An articular index is a formalized method of expressing the severity and extent of joint involvement in inflammatory arthropathies such as rheumatoid arthritis. Rheumatologists agree that articular indices are important in clinical investigations [1], use them in some form in routine clinical practice [2], and when aware of each other’s assessments on similar patients converge on an articular index as the main determinant of their clinical evaluations [3]. It is difficult to conceive of a clinical study of rheumatoid arthritis which would not now include an articular index.

A variety of articular indices have been devised and adopted. If these were simply different but comparable scales by which to measure patients their multiplicity would not cause any difficulty, but this is not the case. Until recently there has been little agreement about which joints should be selected for inclusion in an articular index and how they should be examined [4]. For example, the Ritchie index [5] grades the tenderness of groups of joints, the index described by the Cooperating Clinics of the American Rheumatism Association (the ARA index) [6] counts joints that are tender and/or swollen and the Lansbury index [7] scores the severity of inflammation, weighted for joint surface area. All have been shown to be sensitive to changes in a patient’s condition, but which is the best measure of joint inflammation?

RATIONALE FOR THE STRUCTURE OF AN ARTICULAR INDEX

The clinical measurement of inflammation relies on the assessment of tenderness, swelling and redness by observation and palpation [8]. As any one of the 187 synovial joints may be affected by the rheumatoid process [9], a full articular index might be expected to examine every joint for each of these four classic signs of inflammation. Alternatively, an articular index might be constructed by counting the number of joints with one or more signs of inflammation or any combination of signs. Other indices might be produced by weighting for the severity of the signs or by weighting for joint size, thus producing an almost infinite number of articular indices.

It may, however, be possible to omit some joints without loss of clinical information. In practice, authors have generally decided for a variety of reasons to limit their own articular index to very specific conditions within this very large spectrum. A contrasting approach which we have adopted [10] has been to record separately the data for each of the signs of inflammation for every joint that could be examined by an observer and, by using computer analysis, to evaluate the signs combined in different ways. This included grading for the severity of signs in each joint and weighting for joint size.

WHICH SIGNS TO MEASURE?

Most workers have concentrated on joint tenderness or swelling because of the infrequency of detectable warmth or erythema in the small joints of the hands. However, the correlation between joint tenderness and swelling is low [10], suggesting a rather weak biological link and it has become clear that these two cardinal features of inflammation measure very different aspects of the disease process. Articular indices that use only joint tenderness correlate well with pain scores but poorly with measures of the acute phase response [10]. Joint tenderness is a subjective sign that depends on the ‘pain threshold’ of the individual as well as the strength of the stimulus. The former may be influenced by physical and psychological factors quite separate from the inflammation in the joint, while the latter varies considerably between observers [11]. The use of dolorimeters can reduce variation [12]. Tenderness will also reflect mechanical damage of the articular surfaces. However, despite the complexity of the relationship between synovial inflammation and joint tenderness, tender joint counts were considered the most reproducible with multiple observers by Savage [13] and remain so today [11].

Swelling is a semi-objective sign that depends on the perceptions of the examiner. Swollen joint counts correlate significantly with the erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) but less well with pain scores [10, 14], suggesting a closer relationship with synovial inflammation than tenderness. The inference that swelling is a better measure of synovitis is strengthened by the link between swelling and radiographic joint damage that has not been found with tenderness [15, 16]. Soft tissue swelling can be identified by palpation and observation as in the ARA index, or semi-quantified using jeweller’s rings [17]. Measurement of the reduction in finger joint swelling has been shown to differentiate between the anti-inflammatory and analgesic effects of drugs [18] but the techniques show high inter-observer error and cannot be reliably used by multiple observers [11, 19].

While swelling might be a more accurate measure of synovial inflammation than tenderness, the latter is more sensitive to change [20]. This difference is also found when the signs are combined; thus, counting tender and/or swollen joints is less sensitive than
counting joints both tender and swollen [11]. In keeping with this the Ritchie index showed greater sensitivity than the ARA index.

Thus, tenderness and swelling supply complementary information about joint involvement in rheumatoid arthritis. Tender joint counts are more sensitive to change and are reproducible, factors that are of great importance in clinical trials, but swollen joint counts are a more accurate measure of joint inflammation and predict future joint damage.

WHICH JOINTS TO EXAMINE?

