The 'treatment-resistant' smoker

Strategies to help smokers who are resistant to treatment include intensive combination pharmacotherapies and the use of nicotine replacement therapy to reduce the harm caused by smoking.

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It often amazes healthcare professionals that people with asthma continue to smoke given the widespread information available to them detailing the harmful effects smoking has on health, and on theirs in particular. Recent National Health Surveys have shown that in Australia about 26% of people with current asthma were smokers, which is considerably more than the national average of 17%.[1,2]

Why do people with asthma and others that we see in clinical practice with respiratory, cardiac, vascular and other sequelae from their smoking carry on smoking despite our strong recommendations to them to quit? Why do they continue when they have heard the message to quit 'a million times'? Are these smokers impervious to quit campaigns? Is there something particular about this group, the 'sick smokers'?

There is some evidence that some smokers are in denial about the consequences to them, that they hold a self-exempting belief ('it won't happen to me').[3] However, the group of 'sick smokers' already face the consequences of their smoking. Are they not serious about stopping smoking and only make half-hearted quit attempts? Are they more dependent on smoking than other smokers, and less likely to respond to behavioural or pharmacotherapies? While most smokers want to quit, it is probable that there is a hierarchy of quitting where the more dependent a smoker is, the more resistant they may be to treatment and the more intensive the intervention may need to be in order to effect a positive outcome.[4] Table 1 lists features of smoking that indicate an individual needs more help in quitting.

According to the DSM-IV, the definition of a drug addiction incorporates the fact that 'the substance use is continued despite knowledge

IN SUMMARY

- **There is a hierarchy of strategies available to help tobacco smokers that begins with permanent cessation and provides safe options for those people unable to achieve this.**
- **Some smokers respond well to some pharmacotherapies and others do not. Every smoking cessation pharmacotherapy for which there is substantiated evidence should be tried – a patient just might strike the most suitable one for them.**
- **The harm reduction strategy of reducing smoking by the use of nicotine replacement therapy (NRT) should be considered for treatment-resistant smokers. It is less harmful for a person to smoke while using NRT than it is to smoke without it.**
- **There is good evidence that it is never too late to quit smoking. Reducing smoking by the transient use of NRT may be a gateway to quitting for treatment-resistant smokers.**
- **Algorithms are provided for smoking cessation therapy options and the use of combination NRT in treatment-resistant smokers.**

Table 1. Who needs extra help to quit?

Features indicating more help needed

- Smoking within $^1/_2$ hour of waking
- Multiple short previous attempts to quit
- Smoking or symptoms of nicotine withdrawal while using NRT

Features of little relevance in quitting ability

- Number of cigarettes smoked
- History of smoking
- Brand or strength of cigarette

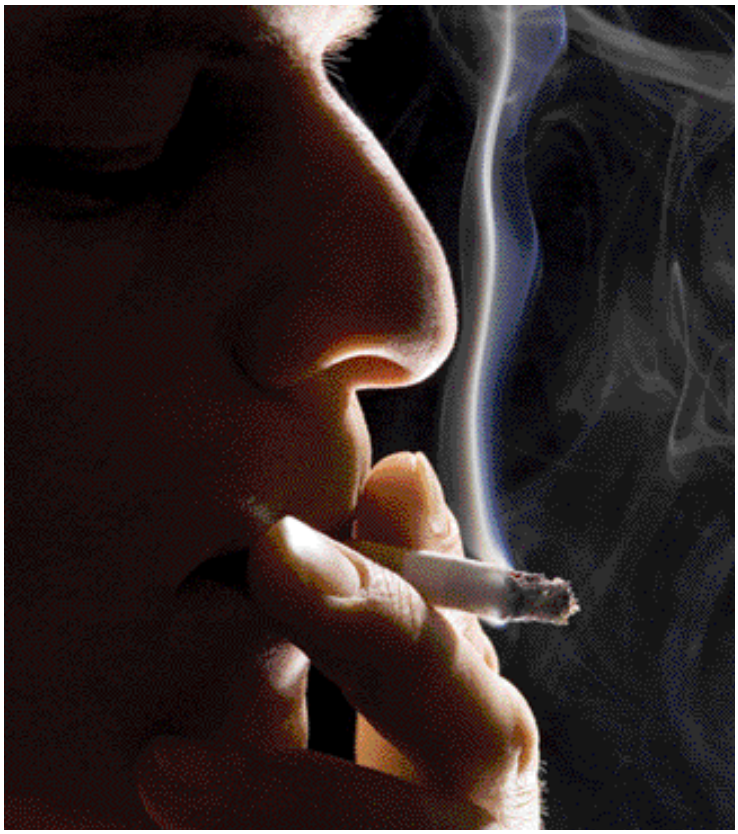
of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance'.[5] Thus the likelihood that these 'sick smokers' are dependent is very high. If they are, then how can we help them? Can we expect spontaneous, unaided quitting in this group? The DSM-IV tells us that this type of tobacco addict cannot quit in this way: 'there is a persistent desire or unsuccessful efforts to cut down or control substance use'.[5] Is the prevalence of smoking in Australia now low enough that those who could quit have quit, leaving a group of hard-core resistant tobacco dependents?

