The recent work on the pathology and genetics of prion disease in humans has several implications for the epidemiological proposals at the end of Professor Matthews's editorial. Firstly, because of the clinical and pathological variability the true incidence of transmissible dementias (prion disease) in humans can be established with certainty only by a combination of genetic screening and immunocytochemical detection of the abnormal isoform of prion protein. Secondly, on the basis of information already available the incidence of the range of prion diseases in humans is (and probably always was) significantly higher than the figures quoted in the editorial. Thirdly, because of this improved rate of detection any attempts at ascertaining the possible impact of foodstuffs contaminated with bovine spongiform encephalitis on the incidence of transmissible dementias must take this apparent rise in the number of cases into account. Finally, the number of familial cases being identified raises the possibility that in humans the prion disease range has more of a genetic basis than hitherto realised.

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SIR,—Drs Christopher Fear and Manikkarasa Devakumar[1] take issue with Professor W B Matthews over his statement that all patients with Creutzfeldt-Jakob disease must be seen by a neurologist who is familiar with the disease[2]: instead they would substitute electroencephalography as a baseline investigation. Those following this recommendation are more likely to miss the diagnosis than a physician or psychiatrist prepared to review the diagnosis at each stage in the light of clinical evidence.

In practice the electroencephalogram is rarely helpful early in the disease, and the best a neurophysiologist reading it can do is to suggest that the test be repeated at intervals. Brown *et al* observed that the characteristic periodic electroencephalogram complexes were found comparatively late in the illness.[3] Although a pathognomic electroencephalogram is eventually seen in about 75% to 80% of patients, this may not be the case in certain groups of patients with Creutzfeldt-Jakob disease —for example, those receiving human growth hormone therapy.[4]

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Non-invasive mechanical ventilation for acute respiratory failure

SIR,—In their paper Dr M W Elliott and colleagues describe the use of nasal intermittent positive pressure ventilation in patients with acute hypercapnic respiratory failure.[1] Of their group, three patients had chronic obstructive pulmonary disease. We have recently managed four patients with this condition with associated acute hypercapnic respiratory failure. Two patients were treated using nasal intermittent positive pressure ventilation, and in the other two patients we used nasal continuous positive airways pressure. The table gives the patients' details. All four patients had known severe chronic obstructive pulmonary disease and were admitted with severe hypercapnic respiratory failure; two of them had associated respiratory acidosis. None of the patients were considered suitable for endotracheal intubation and assisted ventilation because of end stage chronic disease.

All four patients had supplemental oxygen at a flow of between 0·5 l/min and 2·0 l/min entrained through a port in the nasal mask. Arterial oxygen tensions increased in all patients from a range of 3·9-4·7 kPa to 6·3-8·0 kPa with nasal intermittent positive pressure ventilation or continuous positive airways pressure. In three patients there was a fall in arterial carbon dioxide tension; in the other patient, who was treated by nasal intermittent positive pressure ventilation, the arterial carbon dioxide tension was maintained (table). Nasal continuous positive airways pressure was well tolerated, but both patients in whom ventilation was assisted by nasal intermittent positive pressure ventilation required chin straps to prevent excessive air loss during the inspiratory phase.

Two patients survived to be discharged from hospital: one was alive and well several months after discharge, and one died of a bronchogenic carcinoma four months after discharge. Of the two who died in hospital, one died of progressive renal failure despite correction of arterial gas imbalance and the other died of progressive respiratory failure three weeks after admission despite an initial response.

In agreement with Dr Elliott and colleagues we have found nasal intermittent positive pressure ventilation to be of benefit in two patients with severe hypercapnic respiratory failure, but in addition two other patients benefited from the use of nasal continuous positive airways pressure, which has been used previously to manage patients with hypoxia but without hypercapnia[2] and in the treatment of obstructive sleep apnoea.[3] In the two patients described we achieved improvement in arterial oxygen tension with an associated fall in arterial carbon dioxide tension with this technique.

In summary, we believe that both nasal intermittent positive pressure ventilation and continuous positive airways pressure may be useful adjunct treatments in patients with hypercapnic respiratory failure, particularly those who are not suitable for assisted ventilation through an endotracheal tube. In our hands this treatment still requires close supervision by medical, physiotherapy, and nursing staff, and at present we prefer to treat these patients in high dependency settings.

