impossible and it may be necessary to use an alternative gene locus, such as the 16S rDNA or 23S rDNA locus, where phylogenetic data is available for all recognised species within the genus.

In the present study, other species within the genus *Pseudomonas* accounted for 10.2% and 21.4% of the total *Pseudomonas* spp. detected in children and adults, respectively. These values may be clinically significant for two reasons: (i) there may be significant under-reporting of the occurrence and significance of other *Pseudomonas* spp. that have not been described to date as being well-established pathogens of CF, and (ii) other species within the genus *Pseudomonas* may play a role as an early ecological coloniser/successor, thereby preparing a favourable physiological/ecological niche for the colonisation and eventual chronic infection with *P. aeruginosa*.

As not all laboratories employ molecular detection methods for *P. aeruginosa* or other *Pseudomonas* spp., either from culture plates or patients' sputa, small numbers of colonies (n=1–2) may be missed when present in the early stages of colonisation preceding infection of a patient's airway, particularly where single colonies are mixed with other phenotypically similar genera on the primary culture plate.[4]

Pragmatic, practical and cost implications make it impossible to identify the total bacterial microflora qualitatively from sputa on non-selective primary plates. Therefore, any rapid molecular screening method should be encouraged in an effort to detect low copy numbers of organisms in the early stages of colonisation/infection when the main value of the diagnostic assay is the rapid screening of patients with no (or only intermittent) history of colonisation with *Pseudomonas* spp.

Although such assays are not generally available in most clinical diagnostic laboratories, access to such technology is generally available at regional specialist microbiology centres, and therefore it may be prudent to establish routine analysis of CF sputum at annual review. In conclusion, employment of this multiplex PCR assay may permit the rapid detection of other *Pseudomonas* spp. in addition to *P. aeruginosa* directly from the sputa of CF patients. □

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Life-threatening post-partum hypercalcaemia

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A 23-year-old woman presented as an acute medical admission six weeks following the delivery of her second child. She presented with polyuria, polydipsia and lethargy. Blood analysis had excluded hyperglycaemia (random glucose 5.7 mmol/L) but her corrected serum calcium was extremely high at 5.29 mmol/L.[1] The 24-hour urinary calcium was high at 33.3 mmol/day, creatinine clearance 76 mL/h and urine output 5.2 L/day. Parathyroid hormone (PTH) was strikingly high at 1286 pg/L, confirming the diagnosis of primary hyperparathyroidism (PHPT).

Interestingly, her corrected serum calcium had been checked 24-hours post-partum and was found to be elevated at 2.94 mmol/L, but this was not followed up until her presentation as an emergency. She was treated initially with vigorous rehydration and intravenous disodium pamidronate (90 mg over 90 minutes) and after 10 days the serum calcium had fallen to 2.7 mmol/L.

An ultrasound of the neck confirmed a large adenoma (2.5 cm diameter) at the right lower pole of the thyroid. X-ray examination of the hands showed osteopaenia, sub-periosteal bone resorption and acro-osteolysis; and a bone scan showed extensive, generalised increased uptake throughout the skeleton.

A pre-operative vocal cord check was normal. She underwent an open parathyroidectomy two weeks after her emergency presentation. Surgery revealed one large parathyroid adenoma (3.2 x 2.6 x 2 cm), which was resected along with half of one other identifiable gland. Of the remaining glands, one was unidentifiable and the other

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suppressed. Apart from severe hungry bone syndrome requiring calcium supplementation, post-operative recovery was uneventful.

The adenoma weighed 6.5 g and was well encapsulated, with no capsular thickening, no extension of fibrosis into the body of the tumour and no capsular or vascular invasion.

In view of the extreme hypercalcaemia at such a young age, an underlying cause was sought. The family pedigree is shown in Figure 1. Her son's serum corrected calcium was 2.92 mmol/L 48 h after birth (normal range at 24–48 hours: 1.75–3.0 mmol/L.[2] In addition, he was found to have a widened anterior fontanelle, related to diathesis of the sagittal suture, but no focal pathology was noted on a computed tomography (CT) scan of the skull. The calcium fell slightly over two months, reaching a nadir of 2.65 mmol/L.

The patient's daughter (individual III:1), aged four years, had a normal serum calcium. Her father (individual I:4) died at the age of 44 from a myocardial infarction. Interestingly, he underwent frequent 24-h urine collections during life, but it has been impossible to ascertain whether or not this represented part of a follow-up for hypercalcaemia.

