various brands of related drinks in giving the history of sensitivity. Related drinks, sharing the responsible ingredient or ingredients, would probably produce a similar response. We believe that this is the first time that cola drinks have been shown to cause symptoms of asthma.

Whatever the mechanism, the clinical relevance of an increase in airway reactivity is clear. Moreover, this method of testing for food sensitivity in asthma by looking for changes in airway reactivity may have much wider implications. Common ingredients of a normal diet might possibly cause symptoms of asthma insidiously, by increasing airway reactivity. The frequency of ingestion and lack of a direct effect on airway function would make diagnosis difficult. As we have shown that pairs of challenges with histamine performed over short intervals are highly reproducible, looking at changes in sensitivity to histamine is a simple and effective method of testing for food intolerance in asthmatic subjects.

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SHORT REPORTS

Reversal of male-pattern baldness, hypertrichosis, and accelerated hair and nail growth in patients receiving benoxaprofen

Benoxaprofen is a non-steroidal anti-inflammatory drug used to relieve symptoms of rheumatoid arthritis and osteoarthrosis. Reported side effects include photosensitivity, onycholysis, urticarial rashes and pruritus, gastrointestinal ulceration and haemorrhage,[1] and the Stevens-Johnson syndrome.[2] We have reported the development of toxic epidermal necrolysis, leucopenia, and thrombocytopenic purpura[3] in a patient after nine days' treatment with benoxaprofen. We report here on five patients who developed hypertrichosis and accelerated hair and nail growth, two of whom showed reversal of male-pattern baldness.

Case reports

Case 1—A 75-year-old man had hereditary male-pattern baldness since he was 45. At the age of 32 he had developed ankylosing spondylitis, which subsequently affected his lumbar and cervical spine and sacroiliac joints. Treatment with benoxaprofen 600 mg daily gave symptomatic relief. Within a month of starting treatment he developed photosensitivity and onycholysis, which he overcame by using sunscreens and avoiding the sun. After five months' treatment he noticed growth of hairs over an area of scalp that he previously been devoid of visible hair, and on the dorsum of his fingers, hands, and forearms—areas that previously had never had visible hair. He also noticed accelerated facial hair growth. The density of new hair growth on the scalp was equal to that on the areas of his scalp that were not subject to balding. Growth of scalp hair continued when he took a reduced dose of 300 mg benoxaprofen daily.

Case 2—A 39-year-old woman had had rheumatoid arthritis for several years. Benoxaprofen 600 mg daily afforded good symptomatic relief. During the first month of treatment she developed a transient pruritic, erythematous papular eruption on the dorsum of her hands; this cleared within a week. After four months' treatment with benoxaprofen she reported an increased rate of growth of scalp hair. She then developed new hair growth on the dorsum of fingers and toes, areas that had been before hairless to the naked eye. This persisted with benoxaprofen treatment. At no time did she describe photosensitivity or develop onycholysis.

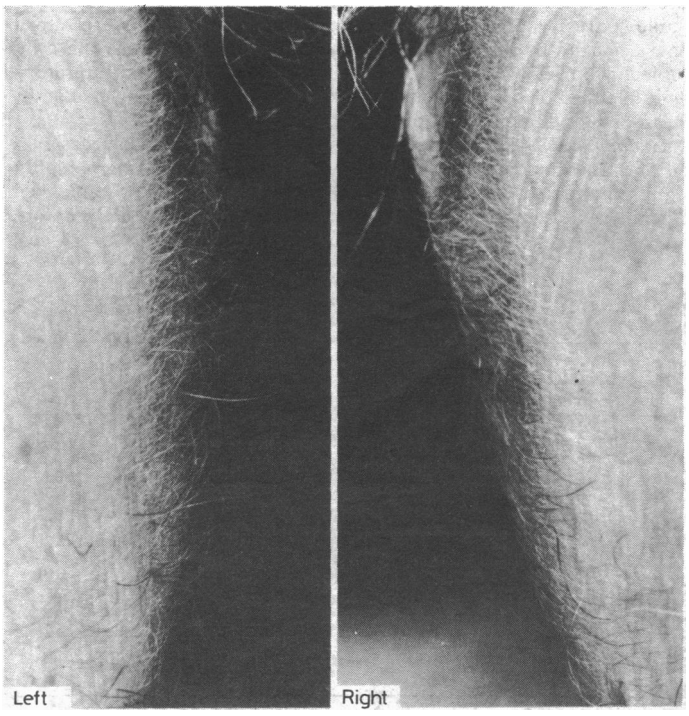
Case 3—A 70-year-old woman with longstanding osteoarthrosis was treated with benoxaprofen 600 mg daily, which afforded an improvement in her symptoms. During the first two weeks' treatment she described photosensitivity on exposure to the sun. After three weeks' treatment she developed a growth of downy blonde hair over her face (figure), limbs, and trunk. The hypertrichosis regressed soon after she stopped taking benoxaprofen.

