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# Early identification of variant Creutzfeldt-Jakob disease

*Some promising approaches but no clear answers yet*

*See pp 577, 593*

Unequivocal evidence now exists that the variant form of Creutzfeldt-Jakob disease is caused by the same strain of agent as bovine spongiform encephalopathy and that this strain differs from other strains isolated from cases of classic sporadic Creutzfeldt-Jakob disease.[1 2] At present definitive diagnosis of either form of the disease is possible only after death, but clinicians are under great pressure to distinguish between the two forms and in particular to be able to identify cases of variant Creutzfeldt-Jakob disease as early as possible.

Exposure of the human population in Britain to the agent causing variant Creutzfeldt-Jakob disease is likely to have occurred in the 1980s through beef products affected by bovine spongiform encephalopathy. Although it is reassuring that there have been only 24 cases of variant Creutzfeldt-Jakob disease (23 in Britain and 1 in France) and that the number of new cases did not increase in the last year, it is impossible to predict how many people are now incubating the variant form of disease. As well as concern over the size of any possible "epidemic" there is also the remote possibility that the level of infectivity outside the nervous system is higher in variant Creutzfeldt-Jakob disease than in the sporadic disease. Preliminary data have shown that necropsy samples of tonsils from patients with variant Creutzfeldt-Jakob disease are loaded with the pathological conformer of the PrP protein,[3] while those of patients with sporadic disease are not.[4] This may increase the risk of accidental transmission by medical procedures. In particular, concern exists about plasma derived products because they are prepared from huge pools, with the chance of including blood from potentially infected donors. Batches of plasma derived products can be withdrawn if a donor is subsequently suspected of having Creutzfeldt-Jakob disease, particularly of the variant form. For all these reasons we need a method of early identification of cases of variant Creutzfeldt-Jakob disease.

From the meticulous work of the Creutzfeldt-Jakob disease Surveillance Unit[5–7] we learn that so far the variant form of disease affects teenagers or young adults (all patients were under 40 years at clinical onset except one who was 48). Usually they present with severe depression (or other psychiatric disorders)[7] or sensory disturbances (disaesthesia or paraesthesia), or both.[5 6] These early and non-specific clinical signs may last several months and most patients turn out not to have either form of Creutzfeldt-Jakob disease.[6] Later during the course of the disease more characteristic clinical signs evolve: dementia, cerebellar and various focal neurological signs, myoclonus or other involuntary movements, and, finally, akinetic mutism.[5 6] The young age, the relatively long clinical course (over a year), the persistent sensory disturbances, an upgaze paresis, and the absence of typical periodic electroencephalographic signs suggest variant rather than sporadic disease.[5 6]

Help may come from neuroimaging techniques. In this issue de Silva and colleagues[8] report reduced brain cortical perfusion in two cases of variant Creutzfeldt-Jakob disease by single photon emission computed tomography (SPECT) analysis. Although this finding is non-specific, it may help to raise the suspicion of disease in young adults presenting with psychiatric disorders where all other routine investigations have been useless. Another promising procedure is cranial magnetic resonance imaging. Although it may give negative results, four patients with variant Creutzfeldt-Jakob disease (3 British and 1 French) had strong signals in the posterior thalamus on T2 weighted images.[6–9] This pattern looks to be specific to variant Creutzfeldt-Jakob disease and, if confirmed, may prove to be the best procedure for differentiating between the two forms of Creutzfeldt-Jakob disease.

The presence of protein 14-3-3 in the cerebrospinal fluid without any other cytochemical abnormalities strongly reinforces the diagnosis of Creutzfeldt-Jakob disease, but this test is equally positive in variant and sporadic disease.[10] Genetic analysis of the PrP gene is important to exclude the familial form of the disease, which may present at a younger age and with a longer duration than sporadic Creutzfeldt-Jakob disease.[11] Also, all cases of variant Creutzfeldt-Jakob disease but only about 70% of sporadic cases are methionine homozygous at the polymorphic codon 129 of the PrP gene.[5 6] At present we can not predict whether heterozygous or valine homozygous subjects at codon 129 are susceptible to variant Creutzfeldt-Jakob disease and, if so, which is the clinical picture that they will eventually develop.

