

Higher survival rates have been associated with referral to specialist centres for a wide range of childhood cancers.⁴ The evidence relating to tumours occurring in adolescents but hardly ever in children is much sparser, though men with testicular teratoma may benefit from initial referral to a specialist centre.^{5,6}

Continuing specialist follow up is essential. Late effects occur, though they are rarely fatal and should be seen in the context of improved survival. They can affect virtually any system and mostly result from treatment rather than the cancer.⁷ Survivors need to be kept under surveillance and, when appropriate, given information on the risk of complications, especially impaired fertility, second cancers, and cardiovascular damage. Nevertheless, it should be emphasised that survivors are in general fit, employable, and in most respects indistinguishable from their peers.

The news about cancer in adolescents is therefore mainly good and should get better as a result of two recent initiatives. This month saw the first international conference on cancer and the adolescent, organised by the Yorkshire Regional

Cancer Organisation. It coincided with the launch of an appeal by the Teenage Cancer Trust aimed at improving facilities for adolescents with cancer. Together these initiatives should stimulate greater interest in a group whose welfare may have been neglected previously.

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Management of women with smears showing mild dyskaryosis

New studies justify immediate referral for colposcopy

Undoubtedly, women with smears showing severe dyskaryosis should have immediate colposcopy; many doctors believe that those with moderate dyskaryosis should be treated in the same way. But what to do about mild dyskaryosis is much less clear cut, and, indeed, the diagnosis is very subjective. According to the NHS cervical screening programme's guidelines, no justification exists for immediate colposcopy for mild dyskaryosis, but the programme wanted further research to determine whether cytological surveillance was as safe and effective as colposcopy.¹ Such research is being conducted prospectively by the Aberdeen birthright project and is reported in this week's journal (p 1399).²

The arguments in favour of immediate colposcopy are that it allows early assessment and diagnosis—useful, given the well documented association between mild cytological abnormalities and high grade cervical intraepithelial neoplasia.^{3,4} In this week's journal, Soutter and Fletcher report that women with mild dyskaryosis are at high risk of developing invasive cervical cancer (p 1421).⁵ Colposcopy should result in reassurance and should protect against the risk of the patient defaulting from cytological follow up. Disadvantages claimed for immediate colposcopy include the cost, which results in suboptimal use of the procedure. There is also a risk of overtreatment, which has increased with the widespread adoption of a "see and treat" policy after the introduction of large loop excision of the transformation zone.

The Aberdeen group addressed the issue of cost and the use of resources. It reported that only one in four smears obtained from women with mild dyskaryosis undergoing cytological surveillance reverted to normal with time and that most women with mild dyskaryosis eventually required colposcopy. In view of this and the need to take additional smears the group believed that a policy of cytological surveillance was likely to be more expensive and less efficient. This hypothesis is also supported by Johnson and colleagues, who used decision analysis to compare the expected mortality and cost associated

with immediate referral with those associated with cytological surveillance.⁶ The risk of ultimately developing invasive cancer was the same in both groups, but the cost was greater if a conservative policy (cytological surveillance) was adopted.

The other important findings in the paper from Aberdeen were that one third of women with cervical intraepithelial neoplasia grade III had an index smear showing mild dyskaryosis and that one in eight women defaulted from follow up. A previous paper has highlighted the risk of defaulting,⁷ and in this week's journal Macgregor and colleagues highlight the increased risk of invasive cervical cancer in women who are screened inadequately, or not at all (p 1407).⁸ Research to identify those women with mild dyskaryosis who may harbour high grade disease has focused mainly on the expression of human papillomavirus types,⁹ although a recent paper reported a strong association between such lesions and smoking.¹⁰ Should women with smears showing mild dyskaryosis therefore be selectively referred?

The remaining potential disadvantage of immediate referral is the risk of overtreatment. The advantages and disadvantages of a see and treat policy are illustrated in the short report by Downey *et al* in this week's journal in a population at high risk of defaulting (p 1412).¹¹ Although large loop excision of the transformation zone is safe and effective,¹² one should aim to avoid unnecessary treatment. Risk factors for overtreatment with large loop excision at the first attendance for colposcopy include minor cytological abnormalities,¹³ and caution should be exercised in patients with such abnormalities. But I believe that this risk is not an argument favouring cytological surveillance in patients with mild dyskaryosis—rather, an indication for a more complete colposcopic assessment before treatment, including punch biopsy of any lesion.

