Letters to the Editor

Sleep apnoea caused by rheumatoid arthritis

Sir, We were interested to read the article by Drossaers-Bakker et al. [1] describing five patients with sleep apnoea syndrome secondary to rheumatoid cervical spine disease. We have also collected a series of five patients with sleep apnoea syndrome: three with rheumatoid arthritis, one with juvenile chronic arthritis and one with seronegative spondylarthropathy. The clinical features of all five patients are described in Table 1. In contrast to the patients described by Drossaers-Bakker, sleep apnoea was diagnosed in patients 2 and 3 when excessive snoring was observed during a period of in-patient assessment. Patients 1 and 5 voluntarily complained of excessive snoring and daytime somnolence, and patient 4 had sleep studies performed after difficulties were encountered with weaning from mechanical ventilation for severe community-acquired pneumonia. In-patient sleep studies in our patients have shown severe sleep apnoea in patients 1–4 [apnoea (A) + hypopnoea index (HI) > 60 events/h] and mild sleep apnoea in patient 5 (A + HI 12 events/h). These studies have demonstrated the presence of mixed central and obstructive components to their sleep breathing disorders. The presence of mixed central and obstructive apnoeas in this group of patients would suggest that the aetiology of their sleep breathing disorder is multifactorial. Factors which may contribute to this include brain stem compression from cervical spine disease, upper airway obstruction [2] from micrognathia, and the use of prednisolone, which may itself cause an increase in neck circumference, weight gain and atrophy affecting upper airway musculature. The death of patient 4, 1 yr after sleep study, from respiratory failure was thought to be due to brain stem compression secondary to inoperable rheumatoid cervical spine disease. We also report the presence of a sleep breathing disorder in a patient with juvenile chronic arthritis and one with seronegative spondylarthropathy. This, to our knowledge, is previously unreported. This observation is not surprising as these patients may also develop micrognathia, reduced mobility of the cervical spine, cervical myelopathy with resultant muscle atrophy and increased body mass index as a result of reduced mobility and steroid therapy. We would like to reinforce the conclusions drawn by Drossaers-Bakker et al. and stress that patients most at risk from sleep apnoea do not always complain of symptoms, and reinforce the observation that a high index of clinical suspicion is required to initiate investigations. We would also suggest that limited sleep studies be extended to include patients with seronegative spondylarthropathies and juvenile chronic arthritis displaying the risk factors illustrated here.


84 Castle Street, Glasgow G4 0SF, UK
Accepted 14 January 1999

Table 1. Clinical features of patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Disease duration (yr)</th>
<th>Diagnosis</th>
<th>Cervical spine MRI</th>
<th>Body mass index</th>
<th>Micrognathia</th>
<th>Snoring</th>
<th>Prednisolone</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>19</td>
<td>Seronegative spondylarthropathy</td>
<td>Erosion and fusion C2–4 II</td>
<td>29.1 mm (53, F)</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>2</td>
<td>32</td>
<td>RA</td>
<td>Cl. 2, 3 laminectomy 1994 (Ranawat grade IIA)</td>
<td>N/A (66.3 kg)</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>RA</td>
<td>Decreased disc spaces</td>
<td>26.1 IIA</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>RA</td>
<td>C5 Diffuse narrowing to level of foramen magnum with pannus formation</td>
<td>20.8 II</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>5</td>
<td>37</td>
<td>JCA</td>
<td>Fusion of upper cervical vertebrae</td>
<td>19.5</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
</tbody>
</table>

© 1999 British Society for Rheumatology
The authors also advocate that this MRI technique be used to assess treatment outcome in RA patients. I suggest that such a statement is premature as it is not clear from this study what the costs of such a technique are, how accessible the appropriate MRI equipment and technical expertise are likely to be outside specialized research MRI units, how much time it takes to acquire these images and how reproducible these results will be when removed from an ideal setting in a dedicated research unit.