Definite diagnosis of all forms of Creutzfeldt-Jakob disease is still possible only by histological examination of the brain, and the only procedures capable of distinguishing between the variant and sporadic forms of the disease are evaluation of neuropathological lesions[5 6] or PrP glycotyping on western blot.[12] Nevertheless

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brain or tonsil biopsies cannot be recommended as a routine procedure in view of the poor benefit for the patient, the risk of contaminating the operating room, and the need to destroy surgical instruments. A simple but specific blood test is badly needed.

Some hope for such a test come from the report of Otto et al, who report in this issue that patients with Creutzfeldt-Jakob disease have a median serum concentration of the brain specific S100 protein higher than that of controls (p 577).[13] Unfortunately the range of values in these patients is wide and overlaps with those in several other neurological disorders, including other dementing illnesses, making the test not very useful for diagnosis in individual patients. Nevertheless, the test is promising and should be quickly validated in a large cohort of patients with Creutzfeldt-Jakob disease and other neurological diseases, a task that should be easily achieved through the European Union collaborative study group for Creutzfeldt-Jakob disease surveillance. Other possibilities for a blood test may come from the recent development of a monoclonal antibody that specifically recognises the pathological conformer of PrP[14] and from the identification that, among the various cells in the blood, only the differentiated B lymphocytes play a crucial role in the pathogenesis of the disease.[15]

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# Medically unexplained neurological symptoms

*The risk of missing organic disease is low*

A psychological component exists in all illness, contributing a variable amount to the clinical presentation. At the benign end of this range are patients who describe their symptoms in more florid terms than seem to be justified. At the malignant end is malingering and the Munchausen syndrome. Between these extremes are a range of patients who present with non-organic signs or symptoms, with or without underlying neurological disease, usually called hysterical elaboration or hysterical conversion disorder.

Again a range of clinical presentation exists. If patients present with apparent non-organic signs or symptoms and are later found to have an underlying disease which might account for some or most of their original problems this is perceived as a hysterical elaboration of the underlying deficit. For example, a patient who seems to have a hysterical paraplegia might be found to have white matter changes on magnetic resonance imaging and oligoclonal bands in the cerebrospinal fluid. Patients already known to have a neurological condition might develop non-organic signs or symptoms, sometimes related to the original condition, but often distinct—for example, the development of pseudoseizures in a patient with epilepsy from childhood associated with an abnormal electroencephalogram. Occasionally patients present with clearly hysterical signs or symptoms but later develop a recognisable neurological disease, which in retrospect might have explained some or all of the original presenting features. Finally, there are patients with hysterical signs and symptoms with no underlying organic disease and in whom no organic disease develops over many years of follow up.

*See p 582*

Crimlisk et al have looked at a small part of this range—patients who presented with purely motor symptoms for which no cause was found on clinical evaluation and investigation (p 582).[1] Only three out of 64 subjects followed for a mean of six years were subsequently diagnosed as having a neurological disorder that could wholly or partly explain the presenting symptoms. One of these patients had a paroxysmal hemidystonia, always a difficult diagnosis and a condition not fully characterised at the time of the original presentation. In one patient the eventual diagnosis was dystrophia myotonica and in another a spinocerebellar degeneration. These conditions are usually diagnosable at presentation, but communication difficulties apparently confused the initial assessment. However, this serves only to emphasise the authors' conclusion that patients who present with medically unexplained motor symptoms and who have been properly evaluated clinically and investigated are unlikely on

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follow up to show evidence of an underlying disease that might have accounted for the presenting features.

