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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³ Way, L W, Admirand, W H, and Dumphy, J E, *Annals of Surgery*, 1972, **176**, 347.

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

obtained during the menstrual cycle,³ pregnancy,⁴ and in cases of amenorrhoea with normal LH and FSH responses to synthetic gonadotrophin releasing hormone and with no pituitary tumour,³ indicating that prolactin secretion is stimulated by endogenous oestrogens. Exogenous oestrogens also stimulate prolactin secretion in women.⁵ Thus oestrogens are an important factor in the control of prolactin secretion in humans. The decrease of serum prolactin levels with age in women and their rising trend with age in men is of practical value in interpreting the results of prolactin assays.

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Ischaemic brain damage of cerebral perfusion failure type after treatment of severe hypertension

Autoregulation of the cerebral circulation is a homeostatic mechanism whereby cerebral blood flow (CBF) is kept within normal limits over a wide range of systemic arterial pressure.¹ In hypertensive patients autoregulation is adapted to a high blood pressure so that symptoms of brain ischaemia may develop during antihypertensive treatment at a blood pressure that is well tolerated by normotensive people.²

Case reports

Case 1—A 60-year-old woman with a BP of 240/140 mm Hg, and bilateral retinal haemorrhages and exudates but no papilloedema, was given in addition to her usual treatment of methyl dopa, 250 mg four times daily, an oral dose of 25 mg bethanidine. Two hours later her BP was 120/85 mm Hg and she was deeply unconscious. A few hours later she was lucid and by next morning had returned to her former mental state. There were no focal neurological signs. Bilateral angiography gave normal findings. The patient died 12 days after the hypotensive episode.

Case 2—A 35-year-old woman with a BP of 240/170 mm Hg, bilateral retinal haemorrhages, and papilloedema, and who had not been receiving treatment for hypertension, was given 2.5 mg pentolinium intravenously. Immediately after the injection, the BP fell briefly to an unrecordable level; 15 minutes later the BP was 120/100 mm Hg and within 24 hours it was 200/140 mm Hg. She remained unconscious for three days with bilateral pyramidal tract signs and, although her conscious level improved thereafter, her mental state remained grossly impaired until she died six months later.

Necropsy showed left ventricular hypertrophy in both cases. In case 1 there was unilateral atheromatous stenosis of the renal artery, and in case 2 the kidneys were small and showed microscopic features of progressive systemic sclerosis. Evidence of "malignant" hypertension was seen in both cases. The brains were fixed intact before dissection. In each there was ischaemic damage in the boundary zones between the major arterial territories (fig) and variable damage in deeper structures. Reactive changes were consistent with the damage having occurred at the time of the recorded hypotensive episodes. Though moderately atheromatous, all the major intracranial and extracranial arteries were patent.

Case 2. Distribution of infarction in the boundary zones between the major arterial territories of the cerebral and cerebellar hemispheres (hatched).

Discussion

The distribution of ischaemic brain damage in these two patients is similar to the commonest pattern found with a precipitate reduction in CBF resulting from a severe episode of hypotension both in man³ and in primates.⁴ There seems little doubt from the clinicopathological correlates that the boundary zone infarction in these cases occurred because of the hypotensive episode precipitated by the anti-hypertensive drugs. In particular, in case 1 the lowest BP recorded was 120/85 mm Hg—a level well above the lower limit of effective autoregulation in a normotensive person.⁵ Hence probably because of impaired autoregulation this patient sustained a critical reduction in cerebral blood flow at a level of BP that under normal circumstances would not have given rise to concern.

Although the advantages of reducing the BP in patients with severe hypertension usually outweigh the dangers of excessive lowering of the BP, the two cases reported here show a potential hazard of lowering it too rapidly in hypertensive patients and emphasise the importance of titrating the dose of hypotensive agent against the level of the blood pressure.

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