Teplitz RL. Analysis of DNA extracted from formalin-fixed, paraffin-embedded tissues by enzymatic amplification and hybridization with sequence-specific oligonucleotides. *Biochem Biophys Res Commun* 1987;142:710-6.

- 3 Feldman GL, Williamson R, Beaudet AL, O'Brien WE. Prenatal diagnosis of cystic fibrosis by DNA amplification for detection of KM-19 polymorphism. *Lancet* 1988;ii:102.

Huntington's disease testing: what and what not to tell

Millan *et al*¹ may be getting on to somewhat of a slippery slope in imagining that they might 'leak' good news about the patient at risk, but withhold bad news, that they happen upon in prenatal exclusion studies for Huntington's disease. In the case of good news, the couple are getting a bonus beyond what they had expected. Great for them: but others in the same boat, through informal and formal Huntington family links, might well get to learn about their happy situation. Those who don't get, or hadn't previously got, good news—and whose 'contract' had been just for testing for prenatal exclusion—may well draw an unfortunate conclusion about their own status. The moral of the story is that, for the greater good, explicit contracts should be made and they should be stuck to.

R J M GARDNER

Department of Paediatrics and
Child Health, University of Otago,
Dunedin, New Zealand.

G R GILLET

Department of Neurosurgery, University
of Otago, Dunedin, New Zealand.

C J CHAPMAN

Department of Laboratory Services,
Wellington Hospital,
Wellington, New Zealand.

- 1 Millan FA, Curtis A, Mennie M, *et al*. Prenatal exclusion testing for Huntington's disease: a problem of too much information. *J Med Genet* 1989;26: 83-5.

Options for prenatal testing for Huntington's disease using linked DNA probes

Fahy *et al*¹ discuss four approaches to prenatal testing for Huntington's disease (HD), which depend on the risk status and desires of the parent at risk. The first is the familiar prenatal exclusion testing option,²⁻⁵ where the

parent at risk seeks to minimise the chance of passing the HD gene to the fetus without changing his or her own risk status. The second and fourth approaches are examples of standard prenatal diagnosis for couples where the at risk partner's status has been clarified either by presymptomatic testing or by early signs of the disease itself. In the third approach,¹ termed 'exclusion-definitive' testing, the initial prenatal exclusion test determines subsequent action. If the fetus has not inherited the HD gene, no further action is taken, the usual practice in prenatal exclusion testing. However, if transmission of the HD gene to the fetus cannot be excluded, a definitive test on the fetus is offered. The attraction of this approach is that it avoids termination of pregnancies where the fetus has a 50% chance of being normal. The disadvantage is that the parent at risk can no longer remain unaware of his or her own risk status.

We have recently been involved in several cases that lead us to propose another approach to prenatal testing for HD. There are two situations which differ slightly. In the first, the parent at risk is homozygous for all linked DNA markers and the HD chromosome cannot be distinguished from the normal chromosome. The usual procedure would be to advise the mother that no prenatal exclusion test is possible and that her child will have a 25% risk of inheriting HD. However, it sometimes happens that linkage data are available for other members of the family, perhaps acquired through research programmes or because someone else in the family has enrolled in presymptomatic testing. If these data indicate that the consultand does not carry the HD gene, we believe that it might be good clinical management

to provide this information even when it represents an unsolicited presymptomatic test.

In the second situation, represented in the figure, heterozygosity of markers in the consultand makes it easy to do a prenatal exclusion test on the fetus. Again, it is possible that other family data may be available that substantially alter the risks of the mother transmitting the HD gene. For example, in the family shown in the figure, the HD gene is segregating with the 17.5 kb fragment at the *D4S10* locus,⁶ and the consultand has not inherited this allele. Thus, if she were to have a chorionic villus biopsy, a 17.5/15.0 genotype in the fetus would carry a risk of about 4% of HD. A 17.5/17.5 genotype would carry a risk of only 0.16%. Against these risks must be set the risk related to the procedure of chorionic villus sampling (CVS), which is of the order of 2%.⁷

In our centre the established presymptomatic protocol requires that additional linkage data acquired through research be regarded as confidential. We would therefore carry out the CVS and then advise the mother of a low risk of HD in the fetus. However, we have recently become dissatisfied at this rather mechanical attitude to the problem. It seems to us that the decision as to whether to proceed with a CVS when fetal risks and procedure risks are nearly matched is one that must be taken by the parents and not by their medical advisers. Thus, in this situation, we are also inclined to provide an unsolicited presymptomatic test to the consultand.

Although the two cases discussed might seem unusual they become a common problem when extensive linkage studies have been carried out in a population and where there is a

Pedigree illustrating the problem of prenatal exclusion testing when the consultand's carrier risk is known to be low. RFLPs at *HindIII* (site 1) for the *D4S10* locus are shown.

vigorous programme of presymptomatic testing. We are therefore proposing an additional prenatal exclusion test option. It is that when the at risk parent's chance of carrying the HD gene is known to be low from other data, the clinical adviser should consider disclosing this information and thus allowing the consultand to decide on whether to proceed with the prenatal test.

