

The intervention reported this week by Aveyard et al was doomed from the start by the requirement that participating teachers should undertake a two day course beforehand. Schools across Britain are unlikely to release one or more teachers for two days' training each year on a topic which, to them, ranks below alcohol, drugs, and sex education in priority. And, short of a ruthlessly enforced decree from the government, few schools will allocate six lessons to smoking in a year (as required here) except as part of a trial.

So it is no surprise that, despite massive efforts since the 1980s to disseminate "effective" programmes requiring training and additional classroom time in the UK and the US, there has been little change in teenage smoking on either side of the Atlantic.<sup>5</sup> Schools simply cannot sustain complex programmes of this kind in the face of competing pressures.

But if the results of this trial had been positive the temptation to launch a massive dissemination programme would probably have proved irresistible. Once the initial enthusiasm had worn off, any early effects would have dissipated just as they did with earlier programmes.<sup>5</sup> And any NHS funding for the programme would have been at the expense of more effective interventions for adults, such as publicity and face to face advice from health professionals.<sup>8,9</sup>

There are no magic bullets to be found in school antismoking programmes: the methods that worked in

the early trials had a delaying effect only,<sup>5</sup> and none have been capable of dissemination on a large scale. Is it too much to hope that this experiment marks the end of attempts to find a quick fix, school based solution to the problem of teenage smoking? If it is, these disappointing findings will be of greater benefit to public health than they appear.

Donald Reid *chief executive*

UK Public Health Association, London SW1P 2HW

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## Fertility after treatment for cancer

### *Questions remain over ways of preserving ovarian and testicular tissue*

An increasing number of people are being successfully treated for cancer, and for those with an expectation of long-term survival the late effects of treatment are of concern. Young people have a particular interest in the impact of chemotherapy or radiotherapy on their future fertility, and recent media reports<sup>1</sup> of the successful transplantation of cryopreserved autologous ovarian tissue into a previously oophorectomised woman with non-malignant disease (K Oktay et al, Annual Meeting of American Society for Reproductive Medicine, Toronto, September 1999) will have caught the imagination of many. If a technique works in this situation, why not for a woman with malignancy whose ovarian tissue might be harvested before the start of sterilising chemotherapy?

Successful transplantation of cryopreserved ovarian cortical tissue into castrated ewes was first performed by Gosden and colleagues in 1994<sup>2</sup>: a return of oestrus cycles was observed, and, after normal mating, conceptions occurred and lambs were born. Further work in women suggests that small pieces of ovarian tissue can be successfully transplanted to an ectopic site within the pelvic cavity (A J Rutherford and R G Gosden, personal communication), and the recently reported case shows that an additional step (a freeze-thaw cycle) before transplantation is also possible.

Is the stage then set for the reversal of treatment induced sterility in women who have had cancer? The technique itself certainly appears to work, but several

questions relevant to patients with cancer need answering: What are the indications for such an approach (not all treatments lead to permanent sterility)? How much tissue should be harvested and when? And, importantly, what is the risk of transmitting disease back into the patient at autotransplantation?

Since 1997, 10 young women at our centre have had ovarian tissue harvested and cryopreserved before receiving high dose chemotherapy for Hodgkin's disease or non-Hodgkin's lymphoma. In each case one whole ovary was removed by laparoscopic oophorectomy and the ovarian cortex (containing primordial follicles) removed en bloc, flattened, trimmed, and then cut into strips before being stored at liquid nitrogen temperature (J A Radford et al, British Cancer Research meeting, Edinburgh, July 1999). Histological assessment has shown varying numbers of primordial follicles and no evidence of disease, though minimal amounts might, of course, remain undetected by these methods, and the results of experiments in which ovarian tissue from patients has been xenografted into immune-deficient NOD/scid mice are, therefore, of great importance (S S Kim et al, annual meeting of American Society for Reproductive Medicine, Toronto, September 1999). If no evidence of tumour transmission is detected, reimplantation of ovarian cortical strips into patients is likely to follow soon afterwards.

