second malignancy of colonic or extracolonic origin may be expected to develop later in about one-third of patients who survive their colonic cancer. The bladder cancer that this patient developed may have been induced by irradiation, since the bladder would have been within the field of treatment thirteen years previously. McIntyre and Pointon⁴ have shown a causal relationship between the development of bladder tumours and previous external pelvic irradiation. In their series of 950 cases they found 16 patients who had developed bladder neoplasm up to 28 years after irradiation, when they would only have expected nine. Castro *et al*⁵ reported 26 patients with colonic carcinoma who had had pelvic irradiation for gynaecological malignancy 5 to 30 years previously. Hence possibly the colonic carcinoma in my patient may also have been irradiation-induced.

This case illustrates two important points: firstly, that radical treatment is not contraindicated for second primary neoplasms; secondly, that routine follow-up after radical treatment and the investigation of new symptoms are worthwhile because of the increased risk of second primary neoplasms. Moertel¹ has shown that the incidence of developing new malignancies increases with each successive new cancer even though the patient's chance of surviving to acquire another lesion decreases progressively with each episode.

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⁴ McIntyre, D, and Pointon, R C S, *Journal of the Royal College of Surgeons of Edinburgh*, 1971, 16, 141.

⁵ Castro, E B, Rosen, P P, and Quan, S H Q, *Cancer*, 1973, 31, 45.

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Incidence of protein-losing enteropathy in primary lymphoedema using chromium-51 chloride technique

Several cases of protein-losing enteropathy (PLE) in primary lymphoedema have been reported¹ but no one has yet attempted to discover the true incidence of PLE in this condition.

Waldmann² has summarised the various radioactive excretory tests used in the diagnosis of PLE.² Our test was based on that described by Walker-Smith *et al*,³ in which ⁵¹CrCl₃ is injected intravenously and faecal loss estimated. The test was modified in that one-third of the dose was used.

Patients, methods, and results

Fifty-five patients, ranging in age from 2 to 72 years, were studied over two years. Their usual mode of presentation was with either unilateral or bilateral lower limb oedema, and some patients also had arm, facial, or genital oedema. Four patients had diarrhoea. ⁵¹CrCl₃ 30 µCi was injected intravenously, and 1 ml of the solution was analysed for a baseline radioactivity count. Stools were collected over the next five days, taking care to prevent urinary contamination, and the radioactivity of the whole stool sample was measured in a large plastic scintillation counter specially constructed at St Thomas's Hospital.⁴ Excretion of more than 2% of the administered dose indicated significant PLE.

We discovered significant PLE in 12 of the 55 patients studied (22%). The percentage ⁵¹CrCl₃ excreted in these patients ranged from 2.5% to 18.4%. Total serum protein was normal in two patients and serum albumin in four patients (see table). Three patients, described elsewhere,⁵ had a segment of small bowel excised and were followed for over a year. They maintained clinical and biochemical improvement, the percentage ⁵¹CrCl₃ loss falling.

Discussion

PLE in primary lymphoedema is due to lymphangiectasia resulting from blockage of the small bowel lymphatics. It must be emphasised

Gut protein loss and serum proteins in patients with PLE in primary lymphoedema

Case No	Age and sex	⁵¹ CrCl ₃ Loss (% of administered dose excreted in 5 days)		Protein (normal 63-79 g/l)	Albumin (normal 38-56 g/l)
		Before operation	After operation		
1	15 F	18.4	9.0*	39	28
2	72 M	16.0		42	24
3	24 F	12.0		47	34
4	52 M	10.8	3.4*	38	29
5	12 M	9.3		55	36
6	2 M	7.2		62	43†
7	2 M	6.6			
8	4 F	6.1		63†	40†
9	15 F	5.9		69†	39†
10	56 M	4.6		51	26
11	11 F	4.0		51	34
12	59 M	2.5	1.5*	60	38†

*Gut resected. †Within normal range.

that serum protein and albumin levels may be normal. In our patients with primary lymphoedema ⁵¹CrCl₃ screening revealed an incidence of PLE of 22%.