Obviously, such a decision would only be taken if there were no other members of the immediate family (such as the consultand's sister) likely to seek prenatal exclusion testing. Gardner *et al.*, in the previous letter, are quite rightly worried about this possibility, and suggest explicit contracts should be made "for the greater good". We are not sure what this means. Doctors make contracts with their patients to provide the best possible care, and not to safeguard the greater good. Our point is that rules have value only when exercised in a context of common sense. We have shown examples where there might be a case for exercising clinical judgement rather than sticking rigidly to the rules.

D J H BROCK
ANN CURTIS
MOIRA MENNIE
J A RAEBURN
*Human Genetics Unit,
Western General Hospital,
Edinburgh EH4 2XU.*

- 1 Fahy M, Robbins C, Bloch M, *et al.* Different options for prenatal testing for Huntington's disease using DNA probes. *J Med Genet* 1989;26:353-7.
- 2 Quarrell OW, Meredith AL, Tyler K, *et al.* Exclusion testing for Huntington's disease in pregnancy with a closely linked DNA marker. *Lancet* 1987;i:1281-3.
- 3 Hayden MR, Hewitt J, Kastelein JJ, *et al.* First-trimester prenatal diagnosis for Huntington's disease with DNA probes. *Lancet* 1987;i:1284-5.
- 4 Millan FA, Curtis A, Mennie M, *et al.* Prenatal exclusion testing for Huntington's disease: a problem of too much information. *J Med Genet* 1989;26:83-5.
- 5 McIntosh I, Curtis A, Millan FA, Brock DJH. Prenatal exclusion testing for Huntington disease using the polymerase chain reaction. *Am J Med Genet* 1989;32:274-6.
- 6 Gusella J, Wexler NS, Conneally PM, *et al.* A polymorphic DNA marker genetically linked to Huntington's disease. *Nature* 1983;306:234-6.
- 7 Rhoads GG, Jackson LG, Schlesselman SE, *et al.* The safety and efficacy of chorionic villus sampling for early prenatal diagnosis of cytogenetic abnormalities. *N Engl J Med* 1989;320:609-17.

Oculocerebrocutaneous syndrome

We read with interest the recent paper by Al-Gazali *et al*¹ on oculocerebrocutaneous syndrome. We would like to report another Dutch patient, add four patients previously reported in ophthalmological publications²⁻⁵ and two recently described cases,^{6,7} and present a follow up of the patient described by Wilson *et al.*⁸

The Dutch patient was the third born male child of healthy, non-consanguineous parents. At birth, skin tags were noted around the left orbit and on the neck. He also had a defect of the left nasal ala, skin hypoplasia above the left ear, and punch-like skin defects around the left corner of the mouth (figure). No anomalies were

Oculocerebrocutaneous syndrome. Note the asymmetrical crying face and that all anomalies are left sided.

found other than on the left side of the face and neck. The left eye, which seemed microphthalmic at birth, gradually started to protrude and an orbital cyst was suspected, which was surgically removed. At operation no connection between the brain and the cyst was found, although the cyst had protruded more when the boy was crying. Histopathology of the cyst showed a neuroepithelial hamartomatous structure. Examination of the right eye did not show any anomalies. Repeated CT scans and MRI of the brain showed agenesis of the corpus callosum and mild constant dilatation of the left ventricle, but no intracranial cysts. Radiology of the thorax and vertebral column gave normal results. Chromosomal studies in lymphocytes and fibroblasts from skin from the left side of the head indicated a normal male karyotype. At present, the patient is 14 months old, has a developmental age of about 12 months, and has not had any epileptic seizures.

The features of this patient and six other reported cases²⁻⁷ are compared with the data presented by Al-Gazali *et al*¹ in the table. In addition we have knowledge of two other unpublished patients (R Gorlin, 1989, personal communication). It is possible that many reported examples of orbital cysts⁹ are in fact incomplete forms of the oculocerebrocutaneous syndrome. The relationship with encephalocraniocutaneous syndrome remains uncertain.^{10,11} Follow up of the patient reported by Wilson *et al*⁸ showed that the girl, now aged 4½ years, has only mild psychomotor developmental delay and is attending a normal school. Her main problems are a disturbed equilibrium and difficulty in co-

Main features of oculocerebrocutaneous syndrome.

	Reference							Present case	Total
	1	2	3	4	5	6	7		
Mental retardation	7/9	+				+		(-)	9/12
Convulsions	7/9		-			+		-	8/12
Generalised asymmetry	3/9		-			-	-	-	3/13
Cleft lip/palate	3/9		-			-	-	-	3/13
Orbital cyst	8/9	+	+	+	+	+	-	+	14/16
Microphthalmia	5/9	+	-		+	+	+	+	10/15
Eyelid coloboma	4/9	-	-	-	-	+	+	-	6/16
Skin tags	8/9	+	-	+	+	+	+	+	14/16
Skin hypo/aplasia	9/9	+	-	+	-	+	+	+	14/16
Punch-like defect	7/9	+	-	+	+	+	+	+	13/16
Skull defects	5/8	-	+		+	+	-	+	9/14
Rib dysplasia	4/9	-					-	-	4/13
Intracranial cysts	6/8		+			+	-	-	8/12
Agenesis of corpus callosum	4/8					-	-	+	5/11