Preliminary Communications

Aldosterone Secretion in Magnesium Deficiency

Indications that aldosterone is closely linked with magnesium metabolism have existed since the first discovery of this hormone. In one of the first cases of primary aldosteronism reported, that of Mader and Iseri (1955), a very low serum magnesium was noted, and in the first case studied by Milne, Muehrcke, and Aird (1957) a low serum magnesium was also present and was restored to normal by removal of the aldosterone-secreting adenoma, the change being accompanied by a strong positive balance for magnesium.

The effect of aldosterone on magnesium metabolism thus revealed has been studied by Hanna and MacIntyre (1960) using rats as experimental animals. These workers showed clearly that in such animals aldosterone increased excretion of magnesium in both urine and faeces, and that this could lead to a severe depletion of muscle magnesium, the effect being more pronounced in adrenalectomized animals. That comparable phenomena occur in the human subject has been shown by Horton and Biglieri (1962). They infused D-aldosterone into an adrenalectomized subject and observed a marked increase in urinary magnesium excretion. This effect was promptly reversed by spironolactone. Urinary magnesium loss was also shown by these latter workers to be increased in cases of primary aldosteronism.

Since the original report of Mader and Iseri (1955), hypomagnesaemia has been found in other cases of primary aldosteronism, although it does not seem to be a usual feature. Horton and Biglieri (1962), for example, found practically normal figures for plasma magnesium in the five patients with primary aldosteronism studied by them.

With the link between aldosterone and magnesium metabolism clearly established, it becomes of interest to determine whether excess or deficiency of magnesium produced in other ways has an influence on the aldosterone secretion rate; whether indeed aldosterone responds to changes in magnesium metabolism in a way comparable to that which occurs with sodium.

Although hypomagnesaemia is not an uncommon occurrence in clinical medicine, suitable cases which are uncomplicated by other electrolyte disturbances are relatively rare. Some of the clinical conditions in which magnesium deficiency may be encountered have been ably reviewed by MacIntyre (1963).

We have had the opportunity to measure the aldosterone secretion rate in two patients with severe and chronic magnesium deficiency relatively free of other electrolyte disturbance, and to repeat the measurement after their magnesium stores had been replenished. The secretion rate method of Cope, Nicolis, and Fraser (1961) was used.

CASE REPORTS

Case 1.—A married man aged 61 was admitted to hospital with a diagnosis of hypomagnesaemia already made by his own medical attendant. The cause was believed to be chronic alcoholism, this addiction having been shown to lead to magnesium deficiency by Heaton *et al.* (1962). No evidence of steatorrhoea was found, but a mild malabsorption state was not completely excluded. Soon after his admission the plasma

magnesium was 0.3 mEq/l. on two separate occasions. Plasma sodium was 130 mEq/l. and remained unchanged throughout his stay in hospital. Plasma potassium was 2.9 mEq/l. at the time of admission, and gradually and steadily rose during the period of study to 4.0 mEq/l. During the period of severe magnesium deficiency the aldosterone secretion rate was 124 μ g./day, an entirely normal figure. Restoration of magnesium stores was effected both by oral supplement and by a final intravenous infusion of 144 mEq daily for three days. Five days after this extensive replenishment plasma magnesium had risen to a steady level of 1.2 mEq/l., plasma sodium was unchanged, and aldosterone secretion rate was now 172 μ g./day.

Case 2.—A married woman aged 48, who was admitted with a severe malabsorption state, was one of the instances of this condition associated with hypomagnesaemia reported by Booth *et al.* (1963). This malabsorption was due to extensive and repeated resections of small bowel for severe Crohn's disease. These resections started in 1945 and were repeated at intervals until 1949. She developed steatorrhoea, and in 1960 a fresh laparotomy revealed two blind loops with fistulae between ileum and transverse colon. A functional anastomosis of ileum to transverse colon was made. On later readmission in 1960 she was wasted and was experiencing tetany. She had a megaloblastic bone-marrow with only traces of vitamin B₁₂ in the plasma. On her admission to hospital her plasma sodium

Relation between aldosterone secretion rate and plasma magnesium.

was 143 mEq/l., plasma potassium 2.7 mEq/l., and plasma magnesium only 0.3 mEq/l. Soon after this time, when both sodium and potassium in plasma were normal, the aldosterone secretion rate was found to be 84 μ g./day on a day when plasma magnesium was still only 0.5 mEq/l. By the 21st day of admission the plasma magnesium had returned to the normal level of 1.4 mEq/l., and on the 36th day, with all three cation concentrations normal, the aldosterone secretion rate was 217 μ g./day.

