(channelling) to patients with high risk for NSAID-induced gastrointestinal injury, with consequent increments in the prevalence of adverse digestive events (7). The prescription of COX-2 inhibitors to patients without risk for NSAID-induced digestive toxicity thus appears to be feasible in conditions of relative safety, and protective therapy with proton pump inhibitors or prostaglandin analogues is not usually recommended (8). However, it remains unclear whether protection of the digestive mucosa should be ensured when prescribing COX-2 inhibitors to patients with specific risk factors. Recent studies have partly challenged previous assumptions underlying the therapeutic rationale for development of selective COX-2 inhibitors. The constitutive expression of COX-2 has been demonstrated in normal digestive tissues, and this isoform can be further induced in proximity of ulcerative lesions, where it might contribute to repairing processes (9). As a consequence, the pharmacological blockade of COX-2 could hamper the mechanisms underlying ulcer healing (10). Overall, COX-2 inhibitors should be prescribed with caution to patients with specific risk factors for adverse digestive events, and revisions of current guidelines should be undertaken to allow a safer use of these drugs in all patient subgroups.

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Circadian profile of serum melatonin in patients with systemic sclerosis

Sirs,

Melatonin (MT) is secreted by the pineal gland, and is believed to be transduction of light exposure into the neuroendocrine system. A circadian rhythm of MT secretion is related to light-darkness exposure. MT modulates immune and endocrine functions (1).

Systemic sclerosis (SSc) is a disease characterized by immune, vascular and fibrotic abnormalities (2,3). *In vitro* studies revealed that low doses of MTexerted a stimulatory effect on fibroblast growth (4). SSc patients have sleep disturbances or depression, the disorders related to MT secretion (5). MT is known as free radical scavenger, and an increased level of free radicals in SSc patients was reported (6).

Nine women with definite SSc, aged 33.7 ± 1.9 yr, and 8 age-matched healthy women were investigated. All investigated subjects were kept at normal light exposure from 6.00 to 22.00. Serum MT was determined with direct RIAmethod.

A circadian rhythm of serum MTwas found in all investigated individuals. MT levels were lower in the SSc patients than in the controls, and AUC during 24 hr as well as during the light or dark period were significantly lower. Maximal MT values were found between 2.00-4.00. Mesor which reflected mean hormone level was shown to be 11.4 pg/ml in the SSc patients and 37.3 pg/ml in the controls (Table I).

The obtained data indicate for suppression of MTsecretion in the SSc patients without alterations in its circadian rhythm. Low MT may be primary or related to other endocrine abnormalities phenomenon (7-10). Further studies are needed.

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Table I. Circadian profile of serum melatonin in patients with systemic sclerosis and healthy controls.

Serum melatonin (pg/ml)	Systemic sclerosis	Healthy controls
8.00 hr	14.68 ± 5.57	33.36 ± 6.92*
12.00 hr	11.72 ± 3.26	30.63 ± 8.40*
16.00 hr	11.22 ± 3.53	28.57 ± 6.31*
20.00 hr	8.68 ± 3.26	28.63 ± 8.65*
22.00 hr	18.18 ± 4.63	42.52 ± 7.34*
24.00 hr	41.19 ± 5.10	75.11 ± 14.81*
02.00 hr	65.86 ± 6.84	89.53 ± 16.16*
04.00 hr	45.68 ± 4.21	62.99 ± 15.98*
06.00 hr	19.43 ± 4.23	36.56 ± 6.29*
08.00 hr	14.10 ± 4.89	34.00 ± 6.50*
AUC 24 hr-period	542.63 ± 45.77	1039.51 ± 189.16*
AUC light period	199.56 ± 28.29	505.17 ± 112.89*
AUC dark period	343.07 ± 31.43	534.34 ± 96.33*
Mesor (pg/ml)	11.4 ± 11.3	37.3 ± 14.5
Amplitude (pg/ml)	23.7 ± 16.2	24.3 ± 14.1
Acrophase (hr)	03 : 02	03 : 18

Statistical significance of the difference between the patients and controls. * $p < 0.001$

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Successful treatment of resistant Behçet's disease with etanercept

Sirs,

Behçet's disease (BD) is a chronic, inflammatory vasculitis characterized by oral and genital ulcerations, ocular and skin lesions, arthritis and neurological involvement (1). We report the case of a resistant BD patient who was successfully treated with etanercept.

