

## MAOIs and anaesthesia: An expert analysis

### Abstract

The main issue in anaesthesia and post-operative care is the avoidance of drugs with SRI potency, particularly opioid analgesics. The confusion of poor publications on this subject is clarified by directing readers to useful recent reviews. The misinformation about the use of pressor agents like adrenaline is addressed. There are several reviews making recommendations about the need to cease MAOI treatment prior to surgery which are poorly informed and misdirected, because the authors have an inadequate understanding of the relevant pharmacology. These are analysed in detail to illustrate the misconceptions that continue to be promulgated.

Surgeons or anaesthetists who unnecessarily instruct patients to cease MAOI prior to surgery, without the approval of the treating specialist, maybe giving advice that is out of step with state-of-the-art knowledge and which will put them at risk of losing a legal case of malpractice, should untoward outcomes precipitate court action.

### Introduction

**Myth:** One cannot give an anaesthetic without ceasing MAOIs first.

The main issue in anaesthesia and post-operative care, in patients taking MAOI treatment, is the avoidance of drugs that act as SRIs, particularly, post-op, opioid analgesics, a few of which have some mild SRI potency; viz. meperidine (pethidine), tramadol, tapentadol, methadone, dextromethorphan, dextropropoxyphene, and pentazocine (other opioids are safe). If high and repeated doses are used in the presence of an MAOI severe ST is possible.

Also, and this is a ‘googly’ (or ‘curveball’ for baseball aficionados) especially for operating theatre situations, **methylene blue MB** (aka methylthioninium) is used (including intravenously) in various circumstances in the belief that it is ‘only a dye’; whereas **it is active as an MAOI in usually administered dosages** [1]. It inevitably interacts with pre-operatively administered SRIs — if they are present at therapeutically relevant concentrations — to precipitate potentially serious, and sometimes fatal, **serotonin toxicity (ST)** [2-5].

Drugs that have clinically significant action as SRIs can precipitate severe ST in a patient treated with either a non-selective MAOI-AB inhibitor, or a selective MAO-A inhibitor (but not a selective MAO-B inhibitor).

Other opioids [bar the above-mentioned] are **safe** (because they have no SRI potency); that includes; **codeine, oxycodone, hydrocodone, buprenorphine, morphine, remifentanyl, alfentanil, sufentanyl, and fentanyl**. These do not act as SRIs and there is no scientific evidence that they are causal, or contributory, in either serious or life-threatening ST — i.e. ST resulting in potentially lethal degrees of hyperthermia, and severe rigidity; see [6].

Poor-quality case reports, often by inexperienced doctors and non-medical commentators (e.g. pharmacists), have been given undeserved attention, by [some commentators](#) and reviewers, and have caused much misunderstanding and misdirection, leading to poor clinical decisions.

**Safe Opioids are: codeine, oxycodone, hydrocodone, buprenorphine, morphine, remifentanyl, alfentanyl, sufentanyl, and fentanyl**

It is important to understand that those opioids that do have weak SRI potency cannot precipitate severe ST when combined with other serotonin reuptake inhibitors, only when they are combined with MAOIs.

**MAOI + SRI — potential severe ST.**

**SRI + SRI — no serious problem.**

Amongst the confusing mass of poor publications there are one or two useful recent reviews, which are summarised and commented on, because they contain material that adds usefully to what I have discussed in my previous papers and commentaries [7-10].

## A storm in a teacup

The eminent clinical toxicologist, Professor Isbister, has explicated the opinion of the world-leading 'Clinical Toxicology Research Group' (from the University of Newcastle) in a recent discussion about CNS toxidromes and antidotes, *'Therapeutics in clinical toxicology: in the absence of strong evidence how do we choose between antidotes, supportive care and masterful inactivity'* [11].

Isbister reminds us that classifying each patient's complex of symptoms and signs is far less important [because specific antidotes are rarely indicated] and can often result in the use of multiple inappropriate antagonists, causing further adverse effects. A proper knowledge of the pharmacology of the implicated drugs, and Bayesian reasoning, is the foundation for analysis and (in)action ('masterly inactivity'); i.e., drug cessation and supportive care is usually the best course of action, not specific antagonists.