Crimlisk et al conclude that repeated investigations for the same problem are unprofitable. In common with other series they found that a good outcome is associated with a short history and warn that conversion disorders do not protect patients from developing other diseases. A previous occurrence of a conversion disorder may delay the diagnosis of another condition. Although these findings can probably be applied to the whole range of non-organic disease, we do not know whether patients with pseudoepileptic seizures, hysterical pain syndromes, hysterical blindness, or non-organic sensory impairment would follow the same pattern.

At least two other series on conversion disorders have been reported from the National Hospital for Neurology and Neurosurgery,[2–4] the most influential being that of Slater in 1962. He analysed 112 patients seen in 1951, 1953, and 1955[2 3] and followed 85 of them for an average of nine years. He identified three groups of patients. About a third were thought to have a hysterical conversion syndrome as well as an organic diagnosis, and on follow up the organic disease prevailed. About a third were initially thought to have pure hysteria, of whom eight later developed an organic disease, and about a third had a psychiatric diagnosis including schizophrenia, depression, and personality disorder. Unfortunately, insufficient details are given to determine whether the subsequent organic disease explained the presenting features, particularly as the eventual diagnoses included trigeminal neuralgia, thoracic outlet syndrome, Takayasu's disease, and cord compression. Three patients went on to develop dementia. Investigations available today would probably have revealed some of these conditions at the first assessment. Twelve deaths occurred, including four suicides, one in a patient with a myopathy and another in a patient with multiple sclerosis. Of the remaining deaths, three were vascular, one due to a brain stem angioma, and one to a glioma. If relevant to the presenting problem most of these conditions would now be diagnosed by magnetic resonance imaging or other relatively non-invasive investigations. Slater did not confine himself to unexplained motor symptoms, so this series cannot be compared directly with that of Crimlisk et al.

Slater concluded that the diagnosis of hysteria was a disguise for ignorance and a fertile source of clinical error. As a result neurologists and psychiatrists became reluctant to diagnose pure hysteria, concerned that they were missing a neurological disease even if some of the neurological features were clearly non-organic. Nevertheless, assuming proper clinical evaluation and negative results on investigation, the chances of a patient developing a neurological disease that might have accounted for the original complaint is very small. Invasive and perhaps dangerous investigations are not appropriate to exclude rare and untreatable conditions; in most patients it is better to recognise the non-organic component of the problem and to seek psychiatric advice. The diagnosis can be reviewed if any new features develop.

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# Not one academy but two

## *The new one should focus on fixing academic medicine*

Everybody in Britain should be grateful if the Academy of Medical Sciences that was launched this week can preserve and promote academic medicine—for it approaches a parlous state. But we don't need yet another body of old men with chains around their necks that dines, processes, and professes and offers a further source of advice to government that it can take or leave to suit its own ends. The academy must target its efforts and aim to be effective not grand.

A Martian—or even an American—might be surprised that after 50 years of unresolved debate about the need for an academy of medicine Britain suddenly has not one but two. The cognoscenti will understand well the difference between the Academy of Medical Royal Colleges and the Academy of Medical Sciences, but few ordinary doctors and almost no members of the public will. Medical students understandably go blank when asked to explain the purposes and structures of Britain's expanding constellation of medical institutions—comprising the BMA, General Medical Council, royal colleges and faculties, specialist societies, and myriad other bodies.

British medicine's problem is not too few organisations, but too many. Given the unimaginable opportunity of starting from scratch, a new chief executive of British medicine would undoubtedly undertake a restructuring more dramatic than anything seen by British Telecom or other liberated monopolies. He or she would slash corporate headquarters, cut overheads, sell off the gowns, cancel the committees, and send people back to their hospitals, surgeries, and medical schools to "add value or go bust." Such dramatic changes are possible only when the country is flattened and the old guard killed off by war, explaining the seeming paradox that countries who lose wars do better economically in the long term than those who win them.

