bone marrow.

Prenatal DNA diagnosis will not only identify males at risk, but also unaffected males and females. These may be potential donors of cord blood stem cells or, later in life, of bone marrow, provided that they are HLA identical. The structure of the XLP gene and the function of its coded protein are still unknown. However, cloning of the entire candidate region using YAC walking technology will permit the identification of the defective gene in the near future. This may allow a direct and a 100% accurate prenatal diagnosis of XLP and may finally offer the opportunity of gene therapy.

This work was supported by the Deutsche Forschungsgemeinschaft (DFG Schu 560/2-3). We wish to thank Dr S Ulhais, Institute of Human Genetics, University of Bonn, for supplying DNA from choriocarcinoma villus biopsy.

<table>
<thead>
<tr>
<th>Table 1 Clinical details of the family</th>
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</thead>
<tbody>
<tr>
<td>Clinical features</td>
</tr>
<tr>
<td>II-4 Well, no bleeding disorder</td>
</tr>
<tr>
<td>II-7 28 years, died severe bleeding disorder</td>
</tr>
<tr>
<td>II-8 15 years, proband of the report in 1993 died of severe haemorrhage</td>
</tr>
<tr>
<td>III-1 9 months, easy bruising and at the age of 6 years had severe bleeding after dental work</td>
</tr>
<tr>
<td>III-2 24 years, osteomyelitis of right femur requiring surgical intervention</td>
</tr>
<tr>
<td>III-3 30 years, has severe infections requiring prophylatic antibiotics. He has alopecia which appears to be connected with his WAS and his blood count and renal and liver function are normal. He has avoided hospitalisation as bleeding has not really been a problem</td>
</tr>
<tr>
<td>III-4 Childhood, allergic eczema, asthma, thrombocytopenic purpura, and recurrent middle ear infections</td>
</tr>
<tr>
<td>III-5 35 years, splenectomy and since has had a normal platelet count</td>
</tr>
<tr>
<td>III-6 37 years, subtotal colostomy and jejunostomy for severe colitis</td>
</tr>
<tr>
<td>III-7 39 years, mesangio proliferative glomerulonephritis, was started on dialysis, and subsequently has had a renal transplant</td>
</tr>
<tr>
<td>III-8 Easy bruising</td>
</tr>
<tr>
<td>V-1 Thrombocytopenia and easy bruising</td>
</tr>
<tr>
<td>V-3 Thrombocytopenia, no evidence of immunodeficiency</td>
</tr>
</tbody>
</table>

Table 2 Summary of the two point lod score

<table>
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<tr>
<th>Lod</th>
<th>0</th>
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<th>0.500</th>
<th>2.500</th>
<th>5.000</th>
<th>7.500</th>
<th>10.000</th>
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</thead>
<tbody>
<tr>
<td>0.00</td>
<td>1</td>
<td>0.000</td>
<td>0.500</td>
<td>2.500</td>
<td>5.000</td>
<td>7.500</td>
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<tr>
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<tr>
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<tr>
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</table>

A variant of Wiskott-Aldrich syndrome with nephropathy is linked to DXS255

Wiskott-Aldrich syndrome (WAS, IMD2 MIM 301000) is an X linked recessive disorder characterised by eczema, thrombocytopenia with small platelets, multiple infections, and susceptibility to malignancy; T and B lymphocyte deficiencies are common. Affected males usually die in the first decade of life though there are exceptions. WAS has been mapped to Xp11.2 and is closely linked to the DXS255 locus that is detected with the hypervariable probe M27P.3 A variant of WAS (MIM 314000) with eczema, thrombocytopenia with small platelets, radial skeletal abnormalities, hypogammaglobulinaemia, and intellectual disability has been observed.5 This syndrome is similar to X-linked lymphoproliferative disease (XLP) which is caused by mutations in the X chromosome having multiple rearrangement. WAS on the other hand is caused by deletions of the X chromosome.

The disease appears to be uniform in the family; affected subjects have easy bruising from an early age and therefore clinically normal males with no history of a bleeding disorder were considered to be normal. A computer simulation of a linkage study showed that it might be possible to confirm linkage to DXS255 with the subjects available.

The alleles were arbitrarily numbered 1 to 4 and the results were analysed by the LIPED computer program.14 The results (table 2) confirm that the condition in this family is linked to the DXS255 locus though the confidence limits for the recombination fraction are wide (0–0–0–15).5 This disorder maps this region as similar to WAS suggesting that it may be allelic with the classical form of WAS. Alternatively it may be caused by a mutation in a closely linked gene. The resolution of these two possibilities may be possible with the isolation of the gene mutated to cause WAS.15

Pedigree and results of M27β typing.


Initially, NHS purchasers were able to refer to the ongoing pilot studies as a reason for not introducing a CF screening service. Now that such studies have shown the feasibility and acceptability of screening, at least in an antenatal setting, new objections are raised. We carried out a successful pilot study for the Yorkshire Regional Health Authority among nearly 6000 pregnancies but our findings have received an unenthusiastic response from local public health professionals. The high cost of the test, the difficulty of finding time for counselling in a busy antenatal clinic, and lack of consensus about the need for screening have all been cited as reasons for inaction. Such arguments make private screening inevitable.

Prenatal screening increases choice, largely but not entirely through the option of avoiding the birth of an affected infant, but as the Nuffield Foundation report and your editorial point out, this must be a properly informed choice. We do not agree, however, that direct marketing necessarily means poorer quality information compared with the NHS. For four years we have marketed prenatal screening for Down's syndrome directly to the public using a nine page patients' guide, a 15 page doctors' guide, and a designated telephone helpline to provide the necessary information. Earlier this year we decided to extend our service to include prenatal screening of couples for CF. A 10 page booklet has been produced giving information on the disorder, the mode of inheritance, the interpretation of carrier test results, and the invasive procedures used for prenatal diagnosis. Couples are encouraged to discuss any aspect of this with us, using the telephone helpline, as well as the Cystic Fibrosis Trust and Support Around Termination for Abnormality (SATTA).

Thornton4 has argued that the demand for any new screening test should not be assessed when it is offered in a state funded programme since acceptance may simply be compliant behaviour. If a test has official approval and is provided free there is a disincentive for the individual person to weigh the benefits and hazards. If so, the growth of a private CF screening market could be of advantage to NHS planners. Commercial push may be a good way of assessing population need.

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A variant of Wiskott-Aldrich syndrome with nephropathy is linked to DXS255.

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