Vaccinating a person with contraindications is justified only when exposure to smallpox has occurred.

Most countries requiring vaccination on entry will waive the regulations if there are contraindications, but this should first be checked with the relevant authority. A doctor's letter, preferably signed and stamped by a vaccinating authority, should then be issued for presentation to the health authority on arrival stating that vaccination is contraindicated for medical reasons.

If despite contraindications a patient must be vaccinated it should be carried out under cover of AVIG. So far as we know transplacental transmission of vaccinia virus has not been reported when this precaution has been taken. Had the simple precautions outlined in the *Memorandum on Vaccination against Smallpox*[2] been carried out the above cases might not have occurred. If those countries still requiring evidence of smallpox vaccination on entry were to abolish this requirement, however. the risks could be completely eliminated.

We thank Professor J Banatvala for helpful criticism and advice, and Professor J W Scopes and Dr B D R Wilson for permission to report these cases.

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(*Accepted 2 April 1979*)

SHORT REPORTS

Reversal of lactic acidosis associated with heart failure by nitroprusside administration

Since Taradash[1] reported the favourable effect of nitroprusside in idiopathic lactic acidosis, no further confirmation of this therapeutic approach has been reported. We describe here another patient with severe lactic acidosis who responded dramatically to nitroprusside.

Case report

A 76-year-old woman was admitted to hospital because of recurrent abdominal pain 15 years after cholecystectomy. She was known to suffer from heart failure and diabetes mellitus. On admission the patient was in shock with profound peripheral vasoconstriction. Her temperature was 37°C. Jugular vein distention, rales at lung bases, and upper abdominal tenderness were noted. Arterial blood disclosed a severe metabolic acidosis (see figure). Blood urea nitrogen was 15 mmol/l (42 mg/100 ml), glucose 8·9 mmol/l (160 mg/100 ml), serum amylase 1230 IU/l, and bilirubin 48 μmol/l (2·8 mg/100 ml). The anion gap was 39 mmol(mEq)/l and attributed to lactate excess.

After 132 mmol bicarbonate the blood pH rose to 7·28 and blood pressure to 120/80 mm Hg. Nevertheless, peripheral cyanosis diminished only very slightly and anuria persisted. Frusemide 80 mg and nitroprusside 0·5-1 μg/kg/min were administered. Peripheral cyanosis gradually disappeared, the skin became warm, polyuria ensued, the blood pH rose abruptly to 7·41, and the anion gap decreased to 20 mmol/l. The patient improved considerably and a few days later was discharged.

Three weeks later she was readmitted in a similar condition, again with considerable peripheral vasoconstriction and a large anion gap metabolic acidosis. Serum lactate concentration was 11·2 mmol/l (100 mg/100 ml). The administration of nitroprusside was again accompanied by a striking diminution of the peripheral cyanosis, an increase in urine output, and a progressive correction of the metabolic acidosis, without further administration of bicarbonate (see figure). Nevertheless, the serum lactate concentration took a further 24 hours to decrease to 2·2 mmol/l (20 mg/100 ml).

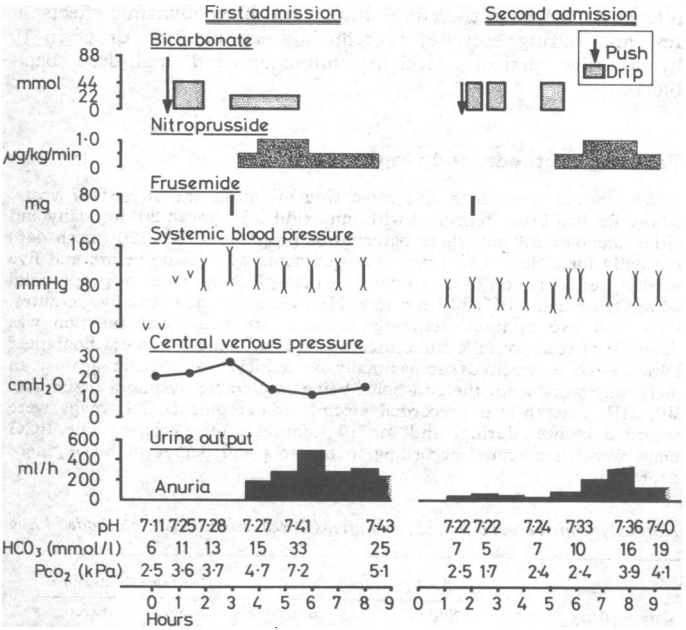
Despite haemodynamic improvement the serum bilirubin concentration rose to 428 μmol/l (25 mg/100 ml). Percutaneous transhepatic cholangiography showed marked dilation of the biliary tree. Owing to the patient's poor general condition an operation was not performed and the patient died.