Until such answers are available and until this technique has been widely validated, it is premature to suggest that it should be included in or replace components of the presently validated and accepted core outcome measurements in the treatment of RA.

Finally, I would appeal to authors, reviewers and editors to resist the tendency to utilize terms such as ‘pannus’ incorrectly in such papers [1], until it is clear whether this specialized region of the synovial membrane is different from the rest of the synovial membrane, with important implications for quantification, therapeutic targeting and patient outcomes.

M. D. SMITH

Re: Assessment of disease activity in rheumatoid arthritis using magnetic resonance imaging: quantification of pannus volume in the hands

Sr, An interesting paper was published recently which, by its title, reported the quantification of pannus volume in the hands of rheumatoid arthritis patients [1].

Most rheumatologists would understand the word pannus to refer to that unique component of the synovial membrane which appears, macroscopically and microscopically, to be eroding hyaline cartilage and subchondral bone. As such, it is likely to be a critically important target for therapeutic interventions and it is clearly important to quantify changes in this region of the joint. It is clear from this paper that, despite the title, the authors did not quantify ‘pannus’ volume, but actually quantified total synovial volume in the joints they studied using magnetic resonance imaging (MRI). At present, the only method available to study adequately the pannus region of a joint is arthroscopy, including arthroscopically directed synovial biopsies of this region. This is likely to be increasingly important, especially if recent evidence [2] that macrophages have a more activated state in this region is validated by further studies.

The authors also advocate that this MRI technique be used to assess treatment outcome in RA patients. I suggest that such a statement is premature as it is not clear from this study what the costs of such a technique are, how accessible the appropriate MRI equipment and technical expertise are likely to be outside specialized research MRI units, how much time it takes to acquire these images and how reproducible these results will be when removed from an ideal setting in a dedicated research unit.

Until such answers are available and until this technique has been widely validated, it is premature to suggest that it should be included in or replace components of the presently validated and accepted core outcome measurements in the treatment of RA.

Finally, I would appeal to authors, reviewers and editors to resist the tendency to utilize terms such as ‘pannus’ incorrectly in such papers [1], until it is clear whether this specialized region of the synovial membrane is different from the rest of the synovial membrane, with important implications for quantification, therapeutic targeting and patient outcomes.

M. D. SMITH

Re: Assessment of disease activity in rheumatoid arthritis using magnetic resonance imaging: quantification of pannus volume in the hands

Sr, An interesting paper was published recently which, by its title, reported the quantification of pannus volume in the hands of rheumatoid arthritis patients [1].

Most rheumatologists would understand the word pannus to refer to that unique component of the synovial membrane which appears, macroscopically and microscopically, to be eroding hyaline cartilage and subchondral bone. As such, it is likely to be a critically important target for therapeutic interventions and it is clearly important to quantify changes in this region of the joint. It is clear from this paper that, despite the title, the authors did not quantify ‘pannus’ volume, but actually quantified total synovial volume in the joints they studied using magnetic resonance imaging (MRI). At present, the only method available to study adequately


Reply

The letter of Dr Hamilton et al. emphasizes the need to be aware of the sleep apnoea syndrome in patients with rheumatic disease. The described cases of sleep apnoea in spondylarthropathy and JCA underscore the necessity to be aware of this syndrome not only in patients with RA. However, the supplied data fail to prove conclusively that a combined apnoea in JCA and spondylarthropathy can be present. To our knowledge, polysomnography is the only definite way to prove the existence of central apnoea and these data are not available.

In addition to our article, we can report that in the 4 yr of follow-up patient A has had a continuous improvement of her apnoea as measured by polysomnography. Patient B died after 2 yr of follow-up because of an unrelated cardiac valve insufficiency, but did not suffer a relapse of apnoea. Patient E is lost to follow-up.

Both Dr Hamilton’s and our observation underline the importance of further study on the recognition and treatment of this syndrome.

