

scientific advances often depend on the apparently unconventional. If the doctor contacts the GMC it will immediately ask for evidence. The preliminary screener of the council has to consider the quality of the evidence that will be adduced because if it is inadequate then the later committees will quickly dismiss the case. One objection people raise against the council is that it has no "police force," but the preliminary screener may ask the council's solicitors to investigate a case if it seems that serious professional misconduct may have occurred. This is naturally a limited investigation, and it is doubtful that the council could have coped with accumulating for itself the evidence that was needed in this case. It took an investigative journalist with the resources of a television programme behind him to gather the evidence, raising questions about the strength of the professional machinery and the unwisdom of being too quick to condemn all "trials by media." In the light of this case the GMC needs to consider hard whether it needs more investigative machinery.

Alternatively, doctors worried about the practices of Sharp and Sultan might have presented their worries to the authorities of the London Bridge Hospital. This naturally would have been an awkward task, but there would also have been worries about how far the hospital would have been able to take the protestations. The hospital had no ethical committee to approve the experiments of Sharp and Sultan, and its medical advisory committee had simply accepted

Sharp's claims to have ethical and scientific backing for what he was doing. Campbell raises questions about the dangers inherent in the expansion of private practice, and these are questions that also worry the GMC. To a large extent the council depends on the NHS machinery for investigating complaints, and because it has no power over specialist registration the council cannot stop doctors in private practice from claiming skills that they do not have. Unscrupulous doctors may prosper within the NHS, but they can prosper much more easily in private practice—as unhappy episodes with slimming clinics, cosmetic surgery, and selling kidneys illustrate. The government is acting this week to outlaw the sale of kidneys, providing another example of failure of professional safeguards and necessity for government action. The ethical dangers in the expansion of private practice have to be recognised and countered.

Finally, as well as the ethics of doctors the practices of the media need to be questioned. The *Daily Express* and the *Daily Telegraph* have reported this dubious treatment, yet they have not publicised the treatment's downfall. They should.

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## Visual disability and the elderly

### *Time for general practitioners to begin preventive screening*

The proportion of the population over 65 is increasing, and more of these people are having to look after themselves. To do so they must retain their faculties, and none is more important than sight.

Surveys of eye disease in elderly hospital outpatients show that the most common referrals are for cataracts (25%), senile macular degeneration (12%), and glaucoma (14%).<sup>1</sup> Although the referral to hospital comes from the general practitioner the diagnosis has usually been suggested by an optician.<sup>2,3</sup> Most referrals result from symptomatic disease and so do not reflect the true prevalence of these diseases in the community.<sup>1</sup> Population surveys provide better estimates.<sup>4,5</sup> These have found cataract or macular disease sufficient to reduce visual acuity slightly (<6/9) in nearly half of the over 75s and glaucoma in about 7%. Though high prevalence does not mean inevitable "blindness," a recent study of patients attending a geriatric day care centre found that one third had unrecognised severe visual loss.<sup>6</sup> These figures suggest a serious underdiagnosis of (commonly asymptomatic) treatable eye disease in elderly patients.

What level of preventive eye care, therefore, should elderly patients be offered? Until now screening for glaucoma has been mainly restricted to patients with a family history of the disease. All patients considered to be at risk should, however, be screened every two years. In addition, because the incidence of open angle glaucoma has been estimated as 0.5% in five years for 65 year olds and 1.1% in five years for 75 year olds<sup>7</sup> two yearly screening should be offered to this population too.

Setting up a screening programme for the elderly would be expensive. A similar programme in the United States was costed at \$100-300m for the first year, rising with rescreening of

the same patients every two years.<sup>8</sup> The chances of additional funding for a similar programme in the United Kingdom are not high, and screening would probably have to rely on existing funds. At present the government pays for screening of the families of glaucoma patients, and it may provide them with free sight tests by opticians in the future. In view of the prevalence of glaucoma in the elderly perhaps screening should also be extended to them.

Who should screen the elderly? At present, almost by default, this is left to ophthalmic opticians. General practitioners refer patients with symptoms and identify those with disease of the outer eye.<sup>3</sup> Diagnosis of diseases in the posterior segment will be made only by ophthalmic opticians until medical students are taught adequate ophthalmoscopy. General practitioners' present degree of proficiency is unfortunate; they are far better placed to examine the individual patients "at risk," and tonometry and ophthalmoscopy take little time for experienced staff.

Most patients referred with asymptomatic early cataract, macular change, or ocular hypertension without glaucoma will require only intermittent observation. As they would far outnumber patients needing treatment any increases in their referral rate would rapidly swamp ophthalmic clinics. As ophthalmic services in the United Kingdom are fully occupied with patients needing treatment this extra burden could be taken on only with a large increase in staffing and facilities.

Cost is another consideration. Hospital visits cost about £30 each, sight tests about £10, and a visit to a general practitioner possibly even less. After an initial hospital referral it would be considerably cheaper for opticians or general practitioners to follow the patients up.<sup>3</sup>

Elderly patients would benefit from free sight tests carried out every two years and from being observed at a local community based centre; they could be referred to hospital should their condition change. Better health care, reduced hospital visits, and improved community care would therefore be achieved. And the elderly would be less neglected than now.

