INCENTIVE FOR MEASLES, MUMPS, AND RUBELLA VACCINATION

SIR,—Dr Miller and colleagues (Feb 4, p 271) suggest that education of parents and professionals could bring about full measles/mumps/rubella vaccination coverage before the child is two years old. Dr Narayan (Feb 4, p 272) suggests monitoring of small-area uptakes and giving authority to the immunisation co-ordinators, in addition to educational campaigns. In England at least, unit managers possess the necessary authority and they receive performance-related pay. We ought to consider seriously the offer of financial incentives to parents willing to present their children for immunisation. A £10 voucher could work wonders for uptake. The risk of contraindications being hidden by a greedy parent could be reduced by ensuring that the money is linked to attendance at the clinic, not to insertion of the needle. A pilot trial is called for.

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INHERITED DELETION AT DUCHENNE DYSTROPHY LOCUS IN NORMAL MALE

SIR,—Detection of deletions in dystrophin cDNA is an accurate method of predicting the inheritance of Duchenne muscular dystrophy (DMD).[1-3] In a letter in *The Lancet* in 1987[4] we described a case of inheritance of a deletion of the intron probe from the DXS206 region in a normal male and his affected sibling. We have now examined this family, using the entire human dystrophin cDNA, to determine the presence or absence of the exons encoded within the region of the familial DXS206 deletion besides the remainder of the gene, to distinguish the normal and affected male siblings. No family members are missing exons in the 5′ half of the dystrophin gene, including the DXS206 region. In contrast, the affected male bears a second distal deletion of two exons in the region of the gene which recognises deletions in 50% of affected males.[1]

The 5′-specific cDNA clone 9–7[1] detected all ten exon-containing *Hind* III fragments in all family members (fig 1). The two intron sequences which detect the proximal deletion (XJ1.1 and XJ10.1;[2] fig 2) define the minimum limits of the familial deletion at the proximal end of the dystrophin gene. The closest exons to this intronic deletion are 7,8 and 9, which are clearly evident in all family members (fig 1). In the lower panel of fig 2, a distal portion of the dystrophin cDNA designated 44-1 was used to detect the exons from the region of high frequency deletion.[1] The affected male (lane 3) carries a deletion of two exons, while all other family members have these exons present. Using a spectrophotometric method for determining dosage[5] we showed that the mother of the affected male has no deletions in this region. It may, therefore, be concluded that this second unique deletion in a region of high-frequency deletion in DMD patients[1] is the DMD mutation in this affected male and not the DXS206 mutation.

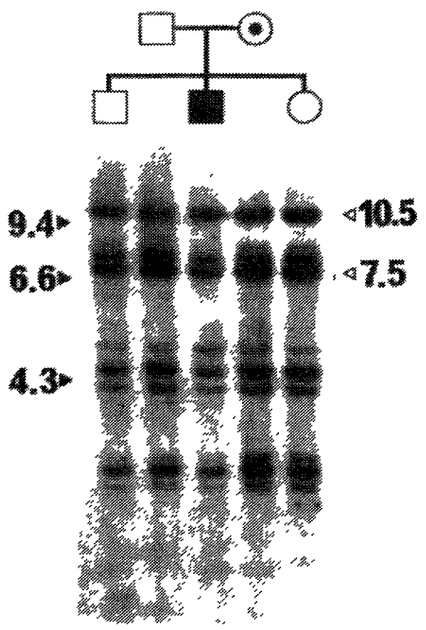

Fig 1—Hybridisation of dystrophin cDNA clone 9-7 to blot of *Hind* III DNA.

All exon containing fragments are present in family members tested. cDNA probes provided by L. Kunkel. Hybridisation and labelling methods essentially as reported.[3]

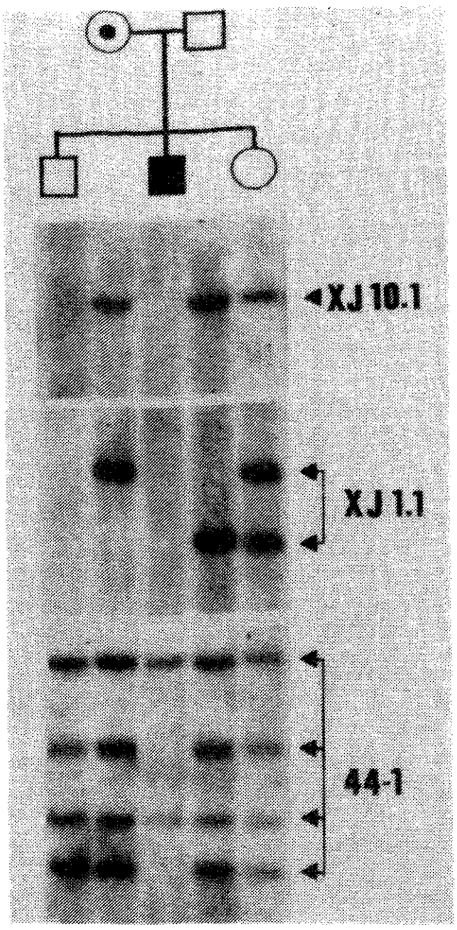

Fig 2—*Taq* I digested family DNA blotted and probed with probes from Duchenne region.

