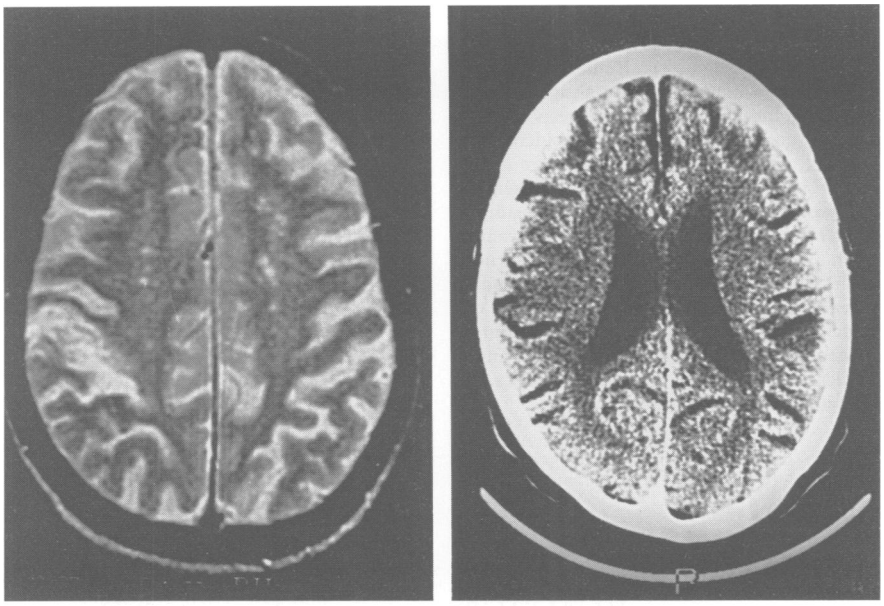

(A) (B)

(A) Sagittal T2 MRI showing a cortical infarct in the right parietal region; (B) CT showing an old cortical infarct in the left parietal region.

Brain CT without contrast showed an old cortical infarct in the left parietal region. Magnetic resonance imaging on the 12th day showed a recent cortical infarct in the high right parietal region, and cortical atrophy localised in the left parietal region, without evidence of callosal lesions. A SPECT examination performed on the 10th day showed a left parietal perfusion deficit with hyperperfusion on the right parietal region. The patient was treated with ticlopidine from the first day; the abnormal motor behaviour as well as the foreign limb sensation gradually disappeared after the first week, but the loss of visual guidance of the affected limb and loss of sensation still persisted on discharge.

The phenomenon that one hand behaves independently of the patient's will was first described by Goldstein[3] in 1908, while studying patients with callosal lesions. Since that initial report, several authors have described similar sensorimotor behaviour in association with lesions involving the corpus callosum, the mesial frontal lobes (cingulate gyrus and supplementary motor areas), combinations of both, or bifrontal lesions.[4] Despite all these clinical descriptions, no unifying criteria were set for the "alien hand syndrome" or "alien hand sign" (depending on the authors). Aetiological theories all have in common some notion of disconnection (right from left, or sensory from motor) and some notion of released inhibition affecting activities of the alien hand.[2] Feinberg *et al*[5] suggested that alien hand syndrome was in fact two different entities, both from a clinical and anatomical perspective: a frontal alien hand syndrome and a callosal alien hand syndrome. The first type would result from damage in the supplementary motor areas, anterior cingulate gyrus and medial prefrontal cortex of the dominant hemisphere, and anterior corpus callosum, and would be clinically related to reflexive grasping and compulsive manipulation. The callosal type would be characterised primarily by intermanual conflict and requires only an anterior corpus callosum lesion.

More recently, alien limbs have also been described with other underlying pathology, such as corticobasal degeneration, and central sensory nuclei (thalamic), occipitoparietal, and internal capsule lesions.[1 6] In all the described cases, callosal, thalamic, or internal capsule lesions, added to cortical lesions were required. Doody *et al*[1] suggest that, alternatively, a large posterior infarct alone may be sufficient to give an alien hand syndrome, although this has never been reported. The clinical picture of these cases also fulfilled the criteria of the feeling of foreignness and autonomous movements seen in classic descriptions. Nevertheless, they also displayed other associated features such as cortical myoclonus, abnormal sensory functions, loss of visual guidance of the affected limb (optic ataxia), or movement disorders.

