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Ion channels

New explanations for old diseases

Ion channels are protein pores in the cell membrane that allow the passage of ions down their respective electrochemical gradients.[1] The ubiquitous presence of ion channels among cells of unicellular and multicellular organisms suggests their importance in maintaining cellular integrity. Our understanding of the part that they play in disease has grown rapidly in the past few years, as a result of being able to explore the functional properties of ion channels in living cells.

Ion channels are classified broadly by the principal ion they carry (sodium, potassium, calcium, chloride) and the mechanisms by which they are opened and closed. Acetylcholine, for example, is a receptor specific agonist that acts at the postsynaptic membrane of the motor end plate to open chloride channels. Changes in membrane voltage or to concentrations of intracellular ions and molecules such as calcium and ATP can also open ion channels. The normal but unequal distribution of ions across the cell membrane can lead to the generation of a membrane potential as great as 100 mV.

Hodgkin and Huxley were the first to study ion channels, in 1952. They examined the squid giant axon using the voltage clamp technique.[2] They focused principally on the ionic mechanisms facilitating communication of information within or between nerve or muscle cells, which led to current knowledge of the action of voltage gated ion channels. Not until Neher and Sakmann developed the patch clamp technique (for which they received the Nobel prize in 1991), however, did it became feasible to study other types of cell and resolve currents passing through single channels.[3] Their work means that conformational changes of biological molecules in situ and in real time can be described, as well as conformational changes in small cells such as lymphocytes or epithelial cells. More important, however, are the changes in the functional properties of ion channels that may be associated with disease processes.

Abnormalities of ion channels were initially believed to be confined to excitable cells. Hyperkalaemic periodic paralysis, for example, arises from a defective voltage activated sodium channel in skeletal muscle.[4] More recently, abnormalities of a calcium dependent potassium channel have been found in cavernous smooth muscle from some men with erectile dysfunction.[5] A complicated regulatory relation exists in cavernous smooth muscle cells between membrane potential, the activity of calcium dependent potassium channels, and voltage activated calcium channels. These voltage activated calcium channels in turn modulate intracellular calcium ion concentration, which is important in the smooth muscle relaxation that precedes an erection. The impaired hyperpolarising ability of corporal smooth muscle arising from defective calcium dependent potassium channels may account for the failure of smooth muscle to relax. This results in impotence.

Even in tissues traditionally not considered to be excitable, however, dysfunction of ion channels has been shown to cause disease. Well known examples include cystic fibrosis and diabetes mellitus. Cystic fibrosis arises from a failure of chloride ions to pass through the so called cystic fibrosis transmembrane regulator protein. In normal cells cyclic AMP activates cyclic AMP dependent protein kinase A, in turn stimulating cyclic AMP dependent transepithelial transport of chloride ions. In cells from patients with cystic fibrosis the cystic fibrosis transmembrane regulator fails to respond to protein kinase A stimulation, resulting in increased intracellular chloride ion concentration.[6] This kind of new knowledge has been applied to devise new therapeutic strategies. In the case of cystic fibrosis, attempts at correcting the abnormal transmembrane regulator have been made by gene therapy, with early favourable reports.[7]

Glucose metabolism is linked to pancreatic cell insulin secretion through a sequence of events entailing changes in the ratio of ATP to ADP concentration, closure of ATP sensitive potassium channels, membrane depolarisation, and the opening of voltage sensitive calcium channels. The rapid influx of calcium results in release of stored granules containing insulin. Defects in this mechanism are thought to contribute to the development of diabetes mellitus.[8] Sulphonylureas, discovered by serendipity many years ago to be effective in treating diabetes mellitus, block ATP sensitive potassium channels.

Recently, evidence has begun to emerge of other roles for ion channels such as in the development of cancer, tumour invasion, and possibly metastasis. Voltage gated sodium channels that are similar to those in excitable tissues are present in small cell lung cancer cell lines[9]; they are also associated with invasion by rat[10] and human[11] prostate cancer cells in vitro. Chloride channels have been identified in primary cultures of cervical epithelium from patients with cervical cancer but not in cultures from patients who do not have cervical cancer.[12 13] The functional role of these chloride

channels in cervical carcinogenesis remains to be determined.

