Reasons behind the changes are difficult to determine. Possibly the tendency was to replace one liquid laxative with another in the belief that liquid preparations are more effective than tablets or fibre products. Thus although the use of senna tablets increased, the rise in the use of senna syrup was much greater, partly because it was given by nursing staff.

Increased prescribing of lactulose may have been due to extensive promotion, the wish to use a liquid preparation, and the perception that the potential lack of griping was an important benefit. Recommendations made to prescribers were not followed, and we conclude that the educational bulletins issued to promote fibre as a first line laxative were not enough to

influence prescribing without some form of reinforcement.

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An endocrine marker for pancreatic cancer

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Although the pancreas is not considered to be a target organ for steroid hormones, abnormally high serum concentrations of sex hormones have been observed in patients with pancreatic diseases.¹⁻³ The purpose of this study was to investigate the role of androgens in pancreatic diseases and the possible diagnostic value of measuring sex hormone concentrations to differentiate between various pancreatic diseases.

Patients, methods, and results

We studied 75 men who were arranged in four groups according to their diagnoses. Group 1 consisted of 14 patients with pancreatic cancer that was confirmed histologically at operation (mean age 55). Group 2 consisted of 26 patients with chronic pancreatitis (mean age 44) with a diagnosis based on the symptoms of insufficient secretion of hormones, typical changes on ultrasonography and pancreatography, and the findings at operation. Group 3 consisted of 19 patients with malignancies of the gastrointestinal tract other than of the pancreas that were confirmed endoscopically and histologically (three oesophagus, six stomach, seven colon, and three papilla of Vater) (mean age 57). Group 4 consisted of 16 control subjects without gastrointestinal or endocrine diseases (mean age 53).

Blood samples were taken between 8 and 10 am. Testosterone, dihydrotestosterone, and androstenedione concentrations were measured by radioimmunoassay,⁴ and the ratio of testosterone to dihydrotestosterone was calculated.

The mean (SD) concentration of testosterone in patients with pancreatic cancer was 7.4 (1.2) nmol/l, which was lower than that in those from the other groups (group 2, 11.6 (6.4) nmol/l; group 3, 7.8 (5.3) nmol/l; group 4, 9.6 (5.3) nmol/l). The differences, however, were not statistically significant. The mean (SD) dihydrotestosterone concentrations were 3.2 (2.3) nmol/l, 1.5 (1.6) nmol/l, 1.9 (0.9) nmol/l, and 1.7 (0.9) nmol/l for groups 1, 2, 3, and 4 respectively. The corresponding androstenedione concentrations were 8.8 (2.5) nmol/l, 9.5 (3.2) nmol/l, 8.2 (3.1) nmol/l, and 9.4 (5.2) nmol/l. There were no significant differences between any of the groups. The mean (SD) ratio of testosterone to dihydrotestosterone was, however, significantly lower in patients with pancreatic cancer than in those with chronic pan-

creatitis (2.5 (1.0) v 9.6 (2.3); $p < 0.01$). In all patients with pancreatic cancer the ratio of testosterone to dihydrotestosterone was less than 4, while it exceeded 4 in all but one patient with chronic pancreatitis (figure). The mean ratio of testosterone to dihydrotestosterone in patients with gastrointestinal cancer other than of the pancreas and in controls was higher than that in patients with pancreatic cancer. The difference was not statistically significant.

Ratio of testosterone to dihydrotestosterone in four groups of patients. Mean (SD) values for each group and the discriminative value are shown

Comment

Our results agree with the previous finding of a decrease of serum testosterone concentration in patients with pancreatic cancer.³ This finding has no diagnostic relevance because similarly low testosterone concentrations have been found in various pathological conditions.⁵ In this study we have shown that the ratio of testosterone to dihydrotestosterone is a valuable marker for differentiating between pancreatic cancer and chronic pancreatitis. This ratio was significantly lower in patients with pancreatic cancer than in those with chronic pancreatitis. The value which discriminated between the two groups was 4.

