Postmortem diagnosis of testicular cancer (letter)

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Published in:
LANCET

doubled when we changed rinses for gel rubs in care units. We did not change to gels for surgical hand disinfection but kept a hand rinse.

Third, Kramer and colleagues put the gel effect before the composition effect. However, the type and number of associated alcohols are perhaps more important than the carrier formulation.

In future gels, which are becoming increasingly fluid and easy to apply, may become as efficient as rinses and as well tolerated as old gels.

Another important issue is efficacy of hand rubs on viruses, which is awaiting European testing. Although, however, the efficacy of the product should be a criterion, if our target is the reduction of nosocomial infections, tolerance and acceptability by health-care workers are also important.

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Authors' reply

Sir—Alcohol-based hand rubs approved for use, whether gels or rinses, reduce bacterial counts on health-care workers' hands more than do antimicrobial soaps or detergents.[1] Rubs are fast-acting, and cause less skin irritation and dryness. We fully agree with John Boyce and colleagues, Peter Hoffman and colleagues, and Dan Diekema that more clinical data are necessary to assess the effectiveness of hand gels. To clarify the issues under discussion, the ultimate goal of hand hygiene is to reduce cross-transmission and infection rates and two main features contribute—adherence to recommendations and agent efficacy.

We have shown previously that factors that determine adherence are multiple,[1,2] but one is health-care workers' acceptance of agents. The concern that rinses might be less accepted than gels is legitimate. Nevertheless, no data yet suggest that adherence is higher when using gels than when using rinses, although the impact on attitudes of an excessively market-driven, health-care industry is clear.[3] Moreover, in one study, fewer than half of health-care workers were satisfied with a newly introduced gel, and more than half found it uncomfortable to use, which threatened adherence (table).[4] To our knowledge, the only reported experience of successful and sustained hand hygiene promotion with a parallel drop in nosocomial infection used a rinse.[2]

We recognise that despite the availability of standard laboratory tests and, especially EN 1500, in no clinical trial has the extent to which hand microbial counts need to be reduced to decrease cross-transmission been established. Whether the difference in log reduction between rinses and gels is clinically important remains unknown. However, if we assume an identical degree of acceptance, the agent with greater efficacy should be favoured until more data from controlled clinical trials are available.

We believe our data raise concern that should stimulate researchers and manufacturers to invest in the development of agents with maximum antimicrobial efficacy, tolerance, and acceptance. Increase of the ethanol content of gels is one step towards improved efficacy. To end the controversy, we invite the scientific community to collaborate to decide international norms for the testing of hand rubs, especially in hospitals, and ideally to assess the dynamics of hand contamination.[5]

In health-care institutions where hand washing with medicated soap is still used, we strongly recommend a change to use of alcohol-based hand rubs, whether rinses or gels, whichever produces the best adherence. In hospitals where adherence has improved and infection rates decreased because of rinse use,[2] we are tempted to say don't change a winning team.

Adherence to hand hygiene is a complex behavioural issue; successful promotion strategies should use multiple methods.[1,2,4] Efficacy, acceptability, and good skin tolerance of hand rubs are important but are only one brick in the wall of adherence.

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	Responses (n=62)		
	Agree	Neutral	Disagree
Item			
Overall, I was satisfied with the hand gel	45%	34%	21%
The gel helped to improve my hand hygiene adherence	42%	23%	35%
The gel was conveniently located	57%	29%	14%
The gel caused less skin irritation than did handwashing	42%	29%	29%
The gel caused a sticky, uncomfortable feeling	53%	24%	23%

Adapted with permission from reference 4.

Healthcare workers' satisfaction and perceptions towards a recently introduced hand gel

Postmortem diagnosis of testicular cancer

Sir—H De Boer and colleagues (May 11, p 1666)[1] describe an adolescent who died 4 days after a car accident. Postmortem diagnosis revealed metastatic testicular cancer. In their accompanying May 11 Commentary, Jeremy Steel and R Timothy Oliver[2] discuss the perils of very late presentation of testicular cancer.

De Boer and colleagues and Steel and Oliver offer several explanations for late presentation. We have started a study on reasons for delay in testicular cancer. On the basis of reports on delay and disease-specific characteristics of testicular cancer, we developed a questionnaire to assess possible characteristics of patients' and doctors' delay.

25 testicular-cancer patients, median age 23 (range 16–43) years, have so far completed the

questionnaire. Median time between awareness of an unexplained symptom and seeking medical consultation was 35 (1–365) days. 12 patients knew of testicular cancer as a disease before diagnosis, but knowledge was not significantly correlated with delay. 21 patients mentioned a change in the testicle as a first symptom, three reported other symptoms (back pain, gynaecomasty) before they discovered a change in the testicle, and one never noted a change in his testicle.

