Cytidine deaminase activity, C reactive protein, histidine, and erythrocyte sedimentation rate as measures of disease activity in psoriatic arthritis

P S Helliwell, A Marchesoni, M Peters, R Platt, V Wright

Abstract
Cytidine deaminase activity, C reactive protein, histidine, and erythrocyte sedimentation rate were measured in 36 subjects with psoriatic arthritis of varying disease duration and severity. Although cytidine deaminase activity may provide an integrated measure of synovial inflammation in rheumatoid arthritis, neutrophil accumulation in psoriatic plaques compromises this measure in psoriatic arthritis. Low histidine concentrations confirm that this amino acid provides a non-specific index of synovial inflammation. In psoriatic arthritis high C reactive protein concentrations seem to be associated with extensive joint destruction. In this study the erythrocyte sedimentation rate was found to be the best laboratory guide to clinical disease activity in psoriatic arthritis.

Clinical and investigative work requires us to assess objectively disease activity and progression. Most investigators rely on a familiar cluster of measurements: some are subjective, such as pain, and some are independent, such as the erythrocyte sedimentation rate. Whereas subjective measures are relevant to the patient, they are liable to be influenced by factors other than those we wish to assess. On the other hand, objective measures may not closely reflect clinical disease activity. A recent editorial stated 'there is a need for markers of disease processes that are specific, sensitive, reproducible, and make sound biological sense'. Such a case has been made for cytidine deaminase activity and histidine concentrations in rheumatoid arthritis.

Cytidine deaminase is a cytoplasmic enzyme whose exact physiological role is uncertain. Cytidine deaminase activity in rheumatoid arthritis is increased in serum and synovial fluids owing to leakage from damaged intrasynovial neutrophils. Such activity is increased in many other conditions also, including septicaemia, ulcerative colitis, and pre-eclamptic toxoaemia. In the chronic inflammatory arthritis of psoriasis cytidine deaminase activity may not be specifically related to synovial inflammation as psoriatic lesions are characterised by neutrophil invasion.

The amino acid histidine originally promised to be a useful marker for rheumatoid arthritis and was thought to be specifically depleted in this condition. Low histidine concentrations, however, seem to be a secondary phenomenon in many types of synovial inflammation, including the seronegative spondyloarthritides. We have previously attempted to characterise inflammatory rheumatic diseases according to their biochemical profile—an exercise of diagnostic and possible aetiological value.

The aims of this study were to relate these new biochemical markers to clinical disease activity in psoriatic arthritis for both the arthritis and the psoriasis, and to identify unique biochemical profiles among the disease subsets as defined by Moll and Wright.

Methods
The diagnostic criteria used for psoriatic arthritis were as described by Wright and Moll. Essentially, these criteria require inflammatory arthritis in three or more joints together with absence of rheumatoid factor and rheumatoid nodules, and the presence of skin or nail lesions consistent with psoriasis. Subjects were mostly selected from a morbidity index derived from a rheumatology outpatient group. After identification they were invited by letter to attend for an examination. The details and purpose of the study were explained in an accompanying note. Other subjects were recruited when routinely attending rheumatology follow up clinic appointments and a few rheumatology inpatients were recruited. Fifty subjects were seen and examined as part of another study of disease pattern in psoriatic arthritis: 36 of these subjects formed the patient group of this study.

For each subject demographic details were recorded and a full history obtained using a standardised proforma. Particular note was made of the onset of psoriasis and arthritis, history of eye inflammation, and an assessment of functional status. Table 1 shows the demographic and clinical details of the subjects.

Clinical examination included a systematic evaluation of most joints, recording the presence of swelling, tenderness, limitation of movement, and deformity. A Ritchie articular index was derived for each patient, in addition to the