K. W. Drossaers-Bakker, H. L. Hamburger, E. B. Bongartz, B. A. C. Dijkmans, R. M. van Soesbergen
Department of Rheumatology, Leiden University Medical Centre, PO Box 9600, 2300 RC Leiden, The Netherlands

Accepted 15 January 1999


Reply

We appreciate your interest and careful comments regarding our article. Although we agree that the word pannus used in the title might lead to some confusion, as you indicated, our understanding is that this medical term has been used to describe the outgrowth of synovial membrane which appears, macroscopically and microscopically, to be eroding hyaline cartilage and subchondral bone. We emphasize that we have no means for quantification or estimation of the pannus volume without dissection until the magnetic resonance imaging (MRI) technique becomes available. The subject we tried to quantify was not ‘just total synovial volume in the joints’, but ‘active’ synovial tissues which have been shown to be successfully visual-
ized by gadolinium-enhanced MRI [1, 2], and such active synovial tissue is likely to be a critically important target for therapeutic interventions. Probably, we could use the words ‘quantitative estimation of pannus’ instead of ‘quantification of pannus’ in our title to be very accurate.

We understand that cost is one of the prime concerns when MRI and post-processing of MRI images are used instead of plain radiography to assess treatment outcome. In this regard, it is not our aim to apply this method to all patients with RA. We believe this technique can be used in a selected population, especially for drug trials. In the clinical trial, not only individual examination fees, but also many other factors, should be taken into account for assessment of the total cost [3]. The total cost for a clinical trial using this radiographic scoring technique includes the overhead costs of the trial ($a_1$), the cost of training a reader to score the radiographs by a particular technique ($a_2$), the amount a reader is paid to score a pair of radiographs ($a_3$) and the average cost per subject in the trial ($a_4$). Here, the total cost ($C$) is derived by $C = a_1 + (a_2 + 2a_3)nk + 2a_4n$, where $n$ is the number of treatment patients and control subjects, and $k$ is the number of readers. In a recent randomized, controlled trial of DMARDs, it was found that radiological damage over 1 yr was similar in both non-DMARD and DMARD groups [4]. If radiological scores had been used to demonstrate the difference between these groups, >500 patients in each group would have been needed to achieve a 5% significance level. Thus, the total cost for a drug trial using radiographic scoring is not necessarily cost effective because of the excess number of patients needed. If MRI is used instead of plain radiography, the number of patients ($n$) could be significantly decreased because MRI can detect drug effect upon pannus before a radiographic response occurs. Further, post-processing of MRI images does not require highly trained readers, therefore $a_2$ and $a_3$ are reduced. Neither does post-processing require multiple readers ($k = 1$ with MRI). The term of the drug trial ($a_4$) may be shortened, and this too will reduce the cost per patient. For these reasons, we believe that quantitative estimate of pannus volume taken from MRI images may be incorporated into efficacy variables in drug trials.

The MRI unit used in our study was not a dedicated research unit. It was installed ~8 yr ago for general medical use at our institution. Likewise, the image sequences were not specially designed for the research. The imaging time required to acquire seven slices using a fat-suppressed T1-weighted sequence was ~3 min, as we reported in our article. Actually, it took ~15 min to complete the whole MRI examination of each hand. All these MRI examinations were performed as ordinary procedures in our hospital.

For post-processing of MRI images, we did not use any dedicated equipment or software. Digitization of the MRI images was carried out using an inexpensive image scanner and general purpose software. Indeed, area measurement was performed with shareware, namely NIH Image. A personal computer was used to measure areas of enhancement. As these computers and software are readily available to the medical community, a dedicated unit is not required to analyse digital images. The image-processing method used in our study is within the reach of all of us.

Finally, we support the instructive comment from Dr Smith in regard to the importance of careful examinations at introducing expensive studies of new generation to the clinics. Nevertheless, we feel that we need to improve the conventional method of assessment in RA clinical trials and hope that many clinicians notice how MRI will benefit it by the early assessment of disease activity.

