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UK clinicians' knowledge of and attitudes to the prenatal diagnosis of single gene disorders

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Abstract

Postal questionnaires were sent to 308 clinicians in the UK (general practitioners, obstetricians, clinical geneticists, neurologists, paediatricians, and paediatric neurologists) to assess their knowledge of, and attitudes to, the prenatal diagnosis of three common single gene disorders, Huntington's disease (HD), cystic fibrosis (CF), and Duchenne muscular dystrophy (DMD). Replies received numbered 213, a response rate of 69%. Overall, 95% of responding clinicians thought that offering prenatal diagnosis for the three test conditions was often or always appropriate. There was a correlation between the clinicians' estimates of life expectancy and their willingness to offer prenatal diagnosis ($p < 0.01$). Among the non-geneticists questioned, fewer than 50% of general practitioners answered correctly regarding the availability of prenatal tests.

Three of the commonest single gene disorders in the UK are Huntington's disease (HD), cystic fibrosis (CF), and Duchenne muscular dystrophy (DMD). DNA probes closely linked to the genes for these diseases are now available, and more recently probes have been developed that identify intragenic defects in most subjects with CF[1] and DMD.[2] Possession of these probes, together with the innovation of chorion villus sampling (CVS), enables prenatal diagnosis to be implemented in some pregnancies at high risk for a single gene disorder as early as 8 to 10 weeks' gestation.[3] In a recent review of the work of a single regional molecular genetics laboratory, 132 prenatal diagnoses had been completed using DNA probes and CVS for these three conditions, and demand was increasing.[4] However, this same survey detected great variability in referral patterns within and between NHS regions. Personal and anecdotal experience suggests that many clinicians are not well informed about DNA testing. Even when clinicians are aware of the availability of tests useful in prenatal diagnosis, their perceptions of the severity of the disease in question, and their attitudes to prenatal diagnosis and termination of pregnancy in general, may have a substantial influence on whether they decide to offer prenatal diagnosis in any given pregnancy.

Professional reticence in offering prenatal diagnosis may have the practical effect of blocking access even when the pregnant woman is fully informed about her options.[5]

A survey of more than 2800 families referred for DNA testing[4] confirmed that most patients were referred by paediatricians, general practitioners, obstetricians, and neurologists.[4] These specialties, and clinical geneticists, were surveyed to assess clinicians' knowledge of the availability of prenatal diagnosis for HD, CF, and DMD, their attitudes to selective termination of pregnancy in the event of a positive prenatal diagnosis for each of the three test conditions, and the extent to which their assessments of the severity of these diseases influenced their willingness to offer to arrange prenatal diagnosis.

Study design

Huntington's disease, cystic fibrosis, and Duchenne muscular dystrophy were selected as 'test diseases' for this survey. Obstetricians, general practitioners, paediatricians, neurologists, paediatric neurologists, and clinical geneticists were selected as 'test subjects'. A random numbers table[6] was used to select them as follows: 50 consultant obstetricians from the list of fellows and members of the Royal College of Obstetricians and Gynaecologists, 50 general practitioners from the list in the Medical Directory, 50 consultant paediatricians from the British Paediatric Association handbook, 50 consultant neurologists from the membership list of the Association of British Neurologists, 62 consultant paediatric neurologists from the list of members of the British Paediatric Neurological Association, and 46 clinical geneticists from the membership of the Clinical Genetics Society. The study took the form of a postal questionnaire, together with an introductory letter. Questionnaires were mailed between December 1988 and February 1989.

The first section of the questionnaire covered knowledge of tests available for prenatal diagnosis, their appropriate timing, and the practical problems of setting up such diagnoses.

Question 1. "I was aware/unaware that DNA probes are now available to enable prenatal diagnosis in some families (depending on family structure, availability of affected persons, and actual results using DNA probes) with HD, CF, or DMD."

Question 2. "I was aware/unaware that prenatal diagnosis of these conditions was possible using chorion villus sampling (CVS) at 8 to 10 weeks of pregnancy in some families."

Question 3. "I was aware/unaware that affected families should preferably be referred before a pregnancy occurs, so that DNA from family members can be examined to determine

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Table 1 Responses to statement "Offering prenatal testing is a reasonable course of action" for each of the test diseases.

	% of clinicians choosing each response					
	Always	Often	Sometimes	Rarely	Never	Score*
Huntington's disease (HD)						
Neurologists	61	27	12	0	0	4·5
Clinical geneticists	62	28	10	0	0	4·5
General practitioners	79	18	3	0	0	4·8
Obstetricians	73	15	8	4	0	4·6
All	69	22	8	1	0	4·6
Cystic fibrosis (CF)						
Paediatricians	73	21	6	0	0	4·7
Clinical geneticists	85	15	0	0	0	4·9
General practitioners	76	21	3	0	0	4·7
Obstetricians	85	12	0	0	4	4·8
All	80	17	2	0	1	4·8
Duchenne muscular dystrophy (DMD)						
Paediatric neurologists	89	9	0	0	2	4·8
Clinical geneticists	87	13	0	0	0	4·9
General practitioners	82	15	3	0	0	4·8
Obstetricians	85	12	0	0	4	4·8
All	86	12	1	0	1	4·8

* Score determined as follows: 5 for 'always', 4 for 'often', 3 for 'sometimes', 2 for 'rarely', 1 for 'never', and total divided by 5.