<table>
<thead>
<tr>
<th>Table 1 Clinical details of subjects (n=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
</tr>
<tr>
<td><strong>Duration of psoriasis (years)</strong></td>
</tr>
<tr>
<td><strong>Duration of arthritis (years)</strong></td>
</tr>
<tr>
<td><strong>Activity of psoriasis</strong></td>
</tr>
<tr>
<td><strong>Area of psoriasis</strong></td>
</tr>
<tr>
<td><strong>Ritchie index</strong></td>
</tr>
<tr>
<td><strong>Number of active joints</strong></td>
</tr>
<tr>
<td><strong>Total number of affected joints</strong></td>
</tr>
<tr>
<td><strong>Erosion score</strong></td>
</tr>
<tr>
<td><strong>Narrowing score</strong></td>
</tr>
<tr>
<td><strong>Severity of arthritis</strong></td>
</tr>
<tr>
<td><strong>Functional score</strong></td>
</tr>
</tbody>
</table>

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A correlation matrix between clinical and biochemical variables was derived from the data. Correlation coefficients between parametric variables were calculated with the Pearson's product moment correlation coefficient r. For the non-parametric variables (psoriasis activity, psoriasis area, severity of arthritis, and functional score) we calculated the Spearman rank correlation coefficient, r_s, correcting for ties as described by Siegel. Levels of significance for r, are quoted for one tail tests. Between group comparisons of parametric data were carried out with Student's t test.

Results

Spinal disease, defined by pain and limitation of movement together with radiological sacroiliitis, was found in 12 subjects (33%). Thirty two subjects had psoriasis vulgaris, two had pustular psoriasis, and two guttate psoriasis. Three subjects had no psoriasis at the time of examination. Dactylitis was present in five subjects (14%). Nails were affected in 24 subjects (67%) and seven had a history of inflammation of the eyes (most having conjunctivitis). Eight subjects had a history of enthesopathy and one subject had enthesopathy of the heel at the time of the examination.

Table 2 shows the correlation matrix between clinical and biochemical variables. Expected correlations between erythrocyte sedimentation rate, haemoglobin, and C reactive protein were found. Although modest reductions in serum histidine occurred (figure), this biochemical

<table>
<thead>
<tr>
<th>Variable</th>
<th>ESR</th>
<th>Hb</th>
<th>CDA</th>
<th>Histidine</th>
<th>CRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (Hb)</td>
<td>-0.35*</td>
<td>-0.29</td>
<td>0.12</td>
<td>0.44†</td>
<td>-0.41†</td>
</tr>
<tr>
<td>Cytidine deaminase activity</td>
<td>0.40*</td>
<td>0.10</td>
<td>-0.12</td>
<td>-0.57</td>
<td>0.04†</td>
</tr>
<tr>
<td>C reactive protein</td>
<td>0.44†</td>
<td>0.16</td>
<td>0.52†</td>
<td>-0.23</td>
<td>0.12</td>
</tr>
<tr>
<td>Psoriasis activity</td>
<td>0.01</td>
<td>0.17</td>
<td>0.75†</td>
<td>-0.11</td>
<td>0.22</td>
</tr>
<tr>
<td>Psoriasis extent</td>
<td>0.38†</td>
<td>0.17</td>
<td>0.20</td>
<td>-0.12</td>
<td>0.27</td>
</tr>
<tr>
<td>Articular index</td>
<td>0.31*</td>
<td>-0.13</td>
<td>0.04</td>
<td>-0.08</td>
<td>0.15</td>
</tr>
<tr>
<td>Number of active joints</td>
<td>0.31*</td>
<td>-0.13</td>
<td>-0.12</td>
<td>-0.20</td>
<td>0.24</td>
</tr>
<tr>
<td>Number of affected joints</td>
<td>0.38†</td>
<td>-0.41†</td>
<td>0.36*</td>
<td>-0.16</td>
<td>0.31</td>
</tr>
<tr>
<td>Functional score</td>
<td>0.08</td>
<td>-0.10</td>
<td>0.17</td>
<td>-0.23</td>
<td>0.35*</td>
</tr>
<tr>
<td>Narrowing score</td>
<td>0.45†</td>
<td>-0.34*</td>
<td>0.47†</td>
<td>-0.27</td>
<td>0.59</td>
</tr>
<tr>
<td>Severity of arthritis</td>
<td>0.31*</td>
<td>-0.34*</td>
<td>0.33*</td>
<td>-0.13</td>
<td>0.48*</td>
</tr>
</tbody>
</table>

*Denotes significant at 5%. †Denotes significant at 1%.

