Special Report: Policy
A review of human carcinogens—Part E: tobacco, areca nut, alcohol, coal smoke, and salted fish

In October, 2009, 30 scientists from 10 countries met at the International Agency for Research on Cancer (IARC) to reassess the carcinogenicity of tobacco, areca nut, alcohol, coal smoke, and salt-preserved fish, and to identify additional tumour sites (table) and mechanisms of carcinogenesis. These assessments will be published as part E of Volume 100 of the IARC Monographs.1

Tobacco smoking is the single largest cause of cancer worldwide. More than 1 billion people around the world are current smokers. New evidence continues to add to the extensive list of tobacco-related cancers (table); there is now sufficient evidence that tobacco smoking causes cancer of the colon1 and of the ovary.1 More than 150 epidemiological studies of tobacco smoking and breast cancer were reviewed. Large cohort studies1,5 published since 2002 consistently show a small positive association (relative risks 1·1–1·3). Many chemicals in tobacco smoke cause mammary-gland tumours in animals, and these carcinogens are stored in breast adipose tissue in women; therefore, the Working Group concluded that there is limited evidence that tobacco smoking causes breast cancer.

A causal link between parental smoking and childhood cancers has been established. Four recent studies showed that children born of parents who smoke (father, mother, or both, including the preconception period and pregnancy) are at significantly higher risk of hepatoblastoma, a rare embryonic cancer. The UK Childhood Cancer Study7 reported a relative risk of 1·86 for paternal smoking only and 2·02 for maternal smoking only, increasing to 4·74 (95% CI 1·68–13·35) when both parents smoke. For childhood leukaemia, a meta-analysis reported an association with paternal smoking before pregnancy (summary relative risk 1·12, 1·04–1·21).8

Second-hand smoke causes lung cancer.2 There is now limited evidence for an association with cancers of the larynx and the pharynx,9 whereas evidence for female breast cancer remains inconclusive. Since second-hand smoke contains most of the constituents of mainstream smoke, it might also be associated with other cancer sites.

Many types of smokeless tobacco are marketed and all contain nicotine and nitrosamines. Hundreds of millions of people use smokeless tobacco, mainly in India and southeast Asia, but also in Sweden and the USA. Earlier findings showed a causal association between use of smokeless tobacco and cancers of the oral cavity and pancreas, and there is now sufficient evidence for cancer of the oesophagus.10

All of the forms of tobacco discussed above induce malignant tumours in laboratory animals. Among the many carcinogens present in tobacco are nitrosamines, including the tobacco-specific nitrosamines 4-(methylnitrosamino)-1-(3-pyridyl)-1-butaneone.
A recent study by the Monograph Working Group, comprising experts from various countries, confirmed that betel quid chewing is carcinogenic to humans. This group concluded that areca-nut-derived nitrosamines, which are formed in combination with tobacco, are carcinogenic to humans and are responsible for several types of cancer, including those of the head and neck, stomach, and esophagus. The Working Group also reaffirmed the carcinogenicity of indoor emissions from households burning solid fuels, which is preventable at an individual level.

The Working Group concluded that tobacco smoking, second-hand smoke, and smokeless tobacco are all associated with the development of oral preneoplastic disorders with a high risk of progression to cancer. Tobacco smoke also contains carcinogens as combustion products, such as arylamines, polyaromatic hydrocarbons, and volatile organics. Many studies have investigated possible associations between polymorphisms in carcinogen-metabolising genes and tobacco-related cancers; most results are ambiguous, with the possible exception of NAT2 in bladder and breast cancers, and GSTM1 alone or in combination with CYP1A1 in lung cancer. Tobacco smoking, second-hand smoke, and smokeless tobacco were all reaffirmed as carcinogenic to humans (Group 1), along with NNK and NNN.

Salt-preserved fish is consumed in several regions around the world. Chinese-style salted fish causes cancer in the nasopharynx and possibly of the stomach, however, the mechanism of carcinogenesis is uncertain. Two hypotheses are nitrosamine formation and reactivation of Epstein–Barr virus. About half the world’s population, mostly in low-income and middle-income countries, uses solid fuels for cooking or heating, often in poorly ventilated spaces. Women and young children receive the highest exposure. The Working Group confirmed the carcinogenicity of indoor emissions from the combustion of coal as household fuel.

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2. IARC. Tobacco smoke and involuntary smoking. IARC Monogr Eval Carcinog Risks Hum 2004; 83: 1–1638.