9 months, while blood and bone marrow smears initially failed to reveal leukaemia.

Bone pain and arthralgias are common presenting symptoms of childhood leukaemia [3], often accompanied by fever and raised ESR. Interestingly, children with leukaemia who present with musculoskeletal symptoms often have low peripheral leukocyte numbers and few, if any, peripheral blasts [7, 8].

In conclusion, periodic fever accompanied by skeletal pain or profound anaemia should alert the physician to the possibility of underlying leukaemia.

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<th>Rheumatology</th>
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<td>Key message</td>
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<td>• Childhood ALL can present as periodic fever.</td>
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The authors have declared no conflicts of interest.

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Interaction between paracetamol and oral anticoagulants

Sir, Paracetamol is a well-tolerated analgesic that is frequently used as a first-line drug in numerous chronic painful diseases, such as osteoarthritis. Paracetamol interacts with certain drugs, including warfarin and some other oral anticoagulant drugs, and can increase prothrombin time. Thus, it has been recommended that the prothrombin time should be carefully monitored in patients taking warfarin sodium who subsequently begin high-dose paracetamol treatment [1]. In spite of this, many warfarin-treated patients are cotreated with paracetamol-containing products [2]. Two main hypotheses can be put forward to explain such a discrepancy. First, some physicians might not be aware of the potential interaction between these drugs as the potential interaction is not reported in some drug dictionaries, such as the French Vidal drug dictionary. Secondly, as the changes in the anticoagulant effect have generally been of limited clinical significance, physicians might consider the combination to be safe. However, physicians should be aware that paracetamol can lead to clinically significant anticoagulant instability. We report here a case of this under-recognized side-effect in a patient receiving fluindione for atrial fibrillation, for whom the anticoagulant response, usually well controlled, was disturbed by paracetamol therapy.

A 72-yr-old man was hospitalized in 2004 for a 2-day history of spontaneous skin haematomas and gingival bleeding. His medical history included diabetes mellitus, blood hypertension and a stroke due to atrial fibrillation in 2001. He had been treated with fluindione for 3 yr. The coagulation was stabilized and the daily dose of fluindione had been unchanged during the 6 months preceding hospitalization (15 mg). The international normalized ratio (INR) had last been determined 2 weeks earlier, with a satisfactory result of 2.3. Compliance with fluindione treatment was correct and no error in anticoagulant dose was detected. Alcohol intake was light to moderate and there were no biological signs of liver disease. On admission, physical examination revealed haematoma of the left arm, right forearm and right thigh. Oral examination showed gingival bleeding and haemorrhagic bubbles. On laboratory examination, the INR was 8. There was a major decrease in serum vitamin K-dependent coagulation factors, whereas other coagulation factors remained within normal limits. No anaemia or thrombopenia was noted and renal function was normal. Because the patient complained of an anterior pain of the right thigh, an abdominal CT scan was performed; it did not reveal any psoas haematoma.

A diagnosis of bleeding due to severe hypocoagulation was proposed. The search for causes of such severe hypocoagulation did not reveal any acute diarrhoea and there had been no change in vitamin K intake or voluntary diet. The patient’s regular treatments (glimepiride, ramipril and digoxin) were not known to interact with anticoagulant therapy and the daily doses had been unchanged recently. No medications had been introduced recently, except for paracetamol, which had been prescribed at the maximal dose (4 g per day) 10 days prior to hospitalization for knee pain. Paracetamol was withdrawn and intravenous vitamin K supplementation and vitamin K-dependent coagulation factors were given. The INR and prothrombin time returned rapidly to normal levels. After 6 days of hospitalization, the patient was discharged.

In our opinion, this unexpected elevation of the INR with haemorrhagic complications in a patient taking oral anticoagulants was due to an interaction between the usual anticoagulant...
treatment and paracetamol. The recent history was suggestive of such an interaction. No intake of another drug which could potentially interact with anticoagulants was found, and there were no other causes, such as a decrease in vitamin K intake, an acute illness or a change in anticoagulant dosage. Moreover, previous reports have suggested that paracetamol can sometimes interact with oral anticoagulants and lead to severe morbidity. In a case-control study evaluating 289 patients treated with warfarin, including 93 with excessive anticoagulation (INR > 6) compared with 196 controls with INR between 2 and 3, the consumption of paracetamol was significantly higher in patients with excessive anticoagulation, independently of other confounding risk factors [3]. Moreover, a dose-dependent relationship was observed between the weekly intake of paracetamol and the risk of anticoagulant instability. In a double-blind crossover study comparing paracetamol (4 g/day) and placebo in patients treated with stable warfarin doses, an increase of 100% or more in the prothrombin time was observed in one-third of the paracetamol-treated patients [4]. This effect was detected after 1 week of paracetamol intake and was maximal during the second week, with great interpatient variability. In the present observation, the oral anticoagulant was fluindione, while most studies have been conducted using warfarin. However, it is likely that the mechanism of paracetamol-induced increased INR is the same for both drugs—probably a decrease in carboxylation.

