Modifying the immunogenicity of tumour cells by inserting genes encoding either cytokines or the products of the major histocompatibility complex can circumvent the problem of the weak immunogenicity of many animal tumour systems. Encouraging results have been obtained by expression of the IL-2 gene in a mouse colonic cancer model¹⁴ and of the IL-4 gene in a mouse renal cancer model.¹⁵ Many clinical studies of genetic immunomodulation are currently under way, particularly in those diseases in which powerful immune responses have been detected, such as melanoma and renal cell carcinoma.

Perhaps the most exciting of future possibilities for genetic intervention in cancer is the direct manipulation of oncogenes or tumour suppressor genes. Although we recognise that cancer is a multigene disorder (with five or six genetic changes needed to induce malignancy¹⁶), some genes may be critical at particular stages and reversal or blockade of a single event may be therapeutically useful. Mutant oncogenes of the *ras* family are found in about a third of all cancers and as many as 80% of pancreatic tumours.¹⁷ This family presents an obvious target for antisense attack, and a protocol to use a retroviral delivery system for antisense treatment in adenocarcinoma of the lung has just been approved in the United States.

The restoration of tumour suppressor gene function has proved an effective strategy for reversing the malignant phenotype in vitro and recently in several animal systems using retinoblastoma gene constructs. Unfortunately we do not yet have good methods to control the quantity of protein produced, and overproduction could adversely affect normal tissue. Indeed, transgenic mice with an extra copy of the RB1 gene are consistently smaller than normal.

Once the entire human genome has been mapped and sequenced it will become amenable to manipulation. Replacing new genes for old—homologous recombination—is now feasible in animal cells, but the technology requires a great deal of refinement before such a feat could be achieved in human somatic cells. Transgenic animals with deleted or mutant tumour suppressor genes provide an elegant model for correction of inherited predispositions to cancer by gene transfer either into particular tissues or into the whole organism.

All new technologies carry risks. Gene therapy is emotive, with potential hazard not only to the patient but also to staff

and the environment. Considerable effort has gone into evaluating the risks and developing ingenious methods to reduce them. Thus disabled viruses that cannot reproduce themselves, suicide marker genes that can destroy cells containing the relevant vector when required, and close examination of clinical protocols by national ethical and scientific committees all help to limit potential problems.¹⁸ A decade ago it would have been inconceivable that we would now know enough about the molecules of cancer to consider genetic intervention. We believe that within 10 years cancer centres will be offering gene therapy as an effective systemic treatment along with surgery, radiotherapy, and chemotherapy.

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Fluoridation in Britain today

Water companies are getting in the way

The recent decision by Welsh Water not to continue fluoridating water in Gwynedd means that the water fluoridation schemes established as part of the Ministry of Health's demonstration study in 1955-6 on Anglesey and in Watford and Kilmarnock have now all stopped operating.¹ That the schemes provided benefits seems undeniable. For example, after the burgh council stopped the Kilmarnock scheme Professor John Mansbridge of the University of Edinburgh continued to monitor the dental health of children in Kilmarnock and in the control community of Ayr. He showed that five years later the dental health of children in Kilmarnock had deteriorated.² At baseline in 1956 the average 4 year old had 7.1 decayed, missing, or filled teeth. By 1961, after five years of fluoridation, the equivalent figure was 3.0; in 1962 fluoridation stopped, and by 1968 the number of decayed,

missing, or filled teeth had reverted to 6.1. Throughout the period 1956 to 1968 the equivalent figure in 4 year old children in the control town of Ayr remained between 6.9 and 7.2.

