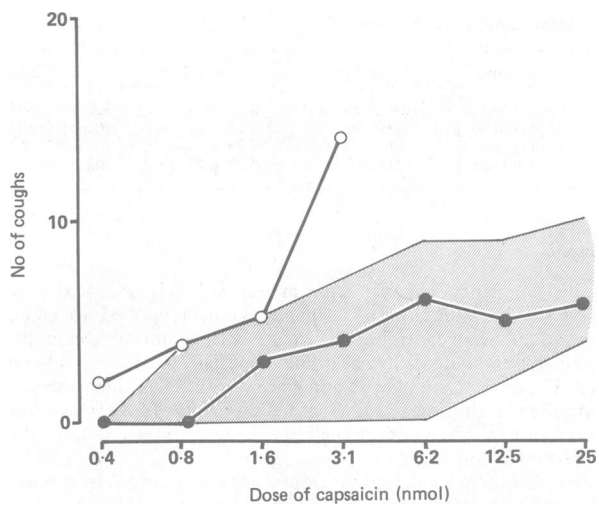
Methods and results

Fifty normal volunteers (21 women) (mean (SD) age 36 (18)) participated in the study, which was approved by the local hospital ethical committee. Five patients (two men) (mean age 60 (12)) had developed cough between one week and six months after starting treatment with either captopril or enalapril for hypertension (four patients) or heart failure. Two patients had stable asthma, which was being treated with inhaled steroids and β adrenoceptor agonists. In all patients cough subsided within one week of stopping treatment. Cough sensitivity to capsaicin was measured while the patients were still taking the drug and one week after treatment was stopped.

Capsaicin (0·01 M in absolute alcohol) was diluted with 0·9% saline to $1·9\times10^{-5}$ to $2·5\times10^{-3}$ M for inhalation. The subjects inhaled single breaths (0·02 ml) of 0·9% saline and all the capsaicin solutions in random order from a nebuliser controlled by a dosimeter (MEFAR, Brescia, Italy) unless the coughing became excessive. The subjects were unaware of the concentration of capsaicin in each inhalation. Coughs were recorded by a microphone connected to a mingograf recorder (Siemens-Elema AB, Solna, Sweden) running at 25 mm/s. The doses of capsaicin that caused two or more and five or more coughs were then calculated.

The figure shows the range of cough sensitivity in the 50 normal subjects. The



Ninety five per cent confidence interval (▒) of number of coughs caused by inhalation of capsaicin in 50 normal subjects and median number of coughs in five patients with cough related to angiotensin converting enzyme inhibitor during (○) and one week after stopping (●) treatment.

geometric mean (95% confidence interval) was 2·5 (1·2 to 3·8) nmol for the dose that caused two or more coughs and 7·7 (6·4 to 9·0) nmol for the dose that caused five or more coughs, and the median (range) maximum number of coughs was 7 (4 to 15). In all the patients the doses required to cause two or more coughs and five or more coughs were lower than normal (0·53 (0·38 to 0·74) nmol and 1·59 (0·75 to 3·36) nmol, respectively) and the maximum number of coughs was higher (median (range) 18 (15 to 20)) during treatment. These values returned towards normal when treatment was stopped, the doses required to cause two or more coughs and five or more coughs being 1·59 (0·75 to 3·36) nmol and 3·61 (1·32 to 9·88) nmol, respectively, and the maximum number of coughs decreasing to 8 (5 to 11).

Comment

Cough while taking angiotensin converting enzyme inhibitors may become a serious problem if the use of such drugs in patients with hypertension and heart failure continues to increase. The temporal relation between taking the drug and developing cough and the cessation of the symptom when treatment is stopped, as seen in all five of our patients, supports the diagnosis. Until now, however, diagnosis has relied on the exclusion of other causes, often by extensive investigations. This study is the first to show that cough associated with treatment with angiotensin converting enzyme inhibitors is caused by an increased sensitivity of the cough reflex. The pathogenesis of this increased sensitivity may entail persistence of inflammatory mediators in the airways. Both bradykinin and prostaglandins are potential candidates. Increased bradykinin concentrations are unlikely to be the cause as another angiotensin converting enzyme inhibitor, ramipril, did not alter the bronchoconstrictor response to bradykinin[4] and bradykinin, unlike prostaglandin D_2,[5] does not alter bronchoconstrictor responsiveness. The cough during treatment with angiotensin converting enzyme inhibitors is caused by an increased sensitivity of the cough reflex, though the cause of this remains obscure.

