that a psychiatric disorder is involved: this was true for three quarters of the cases reported in the series of Wessely and Powell¹² and Mann *et al.*¹³ Depression was the commonest diagnosis, with anxiety and somatisation disorder being less frequent. It has been suggested that depression may be a secondary phenomenon.¹⁴ One important feature that distinguishes patients with the chronic fatigue syndrome from other patients with depression is that they are less likely to report feelings of guilt, unworthiness, and self blame.¹⁵

Strenuous efforts have been made to identify a non-psychiatric explanation, the main proposals having been chronic infection with Epstein-Barr or Coxsackie virus. Immune activation has also been reported.¹⁶ Apart from acute viral infections acting as a trigger, no unequivocal evidence exists for persistent viral infection. Selecting appropriate control subjects has been a problem in studies.

The search for a "physical" cause outside the patient highlights the current unfortunate attitudes towards psychiatric illness, recalling the social stigma attached to tuberculosis or epilepsy in former generations. It also emphasises the regrettable and entirely inappropriate practice of doctors of distinguishing between "organic" and "non-organic" disorders, with the implication that non-organic disorders have no physical basis or even that the symptoms are purely in the mind. The fatigue that patients with the chronic fatigue syndrome experience is an exceedingly discomforting symptom and must have a neural correlate. So far the physiology of subjective central fatigue is largely unexplored, but investigations into the mechanism of objective central fatigue have been initiated.¹⁷

Fatigue is present in many patients with depression. It is also common in Parkinson's disease, when it correlates better with coexistent depression than with the severity of disease but is often independent of both.¹⁸ Interestingly, nearly a quarter of patients in the series reported by Wessely and Powell¹² had no other features of depression or psychiatric disorder. Persistent subjective fatigue may therefore occur in relative isolation, independently of other manifestations of affective disorder. Some progress is being made with the functional imaging of depression by positron emission tomography,¹⁹ and advances in technology could conceivably allow exploration of the anatomical basis of subjective fatigue.

Subjective fatigue is, of course, a normal phenomenon. Possibly the setting of the neural mechanisms responsible for

this sensation is altered in patients with the chronic fatigue syndrome and depression, in the same way that in anorexia nervosa the body image may be altered. Gibson *et al.* have shown that the degree of perceived exertion is significantly greater in relation to the increase in heart rate during incremental exercise in patients with the chronic fatigue syndrome compared with normal subjects.²⁰ This abnormal perception of effort was originally identified by Lloyd *et al.*²¹

The chronic fatigue syndrome reflects a complex interaction between cerebral dysfunction, trigger factors, and social attitudes and is complicated by secondary symptoms. There will be no simple explanation.

P K THOMAS

Emeritus professor of neurology

Royal Free Hospital School of Medicine,
London NW3 2PF

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Screening for cystic fibrosis in primary care

Family practice at last?

A new harmless compound detects carriers of cystic fibrosis by turning their urine blue. When it is taken orally by carrier couples at conception gametes with the cystic fibrosis gene will be inactivated. Cystic fibrosis can be eradicated.

It is not true, of course. Detection of carriers is elaborate; there are over 200 possible mutations, and testing for the more common faults in the gene misses one in six carriers. Even with complete uptake of the test, almost one third of affected fetuses would still reach term.¹ In addition, avoidance of an affected child requires a termination. Before becoming enmeshed in "present imperfect," however, we should examine "future perfect."

Population screening in Britain would mean that almost three million people would need to come to terms with

carrying a defective gene. Families whose beliefs precluded any interference with procreation would be liable to ostracism; criticism from neighbours might even pressure them into participation.² Most children with cystic fibrosis are fit, and their life expectancy is increasing and may soon be greatly improved by gene therapy. Are we in danger of screening for a genetic disorder that will soon cease to be a disease at all?

Countering these arguments is not difficult. Almost everyone carries a severe recessive gene defect. Previously, population screening for such genes has focused on ethnic minorities³—cystic fibrosis merely extends this concept to the population at large. As the human genome project gathers pace we may anticipate the ability to detect all major recessive genes in the near future. When everyone realises that he or she

is a carrier there can be no stigma. Most couples would prefer to know before conception if both partners carry the same gene defect. Few have difficulty accommodating the need to care for the sick who exist while taking steps to avoid recurrence. The minority who chose to continue to term would need support. Nevertheless, experience shows that, in Britain at least, most couples would opt for a healthy child.

