Drug only helps slightly to keep shift workers awake at night

David Spurgeon *Quebec*

Treatment with modafinil, recently approved by the US Food and Drug Administration for treatment of the extreme sleepiness of patients with shift work sleep disorder, reduced this symptom and produced a small but significant improvement in performance in a randomised placebo controlled study (*New England Journal of Medicine* 2005;353:476-86). Yet measured levels of performance were much lower than what such patients need to function at a normal level, and more effective therapies are required, the authors conclude.

Members of the US Modafinil in Shift Work Sleep Disorder Study Group did the study between December 2001 and September 2002. Of 4533 shift workers pre-screened, 204 received the drug and 153 completed the study.

As many as 20% of workers in industrialised nations are shift workers and as many as 10% of these have insomnia or exces-

sive sleepiness and are at increased risk from peptic ulcers, coronary heart disease, insulin resistance, depression, sleepiness related unintentional injury, and curtailed social and family activities. Many of these people work in health care and the transportation industries.

The study found that treatment with the drug resulted in a modest improvement from baseline in what is called night time sleep latency—the interval between the time a person attempts to fall asleep and the onset of sleep. The test was done as an objective measure of sleep tendency during the night, when these patients normally work. Mean sleep latency was longer at night in the group taking modafinil—by 1.7 (standard error of the mean 0.4) minutes $\pm$ 0.3 (0.3) minutes ($P=0.002$)—so their sleep tendency during their night work hours was reduced. Patients receiving modafinil also had reduced frequency and duration of attention lapse dur-

ing night time performance testing on the Psychomotor Vigilance Test (change from baseline, a reduction in lapse frequency of 2.6 compared with an increase of 3.8, $P<0.001$). Proportionally fewer patients reported having had or nearly having had unintentional injuries while commuting home (29% ν 54%; $P<0.001$). Patients treated with modafinil continued to have excess sleepiness and impaired performance at night, however.

An editorial accompanying the article said that modafinil may yet be shown to be an effec-

tive and safe adjunct to comprehensive strategies for shift work sleep disorder (p 519).

Brian Murray, a neurologist specialising in sleep medicine at the University of Toronto and Sunnybrook and Women's College Hospital, commented that the dose used in the study (200 mg) is sometimes doubled in treating narcolepsy or other disorders "so it's possible they could find more of an effect with a larger dose or other strategies. [But] we don't think at this point that the medications can replace the need for sleep." □

As many as 10% of shift workers in industrialised nations have insomnia or excessive sleepiness

Avian flu pandemic could be brought under control in three weeks

Jane Parry *Hong Kong*

An avian influenza pandemic could be prevented but only with swift and targeted intervention at an early stage, say two research papers published online on 3 August in the journals *Nature* and *Science* (www.nature.com, doi: 10.1038/nature04017 and www.sciencemag.org, doi: 10.1126/science.1115717).

Both studies assumed that each person infected would transmit the disease to fewer than two people. Although H5N1 avian flu has very low virulence, no one can predict the reproduction number of any future flu pandemic strain as it could recombine with an existing highly virulent human flu strain. Assuming a reproduction number of less than two, however, both models predict that an outbreak could be brought under control in the first three weeks.

The studies used computer simulations to assess the effectiveness of early intervention in pandemic outbreaks in Thailand, which was chosen for its rich supply of research on social networks rather than because of its likelihood as the origin for an outbreak.

The two computer simulations are part of the Models of Infectious Disease Agent Study research network, which is funded by the US National Institute of General Medical Sciences. "These new models illustrate how the fundamental features of infectious disease spread and can be captured to predict possible outcomes and the potential impact of interventions," said Jeremy Berg, director of the institute.

The studies both evaluated the potential effectiveness of targeted

mass prophylaxis with antiviral drugs and quarantine measures. Research led by Neil Ferguson, professor of mathematical biology at Imperial College, London, and lead author of the paper published in *Nature*, modelled the potential spread of avian flu across the whole population of 85 million people and concluded that if the basic reproduction number of the virus was below 1.8, geographically targeted prophylaxis and social distancing could bring an outbreak under control, and that a stockpile of three million doses of antiviral drugs would be sufficient.

"Policy effectiveness depends critically on how quickly clinical cases are diagnosed and the speed with which antiviral drugs can be distributed," he wrote.

In the paper published in *Science*, Ira Longini, a biostatistician at the Rollins School of Public Health, Emory University, Atlanta, modelled an outbreak in Thailand's Nang Rong region with a population of 500 000 and estimated that, with a reproductive number below 1.6, an

antiviral stockpile of 100 000 to 1 million doses would be sufficient. "If prevaccination occurs, then targeted antiviral prophylaxis could be effective for containing strains with a reproductive number as high as 2.1," he wrote.

The World Health Organization welcomed the research papers and highlighted the need to work with countries currently affected by the outbreak of H5N1 avian flu. "The real question is how do we strengthen surveillance and reporting so that the very brief window outlined in these reports can be utilised? We would work with countries where there have been outbreaks of avian influenza to strengthen their surveillance systems," said Dick Thompson, WHO's spokesman in Geneva.

To date, WHO has only 120 000 doses stockpiled. Roche, the manufacturer of the antiviral drug Tamiflu, announced on 3 August that it is in discussions with WHO to donate a substantial amount of the drug to the organisation. □