

score as well as on the apathy, depression, and anxiety items of the neuropsychiatric inventory.<sup>2</sup> However, when the same drug and outcome were used, no such benefit occurred for patients at a similar severity of disease living in a nursing home setting.<sup>3</sup> Is this difference related to an observer bias, since behavioural problems in dementia are best assessed by interviewing informants who know the patient well—for example, are family members better than professional caregivers at detecting behavioural changes?<sup>4</sup> This is not an issue in Ballard et al's study since all treated patients lived in institutions, and recent data showed good correlation between informant rating and direct observation of behaviours.<sup>5</sup>

Was it appropriate to target agitation in this study? Clearly yes, since agitation is one of the behaviours most commonly related to severity in dementia of various causes and has a marked impact on caregivers,<sup>6</sup> and because uncertainty exists about the best management of agitation, pharmacological or otherwise.<sup>7</sup>

Does the publication by Ballard et al mean that rivastigmine and quetiapine should be avoided in dementia? Evidence from a recently published randomised controlled trial shows that rivastigmine is useful and well tolerated in dementia associated with Parkinson's disease,<sup>8</sup> and in an open label trial quetiapine has been shown to improve psychotic symptoms and cognition in this condition.<sup>9</sup> The evidence for efficacy of rivastigmine and other cholinesterase inhibitors in mild to moderate Alzheimer's disease is established, even by the current report from the National Institute for Clinical Excellence.<sup>10</sup> The issue is whether they are worth their costs from society's point of view.

From a clinical perspective, cholinesterase inhibitors are helpful in the management of many of the symptoms associated with dementia for individual patients. The art of treatment is to use the right drug for the right symptoms at the proper stage of disease,

starting low and going slow. Perhaps clear stopping rules for drugs used in dementia based on evidence from randomised controlled trials and taking into account individual patients' responses to treatment will resolve the current debate about drugs for Alzheimer's disease and related dementias. Ballard et al have added useful information to the body of evidence from randomised controlled trials.

Serge Gauthier *professor of psychiatry, neurology and neurosurgery, and medicine*

McGill Center for Studies in Aging, 6825 LaSalle Blvd, Verdun (Montréal), Québec, Canada H4H 1R3 (Serge.gauthier@mcgill.ca)

Competing interests: SG has accepted honorariums for lectures and is on the scientific advisory board of most companies doing research in dementia including Pfizer, Novartis, Janssen-Cilag, Neurochem, Lundbeck, Merz, Roche, Lilly.

- 1 Ballard C, Margallo-Lana M, Juszcak E, Douglas S, Swann A, Thomas A, et al. Quetiapine and rivastigmine and cognitive decline in Alzheimer's disease: randomised double blind placebo controlled trial. *BMJ* 2005; 330:874-7.
- 2 Gauthier S, Feldman H, Hecker J, Vellas B, Ames D, Subbiah P, et al. Efficacy of donepezil on behavioral symptoms in patients with moderate to severe Alzheimer's disease. *Int Psychogeriatrics* 2002;14:389-404.
- 3 Tariot PN, Cummings JL, Katz IR, Mintzer J, Perdomo CA, Schwam EM, et al. A randomized, double-blind, placebo-controlled study of the efficacy and safety of donepezil in patients with Alzheimer's disease in the nursing home setting. *J Am Geriatr Soc* 2001;49:1590-9.
- 4 Aalten P, de Vugt ME, Lousberg R, Korten E, Jaspers N, Senden B, et al. Behavior problems in dementia: as factor analysis of the neuropsychiatric inventory. *Dement Geriatr Cogn Disord* 2003;15:99-105.
- 5 Cohen-Mansfield J, Libin A. Assessment of agitation in elderly patients with dementia: correlations between informant rating and direct observation. *Int J Geriatr Psychiatry* 2004;19:881-91.
- 6 Senanarong V, Cummings JL, Fairbanks L, Mega M, Masterman DM, O'Connor SM, et al. Agitation in Alzheimer's disease is a manifestation of frontal lobe dysfunction. *Dement Geriatr Cogn Disord* 2004;17:14-20.
- 7 Profenno LA, Tariot PN. Pharmacologic management of agitation in Alzheimer's disease. *Dement Geriatr Cogn Disord* 2004;17:65-77.
- 8 Emre M, Aarsland D, Albanese A, Byrne EJ, Deuschl G, De Deyn PP, et al. Rivastigmine for dementia associated with Parkinson's disease. *N Engl J Med* 2004;351:2509-18.
- 9 Juncos JL, Roberts VJ, Evatt ML, Jewart RD, Wood CD, Potter LS, et al. Quetiapine improves psychotic symptoms and cognition in Parkinson's disease. *Movement Disorders* 2003;19:29-35.
- 10 National Institute for Health and Clinical Excellence (NICE). *Appraisal consultation document: Alzheimer's disease—donepezil, rivastigmine, galantamine and memantine (review)*. www.nice.org.uk/page.aspx?o=245912 (accessed 11 Apr 2005).