The Anglesey scheme operated for over 30 years, albeit rather intermittently for the past few years. Thomas and Kassab recently reported on the substantial benefits of fluoridation for the dental health of women aged up to 32 years who had lived continuously on Anglesey and who were attending St David's Maternity Hospital between July 1986 and July 1987 for their confinement.³ The dentist recording the dental condition of both the women from Anglesey and the control group from the non-fluoridated Gwynedd mainland was blind to women's residential status; those living in the fluoridated area had 30% fewer caries. The fluoridation plant in Watford, also showing signs of age, stopped operating

in 1989. On the positive side, fluoridation continues to provide substantial benefits for the dental health of six million people, many of them living in the west midlands and the north east of England.⁴

The arguments for extending fluoridation are not as overwhelming as they were in 1956. The prevalence of dental caries has fallen in both fluoridated and non-fluoridated districts,⁵ and the costs of fluoridation plant designed to meet modern operating standards are considerable.⁶ It is sensible therefore that the health departments should give priority for new schemes to areas such as the north west of England⁷ and the west of Scotland where the prevalence of dental caries remains high and where large water treatment works allow for economies of scale.

The Water (Fluoridation) Act 1985 placed the responsibility for decisions on water fluoridation with district health authorities, who are required to consult locally before making a formal request to the water undertaker. It was assumed, incorrectly as we now know, that water undertakers would concern themselves mainly with the technical feasibility of the proposal.⁸ Experience in the North Western Region, where 18 district health authorities completed consultation in 1988, and more recently in Strathclyde, Yorkshire, Wessex, and Northern Ireland, clearly shows that health authorities can obtain substantial public and professional support for fluoridation, even though opinion among local authorities remains divided. It is also clear that the cooperation of the water companies cannot be assumed.

For example, the chairman of Welsh Water stated recently that, in spite of assurances from the Drinking Water Inspectorate concerning the safety of fluoridation plant designed according to the Department of Environment's code of practice,⁹ his company would not continue fluoridation on Anglesey or extend fluoridation into the rest of Wales unless

required to do so by the secretary of state. While ministers quite correctly point out that the act requires local consultation, it was surely not the intention of parliament that water undertakers should have such an absolute veto.

The recent fundamental review of dental remuneration by Sir Kenneth Bloomfield called for "a more robust approach" to fluoridation "which would not allow for indefinite procrastination in adopting measures judged by the competent health authorities to be both beneficial and cost effective."⁹ The secretary of state should now require water undertakers to implement fluoridation schemes when they are requested to do so by health authorities, subject to assurances that the proposed schemes are technically feasible and economically sensible.

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Urban slums and primary health care

The private doctor's role

Living in abject poverty and consulting a private doctor seem a contradiction, though not to slum dwellers in many developing countries. In some cities a relative plethora of doctors and rapid urbanisation have led to a boom in private medical practice, which now provides a substantial amount of curative care for the inhabitants, including the poor (p 673).¹⁻³

At the same time as slum dwellers have been queuing to see their local private doctor, ideas from the political right have influenced the policy guidelines of international organisations with clout in developing countries. For example, the World Bank and the World Health Organisation now emphasise private options for health care delivery.^{4,5} This has led planners to focus on the substantial private sector already in existence in some countries. They want to know how this sector can be promoted, how the quality of care can be improved, and how private doctors can participate in national public health policies.^{6,7} Answers to these questions have important implications for slum dwellers, whose only local source of medical care may be private doctors.

The little that has been written about private health care in developing countries suggests great variations among doctors and countries. Excellent care is provided by some, but the general picture is depressing. In particular, it seems that the market forces that opened the doctors' doors in slums

are determining the type and quality of the care that they provide.

Services are predominantly curative. Preventive health care, such as childhood immunisation and health promotion through advice on lifestyle, is uncommon. Consultations, mostly for minor ailments, are characteristically brief. The number of people seen is high—up to 100 patients a day—thus ensuring that unit costs are kept low. Standard medical practice may be ignored, with excessive numbers of drugs or overly expensive formulations being prescribed. For example, in a study of 100 private doctors 80 treatment regimens for tuberculosis were identified. Only four of these followed the standard guidelines of WHO, and the prescribed regimens cost three times as much as the standard protocols.⁸ Some prescribing habits may adversely affect patients' health: systemic steroids for fever, psychotropic drugs for pain, and use of inappropriate antibiotics fall into this category.⁹ When it comes to referral anecdotal reports suggest that informal gratuities are being paid by specialists to doctors for referring patients, potentially leading to overinvestigation and overtreatment.

Have governments a responsibility for actively regulating the private sector? At the very least, they have an obligation to protect their populations from practices that may adversely