magnesium subsequently stabilised at the lower end of the reference range (figure), and no further intravenous magnesium replacement was required.

**Comment**

Calcium and magnesium share a transport system in the gut, and both 1,25-dihydroxycholecalciferol and 1,25 dihydroxycholecalciferol have been successfully used in the treatment of hypomagnesaemia associated with the short bowel syndrome. A recent report describes the use of 1-α-cholecalciferol in a patient with the short bowel syndrome in whom, the authors claim, renal tubular absorption of magnesium was increased. In our case oral magnesium supplements in high doses were associated with diarrhoea, and 1,25 dihydroxycholecalciferol enhanced magnesium absorption and possibly reduced urinary losses. The figure shows that normal serum magnesium concentrations were maintained after the administration of 1-α-cholecalciferol, with resolution of symptoms. Two 24 hour collections obtained while the patient was on 1-α-cholecalciferol contained 5 and 8 mmol magnesium (figure), suggesting that any effect of 1-α-cholecalciferol on renal magnesium conservation was minimal.

The role of vitamin D in the renal handling of magnesium is unclear. Levine et al found a diminution of magnesium tubular reabsorption in vitamin D deficient rats given 1,25 dihydroxycholecalciferol, and Burnatowska et al showed an increased fractional excretion of magnesium in hamsters from which thyroid and parathyroid glands had been removed. Fukumoto et al, however, described a decrease in fractional excretion of magnesium in a hypomagnesaemic patient with the short bowel syndrome who was given large doses of 1-α-cholecalciferol. In their patient, as in our case, the serum concentration of 1,25 dihydroxycholecalciferol was abnormally low, and this was felt to be a factor in impaired renal resorption of magnesium.

More work is required on the effect of 1-α-cholecalciferol on renal magnesium handling, but the case reported here suggests that this drug may be useful in the management of hypomagnesaemia induced by cyclosporin.

**Parathyroid hormone related peptide in ovarian carcinoma**

Hypercalcaemia is one of the commonest paraneoplastic syndromes encountered clinically, being associated with an estimated 10-20% of all solid tumours. Many factors contribute to this syndrome of humoral hypercalcaemia of malignancy (HHM), including cytokines and prostaglandins of the E series. Recently, a peptide structurally and immunologically distinct from parathyroid hormone (PTH), but with parathyroid hormone bioactivity, has been implicated in the pathogenesis of HHM and has been termed parathyroid hormone related peptide or PTHrP.

Hypercalcaemia is associated with ovarian carcinoma frequently enough for the ovary not to be ignored as a primary tumour site in women presenting with clinically unexplained hypercalcaemia. We therefore felt it would be of interest to examine a number of ovarian carcinomas for the presence of PTHrP.

Immunocytochemistry was performed using an antibody raised against the first 34 amino acids of PTHrP (kindly donated by Drs GV Segre and H Jüppner, Boston, Massachussets, USA) and standard indirect immunocytochemical techniques. Two cases of ovarian carcinoma associated with hypercalcaemia (one small cell and one non-small cell type, supplied by Dr GR Dickerson, Boston) were found to contain PTHrP. PTHrP was present throughout the cytoplasm of the tumour cells but was absent from inflammatory and stromal cells and areas of tumour necrosis. The immunoreactivity was completely abolished when the antibody was pre-incubated with PTHrP (1-34) overnight.

Two cases of serous cystadenocarcinoma and two cases of mucinous cystadenocarcinoma of the ovary (from patients who were normalcaemic) were found to be negative for PTHrP.

Normal adult ovary does not produce PTHrP, but the peptide has been detected in the human fetal gonad.

Other work is required on the presence of PTHrP in a hypercalcaemic ovarian carcinoma. While the pathophysiological role of PTHrP is yet to be elucidated, one possibility is that in addition to it inducing hypercalcaemia it may stimulate the growth of tumours in an autocrine manner. It may also regulate the fetal calcium balance.

The widespread presence of PTHrP in lung, renal cell, and squamous cell carcinomas and its presence in small cell ovarian carcinoma, as reported here, suggests that PTHrP is a common manifestation of the transformed cell.

**Prorenin in ovarian cyst fluid**

Aspartic proteinase renin is secreted by the kidneys and, as the initial enzyme in the renin/angiotensin cascade, it is important in the regulation of blood pressure and fluid homeostasis. Recently, high concentrations of the zymogen prorenin have been shown in female reproductive organs. The concentration of prorenin in follicular fluid collected from women undergoing in vitro fertilisation are at least 10 times higher than those in plasma. Immunohistochemical staining has shown that the prorenin is present in the thecal cells lining the follicles from where it is, presumably, secreted into the fluid. As only very low concentrations of active renin are found in the ovary, it has been postulated that ovarian prorenin may be biologically active without any necessity for prior removal of the propeptide. The role of ovarian prorenin is still unclear but it probably operates through the formation of angiotensin I (A1). Studies with the A1 antagonist, saralasin, have indicated a direct role for A1 in ovulation, and, in addition to its effects on steroiogenesis, the vasconstrictor and angiogenic properties may be important for follicular growth.

Cysts are commonly derived from the ovarian follicles and frequently contain a large volume of liquid. It was thus considered of interest to determine whether this fluid might also contain a high concentration of prorenin. The fluid from four cysts was removed at laparotomy was collected, stored at -20°C, and assayed for prorenin by the trypsin-activation method of McIntyre et al. Renin activity was estimated by measuring the rate of angiotensin I (A1) production from human angiotensinogen.

Prorenin was detected in the fluid from four of the cysts assayed—three of follicular origin and one from a mucinous cystadenoma. In two of these cysts two others being virtually negative (table). The concentration of active renin detected in all of the fluids was very low (less than 5% of total) and may have been due to partial activation of the prorenin during collection. This predominance of prorenin over renin is in keeping with previous results for normal ovarian follicular fluid.

**Concentrations of prorenin in ovarian cyst fluid**

<table>
<thead>
<tr>
<th>Age</th>
<th>Prorenin (ng A1/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>Follicular cyst</td>
</tr>
<tr>
<td>20</td>
<td>Follicular cyst</td>
</tr>
<tr>
<td>42</td>
<td>Follicular cyst</td>
</tr>
<tr>
<td>44</td>
<td>Mucinous cystadenoma</td>
</tr>
<tr>
<td>52</td>
<td>Serous cystadenofibroma</td>
</tr>
<tr>
<td>83</td>
<td>Serous cystadenofibroma</td>
</tr>
</tbody>
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12 Concentrations of prorenin in ovarian cyst fluid
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