Case 4—A 70-year-old woman had had osteoarthrosis for about 20 years. Benoxaprofen 600 mg daily afforded good symptomatic relief. During treatment she developed photosensitivity on exposure to the sun. After one month's treatment she noticed a growth of fine blonde hairs on her face and later on her arms and legs. These areas had previously been devoid of visible hair. She continued taking benoxaprofen and the hypertrichosis persisted.

Case 5—A 45-year-old man had had hereditary male-pattern baldness since he was 40. At the age of 39 he had developed psoriatic arthropathy affecting his hands and wrists. He was treated with benoxaprofen 600 mg daily and gained considerable relief of symptoms. Within one month of starting treatment he had developed photosensitivity, which was successfully controlled by use of sunscreens. Onycholysis developed after two months' treatment. After nine months' treatment he noticed an increased growth of hair over the area of scalp previously lacking hair. He also reported an increased rate of growth of his finger nails. Treatment was reduced to 300 mg daily and the growth of new scalp hair and accelerated nail growth continued.

Comment

Hypertrichosis and accelerated hair and nail growth have not previously been described with benoxaprofen. All but one of the above patients had photosensitivity, and generally the new hair grew on sites exposed to sun. The hypertrichosis continued even when



Left and right cheeks of woman with hypertrichosis after benoxaprofen.

benoxaprofen damage was reduced; this may be due to a subclinical photosensitivity reaction, as occurs with onycholysis, which may not be associated with obvious sun sensitivity. It is not yet clear whether the hypertrichosis is simply secondary to the photosensitivity, as is seen in porphyria[4] and when alopecia areata is treated with ultraviolet B or psoralen-ultraviolet A, or whether a different mechanism is entailed, as in hypertrichosis associated with minoxidil.[5]

We thank Dr M Tobin and Dr W E B Preston for permission to report their cases.

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Haemophilus influenza type b resistant to both chloramphenicol and ampicillin in Britain

It is now standard practice to treat severe infections due to *Haemophilus influenzae* with either chloramphenicol alone or a combination of ampicillin and chloramphenicol. We describe a patient who twice became infected with a strain of *H influenzae* type b that was resistant to both ampicillin and chloramphenicol.

Case report

A 9-year-old boy was diagnosed in 1979 as having dermatomyositis, which was treated with prednisolone with a satisfactory initial response. To reduce his dependency on steroids, salicylates, sodium etidronate, and penicillamine were introduced sequentially, starting in January 1981. In April a calcinotic lesion medial to the left knee became infected and discharged pus.

Routine swabs were taken and treatment started with flucloxacillin 50 mg/kg 24 hours and fusidic acid 20 mg/kg 24 hours. *Staphylococcus aureus* sensitive to erythromycin, methicillin, gentamicin, co-trimoxazole, and cefuroxime but resistant to fusidic acid and penicillin, and *H influenzae* sensitive to erythromycin, gentamicin, and cefuroxime but resistant to ampicillin and chloramphenicol were isolated. Flucloxacillin was therefore stopped and intravenous erythromycin started. This caused painful phlebitis, and cefuroxime 56 mg/kg/day was substituted two days later. Intravenous antibiotics were given for a total of nine days. Flucloxacillin 40 mg/kg/day and cephalexin 40 mg/kg/day were given by mouth for a further 12 days. The treatment of his underlying dermatomyositis was then changed to daily high-dose prednisolone and weekly methotrexate because of progressive muscular weakness.