If we are to have another medical institution, then we need either a high level strategic one that points existing bodies in the same direction or one that meets a genuine need. There is a danger that—without focus—

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the new academy may be neither. In 1994 Maurice Shock, a political scientist, famously told British medicine's first summit meeting in 30 years that doctors were not well organised, had failed to see major changes that were happening around them, and needed a top body concerned primarily with strategic and high political matters.[1] Otherwise, he said, "the profession will never be able to punch its weight." The new academy might have been such a body, but it surely now cannot be. Although the fifth aim of the new academy is "to give national and international leadership in the medical sciences," it cannot be a strategic body because it does not bring together the existing powerful and (in some cases) well resourced bodies. Rather, this strategic function might be fulfilled by the "group of nine," a largely invisible body that meets regularly and does include representatives from the major bodies.

If the new academy is not to be strategic then it must be focused, and the right focus is academic medicine. Abundant evidence shows that service and funding pressures, diminished career prospects, problems of accreditation, and the research assessment exercise are eroding Britain's capability in academic medicine.[2–6] Here is real need. To promote academic medicine should be the academy's primary purpose, and it is to be applauded for bringing together clinicians and basic scientists.

Structure, as every first year management student knows, must follow function, and we must worry that the academy's structure will not be best suited to this function. Academic medicine depends critically on bright young people. Without them, the endeavour is nothing. This is why the *BMJ* has argued for the creation of an organisation of "young Turks" to promote research. The new academy may, however, be in danger of excluding these very people. It is to begin with a founding fellowship of 350 nominated by the Royal Society and four other bodies. Aren't these likely to be the same old greybeards that run all the existing organisations? We must hope not.

The new academy may have some spare time and energy to "enhance public understanding of the medical sciences" and "establish itself as an authoritative body to assess and advise on issues of medical science of public concern," but we advise it to concentrate on academic medicine. Fix that, and we will all benefit.

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# At last—maternity statistics for England

*Some trends are apparent but the data still have too many gaps*

After a long gestation the Department of Health has finally delivered a bulletin on maternity statistics.[1] Few routine data on maternity care in England have been published since 1985, the last year of the old Hospital In-patient Enquiry. This lack has been equally frustrating to people who want to compare local performance with national statistics and those who want to monitor national trends.[2 3] Not surprisingly, the new statistics show many changes in maternity care since 1985, while revealing inadequacies in the data.

The Maternity Hospital Episode Statistics system,[4] through which the data are collected, started in April 1989, and the new publication contains data for 1994-5 and trends since 1989-90. It is restricted to data about care during delivery, but a further bulletin with data for 1995-6 and 1996-97, including antenatal and postnatal episodes and data about newborn babies, is promised for the autumn. Subsequent bulletins will then appear annually.

The most dramatic changes are in caesarean section rates and the methods of operative vaginal deliveries (see figure). The caesarean section rate, which levelled off at just above 10% of deliveries in the early 1980s, rose from 11.3% in 1989-90 to 15.5% in 1994-5, mainly due to an increase in the emergency caesarean section rate from 5.5% to 9.0%. The overall level of operative vaginal deliveries changed much less, accounting for 9.7% of births in 1985 and 10.8% in 1994-5. A ventouse was used for only 0.7% of deliveries in 1985 compared with 4.8% in 1994-5, while forceps use declined from 9.1% to 5.8%. Induction rates, which had fallen since the 1970s, fluctuated between 17% and 20% of all deliveries in the early 1990s, while elective caesarean section rates rose from 4.9% in 1985 to 6.8% in 1994-5.

The percentage of deliveries coded as "normal deliveries with no antenatal or postnatal complications" fell from 30.8% in 1989-90 to 18.5% in 1994-5. This could reflect changes in coding practice, but it is ironic that it occurred just when the Changing Childbirth initiative was emphasising that childbirth is essentially a normal process.[5] Probably because of the rise in caesarean section rates, the percentage of women delivered by midwives fell from 75.6% in 1989-90 to 72.3% in 1994-5.

Despite this increase in obstetric intervention, the length of stay has fallen. Three quarters of women delivering in 1994-5 spent fewer than four days in hospital afterwards, compared with just under half in 1985 and a third in 1975. In 1994-5, 10% left hospital on the day they gave birth and 27% the next day.

