Lactic acidosis occurring during phenformin therapy

A. M. Tomkins*
M.B., M.R.C.P.

R. Jones†
M.B., M.R.C.P.

Arnold Bloom
M.D., F.R.C.P.

The Diabetic Unit, Whittington Hospital, London, N.19

Summary
A case of severe lactic acidosis is described in a diabetic taking phenformin who was otherwise healthy. Substitution of metformin for phenformin did not lead to a recurrence of the lactic acidosis.

Case history
The patient was a 47-year-old woman who developed diabetes mellitus in 1965. She was initially controlled on chlorpropamide and phenformin. However, her diabetic control became less satisfactory and insulin therapy was substituted in October 1967. Subsequently her diabetes became unstable and phenformin 100-150 mg daily was added in November 1968. Since then her blood glucose levels have become more steady, but have been high, in the range 240-300 mg/100 ml. Glycosuria appeared occasionally but never ketonuria. She remained well until 30 June 1970 when she was admitted with a 2-month history of malaise, anorexia, weight loss and vague abdominal ache.

On examination she was febrile, not dehydrated and not in shock. Pulse, 72/min; BP, 110/70. Examination of her alimentary, cardiovascular, respiratory and nervous systems revealed no abnormality.

Investigations: Blood glucose, 55 mg/100 ml; Na+, 130 mEq/1; K+, 3.9 mEq/1; urea, 49 mg/100 ml. Astrup, pH 7.32; Pco2, 11 mmHg; plasma HCO3, 11 mEq/1; buffer base, 29 mEq/1; base deficit, -19 mEq/1. Blood lactic acid, 95.2 mg/100 ml (control 6.5 mg/100 ml) (Boehringer kit using u.v. method).

Phenformin was withdrawn and she was treated with intravenous sodium bicarbonate (1 l of 1.4% solution). Twenty-four hours after admission the blood lactic acid had fallen to 56.4 mg/100 ml. She continued to improve on conservative management and 2 weeks later the blood lactic acid was 10.6 mg/100 ml. She was discharged from hospital, and subsequently has been well-controlled on insulin and metformin, with no further episodes of lactic acidosis.

Discussion
Accumulation of lactic acid has repeatedly been shown to result in metabolic acidosis, often with fatal results (Huckabee, 1961). Many reports have described lactic acidosis occurring in diabetic patients taking phenformin (Tranquada, 1964). However, in the majority of these reported cases the lactic acidosis may well have occurred secondary to conditions associated with hypoxia, such as myocardial infarction (Iseri, Evans & Evans, 1963), haemorrhage (Lepage, 1946) or sepsicaemia (Waters, Hall & Schwartz, 1963). Lactic acidosis also has occurred in diabetics treated with other drugs in conjunction with phenformin (Daughaday, Lipicky & Rasinski).

It has been stated (Sadow, 1969) that lactic acidosis is unlikely to occur in patients treated with phenformin unless some other factor is present. In this case, the patient was not otherwise ill and was not on therapy other than phenformin and insulin. Finally, the substitution of metformin for phenformin did not lead to recurrence of lactic acidosis.

Acknowledgments
We are most grateful to Dr Dormandy and his staff for biochemical investigations.

References
Fertility following haematocolpos has rarely been studied. The following case in which unilateral haematocolpos, haematotracehlos and haematometrium was released by making an incision between the two vaginas provided a formerly occluded horn with a 'normal' horn of uterus to act as a control. Both were exposed to the same patient's ova and the same semen. It may be assumed, therefore, that implantation occurred in the more fertile horn.

Case report

On 29 May 1956, at 16 years of age the patient presented with a 2-week history of sharp, stabbing, intermittent lower abdominal pain radiating from the right to the left lower abdomen, recently more severe and accompanied by nausea and vomiting. There were no bowel or urinary symptoms. She had a regular 28-day menstrual cycle lasting 3-4 days. A firm, cystic mass which filled the whole pelvis was explored by laparotomy. On opening the peritoneal cavity, altered blood was seen on the right side. The cystic mass which filled the pelvis appeared to have both cornua of the uterus lying above it and both the Fallopian tubes leading from these appeared normal, though the right one was engorged. The ovaries were both normal. On vaginal examination the cystic mass bulged into the vagina anteriorly. Stale blood was aspirated from this and, on incision of the vagina, 30 fluid oz of stale blood drained. It could now be appreciated by using a uterine sound, that the cervix in the vault of the vagina communicated only with the left cornu of the uterus. Between this cavity (formerly occluded) and the right cornu there was a thin rim of cervix. A tube was temporarily stitched into the incision between the two vaginas. It was noted that the right kidney was absent and the left kidney hypertrophied.

Postoperatively an intravenous pyelogram confirmed absence of the right kidney with normal function on the left.

The patient was asked to attend again if marriage was envisaged.

* Present position and address: Hon. Clinical Assistant Welsh National School of Medicine.

**Pregnancy after haematocolpos**

F. A. Musson*

M.R.C.O.G.

At her next visit 6 years later she proved to be 30 weeks pregnant by dates, with a large foetus. At term the presentation was cephalic but the head high and, at elective lower segment Caesarean section, a live infant weighing 8 lb 1 oz was delivered. The pregnancy proved to be in the right horn of the uterus, the other horn being enlarged to the size of an 8 week pregnancy. The puerperium was uneventful.

A hysterosalpingogram on 2 April 1965 confirmed a uterus bicornis, bicollis with no communication between the horns of the uterus or cervixes. Both Fallopian tubes filled and were patent with free peritoneal spill.

In her second pregnancy in 1969 she had mild pre-eclamptic toxemia at 39 weeks gestation (blood pressure about 140/90 mmHg for 5 days and, once, a trace of albuminuria). She had a high cephalic presentation again. The pregnancy was confirmed to be in the right horn of the uterus at elective lower segment Caesarean section. The liquor was meconium-stained. The infant, which weighed 7 lb 9 oz at 39 weeks gestation, had an apgar score of 6 at birth, but did well. The placenta was heavily infarcted. After delivery she had a *Esch. coli* urinary infection which responded to sulphadimidine.

Her third pregnancy in 1970 was complicated by breech presentation and premature labour at 36 weeks gestation. Sparse, irregular contractions for 5 days culminated in spontaneous rupture of membranes releasing meconium-stained liquor. Lower segment Caesarean section was performed immediately. The child (weight 5 lb 15 oz) being found in the extended breech position in the right horn of the uterus.

The patient was sterilized by excision of both Fallopian tubes. Operative loss was replaced by two pints of blood. Mother and child thrived.

Comment

The case described is of uterus bicornis bicorpus bicollis in the classification of Hunter—one vagina was blind and formed a unilateral haematocolpos, haematotracehlos and haematometrium. After vagi-
Lactic acidosis occurring during phenformin therapy

A. M. Tomkins, R. Jones and Arnold Bloom

*Postgrad Med J* 1972 48: 386-387
doi: 10.1136/pgmj.48.560.386

Updated information and services can be found at:
http://pmj.bmj.com/content/48/560/386

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Notes**

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/