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To Do No Good

Mrs F.W., a 57-year-old nursing home manager, presented with a polyarthritis and plantar fasciitis in association with psoriasis in 2003. She was already taking meloxicam and co-proxamol. Her ESR was 51 and rheumatoid factor was 80. She was labelled as suffering from psoriatic arthritis. Because of indigestion she was changed to celecoxib, which was ineffectve and then valdecoxib (even though it was not specifically licensed for psoriatic arthritis), which she found both tolerable and highly effective. She also continued on the co-proxamol, which she liked.

In January 2005, her GP was unwilling to prescribe co-proxamol following the CSM announcement that it was to be withdrawn. She assures us that she was not consulted by the CSM and therefore regards this as unilateral. She was then tried on co-codamol then tramadol and finally, simple paracetamol. None of these were as effective as the co-proxamol for her. She complained of more pain and was angry that she was refused the co-proxamol. She is told that there is no evidence from studies using aggregated data from large populations that co-proxamol is more effective than other analgesics. She replies that it certainly works better for her and that she was not included in any of the studies. ‘Does the only evidence that applies directly to me not count?’

Worse was to come in April, when valdecoxib was voluntarily (and unilaterally) suspended. She has since been changed to Sulindac, which is not as effective and which she cannot take continuously because of indigestion. “But I am not one of the two people in the UK who got Stevens Johnson from this and as I had been on it for 9 months I understand that my risk was even smaller”.

So, as we sit opposite Mrs F.W. (or any of hundreds of similar patients) in our clinic, we are thinking:

(1) I wonder how many doctors were in the MSD board-room when they decided to withdraw Vioxx? Perhaps there were a few accountants and lawyers who were making a commercial decision on behalf of their shareholders and they interpreted the scientific evidence in the context of the shareholders’ interest. Maybe they got it wrong!

(2) If the evidence is so precise, why have the FDA and the EMEA come to such different conclusions about the CV risks of coxibs and traditional NSAIDs?

(3) How could studies of the wrong dose of the drug in the wrong disease have caused so much trouble for this lady? Imagine the criticism if we were allowed to extrapolate wildly like that in treating patients in other circumstances!

(4) Is the Drug and Therapeutics Bulletin always right?

(5) Should not the benefit/risk ratio for drugs be considered on an individual basis, together with the patient, and in the light of relevant evidence, rather than the paternalistic (and scientifically grossly flawed) way that we are now being asked to adopt without question?

(6) If you just look at the published data without the context of real people who take drugs as they see fit, rather than as per protocol, then you can end up writing a daft editorial on management and conclude that ‘therapeutic touch’ is cost effective for OA [1].

(7) The current ranking of evidence does not take account of the size of the effect – so taping the patella or using a gel have better evidence than knee replacement!

We are most grateful to Binymin and Phillips [2] for engaging in the debate that we have wished to stimulate and providing us with the opportunity to publish this case report. Unfortunately their statement ‘Doubling the risk of myocardial infarction and stroke in order to control chronic dull ache and stiffness due to arthritis seems a logically unacceptable practice…’ is so far away from our patients’ experience that we do not feel we have enough common ground to even have an argument. Twice very little is still very little!

Potential conflict of interests. The authors treat many patients with pain from arthritis. The authors have sat on advisory boards for the drug industry.

Conflict of interest: None of us like sitting opposite patients in pain when there have been better drugs made for them.

D. J. WALKER, L. OTTEWELL, R. J. MOOTS

1 Freeman Hospital, Newcastle NE7 7DN, 1University of Liverpool, University Hospital Aintree, Longmoor Lane, Liverpool L9 7AL, UK

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Correspondence to: Dr D. J. Walker.
E-mail: david.walker@nuth.nhs.uk


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Comment on: Parotid gland biopsy compared with labial biopsy in the diagnosis of patients with primary Sjogren’s syndrome

SIR, We read with interest the report of Pijpe et al. [1] comparing parotid gland with labial biopsy in 35 patients with Sjogren’s syndrome. The authors report a diagnostic sensitivity of 78% with these methods, and a 6% incidence of permanent sensory loss with labial biopsy. In contrast to these findings, we published our experience with an office-based method of labial gland biopsy in which over 100 biopsies were performed, diagnostic sensitivity was 100%, and long-term sensory loss was 0% [2]. Our current experience is with over 350 patients in which only one individual has suffered from permanent sensory loss.

We suggest that the decision as to which biopsy be performed be based on all available techniques, and not be limited to the question of which gland (labial vs parotid) to biopsy.