The more detailed analyses for 1994-5 include some by gestational age and clinical parity, items that are absent from the Office for National Statistics' birth registration data. An estimated 6.2% of singleton deliveries, 46% of twin deliveries, and 79% of triplet and higher order deliveries took place before 37 weeks' gestation. Tabulations by region reveal considerable

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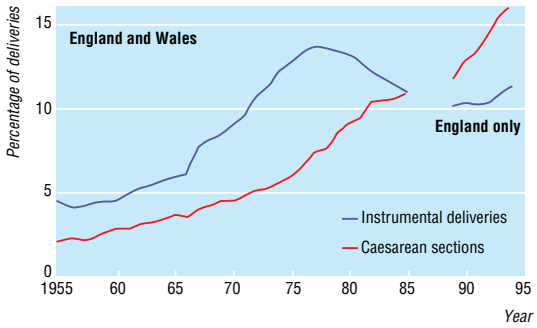


Operative delivery rates 1955 to 1994-5. Data from Maternity Hospital In-patient Enquiry and Hospital Episode Statistics

variations in obstetric practice, but the widest differences occur in the tables that give modes of onset of labour and of delivery for individual trusts.

The most striking feature of these trust tables, however, is their many empty spaces. Records with usable data were available for only 67% of deliveries in England in 1994-5. This ranged from 22-29% of deliveries in the former Yorkshire, North East Thames, and South East Thames regions to over 90% in the former North West Thames, South West Thames, Wessex, West Midlands, and North Western regions. More worryingly, national coverage, which rose from 57% in 1989-90 to 78% in 1992-3, has actually decreased since then. The abolition of regional health authorities, which used to coordinate data collection, may have contributed to this decline.

Several other factors contribute to the gaps. In some units maternity data are collected in stand alone systems that are not linked to the hospital systems from which data are extracted for Hospital Episode Statistics. In others data collection is not computerised. A survey in December 1995 found that only 55% of maternity units in England had a computer system and that only half of the rest were considering buying one.[6]

Given the poor quality of the data, the department's reluctance to publish them earlier is unsurprising. The bulletin's authors, led by Lesz Lancucki, have done much to check not only for non-response bias but also for major errors. Initially they found that 2% of mothers were coded as male, for example, and some caesareans were coded as taking place at home or without any anaesthesia.

Maternity hospital episode statistics have other deficiencies which arise from their episode based nature. The first is the lack of linkage nationally between data on delivery and data about antenatal and postnatal care. Linkage is now becoming possible, as the new NHS number offers the potential for building up a pregnancy based record. Even then, valid comparisons cannot be made between hospital based intervention rates without data about referral patterns and the social composition of the catchment population. These data could be derived, as in Scotland, through linkage with birth and death registration data collected by the Office for National Statistics.

None of this can happen while maternity data remain so incomplete. The bulletin takes a step in the right direction by using the available data to show important trends, while exposing the gaps to public view. These gaps must be filled before this new series of publications can fulfil its promise as a useful resource for monitoring maternity care.

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# Drug treatment in heart failure

## *Lowering heart rate may reduce mortality*

Heart failure is a clinical syndrome in which the heart fails to maintain an adequate output to vital organs. The responses to the resultant low blood pressure and underperfusion of organs include activation of the renin-angiotensin system with retention of salt and water, structural change of the heart and blood vessels with altered arterial compliance, and increased sympathetic drive. These result in an increase in heart rate, peripheral resistance, and myocardial contractility. Although these compensatory mechanisms are effective in the short term, they eventually become harmful. The adverse compensatory activation of the renin-angiotensin system can be modified by inhibitors, which improve symptoms and reduce mortality. Is the long term sympathetic overdrive that occurs as a consequence of heart failure also harmful?