The relation between plasma magnesium and aldosterone secretion rate in these two cases is shown in the Chart.

The final column of the Chart shows an aldosterone secretion of 168 μ g. in an otherwise normal subject whose elevated plasma magnesium was suspected of being due to self-administered magnesium sulphate.

DISCUSSION

In both these subjects the aldosterone secretion rate was found to be in the normal range at a time when magnesium deficiency was severe. After the replenishment of magnesium stores a slight rise in aldosterone secretion rate resulted in both patients, this being larger in the second than in the first. But in neither case was the rise to above normal limits, which in our hands are from 70 to 220 μ g. daily, with a mean of 129 μ g. From the purely teleological point of view, magnesium depletion might be expected to call for a reduction in the secretion of aldosterone. When aldosterone secretion is deliberately inhibited by administration of another sodium-retaining steroid considerably lower figures can be obtained. In

four of our patients treated with 9 α -fluorocortisol in whom a gain in weight resulted, the secretion rates fell to between 20 and 70 μ g./day, with a mean for the four of 45 μ g. In neither of the severely magnesium-depleted subjects was the aldosterone secretion rate low enough to indicate any significant degree of inhibition.

It must be concluded, therefore, that even severe magnesium depletion results in no significant change in the aldosterone secretion rate, and that fluctuations in magnesium metabolism have a negligible influence on aldosterone secretion.

We are grateful to Dr. C. C. Booth and to Professor Russell Fraser for allowing us access to their patients, and to Dr. I. MacIntyre for the plasma-magnesium estimations.

C. L. COPE, D.M., F.R.C.P.
J. PEARSON, B.A.

Postgraduate Medical School of London,
Hammersmith.

REFERENCES

- Booth, C. C., Babouris, N., Hanna, S., and MacIntyre, I. (1963). *Brit. med. J.*, **2**, 141.
Cope, C. L., Nicolis, G., and Fraser, B. (1961). *Clin. Sci.*, **21**, 367.
Hanna, S., and MacIntyre, I. (1960). *Lancet*, **2**, 348.
Heaton, F. W., Pyrah, L. N., Beresford, C. C., Bryson, R. W., and Martin, D. F. (1962). *Ibid.*, **2**, 802.
Horton, R., and Biglieri, E. G. (1962). *J. clin. Endocr.*, **22**, 1187.
MacIntyre, I. (1963). *J. chron. Dis.*, **16**, 201.
Mader, I. J., and Iseri, L. T. (1955). *Amer. J. Med.*, **19**, 976.
Milne, M. D., Muehrcke, R. C., and Aird, I. (1957). *Quart. J. Med.*, **26**, 317.

Medical Memoranda

An Unusual Case of Cardiac Arrest

Cardiac arrest may be due to a variety of causes, many of which are made clear only in retrospect. A large number of cases have now been treated successfully by thoracotomy with direct cardiac massage and, more recently, by the method of external cardiac massage as described by Kouwenoven *et al.* (1960).

CASE HISTORY

The patient, a 48-year-old single woman, had a long history of duodenal ulcer. In 1959 the ulcer perforated, requiring surgical closure. This was followed a few weeks later by a hysterectomy for fibroids. Also in the same year she required a blood transfusion for severe haematemesis. In 1962 her symptoms returned and a barium-meal examination showed duodenal deformity, causing pyloric stenosis. On admission for vagotomy and pyloroplasty her cardiovascular and respiratory systems were clinically normal.

Anaesthesia was induced at 8.25 a.m. with pethidine 20 mg., thiopentone 300 mg. (2½% solution), and suxethonium bromide 100 mg. The patient was inflated for 8–10 breaths with a face-mask, using the Boyle circle absorber. A cuffed orotracheal tube was passed and both lungs were seen to inflate.