A 32-year-old woman was admitted at the Rheumatology Unit of the L. Sacco University Hospital in December 2002 for polyarthritis involving the right wrist, left knee, right elbow, proximal interphalangeal joints of the fingers and metatarsophalangeal joints. She also reported an occasional headache. She had a history of recurrent oral and genital aphtous ulcerations, and papulopustular skin lesions (PPL) which started when she was 26 years old. Physical examination revealed a slight fever (37.1°C) and a blood pressure of 120/70 mmHg. She had lost 3 Kg during the last few months. Laboratory findings were as follows: haemoglobin 10g/dl, WBC 6.500 /mm^3, ESR 55 mm/h, CRP 2.8 mg/dl. The liver and the renal functions were normal.

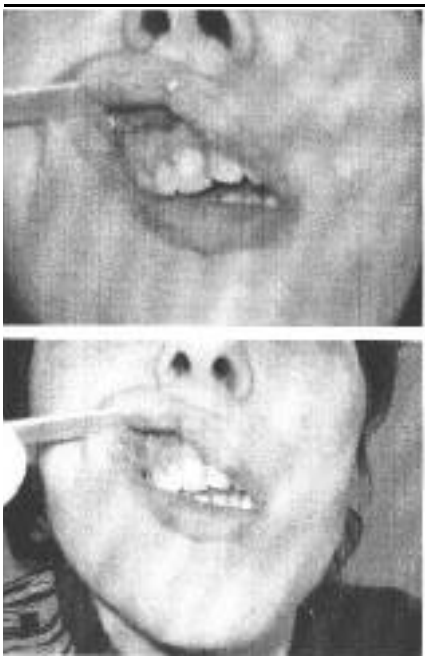

Fig. 1. Oral ulcers in a patient with Behçet disease before and after treatment with etanercept.

RF, ANA and anti-DNA antibodies were negative. Hepatitis B and C, cytomegalovirus, parvovirus B19 and HIV virologies were negative. Anticardiolipin and c and p-ANCA were negative. HLA-B51 was present. Pathergy was negative. Ophtalmological examination detected an anterior uveitis with hypopion. A radiography revealed narrowing of the joint space in the left knee and in the right elbow, erosive changes of the proximal interphalangeal joints, and bone destructive changes in the wrist. Sacroiliac joint involvement was negative.

The diagnosis of BD based on the International Study Group criteria for BD (2) was made and she was treated with oral prednisolone (10 mg/day), methotrexate (MTX) (15 mg/week), and anti-inflammatory agents (NSAIDs). The patient did not tolerate MTX. In April 2003 the disease was severely active. The patient presented with fever, oral ulcers, and polyarthritis; ESR was 99 mm/h, CRPwas 5.3 mg/dl. Prednisolone (25 mg/day) and cyclosporin A (CsA) (250 mg/ day) were introduced. The treatment was well tolerated by the patient and the corticosteroid dose was tapered.

Four months later the patient presented a PPL on the lower extremities and on the face. Three weeks later the patient presented with acne on the lower extremities, on the face and on the trunk, and oral ulcers. CsA was stopped. An improvement of PPL was observed, but in October 2003 the patient presented with a severe episode of oral and genital aphthae associated with polyarthritis. Treatment with prednisolone 25 mg/day was started. PPD test was negative and chest radiograph did not show any nodular infiltrates. Treatment with etanercept, 25 mg subcutaneously twice a week was started (3). After 4 weeks the lesions disappeared and the polyarthritis improved. At present the patient is in clinical remission (Fig. 1). The current therapy is: MTX (15 mg/week), steroids (7.5 mg/day) and etanercept 25 mg (2 sc weekly injections).

The joint symptoms in BD are present in 40-75% of cases of BD (4, 5). According to Vernon-Roberts *et al*. (6) and Nanke *et al*. (7) joint deformities and destruction have been reported in a few cases. In our case the patient had polyarthritis involving the right wrist, left knee, right elbow, proximal interphalangeal joints of the fingers and metatarsophalangeal joints. The treatment with NSAIDs, corticosteroids and MTX was started as a first-line therapy for BD. MTX is efficacious for arthritis, but this patient did not tolerate it. The patient was treated with CsA but a severe PPL associated with an episode of oral ulcers made it necessary to stop the treatment.

Treatment with anti-TNF-α may be useful for the oro-genital ulcerations of BD and for erosive arthritis (8,9). Our findings appear to be the first case in which anti-TNF-α is beneficial in the treatment of genital ulcerations and uncommon erosive arthritis (10).

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Can characterization by traditional Korean medical criteria help in our understanding of patients with rheumatoid arthritis ?

Sirs,

Traditional Korean Medicine (TKM) is an ancient discipline that classifies individuals with musculoskeletal problems using very different terms than Western medicine (1-3). TKM relies more on the clinician's reading of the patient's symptoms and signs with little attention to details of joint findings. The relationship between TKM diagnoses and Western concepts of rheumatoid arthritis (RA) have not been previously ex-