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The effect of adrenergic stimulation on the myocyte is to increase contractility and improve cardiac function. This should be a beneficial effect, yet all clinical trials of positively inotropic drugs have either failed to improve symptoms or have increased mortality in heart failure. The long list of drugs includes the phosphodiesterase inhibitors,[1] dopaminergic inodilators with β adrenoceptor stimulating properties,[2] β adrenoceptor agonists,[3] and quinolone based inotropes.[4] If positive inotropic drugs seem harmful, could reduction in other indices of sympathetic activity be beneficial?

Increased heart rate is known to be an indicator of poor outcome in congestive heart failure.[5] Trials of low dose β adrenergic blockers from as early as 1975 have shown improvements in functional class, exercise

capacity on treadmill testing, and ejection fraction on radionuclide scanning in patients with dilated cardiomyopathy.[6] Carvedilol, a non-selective β blocker with antagonist activity at α1 receptors, improves ejection fraction and ventricular dimensions, albeit without improvement in exercise capacity. There are indications that it may improve mortality in chronic heart failure,[7] but some questions remain, including how to select the patients who might benefit. The reduction in death rate found with carvedilol is consistent with results from using metoprolol[8] and bisoprolol[9] to treat heart failure of idiopathic origin, and with subgroup analysis of patients with heart failure after myocardial infarction.[10] β adrenergic receptor antagonists consistently lower heart rate in the failing heart independent of aetiology.

Angiotensin converting enzyme inhibitors and β blockers share a specific therapeutic effect—a reduction in heart rate.[11] The fall in heart rate with angiotensin converting enzyme inhibitors is not shared by other vasodilators such as minoxidil and flosequinon, which produce reflex tachycardia and have an adverse effect on outcome in heart failure.[12] A reduction in mortality from heart failure was found with a combination of the vasodilator drugs hydralazine and isosorbide dinitrate, which does not substantially alter heart rate. However, when this combination was compared with enalapril, the enalapril treated group showed a further reduction in mortality, from 13% to 9%, in association with a fall in heart rate in the first year.[13] Could this bradycardiac effect add to the clinical benefit derived from other actions of angiotensin converting enzyme inhibitors in heart failure?

Short acting calcium antagonists produce a relative tachycardia and may worsen heart failure, increasing the risk of death in patients with left ventricular dysfunction. The only dihydropyridine calcium antagonist that does not affect heart rate, amlodipine, has no adverse effect on mortality.[14] Amiodarone causes a reduction in heart rate when used to treat heart failure and may reduce mortality depending on the population studied.[15] The decrease in mortality may depend on the size of the reduction in heart rate, which seems to improve the therapeutic efficacy of amiodarone in heart failure.[16]

There is, therefore, an association between a reduction in heart rate and those drug treatments that may be successful in heart failure. It seems unlikely that a decreased heart rate in itself is responsible for the improved outcome: two drugs seem to contradict the possible benefits of reduced heart rate and serve to show that there may be more important underlying influences. Xamoterol is a partial agonist at the β1 adrenoceptor which improves symptoms and effort tolerance in mild heart failure but which is associated with increased mortality in severe disease.[17] Although it causes a small fall in heart rate, xamoterol moderately increases myocardial contractility and, in addition, has 43% of the activity of a full agonist when changes in heart rate are used to assess intrinsic sympathomimetic activity. This supports the concept that positive inotropism with sympathetic stimulation is damaging in heart failure. By comparison, digoxin is a positive inotrope which reduces heart rate, and recent evidence has shown it to have no impact on mortality.[18] Xamoterol has sympathomimetic activity, whereas digoxin increases parasympathetic outflow.[19] Is the adverse effect of positive inotropy outweighed by the benefits of a reduced heart rate and parasympathetic stimulation? Drug treatment in heart failure with β blockers and angiotensin converting enzyme inhibitors increases indices of parasympathetic activity and reduces sympathetic drive,[20] but this does not apply to all interventions. Alteration of heart rate by interference with autonomic drive may be only part of the story.