Table 2 Correlation matrix between clinical and biochemical variables

Laboratory indices in active and inactive psoriatic arthritis. Results are mean plus standard error of mean. None of the differences was significant with Student's t test.

ESR=erythrocyte sedimentation rate; Cyt. deam.=cytidine deaminase activity (IU=10^-4 μmol ammonia/min/ml); CRP=C reactive protein.
marker did not correlate with other laboratory indices of disease activity. The erythrocyte sedimentation rate seemed to be the best indicator of disease activity and severity in this study. C reactive protein was found to correlate with radiographic grade and overall disease severity but not with numerical indices of joint activity such as the articular index.

Cytidine deaminase activity was highly significantly correlated with the activity of psoriatic lesions and the extent of psoriasis, and to a lesser extent with C reactive protein and other indices of arthritic severity.

The study group was divided into those with active arthritic disease and those with inactive disease. Active disease was defined as an articular index greater than or equal to 20 together with at least 30 joints actively inflamed. Seven patients fulfilled the criteria for active disease, 29 for inactive disease; the figure depicts the laboratory data in these groups. Although erythrocyte sedimentation rate and C reactive protein were both higher in the active group, none of the differences was statistically significant.

The study group was further subdivided according to the criteria of Moll and Wright. Twenty six subjects were classified as symmetrical polyarthritis, three as oligoarthritis, and five as predominantly spinal disease. Table 3 presents clinical details of these groups. Of the remaining patients, one had asymmetrical polyarthritis and the other predominantly distal interphalangeal joint disease. These last two cases were not included in the comparisons. Of the laboratory variables, any differences can be accounted for by the greater volume of inflammatory synovial tissues to be found in the group with symmetrical polyarthritis. Cytidine deaminase activity, in particular, was almost the same for the three groups: this contrasts with the strong relation between cytidine deaminase activity and the extent and activity of the psoriatic skin disease.

**Discussion**

Although the study group was selected at random from a morbidity index, there was an unusually high prevalence of male subjects in this group. In other respects our group resembled other recent study groups with psoriatic arthritis. In particular, we confirmed that a symmetrical polyarthritis is the most common manifestation of psoriatic arthritis.

We showed that cytidine deaminase activity is not related to inflammatory activity of the joints in psoriatic arthritis but is strongly related to the extent and severity of psoriatic plaques. Inflamed joints probably make a small contribution to the cytidine deaminase activity as reflected by the significant positive correlation between disease activity and this activity. These results are not surprising as in psoriatic neutrophils accumulate in psoriatic plaques. The pathological features of inflamed synovium in psoriasis are non-specific, including a number of inflammatory leucocytes of which neutrophils are presumably, as in rheumatoid arthritis, a source of cytidine deaminase activity in the serum. Cytidine deaminase activity cannot therefore be used as an integrated marker of synovial inflammation in psoriatic arthritis.

Serum histidine concentration was only modestly reduced in this study. A probable explanation for the low histidine concentration in rheumatoid arthritis is excessive decarboxylation to histamine within the joints. This probably also explains the low serum histidine in other inflammatory synovial conditions, including psoriatic arthritis. In our study histidine concentrations were similar in active and inactive disease.

Overall, the erythrocyte sedimentation rate seemed to be the best indicator of arthritic activity and severity in this study; significant correlations were found between erythrocyte sedimentation rate and the following variables: articular index, number of active and affected joints, functional score, joint narrowing score, and overall severity of the arthritis. These indices of severity depend mostly on the total number of joints affected by the arthritic process: thus a patient with active oligoarthritis would score low on most of these indices. As most patients in this study had a polyarthritis the correlations noted seem valid.

Our patients were also subdivided into the subgroups originally suggested by Moll and Wright. Unfortunately, owing to the high prevalence of symmetrical polyarthritis, numbers in the other subgroups were comparatively small. Nevertheless, we compared the group with symmetrical polyarthritis with the groups with oligoarthritis and predominantly spinal disease. Because many of the laboratory indices reflect the total body burden of inflammatory synovium a meaningful comparison of these groups using these variables is not possible.
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1 Thompson P W. Laboratory markers of joint inflammation and damage. Br J Rheumatol 1987; 26: 83-5.

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