Virtually all kidney tumours of children were Wilms' and there was a striking preponderance in girls. 70% of eye tumours were retinoblastomas. The relative frequency of retinoblastoma was much higher than it is in western countries.

Data from the population-based registries at Bangalore, Bombay, and Madras indicate paediatric cancer frequencies varying from 3-7% to 4%. 2,3 In Dibrugarh in north-eastern India and Chandigarh in the north-west the frequency was 2-4%. International comparisons of cancer incidence are potentially fraught by variability in diagnosis, classification, and coding practices, by competing causes of death, by differential access to medical care, and by incomplete registration, so patterns need cautious interpretation. Leukaemia is the leading type of cancer and malignant tumours of the CNS are the second most common cancer in childhood in several countries. 4-6 Lymphomas are the commonest cancer (59%) among Nigerian children, with Burkitt's lymphoma accounting for 87% of all lymphatic malignancies. 7 A low incidence of Wilms' tumour has been reported from China. 8

Variations in the population distribution of these cancers suggest differences in aetiology. Parental recall of exposure histories has a major role in retrospective studies of risk factors in children, and several factors (genetic factors, birth characteristics, environmental, infectious) have been identified. The establishment of committed paediatric cancer registries in India would contribute usefully to clinical and epidemiological research.

LeVeen shunt with wandering tip

SIR,—The LeVeen peritoneovenous shunt has been used for nearly 20 years in the treatment of intractable ascites due to chronic liver disease. However, the technique has a high failure rate due to shunt occlusion. 1 An uncontrolled study has suggested that the incidence of shunt occlusion due to thrombosis may be reduced if a titanium tip is used (fig 1). 2 This tip is not part of the standard catheter assembly but is attached to the venous end at the time of manufacture. We report here a complication resulting from our first experience of this modification.

The patient was a 52-year-old man with alcoholic cirrhosis developed ascites unresponsive to fluid restriction and diuretics. Twice-weekly paracentesis meant that the patient was unable to resume medical care, and by incomplete registration, so patterns need cautious interpretation. Leukaemia is the leading type of cancer and malignant tumours of the CNS are the second most common cancer in childhood in several countries. 4-6 Lymphomas are the commonest cancer (59%) among Nigerian children, with Burkitt's lymphoma accounting for 87% of all lymphatic malignancies. 7 A low incidence of Wilms' tumour has been reported from China. 8

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Lymphokine-activated killer-cell traffic in metastatic melanoma

SIR,—Mr Swift and colleagues (June 22, p 1511) report the successful imaging of colorectal metastases with 111Indium-labelled tumour-activated killer lymphocytes (TAK). They mention the advantages of TAK cells over tumour-infiltrating lymphocytes (TIL) — in that they are not restricted by tumour histology or stage, are easily handled, and are independent of interleukin-2 support in vivo.

We have lately reported the imaging of melanoma metastases with radiolabelled lymphokine-activated killer (LAK) cells in four of six patients. Additional interleukin-2 infusion was not necessary. 1 Metastases have so far been demonstrated by LAK-cell scintigraphy in 8 (57%) of 14 patients. These cells can be produced quickly and easily. However, only 1×10⁶ to 1×10⁷ cells (which were used in our protocol) can be obtained with ease by leukapheresis. In contrast to TAK, LAK cells were able to image lymph-node, bone, skin, and gastrointestinal metastases, but not parenchymatous metastases.

Two patients gave informed consent for biopsy of scintigraphically-positive metastases, and we could therefore analyse the peritumoural infiltrate with a panel of monoclonal antibodies (APAAP-staining of cryosections). Activated T-helper (CD3, CD4, CD25) lymphocytes were identified as the main population in the reactive infiltrate in these 2 patients. No natural

Fig 1—Titanium tip to LeVeen shunt.
Length 3 cm.

Fig 2—X-ray views of detached tip.

killer (CD16, CD56) cells were seen. This observation suggests that from the heterogeneous cell populations included in LAK-cells, T-lymphocytes but not natural killer cells can migrate to tumour sites in melanoma patients. Tumour recognition and traffic are probably restricted to specific T lymphocytes, as is also suggested by Swift and colleagues' data. However, the peripheral blood seems to contain a considerable number of these T cells, which can be used for tumour imaging after an interleukin-2-induced short-time activation. 3 LAK-cell scintigraphy might use interleukin-2 possibly through a T lymphocyte-tumour cell interaction. 3 Although these preliminary data should be interpreted with caution, we postulate that metastases respond to immunotherapies that use interleukin-2 possibly through a T lymphocyte-tumour cell HLA-DR-dependent interaction. 3 LAK-cell scintigraphy might be a fast and economic method to analyse individual properties and might have prognostic relevance for immunotherapies that use interleukin-2.

