Gestational macromastia: treatment

- support, analgesia
- drugs – testosterone, progesterone, hydrocortisone, bromocriptine, danazol
- surgical excision
- termination of pregnancy

abdomen revealed a gestational age corresponding to 16 weeks. A diagnosis of gestational macromastia was made. The patient was given blood transfusions and the pregnancy was terminated. Hormone evaluation after termination of pregnancy revealed serum luteinising hormone of 8.14 (normal 5–25 IU/l), follicle-stimulating hormone of 5.62 (normal 5–20 IU/l) and serum prolactin of 401 (normal 170–540 mU/l). Danazol 400 mg orally was given daily for 20 days. There was no appreciable decrease in breast size. The patient was subjected to a total mastectomy with nipple and a flap of areola transplanted back. The right breast weighed 5.9 kg and the left 5.6 kg. On cut section fatty tissue was replaced by glandular tissue. Proliferation of fibrous tissue in between the lobules was seen. A solitary abscess was seen in the right breast.

Gestation macromastia is exceedingly rare, Lowison *et al* reported two cases in 56 794 deliveries.¹ Gestational macromastia can manifest either in first pregnancy or after previous normal pregnancies. Manifestations usually begin in the first trimester.² The disorder results from enhanced end-organ response to physiological amounts of various hormones.³ Throughout its development and function breast is a target organ for most hormones. Glandular proliferation which begins at puberty is intensified during pregnancy and is dependent upon progesterone. Oestrogen has a greater effect on ductular growth and prolactin appears important in coordinating these effects. Gestational macromastia in general is massive and frequently results in extensive breakdown of skin, usually around the nipple.² A variety of treatments have been tried (see box).^{2–4} In this patient termination of pregnancy and Danazol 400 mg day (for 20 days) did not appreciably decrease breast size.

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Heterochromatin heteromorphism and variation in apolipoprotein A phenotype – a pilot study

Sir,
Heterochromatin appears as densely stained segments in the terminal ends of chromatin strands, especially in chromosome pairs 1, 9, and 16.¹ Heterochromatin heteromorphism implies a difference in the amount of heterochromatin in the individual chromosomes of a chromosome pair.¹ The amount of heteromorphism may be calculated by subtracting the length of the heterochromatin segments of one chromosome from that of the other in a chromosome pair.¹

We have looked at heterochromatin heteromorphism in the Malmö study, which was designed to investigate factors contributing to the development of acute myocardial infarction in man.² Heterochromatin heteromorphism in chromosome pairs 1, 9, and 16 was investigated in a pilot study of 62 arbitrarily selected individuals and in 50% of these we found a difference in heterochromatin length between the two homologues of chromosome 1. In a second study, the amount of heterochromatin heteromorphism in chromosome pairs 1, 9, and 16 was calculated in 20 consecutive individuals participating in the Malmö study. This subsample consisted of five individuals who did not meet the selection criteria, three controls, and six normotensive and six hypertensive patients. (The selection criteria which were intended to create a normolipidemic normotensive acute myocardial infarction (AMI) group and a normolipidemic hypertensive AMI group, are discussed elsewhere.²) One of the major findings of the Malmö study was the strong correlation between reinfarction in normolipidaemic individuals and low serum levels of apolipoprotein AI.² In the present study we found a significant correlation between the concentration of apolipoprotein AI and the size difference in heterochromatin in the homologous chromosomes 1 ($F = 7.15$, $r = 0.5$, $p < 0.05$). There was no such correlation with the size differences in heterochromatin in the homologous chromosomes 9 and 16, as might have been expected if the apolipoprotein AI concentrations had been reflecting an unspecified mutagenic load, rather than specific qualities linked to chromosome 1.³ Possibly, the heterochromatin areas conserve important sequences of genetic information by protecting against crossing over between heterochromatic segments.

It follows that our observations on apolipoprotein AI concentrations might be explained by the amount of heterochromatin in chromosome pair 1. The apolipoprotein AI gene is not, however, found on the first chromosome; on the other hand, the apolipoprotein AII gene locus is.⁴ Apolipoprotein AII always appears together with apolipoprotein AI in apolipoprotein AI–AII particles. The serum concentration of apolipoprotein AI depends partly on particles with only apolipoprotein AI and partly on particles with both apolipoprotein AI and apolipoprotein AII.⁵ We suggest that the correlation between apolipoprotein AI serum concentration and the amount of heterochromatin heteromorphism in chromosome pair 1 may be interpreted as showing that the formation of apolipoprotein AI–AII particles may be quantitatively regulated by an interaction between the

amount of heterochromatin and the apolipoprotein AII gene in chromosome 1.⁵
Although our primary interest was plasma apolipoprotein AI concentrations, we also determined apolipoprotein AII plasma concentrations in a small subsample of 10 individuals, and, although insignificant, the correlation with the amount of heterochromatin heteromorphism in these few individuals ($F = 3.8$, ns, $r = 0.6$) did not rule out the possibility that our observations on apolipoprotein AI might have been due to such co-variation with apolipoprotein AII regulated by the apolipoprotein AII locus. In conclusion, our results indicate that heterochromatin heteromorphism in chromosome 1 may reflect ability to form apolipoprotein-A-containing particles.

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Post-bulbar chronic duodenal ulcer with major upper gastrointestinal bleeding from the cystic artery

Sir,
Involvement of the cystic artery by a chronic significant post-bulbar duodenal ulcer is reported as a rare cause of major upper gastrointestinal haemorrhage.^{1–3} We present a case of a 93-year-old man who presented with haematemesis and melaena secondary to post-bulbar duodenal ulcer eroding the cystic artery.