Drugs that increase the force of contraction of the failing heart result in increased mortality, and we believe that there should be a halt on further development in this direction. Further studies are needed to establish whether increasing cardiac vagal tone improves mortality.

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# Rewarding healthcare teams

*A way of aligning pay to performance and outcomes*

The American economist Robert Solow argued that labour markets "cannot be understood without taking account of the fact that participants, on both sides, have well developed notions of what is fair and what is not."[1] This may explain why many NHS trusts in Britain have been reluctant to implement local pay mechanisms and performance related pay. As a result the creation of the NHS internal market has not led to a more efficient market for clinical labour. Indeed, opportunities have been missed—the recent review of the distinction award system, for example, paid little attention to incentives for efficiency.[2] Nevertheless, the present government is retaining the purchaser-provider split and is likely to continue to seek efficiencies. With care and a common sense approach, economics can contribute to the analysis and improvement of the clinical labour market.

Some approaches to the analysis of labour markets reflect Solow's common sense approach. Efficiency wage models, for example, accept that workers have discretion over their own performance because of imperfections in managerial monitoring. Workers will adjust their activity according to the wage paid and the fairness of their employment contract. An alternative theory suggests that because of the costs of recruiting and training staff, existing workers (insiders) are more valuable than unemployed alternatives (outsiders). This differential means that (even though the unemployed alternatives may be willing to work for less) employers prefer to keep existing workers at higher wages—which may in turn be enhanced by trade union power.

When these ideas are applied to clinical labour markets, it is apparent that consultants and general practitioners determine not only their own performance, but also that of their clinical teams. Managerial monitoring of performance in health care is difficult as outcomes are difficult to measure. In clinical labour markets medical professionals are insiders and other professions (such as nurses) are outsiders. The medical profession regulates itself, but traditionally the royal colleges, the British Medical Association, and the General Medical Council have been reluctant to manage the outcomes and efficiency of their members and have resisted changes in skill mix.

The asymmetry of information between doctors and their patients and employers means that doctors act as agents for both. One way of getting over this problem is to incorporate employers' goals into an "incentive compatible contract" through financial and non-financial incentives. Trusts might consequently explore the use of short term contracts, although this raises transaction costs and exposes them to risks of discontinuity of care. They might also explore performance related pay, though this is limited by the difficulties of monitoring performance and concern about the fairness of such devices.

An alternative might be to create incentive compatible contracts at the level of the healthcare team. Instead of giving individual consultants distinction awards for successes that are partly due to their team and general practitioners fees for services provided by other team members, the rewards could go to the whole team. The clinical team could be given clinical and other targets, and team members, jointly rewarded, would have incentives to monitor each other's performance.

Again, Solow has suggested that in labour market analysis there is too little emphasis on teamwork and too much on individual performance. "Probably the best possible monitors of work effort are other workers in the same shop floor group. If a major part of compensation for work were tied to group effort or group productivity, which must be easier to observe than individual effort and productivity, it would be in the interest of group members to see that everyone contributed a fair share."[1] If team performance is the measure, then performance related pay may become more practicable in health care, as health professionals may be better able to monitor each other's productivity than a non-clinical manager. This team approach also helps retain clinical freedom while curtailing inefficiency through internal monitoring.[3 4]

An initial application might be to replace distinction awards with targets and rewards for a clinical team. More innovatively, teams could tender to provide an agreed package of care; such teams could exploit changes in skill mix (for example, increased use of nurse practitioners and nurse anaesthetists). Initial experimentation could begin with a waiver of the distinction award scheme, using the freed resources to implement cautious group incentive schemes and outcome measurement. Similar models could be created in primary care. Instead of commissioning care from just general practitioners, purchasers could commission it from teams exploiting the skills of doctors, nurses, pharmacists, and others.

Such ideas should be introduced cautiously, with piloting and quasi-experimental evaluation. Healthcare professionals work in teams, and the internalisation of managerial control within teams offers the possibility of increased accountability and efficiency while preserving the professionalism of health workers. It deserves careful and informed consideration by policymakers.

