fewer found guilty. These checks may thus give rise to a false sense of security and diminish vigilance and supervision. All organisations therefore need careful guidelines governing access to children.

There are also legal problems. As the police cannot be indemnified for incorrect information the employing bodies may be liable for mistakes—if, for instance, the wrong John Smith is checked. Finally, there is the difficulty of interpreting the information received and its relevance to the job in question. For example, the gay movement points out that a conviction for a homosexual offence with, say, a 20 year old is not equivalent to child abuse, and many offences uncovered will have nothing to do with children and may date back many years. The nominated officer may need expert advice in assessing information received.

An attempt to select out those with a relevant criminal background must, however, be made, and if we can bar even one of the multiple child sex offenders much will have been achieved.

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Tetrahydroaminoacridine (THA) in Alzheimer's disease

Not ready for routine use

It must be unique for newspaper headlines describing a new treatment for Alzheimer's disease to be based on reports from a sufferer who claims to have been successfully treated—and a Nobel prizewinning scientist at that.[1] The drug in this case was the anticholinesterase tetrahydroaminoacridine. The sufferer was one in a series of 35 patients,[2] details of whom are not yet published, but the researcher in charge of the study was said in the *Sunday Times* to regard the results as "staggering." The scientist-patient claims that the drug allowed him to be active and creative again after a period of failing memory and long inactivity.

There are good reasons why manipulating the cholinergic system might be effective in treating Alzheimer's disease. A deficit in the cholinergic system in the disease was first described by Davies and Moloney in 1976 and is now well established.[3] The deficit correlates both with the severity of dementia[4] and with measures of the main histological hallmarks of the disease—senile plaques and neurofibrillary tangles.[5] Other neurotransmitter systems are also deficient in Alzheimer's disease: neurochemical analysis of brain tissue at necropsy has suggested that somatostatin[6] and serotonin[7] are deficient, and other studies have implicated deficiencies in dopamine,[8] glutamate,[9] and aminobutyric acid.[10] Neurochemical analysis of biopsy material from patients with Alzheimer's disease has confirmed the cholinergic and serotonergic deficits but not the other deficits.[11]

The successful treatment of Parkinson's disease, another degenerative disorder, with a drug designed to correct a neurotransmitter deficiency has raised hopes that drugs that enhance the cholinergic system would be beneficial in Alzheimer's disease. The early results of such intervention showed that whichever part of the cholinergic system was modified precursor anticholinesterase or receptor agonists were largely unsuccessful.[12,13] Later and more rigorous studies described a modest improvement, especially in older patients with the more "benign" form of Alzheimer's disease[14] who were treated with lecithin[15] and in some patients treated with physostigmine.[16] Trials of receptor agonists RS86, oxotremarine, bethanecol, and arecoline have shown no clinical benefits.[17-20]

Tetrahydroaminoacridine is a potent centrally acting anticholinesterase and cerebral stimulant[21] that has several other postulated actions: selective blockade of potassium channels in the central nervous system (possibly because of its structural similarity to 4-aminopyridine[22]), down regulation of M_1 receptors,[23] alteration in phosphorylation,[24] and at high dosage presynaptic and postsynaptic blockade of both muscarinic and nicotinic receptors.[24] Anticholinesterases increase the need for free choline,[25] which may explain why in some of the few trials of tetrahydroaminoacridine it has been used with lecithin.