It is immediately apparent that the resistant smoker may have issues other than their own physical health regarding their smoking. Smoking in Australia today is associated with poorer mental health.[6,7] Depression and/or a history of depression is a comorbidity extraordinarily common in active smokers,[8-12] and has been strongly linked in smokers with chronic respiratory disease and heart disease.[13,14] Smoking is also linked to socioeconomic status, lower income and poorer education being strongly linked with current smoking.[15]

Nicotine is a formidable antidepressant,[16-18] and self-medicating with it is a feature of smoking. Depression can be measured by the amount of smoking and it is current best practice to assess depression in some format in all chronic relapsing smokers. Even a simple one-line question such as 'Do you feel depressed?' might be a pointer towards risk of relapsing during a quit attempt.[19] A recent Cochrane review acknowledges that 'nicotine may have antidepressant effects that maintain smoking, and antidepressants may substitute for this effect'.[20] Depression may be a feature of a smoker's dependency but, with the exception of bupropion and the anxiolytic nortriptyline, unfortunately there is no evidence to date that currently available antidepressants generally help in smoking cessation.[20] The efficacies of bupropion and nortriptyline are equal to those of nicotine replacement therapy (NRT);[20] bupropion (Clorprax, Prexaton, Zyban SR) has been indicated for smoking cessation but nortriptyline has not.

What then can be done for these 'resistant' or 'harder target' smokers?

The treatment-resistant smoker



Clinical judgement and psychological tact are important in helping smokers quit. Patients who are persistent smokers can be helped towards better health using the strategies of combining therapies or reducing harm. Nicotine replacement therapy is but one of the available therapies.

PHOTOLIBRARY

Table 2. Assessing risk factors for smoking cessation relapse

Time to first cigarette (number and type irrelevant)
- Indicates tobacco dependence, predicts relapse
- Smoking with 5 minutes of waking indicates severe dependence

Psychiatric history
- History of depressive episodes implies need to assess depression during a quit attempt
- Alcohol abuse strongly predicts relapse

Quitting history
- Poor history of previous quit attempts implies need for more intense intervention

Family history
- Strong heritability in dependent smokers

Environmental contexts
- Proximal smoking by others strongly influences relapse

Dealing with the 'been there, done that' patient

We do not know why some smokers respond well to some smoking cessation pharmacotherapies and others do not. Assessing a smoker for risk factors for relapsing will greatly improve your ability to help them on the pathway to quitting (Table 2).

All smoking cessation pharmacotherapies head-to-head have been successful in helping smokers quit. Behavioural interventions have been a great deal less successful. The algorithm on smoking cessation therapies on page 21 shows possible therapies for smokers who are resistant to quit attempts or even to quitting at all. There are no readily available markers, biological or psychosocial, that help us determine who will do better with what sort of treatment. However, pharmacogenetics are increasingly showing promise of polymorphisms that may influence treatment outcomes in both NRT and bupropion therapy. Suffice it to say, every pharmacotherapy for which there is substantiated evidence should be tried – a patient just might strike the most suitable one for them. If one treatment, for example bupropion, is not 'successful' in curtailing tobacco withdrawals in a patient then this does not imply that other treatments may be equally unsatisfactory. Also, a patient doing extremely well on a particular treatment does not imply that he or she was better motivated.

