Karnataka and 258,998 from Maharashtra provinces. In some areas reported attack rates have reached 45% [2].

As there is no vaccine available [2] persons travelling to these epidemic areas should be given adequate advice on personal protection, measures to protect themselves against the bites of the mosquitoes that transmit the virus (including Aedes aegypti), which are active during the daytime.

To avoid mosquito bites:

- Wear full sleeve clothes and long dresses to cover the limbs;
- Use mosquito coils, repellents and electric vapour mats during the daytime;
- Use mosquito nets—to protect babies, old people and others, who may rest during the day. The effectiveness of such nets can be improved by treating them with permethrin (pyrethroid insecticide). Curtains (cloth or bamboo) can also be treated with insecticide and hung at windows or doorways, to repel or kill mosquitoes.
- Mosquitoes become infected when they bite people who are sick with chikungunya. Mosquito nets and mosquito coils will effectively prevent mosquitoes from biting sick people.

As explained earlier, given the strong links between the UK and the Indian subcontinent we feel the awareness regarding chikungunya needs to be increased both in the primary and secondary care setting.

The authors have declared no conflicts of interest.

R. YAZDANI, V.V. KAUSHIK

Lincoln County Hospital, Lincoln, UK
Accepted 23 January 2007

Correspondence to: Dr R. Yazdani, Lincoln County Hospital, Rheumatology Department, Greetwell Road, Lincoln LN2 5QY, UK. E-mail: raminyazdani@gmail.com


2 WHO publication—Chikungunya Fever, a re-emerging Disease in Asia—10th October 2006. Available from: http://www.searo.who.int/en/Section10/Section2246.htm

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Chikungunya fever—reply

SIR, We are grateful to Dr Yazdani and Dr Kaushik for their letter. Since the first outbreak in the Comoro Islands in early 2005, Chikungunya (CHIK) infection has spread to the remaining Indian Ocean islands and then to India [1, 2]. Therefore, while initially CHIK arthropathy was an isolated and rather rare disease, during the last months it has become a frequent arthropathy in travellers returning from these countries. This can create some diagnostic problems. During last year we have seen seven serologically confirmed cases of CHIK arthropathy.

According to Dr Yazdani and Dr Kaushik, features of CHIK arthropathy are quite typical making a clinical diagnosis possible. We summarized some features in Table 1, comparing them with those of reactive arthritis.

The authors have declared no conflicts of interest.

A. VOLPE, P. CARAMASCHI1, A. ANGHEBEN2, A. MARCHETTA G. MONTEIRO2, L. M. BAMBARA1, Z. BISOFFI2

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**Table 1. Clinical features of Chikungunya arthropathy and reactive arthritis**

<table>
<thead>
<tr>
<th>Country</th>
<th>Chikungunya arthropathy</th>
<th>Reactive arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial manifestation</td>
<td>India, Indian Ocean island</td>
<td>Any</td>
</tr>
<tr>
<td>Onset</td>
<td>Self-limiting fever with rash</td>
<td>Urthritis, enteralisity</td>
</tr>
<tr>
<td>Subacute</td>
<td>Symmetric polyarthralgia</td>
<td>Acute</td>
</tr>
<tr>
<td>Arthritis pattern</td>
<td>Wrist, ankle, hand, foot, knee, shoulder</td>
<td>Mono-oligo arthritis</td>
</tr>
<tr>
<td>Involved joint</td>
<td>Absent/mild</td>
<td>Knee, ankle</td>
</tr>
<tr>
<td>Signs of joint inflammation</td>
<td>Normal or slightly elevated</td>
<td>Marked</td>
</tr>
<tr>
<td>ESR/C-reactive protein</td>
<td></td>
<td>Markedly elevated</td>
</tr>
</tbody>
</table>

Sacro Cuore Hospital, Internal Medicine, 1University of Verona, Department of Clinical and Experimental Medicine and 2Sacro Cuore Hospital, Tropical Medicine, Verona, Italy
Accepted 1 February 2007

Correspondence to: Alessandro Volpe, MD, Department of Internal Medicine, Sacro Cuore Hospital, Via Semprebon 5, 37024 Negar, VR, Italy. E-mail: reumatologia@sacrocuore.it


2 WHO publication—Chikungunya Fever, a re-emerging Disease in Asia—10th October 2006. Available from: http://www.searo.who.int/en/Section10/Section2246.htm

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Histoplasmosis in a child with JRA on low-dose methotrexate

SIR, We read the interesting report of Hunstad et al. [1] that described a 7-yr-old girl who developed histoplasmosis while receiving low-dose methotrexate (MTX) to treat juvenile rheumatoid arthritis (JRA). Low-dose MTX is commonly used for treating patients with JRA or psoriasis and, when used without additional immunosuppressive agents, rarely has been associated with opportunistic infections. Only three cases of acute progressive disseminated histoplasmosis (PDH), each in adults receiving MTX for 4 months, 9 years and 17 years, respectively, have been reported in this setting [2]. In the current report, the authors describe a 7-yr-old with new onset JRA treated during a 3-month induction with prednisolone (0.26 mg/kg/day), naproxen and low-dose MTX. A febrile illness began ‘several days’ after completing a prednisolone taper and while receiving MTX. The authors conclude the manifestation experienced by their patient’s illness best fit PDH and that low-dose MTX was a predisposing factor. We believe the data do not support PDH and are most compatible with acute primary pulmonary histoplasmosis [3].