Despite some rationale for its use in Alzheimer's disease it is difficult to see why tetrahydroaminoacridine should be more effective than any other cholinomimetic agent. Kaye *et al* reported only a modest benefit from combined tetrahydroaminoacridine and lecithin (and no benefit from tetrahydroaminoacridine alone),[26] and two reports by Summers *et al* in 1981 and 1986 are the only reports of appreciable clinical benefit.[27,28] These reports have been criticised on several counts: lack of clarity in the inclusion and exclusion criteria, no separate analysis of the blind tetrahydroaminoacridine trial versus the blind placebo trial, the dubious validity of the outcome criteria, no explanation of the apparent absence of a placebo effect, and because the subjects were concomitantly taking lecithin.[29-33] The trials have, however, stimulated more critical examination of the efficacy of the drug. Gauthier *et al* in a double blind study of tetrahydroaminoacridine and lecithin reported a modest but appreciable improvement in both functional ability and cognition over eight weeks[34] but also a high incidence of clinically important side effects, with autonomic symptoms in four fifths of their 51 patients, and hepatotoxicity (based on abnormal results with liver function tests but no biopsy examination) in a third. These side effects were said to be reversible with adjustment of the dose of tetrahydroaminoacridine. The large multicentre trial in the United States[35] was discontinued because of the high incidence of hepatotoxicity[36] but has subsequently resumed.

How serious are the unwanted effects of tetrahydroaminoacridine? Troublesome and occasionally serious cholinergic side effects, including disturbances of the gastrointestinal tract and hypotension,[37] occur at doses lower than those used by Summers *et al*.[27,28] These are reported to be reversible when the dose is titrated. But hepatotoxicity is much more serious and occurs in a fifth to a third of patients; it seems to take the form of an autoimmune granulomatous hepatitis,[38] which is said to be reversible on stopping the drug, but so far few follow up results have been reported.

The story of tetrahydroaminoacridine is a good illustration of the dilemma that faces doctors attempting to treat a devastating degenerative condition: the pressure to do something versus the maxim of "above all do no harm."[35] If tetrahydroaminoacridine is eventually proved to have worthwhile clinical benefits and when there are reliable data

on unwanted effects a judgment may be reached both in general and individual cases on whether its use is justified. Alzheimer's disease is after all a cruel and ultimately lethal disease, and, as with cancer, risky treatment may be acceptable if there are sound reasons to expect benefit from it. At present we have far too few hard facts either on the efficacy of tetrahydroaminoacridine or its dangers to justify its use other than as part of carefully regulated research.

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Control of substances hazardous to health

Far reaching legislation or dead letter?

Described by the Secretary of State for Employment as "the most far reaching health and safety legislation since the Health and Safety at Work Act 1974," the Control of Substances Hazardous to Health (COSHH) Regulations 1988 place specific obligations on employers (including the self employed) to control hazardous substances.[1] The regulations first define a hazardous substance broadly, as something that has the potential to harm health. (Because they are covered by separate legislation medicine for patients, asbestos, lead, radiation, and substances in mines are excluded.) They then require all employers to make, and usually to record, a comprehensive assessment of the risks of using such substances in the workplace. In many cases this must be followed by action to reduce the risk; in some instances monitoring of concentrations of the substance in the air and medical surveillance of the workforce are required. From 1 January 1990 any work with hazardous substances will be prohibited unless an assessment has been made.

The new regulations are well thought out and comprehensive. Furthermore, they have been framed after full consultation with the Confederation of British Industry and the Trades Union Congress. May we therefore expect a substantial improvement in the health record of industry? Unfortunately, there are grounds for pessimism. The Health and Safety at Work Act, in force now for nearly 15 years, was also formed with the best of intentions. It has undoubtedly clarified a lot of obscure legislation and put the responsibility for health and safety at work firmly on employers and employees, and the Health and Safety Commission and the Health and Safety Executive have worked hard to educate and inform industry and to continue a programme of inspection and enforcement. But the fact remains that in those 15 years industry's accident record has not improved—each year still some two workers are killed and 95 are seriously injured among every 100 000 employed.

The Health and Safety Executive has commented on possible causes of this reversal in the downward trend of serious injuries in the workplace, pointing to the possible roles of decreased investment in new machinery, declining standards of maintenance, and reduced resources for safety.[2] To these might be added the unfamiliarity of senior management with the workplace and its hazards, the relative weakness of trades unions with respect to safety, and the need for industry to increase marginal profitability by reducing overhead costs, of which money spent on health and safety may be perceived as a component.

The new regulations come at a time when the public is more aware than ever of the hazards of industry. They provide a clear framework for preventive action. All that is necessary is enforcement. This requires that they are understood by all