Spontaneous respiration began about one minute later and 20 mg. of tubocurarine chloride was given. An intravenous infusion of normal saline was then set up. At 8.37 a.m. she was noticed to be cyanosed, with engorged jugular veins. No radial or carotid pulse could be felt and there were no heart sounds. The pupils were beginning to dilate and inflation with oxygen produced only minimal chest movement.

Immediate thoracotomy was performed, and as the pleura was opened there was an audible hiss due to the escape of gas under tension. The lung was collapsed and the heart flabby and motionless. Direct manual massage of the heart was immediately begun, producing a good carotid pulse. Within one minute a response was obtained and after five minutes the heart was contracting strongly in normal rhythm. The pupils started to constrict and the systolic blood-pressure at 8.50 a.m.

was 80 mm. An infusion of 200 ml. of 2½% bicarbonate solution was started (Brooks and Feldman, 1962).

A more detailed inspection of the lung showed it to be covered with numerous thin-walled bullae, mainly over the lower lobe. There were a few fibrous adhesions between this part of the lung and the diaphragm. A little saline was then instilled into the pleural cavity, and bubbles were seen to be emerging from a small rupture in one of the bullae. This was sutured with catgut and the chest closed with an underwater drainage tube.

At 9.10 a.m. the systolic blood-pressure was 100 mm. and a transfusion of 1 pint (570 ml.) of blood was started. When spontaneous respiration returned at 9.25 a.m. the right side of the chest was seen to have less respiratory excursion than the left and was hyperresonant to percussion. X-ray examination in the recovery room confirmed a tension pneumothorax on the right side.

At this time the patient opened her eyes and objected to the orotracheal tube, which was removed. She then complained of dyspnoea and right-sided chest pain. A dramatic improvement in her symptoms followed aspirating the pneumothorax with a trocar and cannula, which was afterwards connected to an underwater drain. A further x-ray examination showed lung expansion, and at 10.35 a.m. she was well awake and fully orientated, with no evidence of mental impairment.

Daily chest x-ray examination post-operatively showed gradual lung expansion. On the fourth day the needle was removed from the right side of the chest. The next day the patient's breathing became difficult, and a further tension pneumothorax on the right side was aspirated, the needle this time being connected to a low-pressure pump. The tube was removed from the left side of the chest on the sixth day, and the needle from the right side four days later. An E.C.G. showed no abnormality.

The patient was discharged to convalescence three weeks after the cardiac arrest. Throughout a six-months follow-up she has been well, with no gastric symptoms.

COMMENT

Cardiovascular collapse during intermittent positive-pressure respiration (I.P.P.R.) was described by Hunter (1955) in patients with artificially induced pneumothorax. The production of pneumothorax due to rupture of the oesophagus has been reported by Temple (1949) and Dundee (1955).

This case of cardiac arrest was due to bilateral tension pneumothorax. There was no pre-operative evidence of the underlying lung pathology, nor was I.P.P.R. carried out at a pressure greater than that usually employed. It is evident that had external cardiac massage been attempted valuable time would have been wasted. Thoracotomy revealed the cause of the arrest and direct cardiac massage produced a successful outcome. We believe that this method should always be employed where suitable facilities are available. It affords the optimum conditions for observing the heart and returning it to normal rhythm and may reveal intrathoracic causes of the cardiac arrest.

We should like to thank Dr. F. F. Cartwright and Dr. C. D. T. James for their advice, and Mr. L. T. Cotton for permission to publish this case.

C. M. T. GLEAVE, M.A., M.B., B.Chir.,
Senior House Officer in Anaesthetics.
C. P. MONTY, M.B., F.R.C.S.,
Surgical Registrar.

Dulwich Hospital, London.

REFERENCES

- Brooks, D. K., and Feldman, S. A. (1962). *Anaesthesia*, **17**, 161.
Dundee, J. W. (1955). *Ibid.*, **10**, 74.
Hunter, A. R. (1955). *Proc. roy. Soc. Med.*, **48**, 765.
Kouwenhoven, W. B., Jude, J. R., and Knickerbocker, G. G. (1960). *J. Amer. med. Ass.*, **173**, 1064.
Temple, L. J. (1949). *Brit. med. J.*, **1**, 935.