As ion channel subtypes and membrane potential have been implicated in many aspects of cell biology, including the cell cycle, apoptosis, cell adhesion, cell motility, exocytosis, and multidrug resistance, all of which are relevant to the neoplastic process, reports such as these are not surprising.[14 15] The multiple roles of ion channels in normal and altered physiology explain some current pharmacological mechanisms and point to potentially promising new interventions and therapeutic strategies. These include antisense oligonucleotide technology or gene therapy to introduce or restructure ion channels and modify cellular action potentials, ion transport, or the membrane potential profile.[7] Evidence for the role of ion channels in disease continues to grow, and treatments given on the basis of ion channel dysfunction could eventually constitute the basis for an entire new class of interventions to treat disease.

Marc E Laniado *Clinical research fellow in urology*
Paul D Abel *Reader in urology*

Department of Surgery, Imperial School of Medicine, Hammersmith Hospital, London W12 0NN

El-Nasir Lalani *Senior lecturer*

Department of Histopathology

1 Hille B. *Ionic channels of excitable membranes*. Sunderland, Massachusetts: Sinauer Associates, 1992.
2 Hodgkin AL, Huxley AF. A quantitative description of membrane current and its application to conductance and excitation in nerve. *J Physiol (Lond)* 1952;117:500-44.
3 Neher E. Nobel lecture. Ion channels for communication between and within cells. *Neuron* 1992;8:605-12.
4 Hudson AJ, Ebers GC, Bulman DE. The skeletal muscle sodium and chloride channel diseases. *Brain* 1995;118:547-63.
5 Fan SF, Brink PR, Melman A, Christ GJ. An analysis of the Maxi-K+ (KCa) channel in cultured human corporal smooth muscle cells. *J Urol* 1995;153:818-25.
6 Agam G, Aviram M, Zilberman-Kaufman M, Rothstein A, Livne AA. Cyclic AMP-related and cation-affected human platelet chloride transport regulation. *Eur J Clin Chem Clin Biochem* 1995;33:329-35.
7 Korst RJ, McElvaney NG, Chu CS, Rosenfeld MA, Mastrangeli A, Hay J, et al. Gene therapy for the respiratory manifestations of cystic fibrosis. *Am J Respir Crit Care Med* 1995;151:S75-87.
8 Newgard CB, McGarry JD. Metabolic coupling factors in pancreatic beta-cell signal transduction. *Annu Rev Biochem* 1995;64:689-719.
9 Blandino JK, Viglione MP, Bradley WA, Oie HK, Kim YI. Voltage-dependent sodium channels in human small-cell lung cancer cells: role in action potentials and inhibition by Lambert-Eaton syndrome IgG. *J Membr Biol* 1995;143:153-63.
10 Grimes JA, Fraser SP, Stephens GJ, Downing JE, Laniado ME, Foster CS, et al. Differential expression of voltage-activated Na^+ currents in two prostatic tumour cell lines: contribution to invasiveness in vitro. *FEBS Lett* 1995;369:290-4.
11 Laniado ME, Lalani E, Fraser SP, Grimes JA, Bhangal G, Djamgos MBA, et al. Expression and functional analysis of voltage-activated Na^+ channels in human prostate cancer cell lines and their contribution to invasion in vitro. *Am J Pathol* 1997;150:1213-21.
12 Chou CY, Shen MR, Wu SN. Volume-sensitive chloride channels associated with human cervical carcinogenesis. *Cancer Res* 1995;55:6077-83.
13 Shen MR, Wu SN, Chou CY. Volume-sensitive chloride channels in the primary culture cells of human cervical carcinoma. *Biochim Biophys Acta* 1996;1315:138-44.
14 Woodfork KA, Wonderlin WF, Peterson VA, Strobl JS. Inhibition of ATP-sensitive potassium channels causes reversible cell-cycle arrest of human breast cancer cells in tissue culture. *J Cell Physiol* 1995;162:163-71.
15 Kondo S, Yin D, Morimura T, Kubo H, Nakatsu S, Takeuchi J. Combination therapy with cisplatin and nifedipine induces apoptosis in cisplatin-sensitive and cisplatin-resistant human glioblastoma cells. *Br J Cancer* 1995;71:282-9.