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Details of four patients with chronic obstructive pulmonary disease admitted with severe hypercapnic respiratory failure

Case No	Age and sex	FEV_1 (l)	Method of ventilation	At presentation (with air)		Assisted		During convalescence		Outcome
				P_aO_2 (kPa)	P_aCO_2 (kPa)	P_aO_2 (kPa)	P_aCO_2 (kPa)	P_aO_2 (kPa)	P_aCO_2 (kPa)	
1	68 F	1·1	NIPPV	3·9	8·4	8·0	8·6	6·8	5·0	Alive at four months
2*	73 F	0·6	NIPPV	4·7	8·4	6·3	7·8	6·6	6·3	Died after four months
3	70 M	0·6	NCPAP	4·5	7·3	6·4	5·3			Died after three weeks
4	72 F	0·8	NCPAP	4·1	9·0	6·9	5·7			Died after five days

FEV_1 = Forced expiratory volume in one second.
NIPPV = Nasal intermittent positive pressure ventilation.
NCPAP = Nasal continuous positive airways pressure.
*The patient also had kyphasis.

Vasectomy and testicular cancer

SIR,—I agree with Dr A R J Cale and colleagues that the possibility of vasectomy affecting testicular malignancy is important in view of the current trend towards male sterlisation.[1] I disagree, however, that a large prospective study is the best approach at this juncture.

The finding of a significantly higher standardised incidence ratio of testicular tumour for men who had a vasectomy and the short average interval (1·9 years) between vasectomy and malignancy have led Dr Cale and colleagues to suspect "an association" and that "vasectomy accelerates the tumour."[1] Studies on the relation between vasectomy and testicular cancer have been few and the findings tenuous. Vasectomy was not considered as a potential risk factor in a review of the epidemiology of testicular cancer published in 1989,[2] and Moss *et al* did not find an association between vasectomy and testicular cancer among American men aged 18-40.[3] A case-control analysis performed specifically to test this hypothesis did find an association, but it was restricted entirely to Catholic men.[4] The investigators suspected that the finding may have been spurious owing to selective underreporting of vasectomy among the Catholic controls.[4] The finding by Dr Cale and colleagues of an excess of observed number of cases in only the 30-35 age group presents a problem similarly deserving an explanation. An association in time between two variables can be due to many reasons. More convincing evidence is needed before an expensive, logistically difficult, and time consuming prospective approach is to be undertaken.

The incidence of testicular cancer is very low (5·6 per 100 000 white men aged 20-69 in the United States).[4] As Strader *et al* pointed out, even if data of four previous large multicentre studies involving 114 000 men (with an average follow up period of five years) were pooled for analysis the study power would only be 0·2 (for the detection of

a twofold increase of the risk of testicular cancer at the 0·05 level of significance).[1] It is doubtful that one large cohort study could, in fact, produce definitive results to confirm or negate the putative association.

The sample size needed to achieve the desired study power in a case-control study is determined by the prevalence of vasectomy rather than by the incidence of testicular cancer. In a number of countries, including the United Kingdom, about 10% of couples of reproductive age rely on vasectomy for contraception.[5] With this prevalence, a case-control study will need 221 pairs to detect a twofold increased risk for $\alpha=0{\cdot}10$ (two sided) and $\beta=0{\cdot}20$. Only 78 pairs are needed to detect a threefold difference in relative risks for same study power.[6] The prevalence of vasectomy should be higher in big cities where more hospitals are located, and thus fewer testicular cancer patients will be needed. If, in practice, the needed number of cases cannot be reached in a reasonable period of time then multicentre study, retrospective case finding, and increasing the number of controls relative to cases offer solutions. Little suspicion of such an association is entertained by the general population and the exposure variable (vasectomy) is an event not easily forgotten by the study subjects. Both these aspects will help avoid the bias due to selective recall and memory decay, and they will add validity to this much less costly and more easily manageable approach, which produces results more quickly. I believe that the case-control approach is the method of choice.

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Air embolism during transcervical resection of endometrium

SIR,—Dr Ralf Baumann and colleagues in their report point out the risk during transcervical resection of the endometrium from systemic absorption of irrigating fluid from the denuded myometrium and through transtubal loss.[1] We have attempted to reduce transtubal absorption by combining laparoscopic tubal occlusion (using Silastic rings) with transcervical endometrial resection. In nine cases by this combined technique the mean fluid deficit was 259 ml (range 0-900 ml) compared with 643 ml (100-2030 ml) reported by Dr Baumann and colleagues. This small number of cases is insufficient to prove the value of tubal occlusion, but the study gave us the opportunity of observing a hitherto undescribed hazard of endometrial resection.

A 46 year old woman suffering from uncontrolled menorrhagia was found at hysteroscopy to have a small (diameter of 1 cm) adenomatous endometrial polyp. After two months' treatment with danazol she underwent hysteroscopic resection of the polyp followed by total endometrial resection by a modification of the diathermy loop technique.[2] General anaesthesia was induced with propofol and maintained with nitrous oxide, oxygen, and isoflurane breathed spontaneously through a laryngeal mask. The electrocardiogram, blood pressure, and pulse oximetry were monitored continuously. Dextran 40 (10%) was used as the irrigating fluid: 4900 ml was used, of which 4300 ml was recovered.