Table 2 Responses to statement "Supporting a patient's request for termination of pregnancy, in the event of a positive prenatal diagnosis, is a reasonable course of action" for each of the test diseases.

	% of clinicians choosing each response					
	Always	Often	Sometimes	Rarely	Never	Score*
Huntington's disease (HD)						
Neurologists	76	18	6	0	0	4·7
Clinical geneticists	92	5	3	0	0	4·9
General practitioners	70	21	3	0	6	4·5
Obstetricians	89	7	0	0	4	4·8
All	82	13	3	0	2	4·7
Cystic fibrosis (CF)						
Paediatricians	81	13	3	0	3	4·7
Clinical geneticists	92	8	0	0	0	4·9
General practitioners	55	30	6	3	6	4·3
Obstetricians	82	15	0	0	4	4·7
All	78	16	2	1	3	4·7
Duchenne muscular dystrophy (DMD)						
Paediatric neurologists	87	9	2	0	2	4·8
Clinical geneticists	92	8	0	0	0	4·9
General practitioners	59	28	3	3	6	4·3
Obstetricians	93	4	0	0	4	4·9
All	83	12	1	1	3	4·7

* See table 1.

whether or not informative probes are available to enable prenatal diagnosis in a particular family."

The second section covered clinicians' attitudes to the offering of prenatal diagnosis. The statement "Offering prenatal testing (for HD, CF, or DMD) is a reasonable course of action" was followed by a choice of responses.

The third section tested supportive attitudes, should a patient request termination of pregnancy after a positive (affected) prenatal diagnosis test result. For each of the test conditions (HD, CF, or DMD) clinicians were given a choice of response to the statement "Supporting a patient's request for termination of pregnancy, in the event of a positive prenatal diagnosis, is a reasonable course of action."

A supplementary question was included, asking clinicians to estimate average life expectancy for patients with each of the test diseases.

Several parts of the questionnaire took the form of a closed question with a choice of five responses: never, rarely, sometimes, often, or always. For the purposes of analysis, these responses were numerically coded 1, 2, 3, 4, and 5, and an average figure produced for each grouping (tables 1 and 2). Thus a figure of 2·1 indicates that the averaged response of the group is 'rarely', a figure of 4·5 implies that the averaged response lies between 'always' and 'often'.

Results

RESPONSE

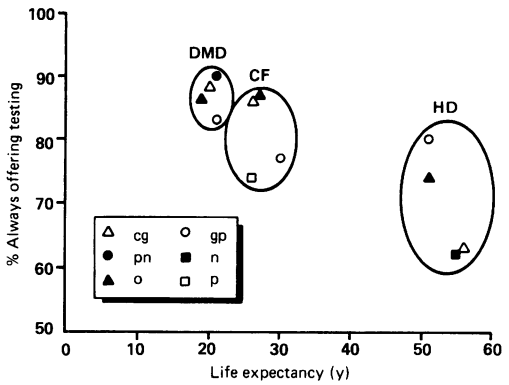
Replies to the questionnaire were received between December 1988 and May 1989. From a total of 308 questionnaires, 213 replies (69%) were received. Analysis of the response rate by specialty is given in table 3.

Table 3 Response rate to questionnaire, analysed by specialty.

Specialty	Mailed	Replied	%
Clinical geneticists	46	39	85
General practitioners	50	33	66
Obstetricians	50	27	54
Neurologists	50	34	68
Paediatricians	50	34	68
Paediatric neurologists	62	46	74
All	308	213	69

Table 4 Knowledge of availability of prenatal diagnosis using DNA probes, and awareness that diagnosis involves chorionic villus sampling (CVS) at 8 to 10 weeks.

Specialty	% of clinicians aware that			
	DNA tests are available			CVS is appropriate at 8 to 10 weeks
	for HD	for CF	for DMD	
Clinical geneticists	100	100	100	100
General practitioners	44	41	47	73
Obstetricians	67	88	77	85
Neurologists	91	—	—	53
Paediatricians	—	100	—	100
Paediatric neurologists	—	—	98	96



The percentage of clinicians, by specialty groups, always offering testing for the three test diseases, and clinicians' estimates of mean life expectancy for the test diseases. Individual estimates as follows: cg, clinical geneticist; pn, paediatric neurologist; o, obstetrician; gp, general practitioner; n, neurologist; p, paediatrician. Ellipses were drawn to delimit the test diseases. The line of best fit for the test diseases showed a negative correlation between the percentage always offering testing and estimates of life expectancy ($r = -0.825$, $p < 0.01$).