The health of gypsies

Lack of understanding exemplifies wider disregard of the health of minorities in Europe

The arrival at Dover of groups of gypsy (Roma) families from Slovakia seeking asylum in Britain has briefly focused the attention of the British media on this poorly understood people.[1] The Roma are one example, albeit a substanial one, of minority communities throughout Europe whose way of life and health needs are largely ignored by the majority communities.

Over 5 million Roma people live in the countries of central and eastern Europe. Originally from north-eastern India, they began a slow westward migration about 1000 years ago. By the fifteenth century they were well established in the Balkans, with smaller groups throughout western Europe. At first they were welcomed, claiming papal protection as penitent pilgrims, but the intolerance that accompanied the reformation and the rise of the nation state in the sixteenth century soon led to persecution. In the eighteenth century Austria-Hungary required Roma children over 5 to be taken from their parents and brought up in non-Roma families. In Romania, Roma people were kept as slaves until the 1860s. Up to 500 000 were exterminated in Nazi camps.

In central and eastern Europe Roma people continue to exist on the margins of society, subject to widespread and often institutionalised racism. Although subject to attempts at forced assimilation by the postwar communist regimes, they were also afforded some protection, but this has largely disappeared in the 1990s, with an increase in racist attacks, often with semiofficial approval.

Against this background, it is unsurprising that health policymakers and researchers have paid little attention to the health needs of Roma people, even though their distinctive way of life suggests these needs may be different from those of the majority population. With estimates suggesting that they account for over 5% of the population in Bulgaria, Hungary, Romania, and Slovakia, they are a far from insignificant minority. This failure to address their needs becomes apparent when a Medline search on the term "gypsy" yields rather more papers on the gypsy variant of the *Drosophila* fruit fly than on the health of the Roma people.

Even the numbers of Roma people are uncertain because of their reluctance to identify themselves and enforced assimilation. In several countries their distinct national identity was recognised in censuses for the first time in the 1990s. The few studies that exist suggest that their life expectancy is up to 10 years less than that of their non-Roma neighbours and that infant mortality is up to four times higher.[2] The much

higher levels of poverty, lack of education, overcrowding, and unemployment suffered by the Roma people probably play an important part, but we know little about their specific patterns of disease and how these differ from those of other groups.[3]

What evidence exists is largely from other parts of the world and is fragmentary. A study in Spain reported a nine times greater prevalence of antibodies to hepatitis A in Roma children than in the non-Roma population.[4] Another Spanish study reported that Roma children were at particularly high risk of lead poisoning.[5] Some Roma groups have a high incidence of inherited congenital malformations.[6] Some small scale research has also been conducted in the Czech Republic and Hungary but most of it is not widely known.

There is also a lack of knowledge about access to health services and how to provide them appropriately. Ethnographic research among American Roma people has identified a strongly held set of health related beliefs in which some diseases are seen as Roma, and thus treated by traditional healers, and others as due to contact with the outside world, requiring the services of the formal healthcare system.[7] Relations with the majority population are governed by a series of rules about what is pure or impure. There are also a range of specific rituals dealing with birth, death, and caring for the ill. These can lead Roma people to accept some aspects of care and reject others, behaviour that is often seen as irresponsible for not fitting in with the norms of the majority.[8]

In central and eastern Europe the principle that public health practitioners should explicitly address the health needs of minorities is not well established. Unfortunately, those in western Europe are not exempt from such criticism. Although much research now exists on some groups, such as south Asians in the United Kingdom, the health needs of many other groups have received little attention; in this sense the Roma people are only one group among several neglected communities, although their situation is particularly difficult.[9]

Some groups have been among us for hundreds of years and are now on the wrong side of a national frontier. Others, such as the Turkish guest workers in Germany, are more recent arrivals. The reasons for not addressing their distinct needs vary, with some countries assuming that equality under the law equates to equality of health and others ignoring those who, while contributing to the economy, are not citizens. Some countries are reluctant to pursue research that might stigmatise groups and make their plight worse. This is a particular concern with regard to the Roma people in the present climate. Any research must obviously be handled with sensitivity to the political and historical environment and may be difficult where there is a long legacy of distrust. Nevertheless, at the end of the twentieth century it should no longer be acceptable for European governments to ignore the health needs of significant numbers of their inhabitants.

