Comment

The toxic shock syndrome was first reported in seven children in 1978[2]; in five of these *Staphylococcus aureus* was isolated from various sites. The occurrence of toxic shock syndrome in menstruating women was first reported in 1980[3]; since then 299 cases have been reported in the United States with 25 deaths.[4] About 95% of these cases have occurred in menstruating women, all of whom had been using tampons. *Staphylococcus aureus* has been isolated from vaginal swabs in more than 90% of cases; blood cultures are always sterile. Our patient had all the features of the toxic shock syndrome, and phage group 1 *Staph aureus* was isolated from her vagina and from the tampon she was using.

The occurrence of scarlatiniform rashes in staphylococcal infections is well known and many of the features of toxic shock syndrome occur in staphylococcal septicaemia; in toxic shock syndrome, however, the organisms have not been found in the blood stream. It has been postulated that staphylococci in the genital tract produce a toxin which causes the syndrome[4]; the nature of this toxin has yet to be elucidated. Because we saw her before the toxic shock syndrome had been associated with tampons, we did not attempt to see if the staphylococcus produced a toxin.

The risk of toxic shock syndrome may be reduced by using tampons intermittently rather than continuously during a menstrual period. The condition should be managed by intensive fluid replacement, and antistaphylococcal antibiotics should be administered after appropriate cultures have been obtained. It is recommended that women who have had an episode of toxic shock syndrome should not use tampons for several menstrual cycles.

I thank Dr H Pullen for permission to report this case admitted under his care.

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(*Accepted 4 November 1980*)

Department of Infectious Diseases, Seacroft Hospital, Leeds LS14 6UH
PAUL HOLT, MRCP, senior registrar

Theophylline and depression

The cerebral stimulant effects of the bronchodilator theophylline are well known. Nevertheless, we have recently seen two cases of severe depression with this drug, a paradoxical and unreported reaction.

Case reports

(1) A 19-year-old asthmatic girl (weight 48 kg) had theophylline 225 mg twice daily added to her standard regimen of inhaled salbutamol and beclomethasone because of increasing bronchospasm. Over a period of one month she unaccountably became depressed and irritable having previously had a stable personality. Her symptoms disappeared promptly on withdrawal of theophylline alone, but its reintroduction two weeks later for an exacerbation of bronchospasm precipitated a further episode of profound depression. Stopping the drug again relieved the symptoms.

(2) An 11-year-old asthmatic girl (weight 31 kg) with eczema and dyslexia was admitted to hospital. Since treatment with salbutamol, beclomethasone, and disodium cromoglycate inhalation was insufficient she was started on theophylline 225 mg twice daily. She was discharged one week later. Shortly afterwards she became acutely depressed, had frequent episodes of crying, and on one occasion admitted to "wanting to take all the tablets and finish everything." Again, no exogenous cause could be identified and after theophylline was stopped her depression disappeared immediately.

Comment

These two cases suggest a paradoxical depressive reaction induced by theophylline. The absence of premorbid depression, the temporal relationship of the onset of symptoms to starting theophylline, their prompt disappearance when it was stopped, and (in the first patient) their return with the reintroduction of theophylline suggest a cause-and-effect relationship. Paradoxical reactions to central nervous depressants are well known and are attributed to selective depression of inhibitory neuronal systems or initial transient release of excitatory transmitters,[1] but we found only one allusion to stimulant-induced depression. This was an authoritative but unreferenced statement that the "CNS excitation produced by large amounts of caffeine is followed by depression."[2] There is considerable experimental evidence that xanthines promote the release of catecholamines from the adrenal medulla[3] and peripheral adrenergic nerve endings.[4] The occurrence of such neurotransmitter depletion in the central nervous system of susceptible individuals could explain the theophylline-induced depression in our patients. Neural catecholamine exhaustion is the basis of Jacobsen's widely accepted hypothesis[5] on the aetiology of depression.

The paradoxical reaction seen in our two patients is obviously uncommon, but clinicians should be aware of it as a possibility in unexpected depression in a patient taking theophylline.

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(*Accepted 24 September 1980*)

Medical Professorial Unit, University College Dublin, St Vincent's Hospital, Dublin 4
MICHAEL B MURPHY, MB, MRCPI, medical registrar
AILEEN DILLON, MB, medical intern
M X FITZGERALD, MD, FRCP, professor of medicine

Controlled trial of bladder drill for detrusor instability

We report a controlled trial of inpatient bladder drill for detrusor instability. Sixty women participated and results were assessed both subjectively and by repeat urodynamic studies.