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Mania induced by biochemical imbalance resulting from low energy diet in a patient with undiagnosed myxoedema

We report a case which is of clinical interest because of the coincidence of two rare features—namely, the occurrence of mania in a patient with myxoedema and the precipitation of mania by biochemical abnormalities resulting from a stringent reducing diet.

Case report

A 68 year old man was referred with a three week history of overactivity, sleeplessness, and damaging household objects. One week before onset he had been seen as an outpatient and prescribed a reducing diet of only two pints (1140 ml) of whole milk a day (3·2 MJ; 760 kcal) and nothing else. A home visit was made, and he was found naked and racing around his home in ceaseless activity. In conversation he was friendly but irritable. He showed flight of ideas and pressure of speech. He made puns and jokes. There was no clouding of consciousness, and he was fully oriented. There were no paranoid ideas or hallucinations. His mood was elated, though he retained insight, which is unusual in mania, and he agreed to immediate hospital admission.

He was married with three adult children and had retired three years previously. His family described him as normally a reserved, quiet man who took his responsibilities very seriously. He had never before needed psychiatric help, but three years previously when he had had a hernia operation he had become restless and had slept badly for a few days. His sister's son suffered from manic depressive illness. The patient had been hypertensive for several years and been taking atenolol and diazoxide as maintenance treatment. (After retirement he had gained 12·7 kg in weight.) One month before psychiatric referral, however, he had been seen by a physician because of bradycardia and hypertension and it was noted that his blood pressure was 170/100 mm Hg with bradycardia considered to be due to the atenolol. This was changed to nifedipine 20 mg twice daily, and he was advised to follow the diet described above. Biochemical check immediately before starting the diet showed mild renal impairment (blood urea concentration 8·5 mmol/l (normal 3·0-6·7), plasma creatinine concentration 148 mmol/l (normal 45-120)).

Examination on admission showed dry skin, a pulse rate of 60/min, and blood pressure 130/80 mm Hg. Supinator and ankle reflexes were brisk with slow

Biochemical values on admission and at discharge

	Normal value	Value on admission	Value at discharge
Haemoglobin (g/l)	120-170	104	124
Urea (mmol/l)	3·0-6·7	11·7	8·6
Creatinine (mmol/l)	45-120	177	143
Urate (mmol/l)	<415	579	445
Alanine transaminase (IU/l)	<40	64	35
Aspartate transaminase (IU/l)	<40	155	51
Cholesterol (mmol/l)	3·6-7·8	7·7	—
Thyroxine (mmol/l)	60-160	16	31
Thyroid stimulating hormone (mU/l)	0·4-4·8	725	>25
Weight (kg)	64-73	85	78

relaxation phases. He was given plentiful fluids and nutritious food and sedated with haloperidol 5 mg eight hourly. Within 48 hours his mental state was much improved and regular sedation was stopped. In view of the hypertensive heart disease thyroxine replacement was started cautiously—25 μg on alternate days, increasing weekly by 25 mg on alternate days to 50 mg daily. Transaminase activities became normal within a week, but renal impairment persisted (see table).

The patient spent one month in hospital, during which his mental state settled gradually and was normal by the time of discharge without psychoactive drugs.

Comment

This case fits the criteria for mania listed by the *Diagnostic and Statistical Manual of Mental Disorders* (3rd edition) and the ninth revision of the *International Classification of Diseases*. The association of mania and myxoedema must be very rare, and we can find no other reported case.[1-5] The two usual psychiatric syndromes seen in myxoedema are, firstly, confusion and cognitive impairment resembling dementia, sometimes with clouding of consciousness; and, secondly, depressed mood with paranoid delusional ideas and often hallucinations.[1,2] Irritability and violence are reported only in association with paranoid cases.[2]

Our patient showed no psychiatric disorder until further metabolic disturbance was superimposed on his thyroid deficiency. After surgery he had a mental disturbance which may have been mild hypomania, which suggests that he may have been particularly susceptible to develop a mental disturbance from metabolic abnormality as an expression of his genetic predisposition indicated by the positive family history.

We thank Professor J T Silverstone for his help and advice in preparing this report.

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Faecal peritonitis induced by Picolax

We report a case of faecal peritonitis after the use of Picolax (sodium picosulphate) before barium enema examination. The cause was a perforated diverticulum of the sigmoid colon 10 cm proximal to an obstructive rectosigmoid carcinoma. We believe that this is the first report of faecal peritonitis after the administration of Picolax.