Martin McKee *Professor of European Public Health*

European Centre on Health of Societies in Transition, London School of Hygiene and Tropical Medicine, London WC1E 7HT

1 Mills H. No gypsies please, we're British. *Observer* 1997; 26 Oct: 19.
2 Braham M. *The untouchables: a survey of the Roma people of central and eastern Europe.* Geneva: UNHCR, 1993.
3 Brearley M. *The Roma/gypsies of Europe: a persecuted people.* London: Institute for Jewish Policy Research, 1996.
4 Cilla G, Perez-Trallero E, Marimon JM, Erdozain S, Gutierrez C. Prevalence of hepatits A antibody among disadvantaged gypsy people in northern Spain. *Epidemiol Infect* 1995;115:157-61.
5 Redondo MJ, Guisasola FJ. An unknown risk group of lead poisoning: the gypsy children. *Eur J Pediatr* 1995;154:197-200.
6 Martinez-Frias ML, Bermejo E. Prevalence of congenital anomaly syndromes in a Spanish gypsy population. *J Med Genet* 1992;29:483-6.
7 Fonseca I. *Bury me standing: the gypsies and their journey.* London: Chatto and Windus, 1995.
8 Sutherland A. Gypsies and health care. *West Med J* 1992;157:276-80.
9 Abel-Smith B, Figueras J, Holland W, McKee M, Mossialos E. *Choices in health policy: an agenda for the European Union.* Luxemburg: Office for Official Publications of the European Communities, 1995.

The use or uselessness of annual public health reports

Time to rise to the challenge of a new role for public health

In the mid 1980s an inquiry into the development of the public health function was established in response to two major outbreaks of communicable disease. The report of the inquiry, chaired by the then Chief Medical Officer of England, Sir Donald Acheson, recommended, among other things, that "community medicine" should be renamed "public health medicine" and that each health authority should appoint a director of public health, who should produce a report on the health of the authority's population each year.[1] After almost 10 years of annual reports from directors of public health the Institute for Public Policy Research has published a review of their purpose and form.[2]

Anne Davies's review is timely because of the huge amount of public health activity taking place nationally. Not only has England its first ever Minister for Public Health, but the current Chief Medical Officer, Sir Kenneth Calman, is also leading a project aimed at developing the public health function. Moreover, Sir Donald Acheson has returned to the fray with additional work on inequalities in health, and a green paper on the government's health strategy *Our Healthier Nation* is expected shortly.

Davies's recommendations are certain to create controversy despite being highly supportive of the concept of reports from directors of public health. The tradition of local annual reports on the public health goes back, with some gaps, to the nineteenth century.[3] Davies's recommendation that reports should in future be produced only every two or even three years will be

seen by some directors as a desirable break from an unwelcome chore. There is, however, no shortage of important public health issues that need to be tackled, and annual reports can, and should be, a catalyst to action. Directors tailor their reports to address various audiences depending on local health problems, but influencing the results of the annual planning cycles of both local authorities and health authorities is an important goal.

Although Davies rightly emphasises the importance of the independent professional nature of the public health report, the net effect of several of her recommendations would be to reduce that independence substantially. In particular, greater government specification of content and centralisation of funding for reports are potentially constraining. The independence of the director of public health needs to be protected, even though some argue that independence is inversely related to influence. There is little evidence of the current independence being abused; indeed, if there is any criticism it is that some directors have not used their annual reports to speak out on the real determinants of ill health.

Public health professionals have recently become even more closely involved with issues in the personal health services, particularly the operation of the internal market. But circumstances have never been more favourable for a return to a much wider public health role. The new and welcome concentration on the social and economic causes of ill health and on health inequalities will highlight the importance of public health leadership. We live increasingly in a world of shared power, where no one organisation has the legitimacy, power, capability, or intelligence to act alone on the causes of ill health.[4] Directors of public health are well placed to act as convenors and catalysts for action in the community, and annual public health reports should be an important tool. Operating effectively in this way will demand a substantial change in approach for many directors, who will also need to avoid the temptation of thinking that the task is merely to "educate" the public about health. When public health professionals talk about educating the public they often mean using more effective means of telling people what, from a professional point of view, is in their best interests.[5] What we need instead is to develop an approach to leadership which mobilises others to take part in collective action on public health issues. The really urgent task is to encourage and empower directors of public health to grapple with the crucial issues of poverty, inequalities, poor nutrition, and bad housing.

