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Comment on the WHO Consensus Statement

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Since the 1960s, it has been argued consistently that anticholinergic agents are overprescribed in patients receiving long-term antipsychotic medication (Morpurgo, 1965; DiMascio & Demirgian, 1970; Klett *et al*, 1972; Rifkin *et al*, 1978). Nevertheless, in many cases anticholinergic drugs are still routinely administered when antipsychotic medication is begun, and then maintained indefinitely. Thus, this WHO statement, reviewing both the adverse consequences and potential benefits of the use of anticholinergics in psychiatry, is to be welcomed. However, presenting itself as a relatively brief policy statement regarding the clinical prescription of anticholinergic agents, it is so compressed that it is only able to hint at a number of issues relevant to the risk:benefit ratio for these drugs, and it is this that I would like to expand upon.

For example, the statement does not specifically mention the potential short-term prophylactic value of these drugs for acute dystonia. This is a painful and distressing side-effect of antipsychotic drugs, particularly the high-potency drugs, usually occurring within a few days of starting treatment. Young males are most at risk. Short-term prophylaxis with anticholinergic medication is likely to be effective and is particularly indicated where there is a previous history of drug-induced dystonia (Keepers *et al*, 1983; Winslow *et al*, 1986; Sramek *et al*, 1986). Further, the statement suggests that short-term prophylactic treatment is particularly useful to avoid the development of akathisia. However, anticholinergic treatment in this condition has an uncertain reputation (Braude *et al*, 1983) and beta-adrenoceptor blockers such as propranolol are probably more effective in the majority of cases (Adler *et al*, 1989).

With regard to drug-induced Parkinsonism, the statement notes that anticholinergics should be used as a treatment only, if "other measures, such as the reduction of neuroleptic dosage or the substitution of the administered drug by another less prone to induce Parkinsonism, have proven ineffective". While manipulation of the antipsychotic dose can be a practical and effective clinical measure (Johnson, 1977), changing an antipsychotic drug cannot be employed as a systematic strategy, as the relative liability for Parkinsonism of the various antipsychotic drugs available cannot be confidently predicted. The statement also suggests that when antipsychotic treatment is started the addition of anticholinergic agents is indicated only if Parkinsonism develops. The anticholinergics should then be stopped later to allow the need for continued use to be assessed. These treatment recommendations are similar to others in the literature (Klett *et al*, 1972; McClelland *et al*, 1974; Pullen *et al*, 1984) which suggest withdrawal of the anticholinergic drugs after three months, as drug-induced Parkinsonism tends to improve spontaneously over this time despite continued antipsychotic medication. Pullen *et al* (1984) added that if long-term anticholinergic treatment for Parkinsonism is indicated in patients on regular depot antipsychotic medication, it may be possible to limit the administration of the anticholinergic to 7 to 10 days after the injection.

This consensus statement from the WHO mainly serves as a warning of the various hazards and side-effects of anticholinergic drugs, although some of those listed, such as the contribution to hyperthermic episodes and the antagonism of the therapeutic effects of antipsychotics, are relatively uncertain. The conclusion is that the prophylactic use of these drugs is not recommended. Although there is little distinction between prophylactic and routine or indefinite administration in the statement, it is clear that the authors see little justification for long-term treatment with anticholinergics. However, if the arguments for and against the chronic administration of anticholinergics are based on the findings of studies of anticholinergic withdrawal the issue seems to be far from resolved. In such studies, the proportion of patients receiving antipsychotic medication who experience relapse of Parkinsonism varies widely, from 68% (Manos *et al*, 1981) to 4% (McClelland *et al*, 1974). In general, investigators who have reported the reappearance of moderate to severe Parkinsonism in a high proportion of those patients withdrawn from anticholinergics, such as Manos *et al* (1981), Rifkin *et al* (1978), and Caroli *et al* (1975), have considered that the risk:benefit ratio is balanced in favour of continuing anticholinergic treatment, while those investigators finding a relatively low recurrence of Parkinsonian symptoms, such as Orlov *et al* (1971), Klett *et al* (1972), McClelland *et al* (1974), and Perenyi *et al* (1983), have concluded that the long-term administration of these drugs is unnecessary for the majority of patients.

One of the possible disadvantages of long-term anti-Parkinsonian treatment mentioned in the statement is that it may predispose to the

development of tardive dyskinesia. It is a commonplace clinical observation that the addition of anticholinergic medication exacerbates existing tardive dyskinesia and that stopping anticholinergics usually improves the condition, and this is supported by experimental and clinical evidence (Klawans & Rubovits, 1974; Greil *et al*, 1984; Kane & Smith, 1982). However, recent reviews (Gardos & Cole, 1983; Yassa, 1988) of the evidence for long-term anticholinergic drug administration acting as a risk factor for tardive dyskinesia have found no convincing support for this idea. One possible explanation for this suspected association is that it is an epiphenomenon. Patients on antipsychotic medication who develop tardive dyskinesia may also have been susceptible to the development of Parkinsonism early in treatment (Crane, 1972; Chouinard *et al*, 1979; Kane *et al*, 1984) and thus more likely to have received anticholinergic drugs.

The statement refers briefly to the danger of an acute toxic state with excessive dosage of anticholinergics. However, toxic reactions to therapeutic doses may also be due to individual sensitivity, with an increased risk in the elderly. Toxic symptoms such as paranoid ideas and hallucinations may be of short duration and not recognised as being drug induced in psychiatric patients (Macvicar, 1977; Crawshaw & Mullen, 1984; Fisch, 1987). Such patients, particularly those with schizophrenia, may be prone to the abuse of these drugs in relatively small, often therapeutic doses in order to produce euphoria and increased sociability (Marriott, 1976; Smith, 1980). This might represent an attempt at self-medication to overcome dysphoria (Pullen *et al*, 1984; Fisch, 1987; Siris *et al*, 1988), although one explanation for the positive perception of anticholinergic drugs by patients may be that they relieve the discomforting experience of bradykinesia or akathisia associated with antipsychotic medication (Johnson, 1981).

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