**Drug cessation and supportive care is usually the best course of action, not specific antagonists**

Baldo & Rose's comprehensive recent review [9] *'The anaesthetist, opioid analgesic drugs, and serotonin toxicity: a mechanistic and clinical review'* contains much of academic value, including a thorough documentation and analysis of the many more recent case reports and the most complete references on basic research about the *in vitro* SRI potencies of opioids. It also further confirms the potential of case reports to mislead, and their limited value. They comment that:

**Anaesthetists must maintain a heightened awareness of its [ST] possible occurrence and a readiness to engage in early treatment to avoid poor outcomes**

This may be supplemented by adding — assuming there is an informed awareness that there could be a problem — that in the majority of cases (which involve SRI + SRI, but not SRI + MAOI) there is little possibility of a serious or fatal outcome (from ST) as a result of a combination of drugs that only have serotonin reuptake inhibition (or other 'non-MAOI' serotonin-related activity) — therefore, Isbister's counsel not to engage in overly aggressive intervention should be noted.

**The only likely cause of peri-operative deaths from ST results from the administration of methylene blue (MB) to someone who has been taking an SRI pre-operatively**

As Baldo and Rose note from the Rickli data, **fentanyl** has no affinity at the SERT and only binds to 5-HT<sub>1A</sub> and 5-HT<sub>2A</sub> 'in the low micromolar

range.’ Only high-dose fentanyl (e.g. 50 microg/kg given rapidly intravenously) will result in micromolar concentrations, and those rapidly decline with redistribution [12]. This further reinforces the conclusion that fentanyl has no relevant actions in relation to ST. SRIs that precipitate ST have potencies in the **single-figure nanomolar** range. Many reviews and comments concern drugs whose potency is orders of magnitude too weak (e.g. fentanyl) to precipitate the hypothesised effects in human clinical situations — such speculations are counter-productive for sensible clinical practice; e.g., the case that Adler et al. [13] reported, about which Rosenbaum and Gillman commented [14]. Another example of a poorly informed and unhelpful case report that good refereeing should have forestalled.

**It is only combinations of MAOI/SRI that have the potential to cause serious and fatal ST — even then specific antidotes (5-HT<sub>2A</sub> antagonists) should be used cautiously.**

Baldo and Rose’s detailed analysis of case reports ascribes more value to them than is warranted: the alternative interpretation is that it illustrates they are of little value: they say ‘*Surprisingly, the non-serotonergic opioid morphine accounted for four cases compared with meperidine (five)*’. There is no surprise, this is as one would expect, especially since none of the cases can confidently be stated to represent definite ST, false positives abound — such case reports are unreliable, as the past history of false alarms about ST with various other drugs has painfully, and counter-productively, illustrated.

The downside to over-interpreting case reports is that they generate misconceptions. Poor data does not produce useful conclusions [15–18]

There are many patients who have features of serotonin excess — that might not reach a degree of severity to justify labelling them as toxicity — solely from therapeutic doses of their SRIs. Putting them in a stressful situation (an illness or condition requiring opioids for example) may be enough to make manifest more pronounced symptoms than usual. Such cases reported as an opioid interaction resulting in ST, where mechanistically an interaction seems unlikely or impossible, may therefore reflect association not causation.

For instance; case reports of rapidly progressive life-threatening complications, e.g. seizures or coma, after low-to-moderate doses of fentanyl in the presence of an SSRI should not be attributed to ST. On the other hand, **non-specific mild-to moderate symptoms** or signs such as agitation, tremor, sweating, and (mild) clonus, have been described in patients on SSRIs receiving opioids that we know have no SRI potency — such symptoms are not necessarily serotonin-mediated, and furthermore do not represent toxicity. They might be contributed to by an indirect effect of decreased GABA-mediated inhibition of 5-HT release [19].

**No other drugs used in anaesthesia have clinically significant SRI properties and therefore there are no other serotonin-related problems or ST.**

## Other drugs of relevance to anaesthesia

Norepinephrine (noradrenaline), epinephrine (adrenaline) and phenylephrine  
See under ‘Major operations’

### *Ketamine*

Clinical doses of ketamine for used for induction of anaesthesia, maintenance of analgesia, or treatment of depression, do not result in serotonin re-uptake inhibition (SRI). Peak concentrations of ketamine when used for induction of anaesthesia may result in inhibition of norepinephrine reuptake and might

theoretically result in exaggerated hypertension when used in the presence of MAO-A or non-selective MAO-AB inhibition; safe concurrent use has been reported in a small number of cases [20-22]. It is clearly prudent to continue monitor such combinations closely.

