announcement in December of the allocation of cash to health regions for 1991-2. Instead of redistributing cash on the weighted capitation basis set out in *Working for Patients*, ministers gave more money than expected to the Thames regions.[2] This provided a safety net to help authorities in London avoid bed closures and cutbacks in services in the first year of the reforms.

Regions such as Wessex and East Anglia, which had expected to gain considerably under the new resource allocation formula, received less money for growth than anticipated. Although ministers declared that they were still committed to achieving equity in the funding of regions, this will not now happen by the original target date of 1992-3. Instead, the aim is to achieve full weighted capitation at regional level "at an early date."

Taken together, these developments point to an important shift in the government's thinking. To some degree this is no doubt motivated by political considerations, in particular the prospect of a general election within the next 18 months. The consequences for the government if its reforms really do put some hospitals into financial difficulty because of an overly aggressive competitive approach are plain to see. For this reason alone the brakes are sure to be kept on until the election is over.

A further factor behind the change of approach is recognition by managers that the reforms simply cannot be implemented quickly. The challenges of negotiating contracts, developing better information about the cost and quality of services, involving doctors in contracting, and the many other items on the reform agenda are immense. Realistically speaking, the government's plans can be taken forward only gradually; hastening implementation would risk disaster.

This, however, creates a difficulty for ministers who continue to claim that the reforms hold the solution to many of the problems of the NHS. If competition is to be implemented slowly and in a way that is carefully managed then efficient hospitals will still be faced with the dilemma that increased productivity is not rewarded with additional resources. Equally, hospitals that perform poorly will not be threatened with the loss of resources to more efficient competitors. Sooner rather than later ministers will have to grasp this nettle and either allow competition to occur or concede that markets have little place in the provision of health services.

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Viruses and cervical cancer

Genital virus infections warrant surveillance rather than radical treatment

Several sexually transmitted viruses are now strongly associated with cervical cancer.[1] The evidence is strongest for human papillomavirus[2] and less strong for herpes simplex virus type 2.[3,4] Indeed, for most of the past decade human papillomavirus has held centre stage as the most probable viral aetiological agent for cervical cancer—but some recent evidence suggests that its contribution may not be exclusive.

DNA from a few of the 60 types of human papillomavirus—particularly type 16 and to a lesser extent type 18—are found in high grade squamous precancer and cancer of the cervix and in endocervical adenocarcinomas.[2] The recently introduced and very sensitive polymerase chain reaction has shown, however, that in some small sample populations of normally sexually active women DNA from human papillomavirus 16 may be almost universal.[5,6] In theory the polymerase chain reaction can detect one genome in a million cells, raising difficult questions about the biological implications of such low level detection.[7-9] Contamination in obtaining a specimen is one problem. Anticontamination primers and the wipe test have shown that contamination of the laboratory by plasmids may produce false positive results.[10,11] Studies discussed at the recent ninth international papillomavirus workshop in Heidelberg showed wide discrepancies in the results of polymerase chain reaction tests in women who were cytologically normal. Careful standardisation, quantification of the amounts of human papillomavirus detected, and quality control of the polymerase chain reaction are all needed before this technique can safely be used in epidemiological studies concerned with the transmission and natural course of genital human papillomavirus infections. Such studies could then provide direct evidence on the contribution of human papillomavirus to human genital cancer.

In spite of its problems, the polymerase chain reaction seems the most promising of the DNA techniques for this type of study, but other techniques have thrown some light on the complex problem. Filter in situ hybridisation[12] has been used most in epidemiological studies, but it is of low sensitivity and the results are often uninterpretable and therefore poorly reproducible. The Southern blotting technique has consistently detected DNA from human papillomavirus 16 in 20-30% of screened women at the level of one copy per cell, but it seems unsuitable for mass use (A Hollingworth *et al*, unpublished data).

What is confusing to the clinician is that many women with DNA from human papillomavirus 16 detected by the most sensitive methods have no more than minor cytological, colposcopic, or histological abnormalities of the cervix with occasional cell positivity for human papillomavirus capsid antigen.[13] These minimal lesions associated with human papillomavirus present a common management problem, for they seem to have a low risk of neoplastic progression, at least in the short term.[14] The current American promotion of mass screening by DNA detection to identify a so called high risk group with human papillomavirus 16 needs to be approached with caution, as has the use of DNA detection in managing women with low grade abnormal smears. The Heidelberg meeting also considered serological diagnosis of the presence of human papillomavirus 16 by using the current generation of fusion proteins and synthetic peptides, but the results were thought to be inconclusive.

Against that background and the difficulties of correlating reproducible colposcopic, cytological, and histological classifications of cervical lesions,[14] the evidence linking human papillomavirus with cervical cancer remains incomplete. By

contrast, much recent experimental evidence now shows that human papillomavirus 16 can produce cellular transformation.[15] Cooperation between human papillomavirus and cellular oncogenes and steroid hormones (especially as in the contraceptive pill) has also been shown in vitro; these experiments may not, however, be directly relevant to human disease.[16-18] Herpes simplex virus and human papillomavirus can cooperate to transform cells into a tumorigenic cell type,[18] and herpes simplex virus-VMW65 protein can transactivate human papillomavirus 18 gene expression.[19] Cellular transcription factors can also regulate gene expression for both viruses.[20,21] Such factors may be tissue specific and could account for the high frequency of neoplastic change in the cervical transformation zone.

Smoking is recognised as an important risk factor for cervical cancer.[22] It may act by influencing the local immune system,[23] which may play an important part in the outcome of human papillomavirus infection, but it may also act through chemical carcinogenesis, as suggested by the finding of smoking related addition products of DNA in the cervix.[24]

Making sense of the evidence

What are we to make of all this seemingly confusing and contradictory molecular and experimental information? Treating everyone with evidence of genital human papillomavirus, even human papillomavirus 16, seems unnecessary. Virus induced vulval warts, containing human papillomavirus 6 and 11, are also associated with cervical intraepithelial neoplasia,[25] in which DNA from human papillomavirus 16 may be present. These cervical lesions are, however, usually small and low grade. Vulval warts should be treated, and if colposcopy is available at the time of treatment it would be prudent to examine the cervix. In the absence of colposcopy, close cytological follow up over the short term should identify accurately the few patients with high grade cervical intraepithelial neoplasia. If the smear at presentation is negative then a repeat should be performed in six months. Taking another smear at 12 months covers the possibility of progression and reduces the false negative rate to a very low level. After this final negative repeat smear, the patient may be discharged to three yearly follow up. Such a schedule would also provide a high level of protection for women with cytological evidence of human papillomavirus infection or borderline nuclear abnormalities, although the cost benefit of obtaining two negative smears after detection of such minor cytological abnormality is uncertain and needs further study. This schedule would place the woman who complies at very little risk of developing unsuspected invasive cancer.

It is important that the detection of these viruses in the genital tract should not add to the already considerable worry, psychosexual difficulties, or confusion that exists in women found to have cervical epithelial abnormalities.

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