medication), and only one in six patients remaining relapse free (and not needing medication) 10-15 years later.⁶ However, recent critiques have shown that recovery and readmission rates in schizophrenia before 1950 were no different⁷ and that antipsychotic agents might even do more harm than good.⁸ Thus the marked decline in the numbers of patients in asylums, from the mid-1950s (in the United Kingdom from some 150 000 in 1956 to under 40 000 in 1990) is usually attributed, at least in part, to effects of the medication. But this decline could equally be seen as socially generated via fiscal policies and community care programmes.⁸ Enhanced biological vulnerability to psychotic relapse might even be a result of the brain being made supersensitive to dopamine,⁹ medication thus acting as a double edged sword, relieving the symptoms of illness but creating an increased potential for relapse once drugs are discontinued.

The World Health Organization's studies of relapse in the 1960s and 1970s showed better outcomes of schizophrenia, surprisingly, in developing countries than in industrialised ones, with over 60% of patients in poor countries asymptomatic after five years compared with only 18% in rich countries.¹⁰ This finding was generally attributed to better social acceptance and support in agrarian communities, but it may have been related to less use of mainstream antipsychotic agents, and continued use of medication correlating with poorer outcome.⁸

Such criticisms rely on a somewhat selective viewing of the literature; more severe illnesses usually require higher doses of medication, thus creating the illusion that the medication creates the severity. More recent appraisals have identified other factors. These include the fact that we now have better definitions of what is and is not schizophrenia. Studies have identified the importance of the family in psychoeducational approaches,¹ especially the need to counter the relapse inducing effects of high expressed emotion (the term used to describe families having persistently critical or hostile attitudes towards their schizophrenic kin). We also know that long term studies show that patients with schizophrenia tend to stabilise anyway after about five years through the natural alleviations of the disease and increasing age and maturity.¹¹ Also we no longer have the large, backward, "demented," long stay asylum population,⁴ and there is agreement that the duration of untreated illness with active symptoms tends to predict the patient's ability to recover—the shorter the better—and that relapse rates can be reduced by continuing with antipsychotics for at least two years after recovery.¹

But there are no grounds for complacency, even with the new atypical agents. These may have their own longer term problems, weight gain and diabetes being the most obvious so far.¹² Treatment with any therapies, should include careful review of physical health, medication dosages, and consideration of graduated withdrawal. Such careful assessments are, of course, made difficult by the patients one cannot research: those who are non-compliant, who use alcohol or illegal drugs damagingly, and who constantly evade even the most diligent community teams.

The history of schizophrenia has shown that it can be a devastating illness and that medication has created at least a cohort of patients more coherent and articulate in describing their experience. But an outstanding need remains for continuity of care, adequately resourced, and for long term studies of outcome and treatments over decades rather than a few months. Such research fits poorly with the short term pressures of the research assessment exercise, drug company marketing policies, or career advancement.

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Hepatitis B infections

Universal immunisation should be preferred in Britain

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The hepatitis B virus causes up to a million deaths worldwide and 16 million healthcare related infections in the tropics every year.^{1 2} In the United Kingdom, 4500 acute hepatitis B virus infections, more than 7500 new cases of chronic infection with hepatitis B virus (mainly in immigrants), and up to 430 cases of hepatitis B virus related hepatocellular carcinoma are estimated to occur each year, with estimated NHS costs alone of £26m-£375m

(\$48m-686m;£37m-538m) per year.³ Approaches to prevention and treatment of hepatitis B have been reviewed in this issue and elsewhere (p 1080).¹⁻⁵ Vaccination and the implications of new screening and treatment strategies for carriers of hepatitis B virus in the Britain are discussed here. Immunisation strategies targeting multiple risk groups have failed to provide adequate coverage in Britain and should be replaced by universal immunisation.