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## Mitochondrial myopathies

### *Mechanisms now better understood*

The mitochondrial myopathies are a clinically and biochemically heterogeneous group of inborn metabolic errors affecting the energy pathways of mitochondrial metabolism.<sup>1,2</sup> Although uncommon, these disorders are increasingly recognised as important causes of diseases of many systems. Any part of mitochondrial metabolism may be affected, and the commonest cause of mitochondrial myopathy is a defect of the respiratory chain.<sup>3</sup> The mammalian respiratory chain and the pathway for oxidative phosphorylation comprise five multimeric enzyme-protein complexes (complexes I-V) located on the inner mitochondrial membrane. These proteins are unique in that they constitute the products of two separate systems of gene expression and protein synthesis: 13 of their 67 subunits are encoded by mitochondrial DNA.<sup>4</sup> Nuclear encoded proteins are transported into mitochondria as precursors either directly or through receptors on the outer mitochondrial membrane. Once inside they are assembled into functional enzyme protein complexes with the products of mitochondrial DNA. Whereas the transmission of nuclear genes is governed by the principles of mendelian inheritance mitochondrial DNA is inherited exclusively through the maternal line. Maternal inheritance of a mitochondrial myopathy with myoclonic epilepsy has been described,<sup>5</sup> and the overall ratio of maternal to paternal transmission of mitochondrial myopathy is 9:1.<sup>6</sup>

Patients with defects in the respiratory chain may present from infancy to late adulthood. Problems associated with early onset may be failure to thrive; hypotonia; respiratory, cardiac, hepatic, or renal failure; mental regression; seizures; ataxia; or visual failure in various combinations. In most affected infants muscle biopsy specimens show cytochrome oxidase (complex IV) deficiency. Prognosis is poor with most patients dying in infancy or early childhood of cardio-respiratory failure and metabolic acidosis. Patients presenting later in life may be grouped into those with progressive external ophthalmoplegia and limb weakness (55%), those with limb weakness alone (18%), and those in whom the central nervous system is affected—with dementia, deafness, seizures, ataxia, and involuntary movements (27%).<sup>7</sup> About a third of patients have a pigmentary retinopathy. Attempts have been made to classify patients into specific syndromes such as the Kearns-Sayre syndrome; the syndrome of mitochondrial encephalomyopathy, lactic acidosis, and stroke like episodes (MELAS); or the syndrome of myoclonic epilepsy with ragged red fibres (MERRF). The considerable overlap among all these groups, however, makes classification by clinical features alone unreliable.

Muscle biopsy confirms the diagnosis in suspected cases. The morphological hallmark of the mitochondrial myopathies is the ragged red fibre—subsarcolemmal accumulations of mitochondria stained red by the modified Gomori trichrome stain. Electron microscopy shows that some patients have intramitochondrial paracrystalline inclusions. The site of the biochemical defect is best determined by polarographic study of respiring mitochondria freshly isolated from skeletal muscle.<sup>8</sup> These studies are supplemented by enzyme assays and cytochrome measurements. In adults respiratory chain defects are most commonly found in reduced nicotinamide adenine dinucleotide coenzyme Q (NADHCoQ) reductase (complex I) and coenzyme Q (CoQ) cytochrome c reductase (complex III). Some patients may have secondary carnitine deficiency. Positron emission tomography scanning has shown that the biochemical defect in skeletal muscle is also expressed in the brains of patients with encephalopathy.<sup>9</sup>

No correlation between the site of the biochemical defect and any of the clinical groups or syndromes mentioned above has been found, suggesting that clinical presentation is determined by the severity and tissue distribution of the biochemical defect(s). Proteins of the respiratory chain may exist in tissue specific forms,<sup>10,11</sup> and this may be important in determining the extent of disease.

Specific deficiencies of nuclear encoded polypeptides have been identified in patients with a defect in complex I or III.<sup>12,13</sup> Deletions of segments of mitochondrial DNA have been shown in the skeletal muscle of about a third of patients with mitochondrial myopathy,<sup>14</sup> suggesting that populations of mitochondria containing deleted and non-deleted DNA coexist in the same tissue. This molecular defect has a clinical correlate—in this study all patients with deletions had ophthalmoplegia and, with the exception of those with the Kearns-Sayre phenotype, none had disease predominantly of the central nervous system. Recent reports have shown that most, but not all, patients with the Kearns-Sayre syndrome have deletions of mitochondrial DNA.<sup>15,16</sup> The pattern of disease in patients with mitochondrial DNA deletions may be determined by the proportion of abnormal mitochondria in any given tissue and their distribution among tissues. The distribution may be governed by random partitioning of abnormal mitochondria during embryogenesis. Tandem duplications of mitochondrial DNA have recently been shown in two patients with mitochondrial myopathy but were absent in unaffected family members. The abnormal mitochondrial DNA was found in muscle, granulocytes, and