Patients, methods and results

Sixty women aged 27-79 with urinary incontinence due to idiopathic detrusor instability diagnosed by pressure-flow studies entered a clinical trial of bladder drill. None was taking a drug known to affect urinary tract function or had coexisting genuine stress incontinence. Cystoscopy and urethral dilatation were performed under general anaesthesia to exclude local disease and measure bladder capacity. Each patient was then allocated at random either to inpatient bladder drill or to serve as a control; controls were advised that they should now be able to hold their urine for four hours, be continent, and allowed home. All patients were reassessed clinically and by repeat pressure-flow studies after three and six months.

Symptoms of patients before and six months after treatment

Symptoms	Bladder-drill group (n = 30)		Control group (n = 30)	
	Before	After	Before	After
Diurnal frequency ..	30	5	30	23
Nocturnal frequency ..	27	3	25	20
Urgency	30	4	30	23
Urge incontinence ..	30	3	30	23
Stress incontinence ..	21	3	20	16

We use the following bladder drill in our unit. (1) The rationale is explained. (2) The patient is instructed to pass urine at specific intervals

during the day (usually every one and a half hours) and must not do so earlier: she must either wait or be incontinent. We ignore the frequency of micturition at night. Once she has reached her target the interval is increased by half an hour daily until she is voiding four-hourly. (3) We encourage the patient to maintain her usual fluid intake and keep a fluid-balance chart. (4) We introduce the patient to someone successfully treated by the drill.

The table lists the symptoms of the 60 patients both before and six months after treatment. The groups were well matched for age, parity, duration of symptoms, and history of gynaecological and urological operations. Bladder capacity measured under general anaesthesia was 650 ml or more in all patients.

After treatment 27 of the 30 patients practising bladder drill were continent and 25 symptom free, whereas only seven of the 30 controls were both continent and symptom free. These results were significant for all symptoms ($p < 0.01$). The mean duration of stay in hospital after cytoscopy was 6·3 days (range 5-13). In no case did the symptoms subside without the cystogram reverting to normal, or vice versa, and only one patient relapsed after apparently successful bladder drill (at four months). The cystometrograms of patients who remained incontinent were closely similar before and after operation.

Comment

Treating detrusor instability with drugs is unsatisfactory, side effects being reported in up to 43% of cases and the cure rate being generally less than 60%.[1] Prolonged cystodistension cured 9% of cases in one series[2] yet 80% in another[3] and carries the risk of bladder rupture, while biofeedback, with a success rate of 81%,[4] is time consuming.

Bladder drill is a simple, effective treatment without side effects. For the best chance of success it should be conducted in hospital, away from the patient's home environment. The mode of action is presumably psychological, encouraging confidence, and its cure rate in an uncontrolled trial was 82·5%.[5] Our 23·3% cure rate after cystoscopy and urethral dilatation may represent a placebo effect. During this trial we omitted all drugs other than night sedation, but in clinical practice bladder drill could be augmented by drug treatment. We conclude that bladder drill is the treatment of choice for detrusor instability in women.

Requests for reprints should be sent to Dr G J Jarvis.

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(*Accepted 1 October 1980*)

The Jessop Hospital for Women, Sheffield S3 7RE

G J JARVIS, FRCS, MRCOG, senior registrar in obstetrics and gynaecology
D R MILLAR, FRCS, FRCOG, consultant obstetrician and gynaecologist

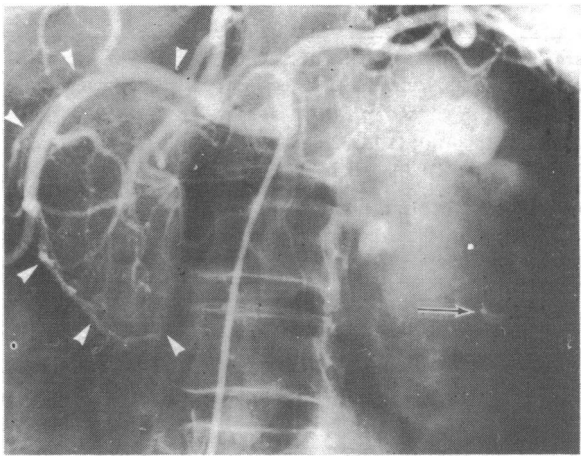
A renal vipoma

Renal tumours are not usually manifested by the watery diarrhoea-hypokalaemia-achlorhydria syndrome.[1 2] Only one renal tumour secreting gastrointestinal hormones has been reported.[3]

