alleles associated with poor metaboliser phenotype is increased by a factor of 2.5.⁶ An alteration in the CYP2D6 gene may therefore also play a part in familial Parkinson's disease.

Segregation analysis was performed in six Parkinson's disease families in which there were at least two affected living patients, with an intragenic microsatellite marker in the CYP2D6 gene. Sixteen patients and 11 relatives were studied. All patients fulfilled the diagnostic criteria for probable Parkinson's disease—namely, (a) at least two of the main features of Parkinson's disease (tremor, rigidity, or bradykinesia), (b) asymmetric onset, (c) pronounced response to levodopa, (d) progressive course, (e) absence of clinical features characteristic of alternative diagnoses or of known aetiology. The mean age at onset was 55 years. DNA was extracted from blood leucocytes, and an intragenic dinucleotide repeat was amplified by the polymerase chain reaction.⁷ Genotypes were determined by hybridisation of a ³²P labelled primer to the polymerase chain reaction product after electrophoresis in a denaturing gel and blotting.

Independent segregation of the microsatellite alleles was found in two of the six families (figure). In family 717, the affected father (II-1) transmitted allele 2 to his affected daughter (III-1) but allele 6 to his affected son (III-2). Although the genotype of the father could only be deduced, false paternity is unlikely, as both children inherited the disease. In family 722, patients III-2 (1/4) and III-10 (2/5) had no marker allele in common, indicating that they do not share an allele of the CYP2D6 gene. These results exclude a defect in this gene as the cause of Parkinson's disease in these two families, unless the disease is not genetic in origin (phenocopy) or there has been a mutation in the dinucleotide repeat. The probability of phenocopy is identical to the prevalence of the disease (0.35%),⁸ and the mutation rate for dinucleotide repeats does not exceed 0.1%.⁹ The combined probability for the occurrence of phenocopies and/or microsatellite mutations in both families is therefore <0.25%. Independent segregation could not be found in the other four families, probably because of their small size.

Although the present study has shown that an allele of CYP2D6 is not responsible for familial Parkinson's disease in two of the six families studied, it cannot be excluded for other cases. Genetic heterogeneity may exist in this disease, as in other neurodegenerative disorders such as Alzheimer's dis-

ease and amyotrophic lateral sclerosis. Poor debrisoquine metabolism may also be a risk factor in the pathogenesis of sporadic Parkinson's disease, a question not considered in the present study.

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A case of Creutzfeldt-Jakob disease presenting with cortical deafness

Cortical deafness is an unusual sign, arising from damage to both temporal or temporoparietal lobes.¹ The clinical, electrophysiological, and neuropathological findings in a patient with sporadic Creutzfeldt-Jakob disease who presented with cortical deafness are described.

A 65 year old man was admitted for investigation of progressive bilateral hearing loss. It had developed insidiously over two months previously. He complained of

"gurgling" noises in his ears, and the loss of hearing could initially be overcome by shouting or increasing the volume of the television. He had difficulty using the telephone. At the time of his admission he could communicate only by writing, and volunteered that his perception of speech was more impaired than his hearing. In the month before admission his wife had noted that he had become more nervous and hesitant. Also during this month, he became unsteady (falling to the left) and developed speech difficulties consisting of hesitancy, stuttering, and a tendency to substitute letters in words ("crudit" instead of "credit").

Rheumatic carditis in childhood had been complicated by mitral valve disease (requiring replacement with a mechanical prosthesis in 1986). A malignant melanoma had been excised in 1991, and a lymph node recurrence treated with excision and radical radiotherapy in 1991. Medication on admission consisted of warfarin, digoxin, Burinex K, and diazepam. There was no family history of deafness or dementia, and no occupational risk factors for cochlear trauma.