In our patient, the feeling of strangeness and imposed involuntary movements, together with the inability to recognise his hand without visual clues, gave the picture of alien hand syndrome. There was no evidence of any frontal, callosal, thalamic or internal capsule lesions. We think that in our case, bilateral dorsoparieto-occipital lesions interfere with peristriate outflow pathways toward parietal zones, where visual-somatosensorial interactions are likely to occur. When bilateral, and in this specific case, synchronous, these lesions could explain the right parietal syndrome together with the loss of visual guidance of the affected limb, that can also result in an alien hand syndrome. Epidemiological studies of alien hand syndrome, then, will be difficult until a clear cut syndrome is defined or there is a consensus about whether there are one or more syndromes and what the relation is between each syndrome and the underlying process.[2]

Our patient shows the multiple anatomical substrates underlying potential alien hand syndrome and the clinical variability (associated cortical symptoms, accompanying movements, duration) of this syndrome. Given the difficulties in a homogeneous assessment and consensus definition, we prefer alien hand sign instead of alien hand syndrome, so that more flexibility in anatomical correlations and associated features can be permitted.

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Antiganglioside antibodies in toxic oil syndrome

Toxic oil syndrome emerged in Spain in 1981, affecting 20 000 people after ingestion of rapeseed oil that was denatured with aniline for industrial use, subsequently refined in an attempt to detoxify it, and fraudulently directed to human consumption.[1] It caused an acute flu-like illness with interstitial pneumonitis that progressed in 15% of the patients to a chronic syndrome, characterised by scleroderma-like skin manifestations, sicca syndrome, arthritis, and various neurological disorders.[2] These were acute encephalopathy, stroke-like episodes, and peripheral nerve lesions with acute or chronic axonal or, less often, demyelinating polyneuropathy. The neuropathy ranged from mild impairment to severe cases, wheel chair bound for months. Around 10% of these patients are still under medical surveillance, due to cardiorespiratory and neurological sequelae. The clinical features and proposed pathogenic mechanism of toxic oil syndrome are similar to the eosinophilia-myalgia syndrome. So far, the toxic substance has not been identified and the mechanisms of lesion of the peripheral nerves has not been established. An autoimmune mechanism has been proposed, but the role of autoimmunity is not clear. We have evaluated the presence of antiganglioside antibodies in patients with toxic oil syndrome and peripheral neuropathy.

Serum samples from 12 patients (two men and 10 women, age range 20–60; mean 43·9 (SD 16·7) years) with toxic oil syndrome and peripheral neuropathy were studied. Neuropathy was not progressive, except in one patient, in whom progression was established by repeated conduction studies. Two patients also had CNS disorders (myoclonia and hyperreflexia). Serum electrophoresis, erythrocyte sedimentation rate, complement study, latex fixation, and

antinuclear antibodies were normal or negative. Sixty eight patients with other neurological diseases and 43 normal subjects were tested as controls. Serum samples obtained during the past year were assayed "blind" for antibodies to ganglioside GM1, GD1b, GD1a, and asialic-GM1 by enzyme linked immunoabsorbent assay (ELISA) according to a modification of the method described by Nobile-Oracio *et al.*[3] Briefly, serum was added to microwells coated with 1% bovine serum albumin (BSA) or ganglioside. Reaction products were visualised with *o*-pheylenediamine as substrate and optical density was read spectrophotometrically in an ELISA reader (Titertek Multiskan plus) at 490 nm. Serum samples were tested in duplicate or three occasions, with a positive sample (a gift from Dr Nobile-Orazio) tested as control in each plate. Results were calculated as the absorbance obtained from the well coated with ganglioside minus the absorbance from the BSA coated well. Samples were considered positive when this difference exceeded 0·1. Antibody titres were considered increased when they were higher than 3 SD from the mean of the results from the 43 normal controls. High titres were confirmed by high performance thin layer chromatography according to the method described by Ilyas *et al.*[4] Positive samples were also studied by immunostaining after absorption in nitrocellulose by a method developed in our laboratory.

Antiganglioside antibodies were found in four patients with toxic oil syndrome. Three (25%) had raised titres of IgM antibodies to ganglioside GD1a (1:800 to 1:400) and one to asialic-GM1 (1:200). Low titres (lower than 3 SD of the controls) of IgM antibodies against GM1, GD1b, and Asialic-GM1 were detected in the GD1a positive patients. Two of these patients had positive titres of IgG anti-GD1a antibodies. In 111 controls tested, two cases of positive IgM antibodies to GD1a were found, one patient with optical neuritis and one with spinal haemorrhage. Reactivity to GD1a was not detected in 43 controls. Anti-GD1a IgM antibodies were significantly higher in patients with toxic oil syndrome than in control groups (ANOVA $F_{2\ 121} = 5{\cdot}71$; $P = 0{\cdot}004$). There was no association between the pattern of clinical signs including proximal *v* distal, motor *v* sensorimotor, and CNS involvement and the positivity of anti-GD1a antibodies. Reactivity showed no significant relation with severity of disease at presentation (Kruskall-Wallis test $\chi = 5{\cdot}02$; $P = 0{\cdot}1$), course (Mann-Whitney U test; $P = 0{\cdot}6$), or age (Spearman coefficient $-0{\cdot}19$; $P = 0{\cdot}53$). Neurophysiological studies showed axonal neuropathy in 10 patients and axonal demyelination in the other two. Nerve conduction blocks were not seen, although a specific search for blocks with proximal evaluation was not carried out.