KNOWLEDGE OF AVAILABILITY OF PRENATAL DIAGNOSIS

This section of the questionnaire was designed to assess clinicians' knowledge of the availability and optimal timing of tests used in prenatal diagnosis for the three test diseases HD, CF, and DMD. Table 4 indicates great variability in awareness among the different clinical specialties, awareness being greatest among clinicians caring for affected persons, intermediate among obstetricians, and lowest (less than 50% for each of the three test diseases) among general practitioners. The general practitioner is often the first clinician to be notified when a pregnancy occurs, and it is a matter of concern that over a quarter of general practitioners were unaware that first trimester CVS could be used in the prenatal diagnosis of the test conditions.

The final question in this section dealt with the practicalities of offering prenatal testing in families where the testing is based on linkage rather than direct analysis of a mutation. Since the questionnaire was written, major technical advances have occurred, and deletions can now be detected in over 50% of boys with DMD, and the ΔF508 mutation can be detected in 70% of subjects heterozygous for cystic fibrosis. Nevertheless, until such advances enable direct mutation detection in nearly all affected subjects, the principle of preconceptual referral still applies. Table 5 shows that the majority of clinicians were aware of the desirability of referral before a pregnancy, with GPs being the least informed group (58%).

ATTITUDES TO OFFERING PRENATAL DIAGNOSIS

Table 1 shows there was a highly consistent response among clinicians from the different specialties, most believing that it is always or often appropriate to offer prenatal diagnosis in pregnancies at risk for the three test conditions (averaged response for HD was 4·5, averaged response for CF and for DMD was 4·8). These results showed some correlation with clinicians' estimates of life expectancy for the three diseases (figure, $r = -0.825$, $p < 0.01$), but there was no correlation with knowledge of availability of prenatal diagnosis by DNA probes ($r = -0.032$, $p = NS$) (table 4).

Table 5 Preconceptual referral: the percentages of clinicians, by specialty group, aware of the desirability of family DNA studies before pregnancy starts.

Clinical geneticists	100
General practitioners	58
Obstetricians	89
Neurologists	88
Paediatricians	82
Paediatric neurologists	91

ATTITUDES TO SUPPORTING A PATIENT'S REQUEST FOR TERMINATION OF PREGNANCY AFTER A POSITIVE PRENATAL DIAGNOSIS

Responses are shown in table 2. Most clinicians believe that it is always or often reasonable to support a patient's request for termination of pregnancy after a positive prenatal diagnosis (averaged response for HD, CF, and DMD was 4·7).

Discussion

Recent reviews of prenatal diagnosis, using molecular genetics techniques in England and Wales[7] and in Scotland[8] show that this approach is becoming established as routine. Our current survey indicates that such a trend is found acceptable by the great majority of clinicians in the UK who are likely to use such services.

The smooth running of a prenatal diagnosis service based on first trimester sampling and analysis requires that referral be made very early in pregnancy, preferably at 6 to 8 weeks' gestation, and if linkage techniques are to be used the family should have been 'worked up' in the laboratory before the pregnancy. Our study highlights two important problem areas: more than a quarter of GPs sampled were unaware of the possibility of first trimester tests, and nearly a half were unaware of the need for previous referral of patients. More encouraging were the results from specialists caring for patients affected by the test diseases; overall they showed a high level of knowledge regarding availability of and optimal timing for prenatal diagnosis using molecular genetics techniques. This is perhaps most likely to ensure success in implementing prenatal diagnosis in autosomal recessive conditions such as cystic fibrosis, where most of the recurrence risk is borne by the immediate family, but less

certain to ensure appropriate referral for X linked diseases, such as Duchenne muscular dystrophy (where carrier females may be distanced both spatially and temporally from the affected male), or late onset autosomal disorders such as Huntington's disease, where regular involvement of a specialist clinician, neurologist, or psychiatrist, may not take place until after the birth of the patient's children or grandchildren. In these latter circumstances, relatives with pregnancies at risk for the disorder will be dependent either on the astuteness of their general practitioner in recognising the genetic risk and making the appropriate referral, or on the efficient running of a genetic register.

This study indicates a need for initiatives to disseminate knowledge of new techniques among general practitioners. This need may be greater than that defined by the study results, since it is probable that those clinicians completing the questionnaire were more informed, or had more experience of the subject matter, than those choosing not to reply. The study also corroborates a recent finding that three-quarters of a sample of Scottish general practitioners were unfamiliar with the details of DNA based linkage analysis.[9]

Our overall conclusion is that the introduction of first trimester prenatal diagnosis for single gene disorders based on molecular genetics techniques is acceptable to the great majority of UK clinicians practising in specialties likely to use it.

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