### *Dexmedetomidine*

Dexmedetomidine is not a problem; it **decreases** 5-HT release [23] and has been used to treat serotonin or serotonin+dopamine+adrenergic (i.e. methamphetamine) toxicity.

### *Ondansetron*

Ondansetron (and related ‘setrons’) used for prophylaxis or treatment of PONV have **not been associated with ST**. Indeed, because **they are serotonin antagonists** (not agonists), there is no pharmacological reason to suppose that they would be capable of that, despite warnings that have been issued by various ‘agencies’ including the FDA and the UK MHRA. These warnings have been criticised and rebutted because they are **based largely on poor quality and second-hand case reports** which do not describe definite symptoms or signs of ST; more importantly, their pharmacological properties make that inherently implausible [16, 24-29]. Even in dosages much higher than those used to prevent or treat PONV, any effect on 5-HT<sub>1A</sub> or 2A receptors would only produce minor alterations in serotonin that would not contribute significantly life-threatening ST when given to a patient on an MAOI or SSRI [30].

### *Drugs with ‘off-target’ action as MAOIs*

It should also be noted that it is important that surgeons and anaesthetists be aware of giving **drugs that have ‘off-target’ action as MAOIs** — examples at the moment are **methylene blue (MB)**, used in various procedures (see other commentaries for details, and [1, 4, 31]), and high-dose linezolid for infections (NB see metaxalone (Skelaxin) below, and the [separate commentary](#) on metaxalone). A proportion of the population take antidepressant drugs that act by serotonin reuptake inhibition (SSRIs and SNRIs), which will interact with MAOIs given ‘peri-operatively’, and thus precipitate ST. Both MB and linezolid do have MAOI activity at high dosage/blood levels, and can thus precipitate serious or even fatal ST in those already on an SRI [4, 5, 32, 33].

Anaesthesia related reviews and guidelines do not include the vital information that MB is a potent MAOI

## History and background

The idea that an anaesthetic cannot be given without first ceasing MAOIs is another of the deeply embedded and ill-founded myths that one encounters about MAOIs. This potentially problematic idea stems from a time when the interactions and toxicities of these drugs were not properly understood and subsequent texts and information for doctors have not since been revised and updated, partly because of the disinterest in MAOI drugs — but also because of poor scholarship, poor pharmacological knowledge, and poor refereeing of papers (see below).

Caution is not always the best choice.

These misconceptions about MAOIs and anaesthesia are of potentially fatal consequence, because poorly informed surgeons (some of whom act as if ‘pharmacology’ was a foreign-language word) may tell patients due for elective surgery to cease treatment, probably without consultation with the prescribing doctor, or being aware of their history, or the possibility of rapid relapse and suicide. I have had experience of suicides from relapse of depression as a direct

result of such ill-advised cessation of treatment — see [\[the farmers story\]](#). Hence, my disparaging view of those surgeons (and anaesthetists) who are too ignorant and arrogant to ask for advice.

MAOIs should not be ceased without prior consultation with the prescribing psychiatrist

## Major operations

First, in ‘uncomplicated’ anaesthesia (not involving pressor agents), aside from avoiding any use of narcotic analgesics with SRI potency, there are no major problems or interactions. The preponderance of informed opinion has agreed with that view for some time [34-41]; however, some reviews and guidelines still contain erroneous information and advice (see below).

For ‘major’ operations that might require treatment to raise or lower blood pressure there are some adjustments of dosage and agents that may be required, but **there are no major obstacles or risks**.

For instance, the hypotensive effect of MAOIs may potentiate blood pressure decreases with general anaesthesia or neuraxial anaesthesia. One retrospective cohort study demonstrated less intraoperative hypotension in 26 patients on tranylcyproline, and no difference in the incidence of tachycardia, hypertension or bradycardia [39].

### *Adrenaline (epinephrine) and noradrenaline (norepinephrine)*

**Adrenaline** (epinephrine) and **noradrenaline** (norepinephrine) are **direct post-synaptic agonists** and therefore do not cause any problematic interaction with MAOIs. Equivocation about that has been evinced repeatedly over the years in most standard texts, yet the lack of any major interaction was established at the dawn of modern pharmacology by researchers whose names, Gaddum and Brodie, among others, are prominent in history [42-44]. That work has been forgotten. It is TCAs that have a more pronounced interaction with adrenaline. Ironically, I cannot recall anyone getting too worried about that.

