

European study reports passive smoking dangers

The results of a long-awaited European study on passive smoking by the International Agency for Research on Cancer (IARC), Lyon, France, show weak but measurable evidence of a dose-response association between lung-cancer risk and exposure to smoke from a spouse or in the workplace, thus adding weight to previous studies.

But the study failed to find an association between childhood exposure to passive smoking in the home and lung cancer. In addition, there was no detectable increase in risk in non-smokers who had not been exposed to smoke for 15 years or more, compared with non-smokers who had never been exposed (*J Natl Cancer Inst* 1998; **90**: 1440-50).

509 women and 141 men who had never smoked but had lung cancer and a control group of 1542 non-smokers without lung cancer were surveyed at 12 centres across Europe. They were asked about their exposure to environmental tobacco smoke

(ETS) during childhood, adulthood, at home, in the workplace, in vehicles, and in public places.

Paolo Boffetta and colleagues report that an increased risk of developing lung cancer is associated with any exposure to ETS in the workplace (odds ratio 1.17) or to a spouse's smoke (OR 1.16). Risk tended to increase with duration of exposure to ETS.

Previous studies linking passive smoking with lung cancer have been criticised for their small size or flawed methodology. But, in

an editorial, William Blot and Joseph McLaughlin (International Epidemiology Institute, Rockville, MD, USA) say that: "The results [of the IARC study] have been eagerly awaited because of the size of the study, the special attempts to minimize misclassification of cigarette smoking status and the ability to control for various potential confounding factors."

Karen Birchard



A hazard of the past

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Necropsy remains an important diagnostic tool

The results of a US study reveal a worrying 44% discrepancy between diagnosis of malignancies and necropsy findings.

Elizabeth Burton's team from New Orleans (LO, USA) studied 1105 necropsies done during 1986-96, identifying 433 tumours of which 250 were malignant. Of the malignant growths, 111 cancers were undiagnosed or misdiagnosed. 57 of the deaths in the people with undiagnosed cancer were directly related to the previously undetected malignancy. "The discrepancy we observed is high. This is alarming in the light of statistics that show the autopsy rate has declined from about 50% in the early 1960s to only 5-10% today", says Burton (*JAMA* 1998; **280**: 1245-48).

Necropsy rates have also been declining in the UK. 98% of UK necropsies are initiated by coroners; only 2% are done at the request of clinicians. Previous studies show that UK necropsies agree more often with pre-death

diagnoses than was recorded in the US study, and James Carmichael (Nottingham City Hospital, UK) is concerned by the size of the discrepancy in the study. "With more high-tech medicine, most clinicians feel confident with diagnostic techniques; this paper clearly shows something is failing but interpreting the data is not straightforward."

Because the patient population chosen by Burton had a low socio-economic status, a higher rate of discrepancy between diagnosis and necropsy findings might be expected than in a wealthier population. People not accessing the health care they need may be a major problem, and according to Burton, "in cases of suspected malignancy, a complete medical workup was initiated but often not completed because of patient mortality. Untangling the web of social and cultural factors involved would need another study", she concludes.

Kathryn Senior

Antibiotic swings and roundabouts

Cutting back on cephalosporin use causes a very rapid fall in bacterial resistance to these antibiotics, according to a US study.

In 1996, the 500-bed New York Hospital Medical Centre of Queens (Flushing, NY, USA) reduced the use of cephalosporin by 80%. The result was a 87% drop in the number of ceftazidime-resistant klebsiella infections in its intensive-care unit, and resistant klebsiella infections throughout the hospital were reduced by 44% (*JAMA* 1998; **280**: 1233-37). But the hospital's policy of using imipenem as its first-choice antibiotic instead of ceftazidime also produced an alarming side-effect—an increase in the resistance of *Pseudomonas aeruginosa* to imipenem from 8.9% in 1995 to 16.7% in 1996.

Gary French, professor of microbiology at St Thomas's Hospital (London, UK), comments that "it is an encouraging result that confirms the evidence we already have" that antibiotic use affects drug-resistance rates. But he was cautious about extending it to other resistant pathogens. "Plasmid-mediated resistance, such as klebsiella's resistance to cephalosporins, can disappear when the antibiotic is withdrawn", but chromosome-borne resistance is more stable, he explains, so the same effect might not occur with bacteria such as methicillin-resistant *Staphylococcus aureus*. In addition, the rapid rise of imipenem resistance following its increased use is "very dramatic and deeply worrying, particularly since imipenem is a last-line treatment for some pathogens", says French. Lead author James Rahal agrees that hospitals must constantly look at the evolution of antibiotic resistance among all their bacterial populations.

Peter Mitchell

Variant penicillin described

A team at Limerick University (Ireland) has designed a variant of the penicillin molecule able to kill penicillin-resistant bacteria. The variant contains a toxic S-amino-sulphenimine group activated only when a bacterium attempts to cleave the penicillin molecule with β -lactamase (Web edition of the *J Organic Chem* Oct 9, 1998; <http://pubs.acs.org/journals/joacah/index.html>).