

neoplasia by testing for the high risk virus types which have been associated with lesions which progress to high grade cervical intraepithelial neoplasia and carcinoma. The hope is that further elucidation of the molecular mechanism that leads to high grade cervical intraepithelial neoplasia will identify those features of viral expression and integration, as well as the aberrations of cellular oncogenes or tumour suppressor genes, that are relevant to progression to carcinoma.

### Understanding and preventing tumour progression

Carcinogenesis is a multistage process. The first stage is known as initiation and is followed by one or more promoting events. Many potentially carcinogenic agents are present in our diet and environment.

Little is known about the factors that govern the fate of precancerous lesions and determine whether a cancer develops and progresses. With cigarette smoking, components of the smoke are thought to promote development of lung cancer in the later stages of carcinogenesis. This tumour progression phase can be retarded by stopping smoking, however long ago the habit was established. In the future, modifications in diet or hormonal status may also be effective in suppressing proliferation and thereby preventing progress to cancer in subjects with precancerous lesions of particular tissues or in those in a high risk group for cancer development.

Central to progress is the need for a clear understanding of the complex biology of the early stages of cancer development and progression. Mechanisms responsible for the control of normal proliferation and differentiation of the various cell types in the body will allow a greater insight into the abnormal growth of malignant cells. Much more needs to be done to identify potential promoting agents for the common cancers and thus the means for intervention in the process of tumour progression.

Over the past decade the emergence of a more

coherent picture of the molecular progression of epithelial carcinogenesis from initiation to promotion has provided the opportunity for developing rational approaches to cancer control. The use of biomarkers, defined as morphological or molecular alterations occurring between initiation and tumour invasion, can have a number of applications for the management of individuals with cancer, or those at risk of developing cancer. A single biomarker, or panels of biomarkers, when rationally assembled, may be used to establish the state of a tissue and provide a clear picture of the state of cancer progression. Biomarkers can be used to help elucidate questions of aetiology and pathogenesis of disease and to refine the understanding of the relations between exposure variables and disease outcomes. Biomarker analysis could also be used in a variety of other cancer related applications, including risk (or susceptibility) assessment, early detection, prognostic discrimination, and disease progression, as well as intermediate end point determination of whether there is progression—for example, in prevention trials which require prolonged follow up.

1 Pike MC, Forman D. Epidemiology of cancer. In: Franks LM, Teich NM, eds. *Introduction to the cellular and molecular biology of cancer*. Second edition. Oxford: Oxford University Press, 1991:49-97.

2 Doll R, Peto R. *The causes of cancer*. Oxford: Oxford University Press, 1981.

The concluding part of this article will be published next week.

### Correction

#### Screening for cervical cancer

An editorial error occurred in this article, the seventh in the series on cancer prevention in primary care by Joan Austoker (23 July, pp 241-8). The first sentence in the penultimate paragraph under the heading "Interpreting and managing results of smear tests" should have read: "In practice, mild and moderate dyskaryotic smear test results do not correlate well with the histological diagnosis of mild or moderate dysplasia—that is, grade I or II cervical intraepithelial neoplasia."

## A MEMORABLE PATIENT

### "I'm willing to come for your research"

The surgeon's interview with patient and spouse after cancer surgery usually has a rare blend of intimacy, tension, and poignancy. This one was no exception. The patient had been expecting the worst: the significance of the painless jaundice and recent weight loss had not been lost on him. So he took the news calmly, but not too bravely as evidenced by the tight grip he had on his wife's hand. His retirement, recently started, was obviously not destined to be a long one. He thoughtfully gave me absolution for my medical impotency to cure him, reassuring me that the combination of his faith in God and the devotion of his wife would enable him to face anything, even death.

Discharged early on the fifth day after the operation, the palliative procedure seemed to give him a new, if temporary, lease on life. His first visit came and went; the celebrations of his 40th wedding anniversary reportedly raised quite a stir in the small country town where he lived 100 km from the university department of surgery.

At the time, some colleagues and I were recruiting cancer patients who were losing weight for a study of cancer cachexia.<sup>1</sup> The subjects were asked to undergo a two hour ordeal consisting of a hyperinsulinaemic euglycaemic clamp (intravenous infusions of glucose and insulin) and indirect calorimetry where respiratory gas exchange was measured using a ventilated hood canopy. The project was funded by a grant from the New Zealand Cancer Society and, somewhat parochially, the regional daily newspaper had deemed this newsworthy and carried a short paragraph on the research project.

Several months later I received a letter from my patient. Near death and even too weak to hold a pen, he said via his wife's transcription:

"I apologise that I am not well enough to keep my next outpatient clinic appointment with you—it is simply too far to come. However, I saw your cancer research project reported in the newspaper and if I can help in any way, I'm willing to come for your research."

He never did—nor could he have, of course. As it was, my reply letter by return mail gently declining his offer reached him just before he died.

He exemplifies the many patients who, in addition to the trials of their illnesses, are prepared to enrol in research studies with cheerfulness, courage, and not a little personal inconvenience. The detached style we conventionally use in reporting scientific work is out of place when acknowledging the debt we owe to these willing collaborators.

I offer this as a tribute to my memorable patient's memory and to all others like him.—BRYAN PARRY is a consultant surgeon in Singapore

1 McCall JL, Tuckey JA, Parry BR. Serum tumour necrosis factor alpha and insulin resistance in patients with gastrointestinal cancer. *Br J Surg* 1992;79:1361-3.

We are delighted to receive submissions of up to 600 words on *A paper (or patient or book) that changed my practice, A memorable patient, The one message I would like to leave behind, or related topics.*