The ⁵¹CrCl₃ isotope test is a simple and convenient clinical method of screening patients for PLE in primary lymphoedema. It is also reliable as the isotope has a long bench storage life, and less than 1% of the excreted isotope is reabsorbed in the bowel. The test can be performed on outpatients. An adequate stool output is essential and care must be taken to prevent urinary contamination of the stool (especially in children) as up to 30% of the isotope is excreted in the urine.³

We thank Professor J B Kinmonth, under whose care these patients were admitted.

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⁵ Kinmonth, J B, and Cox, S J, *British Journal of Surgery*, 1974, 61, 589.

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Residual biliary calculi: dispersal by irrigation of common bile duct

When residual gall stones are shown in the bile duct after exploration further surgery is usually advised, but this is fraught with technical difficulties and a high mortality rate. A reliable non-operative method for removing such stones would obviously be welcome and recently success has been reported using a simple washout technique. This paper reports two further successful cases using this procedure.¹

Technique

Before starting the washout procedure bile is cultured and, if infected, the patient is started on the appropriate antibiotic. Bile is further cultured if indicated clinically. The washout is performed by connecting the T-tube to a litre of sterile 0.9% saline, to which 40 ml of 1% lignocaine has been added. Probanthine 15 mg is given intramuscularly 30 minutes before the start of the irrigation. The saline is initially dripped in slowly, but once discomfort has settled the saline is allowed to flow rapidly through the T-tube. At the end of the procedure the T-tube is clamped. The criterion for success is a post-washout choledochogram showing the disappearance of the stone(s).

Case reports

Case 1—A 51-year-old woman was admitted for cholecystectomy; at operation a peroperative choledochogram showed an enlarged duct with the suspicion of a stone within it. Formal supraduodenal exploration, together with transduodenal sphincterotomy, was performed and two stones removed. The post operative T-tube choledochogram showed two residual stones in the lower end of the duct. Three washouts were performed over the next few days and a T-tube choledochogram after the last washout showed no evidence of residual calculi. The T-tube was removed and the patient has remained well.

Case 2—This man presented with recurrent episodes of cholangitis. At operation the choledochogram showed a stone in the lower end of the duct but none was found on exploration and transduodenal sphincterotomy. Two postoperative T-tube choledochograms showed two residual stones in the lower end of the bile duct. Re-exploration was performed and one crushed stone removed. A repeat choledochogram showed one residual stone and a biliary washout was then performed. A T-tube choledochogram two days later showed free flow of the contrast medium into the duodenum and no evidence of the residual stone. The T-tube was removed and the patient has remained well.

Discussion

The value of peroperative choledochograms in biliary surgery is now well established, and their use reduces substantially the incidence of residual stones. Despite these radiological aids, however, there remain a small percentage of patients in whom retained calculi can be shown after operation. Further surgical exploration of the bile duct is usually recommended, but recently there has been renewed interest in non-operative procedures, including instrumental extraction, biliary washout, and chemical dissolution, with heparin² and sodium cholate³⁻⁵ being the solvents of choice.

The washout technique depends for its action on the rapid rate of the infusion to flush the stone through the lower end of the bile duct.

Non-operative treatment of residual stones in lower end of common bile duct

Reference	Technique	No of patients	No of patients in whom treatment was successful
Gardner (1973) ²	Heparin infusion	5	5
Lansford <i>et al</i> (1974) ⁴	Sodium cholate infusion	5	5
Britton <i>et al</i> (1975) ⁵	Sodium cholate infusion	4	4*
Catt <i>et al</i> (1974) ¹	Saline washout	6	5
Present series	Saline washout	2	2
Total		22	21

*Includes one case where stone in the lower end was removed successfully but a calculus just proximal to T-tube remained.