H. Sugimoto, A. Takeda
Department of Radiology, Jichi Medical School, 3311 Minamikawachi-machi, Kawachi-gun, Tochigi-Ren, 329-0498, Japan


Erratum

While we were preparing this reply, we noticed an error in the above article.
Page 855, line 2 of the left column;
$SI = \frac{([S_1 - 2s.d._1] - [S_2 + 2s.d._2])}{2}$
the correct equation should have been:
$SI = \frac{([S_1 - 2s.d._1] + [S_2 + 2s.d._2])}{2}$

Relevance of tumour necrosis factor alpha gene polymorphism in rheumatic disease
Sir, We read with interest the recent editorial by Verweij and Huizinga [1] on the relevance of the tumour necrosis factor alpha (TNF-α) gene polymorphism in rheumatic diseases. The biological activities of TNF-α, and its gene location within the MHC, make it an attractive candidate gene in diseases with an MHC association and a marked inflammatory component.
One of the major problems in dissecting the contribution of TNF-α polymorphism to a disease is the strong linkage disequilibrium that exists across the MHC region. For instance, in one study, TNF-308A was present on all 22 HLA A1-B8-DR3-DQ2 haplotypes [2]. This greatly complicates the identification of the primary disease gene. One way of overcoming this problem is to perform genetic studies in ethnic groups that have different patterns of linkage disequilibrium across the MHC. Genetic studies in African-Americans have, for example, revealed linkage disequilibrium between TNF-308A and DRB1*15. A study of TNF and DR alleles in African-Americans demonstrated associations of DR15 and TNF-308A with SLE; however the TNF genetic association was thought to be independent of DR alleles [3]. Finer mapping, using more markers within the class III region, in different ethnic groups will be a powerful method of localizing the important gene variants that contribute to the MHC genetic background of SLE.

Although ankylosing spondylitis is strongly associated with HLA-B27, several groups have tested for an independent contribution from the TNF locus. A large study has recently reported that carriage of TNF-308A is associated with lower disease susceptibility in HLA-B27-negative patients [4].

Some large studies have shown contradictory results in RA [5, 6], and further studies are awaited. In this disease, however, genetic variation within the MHC is perhaps more important in determining the clinical severity of disease. Studies examining the associations of disease severity and TNF alleles are, therefore, eagerly awaited.

The effects of the -308 polymorphism on gene function have been studied by several groups. The results are not all in agreement, but most have found that the TNF-308A promoter fragment is a stronger transcriptional activator than the common allele in reporter gene assays [7–9]. A fourth group examined DNA-binding protein at the polymorphic site and found, in macrophages, that only the TNF-308A allele bound a nuclear protein [10].

We agree with the authors that a further range of genetic studies are essential to determine whether TNF-α polymorphism contributes susceptibility to, or severity of, autoimmune rheumatic diseases. The matter becomes more important in pondering the pharmacogenomic aspects of treatment.

A. G. Wilson, G. W. Duff
Division of Molecular and Genetic Medicine, University of Sheffield, Royal Hallamshire Hospital, Sheffield S10 2JF, UK
Accepted 15 January 1999


Reply

We thank Drs Wilson and Duff for their comments. All investigators agree that the strong linkage disequilibrium poses a problem in the determination of the relevance of TNF gene associations with disease. On the other hand, the data suggest a secondary contribution of TNF polymorphisms in SLE in the European population, whereas on the other hand evidence exists for an independent role of TNF gene variants in SLE among African-Americans [1, 2]. In ankylosing spondylitis, results on an independent contribution of TNF gene variants in disease susceptibility are also contradictory. Although it was recently reported that TNF gene variants independently contribute, our data indicate that the association was secondary to HLA-B27 [3, 4]. In addition, Wilson and Duff are right to say that contradictory results have also been reported in RA [5, 6]. Extensive haplotype analysis including numerous MHC localized genetic variants in combination with functional analysis is required to identify the disease-causing gene(s).