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Most deaths from hepatitis B virus are due to chronic carriage (presence of virus for more than six months), leading to inflammation, cirrhosis, and cancer of the liver. Since most infections in the tropics occur perinatally or in early childhood, prevention strategies for such areas have focused on universal immunisation early in infancy. In countries with low endemicity such as the United Kingdom, most indigenous infections occur in early adulthood owing to sexual transmission or related to intravenous drug misuse, and universal immunisation in adolescence may be more appropriate. As the cost of vaccines has fallen, universal immunisation strategies have been adopted by over 150 countries, with evidence of effectiveness lasting more than 10 years in preventing infection, carriage, and hepatocellular carcinoma.

Prevention in Britain has relied on identifying and immunising members of various high risk groups, of which 12 are currently identified.⁶ This has generally failed, and even in situations where recent changes have been successful—such as the introduction of universal antenatal screening for maternal carriage of hepatitis B virus—onward referral of carrier mothers for specialist assessment and immunisation of family members other than the neonate have often faltered, despite their increased risk.⁷ Vaccination of intravenous drug users, prisoners, and their contacts has been patchily instituted although even incomplete opportunistic immunisations will provide substantial protection in these groups.⁸ More than 90% of hepatitis B virus related cases of chronic disease and hepatocellular carcinoma in some northern European countries are said to be due to immigration, but these models exclude transmission within prisons, between drug users, and in other high risk groups.⁹ Prevention models based on vaccinating heterosexual attendees at genitourinary medicine clinics have been less successful than among communities of men who have sex with men. Selective vaccination of these and other high risk groups—such as patients with renal disease—will still be required for some years even if British policy eventually moves towards universal immunisation.

The B cell dependent immunity that develops after active immunisation lasts for over 10 years in endemic settings, and anti-HBs antibody concentrations rise rapidly again after antigenic challenge.¹⁰ Seroconversion (anti-HBs antibody concentration 1×10^4 IU/l) should be confirmed in blood taken from people who have been vaccinated six to eight weeks after the final dose of a conventional 0, 1, and 6 month immunisation schedule, or after one of the accelerated schedules (0, 1, 2, and 12 months, or 0, 7, 21 days, and 12 months). Many apparent non-responders will seroconvert after a further two or three doses. Despite current recommendations made in 1996,⁶ responders probably do not need further boosters after a documented successful primary course unless they are at particularly high risk or are immunosuppressed—for example, as a result of renal failure or HIV infection.¹⁰ Vaccines available in the United Kingdom are interchangeably immunogenic, can be given with hepatitis A vaccine, and provide protection when rapid schedules are used. Newer vaccines are more immunogenic and may overcome vaccine escape by mutant virus.¹¹

Circulating “e” antigen (HBeAg) has historically been used as a surrogate for high circulating concentrations of hepatitis B virus DNA, and carriers

with detectable HBeAg are more infectious and at higher risk of active hepatitis, cirrhosis, and hepatocellular carcinoma. They are also more likely to respond to antiviral treatment. However, precore mutations in the hepatitis B virus genome, leading to high circulating concentrations of hepatitis B virus DNA despite undetectable HBeAg, are increasingly recognised and can cause fulminant hepatitis in neonates and serious chronic liver disease in carriers. Such carriers with higher concentrations of hepatitis B virus DNA do respond to antiviral treatment, and guidelines have to be redefined for screening for hepatitis B virus DNA and follow up of all HBeAg negative carriers. Possibly, British healthcare workers who are HBeAg negative carriers with moderate hepatitis B virus viral loads (10^3 – 10^5 genome equivalents/ml) may be allowed to perform exposure prone procedures if antiviral treatment consistently reduces their viral load.¹²

Although treatment with interferon alpha, lamivudine or adefovir is successful in clearing hepatitis B virus in some patients, long-term suppressive treatment (with risks of viral resistance and rebound) is the only option for most patients. Antiviral monotherapy predictably leads to resistance, and drug combinations have yet to be identified to prevent this and to produce the dramatic benefits seen following combined therapy of infections such as HIV, hepatitis C, and tuberculosis. Complex interactions with highly active antiretroviral therapy given for HIV mean that the management of hepatitis B and HIV coinfection requires specialist expertise. This may present unexpected problems in resource poor settings in which highly active antiretroviral therapy is being introduced on a wide scale.

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