The activities of aromatase and 5- α -reductase are high in pancreatic cancer cells.³ These enzymes convert testosterone to oestrogens and dihydro-

testosterone. The increase in their activities may lead to a low testosterone concentration and a high dihydrotestosterone concentration. These changes may explain the reduced ratio of testosterone to dihydrotestosterone found in patients with pancreatic cancer.

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Isolated central respiratory failure due to syringomyelia and Arnold-Chiari malformation

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We report on two patients without pre-existing neurological abnormality who presented to hospital with acute central respiratory failure. Both showed syringomyelia and an Arnold-Chiari malformation on magnetic resonance imaging, and both improved after decompression of the foramen magnum. Isolated respiratory failure has not to our knowledge been reported in association with syringomyelia.

Case reports

Case 1—A healthy 26 year old woman became breathless over two weeks. She became lethargic, tended to fall asleep at work, and finally was found unconscious in bed. On admission she was cyanosed, hypothermic, and unconscious. Analysis of blood gases while she was breathing air showed a pH of 6.82, arterial carbon dioxide tension of 22.9 kPa, and arterial oxygen tension of 5.3 kPa. After intubation and ventilation she became fully conscious. Neurological examination showed brisk reflexes and inadequate spontaneous ventilation; her arterial carbon dioxide tension rose to 8.0 kPa over six hours. A computed tomogram was normal, but magnetic resonance imaging showed an Arnold-Chiari malformation with syringomyelia extending from the medulla to the thoracic spinal cord (figure). Bilateral paralysis of the

diaphragm was confirmed by radiography, and she communicated that she was afraid to fall asleep without the ventilator in case she stopped breathing. Capnography and spirometry showed that arterial carbon dioxide tension increased and ventilation decreased when she fell asleep (Ondine's curse). Decompression of the posterior fossa, duroplasty, and aspiration of the syrinx were performed. Within 10 days she was able to breathe spontaneously when awake but required ventilation to sleep. Though she needed long term nocturnal ventilation through a close fitting nasal mask, she continued to improve and returned to work.

Case 2—A healthy 58 year old woman became confused over two days. She stumbled and struck her head against a table but did not lose consciousness. She was referred for neurosurgical assessment because of confusion. No skull fracture or neurological abnormality was present, but analysis of blood gases when she was breathing air showed a pH of 7.33, arterial carbon dioxide tension of 8.8 kPa, and arterial oxygen tension of 7.6 kPa. A computed tomogram showed a shallow posterior fossa, and magnetic resonance imaging showed a syrinx extending from the medulla to the conus. Spirometry showed a reduction in vital capacity. After decompression of the posterior fossa and duroplasty her arterial carbon dioxide tension fell to 5.3 kPa and arterial oxygen tension to 8.0-8.6 kPa on air. She became fully lucid and more active than before admission.

Comment

Central respiratory failure has been described in neonates in association with Arnold-Chiari malformation, hydrocephalus, and spina bifida, and decompression of the foramen magnum has been recommended when lower cranial nerve or respiratory dysfunction occurs.¹ Central respiratory failure has occurred in association with Arnold-Chiari malformation and with syringomyelia and lower cranial nerve palsies,² and in one case respiratory failure was attributed to insensitivity of peripheral chemoreceptors resulting from lesions of the ninth cranial nerves.³

Both our patients had large syrinxes, yet neither exhibited the classic symptoms or signs of syringomyelia before presenting with acute respiratory failure. In both cases radiographs of the diaphragm confirmed phrenic nerve dysfunction, which improved after operation. Phrenic motor neurons are located more medially in the anterior horn than other motor neurons and may be vulnerable to compression by an expanding syrinx.

Central respiratory failure in these patients may have been due to compression of the medulla by the Arnold-Chiari malformation or to the syringomyelia. The effect on the phrenic nerve suggested that the syringomyelia was important, although Arnold-Chiari malformation alone has caused respiratory failure.⁴

Both patients were diagnosed by magnetic resonance imaging, and in one case the computed tomogram was normal. Magnetic resonance imaging of the cranio-vertebral junction should be considered in patients

Sagittal magnetic resonance images before and after operation (case 1), showing a large syrinx that collapsed after surgery and descent of tonsils to level of C1