies



had found weaker associations between smoking and bladder cancer, the researchers hypothesise that changes in cigarette design may account for the differences. Modern cigarettes contain less nicotine and tar, but are richer in some known bladder carcinogens, such as β -naphthylamine. Better detection efforts among smokers could also explain the stronger association.

The US Preventive Services Task Force recently reviewed the evidence on screening for bladder cancer in asymptomatic adults (*Ann Intern Med* 2011;155:246-251). The evidence was deemed insufficient to assess the balance of benefits and harms.

Freedman ND, et al. *JAMA* 2011;306:737-745.

BRIDGET FARHAM

SINGLE SUTURE

Cause found for ambiguous genitalia

A sexual development disorder in baby boys may be due to the absence of a hormone-production pathway identified in wallabies. The finding could help to diagnose cases of ambiguous genitalia.

One in 4 500 babies has gene mutations that disrupt normal development of testes or ovaries in the womb. These children can be born with external genitalia that do not look typically female or male.

In humans, normal development of the testes relies on testosterone and dihydrotestosterone (DHT). The latter is the more potent and is produced when testosterone is broken down.

Wallabies and some rodents are known to be able to make DHT via two different routes, one of which bypasses testosterone completely. The process works by converting cholesterol, the precursor to testosterone, directly into DHT.

To find out whether a similar 'back door' pathway exists in humans, Anna Biason-Lauber and her colleagues at the University Children's Hospital Zurich in Switzerland investigated the genetic make-up of a family, three of whom have ambiguous genitalia. As these individuals were all able to produce DHT from testosterone, multiple attempts to diagnose the cause of their symptoms had failed.

Biason-Lauber's team screened all the family members for mutations in four genes - *AKR1C1* to *AKR1C4* - known to be involved in producing DHT from cholesterol in the wallaby. They found that two of the genes were mutated only in the three affected individuals, suggesting that they were unable to make DHT using this pathway.

Further screening of 34 people with similar disorders revealed a mutation in one of these genes in four of them.

'This unique, newly described form of developmental sexual disorders establishes that the back door pathway is essential for normal male sexual development,' says Biason-Lauber.

'It certainly could explain some of the undiagnosed patients,' says Jacky Hewitt at the Murdoch Children's Research Institute in Melbourne, Australia, who recently found that 43% of people with sex disorders do not receive a definitive diagnosis.

New Scientist 27 August 2011, p.10.