Although studies show association between the TNF-308 polymorphism and disease, the functional relevance of this polymorphism is still uncertain. Several groups reported on increased transcriptional activity of the –308A allele [7–9], whereas in at least three studies...
no difference between the two alleles was found [10–12]. In that sense, we feel that firm statements on the functional relevance require some caution and are therefore not appropriate. Further studies are needed to make conclusive statements on the functional relevance of the TNF-308 G to A transition.

C. L. VERWEIJ, T. W. J. HUIZINGA
Department of Rheumatology, Leiden University Medical Centre, PO Box 9600, 2300 RC Leiden, The Netherlands


Doctors' handwriting—does size matter?

Sr, We have observed over the past few years that the handwriting of our senior house officers seems to be becoming larger. Not only is the size of letters bigger, but the spacing between words and lines is greater, so

Senior Consultant :
Senior Registrar :
Specialist Registrar :
Senior House Officer :

Fig. 1. Examples of handwriting.
Wegener’s granulomatosis and diabetes insipidus

Snr, Wegener’s granulomatosis (WG) is a disease of unknown aetiology characterized by granulomatous necrotizing vasculitis of the upper and lower respiratory tracts and the kidneys [1, 2]. Diabetes insipidus (DI) is a rare complication of WG; only seven cases with this complication have been published in the literature. We report an additional case in which, unlike the previously reported cases, MRI failed to show any abnormalities in the pituitary gland, sella turcica or hypothalamus.

SS is a 21-yr-old previously healthy female who was admitted to our medical centre in January 1997 with a 1 week history of arthritis that started in her left knee and later progressed to involve both knees, wrists, metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints, associated with fever and bilateral eye redness. Her system review revealed a 2 month history of chronic sinusitis and epistaxis, for which she was operated on 6 weeks prior to her admission. The diagnosis of WG was suspected. Physical examination revealed a temperature of 39°C and polyarthritis involving the knees, MCP and PIP joints of both hands. Rhinological examination showed a severely hyperaemic mucosa with crusting and polypoid changes. The nasal septum had a purulent cobblestone appearance. Ophthalmological work-up showed bilateral conjunctivitis and marginal keratitis.

Her laboratory studies showed white blood cells (WBC) 15 200 cells/mm³ (75% neutrophils, 12% lymphocytes, 8% monocytes, 5% eosinophils), platelet count 410 × 10³ cells/mm³ and erythrocyte sedimentation rate 111 mm/h. Antineutrophil cytoplasmic antibodies were 33 IU (normal level: <10). Left knee synovial fluid examination showed WBC 47 000 cells/mm³ (90% neutrophils) and a negative culture. Urine analysis, kidney and liver function tests were normal. Chest radiograph showed infiltrates in the anterior segment of the right upper lobe. CT of sinuses showed soft-tissue thickening and fluid in maxillary, sphenoid and ethmoid sinuses, causing almost complete obliteration of paranasal sinuses and erosion of the medial wall of maxillary sinuses (Fig. 1). Angiography of major abdominal vessels showed multiple arteritic changes affecting the arterial tree of the liver. Pathology of sinus mucosa showed necrotizing chronic inflammation with microabscess formation.

In the hospital, she started to complain of polydipsia and polyuria, so DI was suspected. After 2 h of water deprivation testing, she lost 1.5 kg (3%) of body weight. Baseline serum osmolality was 296 mosm/kg and rose by 2 h to 330 mosm/kg, while baseline urine osmolality was 56 mosm/kg and reached a maximum of 81 mosm/kg. After the s.c. injection of 2 μg of desamino D-arginine vasopressin (DDAVP), urine osmolality rose...
within 3 h to 293 mosm/kg. MRI of the brain was performed with axial proton density before and after gadolinium contrast enhancement and this showed no intra-axial or extra-axial masses. The pituitary gland was normal in size and showed normal signal intensity with no focal lesions. The pituitary stalk showed no abnormalities and was in the midline.