Comment

Recurrent lactic acidosis in this patient was due to advanced heart failure with decreased peripheral tissue perfusion decompensated by pancreatitis and obstructive jaundice.[2] Further myocardial depression by acidosis precipitated circulatory collapse with extreme vasoconstriction, oligoanuria, and perpetuation of lactic acidosis.

By improving cardiac performance and tissue perfusion nitroprusside prevented intracellular anaerobic metabolism and allowed for a rapid reversal of lactate production. The ensuing complete correction of acidosis contrasted with the small changes in pH induced by the bicarbonate administered before nitroprusside, creating even a transient "overshoot alkalosis"[3] during her first admission.

The concurrent correction of metabolic acidosis with the administration of nitroprusside is surprising in view of the potentially increased production of lactate by cyanide.[4] Nevertheless, the repetition twice of a similar sequence of events and its resemblance to the events reported by Taradash[1] weigh heavily in favour of a cause-and-effect relationship.



Serial arterial blood gases and haemodynamic parameters before, during, and after treatment on first and second admission.

***Conversion:* *SI to traditional units*—HCO_3: 1 mmol/l=1 mEq/l. Pco_2: 1 kPa≈7·5 mm Hg.**

Interestingly, during the first admission the anion gap returned towards normal as soon as acidosis was corrected whereas in the last admission the serum lactate remained raised for several hours after the correction of acidosis. This lag period[5] may have been due to the onset of hepatic insufficiency on the second admission. On that occasion the liver may have failed to remove lactate efficiently from the extracellular space, although improved tissue oxygen delivery had already reversed intracellular lactic acid production.

These data support the concept that nitroprusside may be an important therapeutic agent in combating "overproduction" lactic

acidosis due to tissue hypoperfusion, such as occurs in advanced heart failure.

We are indebted to D Ben-Yshai and M Bassan for helpful advice.

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Reduction of beta-blocking drugs in hypertensive patients treated with minoxidil

Combining high-dose beta-blocking drugs with minoxidil has proved valuable in severe hypertension.[1] Brunner *et al*,[2] however, suggested that beta-blocking drugs may be reduced or even withdrawn in patients taking long-term minoxidil without loss of blood-pressure (BP) control or occurrence of reflex tachycardia. This might also be expected to improve left ventricular function and increase exercise tolerance. We have therefore studied the haemodynamic effects, at rest and during exercise, of reducing beta-blocking drugs in 10 hypertensive patients receiving minoxidil and high-dose beta-blockade.

Patients, methods, and results

We studied seven men and three women (mean age 56±SD 7 years) whose BP had been controlled with minoxidil 5-50 (mean 20) mg daily and either atenolol 200 mg (three patients) or propranolol 320-720 (mean 446) mg daily for at least two years. Measurements were made before and five weeks after reduction (over 10 days) of beta-blocking drugs to propranolol 40 mg twice daily. BP and heart rate (HR) were recorded after five minutes' lying and two minutes' standing. Resting left ventricular function was determined from systolic time intervals and "M"-mode echocardiograms.[3] Patients were exercised submaximally on a bicycle ergometer against an increasing work load, the end-point being intolerable dyspnoea or fatigue. BP, HR, and 16-lead precordial electrocardiographic (ECG) maps were recorded before, during, and for 10 minutes after exercise. The ECG maps were then scored according to the area and degree of ST-segment depression.[4]

In two patients BP rose sharply within five days after halving the dose of beta-blocking drugs and the original doses were restarted. In the remaining eight patients erect diastolic BP and HR rose significantly both at rest and during exercise (table). Resting left ventricular function, however, was not significantly altered, and neither maximum work capacity nor the duration of submaximal exercise was increased. New ST-segment depression was seen on the ECG maps of three patients at rest and in one further patient during exercise only. In this patient it was associated with angina pectoris. Maximum exercise HR and mean BP product, reflecting myocardial oxygen consumption,[5] was also significantly increased. (The dose of propranolol had to be increased to 160 mg daily in three other patients within 12 weeks after the initial reduction to maintain BP control.)