The authors have declared no conflicts of interest.
Sir, We thank Dr Friedman and Dr Miller for their remarks regarding the observed 6% of long-term loss of sensibility of the lip after taking a labial biopsy for diagnostic purposes in our study [1]. According to their letter, they did not observe any long-term sensory loss after taking a labial biopsy using the technique described in their article [2]. Their technique for taking a labial biopsy consisted of an office-based method of taking labial gland biopsies applying a very small incision that even did not need suturing in all cases. Although Friedman and Miller stated in their letter that they had not observed permanent sensory loss in their study sample (118 patients), they reported two cases of long-term numbness in their paper (2%) [2]. Moreover, their paper does not provide a description of how the sensory function was evaluated. Such information is essential as judgement by an independent researcher, being not the surgeon who took the biopsies, will provide an unbiased outcome in this respect. Therefore, we feel that our data are more reliable in this respect than figures provided after judgment by the physician who performed the biopsy. Furthermore, the sensory losses of 2 or 6% as reported in their and our paper, respectively, are both on the lower end of sensory loss after labial biopsies as reported in the literature [1]. Moreover, it is unrealistic that in larger labial biopsy series no cases of permanent numbness will occur. In their anatomical study Alsaad et al. [3] revealed that there is no safe anatomical space for minor surgical procedures in the lower lip to avoid cutaneous numbness. Finally, we do not understand what is meant by a diagnostic sensitivity of 100% as mentioned in their reply. Such a diagnostic sensitivity of labial biopsies, for example, Sjögren’s syndrome is unrealistic and not supported by the data reported in their study. Friedman and Miller [2] reported in their study that the labial biopsies of 66% (and not 100%) of the patients referred for diagnostic evaluation of the clinical diagnosis of Sjögren’s syndrome were positive. It is, however, hard to interpret their data as there is no mention in their paper which diagnostic criteria for Sjögren’s syndrome they have used. It even might have been that they diagnosed Sjögren’s syndrome only on the basis of the labial biopsy.

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J. PIJPE, A. VISSINK, C. G. M. KALLENBERG, F. K. L. SPIKERVET

University Medical Center Groningen, Oral and Maxillofacial Surgery, and 1University Medical Center Groningen, Clinical Immunology, Groningen, The Netherlands

Correspondence to: C. G. M. Kallenberg.
E-mail: c.g.m.kallenberg@int.umcg.nl

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Comment on ‘Drug-related pulmonary problems in patients with rheumatoid arthritis’

Sir, The editorial by Dr Saravanan and Dr Kelly about drug-associated lung disease in rheumatoid arthritis (RA) [1] is welcome and timely. However, we think that there are two important issues related to the passage: ‘...The reported incidence of “methotrexate pneumonitis” in RA varies widely, from 0.86% to 6.9%, the risk being maximal in the first year of treatment. Its overall frequency is 1 in every 100 patient-years [15].’

(1) The sources related to the frequencies for methotrexate pneumonitis should be provided and clarified. In Table 3 of reference 15 of the editorial [2] this frequency is given as 0.7% (16/2436). We, however, understand from the text and Table 7 that there were only 13 courses (13/2436 = 0.5%) of methotrexate that needed to be stopped due to pneumonitis. In any event either percentage is lower than the lowest frequency quoted in the editorial. This needs clarification. It should also be added that the editorial gives the adverse effect frequency as patient-years while the quoted Grove et al.’s study [2] gives the frequency as courses of methotrexate that needed to be stopped due to toxicity.

We also surely need to know more about the source especially for the alarming 6.7% frequency of pneumonitis with methotrexate, the anchor drug in RA treatment. We had previously reported our experience with methotrexate in a weekly academic rheumatology clinic over 13 years in 248 patients and among these, in only three patients the methotrexate had to be stopped due to any pulmonary problems [3].

(2) On the other hand the latter part of the passage provides a good example why the imprecise patient-years unit should be abandoned in giving incidences related to adverse effects. Like others in the past [4, 5], we also have recently stated [6] this practice had problems. Some drug reactions as a rule occur early in the treatment course and in only a few individuals, as, we understand, in the case of pneumonitis during methotrexate use under discussion. Apart from the relatively few patients with these early adverse effects, the remaining patients who are prescribed the drug will never get these reactions however long they use the drug. This unduly inflates the denominator of the related incidence ratio and thus will have the potential of under representing the problem related to this particular adverse effect.

The same is also true for late appearing adverse effects. If the effect is a late appearing event—like neoplasms after...