She was started on pulse steroid (1 g of i.v. methylprednisolone daily for 3 days) with marked improvement and complete resolution of her arthritis, then she was maintained on 80 mg prednisolone/day with methotrexate (7.5 mg/week). She also received DDAVP as two nasal puffs bid to control her DI. Two weeks later, her polypidysia and polyuria improved, and the dose of DDAVP was reduced to one puff b.i.d. On her last follow-up in November 1998, she was asymptomatic on prednisone 2.5 mg/day and methotrexate 25 mg/week.

The results of the water deprivation test are inconclusive. Central DI due to antidiuretic hormone deficiency would have been expected to show a better response of urinary osmolality to DDAVP (normally >600 mosm/kg). The suboptimal response is consistent with either a partial nephrogenic DI or due to the fact that DDAVP was given s.c. rather than i.v. Moreover, the adequate subsequent clinical response to twice-daily intranasal DDAVP makes nephrogenic DI unlikely and is consistent with central DI.

DI is a rare complication of WG. In reviewing the literature, there were only seven published cases [3–5]. The suggested causes of this complication include granulomatous lesions encroaching on the nervous system by contiguous invasion from nasal or paranasal granuloma, in situ granuloma formation in the posterior pituitary gland, and vasculitis of posterior and/or anterior pituitary blood vessels causing arterial lumen narrowing, secondary ischaemia and gland destruction [3]. All of the reported cases showed either local erosion of the pituitary gland or intracranial granuloma, except for one case reported by Hurst et al. [6] in 1983, with a normal CT scan of the brain. However, CT scan of the brain is not the best modality to demonstrate hypothalamic or pituitary abnormalities, compared to MRI, which is considered the best imaging modality [7]. In our case, MRI detected no pituitary or hypothalamic erosions, and no granulomas. A small-vessel vasculitis, not detected by MRI, may be the cause of central nervous involvement in our patient.

R. A. HAJI-ALI, I. W. UTHMAN, I. A. SALTI1
G. S. ZAATARI2, M. C. HADDAD3, F. W. NASR

Divisions of Rheumatology and 1Endocrinology, Department of Internal Medicine, 2Department of Pathology and Laboratory Medicine and 3Department of Diagnostic Radiology, Faculty of Medicine, American University of Beirut, Beirut, Lebanon
Accepted 29 January 1999

Correspondence to: R. A. Haji-Ali, American University of Beirut, Medical Centre, PO Box 113-6044, Beirut, Lebanon.


Sjögren’s syndrome: a community-based study of prevalence and impact—comment on the article by Thomas et al.

Sir, We read the recent paper on the above topic with great interest. In their report, Thomas et al. [1] stated that Sjögren’s syndrome (SS) has affected ≈3–4% of adults, aged 18–75 yr, in the general population. Thirteen subjects (3.8% of the 341) satisfied their definition of SS, among them four subjects taking antidepressants or diuretics. Six subjects (46.1% of the 13) were ≥55 yr old. The serological criterion was fulfilled in the presence of at least one of the following serum antibodies: antibodies to Ro/SS-A or La/SS-B, antinuclear antibodies, rheumatoid factor. Serum antibodies to Ro/SS-A or La/SS-B were present in 32 participants (9.4% of the 341). The unstimulated salivary flow (USF) test was considered positive if the flow was ≤0.5 ml in 5 min.

Their study protocol was designed based on the ‘preliminary classification criteria’ for SS [2]. However, they were unable to apply these criteria exactly as proposed by the authors. Briefly, the Rose Bengal score, salivary scintigraphy and histopathological investigation of the minor salivary glands were not performed. In addition, according to validated classification criteria for SS, the diagnosis is established by the presence of any four of the six items of the criteria set (serological tests for autoantibodies being limited to the presence of Ro/SS-A or La/SS-B antibodies, or both, and therefore not including antinuclear antibodies and rheumatoid factor) and in the absence of any disorder listed among the exclusion criteria including the use of antidepressants, antihypertensive drugs, neuroleptics and parasympatholytic drugs or any disease potentially associated with SS [3]. Even more, Schirmer’s I test and the USF test had been found to be significantly reduced in the elderly [4], so it was decided not to consider these two tests in any individual older than 60 yr [3]. In addition, the generally accepted USF test is considered positive if the flow is ≤1.5 ml in 15 min.
We believe that in the report by Thomas et al., SS should not be established in subjects older than 60 years as well as subjects taking antidepressants or diuretics. According to these data and the surprising high prevalence of antibodies to Ro/SS-A or La/SS-B, we presume that the reported prevalence of SS is probably overestimated.