Fertility after treatment for cancer is not only of interest to women. Men under the age of 55 have the

option of cryobanking semen before the start of sterilising chemotherapy,<sup>3</sup> but this is a finite resource, it does not permit a natural conception, and it is not an option for prepubertal boys. Furthermore, a recent study of 115 men who cryobanked semen before receiving treatment for Hodgkin's disease showed that after prolonged follow up only 33 had used these stored gametes and, of those who did, only 8 were rewarded with a live birth (FH Blackhall et al, unpublished). It would appear, therefore, that this is not a very popular or successful way of achieving pregnancy and other strategies need to be considered.

In 1994 Brinster and colleagues in Philadelphia described how spermatogenesis could be reinstated in mice sterilised with busulphan by injecting their seminiferous tubules with a suspension of testicular cells derived from an allogeneic donor.<sup>4</sup> These remarkable results suggested that human testicular cells might be harvested and cryopreserved before the start of chemotherapy and reintroduced into the testis on its completion. A clinical trial testing this hypothesis is currently under way in adults: 11 men have had testicular tissue harvested and cryopreserved as a single cell suspension (J A Radford et al, British Cancer Research meeting, Edinburgh, July 1999, and PF Brook et al, unpublished), and five who have now successfully completed treatment for cancer have had this material injected back into the donor testis. Results of follow up semen analysis are awaited with interest.

These developments and work in progress suggest that it may soon be possible to preserve the fertility of patients requiring treatment for cancer which ordinarily would lead to permanent sterility. Understandably, this makes exciting news but several important issues still need to be resolved and, until they are, the various techniques should be confined to ethically approved clinical trials where efficacy and safety can be fully evaluated. Although patient pressure is likely to be intense, we should proceed cautiously until we have a clearer view of the possible benefits and pitfalls. The alternative—the uncontrolled harvesting, cryopreservation, and reimplantation of gonadal tissue in a wide range of circumstances—may, at best, be ineffective or unnecessary and, at worst, life threatening.

JA Radford *senior lecturer in medical oncology*

SM Shalet *professor of endocrinology*

Christie Hospital, Manchester M20 4BX

BA Lieberman *consultant gynaecologist*

St Mary's Hospital, Manchester M13 0JH

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## Stumbling into rationing

*A national debate on values is needed to sustain the NHS*

Muddling through is the British way. While some countries may tackle a problem like the rationing of health care head on—admitting the problem at the highest level, analysing it, declaring their values, and beginning work on a just, transparent solution—the British deny the problem and nibble at its edges. Surely we can do better. This government, like the last, avoids the word rationing, but it knows that not everything can be done for everybody. So it has constructed machinery with Orwellian names—health improvement plans and the National Centre for Clinical Excellence (NICE)—to do some of the inevitable job of denying access to effective interventions.

It was a step forward when the government declared that sildenafil (Viagra) would not be available to all who might benefit. It botched the job by suggesting that psychological causes of impotence were less “worthy” and by diverting debate into silly discussions over sildenafil being abused by ageing lotharios. But the job was done.

Now Britain is making further progress by NICE advising that zanamivir, the new anti-influenza drug, should not be made available throughout the NHS. What we need, however, is a deep, national debate on the values that should be used to make these decisions. Whether or not zanamivir is to be made widely available is not ultimately a technical decision. It may be dressed up as a technical argument, but it's a value judgment. And many, including the *BMJ*, do not feel

comfortable with those value judgments being made simply by technical advisers, ministers, and civil servants.

The other problem with NICE is that it's concerned with what's new. Just, transparent, and efficient rationing would think about the old as well as the new. (Thus the main argument for NICE advising against zanamivir is that it has not been adequately tested in high risk groups like the elderly, but this is a problem with many routine treatments.) Otherwise, NICE may come to be seen as anti-innovation, keeping the NHS firmly in the past. The government might argue that health improvement programmes are about “deciding local priorities”—that is, rationing—but does the public understand that? No, and the name doesn't help.

The NHS has survived so long because it has been an institutional expression of deeply held values. But we cannot have universal access free at the point of delivery, comprehensiveness, and high quality on current resources. If the government wants to sustain the NHS then it needs to engage the public in deciding how to trade those values. That engagement might also lead to more resources being put into the NHS.

Richard Smith *editor, BMJ*

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