Therefore, if vasopressor agents are required **directly acting alpha agonists** may have their effects potentiated — initial doses of **norepinephrine (noradrenaline), epinephrine (adrenaline) and phenylephrine** need to be lower when used in patients taking MAOIs [45]. These initial lower doses may then be promptly titrated as needed, without significant difficulty or inconvenience.

Care may be required where copious amounts of ‘topical’ **phenylephrine** are used to control bleeding vascular beds (e.g., in ENT surgery), hypertension and vascular incidents have been reported **even in the absence of MAOIs**. Oxymetazoline may be a better option [46].

In dental anaesthesia, if it is preferred to avoid adrenaline, then **felypressin** can be used instead.

### *Ephedrine*

What were formerly referred to as ‘**indirectly acting**’ agents (**ISAs**, now **commonly referred to by the preferred term ‘releasers’**), like **ephedrine**, are the agents that are best avoided because they produce more pronounced and less predictable or controllable elevations of blood pressure.

### *Oxymetazoline and xylometazoline*

Oxymetazoline and xylometazoline are both alpha-adrenoceptor agonists and are negatively coupled to adenylate cyclase which thus decreases cAMP. Activation of 2A-adrenoceptors causes inhibition of neurotransmitter release [47]. They are

used during surgery and as nasal mucosa decongestant and for common colds etc. **They are safe with MAOIs.**

## A typical misleading case report

Pay-to-publish journals specialising in case reports have produced a veritable tsunami of nonsense which does not look like abating any time soon. Many such reports are being published without any meaningful refereeing whatsoever. The FDA 'FAERS' system is worse because it includes self-reports from the public (these are included in Baldo & Rose's review and they rightly seem to imply reservations about these, which one might further amplify).

Science is going, has gone, to the dogs.

For instance; a case report of an adult on HAART for HIV taking escitalopram and up to 40 mg of oral ondansetron daily [48] describes paroxysmal **myoclonus\*** (NB clonus, not myoclonus, is diagnostic of ST) that abated with a change in HAART with reduced nausea, and reduction, then discontinuation, of ondansetron. This may have been associated with increased serotonergic neurotransmission related to a pharmacokinetic interaction that would elevate escitalopram blood levels, and thus increase its SEs.

No other symptoms of ST were present; thus, this is not definable as definite ST, or hardly even possible ST, and this report is unhelpful. It is jumping on the bandwagon of reporting supposed ST when it is merely describing a known side-effect that has been recognised for over half a century. **It is unwarranted to describe it as toxicity.**

**Myoclonus is not the same as clonus, and myoclonus is not a diagnostic feature of ST**, although it is sometimes seen (~10% of cases), but not in isolation [personal communication: data courtesy of Prof Whyte from their database, Nov 2019]. It is also seen in therapeutic doses as an idiosyncratic, seemingly serotonin-mediated, SE with many SRIs, often occurring hypnagogically, and was recognised with clomipramine 50 years ago [50, 51]).

One strongly suspects most of these poor case reports have not observed true pathological clonus: such reports rarely contain essential details, like how many beats of clonus, whether it was present in the calf, or greater in the lower than the upper limbs (as is typical in ST). Likewise, when reporting elevated temperature measurements, they never state how it was measured, where it was measured, or for how long it was elevated. That is poor science, especially in view of the established imprecision of temperature measurements (especially aural IR).

Case reports do not give essential details, how many beats of clonus, whether it was present in the ankle or calf, or greater in the lower than the upper limbs

## Provenance of case reports

**The experience and expertise of the people writing case reports (and reviews) is of great relevance when interpreting them and must be taken into account when assessing the value.** The above references are a good example of this, one of them being from Prof Isbister, who is a distinguished clinical toxicologist who has extensive experience in treating drug toxicity, including ST, (a long-time colleague of Professor Whyte at the Clinical Toxicology Research Group, University of Newcastle). It would be prudent to

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\* the essential difference is that myoclonus is irregular, biphasic, and usually involves groups of muscles, not single muscles. Clonus is mono-phasic, regular, and involves one set of opposing muscles (like the calf or biceps) 49. Faught, E., *Clinical presentations and phenomenology of myoclonus*. *Epilepsia*, 2003. 44: p. 7-12.. **Pathological clonus manifests with 10-12 beats or more, 2 or 3 beats is not clinically significant clonus**, [see this video of clonus](#)



take a great deal notice of what is said by these authors, from this world-renowned research unit.