It has been hypothesised that patients with 'rogue' or mutant neuronal nicotine receptor subtypes are poor responders to conventional pharmacotherapies. As newer pharmacotherapies become available that target these receptors, a patient may just 'luck-in' and respond to these agents; hence we recommend that smokers continue to try any evidence-based new product that becomes available.

In Australia, NRT has had the broadest usage of all pharmacotherapies to date for smoking cessation, primarily because it is now available without prescription. Our long experience with NRT has led us to develop an algorithm for the use, either alone or in combination, of the various forms of NRT (transdermal patches, chewing gums, lozenges, inhalers and sublingual tablets) in treatment-resistant smokers (see page 22).[21] Although the algorithm is self-explanatory, some of the content may be counterintuitive and 'off-label,' but we are finding that more and more patients are requiring higher doses of nicotine as 'replacement' to effect successful outcomes. We have also found that these intensive interventions are both safe and effective.

In other countries where antismoking campaigns have been similarly strong, more intensive combination treatments have also been devised to target this growing resistant group. Steinberg and colleagues in New Jersey have shown that the use of combinations of NRT with other pharmacotherapies for longer durations have shown excellent outcomes.[22] Specialists in smoking cessation around the world are increasingly taking up the slogan, 'More better, longer better', regarding NRT.

Dealing with the 'too late to quit' patient

Psychologically, it is advisable to avoid mentioning the 'Quit or you'll die' black and white dogma in smokers who consider it is too late to quit smoking. They have invariably heard this before (probably from you). Also, some patients may be distressed by this 'threat', and this may lead to a more anxious smoker. There is good evidence that it is never too late to quit. Every single smoker, irrespective of age and history of smoking, can at least improve their oxygen carrying capacity, notwithstanding the potential improvement of respiratory and vascular functions.

Achieving cessation in this group of smokers may require the delicate politics of easing into quitting – a softer approach. Try describing and prescribing the transient use of NRT to reduce the number of cigarettes smoked. We know that 25% of Australians smoke while using NRT, and that when smoking while using NRT their nicotine intake is suppressed and the intakes of particulate matter and gas are also reduced.[23,24] It is, therefore, less harmful for a person to smoke while using NRT than it is to smoke without it. Reducing smoking in this manner may be a gateway to quitting.[25] The fourth pillar of the WHO Framework Convention on Tobacco Control (to which Australia is a signatory) is 'harm reduction and the international human right to health'.[26]