While it might be theoretically best to examine all joints, some joints, although undoubtedly involved in inflammation, are difficult to examine reliably. The concept of examining 'signal joints' was introduced by Ward et al., who suggested identifying a few key joints and following their progress [21]. While this method is attractive, allowing the physician to tailor a measure of significant improvement at any stage of the disease, it is limited in its capacity to describe deterioration, particularly when there is deterioration in non-signal joints. Egger et al. compared the use of signal joints with full and reduced joint counts in the context of two clinical trials [22]. They found the signal joint technique to be less sensitive than full joint counts but a 36-joint subset was of similar sensitivity and reliability to the full index and was recommended on grounds of practicality. We have confirmed that omitting certain joints does not weaken the qualities of an articular index and have devised a 38-joint index [10]. Fuchs et al. evaluated a 28-joint index in cross-sectional studies and found it to be as effective as indices including more joints [23]. These results were extended by the authors in longitudinal comparative studies using tenderness and swelling as separate measures [24]. This has been confirmed by independent workers [25, 26]. It seems unlikely that further reduction in joint numbers will be of great practical advantage and may result in loss of important clinical information.

GRADING AND WEIGHTING?

Ritchie and colleagues designed their articular index to detect changes in joint tenderness [5]. They adopted the grading system of Bunim et al. [27] and argued that a graded examination would improve discrimination between patients. The disadvantage was a reduction in inter-observer reproducibility so that they concluded 'the index is invalid if observations are made on the same patient by different clinicians'. We confirmed this finding, demonstrating that grading the severity of tenderness using the Ritchie index resulted in greater variation between observers, perhaps because of differences in the strength of the pain stimulus as suggested by the patients' responses at interview, or variation in the patients' responses to the observers as suggested by the assistants [11]. This has also been found by others [28]. The results support the contention that grading is an important source of error in the Ritchie index [29]. Thus, grading for the severity of signs produces a small improvement in sensitivity to detect change at the cost of increased observer variation.

Lansbury contended that an articular index designed to measure the total amount of joint inflammation should be weighted for joint size because the volume of inflamed synovium would be proportional to the articular cartilage surface area [7]. We explored this further by correlating joint counts and articular indices weighted for joint surface area with the serum CRP [10]. The rationale was that CRP is produced in response to synovial inflammation and should be a gross measure of total joint inflammation. Our results showed significant improvement in the correlation with CRP when joint counts were weighted for size. This finding is confirmed by Stucki et al. [30] who found that weighting swollen joints consistently improved correlation with CRP as well as with other indices of disease activity such as grip strength, morning stiffness and patient global assessment. However, similar correlation was not found in a longitudinal study by Prevoo et al. [31]. Moreover, weighting for joint size significantly reduces the sensitivity of an index to change [23] and increases observer variation [11].

SELF-REPORT ARTICULAR INDICES

In 1989 Stewart et al. described a self-reported articular index based on the identification of 'joints which are tender and inflamed' weighted for joint size [32]. They showed good correlation between the self-reported score and those undertaken by a rheumatologist (r = 0.83), and reasonable test–retest reliability. However, the self-report index did not correlate with serum CRP, in contrast to the rheumatologist scored index, suggesting that it measured a slightly different aspect of the disease. It may be that patients place more emphasis on tenderness than does the rheumatologist or that the term 'inflamed' was interpreted differently to swelling.

In order to avoid the preconceptions built into existing articular indices devised for use by health-care assessors, Hewlett and colleagues adopted the approach of having patients record their perceived joint signs and symptoms and used computer analysis to seek the best combination of joints and self-reported signs for correlation with the CRP [33]. Although a correlation between patients and health-care workers could be shown for some combinations, no correlation with CRP could be obtained with any combination of patient-perceived signs and symptoms.

The rapid assessment of disease activity in rheumatology (RADAR) questionnaire similarly includes a self-report articular index that grades joints for the severity of tenderness from 0 to 3 [34]. Agreement between patient and rheumatologist was again reasonable, both cross-sectionally and longitudinally. However, these indices have not been tested in the context of clinical trials and further work is required to determine their ability to accurately assess joint swelling.

COMPOSITE INDICES

Steinbrocker and Blazer were the first to describe a composite index of joint inflammation (the therapeutic
score card of 1946) based on sedimentation rate, pain, range of movement, joint tenderness, anaemia, functional status and mood [35]. Each parameter was arbitrarily weighted and the scores subtracted from 100. In 1956 Lansbury described his systemic index of rheumatoid activity, a composite index of morning stiffness, fatigue, aspirin consumption, grip strength, ESR and haemoglobin [36]. He later combined this with an area-weighted articular index [7] to form a Comprehensive Index. Other composite indices were also produced during this time (see Lansbury for a detailed review [37]). Much debate followed and an editorial in 1967 about the role of composite indices of disease activity in clinical trials concluded that the technique ‘muddles the whole affair’ and should not be applied in therapeutic practice [38]. Despite these sentiments much further work has been undertaken and there have been considerably advances in the statistical techniques used to define and evaluate new indices [39]. Notable steps have been the index of disease activity of Mallya and Mace [40], the pooled index [41] and the Stoke index of Davis et al. [42] and the development of the disease activity score (DAS) [43]. The Mallya and Mace index has been shown to be less able to discriminate between patients than do the DAS or Stoke indices [44]. However, both the Stoke and the Mallya and Mace indices require more clinical data and are more complicated than the DAS. Furthermore, the DAS index has been independently verified [45]. All these recent indices include some type of articular index. The DAS, now modified to include the reduced 28-joint counts for tenderness and swelling, has been shown to be as valid as disease activity scores that include more comprehensive articular indices [46].