The Walczyk reference reporting ST with tapentadol is from a group of pharmacists — none of the four authors are doctors, never mind clinical toxicologists. A pharmacist cannot make a reliable and informed report like this, which depends on first-hand observation and experienced interpretation of complex clinical signs in a case of toxicity (cf. clonus and myoclonus). I hope readers give such reports the scant attention and credibility they deserve.

If you had a high-performance sports car, would you take any notice of what a bicycle repair man said about what might be wrong with it?

Professor Isbister commented on Walczyk's report, dismissing the notion it represented ST, and I quote from Isbister's response:

In all cases, the treatment must focus on removal (or reduction) of the implicated agent. Classifying each patient's complex of symptoms and signs is far less important and can often result in the use of multiple inappropriate antagonists, causing further adverse effects. Supportive treatment is far more important than the use of specific antagonists. ... Cases such as this one reported by Walczyk et al are best looked at through the lens of Bayesian analysis as to the most probable cause of the symptoms, with ideally an emphasis on supportive care of the overdose.

## Recent demythologizing data

### *MAOIs and enzyme inhibition*

More recent and reliable data on the effect of MAOIs on metabolic enzymes emanates from the research group of Prof Glen Baker (DSc) whose members have done much work in this area. In a more recent paper, they state [52], of MAOIs:

None of these inhibitory effects are considered clinically significant at usual therapeutic doses. However, in certain situations such as high dose tranylcypromine therapy, or in poor metabolizers of CYP2C19 substrates, clinically significant interactions might occur, particularly when tranylcypromine is co-administered with drugs with a narrow therapeutic index.

Essentially, this is because none of the 'irreversible' MAOIs act as anything other than **weak competitive inhibitors of CYP450 enzymes** that only have significant inhibitory action in the micromolar range, which is more than one thousand times higher than the concentrations achieved **therapeutically\***. Since tranylcypromine has a half-life of about two hours, it is impossible it could maintain concentrations able to cause inhibitory interactions.

Much of the misunderstanding that has been thoughtlessly promulgated in the literature originates from this old paper by Clark [57], which, it should be noted, predates the more sophisticated understanding of cytochrome P-450-based drug

\* After a single oral dose of 20 mg, mean peak plasma concentration in 9 subjects was 0.112 mg/L (range 0.05 – 0.2 mg/L) 53. Mallinger, A.G., et al., *Pharmacokinetics of tranylcypromine in patients who are depressed: relationship to cardiovascular effects*. Clin Pharmacol Ther, 1986. **40**(4): p. 444-50, 54. Mallinger, A.G. and E. Smith, *Pharmacokinetics of monoamine oxidase inhibitors*. Psychopharmacol Bull, 1991. **27**(4): p. 493-502.. Tranylcypromine 400 mg concentration was 0.5 mg/L with mild symptoms of intoxication 55. Twersen, S. and A. Schmoldt, *One fatal and one nonfatal intoxication with tranylcypromine. Absence of amphetamines as metabolites*. Journal of Analytical Toxicology, 1996. **20**(5): p. 301-4.. In a fatal overdose estimated at 550 mg, antemortem tranylcypromine blood concentration was 0.611 mg/L 56. Crifasi, J. and C. Long, *The GC/MS analysis of tranylcypromine (Parnate) in a suspected overdose*. Forensic Sci Int, 1997. **86**(1-2): p. 103-8..

interactions. It only suggested inhibition at concentrations **way beyond the concentration achieved therapeutically**.

### *SRI potency of opioids updated*

Being frequently obliged to make negative comments about publications in the 'ST space', it is good to be able to recommend the review by Baldo & Rose in the Br. J of Anaesthesia [9] which is a thorough and up-to-date review of many significant and recent references [7, 58-62]. It is the best and most recent source of references and data relating to SRI potency of opioids. These data confirm what I have reviewed in previous publications, which is repeated above.

See also subsequent data from Olson [63].

## Guidelines and other pontifications: Ultracrepidarian issues

If anyone's feathers are ruffled by my use of the word pontification, then take a deep breath and read on.

Since I initially posted this commentary one or two noteworthy publications have appeared including De Hert et al.; '*Pre-operative evaluation of adults undergoing elective noncardiac surgery: Updated guideline from the European Society of Anaesthesiology*' [64]. I note that there is an amusing incongruity in a publication by the first author (De Hert), who later co-authored a paper concerning the unreliability of guidelines (*Pitfalls of clinical practice guidelines in the era of broken science: Let's raise the standards*), with which [I heartily agree](#) [65].