An oral pantomograph (OPG) was normal (excluding fibro-osseous jaw tumours), as were fasting pancreatic hormones (gastrin, pancreatic polypeptide, glucagons, vasoactive intestinal peptide and neurotensin), 24-h urinary vanilmandelic acid (VMA) and serum prolactin, excluding associated multiple endocrine neoplasia (MEN) syndromes.

A renal ultrasound showed nephrocalcinosis but no other features of note, and, in particular, no evidence of Wilms' tumour. Interestingly, an abdominal X-ray did not show any signs of nephrocalcinosis. A brain magnetic resonance imaging (MRI) scan, requested during the investigation of unrelated episodes of collapse, showed no intracranial pathology but did reveal a benign osteoma in the vault. Osteomas have not been reported in familial PHPT syndromes. While this could represent a coincidental finding, the possibility of an association between osteomas and familial PHPT syndromes cannot be ruled out.

At follow-up, two years after original presentation, the patient remained asymptomatic, with normal serum calcium and PTH levels. Her bone density scan showed osteopaenia in the lumber spine (T score: 0.5 SD, Z score: 1.3 SD) but was unremarkable at the left hip.

Primary hyperparathyroidism is a common condition. The incidence since the introduction of multichannel analysers is approximately 1 in 1000, with the relatively asymptomatic older female being the typical patient.[3] A prevalence of up to 2.1% in post-menopausal women has been reported in population-based health screening.[4]

Primary hyperparathyroidism is predominantly a sporadic disorder.[5] However, in the minority (<10%) of affected patients, PHPT is associated with a number of distinct hereditary syndromes including multiple endocrine neoplasia (MEN) types 1 and 2A (MEN 1, MEN 2A), hyperparathyroidism–jaw tumour (HPT–JT) syndrome[6] and familial isolated hyperparathyroidism (FIHP).[7]

Primary hyperparathyroidism is caused primarily by a benign single adenoma in approximately 80% of patients. Multinodular parathyroid hyperplasia accounts for 15–20% of cases and only occasionally is PHPT caused by parathyroid carcinoma. Distinguishing between benign and malignant parathyroid tumours can be difficult.[8] Sandelin *et al*. reported a series of parathyroid carcinomas in which the initial diagnosis was benign in 50% of cases.[9]

Although there is no definite evidence of other affected family members in this report, it is difficult to rule out the possibility, particularly in view of the history of frequent 24-h urinary assays in the patient's father. Gross hypercalcaemia at a relatively young age makes the diagnosis of familial hyperparathyroidism likely.[7]

The dominant mode of inheritance, the occurrence of asymptomatic gene carriers and the increased risk of parathyroid carcinoma or associated malignancies in other endocrine glands or the kidney, make it essential to exclude or confirm the diagnosis of familial hyperparathyroidism in all relatives whenever the diagnosis has been entertained or made in one member of the family. Long-term follow up is essential in order to confirm FIHP, as many families with MEN may present initially with parathyroid tumours and then other endocrine tumours are diagnosed a few years later.

The penetrance of fibro-osseous jaw tumours and Wilms' tumour is low in HPT-JT[6] but it is possible that the patient described here, or other family members. may present with these tumours at a later stage. Hence, long-term surveillance is indicated.

Primary hyperparathyroidism is relatively uncommon in pregnancy, with figures available pointing towards 0.8% of all female patients with PHPT presenting at this time.[10] However, the exact incidence is unknown because many patients will remain asymptomatic and there is no routine screening in place. In sporadic PHPT there is no apparent familial inheritance and the level of hypercalcaemia is often relatively mild, as the expanded plasma volume and the increased uptake of maternal calcium by the placenta result in a relatively low serum calcium.

Suggested parameters for biochemical diagnosis of PHPT during pregnancy are: total serum calcium >2.53 mmol/L during the first trimester, >2.42 mmol/L during the second trimester or >2.29 mmol/L during the third trimester.[11]

Primary hyperparathyroidism increases the risk of fetomaternal complications throughout pregnancy. Maternal complications include constitutional symptoms, nephrolithiasis, bone disease, pancreatitis, hyperemesis, muscle weakness, mental status changes and hypercalcaemic crises.[12] Post-partum hypercalcaemic crises may be seen once the placenta is delivered, as active placental calcium transport may be protective.[13] This appears to have been the mechanism of presentation in the patient reported here. Fetal complications may include intrauterine growth retardation, low birthweight, preterm delivery, intrauterine fetal demise, post-partum neonatal tetany and permanent hypoparathyroidism.[12]

Typically, serum calcium in an infant born to a mother with PHPT would be low. The placenta transports maternal calcium ions to the fetus against a concentration gradient, resulting in relatively high fetal calcium, suppression of fetal PTH and stimulation of fetal calcitonin. As placental calcium is withdrawn, the newborn infant becomes functionally hypoparathyroid. Fetal serum calcium level reaches a nadir at three to four days of life, and subsequently PTH rises, calcitonin falls and calcium rises.[14] Interestingly, the patient's newborn boy had a serum corrected calcium at 48 h at the upper limit of the reference range.

