warranted. The findings of this study, taken alongside our previous work, suggest that the association between gout and OA is mediated by local mechanical factors rather than systemic or genetic factors.

**Rheumatology key message**
- OA influences local MSU crystal deposition but does not appear to be a risk factor for the development of gout per se.

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How much of what we do as doctors is *iatrocebo*?

**Iatrocebo** derives from the Greek *iatro* meaning ‘physician, medicine or treatment’ and *placebo* meaning ‘an inert substance given as a medicine for its suggestive effect’. *Iatrocebo* is defined as ‘an observed therapeutic effect erroneously put down to an evidence-based medical intervention’.

The lady in question presented with an unusual pain syndrome with no clear diagnosis nor successful treatment plan. She was guardedly pleased to see me. I asked her what specifically she had thought had been helpful from our unified approach. Was it the listening? Was it the ‘coping strategies’? Was it the tablets? No, she sheepishly replied. She had not found any of that in the blindest bit useful. In fact, she had occasionally found us annoying as we had got in the way of her vet’s appointments. The truth, she said, was that she had bought a cat who had unconditionally loved her from the time she brought it home. She in turn cared deeply for it and loved it back. She found the confidence to practise her piano and had eventually got better.

As a doctor, I reflected on the number of patients ‘healed’ by my evidence-based interventions. But how many times had the patient received other help without my knowledge? How many times had the patient not taken the tablets and yet not told me? How many times had the patient not taken the tablets and yet not told me? How many times had the patient received other help without my knowledge? How many times had the patient not taken the tablets and yet not told me? How much of what we do is iatrocebo?

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**Rheumatology key message**
- *A patient’s improvement erroneously thought to be due to medical intervention defines the neologism ‘iatrocebo’.*

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**Purified protein derivative reaction is not augmented in Behcet’s syndrome patients**

Sir, In a recent position paper about the emerging role of TNF-α antagonists in managing Behcet’s syndrome (BS), the importance of screening BS patients for latent tuberculosis before starting treatment with these agents has been emphasized [1]. This is especially important since in geographies where BS is endemic, the prevalence of tuberculosis is also relatively high. Guidelines recommend screening all patients with a tuberculin test and chest X-ray before starting treatment with TNF-α antagonists [2]. Case reports suggest that false positive results can be obtained with the tuberculin test due to the pathergy phenomenon observed in BS patients [3, 4]. However, this has not been formally surveyed.

During a recent study, in which we looked at the effect of infliximab on the tuberculin test [5], we had included 82 BS

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patients, 81 infliximab naive RA patients and 47 healthy subjects as controls. At the same time and apart from the purposes of that study, we also had done a pathergy test in those subjects who agreed to participate, with the aim of determining the effect of the pathergy phenomenon on the response of BS patients to the tuberculin test. Informed consent was obtained from all subjects. The study was approved by the ethical committee of Istanbul University, Cerrahpasa Medical School.

Eighty BS and 61 RA patients and 38 healthy controls participated. The tuberculin test was administered with the Mantoux technique, using 5 IU of purified protein derivative (PPD) solution, which was injected intradermally into the forearm by a nurse. The pathergy test was done at three sites on each forearm by inserting six sterile 20-gauge needles intradermally, on the same day as the tuberculin test. Both the tuberculin test and the pathergy reaction were evaluated 48 h later, by two independent observers in a blinded manner. Subjects put their arms through a curtain and their hands were covered to prevent the observers from recognizing the subjects, or any deformities revealing the diagnosis. PPD reaction was evaluated by measuring the transverse diameter of the induration. A positive pathergy test was defined as a papule or a pustule at the insertion site of the needle. The number of subjects with a positive PPD test (≥10 mm) in each group was compared and the relationship between PPD positivity and the pathergy phenomenon was sought.