WHICH ARTICULAR INDEX?

The results of these studies suggest that there is no single articular index that will produce optimal results in all conditions. However, the data presented above provide a method by which rheumatologists may choose an articular index relevant to their specific needs. This goes some way to answering the call for properly evaluated clinical measures [47].

It is clear that tenderness and swelling supply different information about the disease process. Tender joint counts are more sensitive to change and correlate best with pain, a property considered important by patients. By comparison, swollen joint counts measure synovial inflammation and predict joint damage. Both these properties influence the choice of treatment so it follows that both tenderness and swelling should be included in an index.

Grading the severity of the signs improves the sensitivity of an articular index but decreases its reproducibility between observers. Weighting for joint size improves correlation with the acute phase response, suggesting a more valid measure of total synovitis, at the cost of reducing observer reproducibility.

The Committee on Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) has recently defined a core set of disease activity measures that include a tender joint count and a swollen joint count separately [48]. Similarly, the EULAR Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT) has published a core set which includes the 28-joint tenderness and 28-joint swelling counts [49]. It seems likely that these will become the standard outcome articular indices for clinical trials for the next decade (Fig. 1), although it
is possible that for other purposes such as prognostica-
tion it may be worth combining the observations
mathematically.

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REFERENCES


NEUROLOGICAL INVOLVEMENT IN SYSTEMIC SCLEROSIS

Although systemic sclerosis (SSc) is a multisystem disease, neurological involvement was only rarely documented in large series of SSc patients [1–3] and so, until recently, was considered unusual. However, we now know that neurological involvement occurs in a significant proportion of patients with SSc, and many have subclinical neuropathy.

Several forms of neurological involvement occur. Cranial nerve abnormalities, peripheral neuropathy, central nervous system involvement and autonomic peripheral neuropathy, have all been described. A patient with SSc and pulmonary fibrosis has been reported, in whom the left hemidiaphragm became elevated prior to a fatal clinical deterioration [4]. The authors postulate that phrenic nerve palsy developed as a manifestation of the SSc and contributed to the patient’s death. The implication, therefore, is that in certain clinical circumstances neuropathy in SSc may be life threatening.

Clinically apparent neuropathy in SSc has been described mainly in case reports and small series. Some larger studies have also been reported. Lee et al. [5] studied neurological involvement prospectively in 125 patients with SSc and found four cases of carpal tunnel syndrome, and one each of peripheral neuropathy, trigeminal neuralgia and mononeuritis multiplex. A recent retrospective study suggested that 40% of 50 patients with SSc had neurological abnormalities, but the inclusion of patients with muscle involvement contributed to this high frequency [6].

To consider the different neuropathies associated with SSc in turn, trigeminal sensory neuropathy is the commonest clinically manifest neuropathy in patients with SSc, and was reported in 4% of a series of 442 patients with SSc [7]. Trigeminal neuropathy often occurs early in the course of SSc and may be the presenting feature. Other cranial nerves may be involved in association [8].

Although peripheral neuropathy in patients with SSc has been described in a number of case reports, this is uncommon. It is usually of mixed sensory and motor type. However, a study of peripheral nerve function in SSc, in which sensory thresholds, nerve conduction and sympathetic skin responses were assessed in 29 patients, demonstrated subclinical peripheral nerve dysfunction in a significant proportion of patients, more marked in the feet than the hands: tactile sensitivity in the foot was impaired in 50% of patients [9]. Other forms of peripheral nerve involvement in SSc have also been reported, albeit infrequently: entrapment neuropathies, particularly carpal tunnel syndrome [5] and mononeuritis [5, 10, 11].

Central nervous system involvement is rare. The high incidence of ‘cerebral disease’ originally reported in patients with SSc was usually secondary to cardio-pulmonary or renal disease [3]. Isolated cases of cerebral vasculitis have been described. Averbuch-Heller et al. [6] in their series of 50 patients, reported a myelopathy in four and cerebrovascular disease in three, but most clinicians believe that the central nervous system is almost always spared. In a recent study of central nervous and psychiatric involvement in SSc, neuropsychiatric symptoms were present in five of 32 patients, but it was not possible to ascribe these to...