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). In a letter in The Lancet in 1987 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.

The 5'-specific cDNA clone 9-7 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) (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. 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 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 is the DMD mutation in this affected male and not the DXS206 mutation.

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 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. 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 iontron 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 DXS206 deletion, genetic counselling must address this potential increased risk of bearing an affected male.

We acknowledge support from the Muscular Dystrophy Association of the USA through clinical research grants (R. J. B., A. D. R.) and a postdoctoral Fellowship (A. P. W.), from the National Institutes of Health (NS19999), and from the Neuromuscular and Telethon Foundations of Western Australia (N. G. L., A. D. R.).

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