Upper two panels are probed with indicated intron-specific probes from DXS206 region.[2] Both male offspring demonstrate deletions in DXS206 region, whereas only affected offspring carries a deletion recognised by distal 44-1 cDNA probe. XJ1.1 and XJ10.1 probes were from P. Ray and R. Worton.

These data illustrate the paradoxes that may arise during carrier detection and prenatal diagnosis in DMD families. The origin of the deletion in the DXS206 region in this pedigree must have been complex, as shown by the absence of hybridisation in two intronic probes XJ1.1 and XJ10.1[4] which are believed to be between exons 7 and 8. Since all exons from this region were present (fig 1), it is assumed that this DXS206 deletion permitted the proper co-linear expression of these 5′ exons. To confirm this, the presence of all of the first ten exons in the dystrophin transcript of the two siblings will need to be examined at the RNA level.[6] Had the DNA from the normal male been presented for prenatal study with the commonly available DMD probes, this deletion would have predicted DMD and the probable pregnancy outcome would have been termination. When the dystrophin cDNA probes were used the normal and affected males produced the same results in the DXS206 region. These males are distinguishable on the basis of what appears to be a new mutation (a second unique deletion) in the distal portion of the

affected sibling's dystrophin gene. Thus, prenatal diagnosis with intron probes may sometimes yield erroneous diagnoses.

The possibility that the DXS206 deletion in one of the mother's X chromosomes may have contributed to the unique second deletion in the affected male is intriguing. Because daughters of the unaffected male sibling may inherit this same DSX206 deletion, genetic counselling must address this potential increased risk of bearing an affected male.

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YOUNG DYSPEPTIC PATIENTS

SIR,—Dr Williams and colleagues (Dec 10, p 1349) contribute to the debate on routine endoscopy in patients with dyspepsia. The results of their study are reassuring in that the incidence of malignant disorders in young patients with dyspepsia was low so that the risk of delaying a diagnosis of cancer by postponing endoscopy is negligible. However, cancer detection is not the only reason for endoscopy in dyspeptic patients, whatever their age.

Dyspepsia is a heterogeneous condition, the causes of which include both peptic ulcer and non-ulcer disease. Non-ulcer dyspepsia may be related to mucosal alterations (inflammatory changes, erosions) or to motor abnormalities.[1] Treatment must therefore depend on the pathogenetic factor(s) underlying the dyspepsia. Endoscopy may "not ultimately change the treatment", but that merely highlights the fact that many physicians are more interested in achieving rapid, albeit temporary, symptom relief than in trying to remove the causes of dyspepsia. We (and others[2]) do not subscribe to Williams and colleagues' advice that young patients with dyspepsia be treated first with H_2-receptor antagonists. The effect of these drugs on symptoms in non-ulcer dyspepsia is controversial,[3-5] probably because in some studies most of the patients had motility disorders rather than acid hypersecretion. Also in some subpopulations of dyspeptic patients, symptom relief by H_2-blockers is seldom associated with improvement of mucosal alterations. Ranitidine and sucralfate are equally effective in treating dyspepsia in symptomatic patients with non-erosive gastritis (symptom relief being faster with the H_2-receptor antagonist), but sucralfate is significantly superior in promoting endoscopic and histological healing or in improving mucosal inflammatory changes.[6] Dyspeptic patients with erosive duodenitis can find relief to the same extent with either ranitidine or pirenzepine, but pirenzepine is significantly more effective in respect of disappearance of duodenal erosions.[7] Thus the indiscriminate use of H_2-receptor antagonists in patients with dyspepsia of unknown origin is irrational and endoscopy remains the only way of achieving the correct diagnosis and identifying the therapy required. It has been suggested that with non-ulcer dyspepsia cimetidine responders might be identified by the presence of symptoms suggestive of reflux oesophagitis,[8] but this is yet to be confirmed.

If an attempt to reduce unnecessary endoscopy has to be made, then antacid prescription for a few days would seem to be more reasonable.[2,9] Although the efficacy of antacids in relieving dyspeptic symptoms has also been questioned,[4] at least they are cheaper and less potent drugs, with a lower risk from self-prescribed, long-term use.

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EXCRETION OF PLATINUM INTO BREAST MILK

SIR,—There are few data on the excretion of antineoplastic agents into milk of lactating patients. Methotrexate, cyclophosphamide, doxorubicin, and hydroxyurea have been recovered from breast milk.[1-4] Egan et al did not find cisplatin in milk of a patient treated with cisplatin and doxorubicin for ovarian cancer.[3]

We have treated a 24-year-old woman who underwent a caesarean section at 33 weeks' gestation because of entodermal sinus tumour of the left ovary. 6 days after delivery she was treated with cisplatin 30 mg/m^2 intravenously over 4 h on days 1–5 with hyperhydration, etoposide 120 mg/m^2 on days 1, 3, and 5, and bleomycin 30 mg on days 2, 9, and 16. The patient was advised not to breastfeed her child. On the third chemotherapy day, 30 min before the cisplatin infusion, breast milk and blood were collected. Platinum content was measured by atomic absorbtion spectrometry. The breast milk contained 0·9 mg/l and plasma 0·8 mg/l.

Although most of the platinum in the breast milk is probably bound to protein, this does not exclude the possibility of harm to the child. Hegedus et al[5] found that at least some protein-bound platinum can react with strongly nucleophilic substances. We therefore think that a mother should not breastfeed while receiving cisplatin chemotherapy.

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