Examination showed cachexia but no lymphadenopathy. Severe bilateral hearing loss was confirmed with only non-discriminating perception of sounds. His speech was consistent with deafness (vowel lengthening), but also showed evidence of a more central language disturbance (phonological errors). He had horizontal nystagmus on gaze to the left, and predominantly left sided finger-nose ataxia. The rest of the examination was unremarkable.

The following investigations were normal or negative: routine biochemistry and haematology, erythrocyte sedimentation rate, autoantibody profile, chest radiograph, syphilis serology, international normalised ratio, and serum ammonia. Liver function tests were abnormal (albumin 32 g/l (normal 35-50), bilirubin 37 µmol/l (5-20), alanine aminotransferase 44 U/l (<40), aspartate aminotransferase 62 U/l (<40), alkaline phosphatase 599 U/l (70-350) and γ-glutamyltransferase 222 U/l (<50)). Examination of CSF showed less than 5 nucleated cells per mm³ and 0.45 g/l protein. Imaging by CT and MRI (with gadolinium) showed no abnormalities. EEG showed prolonged runs of repetitive sharp wave complexes bilaterally. Pure tone audiometry could not be carried out due to lack of cooperation. Brainstem auditory evoked potentials were performed with a suprathreshold 90 dB click stimulus, and showed waves 3-5 and wave 3 on stimulation of the right and left sides respectively. Cortical auditory evoked potentials (CAEPs) were recorded with an 85 dB burst stimulus. These showed normal waveforms bilaterally and normal absolute latencies of the N1 response (89.5 ms on right, 99.0 ms on left).

He deteriorated rapidly, becoming confused, agitated, and more ataxic. He developed paratonic rigidity of all four limbs and primitive reflexes recurred. There were spontaneous myoclonic jerks and a prominent startle response (to touch). He became akinetic and mute, and probably blind (no response to visual menace). He died two weeks after admission.

The immediate cause of death at necropsy was bilateral acute bronchopneumonia. No evidence of residual or metastatic melanoma was found. The prosthetic mitral valve was satisfactory and appreciable left ventricular hypertrophy was noted. The

Partial pedigrees of families 717 and 722. Genotypes for CYP2D6 are indicated by large numbers below each tested person. Genotype in parentheses is deduced.

brain weighed 1333 g and showed mild cortical atrophy. Histological examination found widespread subacute spongiform encephalopathy with vacuolation in the frontal, occipital, and both temporal lobes, basal ganglia, thalamus, and cerebellum. The brainstem and spinal cord seemed spared. In the areas of severe spongiform change in the temporal lobes there was extensive neuronal loss and reactive astrocytosis.

Immunocytochemistry for the prion protein (antibody provided courtesy of Dr J Hope, Neuropathogenesis Unit, Edinburgh) showed a positive reaction around areas of confluent vacuolation. These changes were present in both transverse temporal gyri, but the underlying white matter and medial geniculate bodies were unaffected. No amyloid plaques were identified on immunocytochemistry and there was no evidence of any other disease process in the brain. Molecular biological examination of the open reading frame of the prion protein gene showed no mutations and he was methionine-valine heterozygous at codon 129.

Disturbed hearing is unusual in the early stages of Creutzfeldt-Jakob disease. Although six out of 100 experimentally transmitted cases were reported to have "auditory sensory disturbances" in the first stage, these were not defined.² Will and Matthews subsequently described the clinical features in 137 pathologically or electrophysiologically confirmed cases, and none of these had auditory symptoms as presenting features or during the course of the illness.³ Visual disturbance, by contrast, was commoner, with 9% of patients complaining of visual disturbance at the start and 13% exhibiting cortical blindness during the course of the illness. This difference may in part be due to the difficulty in assessing hearing in patients with rapidly progressing dementia. The finding of spongiform change affecting both transverse gyri supports the clinical suspicion of cortical deafness as the cause of this man's hearing loss. The normal CAEPs were unexpected, but as pointed out by Graham *et al*⁴ these may be preserved in cortical deafness. It is arguable that these clinical features in the presence of normal CAEPs should be regarded as auditory agnosia, but we prefer to regard the entities of auditory agnosia and cortical deafness as part of a continuum (as do Graham *et al*⁴). It is also of note that normal flash visual evoked potentials have been recorded in cortical blindness.⁵ In conclusion, this pathologically verified case of Creutzfeldt-Jakob disease presented with cortical deafness. This is, to our knowledge, the first description of such a presentation, and emphasises the variety of cortical disturbances with which this disease can present.

