bone marrow.^{12,13} 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.

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

Wiskott-Aldrich syndrome (WAS, IMD2 MIM 301000¹) is an X linked recessive disorder characterised by eczema, thrombo-

Table 1 Clinical details of the family

Clinical features	
II-4	Well, no bleeding disorder
II-7	28 years, died severe bleeding disorder
II-8	15 years, proband of the report in 1932 died of severe haemorrhage
III-1	9 months, easy bruising and at the age of 6 years had severe bleeding after dental work
	24 years, osteomyelitis of right femur requiring surgical intervention
	30 years, chronic chest infections requiring prophylactic 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
III-3	Childhood, allergic eczema, asthma, thrombocytopenic purpura, and recurrent middle ear infections
	35 years, splenectomy and since has had a normal platelet count
	37 years, subtotal colectomy and ileostomy for severe ulcerative colitis
	39 years, mesangioproliferative glomerulonephritis, was started on dialysis, and subsequently has had a renal transplant
III-10	Easy bruising
V-1	Thrombocytopenia and easy bruising
V-3	Thrombocytopenia, no evidence of immunodeficiency

cytopenia with small platelets, multiple infections, and susceptibility to malignancy; T and B lymphocyte deficiencies are common.^{2,3} Affected males usually die in the first decade of life though there are exceptions.⁴ WAS has been mapped to Xp11.2 and is closely linked to the DXS255 locus that is detected with the hypervariable probe M27β.⁵⁻⁷ A variant of WAS (MIM 314000¹) with eczema, thrombocytopenia with small platelets, raised serum IgA, virtually intact immunity, a mild nephropathy, and normal life expectancy has been reported.^{8,9} Gutenberg *et al*⁸ reported the results of renal biopsies in three males from the same family.

A brief description of the family is given in table 1 and the figure. This family presented to the Genetics Clinic at Guy's Hospital when IV-2 was pregnant. The family was reported in 1932,¹⁰ and the proband was included in a later report.¹¹ Ata *et al*¹² extended the pedigree and showed that there was no linkage between the condition and the ABO, Rh, MNSS, Duffy, and Xg^b blood groups. One affected male who has mesangioproliferative glomerulonephritis was started on dialysis and subsequently had a renal transplant.¹³ The clinical picture is similar to the variant of WAS reported previously.^{8,9}

The disease appeared 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 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 ($\theta = 0-0.18$).¹⁵

This disorder maps to the same region as 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.¹⁶

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Table 2 Summary of the two point lod score

Lod	θ
0.000	0.5000
0.567	0.4000
1.253	0.3000
1.935	0.2000
2.565	0.1000
2.857	0.0500
3.130	0.0010
3.135	0.0000

Pedigree and results of M27 β typing.

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Direct marketing of cystic fibrosis carrier screening: commercial push or population need?

A recent editorial in this journal¹ expresses concern about the direct marketing of cystic fibrosis screening outside the NHS. The potential hazards of screening are stressed and it is postulated that these negative aspects may be ignored under commercial pressure.

In our view the greater danger is that the potential benefits of screening will be ignored because of inertia within the NHS. Prenatal screening for neural tube defects was first shown to be feasible in the late 1970s but did not become widespread in the NHS for another decade. Biochemical screening for Down's syndrome is experiencing a similar lag time between research and implementation. At this rate a reasonable CF screening provision would not be expected before the next century.

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,²⁻⁶ 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 report⁷ 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 (SATFA).

Thornton⁸ 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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