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# Meeting the challenge of genetic advance

*Requires rigorous navigation between laboratory, clinic, and society*

See p 618

Advances in molecular genetics over the past decade have been remarkable. Soon the entire human genome will have been sequenced and most of the genetic loci associated with human disease identified. These advances have greatly enhanced understanding of disease mechanisms and begun to explain why the clinical course of common disorders such as diabetes, asthma, and rheumatoid arthritis is so variable, as Bell discusses in the first of four articles on the broader implications of the new genetics (p 618).[1] In future presymptomatic population based genetic testing for common late onset disorders such as Alzheimer's disease[2] and colon cancer may become widespread and bring important health benefits. Genotyping may become part of routine investigations to help clinicians tailor drug treatment effectively.

But in what has been dubbed the "post-genome" era, increasing attention is now being paid to the limitations as well as the potential of DNA based genetic tests. The ability to detect genes greatly exceeds our understanding of what they do. Even in the simple Mendelian disorders the relation between the DNA sequence of a gene and the corresponding phenotype is far from clear. In late onset conditions, such as coronary heart disease and diabetes, where genetic, social, biological, and environmental factors interact over time, predicting the clinical importance in a given patient of several different mutations of low penetrance genes is very difficult.[3]

Some mutations—for example those associated with type 1 diabetes—have a high population frequency and may therefore be protective. Early optimism about the potential value of screening for breast cancer genes has been replaced by recognition that the prognostic meaning of the mutations is unclear[4] and that taking action on "gene based statistical prophecies" may not be in patients' interests.[5] In Britain the Human Genetics Advisory Commission has concluded, "It is unlikely that actuarially important genetic predictions of common causes of adult death will be available and validated for some time."[6] Genetic epidemiology is in its infancy.

Whether testing will inevitably become widespread as more tests become available is uncertain. Much depends on the severity of the disease and the scope for effective treatment or prevention. Readiness to undergo testing also depends on how testing is offered and on personal, social, and psychological factors; the more well informed people are, Marteau suggests in next week's article in the series, the less likely they are to want testing.

Rigorous assessment of the benefits and costs, both economic and psychosocial, of introducing new genetic screening tests is essential, not least because information from genetic tests carry implications for families as well as individuals. The problems of testing children who are too young to give informed consent are well recognised, and there is broad agreement that predispositional testing for late onset disorders should not be done.[7] Prenatal screening remains contentious because of the fine line between allowing couples to make informed choices and pressurising them to terminate affected fetuses. Some argue that the intention of much genetic research is eugenic by implication,[8] and legislation in China which has made this explicit has provoked passionate controversy.[9]

Among the public, upbeat reporting of the identification of new genes and the ability to test for them has raised both interest and concern. Fears about discrimination by insurance companies and employers is understandable despite the introduction in America of a federal law to protect against such discrimination and in Britain reassurance from the Association of British Insurers. As studies to correlate genetic predisposition with clinical disease increase, issues of confidentiality and informed consent warrant more attention.[10] The inadequate counselling and failure to obtain written consent from most subjects in a recent study of testing for the adenomatous polyposis gene is worrying, as is the fact that many doctors requesting the test did not recognise its limited predictive value.[11]

Failure to appreciate the complexity and limitations of genetic tests and the fact that testing may provoke rather than allay uncertainty must be tackled. The difficulty in ensuring appropriate use of tests for prostate specific antigen is instructive.[12] Even a small increase in genetic testing for predisposition to common diseases will severely test the current supportive medical model with its intensive pretest counselling and post-test follow up.

Inevitably the brunt of dealing with the public's hopes and fears will fall on doctors in primary care. We urgently need to define likely service needs and how best to establish collaboration between geneticists, public health specialists, and primary care teams. Meanwhile, those engaged in genetic research have a responsibility to draw attention to the limits as well as the potential of their findings and to foster balanced media reporting. And in discussions over public policy, expert committees must fully recognise the importance of open debate.

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