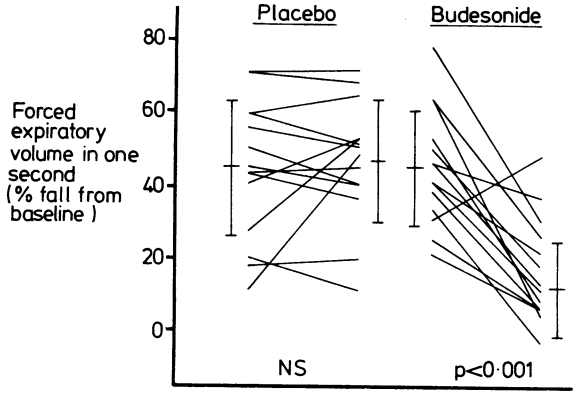
Patients, methods, and results

Sixteen children aged 8 to 15 (mean 10·9) years with perennial asthma were selected on the basis of >20% decrease in lung function after exercise. None had received corticosteroids within the past three months. Sodium cromoglycate was stopped 24 hours before the study and inhaled B_2 agonists eight hours before visits.

The study consisted of two three week treatment periods separated by a fortnight's wash out; during each treatment period participants received 200 μg budesonide aerosol twice daily through a 750 ml cone spacer or a placebo with a double blind randomised crossover protocol. Immediately before and at the end of each treatment period the children performed an exercise test and delivered a 24 hour urinary sample for analysis of cortisol. The exercise challenge consisted of five or six minutes of continuous running on a treadmill at individually adjusted, submaximal workloads. Heart rate was measured by radiotelemetry, and all subjects wore a nose clip during exercise. The absolute humidity was recorded.

Forced expiratory volume in one second was recorded on a dry spirometer (Vitalograph) before exercise (baseline) and three or five, 10, and 20 minutes after exercise. Results were expressed as the maximal percentage fall from the baseline value. Urinary cortisol was measured by radioimmunoassay. Two



Individual percentage falls in forced expiratory volume in one second induced by exercise before and after three weeks' treatment with budesonide aerosol and its placebo. Means (SD) are shown.

way analysis of variance and *t* tests for paired comparisons (two tailed, 5% level) were performed.

Fourteen children completed the study. Mean (SD) baseline forced expiratory volume in one second (% predicted) improved from 84 (17)% to 94 (16)% ($p<0·02$) during treatment; placebo showed no effect. Budesonide reduced the mean fall in forced expiratory volume in one second from 45 (16)% to 17 (14)% ($p<0·001$) (figure). No carryover effect from the treatment was detected after wash out. No significant changes occurred in the test conditions (absolute humidity, final heart rate, and workload). The mean 24 hour urinary free cortisol excretion was 94 (55) nmol/l (3·4 (2·0) μg/100 ml) and 116 (55) nmol/l (4·2 (2·0) μg/100 ml) before treatment and 96 (34) nmol/l (3·5 (1·2) μg/100 ml) and 85 (34) nmol/l (3·1 (1·2) μg/100 ml) after placebo and budesonide, respectively ($F=1·64$; df 3·44, NS). One case of hoarseness during budesonide treatment was the only side effect reported.

Comment

Budesonide given by inhalation for three weeks afforded significant protection against exercise induced asthma in most children without appreciable suppression of adrenal function. Improvement in baseline airway function cannot explain the effect of budesonide on exercise induced asthma.[4] Normal 24 hour urinary free cortisol excretion cannot exclude more subtle degrees of adrenal suppression.

The present results and the finding that the immediate reaction induced by allergen was blocked after a week's treatment with prednisone[5] show that regular steroid treatment attenuates some immediate asthmatic reactions. The pathogenesis of exercise induced asthma and the precise modes of action of steroids, however, are incompletely understood. It is generally accepted that the airway cooling that occurs during exercise initiates the bronchoconstriction, but the mechanism is unknown. The decrease in bronchial reactivity during steroid treatment might result from decreased mucosal inflammation, reflex activity, or mediator release.

Inhaled B_2 agonists are the most effective drugs against exercise induced asthma, though the duration of action of bronchodilators is short and the effect sometimes insufficient, especially in severe cases. Additionally, children often forget to use or refrain from using prophylactic medicine when necessary. The present results suggest inhaled steroids may be valuable in managing troublesome exercise induced asthma.