Gabriel Scally *Regional director of public health*

South and West Regional Office of the NHS Executive, Bristol BS12 6SR

1 Public health in England. The report of the inquiry into the future development of the public health function in England. London: HMSO, 1988 (Cmnd 289).
2 Davies A. *Reporting the public health: a new role for annual public health reports.* London: IPPR, 1997.
3 Chave SPW. The rise and fall of the medical officer of health. *Community Medicine* 1980;2:36-45.
4 Bryson JM, Crosby BC. *Leadership for the common good: tackling problems in a shared power world.* San Francisco: Jossey-Bass, 1992.
5 Mathews D. Public-government/public-schools: insights from another disconnect. *National Civic Review* 1996;85:14-22.

Screening for fragile X syndrome: a model for genetic disorders?

The merits of screening should be considered separately for each disorder

The fragile X syndrome is often cited as the commonest inherited cause of mental handicap. It was described after the finding that a fragile site at the distal end of the X chromosome was associated with mental handicap. The X linked inheritance pattern is atypical; female carriers may show some features, and males may also occasionally be asymptomatic carriers. Fragile X syndrome was the first of an increasing number of neurological genetic conditions in which a dynamic mutation of a triplet repeat was identified, where instability between generations explained the unusual inheritance pattern.[1] The documentation of the molecular pathology in fragile X allowed confirmation of carrier status in both male and female family members. The growth in understanding of the condition led to early calls for screening,[2] proposed both to implement early therapy and to reduce the birth prevalence.

Several approaches to screening are possible, broadly divided into either case finding with cascade screening (of relatives at risk in the extended family) or population screening for carriers, most commonly suggested during pregnancy.[3] Case finding in childhood would allow early intervention, and, although there is no cure, some manifestations do respond to mainly behavioural management strategies.[4] Early diagnosis may reduce lengthy and distressing investigations for developmental delay and permits genetic advice to be given to a family. However, the diagnosis may not be made until after the birth of a sibling. Carriers identified by cascade screening can consider reproductive choices, including limiting family size, use of donor gametes, and prenatal diagnosis with the offer of selective abortion.

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Turner et al show the effectiveness of a case finding programme with active cascade screening (p 1223).[5] Their service has been running in New South Wales for 10 years and is based on active searching for affected adults and school age children. A reduction in birth prevalence from 2.5 to 1 per 10 000 has resulted from follow up of extended families. Although British genetic centres offer testing to relatives of individuals with fragile X syndrome, active case finding is not systematic. The relatively poor performance of cascade

screening in Britain and parts of Europe[6] may result partly from social differences between these populations and that in New South Wales. However, the results of cascade screening may take some time to emerge. The Australian team emphasises how family dynamics may change, with testing becoming acceptable long after the original approach by genetic services (G Turner, personal communication).

Antenatal screening is attractive as a potential approach to reducing birth prevalence; since no affected child has been born to a woman who is not a carrier, it could identify all pregnancies at risk of being affected. Nevertheless, several potential pitfalls exist. Prime among these is the lack of information about the natural history of fragile X syndrome. Measurement of the size of the triplet repeat in the gene gives some information about the risk of unstable transmission, but other factors which determine instability are poorly characterised in fragile X families, so extrapolation to the general population is premature. Preliminary data even suggest that repeat sizes at the upper limit of the "normal range" may be overrepresented in boys with special educational needs.[7] Present technology would identify about 1 in 259 women as being at risk of transmitting the condition.[8] While the clinical outcome for male fetuses of carrier females is readily predictable from prenatal testing, that for female fetuses is less clear.[9] Furthermore, as Turner et al point out, the demands of counselling those identified as being at risk will be enormous, and a great deal of anxiety (much of it needless) will be engendered. Further research is needed to answer the questions posed about antenatal screening in the general population. In the meantime case finding and cascade screening is probably the best approach for fragile X syndrome. In the long term, this will provide a firm foundation for broader population testing in future.

