MCQs

1 Depot injections:
a overcome covert non-adherence
b are administered every 1–6 weeks
c are administered subcutaneously
d enhance relapse prevention
e are available only for typical antipsychotics.

2 Treatment adherence for antipsychotics:
a is considerably worse than that for other drugs and other illnesses
b is dependent on the patient's health beliefs
c is unrelated to the patient's personal opinion regarding their susceptibility to relapse
d is always accurately predicted by a patient's verbal report of their adherence behaviour
e is mainly dependent on the drug's side-effect profile.

3 Reasons for depot underutilisation include:
a depot clinics are expensive to run
b patients naturally prefer oral to depot formulations
c depots have an image problem
d depots are associated with coercion
e suboptimal prescriber knowledge regarding these drugs.

4 Advantages of depot antipsychotics (compared with oral) include:
a easier early detection of relapse
b reduced consistency between the drug prescription and drug delivery
c more variability between patients in steady-state blood levels for a given dose
d reduced rehospitalisation rates
e reduced risk of deliberate self-poisoning.

5 Regarding the future use of depot antipsychotics:
a depot utilisation rates will be affected if new legislation includes a community treatment order
b availability of atypical depot antipsychotics will have no impact on depot prescribing
c prescribers require more information regarding switching to depots
d NICE does not advocate the use of typical depot antipsychotics
e the decision to switch to a depot should be openly discussed with the patient and carer beforehand.

MCQ answers

1	2	3	4	5
a T	a F	a F	a T	a T
b T	b T	b F	b F	b F
c F	c F	c T	c F	c T
d T	d F	d T	d T	d F
e F	e F	e T	e T	e T

Why indeed?

Invited commentary on... Why aren't depot antipsychotics prescribed more often and what can be done about it?

Thomas R. E. Barnes

A recent review concluded that replicated, evidence-based studies have demonstrated several areas of advantage for long-acting antipsychotics over oral antipsychotics. These include improved global outcome and reduced risk of rehospitalisation, psychopharmacological benefits such as more consistent bioavailabilty and more predictable dose–blood level correlations, an improved pharmaco-kinetic profile allowing lower dosages to be used with a consequent reduced likelihood of side-effects, and a reduced burden of care when injections are required only every 2–6 weeks (Robert & Geppert, 2004). Further, if a patient relapses despite receiving uninterrupted depot treatment, this indicates the need to consider reasons for deterioration other than poor adherence. However, perhaps the critical advantage over oral preparations is the avoidance of covert non-adherence (Barnes & Curson, 1994). With depot treatment, any decision by the patient not to continue medication will be signalled by failure to attend for, or refusal of, injection. The clinical team can therefore act to intervene appropriately,

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bearing in mind that non-adherence may be both a cause and consequence of worsening of illness. Lastly, with depot preparations the risk of self-poisoning is reduced.

The disadvantages relate to the relatively stable plasma drug concentrations, leading to a lack of flexibility should side-effects develop or when titrating the dose clinically. However, clinical experience suggests that long-acting formulations in standard dosage have a relatively low side-effect burden, and specific notions that such preparations are associated with an increased risk of neuroleptic malignant syndrome and extrapyramidal side-effects, particularly tardive dyskinesia, have not been supported by reviews of the published evidence (Glazer & Kane, 1992).

An image problem

Given the apparent benefits of depot preparations, why, as Patel & David (2005, this issue) ask, are they not used as often as they used to be? These authors essentially give two main reasons. First, they refer to an 'image problem': clinicians believe that patients and the wider community have negative attitudes to depot. Patel & David argue that this is a mis-apprehension, and adduce results from a host of studies that suggest that at least a proportion of people with severe, enduring mental illness prefer depot administration of antipsychotics, because of its perceived efficacy, its function as a 'safety net' protecting them from risk of relapse and hospitalisation (Svedberg *et al*, 2003) and its usefulness in obviating the need to remember to take tablets on a daily basis. Nevertheless, despite such positive reports, people switched from a depot first-generation antipsychotic to an oral second-generation drug may favour the latter (Desai *et al*, 1999; Godleski *et al*, 2003).

Demonstrating that some patients are satisfied with their current treatment does not address what is perhaps a broader image problem for depot medication. Clinicians may have a lingering concern that, in the public perception, the parenteral route of administration is associated with the patient as a passive recipient at best, and with coercion at worst. The use of the depot route may be seen as the cautious choice for clinicians faced with cultural, ethnic or communication barriers (Ziguras *et al*, 1999). There is also the awareness that, with their long half-lives, depot preparations inevitably delay the opportunity for a patient to reverse any decision about continuing with medication. Thus, clinicians may fear that the process of the regular administration of injections, apart from having the potential to be rather ignominious and painful, might symbolise a relationship between prescriber and patient that is incompatible with a clinical culture that seeks to approach patients in a respectful and empathic manner and encourage communication of any treatment concerns. But it is precisely in the context of such a culture of concordance, involving informed choice and unbiased discussion of the treatment options available, that the ethical and clinical issues surrounding depot treatment can be adequately addressed, and the restrictive notion of depot as a 'treatment of last resort' dispelled (Robert & Geppert, 2004).

The restricted evidence

The second main reason propounded by Patel & David for the reduction in depot use is that clinicians may not adequately consider the risk–benefit balance with depot antipsychotics. This may partly reflect the nature and amount of relevant evidence available. For example, the studies comparing depot and oral medication in terms of risk of relapse that show only modest differences may for two reasons underestimate the value of depot in clinical practice. First, as Patel & David point out, in most cases the trial period was too short to reveal the longer-term benefits of depot treatment. In one of the longer studies comparing depot and oral antipsychotic treatment, Hogarty *et al* (1979) found no difference in the proportion relapsing within the first year, but a significant advantage for depot emerged in the second. Second, the patients for whom depot is commonly indicated, that is, those with a history of poor adherence, may be underrepresented in the studies. Recruitment seems to have been biased towards the inclusion of patients with a lower risk of non-adherence to treatment (Schooler, 2003), which would serve to diminish any advantage for depot compared with unreliable tablet-taking in the oral treatment group. That patients consenting to participate in clinical studies will tend to be more treatment adherent than those failing to consent is a problem relating to generalisability of results that may be ubiquitous in trials in schizophrenia (Bowen & Barnes, 1994).

Clinicians will face a similar lack of robust evidence if they try to weigh the possible risks and benefits of traditional depot drugs, all of which are first-generation antipsychotics, against those of a second-generation drug, only one of which, risperidone, is as yet available as a long-acting injection. There is accumulating evidence that the second-generation drugs may have advantages over those of the first-generation in terms of efficacy, including relapse prevention (Leucht *et al*, 2003), and safety, with a lower liability for extrapyramidal side-effects, including tardive dyskinesia (Correll *et al*,

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2004), but these findings predominantly relate to comparisons of oral first- and second-generation antipsychotics. At present, there is a paucity of long-term trials systematically comparing depot formulations and oral second-generation drugs on key clinical outcome measures.

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