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Fatal exacerbation of systemic lupus erythematosus after treatment with griseofulvin

Most cases of systemic lupus erythematosus pursue a chronic relapsing course. Some drugs that are commonly prescribed and considered to be fairly safe can exacerbate existing disease, unmask a lupus diathesis, or produce a drug induced lupus syndrome. Awareness that drugs can adversely alter the course of systemic lupus erythematosus could prevent morbidity and death. We report a fatal exacerbation of systemic lupus erythematosus presumed to be due to griseofulvin.

Case report

A 22 year old woman with a six year history of systemic lupus erythematosus was admitted after one month of malaise, sweating, and fever. The diagnosis had initially been made on the basis of fever, lymphadenopathy, Raynaud's phenomenon, digital vasculitis, photosensitivity, and butterfly rash. Antinuclear and native double stranded deoxyribonucleic acid (DNA) antibodies were present in considerable but varying titres. She subsequently developed proteinuria. Renal biopsy showed focal proliferative glomerulonephritis; cerebral lupus was presumed to be present because of changes in personality; and an electroencephelogram showed diffuse slow wave activity. She was given maintenance treatment of prednisolone 7 mg on alternate days.

Over the month before admission her general practitioner had prescribed ampicillin and erythromicin for a presumed respiratory tract infection. Griseofulvin had been prescribed seven days before admission; although the precise amount was unknown, the total dose could not have exceeded 1 g.

On admission she looked unwell and had a fever of 38·7°C, pulse rate 110 beats/min regular, and blood pressure (supine) 120/100 mm Hg. Results of examination were otherwise normal with no cutaneous signs of systemic lupus erythematosus and no obvious source of sepsis. White cell count was $3·9\times10^9$/l, haemoglobin concentration 10·5 g/dl, and erythrocyte sedimentation rate 121 mm in the first hour; C reactive protein was absent, and blood, sputum, and urine cultures yielded negative results. Renal function, electrolyte concentrations, and results of a short Synacthen test were normal. Liver enzyme activity (aspartate transaminase, alanine transaminase, and γ glutamyl transferase) and bilirubin concentrations were normal, as was a chest *x* ray film. DNA binding was 41% (normal < 30%). She was presumed to have an exacerbation of her disease rather than infection, and prednisolone was increased.

On the second day in hospital she developed symptoms of a peripheral, sensory polyneuropathy and left lateral popliteal nerve palsy. Examination of cerebrospinal fluid showed a normal cell count and protein concentration. Results of gram staining and culture were negative. An intravenous bolus of methylprednisolone 1 g was given with symptomatic benefit. Further neurological signs did not develop, but nausea and a low intake of fluid necessitated intravenous fluids.

On the fourth day a further 1 g methylprednisolone was given for weakness. Objective and biochemical evidence of myositis was absent. Urea and creatinine concentrations had risen to 16 mmol/l (96 mg/100 ml) (normal 2·5-8·0 mmol/l (15-48 mg/100 ml)) and 180 μmol/l (2·0 mg/100 ml) (normal 40-130 μmol/l (0·5-1·5 mg/100 ml)) respectively. Intravenous fluids were increased to maintain a positive fluid balance.

The next day she developed fulminant small vessel vasculitis, which manifested as truncal livedo reticularis and florid butterfly rash. Despite further methylprednisolone ischaemia of the right hand and severe generalised myositis developed (creatine phosphokinase 8100 U/l, lactate dehydrogenase 800 U/l), and subsequent respiratory distress necessitated positive pressure ventilation. Her condition continued to deteriorate with progressive renal failure and digital gangrene despite further pulses of methylprednisolone 4 g daily and infusion of epoprostenol (prostacyclin). She died on day 10.

Comment

Drugs, infection, and sunlight are major precipitating factors of systemic lupus erythematosus; as no treatment has been shown to alter the course of the disease, management aims at treating symptoms and preserving function of the major organs. Avoidance of precipitating factors is therefore important.

The indication for griseofulvin in this case remains unclear. Exacerbations of systemic lupus erythematosus and unmasking of lupus diathesis have been reported after treatment with griseofulvin,[1-3] but the mechanism is unknown. Any drug administered to patients with systemic lupus erythematosus should be considered to be potentially harmful and treatment begun only if absolutely necessary.