'*Management of Psychiatric Medications During Perianesthesia Period*' by Trigo-Blanco & Oprea is another recent breath of fresh air and contains generally accurate information about MAOIs [66], although a citation they rely on [67] is less satisfactory and has some misinformation.

The authors of the De Hert et al. Guideline, have got themselves into a tangle and been 'hoist by their own petard'. They state:

We recommend stopping irreversible MAOI at least 2 weeks prior to anaesthesia. In order to avoid relapse of underlying disease, medication should be changed to reversible **MAOI** [68]\*.

First; patients are likely to have been exposed to a 'reversible MAOI' unsuccessfully prior to being put on an irreversible MAOI, making that suggestion superfluous (moclobemide is the only reversible MAOI on the market, and only in a few places — it was never approved for use in the USA). Furthermore, most psycho-pharmacology specialists regard moclobemide as being substantially less effective. They also mention 'third generation MAOIs' without indicating what that term means, if they know — indeed, the meaning is certain to be opaque to everyone, since this expression is not in common currency. To my knowledge, as an MAOI expert, it has only ever been used once in the literature [69]. Ultracrepidarian (opining about things beyond one's expertise).

Furthermore, De Hert et al. misrepresent the paper by Castanheira et al. [68] which states:

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\* This reference [67] is Castanheira and Mercado.



Thus, for patients undergoing elective surgery without major psychiatric risk to stopping therapy, it would be prudent to withhold MAO inhibitors; but, for patients undergoing urgent **surgery\*** or who are psychiatrically unstable without them, it appears that MAO inhibitors can cautiously be continued, along with care to avoid or minimize sympathomimetics, anticholinergics and meperidine’.

Castanheira et al. ‘*Guidelines for the management of chronic medication in the perioperative period: systematic review and formal consensus*’, [68] give no indication whatsoever of what an ‘MAOI-safe technique’ might be (it is not a properly defined or recognised concept, but appears to refer to avoidance of pethidine — at least that is one step in the right direction!). They provide no original data, but simply (mis)cite yet another paper (which self-cites a paper by the same senior author). Such citation practices do not constitute scientific evidence (or any evidence) to support their contention. The comment ‘*care to avoid or minimize sympathomimetics, anticholinergics and meperidine*’ suggests they are woefully ill-informed (no mention of other ‘SRI’ opioids). Ultracrepidarian. And disappointing for something produced in the third millennium.

In support of their pontifications the Castanheira paper states ‘others agree’ (which hardly constitutes a scientific position or argument) and cites Mercado [70], which is a self-citation. It is reassuring to know that Dr Mercado agrees with herself.

Mercado is opining in a vague and poorly informed manner. Ultracrepidarian.

In stating ‘*Thus, for patients undergoing elective surgery without major psychiatric risk to stopping therapy*’ there is not recognition of the fact that it is unlikely that patients would be continuing such MAOI therapy, unless there was a significant risk of relapse on cessation. **These are not the kind of drugs that are taken for trivial reasons.** They provide no references or explanation for their view and evince no understanding of the pharmacological interactions that are relevant. Ultracrepidarian.

Mercado also cites Michaels [71] in support; that paper is horribly misinformed (it classifies TCP as a **reversible** MAOI — a serious and consequential error of fact) and is way out of date; Mercado cites also El-Ganzouri [34] which is 30 years out of date, but at least it does contain a little relevant original data.

**In summary: De Hert et al. (on behalf of the European Society of Anaesthesiology) do not appear to understand the pharmacology relevant to the subject and have selected inappropriate references which they have then misinterpreted or mis-cited — how inept can one get?**

**The answer, according to that splendid curmudgeon, Cecil Northcote Parkinson; have even more members on your committee.**

Same man as the eponymous Parkinson's law:

Work expands so as to fill the time available for its completion

A recent review of anaesthesia for ECT by Zafirova does not recommend cessation MAOI treatment, although it is yet another example of a review by authors who obviously do not understand ST [72]. It is enough to make one weep in despair because it is full of misconceptions and inappropriate references [73].

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\* this is a thoughtless and illogical comment because the effect of irreversible MAOIs last for many days, even several weeks. Therefore, ceasing them before ‘urgent surgery’ would be completely pointless since their pharmacological effect would remain.