The presumptive diagnosis of histoplasmosis resulted from chest radiography that demonstrated an isolated pulmonary nodule and mediastinal adenopathy. Histopathological examination of affected lymph nodes showed necrotizing granulomas that contained giant cells and yeast forms compatible with *Histoplasma capsulatum*. The diagnosis was later confirmed by demonstrating seroconversion of complement fixation and immunodiffusion titers. Evidence presented to support PDH included, ‘persistent fever, splenomegaly, anaemia, elevated ALT and significant antigenuria in the setting of non-diffuse pulmonary involvement’. However, as noted by the authors, the defining feature of PDH is extrapulmonary dissemination of fungal infection that results from progressive fungal dissemination [1, 3]. This must be distinguished from the early, self-limited dissemination that almost uniformly accompanies primary pulmonary infection and that is aborted by the development of an adaptive cellular immune response to the fungus [3]. In the reported case, neither the laboratory nor radiographic evidence presented was suggestive of extrapulmonary infection. We believe that the low level *Histoplasma* antigenuria [4] of 3.5 units; (normal range <1 unit; Mira Vista Diagnostics, Indianapolis, IN, USA) was reflective...
of primary, rather than progressive, dissemination since transient antigenuria is found in 75–81% of patients with primary pulmonary infection [5]. Prolonged fever and mild anaemia, are common in primary pulmonary histoplasmosis. What were absent were more distinctive haematological features [6, 7] of PDH during childhood, including leucopenia, thrombocytopenia and coagulopathy. Blood cultures were negative as expected in all instances of acute pulmonary infection but in only 50% of PDH [5]. Neither isolated splenomegaly nor the minimally elevated ALT is predictive of PDH. Finally, the authors cite a reference [8] to establish the diagnosis of PDH using the definition, ‘...in the absence of extrapulmonary cultures, symptom duration has been used to distinguish disseminated disease from self-limited infections, which generally resolve within 14 days.’ Yet, this source predicated the use of this definition with ‘in addition to clinical progression, dissemination had to be documented by...histopathological sections showing yeast forms compatible with H. capsulatum from extrapulmonary tissues or extrapulmonary granulomas without visible organisms.’ [8]

We agree with the decision to use an antifungal agent to treat this infection, which we believe is most compatible with acute pulmonary histoplasmosis. However, since fever in this setting may last for 2–3 weeks and spontaneously resolve [9, 3]. It is uncertain whether the illness may have resolved with additional observation. We concur with the authors’ conclusion that opportunistic infections should be considered in febrile patients who are receiving low dose MTX. However, considering the frequency and extended durations with which patients are treated with this regimen, combined with the rarity of opportunistic infections caused by H. capsulatum, we believe the risk is extremely low.

LJW is the owner of MiraVista Diagnostics, a laboratory that performs the histoplasma antigen test.

M. B. KLEIMAN, L. J. WHEAT1, S. BOWYER2

Section of Infectious Diseases, 1MiraVista Diagnostics and Mirabella Technologies, Indianapolis, IN, USA and 2Section of Rheumatology, Department of Pediatrics, Indiana University School of Medicine

Correspondence to: M.B. Kleiman.
E-mail: mkleiman@iupui.edu


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RE: Histoplasmosis in a child with JRA on low-dose methotrexate

SIR, We appreciate the comments of Kleiman et al., which serve to clarify current thinking about the outcomes of Histoplasma acquisition, the interpretation of available laboratory studies, and the classification of infected patients. The diagnosis of Histoplasma infection in our patient is not in question. We further agree that our patient did not meet criteria for acute progressive disseminated histoplasmosis (PDH), as outlined by Kleiman et al. In fact, we took great care in the preparation of our report to avoid assigning the diagnosis of PDH to our patient. Her clinical course and laboratory data did suggest early dissemination and support our decision to offer antifungal treatment in the context of her underlying disease and its therapy. These distinctions should not distract from our conclusion that opportunistic infections should be considered in acutely ill patients receiving therapeutic regimens considered to be mildly immunosuppressive.

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DAVID A. HUNSTAD, ANTHONY R. FRENCH

Divisions of Infectious Diseases and Rheumatology, Department of Pediatrics, Washington University School of Medicine, USA
Accepted 30 March 2007
Correspondence to: Anthony R. French.
E-mail: french_a@kids.wustl.edu