Temporary abstinence using NRT

Using NRT to provide temporary abstinence is a strategy commonly used by

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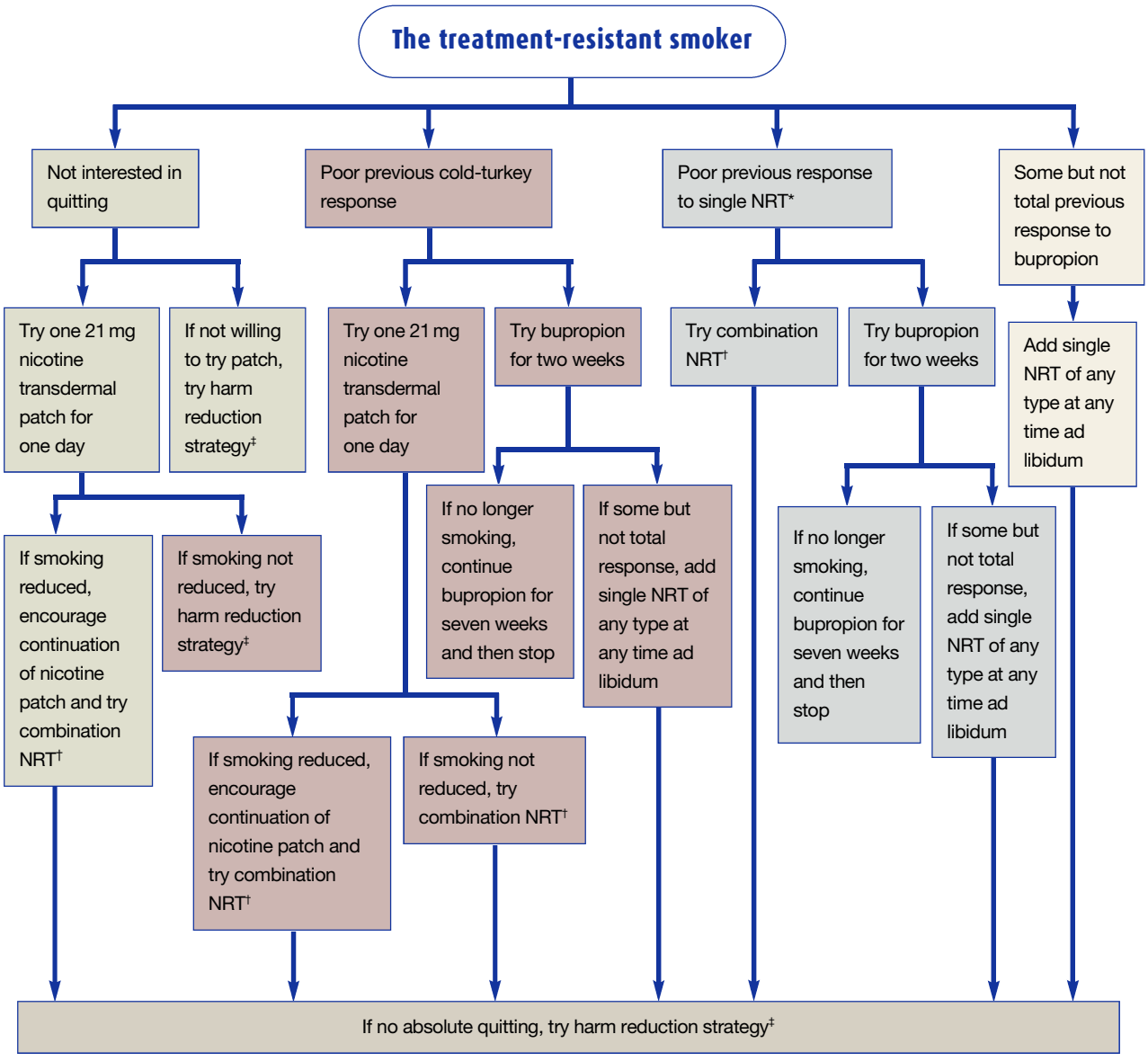
Smoking cessation strategies for the treatment-resistant smoker



* NRT = nicotine replacement therapy.
† Combination NRT = transdermal nicotine patch plus nicotine gum, lozenge, inhaler or sublingual tablet.
‡ Harm reduction strategy = alternating NRT with smoking to reduce number of cigarettes smoked or achieve temporary abstinence.

Note contraindications and that new drugs will be available soon.

smokers in situations where they are unable to smoke, such as during smoke-free flights. This is safe and should be encouraged as harm reduction. The British Group ASH (Action on Smoking and Health) advocate a cutting down to quit regimen that involves daily alternating smoking a cigarette with any form of NRT. The regimen, called NARS (Nicotine Assisted Reduction to Stop), has shown good unintentional long-term quitting rates.[27]