Note that Mercado is the ‘senior author’ of the Castanheira et al. paper and is a general physician with no publications relevant to this subject, nor any apparent expertise in psychopharmacology. Mercado’s text contains various errors, is and is out of date, being now 15 years since publication — not the most felicitous of references to have used.

Yet more errors are evident in a somewhat more recent citation; ‘*Antidepressants and antipsychotics: anaesthetic implications*’ [74], where Rasool says:

‘MAOIs decrease the dose requirement of **thiopentone\***.’ Phenelzine decreases plasma cholinesterase concentration and prolongs the action of suxamethonium.

It is poor academic practice to make general statements, as above, about the pharmacological properties of a group of drugs. Such statements are almost inevitably going to be wrong, especially since many classes of drugs are defined as such via non-pharmacological properties.

### *Incidentally*

Incidentally, not one of these guidelines or pontifications even mention **methylene blue** (which may be used intra-operatively — e.g., in thyroid surgery). Considering how long the knowledge of MB’s MAOI potency has been in the academic space [1, 3] that reflects poor academic knowledge and thoroughness. This is a serious error, since these interactions (MB/SRI) have undoubtedly caused deaths.

These papers and guidelines have egregious errors, as evidenced by the omission of MB

Anyone who thinks my criticism of guidelines and similar documents is harsh might like to remember this example. I am in good (and distinguished) company in my cynical opinions, as was drawn to my attention by Professor Whyte who quoted John Ioannidis [75] from his recent editorial discussing the removal of Peter Gøtzsche from the Cochrane group, under unsatisfactory and controversial circumstances:

Despite valiant efforts to make them more evidence-based, guidelines, recommendations and exercise of policy power unfortunately remain among the least evidence-based activities, impregnable strongholds of expert-based insolence and eminence-based innumeracy [75].

‘**Impregnable strongholds of expert-based insolence and eminence-based innumeracy**’ — it is refreshing to see someone distinguished expressing clear and forthright opinions about such matters without equivocation and the usual pandering to propriety.

There are 1001 perceptive and acerbic quotes about committees, which may be applicable.

As Cecil Northcote Parkinson [his most well-known and eponymous quote is ‘*work expands to fill the time available*’] said; ‘*Deliberative bodies become decreasingly effective after they pass five to eight members*’. Most guidelines committees have more than eight members! But perhaps we should allow Robert Copeland the last word, ‘*To get something done a committee should consist of no more than three people, two of whom are absent*.’

None of the above papers define what they mean when they use terms like first and second generation MAOIs, neither do they even mention selegiline or rasagiline or any of the other newer drugs that are being used for Parkinson’s disease. While vigilance is always indicated, use of MAO-B inhibitors like rasagiline (Azilect) and selegiline (Eldepryl, Zelapar) does not require avoidance of medications with SRI properties or norepinephrine releasers (e.g., ephedrine). Patients who are using these medications at the recommended doses for the treatment of Parkinson’s disease should therefore not discontinue them peri-operatively.

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\* That is incorrect, and obviously is not true of all ‘MAOIs’, even if it could be true of one of them, even though the evidence they produce is weak and unreliable. Either way, it’s a trivial non-problematic effect (see below).

It hardly needs saying that the authors of these documents evince a limited understanding of ST. They come nowhere near explaining the pharmacology or rationale of these interactions, which is necessary if doctors are to learn and be enabled to practice logical and sensible medical pharmacology.

Will no-one protect us from the self-appointed experts who sit on these guideline committees? It is high time such people were held to account for the guidelines and pontifications that they pretentiously and portentously promulgate.

## Myth and misinformation cost lives

These examples help readers to understand that the epithet of *caveat lector* must constantly be borne in mind, because myth, misinformation, and ultracrepidarianism cost lives. We are deep into the territory in of unsubstantiated rumour and myth, carelessly repeated, by supposed experts, *ad nauseam*.

These patterns of iterations of misquotation and misunderstanding by authors who seem to be wanting in their understanding of pharmacology are now tediously and embarrassingly common in modern academic writing. No one seems to check their references, and worse still, nor do the referees.

I have lectured before about how [the standards in the medical scientific literature](#) have reached an all-time low.

A clear definite conclusion regarding case reports is that they have caused misunderstanding and confusion and been of slight help in elucidating matters related to ST.

**In summary: we have a lamentable and dispiriting procession of poor scholarship, misunderstanding, misinformation, misinterpretation, mistakes, and misattribution. It reflects little credit on academia and much of it represents the blind leading the blind. Blindly.**

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