Speech assessment was performed by Mr Cameron Sellars, genome analysis was undertaken at the AFRC Centre for Genome Research in Edinburgh by Dr Otto Windl and Ms. Maureen Dempster, and Dr Robert Will gave encouragement and guidance.

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Late recurrence of craniopharyngioma in the cerebellopontine angle in a fertile woman

Suprasellar craniopharyngiomas account for about 3% of intracranial tumours. They are regarded as slowly expanding and arise from remnants of Rathke's pouch epithelium or from metaplasia of pituitary cells.¹ Their tendency to local infiltration makes total surgical removal difficult. Recurrence is to be expected in incompletely removed cases. Postoperative irradiation is generally agreed to be of benefit, but the risk of long term hypopituitarism may be increased.² We report a case of craniopharyngioma treated by surgery and cobalt irradiation, which recurred in the cerebellopontine angle 26 years later, in a woman with normal fertility.

A 33 year old woman presented with a 12 week history of left facial numbness and paraesthesiae. There was no visual loss, headache, or urinary symptoms. She had a suprasellar mass removed in 1963 when aged seven and postoperative radiotherapy consisting of 3000 rads of cobalt was given from both sides. The estimated field was 10 cm. There were no records available of the original surgery but the mass was regarded as entirely suprasellar, probably incompletely removed, and the histological diagnosis was craniopharyngioma. She did not receive

replacement hormone treatment and had no symptoms until this presentation. She had a normal menarche and had one healthy child delivered by caesarean section. On examination she was small (148 cm), obese, and was 18 weeks pregnant. She had sensory diminution in the ophthalmic and maxillary divisions of the left trigeminal nerve, with an absent left corneal reflex. Visual fields and acuity, and the remaining cranial nerves were normal. General systemic examination, full blood count erythrocyte sedimentation rate, biochemical profile, plasma thyroxine, urinalysis, chest radiograph, left facial electromyograph, visual evoked responses, and CSF analysis were all normal. Computed tomography showed a large contrast enhancing mass in the left cerebellopontine angle extending from the clivus and continuous with an area of dense suprasellar calcification. Left vertebral and carotid arteriography showed posterior displacement of the vertebral artery. There were no feeding vessels. MRI (figure (A)) outlined the mass in the cerebellopontine angle, not involving the internal auditory meatus. The tumour was heterogeneous with areas of calcification and probable necrosis. The T1 and T2 weighted sequences suggested a fat or cholesterol containing tumour such as craniopharyngioma. Surgery was performed six months after delivery of her baby. The trigeminal nerve was stretched over a cyst containing brown fluid. The wall was excised but only limited resection could be done on the calcified anterior portions. A catheter was inserted into the residual cyst, and a Pudenz reservoir placed subcutaneously below the left ear. Postoperatively facial sensation returned to normal and she remains well two years later. The cyst contents have been aspirated on two occasions because of headache.

Endocrine function 14 days after craniotomy was normal as assessed by a Synacthen test, an LHRH test, and plasma thyroxine, and prolactin concentrations. A growth hormone secretion test and TSH measurement were not done. Histological examination of the tissue showed adamantinomatous type epithelium with foci of cystic degeneration, squamous epithelium, calcification, and ossification typical of an adamantinomatous type of craniopharyngioma (figure (B)). The fluid contained polarisable crystals. This case has several

(A) Mass of the tumour outlined by MRI.
(B) Histological section of the tumour.