scientific paradigm. To do so would, in their view, be to create a medicalised version of the therapy, denying its philosophical underpinnings.

Statutory regulation is not remotely feasible unless a therapy has a single unified professional voice. Many therapies are characterised by a diversity of underlying philosophies. This plurality would almost certainly be lost in a statutory scheme, which would gravitate towards the most established or dominant schools of thought to the exclusion of opposing views. A further practical consideration for therapists is that professional subscriptions would need to increase enormously to support a statutory infrastructure, the benefits of which would be largely illusory.

For most therapies, the rush towards statutory regulation as opposed to professionalisation is misguided. Rather than binding themselves within an inappropriate statutory straitjacket, most therapies should continue working towards accreditation and the development of national standards of training and competence. Consumers will be best protected by a dynamic, ethics led approach to voluntary self regulation in which standards of practice and visible and effective disciplinary procedures are given higher prominence than the pursuit of professional status.

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Ecstasy and neurodegeneration

Ecstasy's long term effects are potentially more damaging than its acute toxicity

Publicity in the popular press and medical journals[1] on the dangers of using ecstasy (3,4-methylenedioxymethamphetamine) has concentrated almost exclusively on the problems of acute toxicity. While the unnecessary death of any young person is rightly deplored, it is strange that so little attention is being paid to the long term effects of this recreational drug. This lack of attention is particularly surprising because evidence has been available for several years that ecstasy induces neurodegeneration in the brains of experimental animals.[2] If young people continue to use the drug socially they should at least be fully informed of the risks.

Administration of ecstasy to various animals has been shown to cause long term destruction of serotoninergic axons and axon terminals in the brain. This damage occurs in rodents' brains and in several species of primate.[2] Some reinnervation may occur after several months, but in squirrel monkeys several brain regions showed no recovery even after a year, while in areas where it did occur the innervation was often highly abnormal.[3] This long term damage to serotoninergic neurones can occur in rats and primates after a single high dose of ecstasy (20 mg/kg) or several lower doses (4×5 mg/kg). A recent study in rats, however, found considerable degeneration after a single dose of 10 mg/kg, which produced plasma concentrations in the same range as those seen in patients admitted with an acute toxic response to the drug.[4] Only 5 mg/kg of the major metabolite of ecstasy, 3,4-methylenedioxyamphetamine, was needed to produce similar damage.[4]

Many of the acute toxic effects of ecstasy are probably due to the parent compound and its effect of releasing serotonin from nerve terminals. Neurodegeneration, however, seems to result from metabolites of ecstasy; these oxidise to products that give rise to free radicals, which in turn induce oxidative stress and membrane damage.[5] Tucker *et al* used a yeast microsomal preparation expressing the human enzyme to provide evidence that the rate of metabolism of ecstasy is probably linked to whether a person taking the drug is an extensive or poor metaboliser of debrisoquine (via the CYP2D6 enzyme).[6] They proposed that extensive metabolisers may be at less risk of an acute toxic reaction to ecstasy but in more danger of long term neurodegeneration.

The prime example of a recreational drug producing long term neurotoxic degeneration occurred in a group of subjects who ingested a meperidine analogue, which was contaminated with MPTP (N-methyl-4-phenyl-1,2,3,6-tetrahydropyridone). After ingestion this was metabolised to MPP^+ (1-methyl-4-phenylpyridinium), a compound that produces free radicals.[7] The accidental ingestion of MPTP by these individuals resulted in the appearance of a severe and irreversible form of Parkinsonism, caused by neurotoxic degeneration of dopaminergic neurones in the nigrostriatal pathway.[8] The neurotoxic damage produced by MPTP is not only demonstrable in rodents and primates but also occurs at much lower doses in humans.[2] In humans ingestion of large amounts of MPTP rapidly produces overt signs of neurological damage, but there is now evidence that low doses or transient exposure produce occult effects revealed only by brain imaging.[9]

No unequivocal evidence yet exists that regular users of ecstasy have brain damage, but the studies that have been performed give no grounds for reassurance. McCann *et al* reported that 30 regular users of ecstasy had lowered concentrations of the serotonin metabolite 5-hydroxyindole acetic acid in their cerebrospinal fluid,[10] a change also reported in primates with brain damage induced by ecstasy.[11] Since serotonin plays a major part in the control of mood, regular use of ecstasy might be expected to lead to psychiatric abnormalities. There are case reports to support this expectation,[2 12] but the interpretation of such data is difficult.[2] What is of great concern is the possibility that the neurotoxicity in humans might be slow and insidious and that problems such as major depression will appear only in several years' time.