In our two cases this was obviously facilitated by the associated transduodenal sphincterotomy performed at the time of the original operation. Post-washout pyrexia, probably due to transient bacteraemia from cholangiovenous reflux,¹ has been reported. Bile should therefore always be cultured before irrigation of the bile ducts and the patient treated with the appropriate antibiotic. Reports indicate that in both chemical dissolution and the washout technique excellent results are obtained when the stone is in the lower portion of the bile duct (see table). The evidence supports the argument that non-surgical procedures have a significant place in the management of the patient with a residual stone, particularly if this is in the lower portion of the bile duct.

We thank Mr Philip Shemilt for allowing us to report details of the second case.

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⁴ Lansford, C, Menta, S, and Kern, F, *Gut*, 1974, **15**, 48.

⁵ Britton, D C, *et al*, *British Journal of Surgery*, 1975, **62**, 520.

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Influence of age on serum prolactin levels in women and men

The purpose of the present study was to investigate the changes in prolactin secretion with age in women and to correlate them with reported changes in ovarian oestrogen production. To elucidate whether factors other than ovarian oestrogens might also be involved the influence of age on prolactin secretion in women was compared with that observed in men.

Materials, methods, and results

Single blood samples were collected between 10 am and 4 pm from 86 women and 241 men blood donors aged 18-65 years from the Saint-Pierre Hospital, Brussels. Serum prolactin was measured by a homologous human radioimmunoassay method.¹ Human pituitary prolactin (HPR VLS-1) was obtained from the National Institute of Arthritis, Metabolism and Digestive Diseases, USA. The rabbit anti-prolactin serum was obtained against pituitary prolactin from culture medium of human fetal pituitaries.¹ The assay results are expressed here in mU of a research standard (MRC 71/222) of human pituitary prolactin distributed by the Division of Biological Standards, National Institute for Medical Research, London; 1 mU of this pituitary prolactin was found to be equivalent to 42 ng of the pituitary prolactin preparation (HPR VLS-2) with 95% fiducial limits at 55 and 32 ng. The distribution of the individual values within each age group was found log-normal by Rankit-test. Homogeneity of variances among age groups and the significance of differences between means (*t* test) were tested as described by Snedecor.

There was a progressive decline ($t = 3.84$ with 25 degrees of freedom; $P < 0.001$) in serum prolactin concentration with age from 443 mU/l in women aged between 15 and 25 to 218 mU/l in women aged between 55 and 65 (see fig). The decrease was already significant ($t = 2.81$ with 32 degrees of freedom; $P < 0.01$) between the ages of 45 and 55 (291 mU/l) compared with the mean value in the youngest group. The difference was also significant ($t = 3.74$ with 32 degrees of freedom; $P < 0.001$) between the age group 55-65 (218 mU/l) and the age group 35-45 (353 mU/l). Serum prolactin in men rose slightly with age. Between the ages of 55 and 65 the mean value (320 mU/l) was significantly higher ($t = 2.06$ with 79 degrees of freedom; $P < 0.05$) than between the ages of 35 and 45 (216 mU/l).

The average value was 333 mU/l in women and 239 mU/l in men, and in the age group 55-65 the serum prolactin concentration was significantly higher ($t = 2.04$ with 21 degrees of freedom; $P < 0.05$) in men (320 mU/l) than women (218 mU/l). At younger ages the average values of circulating prolactin were higher in women than in men (see fig).

Mean serum prolactin (mU of human pituitary research standard MRC 71/222) in men and women of different age groups. Vertical bars represent standard error of the means. Number of single determinations indicated in each column.

Discussion

Serum prolactin levels in women decrease steadily with age with a significant decline at the menopause which continues even further during the next decade. This contrasts with men, whose levels tend to rise after the age of 45. The study, however, should be extended to see whether this continues beyond the age of 65.

The fall in serum prolactin with age in women is parallel to the fall in circulating and urinary oestrogens² and is consistent with data