In short, the capacity to screen for carriers of cystic fibrosis is set eventually to carry genetics if not into every living room, at least into every health centre. For it is there that most people would prefer to have such investigations.⁴ Is it now time to start the general introduction of genetic screening? The two studies reported in this issue explore the options and illustrate many of the problems.

The paper by Bekker and colleagues introduced a member of the research team to a London practice (p 1584).⁵ A lack of interest in carrier testing emerges, which is perhaps unsurprising: an inner city practice will always be a tough test of any preventive programme. The authors found that the only effective screening option in terms of uptake was to collect samples opportunistically, a similar finding to that reported by Watson *et al.*⁶ Although the authors feared that this might reflect inappropriate "selling" of the test, it seems at least as likely that people will not inconvenience themselves for a test that they do not think they need. People without a family history "feel lucky."

Harris and colleagues got general practitioners in several practices to target the first antenatal visit (p 1580).⁷ Enthusiasm among general practitioners in Manchester may have reflected the persuasive powers of the study group, but a more likely explanation is that, given adequate support, general practitioners have a natural affinity for the study of genetic disorders in families and adapt readily, using the cystic fibrosis carrier test as a means of introduction.

Different approaches to carrier testing are likely to be complementary; our own pilot study is looking at using a preconception clinic, a "well couple" clinic. Most regional genetic centres now offer cascade carrier detection⁸ by approaching the relatives of known carriers. This has the advantage of precision and limited cost but depends on the birth of an affected child. Testing in antenatal clinics is

feasible⁹ but introduces additional stress on the family and the system. Telling couples only if both carry the gene¹⁰ reduces the need for counselling but is counter to the longer term need for the population to recognise that recessive carrier status is a normal fact of life. This could be merged with the health centre's antenatal booking clinic to make genetic advice available to couples planning, or about to have, a baby.

Introducing carrier screening to senior school students and linking it to a health education programme¹¹ is a possible "turnstile" for the future. Our first need is to educate the health care professionals. At the end of this decade couples will want to know which recessive genes they carry. If they don't get the answer they will at least expect their doctor to understand the question.

Carrier testing cannot easily be blocked by purely economic arguments as the fall in health costs from fewer children born with cystic fibrosis would more than offset the cost of screening.¹ It seems set to come into wider use with the usual debate over resources, cost-benefit analysis, public understanding, the changing clinical burden, and the ethics of termination. It heralds the beginning of true primary care genetics. Should it perhaps be called family practice?

JOHN BURN

Professor of clinical genetics

Northern Region Genetics Service and
Division of Human Genetics,
University of Newcastle upon Tyne,
Newcastle upon Tyne NE2 4AA

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Who's for continuous ambulatory peritoneal dialysis?

Most patients with end stage renal failure, especially those with a chance of receiving a transplant

Continuous ambulatory peritoneal dialysis is now an established treatment for patients with end stage renal failure and accounts for over half the patients managed with dialysis in Britain.¹ Despite teething troubles in the early 1980s² patient survival is currently the same with both continuous ambulatory peritoneal dialysis and haemodialysis, and the survival of the technique of continuous ambulatory peritoneal dialysis is approaching that of haemodialysis.^{1,3} Morbidity is similar,^{3,4} but the rate of admission to hospital is lower with haemodialysis.^{3,5}

Yet the proportion of patients treated with continuous ambulatory peritoneal dialysis varies considerably from country to country: whereas in Britain it is 52%, in Sweden it is 33%, in the United States 17%, in Germany 9%, and in Japan 6%. Why are patients preferentially given haemodialysis in most parts of the developed world?

Non-medical considerations seemingly have a substantial

impact on the choice of treatment, with financial factors predominating.⁶ The rates of use vary according to how much doctors and renal units are reimbursed for treatment. Countries with fixed annual allocations for health care favour continuous ambulatory peritoneal dialysis, presumably because it is cheaper.

This most obviously occurs where facilities for maintenance haemodialysis are limited, as in Britain. In countries where reimbursement differs less between continuous ambulatory peritoneal dialysis and haemodialysis, the lack of adequate training of nephrologists and nurses, bias among doctors, the availability of resources, and social mores are more important.

The only genuine medical contraindications to continuous ambulatory peritoneal dialysis are active bowel disease, abnormalities of the abdominal wall, and the inability to learn or perform the technique. Although more high risk patients