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Prescribing antidepressants in general practice

Watchful waiting for minor depression, full dose treatment for major depression

See pp 858, 860, 861

This week's *BMJ* includes three studies of the use of antidepressant drugs in general practice. MacDonald *et al* (p 860) looked at patient specific dispensed prescribing and hospitalisations for possible adverse effects, using a record linkage database covering Tayside, Scotland.[1] They found prescribing of tricyclic antidepressants to be generally safe: the drugs were rarely used in the presence of contraindications and did not lead to an excess of hospitalisations for adverse cardiovascular effects. The authors say, however, that this may have been because about three quarters of prescriptions were for less than the recommended dose for major depression (125 mg of amitriptyline or equivalent a day[2]) and most were for less than 60 days.

These findings are not new: studies going back more than 20 years have consistently found that tricyclic antidepressants are usually prescribed at low doses for short periods in general practice.[3-5] So why do practitioners continue to prescribe in such a way, and are they really wrong to do so?

Low dose tricyclic antidepressants for migraine prophylaxis, neuralgia, and nocturnal enuresis account for only a small proportion of prescriptions; most are used for a diagnosis of depression.[5] However, the doses used are often limited by side effects, whether experienced by the patient or anticipated by the doctor. Tricyclic antidepressants are started at a low dose and stepped up.[2] Many patients object to the side effects of higher doses and stick with a lower dose, often because it helps them to sleep. General practitioners are understandably wary of pressing increases on patients who have to continue to work and drive their cars.[4] Once they begin to feel better, many patients discontinue treatment within a few weeks, often without telling their doctor.[6]

The paper by Priest *et al* (p 858) sheds light on patients' reluctance to take antidepressants.[7] A doorstep survey of more than 2000 people found that only one in six thought people suffering from depression should be offered antidepressants. The large majority considered them addictive. Most thought that depression was caused by adverse life events, and nine out of 10 thought that counselling should be offered.

Such considerations help explain why most patients take only low doses of tricyclic antidepressants for short periods. While an evidence based approach suggests that this represents inadequate treatment for the 5% of patients with major depression according to strict diagnostic criteria,[8] the controlled trials that have been carried out have usually included only narrowly selected groups of patients. There has been relatively little research on the efficacy of lower doses of tricyclic antidepressants for those presentations which more commonly demand help from a general practitioner—minor depression, often mixed with anxiety and perhaps accompanied by increased alcohol consumption, in the context of adverse life events or social problems which the doctor has little chance of influencing.

One careful trial found that a median daily dose of 125 mg of amitriptyline was no better than placebo in mild depression, although the trial excluded patients with problems of alcohol or drug misuse or minor depression associated with anxiety disorders.[9] Two trials in general practice concluded that a daily dose of 75 mg was ineffective in minor depression. However, one of the studies was performed in Australia (which may not be generalisable to British patients) and did not include measures sensitive to changes in symptoms of anxiety,[10] while the other suffered from a small sample size and a high drop out rate.[11] Conversely, a randomised controlled trial in psychiatric outpatients suffering from minor depression, anxiety disorder, or panic disorder found average daily doses of only 45 mg of dothiepin to be effective.[12] Further research is addressing whether 50-75 mg of dothiepin is effective for minor depression in patients in general practice (G Lewis, personal communication).

Meanwhile, prescribing habits are changing, perhaps owing to the Defeat Depression Campaign, which is aimed at increasing general practitioners' awareness of depression, and to the advent of the selective serotonin reuptake inhibitors. On p 861 Donoghue *et al* report the analysis of a large general practice computer prescribing database showing that, between 1993 and 1995, the number of prescriptions for depression increased by nearly 30%, mostly due to increased prescribing of selective serotonin reuptake inhibitors.[13] As a result, the proportion of patients receiving doses that were effective for major depression increased from 40% to 54%. Selective serotonin reuptake inhibitors are much easier to prescribe than tricyclic antidepressants because they are usually started at a therapeutic dose and seem to be better tolerated. Discontinuation rates are lower, though only by 5-10%,[14 15] which seems to be due to their having fewer side effects rather than greater efficacy.[16]

While the use of newer drugs means more patients will receive doses of antidepressants acknowledged to be effective, the problem remains that many people with only mild depression are probably being given a placebo with side effects, while others who would benefit from treatment for major depression go unrecognised.[17] Research so far justifies antidepressants only for major depression, a diagnosis requiring the presence of low mood or loss of interest and pleasure that has continued for most of the day for at least two weeks, plus four out of seven symptoms—namely, change in appetite, change in sleep, low energy or fatigue, impaired concentration, guilt or feelings of

worthlessness, retardation or agitation, and thoughts of suicide. Doctors should run through this list of symptoms when they suspect depression and refrain from prescribing unless the depression is severe enough.