Case report

A 64-year-old woman with treated thyrotoxicosis and longstanding goitre presented in February 1979 with watery diarrhoea for three months. She had not lost weight and denied other symptoms. Findings on examination and sigmoidoscopy were otherwise normal, as were barium enema appearances, thyroid function values, full blood count, and renal and liver function values. Small-bowel barium meal showed an increase in jejunal diameter and thickness of mucosal folds, and xylose absorption was abnormal (14% excretion in five hours). In October she was admitted with an exacerbation of her diarrhoea, epigastric pain, and vomiting. She was dehydrated, hypotensive, and in fast atrial fibrillation. Serum potassium concentration was 2·1 mmol (mEq)/l. Despite intravenous fluids she deteriorated, passing 6 l watery diarrhoea daily and having 5·7 l alkaline fluid (pH 7·5-8·0) aspirated daily from her stomach. She became clinically acidotic (arterial pH 7·2), and serum potassium concentration fell to 1·9 mmol/l. Paralytic ileus developed.

In view of a clinical diagnosis of watery diarrhoea-hypokalaemia-achlorhydria syndrome treatment with steroids, intravenous fluids, and potassium supplements was instituted. Pancreatic angiography (figure) showed an expanded hypervascular pancreatic head with vessels of irregular calibre and a prominent venous blush. Calcification in the region of the left kidney was seen, and a left renal arteriogram confirmed a tumour at the lower pole. Radioimmunoassay disclosed grossly raised plasma concentrations of vasoactive intestinal polypeptide (over 400 pmol/l (13·2 pg/100 ml); normal below 30 pmol/l (1 pg/100 ml) and pancreatic polypeptide (over 1000 pmol/l (42 pg/100 ml); normal below 100 pmol/l (4·2 pg/100 ml)). At laparotomy an enlarged, firm pancreas was seen, with no tumour palpable. Multiple biopsy specimens from throughout the gland showed no evidence of adenoma or islet-cell hyperplasia at frozen section. The head and body were resected, leaving the tail in situ. The tail lifted easily off the left kidney, disclosing a large intracapsular tumour at the lower pole. Left nephrectomy was performed. Vasoactive intestinal polypeptide concentrations in portal and peripheral venous blood were similar, while there was a threefold increase in blood from the left renal vein.



Coeliac axis arteriogram showing expanded head of pancreas containing increased number of irregular calibre vessels (large arrows) and calcification in left kidney (small arrow).

Histologically the pancreas showed reduction in acinar and islet cells with increased fat and fibrosis (consistent with chronic pancreatitis), but no adenoma or islet-cell hyperplasia. The renal tumour was a typical malignant apudoma. The pancreas contained normal amounts of vasoactive intestinal and pancreatic polypeptides, somatostatin, and glucagon, whereas excessive quantities of immunoreactive vasoactive intestinal and pancreatic polypeptides were found in the renal tumour. Electron microscopy confirmed the presence of secreting granules 155-200 nm diameter, typical of vipoma.

The patient recovered well initially and her bowels returned to normal. Twelve days after operation, however, she developed septicaemia from a pancreatic abscess, from which she died. There was no residual tumour at necropsy, but the pancreatic tail had been destroyed by abscess.

Comment

Although this patient's symptoms were unequivocally the result of a functioning vipoma of the left kidney, we cannot exclude the possibility that this was a metastasis from an unrecognised primary lesion in the pancreatic tail. Such a tumour may metastasise while small enough to be overlooked at angiography and laparotomy. Nevertheless, the renal tumour was calcified, suggesting that it had been present for some time, and the patient's symptoms responded to its removal. A renal tumour producing enteroglucagon has been described,[3] and the presence of multiple pancreatic hormones in the tumour is not in itself evidence of a pancreatic origin.[4] The pancreas showed no evidence of the D-cell hyperplasia often seen in association with unrecognised adenoma.[5] A primary renal origin for this tumour therefore seems likely.

We are grateful to Dr C K Anderson and Dr J M Polak for the histological and histochemical reports; to Dr S R Bloom for hormone assays; to