Erosions are like cockroaches, when you see one there are many others you do not see. It's just one erosion! No, it is not!

Sirs,

When we see a cockroach we know that there are many others we don't see. (Exterminators estimate there are hundreds we don't see. [PC2] When we see an erosion on conventional radiology in rheumatoid arthritis (RA) we suspect there are others. But our radiographic studies usually just quantitate erosions and joint space narrowing of the hands, wrists and feet (1). We know from using Ultrasound, CT and MRI studies when looking at the hands that there are other erosions we don't see by conventional radiology (1, 2). The Modified van der Heijde Sharp Score of erosion and joint space narrowing is 380x or a total Genant Score is 290 but these are not tabulated beyond the hands, wrists and feet, yet our patients have erosive disease and joint space narrowing in many other locations (1, 2). There are 360 joints in the body but not all are ever involved by RA. We have no studies that have quantitated how many total types of erosions at all sites there are in a patient when we find one erosion. We sometimes are told "it is just one erosion", but is it really? No, it is not!

Beyond erosions and joint space narrowing we also should consider measurement of synovitis, osteitis and tenosynovitis using such modalities as ultrasound and MRI (3-5). Erosions and joint space narrowing indicate damage, which could be former damage or ongoing erosive damage but synovitis, tenosynovitis and osteitis are a measure of the presence of ongoing active disease. Thus it is important to look at and define active RA and decide what to measure.

We need a programme that can quantitate "systemic erosion, joint space narrowing, synovitis, osteitis and tenosynovitis" as part of a damage risk assessment. (Table I) Our clinical assessment of disease activity measures tells us a lot, but still lacks the precise objectivity we need. Tender and swollen joint counts of the hands, wrists and feet are far from narrow objective measures and have large smallest detectable differences of 4.8 for Tender Joint Count and 3.5 for Swollen Joint Count (6). Even conventional radiograph readings in studies have smallest detectable changes or differences of 4.6 to 5.92 for the Behandel Strategieën (BeSt) study, 6.2 in TEMPO, and 6.23 by Ejbjerg with simultaneous MRI SDD from 1.24 to 4.19 depending on the site (7-9). Furthermore, rheumatologists and radiologists differ in the same patient (10). Yet imaging including CT has still been our best objective measure (11, 12). The VECTRA-DA® is a multi-biomarker disease activity (MBDA) score. It includes 12 biomarkers: VEG-F, EGF, TNF-α –RI, IL6, MMP-1, MMP -3, YKL-40, VICAM 1, SSA, CRP, Leptin and Resistin. It has a precision of 1.6%. [Median Coefficient of Variation was 1.6% (range: 0.0% to 6.4%)] (7, 13, 14). Other biomarkers are also being evaluated such a 14-3-3η and microchip arrays. The MBDA has shown a good ability to predict erosions and joint space narrowing using the modified van der Heijde Sharp Score but obviously is influenced by disease activity beyond the hands and feet (7, 13, 14). It can be a semi-surrogate for systemic erosive disease and has been associated with MRI identified active synovitis and osteitis (7, 13, 14). The MBDA has been called the "Rheumatoid Arthritis Thermometer" by Professor Iain McInnes.[PC3] The MBDA is a portion of large pool of inflammatory biomarkers, proteins and enzymes known as the "Immunologic Cesspool" by Greg Silverman [PC4]. In perspective the amount of total synovitis in the smaller joints of the fingers and toes is much less that the total amount of synovitis in the intermediate and larger joints.

The MBDA can also quantitate and report the individual 12 biomarkers as a way to look at some of the immunologic activity included in the ongoing inflammation in the RA patient. In looking at the activity of the individual biomarkers, Professor Iain Mc-Innes uses the term "immunologic stethoscope" to look at these biomarker players in this active immune disease [PC3]. This delineation of the quantity of these and other biomarkers may eventually give clues to disease activity and suggest mechanisms of action and how this can be evaluated and what type of intervention we may consider.

This article is a proposal to assist the Rheumatologist in assessing the "Rheumatoid Arthritis Damage Load" using imaging with disease activity composite measures, functional measures and a biomarker score. (Table I) (20). We need to keep the perspective of this "RA Damage Load" that incorporates such a damage score or damage index and integrates the imaging, laboratory, systemic disease, functional guides and socioeconomic issues that we use to care for our patients. We know there is still active disease even with a DAS score remission of any type, an ACR/EULAR Boolean Remission or MBDA remission. New erosions and synovitis can occur (7).

RA is a systemic disease and our target of therapy needs to be directed to all of its manifestations. The joint is our target as it is the calling card to this disease. And although it is our target, when we treat RA there are many other systemic targets so that we need a "RA Carry Permit" to describe our ammunition. (Table II) The "RA Carry Permit" contents are impacted by scientific reasons related to the total disease process and geo political regulations from government policies to insurance programmes. Here we are emphasising the need to focus on the "RA damage load" and see if all of the foci of extra-articular disease are included in our aim can be targeted; including extra-articular systemic disease such as cardiovascular disease, pulmonary disease, vasculitis, nodular disease and eye disease as well as articular, tendon and additional soft tissue damage.

As a clinician we need as many tools as possible to assess and help our patients. Outcome studies incorporating the measurements in the "RA Damage Load" will be important. We know from studies in-

Table I. Clinician needed tools: Rheumatoid Arthritis Damage Load to develop a rheumatoid arthritis patient assessment to develop rheumatoid arthritis targets for therapy.

Rheumatoid Arthritis Damage Load
Specific Measures
Erosion Score
Joint Space Narrowing Score
Synovitis Score
Bone Marrow Oedema/Osteitis Score
Tenosynovitis
Disease Activity Measure Score
Functional Score
Biomarker Score
Systemic Disease

Table II. "Rheumatoid Arthritis Carry Permit" – therapies available for the rheumatologist to aim for treatment to target.

Rheumatoid Arthritis Carry Permit
NSAIDS
Corticosteroids
DMARDS – non-biologic
DMARDS – small molecules
DMARDs – biologic
Therapies for systemic disease
Other comorbid disease therapies

corporating x-ray Sharp Score probability plots that people on therapy can get progressive worsening on imaging (15). We need investigative data to validate and integrate all of our patient's damage since it can lead to impairment, disability and death. We want these outcome measures to relate to the individual patient. We also know that continued elevation of MBDA correlates in patients treated with methotrexate or TNF inhibitors with worsening of clinical response, increasing x-ray damage and suppressing the MBDA leads to less x-ray damage (16, 17, 18). As these measurements, as well as cardiovascular and other extra-articular systemic outcomes are included in clinical studies we will have a clearer idea of their impact on many outcomes.

This article proposes guidelines to assist the rheumatologist beyond the present treat-to-target algorithm which has information shortcomings (19). As clinicians we always desire as much credible information as possible. Our ability to integrate established and new data including investigational studies is what we do daily using our clinical gestalt. This article emphasises that when we see an individual patient there are many measurements we need to utilise the "RA Carry Permit". We integrate data from large studies and distill it to the individual patient. As we discuss these findings during the direct patient physician relationship we want to be in win-win clinical setting. Every bit helps, large and small.

The damage load will help to enrich our "Physician Gestalt" which manages the complexity of the various disease activity measures to decide when we need to treat the patient and what guidelines we use. The term "erosions" in this article is an allegory to all of our measurements. Once we define a more complete RA disease damage and activity algorithm, the better we can use the "RA Carry Permit" filtered through the "Physician Gestalt" to treat active RA.

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