Previous reports have shown that conservative

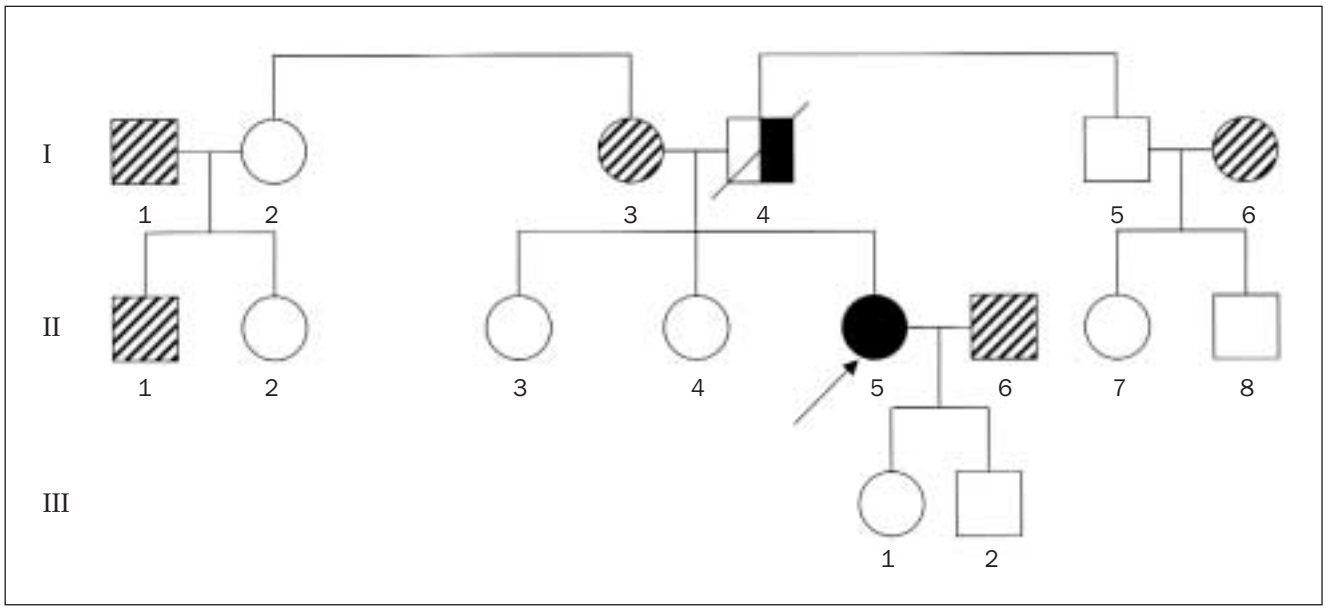

Fig. 1. Pedigree of a family showing possible autosomal dominant inheritance of familial isolated primary hyperparathyroidism. Affected individuals are represented by black symbols, unaffected individuals are depicted as open symbols, and members who were not investigated are represented by hatched symbols. Patient I:4, in whom a definitive diagnosis has not been made, is shown by a half-filled symbol.

management in the first trimester (and possibly the whole duration of pregnancy) is safe when there is mild, asymptomatic PHPT.[15] Surgery is generally advised in symptomatic patients during the second trimester, but may be safe even in the third trimester.[16–18] Surgery has been shown to reduce both fetal and maternal complications of PHPT during pregnancy.[19] Given the reluctance to use pharmacological therapy during pregnancy, surgery does appear to be the natural option when symptoms dictate that conservative management is no longer appropriate.

Increasingly sophisticated surgical techniques, including minimally invasive techniques using intra-operative PTH monitoring, mean that surgery should be safe and effective, with a short recovery period.[20–22] However, the lack of routine biochemical screening at the beginning of pregnancy means that many such cases initially will go unnoticed. The result is that both the fetus and the mother are at risk during the initial period until symptoms develop, and are then at greater risk due to late presentation.

Screening is simple, cheap and accurate; serum calcium could be checked at the same time as the blood glucose. It would appear that pregnancy-associated PHPT meets the standard criteria for screening programmes (condition leads to severe illness if left untreated, condition is treatable, condition is relatively common and the screening test is cheap and reliable) and should be considered for the routine antenatal screening process.

