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.[1 2] 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.[3] 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.[4] 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,[5] and the overall ratio of maternal to paternal transmission of mitochondrial myopathy is 9:1.[6]

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 cardiorespiratory 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%).[7] 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.[8] 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.[9]

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,[10 11] 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.[12 13] Deletions of segments of mitochondrial DNA have been shown in the skeletal muscle of about a third of patients with mitochondrial myopathy,[14] 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.[15 16] 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

lymphocytes of one of the patients but not in bladder epithelial cells or hair.[17]

Effective treatment of the mitochondrial myopathies remains limited. Acute exacerbations with severe lactic acidosis precipitated by exercise, infection, or alcohol may be improved by correcting the acidosis with a slow infusion of sodium bicarbonate. Patients with carnitine deficiency associated with a respiratory chain defect may improve with oral carnitine. Ubiquinone, ascorbic acid, menadione, and steroids have all been tried with varying success. Clearer understanding of the molecular mechanisms underlying these metabolic defects may lead to more effective treatment.

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NHS review: the first three months

Time for the posturing to stop

Much of the style and content of the government's white paper on the NHS was bound to provoke antagonism.[1] Firstly, the timetable requiring the first hospital trusts and budget holding practices to be operational by the end of 1991 is widely regarded as all but impossible. It permits no time for evaluative studies or demonstration projects. Secondly, the government's apparent determination to impose the full set of changes on a reluctant service is abrasive and confrontational. By defending the white paper hook, line, and sinker the government has failed to allow the service to respond to the positive features while seeking further clarification of the more questionable elements.

Thirdly, the vagueness of many of the white paper's proposals does not encourage the belief that their consequences have been carefully anticipated and approved. The absurdly fine detail in which the valuation of capital assets has been described (requiring, for example, the separate valuation of every individual item above £1000) emphasises the paucity of detail supporting innovative proposals such as creating hospital trusts and pricing and selling services. Virtually nothing has been said about the implications of these profound changes for community care, medical manpower planning and training, strategic planning of health care services, management and accounting costs, or pursuit of social and geographical equity in health care. Nowhere has it been explained exactly how patients will have a greater choice of health care at no less inconvenience than at present. All that has been offered are broad assurances that all will be well.

Beneath the justifiable demands for detailed answers to questions such as these are deeper fears about long term objectives and implications. The white paper is to be understood as a political statement, not as a planning document; it seeks to apply to health care many of the principles of change that are being implemented throughout the public sector services. Its effect will be to destabilise the NHS, a process that may be intensified through government policies for the future funding of the service. Although the review was set up amid widespread fears about the underfunding of the NHS, the white paper offers no prospect of change in either the level or the source of funds. Indeed, the 1989 Public Expenditure White Paper,[2] published the day before the white paper, forecast annual increases in total NHS expenditure of only 7·7%, 5·3%, and 4·2% respectively over the next three years. These figures do not allow for inflation, nor do they take account of demographic or technological changes. Circumstances could easily arise (such as the continuation of high inflation) in which these figures would become real cuts.

The destabilisation of the NHS, the absence of increased expenditure, and the introduction of the principle of tax relief on private health insurance premiums have fuelled fears that the proposals are an interim step towards privatisation. Although any such intent has been denied by Mr Clarke, the fear is reasonable. The government believes in the power of market forces to produce an efficient allocation of goods and services, and it has implemented that belief in public services that 10 years ago almost nobody thought could be privatised. There is no reason why this long term political programme should stop short at the NHS.

It is regrettable, however, that the intense hostility engendered by the white paper has obstructed much real debate about its meritorious features. That the hostility has spilt over to the proposed new contract for general practitioners has exacerbated the tendency to simplify and polarise opinion, as though there are no midway points between an uncritical belief in the rightness of the government's proposals and an implacable opposition to every last detail.

Several features of the white paper do reflect and develop ideas that have been discussed for some time and that until