Fragile X syndrome cannot, however, be used as a model for all genetic disorders. For some conditions, such as phenylketonuria, neonatal screening is well established, allowing both early treatment and genetic counselling. Neonatal screening programmes for other genetic diseases will be appropriate where treatment started in asymptomatic affected individuals can prevent death and disability, a good example being medium chain acyl CoA dehydrogenase deficiency.[10] For recessive disorders (where the status of both partners determines risk) antenatal screening may be the most appropriate. An example is haemoglobinopathy screening, well established in many parts of Britain, although for the most informed reproductive choices, genotype needs to be known before pregnancy.[11]

The technology for screening for genetic disease is progressing rapidly, both as the molecular pathology of more disorders is elucidated and as relatively cheap, large scale testing becomes available. Alongside these developments, it is also important to consider for each disorder much wider issues, including the pattern of inheritance, provision of accessible information, and possible interventions before deciding on whether and how to screen.

Angela Barnicoat *Consultant clinical geneticist*

Great Ormond Street Hospital for Children NHS Trust, London WC1N 3JH (abarnico@ich.ucl.ac.uk)

1 Verkerk AJMH, Pieretti M, Sutcliffe JS, Fu Y-H, Kuhl DPA, Pizzzuti A, et al. Identification of a gene (FMR-1) containing a CGG repeat coincident with a breakpoint cluster region exhibiting length variation in fragile X syndrome. *Cell* 1991;65:905-14.
2 York-Moore D. New developments in the fragile X syndrome. *BMJ* 1992;305:208.
3 Murray J, Cuckle H, Taylor G, Hewison J. Screening for fragile X syndrome: information needs for health planners. *J Med Screen* 1997; 4:60-94.
4 Turk J, Sales J. Behavioural phenotypes and their relevance to child mental health professionals. *Child Psychol Psychiatry Rev* 1996;1:4-11.
5 Turner G, Robinson H, Wake S, Laing S, Partington M. Case finding for the fragile X syndrome and its consequences. *BMJ* 1997;315:1223-6.
6 Van Rijn MA, de Vries BBA, Tibben A, van den Ouweland AMW, Halley DJJ, Niermeijer F. DNA testing for fragile X syndrome: implications for parents and families. *J Med Genet* (in press).
7 Murray A, Youings S, Dennis N, Latsky L, Linehan P, McKechnie N, et al. Population screening at the FRAXA and FRAXE loci: molecular analyses of boys with learning difficulties and their mothers. *Hum Mol Genet* 1996;5:727-35.
8 Rousseau F, Rouillard P, Morel M-L, Khandjian EW, Morgan K. Prevalence of carriers of premutation size alleles of the FMR-1 gene- and implications for the population genetics of fragile X syndrome. *Am J Hum Genet* 1995;57:1006-18.
9 Steinbach P, Wöhrle D, Tariverdian G, Kennerknecht I, Barbi G, Edlinger H, et al. Molecular analysis of mutations in the gene FMR-1 segregating in fragile X families. *Hum Genet* 1993;92:491-8.
10 Sweetman L. Newborn screening by Tandem Mass Spectrometry (MS-MS). *Clin Chem* 1996;42:345-6.
11 Department of Health (1993) Report of a Working Party of the Standing Medical Advisory Committee on Sickle Cell, Thalassaemia and other Haemoglobinopathies. London: HMSO.

Replacing the NHS market

The white paper should focus on incentives as well as directives

The British government is working on a white paper to be published by the end of the year outlining its plans for replacing the NHS market. The likely flavour of the white paper has already been indicated in ministerial speeches that have emphasised the government's desire to avoid another reorganisation, to pilot its own policies before they are implemented across the NHS, and to encourage cooperation and team working. The test will be the ability of the white paper's authors to translate these aspirations into practical proposals. Three central questions have to be addressed: If competition is to be abolished, should the separation between purchasers and providers be maintained? What will happen to general practitioner fundholding? And, without competition, what incentives will there be to improve performance, especially when funding is tight?