M. Tomsic, B. Rozman

University Medical Centre, Department of Rheumatology, Vodnikova 62, 1000 Ljubljana, Slovenia

Accepted 29 January 1999


Reply

We thank Drs Tomsic and Rozman for their comments on our paper [1]. As we clearly stated there, scintigraphy and biopsy were not appropriate for use in a community survey. Given that the published rules for case definition [2] gave equal weight to all features, the absence of results from these tests could only have served to underestimate the prevalence of Sjögren’s syndrome, as was stated in our paper [1]. We also note the comments of Drs Tomsic and Rozman regarding the incorporation of positive tests for rheumatoid factor (RF) and anti-nuclear antibodies (ANA) in our case definition. In fact, we did follow the published criteria, which include these autoantibodies, if excluding subjects with non-Sjögren’s connective tissue disease as an explanation for positivity to either of these antibodies.

We agree that medication history is important, but we had presented the data indicating that only four of the cases were taking either anti-depressants or diuretics. Finally, in the criteria suggested by Vitali et al. [2], the unstimulated salivary flow (USF) test is considered positive if <1.5 ml in 15 min. This is a test that causes some discomfort and, in the community setting of our study, we adopted a practical reduction in the duration of the test to 5 min and hence a salivary flow cut-off of <0.5 ml. We do not think it is likely that this would have altered our results.

E. Thomas, E. M. Hay, A. Hajeer, A. J. Silman

ARC Epidemiology Research Unit, Stopford Building, University of Manchester, Manchester M13 9PT, UK


The underlying colonic or hepatic disease may promote the overgrowth of *S. bovis* and its translocation from the intestinal lumen into portal venous or lymphatic systems [2]. Musculoskeletal manifestations (myalgia, articular pain, aseptic arthritis, low back pain and osteomyelitis) are among the most common complaints found in 28–44% of patients with infectious endocarditis. The incidence of osteomyelitis is <5%. Spondylodiscitis is the most common location and has been associated with haematogenous spread [3]. Its most frequent localization is lumbar (70%), thoracic (10–15%), cervical (7–10%) and bifocal (10%) vertebrae. Back pain, fever and stiffness are the major symptoms of both spondylodiscitis and endocarditis. The non-specific clinical presentation of pyogenic vertebral osteomyelitis may result in frequent misdiagnosis. Moreover, its diagnosis is based on blood cultures and imaging tests, in which certain abnormalities have recently been found. Radiological abnormalities do not appear before 2–8 weeks of the disease’s evolution [4]. Because it is highly vascularized, the vertebral end plate is usually the initial site of infection in haematogenous osteomyelitis. Thus, CT scan can detect erosions in vertebral end plates in 89% of patients at an early stage, when the plain radiographs still reveal nothing. CT can also identify the best site for diagnostic aspiration or open biopsy, if considered necessary [5]. However, MRI can reveal abnormalities earlier [4]. Radionuclide bone scans with gallium-67 (67Ga) or technetium-99m (99mTc) are very helpful at the initial stage of the infection because they can provide evidence of bone infection within the first 48 h [6]. Clinical manifestations, positive blood cultures and typical imaging findings are generally enough for appropriate diagnosis. When this is uncertain, needle biopsy should be performed [4]. It is important to note that the main differential diagnosis of spondylodiscitis is metastatic malignancy, especially when multiple vertebral affection exists. The association of spondylodiscitis and *S. bovis* endocarditis was first reported in 1981 by Allen *et al.* [7]. Since then, only 10 cases have been described in the literature. This association has been observed predominantly in men in the seventh decade of life, and their main clinical findings were back pain and fever. The prognosis of all these patients was determined by endocarditis. Marsal *et al.* [8] and Carrasco *et al.* [9] described two patients with two disc spaces affected, but the rest of the authors have reported the involvement of one disc only. Our case is the first with multiple spondylodiscitis.