Primary hyperparathyroidism is a relatively common disorder that may occur during pregnancy. Untreated PHPT in pregnancy may have serious outcomes for both mother and child, but early identification of the disorder permits appropriate monitoring and treatment as required. At present, the treatment of choice would appear to be surgery, when conservative measures have failed.

Finally, the possibility of hereditary hyperparathyroidism should be considered, as some individuals presenting with PHPT during pregnancy will be manifesting the first features of one of these syndromes. Thus, routine screening for hypercalcaemia during pregnancy needs to be debated.

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A case of 'crouching' triglyceride and 'hidden' cholesterol

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Fasting specimens are recommended for full lipid profile testing by the third report of the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP III) because of the well-known errors in the Friedewald estimation of low-density lipoprotein cholesterol (calculated LDL-C) for non-fasting samples. The report remains highly focused on LDL-C management and includes the definition of target values; however, non-high-density lipoprotein cholesterol (non-HDL-C) may play an important role as a secondary therapeutic goal for initiation of LDL-lowering.[1]

Recently, a case of ischaemic heart disease (IHD) complicated with acute pulmonary oedema (APO) was encountered. The fasting plasma lipid profile results for the 70-year-old female patient showed total cholesterol 5.2 mmol/L (reference value <5.2), triglyceride 5.8 mmol/L (<1.7) and HDL-C 0.19 mmol/L (>1.0). Intriguingly, because LDL-C calculation is invalid when TG level is >4.5 mmol/L, LDL-C was measured by a direct surfactant method (homogeneous enzymatic, Hitachi 912, Roche Diagnostics) and was found to be very low (0.2 mmol/L). Apolipoprotein B100 (apo B) was, however, 1.20 g/L (0.41–1.07) and apo A1 was 0.73 g/L (1.20–2.00).

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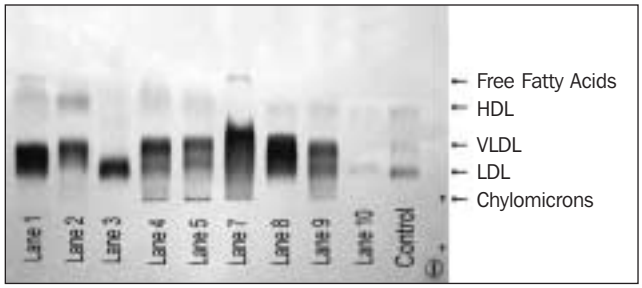

Fig. 1. Lipoprotein electrophoresis of the patient's plasma sample. Lane 3 shows a dense and distinct β-lipoprotein band, which is compatible with lipoprotein(a).

The sample appeared clear. Lipoprotein electrophoresis of the plasma sample revealed a dense and distinct β-lipoprotein band; however, the pre-β fraction was absent and there was no chylomicron at the origin. The faint α band was consistent with the low plasma HDL-C level (Fig. 1, Lane 3). Lipoprotein(a) (Lp[a]) was measured and found to be 505 mg/L (Immage immunochemistry system, Beckman Coulter).

The patient was on warfarin but not on any lipid-lowering drugs. Although the presence of other classes of triglyceride-rich lipoproteins could not be excluded, the lipoprotein pattern appeared unremarkable. Presumably, the presence of a high level of endogenous free glycerol (measured as triglycerides by a non-blank method) in patients under stress (IHD and APO) may account for the high plasma triglyceride result in this patient. Of concern, however, was the extremely low LDL-C concentration by a direct surfactant method.

The patient showed no evidence of obstructive liver disease or cholestasis, so the presence of LPX (which lacks apo B) or LPY (a triglyceride-rich lipoprotein) becomes unlikely. So, where had all the cholesterol gone?

Lipoprotein(a) is a cholesterol-rich lipoprotein that resembles LDL in size and lipid composition, yet contains apo(a), a structural glycoprotein that is covalently attached, via a disulphide linkage, to the apo B moiety of the LDL-like particle. The concentration of Lp(a), measured as its protein moiety of apo(a), by an immunonephelometric assay (Beckman Coulter Array system) was found to be very high in this sample. Although a method for directly determining Lp(a) cholesterol using lectin-bound plasma technology[2] was not available at the time of testing, following the approach proposed by Scanu,[3] the estimated cholesterol content of the Lp(a) protein based on the known chemical composition of Lp(a) was 3.2 mmol/L.

Unfortunately, Lp(a) is not included as part of most routine lipid profiles. Although its omission is inconsequential in individuals with low plasma Lp(a) levels,