Comment

The increases in erect BP and HR, although small, suggest that despite prolonged control of the BP with minoxidil the baroreflex-mediated increase in sympathetic activity continues. The ischaemic changes on the ECG maps and the increased myocardial oxygen consumption are probably mediated by sympathetic overactivity, and relative myocardial ischaemia may account for the lack of improvement in left ventricular function. This in turn would limit exercise tolerance. Reducing the dose of beta-blocking drugs does not appear to confer any benefit to set against some impairment of BP control and the appearance of ischaemic ECG changes. These results do not support the findings of Brunner *et al*.[2] High-dose beta-blocking drugs should not therefore be routinely reduced in patients receiving long-term minoxidil treatment.

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Corrections

Respiratory influence on heart rate in diabetes mellitus

We regret that an error occurred in the paper by Dr G Sundkvist and others (7 April p 924). In the second sentence below the figure on p 925, "Diabetics with sensory neuropathy . . . were taking significantly more insulin" should be corrected to ". . . significantly less insulin."

Campylobacter enteritis associated with consumption of unpasteurised milk

In the paper by Dr D A Robinson and others (5 May, p 1171) Dr Edgar's initials should be W M and not W J.

Haemodynamic values before (1) and after (2) reduction of beta-blockade in hypertensive patients taking minoxidil

Case No	Beta-blockade* (mg)	Minoxidil (mg)	Blood pressure (mm Hg) Supine 1	Supine 2	Erect 1	Erect 2	Heart rate (beats/min) Supine 1	Supine 2	Erect 1	Erect 2	Maximum exercise blood pressure (mm Hg) 1	2	Maximum exercise heart rate (beats/min) 1	2	Maximum heart rate and mean blood pressure product 1	2	Duration of exercise (min) 1	2	PEP/LVET† (%) 1	2	Echo left ventricular ejection fraction (%) 1	2	Resting ST-segment depression (mm) 1	2
1	p480	15	150/92	245/170	168/93	174/124	52	57	62	66	Restarted on high-dose beta-blockade													
2	a200	50	144/95	195/116	150/100	166/118	64	66	74	72														
3	a200	5	152/98	143/98	133/89	149/102	72	80	74	82	176/100	194/120	115	143	14375	20375	7·0	9·0	36	34	56	58	0	0
4	p320	30	136/84	148/81	138/84	127/93	68	70	64	67	180/108	190/115	115	130	15180	18200	4·0	4·0	28	24	73	70	0	3
5	a200	15	141/77	143/98	131/79	146/98	54	64	69	80	190/94	224/118	105	133	13230	20349	6·0	7·0	24	31	57	48	3	4
6	p720	30	126/86	150/97	124/84	131/91	56	72	60	76	160/100	156/102	110	125	13200	15000	8·6	13·0	16	19	45	44	0	0
7	p480	10	131/85	125/85	116/76	128/80	65	82	66	85	120/70	160/100	90	95	7830	11400	3·5	3·8	35	41	62	64	0	0
8	p320	10	150/84	146/84	130/79	132/90	64	74	62	86	190/100	182/105	110	125	14300	16250	2·0	3·0	30	30	42	—	0	0
9	p480	15	148/88	155/105	146/90	149/103	66	80	74	80	198/100	188/120	95	110	13205	15620	3·0	2·0	27	30	69	63	0	0
10	p320	20	175/95	150/71	169/84	159/94	76	78	76	82	190/98	210/120	105	110	13440	15000	4·0	3·0	23	30	45	32	5	9
Mean	p446	20	145/87	145/90	135/83	140/94§	65	75	68	80	176/98	188/112§	106	120	13095	16569	4·8	5·6	27	30	56	54		
SE of mean			6/3	3·4	6/2	5·2	3	2	2	2	9·5	9·3	3	6	848	1167	0·8	1·5	3	2	5	5		
P‡			NS		§<0·002		<0·02		<0·002		§<0·005		<0·04		<0·01		NS		NS		NS			

*P = Propranolol. a = Atenolol.
†PEP = Pre-ejection period. LVET = Left ventricular ejection time.
‡Significance determined by Mann-Whitney U test. NS = Not significant.