In conclusion, spondylodiscitis should be considered in patients with *S. bovis* endocarditis, or other infective endocarditis, especially if there is persistent back pain, even though vertebral involvement is multiple.

G. García-Pardo, T. Auguet, J. L. Blanco, O. Araújo, A. Lorenzo, C. Richart
Internal Medicine Department, Hospital Universitari de Tarragona Joan XXIII, Rovira i Virgili University, Tarragona, Spain
Accepted 25 February 1999
Correspondence to: G. García-Pardo, Internal Medicine Department, Hospital Universitari de Tarragona Joan XXIII, c/ Mallafré Guasch, 4 43007-Tarragona, Spain.


Re: Estimating the prevalence of delayed median nerve conduction in the general population [1]

Str, I would like to ask for clarification about the nerve conduction testing procedure. Most of those involved in performing nerve conduction studies would perform an actual measurement of distance and then a velocity worked out from the latency divided into the distance, or would use a standardized length, or compare distal latencies of median and ulnar nerves. Was any of these the case here?

Were any studies done on any other nerve to confirm that the patient did not have a generalized peripheral neuropathy, as this would give delayed median nerve conduction on its own without any suggestion of carpal tunnel compression being involved? It would be usual practice to examine at least an ulnar nerve in comparison with the median nerve. Without this information, the findings of delayed median nerve conduction are clinically meaningless.

Finally, the summary says: ‘The conclusion reached was that carpal tunnel syndrome, as assessed by delayed median nerve conduction, is common in the general population’. As the authors make clear in the second paragraph of their Introduction, there is a group of patients with carpal tunnel syndrome and normal sensory nerve conduction studies, and other members of the population who are symptom free but may have delayed median nerve conduction. Is it possible to diagnose carpal tunnel syndrome when there are no symptoms, and would the authors not have been better simply to report their finding of delayed median nerve conduction and not extrapolate this by suggesting that all such subjects had carpal tunnel syndrome?

I. M. Morris
Kettering General Hospital NHS Trust, Rothwell Road, Kettering, Northants NN16 8UZ, UK
Accepted 4 March 1999

Reply

We are happy to respond to the comments raised by Dr Morris.

The velocity was indeed calculated by dividing the latency by the distance. In most instances, the latter was 7–8 cm.

We agree that in clinical practice it is appropriate to compare the latencies from the median nerve with those from the ulnar nerve. We did, in fact, attempt this in a pilot sample of participants at the commencement of this study. We decided not to continue with the ulnar nerve testing for two reasons: (1) the extra study added to the discomfort and inconvenience of the study participants who were essentially volunteers, in contrast to the situation in the clinic; (2) similarly in this population sample, we assumed that the prevalence of peripheral neuropathy would be very low, again this is in contrast to the need for greater diagnostic stringency in clinic referred patients.

We agree with Dr Morris that our study was focused on the prevalence of delayed median nerve conduction. This is clearly stated in the title and the objectives. All the tables just refer to the prevalence of delayed nerve conduction. Our brief mention of carpal tunnel syndrome was meant just to be a marker for a clinical audience of the possible significance of our findings. We are happy to make clear, as we believed we had done in the paper, that this was only a study on the prevalence of delayed median nerve conduction.

S. Ferry, T. Pritchard, J. Keenan, P. Croft, A. Silman
ARC Epidemiology Research Unit, Stopford Building, University of Manchester, Manchester M13 9PT, UK