The time has come to review the recommendations for managing women in whom a smear shows mild dyskaryosis. A

case can be advanced for selectively referring smokers with mild dyskaryosis for immediate colposcopy and for continuing with cytological surveillance for non-smokers. The data now available, however, justify a policy of immediate referral of all such patients for colposcopy. This would result in some increase in colposcopic surveillance but is surely preferable to cytological surveillance in a group with a high incidence of important disease who will ultimately need colposcopy, especially when there is a substantial risk of patients defaulting from follow up.

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Aminophylline in the hospital treatment of children with acute asthma

On the way out

In 1971 Pierson and colleagues showed that in children with acute asthma, intravenous aminophylline provided additional benefit when added to a regimen of hydrocortisone and sympathomimetic drugs.¹ As these drugs are pharmacologically different and each causes bronchodilatation it seemed reasonable that together their effect would be additive. For children with poor pulmonary function (peak flow <25% expected) or with hypercapnoea (arterial carbon dioxide pressure >5 kPa) this combination seemed to work²: less severely ill children recovered when given oral prednisolone and nebulised salbutamol and did not need inpatient care.

For nearly 20 years children with acute asthma have been managed along these lines. Recent practice, however, has seen the intravenous treatment of children with severe asthma replaced by the regimen now used to treat less severely ill children: oral prednisolone and nebulised β agonists. This combination seems to be efficacious and free of serious side effects and is now recommended for all but life threatening asthma.³ What then is the role of aminophylline in the management of acute asthma in children?

Several recent articles are relevant. Singh and Kumar reported that in a group of moderately ill inpatients a single dose of oral prednisolone 1.5 mg/kg together with salbutamol given continuously by nebuliser at a dose of 0.15 mg/kg/h resulted in more rapid improvement than intravenous aminophylline at 0.9 mg/kg/h given with intravenous hydrocortisone and intermittent nebulised salbutamol. Unlike those receiving the aminophylline regimen, most children who received the continuous salbutamol regimen had peak expiratory flows of >75% expected at 24 hours and could be discharged from hospital.⁴ Other studies have shown that in children with moderately severe asthma no appreciable benefit resulted from adding intravenous aminophylline to nebulised salbutamol and intravenous steroids in terms of clinical improvement and the time for which supplemental oxygen was needed⁵ or the rate of improvement in pulmonary function.^{6,7} No study has examined the value of aminophylline in children with very severe acute asthma who need or may need ventilatory support. The most likely explanation for the lack of added benefit from aminophylline in recent studies is the

difference between the sympathomimetic drugs used now and those used in earlier work. Modern β agonists act for longer and are probably used in larger equivalent doses than their predecessors, such as isoprenaline.

Although some anxiety about cardiotoxicity always exists when aminophylline is used in adults, in children there is much less concern about this potentially serious side effect. In a group of clinically stable asthmatic children who underwent Holter monitoring and a maximal treadmill exercise test, neither theophylline alone nor theophylline combined with salbutamol was associated with any substantial adverse cardiovascular effect, including arrhythmias.⁸ Nausea, vomiting, headache, and abdominal pain were more common in children with acute asthma who received aminophylline as well as salbutamol.⁷

Aminophylline therefore seems to have nothing to add to corticosteroids (either oral prednisolone or intravenous hydrocortisone) and a nebulised β agonist in the hospital treatment of acute asthma for most children. But two groups need further consideration. As the value of aminophylline in life threatening asthma is unknown, withholding it seems unreasonable as a small benefit could make a large difference in outcome. For those children who do not improve when given a corticosteroid and β agonist consideration could be given to adding aminophylline as well as excluding alternative or coexisting diagnoses, such as an inhaled foreign body or pneumonia.

The second group that needs to be considered is children in developing countries and countries in eastern Europe and the former Soviet Union. In these countries aminophylline is cheaper and readily available more than β agonists. For as long as this is true aminophylline will remain a valuable drug for many children in the world who need treatment in hospital for acute asthma.

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