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PERSPECTIVE

Tackling the real issues

Successful prevention requires attacking the causes, says **Stephen S. Hecht** — and the main target remains tobacco.

The best way to control cancer is to prevent it from happening. Data from the United States indicate that the age-standardized incidence of cancer continues to decrease in this century, mainly owing to decreases in the major cancers: lung, prostate and colorectal in men; breast and colorectal in women¹. Similar trends exist in other Western countries, although not in less developed or transitioning ones^{2,3}. These decreases are largely attributable to cancer prevention. Millions of lives have almost certainly been saved.

Unlike prevention of heart disease, which is now a commonly understood goal of a healthy lifestyle, the concept of cancer prevention gets little attention. Curing cancer is newsworthy and glamorous. Prevention is not. One can meet the survivors of childhood leukaemia or breast cancer and marvel at their good fortune. It is difficult to write an engrossing story of cancer about a person who did not get cancer in the first place.

We now know a great deal about the causes of common cancers — and the better we understand cause, the more able we are to conceive of effective preventive measures. Geographic and economic differences in cancer incidence and mortality are striking. Common forms of cancer vary greatly between high-income countries and low- to moderate-income countries^{2,3}. Wealthy countries are beset by high incidences of lung, breast, prostate and colorectal cancers. Migrants from one geographical area to another adopt the risk factors of their new

homes. Furthermore, the lifestyle habits of certain groups, such as Mormons and Seventh Day Adventists, lead to significantly lower cancer rates, in part because of their abstinence from tobacco and alcohol³. These facts unmask the role of lifestyle factors in the common cancers and illustrate the huge potential of cancer prevention (see *Breaking the cancer habit*, page S16).

Cigarette smoking, the cause of 90% of lung cancer, stands out as one of the best examples in which cause and prevention are intimately linked. Smokers are exposed to multiple DNA-damaging carcinogens and consequently have acquired multiple mutations in genes that control cellular growth⁴. They are also exposed to multiple tumour promoting substances and inflammatory agents that exacerbate the process. The addictive power of nicotine perpetuates the persistent exposure to these toxicants.

Effective tobacco control — led by clean air legislation, taxation, and anti-tobacco advertising — is contributing to decreased lung cancer incidence and in some Western countries. We can expand our preventive activities against tobacco-related cancer by achieving a better understanding of the biochemical, genetic and behavioural mechanisms of smoking. This knowledge could help us identify people who have a particularly high susceptibility to these cancers; we could then target those individuals for new prevention measures, such as a nicotine vaccination and chemoprevention.

We know less about major causes of breast, prostate and colorectal cancer. Estrogen is clearly involved in breast cancer aetiology and androgens are critical in prostate cancer development. Consumption of red meat cooked at high temperatures plays a role in colorectal cancer. We must expand our understanding of the causes of these cancers and translate it to cancer prevention strategies.

There are other significant and successful strategies for primary and secondary cancer prevention: vaccination and screening for cervical cancer; vaccination against hepatitis B and avoidance of aflatoxins for liver cancer; avoidance of excessive sunlight exposure for skin cancer; limiting alcohol consumption for head and neck cancer, and liver cancer.

Education and public outreach are critical. Here, we might emulate our colleagues in cardiovascular disease prevention research. There is a sharply increased awareness of the preventive power against heart disease of low-fat diets, cholesterol reduction (in part owing to statins), treatment of hypertension, exercise, and avoidance of tobacco. This awareness, along with improved medical care, has led to a significant reduction in deaths from heart disease — from about 320 deaths per 100,000 people (younger than 85 years) in 1975 to 130 deaths per 100,000 people in 2006. This almost 60% drop in mortality rate far exceeds the 11% decrease in the rate of cancer deaths (from 180 to 160 per 100,000 people) over the same period¹.

As we allocate research resources on the life-saving potential of cancer prevention, we need to keep in mind the prime importance of lifestyle factors in cancer aetiology, and continue to support studies to better understand the specific causes and mechanisms of common cancers. We need to identify susceptible individuals and target them for preventive interventions, including chemoprevention using non-toxic or dietary agents with demonstrated efficacy. We should not be distracted by fleeting, flamboyant approaches that take us off the main task of dealing with the lifestyle factors that link cause and prevention. ■

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3. Boyle, P. & Levin, P. *World Cancer Report*, 2008. (IARC, 2008).
4. US Department of Health and Human Services *How Tobacco Smoke Causes Disease*, 221–353 (DHHS, 2010).