In this sample of patients with toxic oil syndrome the main finding was the presence of high titres of anti-GD1a antibodies in three. These had no relation with the clinical features evaluated in this small sample. Diverse immunological disorders have been reported in patients and animal models of toxic oil syndrome, such as increased serum IgE or IgM, positivity of antinuclear antibodies, and of several tissue specific antibodies against glomerular basement membrane or collagen, but there are no previous reports of antiganglioside antibody reactivity in this syndrome. Data from the medical literature point to a chronic T lymphocyte activation in toxic oil and eosinophilia-myalgia syndromes. Chronic inflammation could facilitate antigen exposure that induces an immune response to neural ganglioside. Although increased titres of antiganglioside antibodies are associated with lower motor neuron diseases and predominantly motor neuropathy,[5] their role is not understood. The relevance of this reactivity in our patients is also not clear, but in our opinion, the finding provides new insight about the pathogenesis of toxic oil syndrome, suggesting an immune mechanism implicating antiganglioside antibodies, and expands the range of diseases with antiganglioside antibodies.

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Dose standardisation of botulinum toxin

Several studies have shown that botulinum toxin A is the treatment of choice in blepharospasm and hemifacial spasm. There is no dose standardisation, however, between the two commercial preparations available—namely, Botox (Allergan, 100 U/vial), and Dysport (Speywood, 500 U/vial); 1 U or μg of one is not equivalent to 1 U or μg of the other. Quinn and Hallet[1] drew attention to the need for a comparative study. Schantz and Johnson[2] replied but in basic biological terms. Brin and Blitzer[3] suspected that 1 U of Botox is roughly equivalent to 4 to 5 U of Dysport, but there was a much wider range in their accompanying table of "standard injection doses" of the two products. Marsden[4] also suggested that 1 U of Botox is roughly equivalent to between 4 and 5 U of Dysport, but pointed out that the exact equivalence should be resolved as soon as possible. Pickett and Hambleton[5] suggested an equivalence of 1:3, based on "clinical observations", but gave no details and the same authors[6] recently found a similar equivalence using a mouse essay. We now wish to report a study of the clinical equivalence between the two preparations of botulinum toxin.

We selected 74 patients, 37 with idiopathic blepharospasm and 37 with hemifacial spasm. All patients had responded favourably and repeatedly to Dysport for at least 12 months (table). We injected increasing doses of Botox until a satisfactory response lasting as long as with Dysport was obtained (patients serving as their own controls). The injection technique was otherwise unchanged. Botox (like Dysport) is presented as a powder in a vial to be dissolved. We always injected the same volume with each toxin; we obtained a higher dose of Botox by using less diluent. Our initial dilution with 4 ml saline gave a satisfactory response in less than 50% of patients. Dilutions with 3 ml, 2·5 ml, and 2·0 ml all produced a similar poor response rate (<50%). Finally, when we used 1·5 ml saline, we obtained a satisfactory response in all patients lasting as long as with Dysport (table) without side effects such as ptosis or diplopia. The total number of patient injection episodes was 59 for blepharospasm and 52 for hemifacial spasm; some patients were injected more than once, but a three month interval between injections was always respected.

The final dilution of 100 U of Botox with 1·5 ml saline gives a concentration of 67 U/ml; 500 U of Dysport is dissolved in 2·5 ml saline to give a 200 U/ml concentration. Hence, we arrived at a clinical equivalence of 67 U Botox equal to 200 U Dysport—that is, a ratio of 1:3. We think that this will be a useful guideline, particularly when clinicians attempt to change from one toxin to the other.

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Equivalence of Dysport and Botox in treatment of blepharospasm and hemifacial spasm

	No of patients	*Sex (n)*	*Mean (range) age at onset (y)*	*Mean (range) duration (y)*	*Mean dose of Dysport (Dysport U)*	*Mean effective dose of Botox (Botox U)*
Hemifacial spasm	37	M (14) F (23)	54·6 (32–89)	8·16 (3–22)	85	32
Blepharospasm	37	M (7) F (30)	54·7 (33–80)	8·34 (1·5–24)	223	77