A fairly fit and alert 93-year-old man was referred with a history of a single large episode of red bleeding per rectum. There was no previous history of either upper or lower gastrointestinal symptoms prior to this episode. He was taking a nonsteroidal anti-inflammatory drug for gout. On admission he was in a stable condition; abdominal and rectal examination was unremarkable. A

presumptive diagnosis was made of bleeding from colonic diverticular disease and in view of his age he was treated conservatively. Over the next 48 hours he had two further episodes of rectal bleeding suggesting melaena associated with an episode of haematemesis, hypotension and tachycardia with a fall in haemoglobin requiring six unit blood. An emergency gastroscopy revealed blood in the duodenum but no other lesion was seen. At operation a large chronic post-bulbar duodenal ulcer was discovered which was eroding into the neck of the gall bladder and the anterior branch of the cystic artery. A partial (Billroth II) gastrectomy was performed and the patient made a full recovery.

Various emergency treatment modalities to arrest cystic artery haemorrhage include endoscopic electrocoagulation or laser therapy, embolisation⁴ of the cystic or right hepatic artery and surgery. The former two options are feared with higher risk of infarction of the gall bladder. At surgery, cystic artery ligation with cholecystectomy has been recommended because ligating the artery and leaving the gall bladder *in situ* could lead to infarction.¹ This was certainly not the case in our elderly patient where we simply tied the cystic artery, probably the anterior branch and performed a Billroth II gastrectomy.

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Iatrogenic gall bladder perforation

Sir

Gall bladder perforation is an uncommon complication of percutaneous kidney biopsy. Several cases have been reported previously, though over 25 years ago^{1–3} and we describe another, in a 70-year-old man with suspected polyarteritis nodosa.

Biopsy of the right kidney was carried out with the patient in the prone position and a pillow under the abdomen. The longitudinal axis of the right kidney was outlined by means of ultrasound scanning by a ultrasonographer using a 3.5 MHz curvilinear phased crystal array probe. On scanning, the right kidney was situated in a normal anatomical position. The depth of the lower pole of the kidney was determined using a lumbar puncture needle as well as by ultrasound. One vertical pass to the lower pole of the right kidney, by an experienced operator (MJF), was made with a 1.6 gauge menghini needle and a good sample obtained.

Immediate right-sided flank pain occurred. Post-biopsy blood pressure was stable at 180/90 mmHg and he subsequently passed 300 ml of clear urine. His severe flank pain persisted. Abdominal examination revealed right flank tenderness with guarding and normal bowel sounds. Ultrasound scan showed a 2–5 cm haematoma over the lower pole of the right kidney and free fluid ('probable blood') over the right lobe of the liver.

The patient settled with analgesia, remaining haemodynamically stable and passed a further 250 ml of rose-coloured urine. Fifteen hours post biopsy his blood pressure dropped acutely to 100/60 mmHg and he developed generalised abdominal discomfort. His temperature was 37.5°C and he was sweaty with clinically evident generalised peritonitis.

Laboratory investigations revealed: haemoglobin 16 g/dl, white cell count $12 \times 10^9/l$, platelets $185 \times 10^9/l$ plasma urea 17 mmol/l, sodium 143 mmol/l, potassium 5.1 mmol/l, bicarbonate 20 mmol/l, chloride 109 mmol/l, creatinine 320 $\mu\text{mol/l}$, and amylase 320 Somogyi Units (normal < 250). There was no free gas on abdominal or chest X-ray.

After rapid resuscitation he underwent emergency laparotomy where bile-stained peritonitis with collections under both diaphragms and in the pelvis was found. There was a pinpoint perforation in the fundus of a small gall bladder which was lying in a normal anatomical position and displayed no evidence of acute inflammation. The omentum had migrated towards the gall bladder but had not sealed the hole. He underwent oversewing of the gall bladder, peritoneal lavage and peritoneal drainage.

He spent 21 days in hospital, his stay being complicated by a lower respiratory tract infection. His impaired renal function remained stable. Report of the biopsy confirmed kidney tissue, but there was no gall bladder tissue present.

Haemorrhagic complications of percutaneous renal biopsy are common (see box), but these are not usually life threatening and serious complications are rare.^{1–5}

Usually patients with iatrogenic perforated gall bladders develop pain and hypotension

shortly after the incident. If there is no underlying obstruction of the biliary tree the abdominal pain and hypotension are usually self-limiting, not resulting in peritonitis.⁶

Our case of gall bladder perforation was complicated by peritonitis. We therefore suggest that if a patient develops abdominal pain post renal biopsy he/she should be observed closely and an ultrasound scan performed. Conservative management for a short time is appropriate but early signs of peritoneal irritation demand surgical intervention, acknowledging the possibility of a perforated viscus as a potentially serious complication of a relatively safe procedure. The use of real-time ultrasound during biopsy may help reduce the number of complications.

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Complications of percutaneous renal biopsy

Minor

Haemorrhagic:

- microscopic and macroscopic haematuria (50%)
- intra- or peri-renal haemorrhage
- peri-renal haematoma (1.4% clinically, > 50% on CT scanning)
- retro-peritoneal haematoma (5–10%)

Pain: abdominal or flank (5–10%)

Infection: renal (0.18%)

Arteriovenous fistula: renal (0.1%)

Major

Perforation: pleura, bowel, mesenteric artery, gall bladder

Laceration: liver, spleen, adrenal, pancreas