Of the 24 patients who reported an abnormal testicle, only four thought of cancer as a possibility, ten had no explanation, and ten attributed their symptoms to another illness. Six patients expressed embarrassment about the abnormality in the testicle. Embarrassment was strongly related to patients' delay. All 24 patients consulted their family physicians about the abnormality in the testicle and ten were immediately referred for further examination. The remaining 14 patients were initially misdiagnosed, which led to delays of up to 112 days, although the median doctor delay was only 12 days.

The median delay for patients and doctors is limited, but the range is large. An unanticipated result was that interpretation of symptoms was an important determinant of delay, whereas patients' knowledge of testicular cancer seemed unimportant. The low prevalence of testicular cancer and vagueness of the symptoms augment the chances for misinterpretation. Delay in diagnosis of the disease may lead to more extensive disease, combined methods of treatment, and a reduction in disease-free survival.[3] Therefore, family physicians should always bear testicular cancer in mind when adolescents and young men present with inguinal or scrotal complaints.

We agree with Steele and Oliver, that continuous education is needed for patients as well as medical professionals to alert them to the fact that testicular abnormalities may constitute medical emergencies.

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1 de Boer HD, Haerkens MH, van der Stappen SW, van Ingen G, Wobbes T. Testicular carcinoma: postmortem diagnosis after a car accident. *Lancet* 2002; **359:** 1666.
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Use of galantamine to treat vascular dementia

Sir—The masking of treatment assignment prevents bias at several stages of randomised controlled trials. Doubts on this pivotal trial feature are legitimate for Timo Erkinjuntti and colleagues' study (April 13, p 1283)[1] of galantamine in dementia.

In obtaining consent for randomisation, patients and caregivers are informed of potential adverse effects of the drug under study. As with all cholinesterase inhibitors, galantamine has notable cholinomimetic side-effects. The frequency of nausea (24%) and vomiting (13%) reported in the galantamine group was substantially higher than that in the placebo group (7% and 6%, respectively). Given the high frequency of gastrointestinal side-effects and the knowledge of its hidden meaning in physicians, patients, and caregivers, it is highly unlikely that the masking of treatment was maintained throughout the entire study period for all patients.

Erkinjuntti and colleagues do not address the issue of unintentional loss of blinding similar to other studies on cholinesterase inhibitors, blinding at the time of randomisation is simply stated as a matter of fact, but data are lacking that support its success rate and preservation throughout the study. The burden of proof for effective blinding, however, rests on the investigators. At the last visit, patients, caregivers, and physicians should be asked to guess what treatment was provided. If the number of correct responses does not exceed the level of chance, it is reasonable to assume that blinding was successfully maintained. If such hindsight on blinding is not provided, however, there is room to speculate that small effect sizes, such as noted by Erkinjuntti and colleagues, may be due to bias that is based on knowledge of treatment assignment in patients, caregivers, or physicians.

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1 Erkinjuntti T, Kurz A, Gauthier S, Bullock R, Lilienfeld S, Damaraju CV. Efficacy of galantamine in probable vascular dementia and Alzheimer's disease combined with cerebrovascular disease: a randomised trial. *Lancet* 2002; **359:** 1283–90.

Sir—Timo Erkinjuntti and colleagues' report on galantamine[1] will fuel the debate over whether cholinesterase inhibitors are a rational treatment choice for patients with vascular dementia. Despite evidence from preclinical and postmortem studies that the pathological changes in vascular dementia seem to be associated with cholinergic deficits, some experts remain unconvinced.

Erkinjuntti and colleagues provide convincing evidence that the acetylcholinesterase-selective inhibitor galantamine is effective in patients who have Alzheimer's disease with cerebrovascular disease (mixed dementia). However, galantamine provided no significant benefit over placebo in patients with pure vascular dementia. The researchers suggest that this lack of effect was due to the study not being powered to detect significance in the pure vascular dementia subgroup, and because there was a slow placebo decline.[1] However, the results will inevitably be interpreted by some critics to suggest that the efficacy of galantamine in mixed dementia stemmed only from the drug's effects on the Alzheimer's features of the disorder.

We challenge such interpretations and express our support for the continued study of cholinesterase inhibitors in patients with vascular dementia. Existing data provide evidence that the cholinergic hypothesis is applicable, and that cholinesterase inhibitors may provide benefits in patients who have dementia with a vascular component.

We have published data from a small study in patients with frontosubcortical vascular dementia, showing that 3–6 mg rivastigmine daily—an acetylcholinesterase inhibitor and butyrylcholinesterase—improved executive function and behaviour for 12 months, compared with baseline and a control group receiving cardioaspirin.[2] These are the two domains that characterise frontosubcortical vascular dementia. These benefits were maintained over 22 months of treatment[3] and may reflect the drug's effects on the cholinergic system, and its particular activity in frontal areas of the brain.[4] Furthermore, Kumar and colleagues,[5] in a large randomised study, showed that rivastigmine provided even greater benefits in patients with Alzheimer's disease and vascular disease than in patients with pure Alzheimer's disease. Rivastigmine was well tolerated in both studies.[2,3,5]

We agree with Erkinjuntti and colleagues that there may be a cholinergic deficit in patients with