## Human and veterinary medicine

*Theme issue will look at ways in which doctors and vets can work together*

Traditionally, human medicine and veterinary medicine tend to be viewed separately. Doctors treat people, and vets look after animals. Of course differences exist between the two types of patients and options for treatment. Euthanasia, for example, tends not to be looked on favourably in humans, whereas in veterinary medicine it might be the best approach. Similarly, culling infected individuals or those suspected of being infected is not an option for controlling an outbreak of infectious disease in humans but may well be so in animals. Doctors usually have the advantage over vets in that they can talk to their patients; for vets, life would be so much easier if their patients could talk.

Despite the differences between the two professions they have common interests and share challenges. Vets and doctors are having to work together more and more—for example, over fears that avian

influenza could be the harbinger of a human pandemic<sup>1</sup> and over control of food borne zoonoses.

Without adequate safeguards, diseases of people and animals can now move more quickly around the world. Controls and contingency plans must be drawn up in tandem, whether the disease threat is natural, as with SARS, or caused by humans, as in a potential bio-terrorist attack. Antimicrobial resistance also presents challenges to doctors and vets alike.

With increasing urbanisation we can easily forget the extent to which people depend on animals. In the developing world many people rely on animals for food and transport (whether of people or goods)—and the health of those animals can mean the difference between life and death. Closer to home, livestock are important economically but animals are also a source of companionship. Half of all households in the United Kingdom own a pet (www.pfina.com/public/

*BMJ* 2005;330:858-9



A pet and bird shop owner in Taiwan gets vaccination for avian flu

petownership\_stats.htm), and many pets are just as important as a family member or friend, sometimes more; for them, the same level of health care is expected. Cost of treatment and subsequent quality of life is an issue for the care of animals and humans.

Doctors may not fully appreciate the importance of the relationship between owners and their animals. This may be relevant when, for example, advising immunocompromised patients of any risk from their pets, or considering the implications of taking an

elderly pet owner into care in an environment where animals are banned. When advising patients about owning pets, doctors now have to weigh up the risks of developing allergies.<sup>2</sup>

The *BMJ* and the *Veterinary Record* plan simultaneous publication of theme issues exploring how the two professions can collaborate for mutual benefit. We would like to cover topics such as the investigation and control of infectious diseases; zoonoses; medical and veterinary education; professional regulation; and issues related to pet ownership. The theme issues, to be published in November 2005, will be a mix of papers, debate pieces, editorials, and reviews. We are particularly interested in original research relevant to both disciplines. The deadline for submissions of original research is 30 May 2005.

Martin Alder *editor Veterinary Record*

London W1G 9NQ  
(editorial@bva-edit.co.uk)

Graham Easton *assistant editor BMJ*

London WC1H 9JR  
(geaston@bmj.com)

Competing interests: None declared.

- 1 Parry J. Officials report first Cambodian case of avian flu. *BMJ* 2005; 330:273.
- 2 Ownby DR, Johnson CC, Peterson EL. Exposure to dogs and cats in the first year of life and risk of allergic sensitisation at 6 to 7 years of age. *JAMA* 2002;288:963-72.

## Treatment of postmenopausal osteoporosis

*Has improved owing to the availability of many drugs that prevent fractures*

Osteoporosis is characterised by bone fragility due to low bone mass and modifications of the internal bone structure, with alterations of its microarchitecture. Of various fragility fractures that represent the major complication of the disease, vertebral and hip fractures are associated with pronounced morbidity and increased mortality.<sup>1</sup> Several agents have been used for many years to prevent or treat osteoporosis. However, methodologically sound randomised controlled trials assessing their efficacy against fractures at the axial (vertebral) and appendicular (non-vertebral) sites have become available only in the last 15 years. Most of these trials were recently summarised in systematic reviews.<sup>1-3</sup>

Bisphosphonates are potent inhibitors of resorption and represent 70% of the worldwide market for drugs used to treat osteoporosis. Alendronate and risedronate were both investigated in well designed, randomised controlled trials, where their ability to reduce vertebral, non-vertebral, and hip fractures was shown—the latter mainly in women with severe osteoporosis (low bone density and prevalent fractures).<sup>2-6</sup> Both are widely available as daily or weekly oral formulations. No head to head comparisons between alendronate and risedronate have been made. Results of published randomised controlled trials or meta-analysis do not provide compelling evidence for statistically significant differences in their efficacy or

safety. Both compare favourably with etidronate, the first bisphosphonate developed, which in the absence of an unequivocal effect on non-vertebral fractures seems outdated. Ibandronate reduces vertebral fractures, but its effect on non-vertebral fractures has so far only been shown in a post hoc analysis performed on a high risk subgroup.<sup>7</sup>

Selective oestrogen receptor modulators act as oestrogen agonists or antagonists depending on the target tissue. Raloxifene reduces vertebral fractures across different degrees of skeletal fragility, ranging from low bone density to severe osteoporosis,<sup>8</sup> but little evidence of efficacy in preventing non-vertebral fractures is currently available.<sup>3 4 8</sup> Major non-skeletal benefits have been documented (in breast cancer) or are under investigation (cardiovascular disease) and should be considered when assessing the overall risk to benefit ratio of selective oestrogen receptor modulators.

The efficacy of hormone replacement therapy against fractures has been derived mainly from case-control and cohort studies.<sup>2</sup> Although not conducted in women included on the basis of an increased risk of skeletal fragility, the women's health initiative trial,<sup>9</sup> a randomised controlled trial designed to assess the major health benefits and risks of the most commonly used hormone replacement therapy in the United States, reported a significant reduction in verte-