The argument for ending the separation between purchasers and providers rests on the view that these responsibilities are intrinsic to the NHS market and that a commitment to replace the market should logically result in the integration of health authorities and NHS trusts. As experience has shown, however, there is value in maintaining a separation of responsibilities, even if competition is no longer the preferred way of allocating resources. Not least, such an arrangement

enables health authorities to concentrate on assessing the population's health needs and promoting the public health, unencumbered by responsibility for running services. Equally, hospitals can run their affairs without having to refer matters upwards. Above all, the separation helps to ensure greater transparency in the use of resources and enables health authorities to hold providers accountable. The white paper should therefore retain this separation while reinforcing the position of health authorities as the bodies responsible for taking a strategic view at a local level and bringing together different agencies to plan necessary changes to improve the population's health and health services.[1]

What then should happen to fundholding? Critics of fundholding argue that it runs counter to the NHS's principle of equity by reinforcing differential access to hospital services. They also claim that fundholding increases management costs and makes it difficult to plan services for a population. Against that is evidence that some fundholders have achieved improvements in services for their patients,[2] not to mention the political difficulties of ending a scheme which several general practitioners appear passionately attached to. The issues here are compounded by the emergence of a wide variety of approaches to general practice commissioning.[3]

Given this mosaic of primary care led commissioning and provision,[4] any single model, such as the locality commissioning groups proposed when the Labour party was in opposition, is unlikely to be appropriate in all circumstances. The white paper should therefore offer a range of options and allow health authorities and general practitioners to adapt these options to fit existing arrangements. While there are strong arguments on the grounds of both equity and cost to move away from single practice fundholding towards more collective approaches, these approaches must retain the commitment of people working in primary care. This suggests that control over budgets by general practitioners should continue to be an option under collective commissioning, alongside stronger accountability for their use. And while the government's concern to raise standards in primary care by targeting poor performers is welcome, this should not be at the expense of the innovators, whose enthusiasm will rapidly be lost if the incentives to deliver change are removed or diluted.

This relates directly to the third question: how will performance be improved in the absence of the market? One possibility is that the NHS will revert to a more centralised approach in which clear targets are set in the NHS Executive and achievement against these targets are rigorously monitored at all levels. Another option is to make use of comparative information on performance and to use this to bring the poor performers up to the level of the best. A further possibility, perhaps to be used alongside other approaches, is to retain the option of services moving from one provider to another to keep providers on their toes. I have described this as contestability and suggested that it offers a middle way between planning and competition.[5] In a contestable health service the assumption is that purchasers and providers should work together to improve performance, not that contracts should move regularly in the quest for short term gains by purchasers. Only if collaboration fails would purchasers consider alternative suppliers. The knowledge that contracts may move serves as a stimulus to increase efficiency and enhance responsiveness. By focusing contestability on quality and outcomes rather that just cost and activity, the government may be able to turn policies designed for other purposes to its own ends.

To make this point is to suggest that Labour's approach needs to be eclectic, willing to use a range of instruments wherever they offer the prospect of advancing its aims. Centrally led performance management has a contribution to make, but empowering entrepreneurial professionals to improve care is equally important. Just as the government's education reforms have focused on raising standards in the classroom, so the test of the health reforms will be their ability to make a difference in the surgery, the clinic, and the ward. A carefully crafted mixture of incentives and directives is the most promising way of tackling low standards and encouraging innovation.

Chris Ham *Director*

Health Services Management Centre, University of Birmingham, Birmingham B15 2RT

1 Ham CJ. *Public, private or community: what next for the NHS?* London: DEMOS, 1996.
2 Audit Commission. *What the doctor ordered.* London: HMSO, 1996.
3 Mays N, Dixon J. *Purchaser plurality in UK health care.* London: King's Fund, 1996.
4 Smith J, Bamford M, Ham C, Scrivens E, Shapiro J. *Beyond fundholding.* Birmingham: Health Services Management Centre, University of Birmingham, and Centre for Health Planning and Management, University of Keele, 1997.
5 Ham CJ. Contestability: a middle path for health care. *BMJ* 1996; 312:70-1.