Case report

A 73 year old man was admitted to hospital complaining of abdominal pain of sudden onset that had become worse in the hour before admission. On examination the abdomen was distended, silent, and rigid. Blood pressure was 100/80 mm Hg and the pulse rate 120/min. An erect chest radiograph showed gas under both diaphragms. At laparotomy liquid faeces were found in the peritoneal cavity and the sigmoid colon proximal to an obstructing carcinoma of the rectosigmoid junction was perforated. There was moderate diverticular disease of the descending colon above the perforation. Hartmann's procedure and peritoneal lavage were performed. Histological examination of the resected specimen showed a moderately differentiated adenocarcinoma of the sigmoid colon and a perforated diverticulum 10 cm proximal to the carcinoma; there was spread to the lymph nodes. The intervening colon was reported as being normal. Postoperatively the patient developed septicaemic shock and renal failure, which failed to respond to treatment. He died three weeks later.

One month before admission the patient had attended the outpatient department complaining of diarrhoea and abdominal pain. He did not give a history of passing blood, and a rigid sigmoidoscopy to 15 cm did not show any abnormalities. A barium examination of the colon was planned for the day on which he was admitted. During the evening before admission he had taken two sachets of Picolax in preparation for the barium enema.

Comment

Carcinoma and diverticular disease are common disorders of the colon. Their diagnosis often depends on a barium enema or colonoscopic examination, which in turn depend on good preparation of the bowel. Picolax is a stimulant laxative containing sodium picosulphate and magnesium citrate that has been used for both barium and colonoscopic examinations with good results.[1,2] The perforation in this case was due to diverticular disease and was precipitated by Picolax and the distal obstructing carcinoma. Rose *et al* stated that Picolax should be used with caution in patients with potentially obstructive lesions or diarrhoea,[2] and we endorse this view. We would add that any patient suffering from diarrhoea or abdominal pain in whom a carcinoma is suspected should undergo flexible sigmoidoscopy before being given Picolax. If there are clinical signs of obstruction Picolax should not be used. In cases in which the bowel appears normal on flexible sigmoidoscopy we believe that Picolax should be given under medical supervision—that is, while they are in hospital for the ensuing examination.

We emphasise that Picolax is a safe and efficient means of colonic preparation. For its safe record to be maintained patients at risk must be preselected for careful assessment before it is used.

We are grateful to Dr J Burston for the histological examination and to Anne Reavley for secretarial help.

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Incidence of the premenstrual syndrome in twins

The premenstrual syndrome is a recognised clinical entity with both psychiatric and physical symptoms,[1] but its cause remains in dispute.[2] This study was instituted to determine whether a genetic factor is concerned.

Subjects, methods, and results

The premenstrual syndrome is defined as the recurrence of symptoms limited to the premenstruum with complete absence of symptoms for at least seven consecutive days in the postmenstruum.[2] Subjects were drawn from a premenstrual syndrome clinic run by KD, and all 108 index patients had completed a three month prospective menstrual chart that had resulted in a positive diagnosis of the premenstrual syndrome. There were 15 pairs of monozygous twins and 16 pairs of dizygous female/female twins; their zygosity was determined from their medical records after the diagnosis of the premenstrual syndrome had been confirmed. Controls with confirmed premenstrual syndrome and at least one sister were enlisted between May and October 1986. Siblings were regarded as suffering from the syndrome if they had received treatment for it and it had been confirmed by a menstrual chart. The female siblings of 68 (52%) of the subjects were interviewed, information on the remaining siblings being obtained from the subjects' personal knowledge or from correspondence. No twins or control siblings had been reared separately. Any previous medical and psychiatric illnesses in index subjects and in male and female siblings were also recorded. The data were analysed by the χ^2 test.

Among the 15 sets of monozygous twins both twin siblings suffered from the premenstrual syndrome in every case except one, whereas in the group of dizygous twins only seven of the 16 twin siblings suffered. The 77 controls had 121 female siblings, of whom 38 suffered from the syndrome. This gives a p value of $<0{\cdot}001$ for monozygous twins versus controls but no significant difference between dizygous twins and controls. The incidence of previous medical or psychiatric illness among twins, controls, and their siblings was similar.

Comment

Twin studies are a useful method of illustrating "horizontally" the genetic element of disease.[3] In the one monozygous twin pair in which only the index patient had the premenstrual syndrome she had started to suffer from it after the birth of the first of her two children, whereas her sibling was nulliparous.