7 of 59 patients with generalised neurofibromatosis. Of these, 4 had pulsating eyeballs and 2 had exophthalmos.

Unilateral pulsating exophthalmos in patients with generalised neurofibromatosis is a sign of considerable clinical importance, both in differential diagnosis and in prognosis. This view is supported by a patient with pulsating exophthalmos and neurofibromatosis, with a congenital defect in the left posterior orbital wall, whom I have followed up for 25 years. During this period diplopia developed due to ocular muscle paresis and progressive deterioration of vision in the left eye, but he is otherwise symptom-free and in full-time employment.

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1. Burrows EH. Bone changes in orbital neurofibromatosis. *Br J Radiol* 1963; **36:** 549–61.
2. Burrows EH. Orbitocranial asymmetry. *Br J Radiol* 1978; **51:** 771–81.

VISIONS THAT TALK

SIR,—Dr Deahl (April 4, p 812) questions the validity of a polysensory combined visual/auditory hallucination in which people are visualised who also talk.

More than 20 years ago at the Brook Hospital, Woolwich, I saw a woman aged about 45 who was holding a conversation with a visual hallucinations of visions that talked. Other diseases of the corpus disorientated, and demented. She had been in hospital for about a week and told the nurses that she could see people by her bed and was often seen conversing with them. She had drunk large amounts of wine during the previous 2–3 years and had become a prostitute for small amounts of money. She died a few weeks later. At necropsy the brain showed several round areas of necrosis with demyelination in the corpus callosum. She had Marchiafava-Bignami's disease.

Deahl mentions a chronic alcoholic patient who described hullucinations of visions that talked. Other diseases of the corpus callosum, such as tumours and angiomas, may also produce hallucinations. The talking visual hallucination is a real syndrome with an organic basis and occurs with diseases of the corpus callosum.

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BOTULISM AND GUILLAIN-BARRÉ SYNDROME

SIR,—Dr Sonnabend and colleagues (Feb 14, p 357) describe a case of botulism type F associated with Guillain-Barré syndrome (GBS). The mechanism of action of the toxin is thought to be restricted to the neuromuscular synapse, which may be why the possibility that the botulism toxin might have caused the signs and symptoms of GBS was not discussed. Our findings in the canine equivalent of GBS indicate that such an explanation may not be unreasonable.[1,2] The clinical signs in six dogs initially suggested GBS but subsequently were found to be due to a severe food-borne type C botulism. Electrophysiological studies indicated a significant slowing of sensory nerve conduction velocity and a significant change in the shape, amplitude, and duration of action potentials recorded adjacent to the nerve; these changes reversed in parallel with clinical improvement. These findings indicate a sensory nerve dysfunction not adequately explained on current knowledge of the action of botulism toxin on cholinergic nerve endings. It was therefore suggested that botulism toxin interferes with peripheral nerve conduction as well. Sonnabend et al suggest that patients with GBS should be examined for botulism. I suggest that sensory nerves should be studied in cases of botulism.

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1. Cornelissen JMM, Haagsma J, van Nes JJ. Type C botulism in five dogs. *JAAHA* 1985; **21:** 401–04.
2. van Nes JJ, van der Most van Spijk D. Electrophysiological evidence of peripheral nerve dysfunction in six dogs with botulism type C. *Res Vet Sci* 1986; **40:** 372–76.

PAIN IN THE PLURAL

SIR,—Dr Olson (March 28, p 755) finds that Australian patients often refer to their painful symptoms in the plural when the aetiology is other than organic. I too have been using this as a rule of thumb since I have found it to be valid in the West Indies and West Africa.

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EARLY EMBRYO LOSS

SIR,—Early embryo loss within 14 days of conception is probably unrecognised by most women because menstruation occurs at or about the expected time. Surveillance of early embryo loss therefore requires the co-operation of a representative sample of couples and a reliable assay to establish the presence of an embryo within the female reproductive tract. The first report about early embryo loss was a study which was published in 1959 of "therapeutic" hysterectomy in 210 fertile women aged below 42.[1] 107 women fulfilled the criteria for possible conception—ie, no abnormality likely to prevent conception was identified in the upper reproductive tract and coitus had occurred within 24 h of known ovulation. In these 107 hysterectomy specimens, 34 early embryos were identified, ranging from a 2-cell tubal embryo to a 17-day villous embryo. 10 of these embryos were so abnormal as to be incapable of survival—ie, early embryo loss was 29%. However, women undergoing hysterectomy during the 1940s and 1950s were unlikely to be a representative sample. Furthermore, the female upper reproductive tract is a vast area to sample and the contents are difficult to retain. Nevertheless the study is frequently quoted and the data have been reanalysed to give estimates of early embryo loss ranging from 35 to 78%.[2,3]

The chorion begins to secrete human chorionic gonadotropin (HCG) from day 6 of embryogenesis[4] and an embryo within the reproductive tract may be detected by a positive HCG assay in maternal serum or urine after that time. The initial immunological assays cross-reacted and were insensitive at low levels of HCG; the radioimmunoassay for the β-subunit of HCG is more specific. Serum HCG assay in luteal phase cycles of 200 women with copper intrauterine contraceptive devices showed that conception occurred in 12–19% of such cycles.[5] In a study over 198 cycles in a normal population of 82 women (41 were nulliparous) attempting to conceive, control urinary values were obtained from a group of sterilised women.[6] Anovulant contraceptives had been discontinued for 3 months and urinary samples were collected on alternate days from day 21 of the cycles. HCG was increased in 118 cycles, of which 51 (43%) resulted in clinical pregnancy—ie, a 57% loss of early embryos. The same group had previously assayed urinary β-HCG to monitor conception attempts in 197 women of whom 101 were nulliparous. Urinary samples were collected daily from day 21 of 623 cycles; 152 conceptions were detected, of which 50 were lost at the next menstrual period—ie, early embryo loss was 33%.[7] Serum β-HCG has also been studied in 226 cycles in 91 normal healthy women (23 were nulliparous) who wished to conceive.[8] During 3 preceding cycles, when barrier contraceptives were used, weekly serum samples provided control levels. During the investigation proper, serum samples in the week before expected menstruation revealed increased levels of β-HCG in 92 cycles, of which 7 ended in normal menstruation. In the remaining 85 cycles, menstruation did not occur and a diagnosis of clinical pregnancy was made, of which 11 ended as spontaneous abortions. The incidence of clinically unrecognised early embryo loss was therefore only 8%.

However, any estimate of early embryo loss derived from HCG or β-HCG assays cannot include those embryos who fail to reach the stage of HCG secretion. Surveillance of embryo loss during the period from conception to blastocyst formation requires some other means of identification of the zygote, morula, or early blastocyst within the reproductive tract. In the mouse, conception is followed by maternal thrombocytopenia which is sustained until implantation.[9] This effect is caused by the embryo because it is observed after the transfer of early embryos to foster mothers,[9] and after the injection of normal females with the in-vitro fertilisation