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Detection of Chlamydia trachomatis in the vaginal vault of women who have had hysterectomies

Chlamydia trachomatis is thought to infect the columnar epithelium of the endocervix but not the squamous epithelium of the vagina.[1] After a report of chlamydial vulvovaginitis in a woman who had had a hysterectomy[2] we screened women who had had hysterectomies to determine the prevalence of *C trachomatis* in the vagina.

Patients, methods, and results

In the last three months of 1984, 17 women who had had hysterectomies attended the Praed Street Clinic. In addition to performing microscopy of Gram stained urethral and vaginal smears and dark ground microscopy of a wet smear from the vagina we collected urethral, vaginal, and rectal specimens for culture of *Neisseria gonorrhoeae* and took a smear from the vaginal vault to be examined for *C trachomatis* using a direct monoclonal antibody test (Syva).[3]

C trachomatis was detected in smears from four of the 17 women (table). All had had their ovaries conserved at hysterectomy, and serum follicle stimulating hormone and luteinising hormone concentrations of < 15 U/l confirmed that they were premenopausal[1].

At the next visit the women were examined colposcopically. Of the three who had presented with vaginal discharge, two (cases 3 and 4) had vaginal inflammation most pronounced in the vault, with a white mucous discharge. One patient (case 1) had been treated for gonorrhoea one week previously, and examination confirmed that her discharge had resolved. Four ulcerated areas were seen in the upper third of the vagina in case 2, from which herpes simplex virus was isolated in cell culture. No cervical remnants were present in any of the women.

All patients were treated with doxycycline 100 mg twice daily for seven days. The vaginal discharge in cases 3 and 4 resolved; repeat examination confirmed the absence of vaginitis, and tests for *C trachomatis* one and four weeks after treatment gave negative results.

The sexual partners of the patients were examined and tested for *C trachomatis* (table). The husband of one patient (case 2) had urethritis and was the only contact whose urethral smear was positive for *C trachomatis*. The husband of the patient in case 1 was being treated for gonorrhoea; although *C trachomatis* was not detected in his urethral smear, he subsequently needed treatment for postgonococcal urethritis.

Comment

Vaginal colonisation by *C trachomatis* in neonates results from maternal contamination during delivery.[4] It is generally accepted, however, that chlamydiae do not infect squamous epithelium. The report of chlamydial vaginitis in a postmenopausal woman with cervical carcinoma and an irradiated atrophic vagina was, therefore, surprising. No less surprising was our finding of chlamydiae in 24% of vaginal smears from otherwise healthy premenopausal women who had had hysterectomies. Hitherto such women have not been considered to be at risk of harbouring chlamydiae in the vagina. As we believe that our patients were an unbiased sample of our clinic population, we would expect further studies to find a similar prevalence.

Two patients had vaginitis, which resolved after antichlamydial treatment. Whether *C trachomatis* can truly infect the vaginal squamous epithelium and cause vaginitis, however, is uncertain. The organisms may have contaminated the surface of vaginal cells, having been derived from close anatomical sites—namely, the urethra, rectum, and Bartholin's glands—or from a sexual partner. Indeed, as a urethral rather than a vaginal specimen is more likely to be positive for *N gonorrhoeae* in women who have had hysterectomies[5] the prevalence of *C trachomatis* may have been underestimated in our study because other sites were not sampled. Nevertheless, the identification of *C trachomatis* in the vaginal vaults of women who had had hysterectomies is important for two reasons: firstly, the organisms may serve as a source of infection for the patients' sexual partners, and, secondly, they may cause symptoms in these patients. Sexually active women who have had hysterectomies should therefore be screened for vaginal chlamydiae, particularly as these may be eliminated by treatment.

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Details of women who had had hysterectomies in whom Chlamydia trachomatis was detected in the vaginal vault

Case No	Age (years)	Reason for hysterectomy	Presenting complaint	Concurrent infection	Sexual partners in previous three months
1	24	Pelvic tuberculosis	Vaginal discharge	Gonorrhoea	Husband had postgonococcal urethritis; 10 contacts untraceable
2	49	Fibroids	Genital ulceration	Herpes simplex	Husband had non-gonococcal urethritis; positive for *C trachomatis*
3	43	Sterilisation	Vaginal discharge		Regular boyfriend asymptomatic, negative for *C trachomatis*
4	44	Menorrhagia	Vaginal discharge, dyspareunia		Husband asymptomatic, negative for *C trachomatis*; casual boyfriend untraceable