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Clinical spectrum of mitochondrial DNA mutation at base pair 8344

Sir,—Dr Hammons and colleagues (June 1, p 1311) identify a mutation at base pair 8344 of the mitochondrial genome in blood samples of 5 of 7 patients with the syndrome of myoclonic epilepsy and ragged red fibres (MERRF), confirming previous studies with muscle mitochondrial DNA. 1,2 This mutation, which is in the mitochondrial gene for lysine transfer RNA (tRNAlys), was also found in 1 patient with myoclonus and ataxia who lacked ragged red fibres, but was absent in many other syndromes associated with mitochondrial disease. We describe further phenotypes associated with this mutation.

The clinical spectrum of MERRF is broad relative to the other causes of progressive myoclonic epilepsy from which it should be distinguished. 3 We have reported 13 patients with MERRF, including one family with 6 affected members. 4 The 2 most severely affected (subjects 5 and 6) had the pathological features of Leigh's syndrome, in addition to the system degeneration characteristic of MERRF. 4 We have now identified the tRNAlys mutation in this family. This confirms Hammons and colleagues' observation of Leigh's syndrome lesions at necropsy in 1 of their MERRF patients with this mutation. The neuropathological lesions characterising Leigh's syndrome are strikingly different from those in uncomplicated cases of MERRF, yet they now seem to be consequences of the same mitochondrial DNA mutation in some families. On the basis of positron emission tomographic data, 5 we have suggested that such clinical-pathological diversity can be explained by the peculiarities of mitochondrial inheritance, resulting in a spectrum of severity of cerebral metabolic deficits. In the more severe cases, sudden clinical and metabolic deterioration can happen with additional stresses, such as fever, resulting in the pathological picture of Leigh's syndrome.

The proband of our MERRF family also had large disfiguring axial lipomas characteristic of multiple symmetric lipomatosis (MSL). 6 Morphological and biochemical evidence suggests that familial and sporadic MSL is associated with mitochondrial dysfunction. 6 An additional patient in our series of MSL, 7 who did not have myoclonus epilepsy, also had the tRNAlys mutation. Moreover, the index case of the US family in whom the MERRF mutation was originally described now also has lipomas (J. M. Shoffner, personal communication). It thus seems that MSL, at least in some cases, is a manifestation of this mutation.

Although the clinical features of the mitochondrial encephalopathies are diverse, there are recognisable clinical patterns, for which genotypic specificity is emerging. The clinician should now ask for analysis of mitochondrial DNA from blood or muscle to search for the tRNAlys mutation in cases of possible MERRF, MSL, or Leigh's syndrome. However, all three of these clinical phenotypes are probably also caused by other yet to be discovered molecular lesions.

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Severity of cystic fibrosis

Sir,—Dr Johansen and colleagues (March 16, p 631) report that just over three-quarters of patients with cystic fibrosis are homozygous for the AF508 mutation. The rest have other mutations, many of which have been recognised, raising the possibility that the clinical expression of the disease is determined by the mutation that is present. We report a 45-year-old man in whom the disease has been unusually mild and whose genotype has been determined.

The patient was an only child born in 1946. At 5 years old he had steatorrhoea and respiratory infections, and fibrocystic disease of the pancreas was diagnosed. He was treated with pancreatic enzyme supplements and made such good progress that by age 15 the diagnosis was thought to have been incorrect and the enzyme supplements were stopped. In his early twenties steatorrhoea recurred and a jejunal biopsy showed an abnormality consistent with coeliac disease. Failure of his symptoms to resolve completely on a gluten-free diet was attributed to non-compliance. At the age of 27 intestinal obstruction developed and at laparotomy the terminal 0-6 metres of ileum proved to be occluded by inspissated faecal-like material. At about this time he was investigated for a persistent productive cough and bronchotherapy showed bilateral bronchiectasis.

By age 38, when he moved to Devon, he was beginning to be troubled by breathlessness on exertion. Since then he has had planned admissions for physiotherapy about twice a year in addition to postural drainage at home, but he has never required admission for an acute infective exacerbation. Chest radiography showed extensive basal emphysema with upper zone fibrosis. His lung function has declined over the past 7 years (FEV1, 925 ml and FVC 1929 ml in 1984; and 550 ml and 1350 ml, respectively, in 1991), and Pseudomonas aeruginosa has frequently been cultured from his sputum. His sweat sodium concentration was 124 mmol/l in 1984. He has maintained a steady weight during this time (51 kg, height 1929 cm in 1984; and 180 cm, respectively, in 1991).