On completion of the resection the pelvic organs were inspected by laparoscopy, with the patient in a head down position. The uterus was intact but there was congestion of the broad ligaments, from which air bubbles could be seen entering small calibre veins in the lateral pelvic wall. Over the next four minutes the patient's oxygen saturation fell from 97% to 84% and her pulse rate rose from 72 to 110 beats/min, consistent with air embolism. Her blood pressure was unchanged. The head down position was reversed and positive pressure ventilation started with 100% oxygen. The oxygen saturation and pulse returned to normal within 10 minutes and the patient made a full recovery.

Air emboli can occur during surgery whenever a vein is open and the air pressure exceeds venous pressure. This can be the result of a rise in air pressure, such as occurs during insertion of a cemented femoral prosthesis,[3] or a fall in venous pressure caused by raising the operative site above the level of the heart, which is a particular risk when the patient is breathing spontaneously. Air emboli have been reported to occur during neurosurgery[4,5] and less commonly during caesarean section[6] and transurethral resection of the prostate.[7]

We present these data to warn others embarking on the newly developed procedure of transcervical resection of the endometrium that an anaesthetic technique employing positive pressure ventilation may be preferred. Our experience also suggests that patients should not be nursed in a head down position after operation.

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Portal vein thrombosis in myeloproliferative disease

SIR,—The extensive thrombosis of the portal venous system that may accompany the myeloproliferative diseases was clearly described in the recent Hammersmith Hospital staff round report.[1] Haematological disorders, however, represent only one of several possible aetiologies of portal vein occlusion, which include congenital malformations, trauma, sepsis, tumours, and invasive procedures such as catheterisation of the umbilical vein. Our recent analysis of portal venous occlusion in 27 patients suggested a relation between the aetiology and the anatomical distribution of the occlusion. Each patient was investigated with digital subtraction angiography, and the anatomical features were interpreted by one observer (JK), who was without knowledge of the clinical history of the case. The angiographic features were classified into four main groups:

(1) Seven patients had occlusion of the main portal vein and bifurcation. Five of these had no history of important illness and one patient had undergone an operation for duodenal atresia. Cavernous transformation of the portal vein was seen in patients in this group, which might have represented a congenital anomaly of the portal vein.

(2) Five patients had occlusion of the main portal vein and distal intrahepatic branches. Four of these had a history of severe illness and two had undergone neonatal catheterisation of the umbilical vein.

(3) Six patients had total occlusion of the portal venous system excluding the splenic vein. Five of this group had been treated for abdominal problems and two had undergone catheterisation of the umbilical vein.

(4) Nine patients had total occlusion of the portal venous system. Six of these patients had haematological abnormalities including polycythaemia, prekallikrein deficiency, and myeloid dysplasia. Three had associated hepatic vein occlusion (the Budd-Chiari syndrome). No haematological anomaly was found in three patients, who had histories of pancreatitis, surgical trauma to the superior mesenteric artery, and catheterisation of the umbilical vein.

The preliminary analysis of patients with portal venous occlusion suggests that congenital anomalies may spare the splenic and superior mesenteric veins, which may be used for surgical decompression if indicated. At the other end of the range total occlusion of the splanchnic veins may indicate an underlying haematological disorder. Catheterisation of the umbilical vein and intra-abdominal sepsis are associated with occlusions of variable extent that usually extend beyond the portal vein itself.

In conclusion, accurate visualisation of the anatomical distribution of venous occlusion may be helpful in determining the aetiology of as well as in managing extrahepatic portal hypertension.

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Clinical directorates

SIR,—Mr J N Johnson's editorial on clinical directorates raises several important issues in the style of hospital management, both the version that has evolved (and is still evolving) at Guy's Hospital and the predictably different versions that need to be constructed flexibly to fit local circumstances.[1] I will do little more than offer a few personal observations from the vantage of my fifth (and last) year as director of clinical services in medicine at Guy's Hospital. Some of my fellow directors may see things in a different light; Professor Cyril Chantler, who was largely responsible for introducing the system at Guy's, has written about it before.[2]

I agreed to take on the task reluctantly, seeing it partly as a device for administering unpleasant medicine to my colleagues which they might accept less readily from a lay manager. There was indeed much foul tasting medicine to be swallowed in our first few years as we "slimmed down" to try to live within budget. It became clear that we had to do that if only to practise the best medicine possible under the circumstances; it was equally clearly my responsibility to identify where that "best" was not good enough and to argue forcibly against the constraints, sometimes almost crippling, that we