A recent editorial argued against legalising ecstasy because of the problems of acute toxicity. To this we add that no one should seriously consider legalising a compound that can be shown to cause long term neurodegeneration in rodents and primates at doses that differ little from those used recreationally by humans.

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Pharmaceutical representatives

Effective if used with caution

Pharmaceutical representatives are the "stealth bombers" of medicine: they swoop in, change physicians' prescribing habits (better than any journal article or formal educator), and disappear again. In the United States there is one drug representative for every 15 practising physicians—a teacher to student ratio that would be the envy of many universities. Though some doctors welcome the free samples and gifts, most dismiss representatives' information as a sales pitch. However, when their advice is actively sought and treated with caution, they can be a valuable source of new information for a busy doctor.

Obtaining information from drug representatives requires minimal effort. As communication experts, drug representatives package their messages into tight bundles, delivering them neatly between patients, often accompanied by a free lunch. Their bottom line message—"prescribe my drug"—is seemingly supported by medical evidence, yet this is frequently intermingled with emotional appeals and logical fallacies.[1] Consumers of this information must be constantly vigilant in order to separate the wheat from the chaff.

In this sifting process two factors must always be considered: the relevance and validity of the information presented.[2] However easily obtained, if information is irrelevant or invalid it is useless. The standard sales pitch is rife with information on a drug's effect on cellular receptors, its in vitro inhibitory activity, or its effect on serum concentrations. These intermediate outcome measures are a far cry from answering the question that patients would ask: "If I use this drug is it likely to make me live a longer, healthier, more productive, and symptom free life?" Clear thinking is needed to avoid being misled by irrelevant claims of benefit.

The validity of information presented by drug representatives varies with their level of knowledge and their zeal in conveying their message. A recent analysis of the accuracy of information from representatives found that one in 10 statements—all of which favoured their product—were at odds with the company's own literature.[3] Unfortunately, only one in four clinicians was aware that the information was incorrect. Scepticism is the key to obtaining valid information.

One useful way to evaluate information from drug representatives is "STEP,"[4] an acronym for safety, tolerability, effectiveness, and price. All four attributes should be considered when weighing the purported advantage of one drug over another. Safety applies to the likelihood of long term or serious side effects caused by the drug. Tolerability is best measured by comparing the pooled drop out rates between the new drug and a competitor drug, rather than trying to weigh the relative incidence of side effects. The best way to evaluate effectiveness is to compare the new drug with your current favourite. The necessary information may be hard to come by, especially since research funded by a drug company may not be published if the results show no benefit of its drug over that of its competitor.[5] Lastly, the price of the drug should include not only its direct costs but any indirect costs, such as additional monitoring or extra visits to a doctor. So, until your drug representative produces valid data that a drug is at least one STEP better, your current practice need not change.

Information such as this is not the only stock in trade of drug representatives: they also provide gifts, food, and other inducements to convince doctors to prescribe their drugs. Since reciprocity is so much a part of human nature, doctors must guard against a feeling of indebtedness that might overwhelm the rational approach outlined above. An adage well known in the world of marketing is that advertising works best when its audience does not think it is being "sold" anything.

The best way to avoid "stealth" attacks by drug representatives is to put them to work for you, checking for new information about their drug that is both relevant and valid. Use them to identify and to bring you the facts about their drugs that fit into the STEP approach. Tell them what information you need—"patient-oriented evidence that matters"[6] not a "mishmash of preclinical data."[7] Do not trust them to précis information into a conclusion; reserve that crucial process for yourself. The primary goal of drug representatives is to promote a product, but an active approach by doctors can transform them into a useful and accurate source of information.

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