Patients with minor depression will often recover without drug treatment within a relatively short time. Initially, the doctor should sit tight and listen—help the patient to talk through the problem but not prescribe until it is clear that enough symptoms have been present for at least two weeks, suggesting that drug treatment will be beneficial ("Don't just do something, sit there"). If a patient with major depression is unable or unwilling to take higher doses of a tricyclic antidepressant, switching to a newer drug might ensure that an adequate dose is given where it is really needed.

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Hepatitis B and admission to medical school

More flexibility should allow infectious applicants to follow non-invasive medical careers

See p 856

In 1994, Britain's Committee of Vice-Chancellors and Principals issued guidance to universities on medical and dental students' fitness to practise in relation to hepatitis B[1]; it was immediately controversial.[2 3] The main arguments were whether being an infectious carrier of hepatitis B virus should preclude having a career in medicine, and whether the requirement to have been screened, immunised (if necessary), and shown to be immune before entry to medical or dental school was either necessary or practicable. The NHS Management Executive had earlier issued guidelines to health authorities and trusts that included reference to medical students,[4] but the guidance to universities went further by saying that students infectious for hepatitis B should be excluded from the clinical course; for them there would be no option of a restricted choice of specialty in which their infection would not pose a hazard. Despite the opposition, the guidelines have not been relaxed, except that a revision issued in April 1995 made it clear that, provided the student had been given vaccine, as appropriate, it was not necessary to show that he or she was immune[5]; non-responders could be accepted on to medical or dental courses provided it was known that they were not infectious.

The guidance does not include any indication of which markers of hepatitis B virus infection are necessary to determine a student's acceptability. It is perhaps not surprising therefore that a survey of medical schools published in this week's issue of the *BMJ* (p 856) reveals some confusion.[6] Most of the schools required the results of hepatitis B virus markers before registering a new student, and half required that the student should have at least started the course of immunisation. Which hepatitis B virus tests were required varied, in some cases suggesting a lack of understanding of hepatitis B virus serology. This was demonstrated by a question asking under what circumstances a student would be refused entry, or removed from a course; two schools replied that students would be excluded if hepatitis B virus surface antibody were positive, which would exclude students who were immune, and five schools replied that they would exclude students if hepatitis B virus surface antigen were positive, regardless of "e" marker status, which goes much further than required by the NHS guidance.

In a low prevalence population, such as medical students, the most economical strategy for achieving confirmed immunity to hepatitis B is to immunise all and to test serologically after the third dose. To screen before immunisation and confirm immunity afterwards requires more tests and saves very little vaccine, but this would identify carriers of hepatitis B virus infection earlier.

Which tests should be used? Detectable antibody to hepatitis B virus surface antigen indicates immunity to infection, whether natural or vaccine induced, and a lack of infectivity (table 1). If antibody to surface antigen is not detectable after vaccination, this may be due to a failure to respond to the vaccine or due to the individual already being infected; a test for hepatitis B virus surface antigen, if positive, would confirm current infection. If neither surface antigen nor antibody are detected, a test for antibodies to hepatitis B virus core antigen will distinguish non-responders to the vaccine (hepatitis B core antibody negative) from those who have had hepatitis B in the past but do not have a detectable response to hepatitis B surface antigen (hepatitis B core antibody detectable). Non-responders to vaccine may be given one or more further doses, but a residual group of non-responders will remain.

Most students found to have hepatitis B surface antigen in their serum will prove to be carriers (defined as someone with detectable surface antigen for more than six months) rather than to have acute infection. The critical question is whether a carrier is to be considered infectious. The guidance from the NHS Management Executive is for this to be determined by tests for hepatitis B e antigen[4]; if this marker is detectable, the individual should be considered infectious and is not permitted to undertake exposure prone procedures. For medical students, the implication is that if the guidance from the Committee of Vice-Chancellors and Principals is followed, they should be refused entry, or not allowed to continue to the clinical course. If hepatitis B e antigen is not detectable,