Six weeks after stopping antibiotics he had a general anaesthetic for insertion of grommets and simultaneous plastic surgery to repair a persistent skin defect over the left knee. One week later he developed pneumonia with production of purulent sputum. Chest radiography showed no acute changes. Sputum samples grew *H influenzae*, again resistant to ampicillin and chloramphenicol but sensitive to gentamicin. This was successfully treated with intravenous gentamicin and flucloxacillin. His general condition continued to deteriorate, however, and despite intensive treatment including plasmapheresis he died one month later.

Bacteriology—On both occasions the organism was initially identified as *H influenzae* by its morphological appearance when cultured on blood and chocolate agar. This was confirmed by its nutritional requirements of haeme and diphosphopyridine nucleotide (X and V factors). The isolate from the sputum was cultured on chocolate agar and then slide agglutination testing performed (Wellcome Foundation Ltd) which showed it to be serotype b. Beta-lactamase activity was shown by the method of McGhie *et al.*[1] The minimal inhibitory concentration was tested by the agar dilution method of susceptibility testing, which is not critically dependent on the inoculum (Adatab, Mast Laboratories Ltd). The minimum inhibitory concentration of chloramphenicol was 16 mg/l (control strain <2·0 mg/l) and that of ampicillin 32 mg/l (control strain <1·0 mg/l). All the other sensitivities were determined by routine antibiotic disc sensitivity testing (Mast Laboratories Ltd). The disc strength of cefuroxime was 30 μg.

Comment

Chloramphenicol-resistant, ampicillin-sensitive *H influenzae* was first reported from the United States in 1972.[2] In 1977 a child in Oxfordshire survived meningitis caused by *H influenzae* with the same antibiotic sensitivities.[3] In 1979, however, *H influenzae* type b resistant to both ampicillin and chloramphenicol caused an outbreak of meningitis in Bangkok in which three children died.[4] In the same outbreak one child with *H influenzae* type b meningitis was successfully treated with rifampicin and co-trimoxazole. The organism in our patient was sensitive to co-trimoxazole, and also to cefuroxime, which should be regarded as a therapeutic alternative when treating meningitis due to a similarly resistant organism as it penetrates adequately into the cerebrospinal fluid.[5] If this strain of *H influenzae* becomes more common the recommended antibiotic treatment for conditions such as epiglottitis and meningitis will have to be altered.

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Hypersensitivity to local anaesthetics: a direct challenge test with lignocaine for definitive diagnosis

Local anaesthetics hold a key position in medical and dental practice. When hypersensitivity (allergy) to them is suspected an accurate diagnosis must be established or a local anaesthetic found which the patient can take safely. Many tests have been advocated for this, but unfortunately, in-vitro tests have proved unreliable, and other procedures, such as nasal challenge and skin tests, have not been validated by controlled series. Indeed, in our own studies on skin testing with lignocaine a false-positive rate of one in four occurred among atopic subjects (unpublished observation).

We present here the details and results of a direct challenge test with lignocaine on eight patients with histories of hypersensitivity reactions attributable to this drug. Similar regimens have been reported[1 2] but mainly to evaluate a suitable alternative local anaesthetic to that suspected as an allergen. In our regimen a solution of lignocaine was administered in saline without preservative or vasoconstrictor, thereby avoiding any possible contribution from these substances.

Patients, methods, and results

Seven women and one man (aged 18-56 years) were investigated after one or more suspected reactions to lignocaine with at least one of the following features: swelling of the lips and cheek, urticaria, wheeze, severe dyspnoea,