The number of patients with a positive pathergy reaction, a positive PPD test and the mean PPD induration of each group are shown in Table 1. The mean diameter of the PPD induration was lower among RA patients \((H_{\text{Mann–Whitney}} = 20.1, P < 0.001, \text{Kruskal–Wallis})\) when compared with BS patients and healthy controls. The mean indurations in BS patients and healthy controls were similar \((H_{\text{Mann–Whitney}} = 2.0, P = 0.163, \text{Kruskal–Wallis})\). Inter-group comparisons revealed that mean PPD induration was similar among BS patients and healthy controls \((\text{Mann–Whitney } U = 1207, P = 0.163)\). PPD indurations in both BS patients and healthy controls were higher than in RA patients \((\text{Mann–Whitney } U = 1595, P < 0.001\) and Mann–Whitney \(U = 568.5, P = 0.001, \)respectively).

The number of patients with a positive PPD test was also lower among RA patients than the other two groups \((\chi^2 = 19.246, P < 0.001)\). Inter-group comparisons showed that the frequency of PPD positivity was similar among BS patients and healthy controls \((P = 0.2)\), and higher in both BS patients and healthy controls when compared with RA patients \((P = 0.002\) and \(P < 0.001\), respectively).

Then, we looked at the association between having a positive pathergy test and the size of the PPD reaction. The mean PPD induration was similar among BD patients with a positive pathergy test and among those with a negative test \((9.8 \pm 7.1 \text{ mm} v. 11.9 \pm 7.7 \text{ mm}; P = 0.316)\). The number of patients with a positive PPD test was also similar among BS patients with and without a positive pathergy reaction \((12/18, 67\% \text{ vs } 38/62, 63\%; P = 0.79)\). Forty-seven of the BS patients were using immunosuppressive drugs such as AZA and CsA. The frequency of a positive PPD test was not different between the patients who were receiving immunosuppressives and those who were not \((30/47 \text{ vs } 21/33, P = 0.6)\). Similarly, the mean PPD induration was not different between those who were receiving immunosuppressives and those who were not \((11.3 \pm 7.5 \text{ mm} v. 11.5 \pm 7.5; P = 0.947)\).

The frequency of a positive pathergy test among BD patients was somewhat lower than previously reported [6]. The patients we included were patients who were being followed in our clinic for some time. This might have resulted in a lower frequency of pathergy positivity when compared with a newly diagnosed group of patients.

Our findings showed that the PPD reaction was not augmented among BS patients and its induration size was not affected by having a positive pathergy test.

Rheumatology key message

- The PPD reaction is not augmented in BS patients and it is not affected by the pathergy phenomenon.

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Occurrence of cold agglutinin disease in RA patient during etanercept therapy successfully treated with rituximab

Sir, Cold agglutinin disease (CAD) is characterized by the presence of cold agglutinins (CAs), directed against the I/i carbohydrate antigens on the surface of red blood cells (RBCs), causing haemagglutination and haemolysis [1]. Pathogenic CAs are generally of the IgM isotype and derive from monoclonal B-cell expansions [2], exclusively encoded by the VH4-34 segment of the rearranged heavy chain gene [3].

Chronic CAD is usually idiopathic, but it has been occasionally described in patients with autoimmune diseases such as SLE, RA, adult onset Still’s disease, SS, SSc or lymphoproliferative disorders [4, 5]. It has been shown that the primary form frequently represents a lymphoproliferative bone marrow disorder characterized by clonal expansion of B cells [4, 5]. Conventional treatment with corticosteroids, alkylating agents, immunosuppressive drugs, IFN-α or cladribine are usually ineffective in CAD [6]. Conversely, the chimeric monoclonal anti-CD20 antibody rituximab, that is currently used for the treatment of non-Hodgkin

<table>
<thead>
<tr>
<th>BS (n = 80)</th>
<th>RA (n = 61)</th>
<th>Healthy controls (n = 38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A positive pathergy test (%)</td>
<td>18/80 (23)</td>
<td>4/61 (7)</td>
</tr>
<tr>
<td>A positive PPD test (%)</td>
<td>50/80 (63)</td>
<td>21/61 (34)</td>
</tr>
<tr>
<td>Mean PPD induration (mm) (±S.D.)</td>
<td>11.4 ± 7.6</td>
<td>6.8 ± 7.1</td>
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