Numerous arthritic patients are cotreated with paracetamol and oral anticoagulants. Regarding the frequency of coprescription, in most cases the potential biological interaction does not lead to any clinical adverse effect. However, the present observation shows that this combination is not as safe as generally believed and can sometimes induce life-threatening hypocoagulopathy, and suggests that INR monitoring should be intensified in patients treated with oral anticoagulants to whom paracetamol is given.

**Key messages**

- That the association between paracetamol and oral anticoagulants can sometimes induce life-threatening hypocoagulation.

No conflict of interest has been declared by the authors.

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**A case of eosinophilic enteritis and rheumatoid arthritis**

Sir, Peripheral blood eosinophilia is a well-recognized finding in patients with rheumatoid arthritis (RA) and may be associated with increased disease activity or use of disease-modifying drugs [1, 2]. The relationship between tissue eosinophilia and RA is, however, unclear. We report here a case of eosinophilic enteritis (EE) in a patient with RA.

A 71-yr-old Indian woman presented with a 2-month history of worsening peripheral oedema, right iliac fossa pain and weight loss. She had two similar previous but milder episodes (4 and 6 yr before this presentation) which resolved spontaneously. She had a 10-yr history of seropositive RA and suffered from secondary Sjögren’s syndrome, hypothyroidism and vitamin B12 deficiency. Her medications included sulphasalazine, methotrexate, thyroxine, Calcichew D3 and vitamin B12. She was born in East Africa, has been resident in the UK for 42 yr and visits India and the Middle East frequently. Physical examination revealed bilateral pitting oedema of the thigh and right iliac fossa tenderness. Her RA was clinically inactive with no swollen or tender joints. There was no evidence of lymphenadenopathy, cardiac failure or other abnormal clinical findings.

Investigations revealed an iron deficiency anaemia (9.3 g/dl), peripheral eosinophilia (1.4×109/l; 17% of total white cell count), hypoalbuminaemia (17 g/dl), hypocalcaemia and hypo-gammaglobulinaemia. Electrolytes, transaminases, thyroxine and prothrombin time were normal. The erythrocyte sedimentation rate was 16 mm/first hour and the C-reactive protein 29 g/dl. Urinalysis revealed no active sediment or proteinuria. Analysis of tumour markers (CA-125, CA19-9, carcinoembryonic antigen, α-fetoprotein) and peripheral blood gene rearrangement were negative. Three separate stool cultures and serology for parasites were negative. A small bowel follow-through study showed irregularly thickened mucosal folds in the jejunum consistent with small bowel lymphoma, hypereosinophilic syndrome, Whipple’s disease or parasitic infections. Upper and lower gastrointestinal endoscopies and duodenal biopsy were normal. Enteroscopy showed patchy erythema in the jejunum but the biopsy was normal. An 111indium-labelled transferrin isotope scan demonstrated reduced retention of labelled transferrin, indicative of protein-losing enteropathy. Laparoscopy revealed a thickened proximal jejunum on palpation and a full-thickness biopsy was taken. Histology revealed a prominent mucosal and submucosal eosinophilic infiltrate accompanied by mild oedema. Small focal eosinophilic aggregates were also seen in the muscularis propria and subserosa (supplementary Figure 1; may be viewed in colour as supplementary data at Rheumatology Online). The villi were normal and no parasites were identified. There was no evidence of vasculitis or lymphoma. These features are those of EE of submucosal type. A diagnosis of protein-losing enteropathy secondary to EE was made. Her symptoms improved with frusemide, protein supplementation, calcium and vitamin D.

Investigations into previous laboratory data over the last 10 yr revealed fluctuating eosinophil counts (absolute levels...