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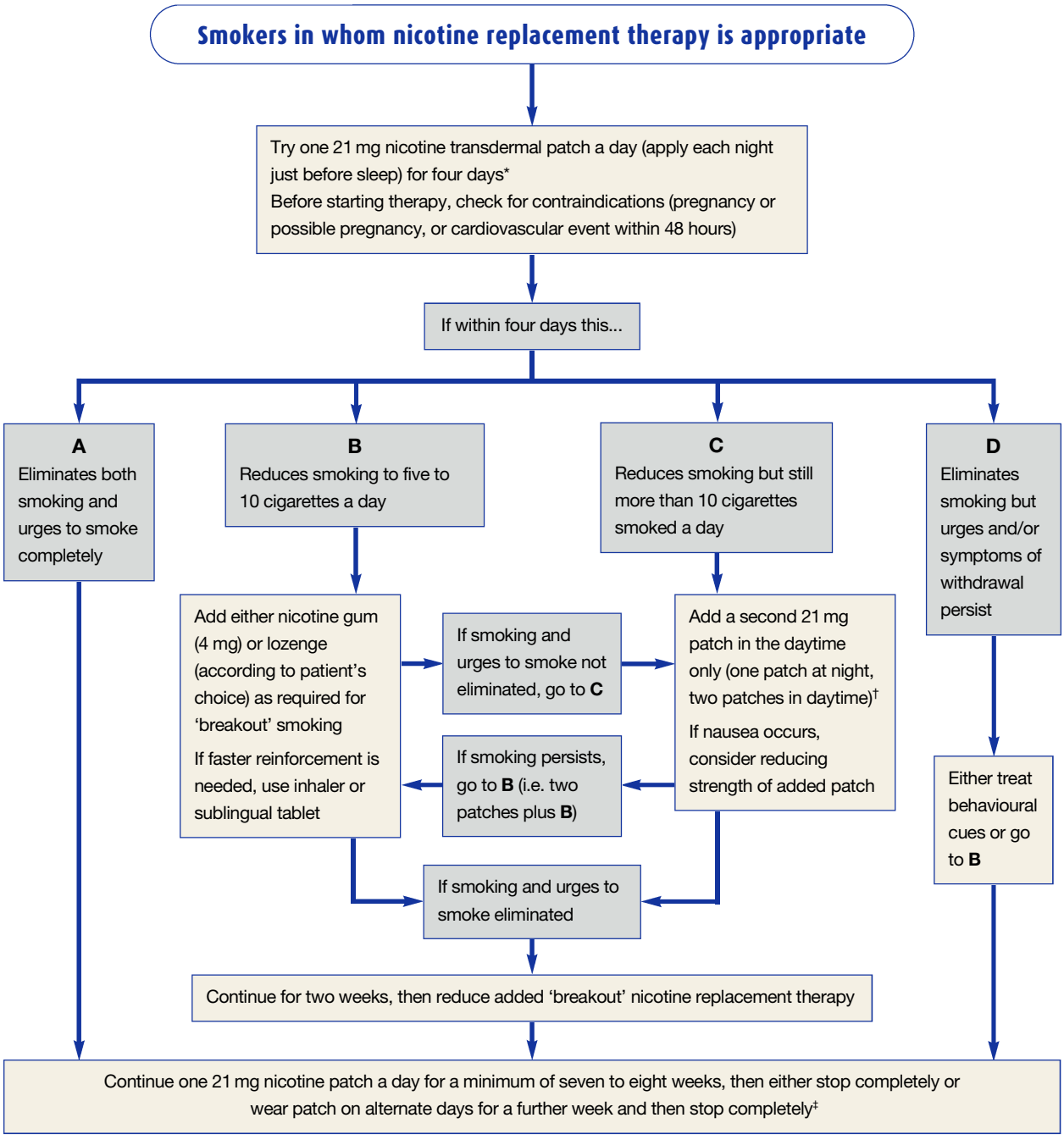
Bittoun combination nicotine replacement therapy algorithm



* Applying patch before sleep allows the slow rise of nicotine overnight, strongly reducing the 'urge' for the first cigarette of the day.
† No evidence in the literature or in the author's experience of toxicity.
‡ No evidence in the literature for weaning (or reduction) of patch strengths.

Source: Bittoun R. A combination nicotine replacement therapy (NRT) algorithm for hard-to-treat smokers. *J Smoking Cessation* 2006; 1: 3-6.

Temporary abstinence using NRT has the following benefits:

- relief of cravings and other nicotine withdrawal symptoms
- reduced cigarette consumption and prevention of compensatory smoking
- smokers may learn that they can manage without tobacco for several hours, which may increase their motivation to quit completely.

Using NRT to provide temporary abstinence is an appropriate strategy for attempting smoking cessation in psychiatric patients, a group in whom the prevalence of smoking remains high in Australia.

Indigenous smokers

The peculiarity of very high rates of smoking among indigenous peoples is not particular to Australia alone. It represents a typical confounding dilemma of smoking in lower socioeconomic, poorly educated groups. Indigenous smokers constitute a combination of all types of smokers ranging from the less dependent to the highly dependent, much more like the general population of Australia two decades ago than the current highly dependent non-Indigenous population. Identification, education and brief intervention are just some of the basic strategies aimed at this group, and culturally appropriate strategies such as these will, in time, reduce smoking rates in this group as well.

It should be noted that there are racial and ethnic (and also gender) differences in nicotine metabolism through the CYP2A6 gene, and that these differences affect ability to quit smoking.[28] These variants have not been studied in Australian populations.

Conclusion

As with all medical conditions, clinical judgement and psychological tact are important in helping smokers quit. The strategies of combining therapies or reducing harm are important avenues in these matters and can be pursued by clinicians keen to help their persistent smoking patients towards better health. MT

A list of references is available on request to the editorial office.

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