was dystonic posturing and clawing of both hands. Power was reduced (grade 4) at the wrist and in the hands, worse on the right.

The right leg was flaccid, and there was no movement at the right ankle. Power was reduced (grade 4) proximally in both legs. The right ankle jerk was absent, but all the other tendon reflexes were brisk. The right plantar response was absent, the left exten-
sor. There were no cerebellar or sensory signs. General examination was normal.

The following investigations were normal or negative: routine haematology and bio-
chemistry, serum copper and caeruloplasmin, serum and urinary amino acids, syphilis serology, antinuclear factor, lupus anticoagulant, and antiphospholipid antibody. Constituents of CSF were normal including lactate (1-15 mmol/l; normal range: 0-5-1-8 mmol/l), and pyruvate (83 mmol/l; normal range: 40-138 mmol/l). Motor and sensory nerve conduction velocities and amplitudes were within normal limits.

Brain MRI showed large CSF spaces around the anterior portions of both tempo-
ral lobes (figure). There was also a mild degree of generalised cortical atrophy and focal areas of signal abnormality in the white matter of both cerebral hemispheres. A trace of glutaric acid was present in the urine, with a small peak of 3-hydroxyglutaric acid. Glutaryl CoA dehydrogenase activity, mea-
sured by release of labelled CO₂ from [1,5-
13C]glutaryl CoA by cell homogenate, was undetectable in cultured skin fibroblasts (0-0 and 0.0 compared with 12-9, 13-9, 19-6, 20-1, 12-5 and 12-7 pmol/mg protein/min in simultaneous controls) and was <1% of normal in blood lymphocytes (0-06 and 0-02 compared with 11-3 and 10-8 pmol/mg protein/min in a simultaneous control) confirming a diagnosis of GA-1.

The dystonia and dyskinesia with severe dystarthis but relative preservation of cogni-
tive function in this patient is typical of GA-1. In addition, the bitemporal enlargement of CSF spaces on MRI, although occasion-
ally reported in other conditions, is strongly suggestive of GA-1. No other cause was identified for this patient's neurological dis-
order.

Most patients with GA-1 present in the first year of life with acute metabolic decompen-
sation and encephalopathy. A recent review of reported cases suggests that 97% of those surviving an acute encephalopathic onset are likely to have sequelae.1 Our patient presented with delayed walking and dragging the right leg. Up to 25% of cases may present insidiously and there is some evidence that the prognosis in this group is better with only 48% being left with severe disability.2 It is rare for new neurological deficits to develop after the age of 3 years, and after this age any residual disability remains static.3 Our patient is unusual in that, after a gradual onset, there was further deterioration in neurological function at the age of 7. The details of that episode are lim-
lit, but as the neurological sequelae are typical of GA-1, it seems reasonable to attribute it to GA-1 rather than to implicate a second disease process. From the age of 7 until 50, her neurological state remained stable. The current decline in mobility was thought to be related to degenerative joint disease rather than neurological deteriora-
tion.

The proportion of cases diagnosed in infancy that had a later, adult-onset as is, yet, unknown given that GA-1 was first described only 20 years ago. At the age of 50 years, our patient is the oldest documented case with GA-1. Four other clinically affected patients aged 50 years, in whom the diagnosis was made after the age of 18 (aged 19, 23, 28, and 37), have been reported.4 It is likely that there are other unrecognised cases of GA-1, born before the condition was first described, who have survived into adulthood.

The diagnosis of GA-1 in clinically sus-
ppected cases is usually made by demonstrat-
ing excetration of 3-oxo-3-hydroxybutyric acid and 3-hydroxyglutaric acid in urine. Glutaric acid is found in the urine in other metabolic disorders such as methylmalonic aciduria, 3-hydroxyglutaric aciduria, but the presence of 3-
hydroxyglutaric acid makes the diagnosis of GA-1 almost certain, as it has not been found in any other condition.5 However, during periods of neurological stability, which will invariably be the case in adults, excetration may be largely undetectable.6 Neuroradiological findings (enlarged frontotemporal CSF spaces and signal abnor-
malities in cerebral white matter and, in severe cases, in the basal ganglia) may also help to suggest a diagnosis of GA-1, but they are not specific. Similar abnormalities are seen in the basal ganglia in the mitochondrial encephalopathies and in Leigh's syndrome. Although dystonia may be prominent in Leigh's syndrome,7 the presence of other features such as retinopathy, peripheral neu-
ropathy, and dysmorphism help to distin-
guish it from GA-1. In addition, enlarged frontotemporal CSF spaces are not found in Leigh's syndrome. To confirm a diagnosis of GA-1, glutaryl CoA dehydrogenase activity must be measured in cultured skin fibro-
blasts or blood lymphocytes.8 It is usually undetectable in homozygotes.

GA-1 is thought to be rare in adults, and there are almost certainly unrecognised cases among populations of adults with sta-le neurological deficits acquired in childhood. This report illustrates the clinical and neuroradiological findings that may be seen in adults and extends the clinical range of GA-1.

1 M C PREVETT
2 R S HOWARD
3 Department of Neurology,
4 St Thomas’ Hospital,
5 Guy’s and St Thomas’ NHS Trust,
6 Lambeth Palace Road,
7 London, UK
8 R N DALTON
9 Department of Paediatrics, and
10 Child Development Services,
11 Sheffield Children’s Hospital,
12 Sheffield, UK
13 S E OLPIN
14 Department ofNeural Scanning and Metabolic
15 Disease, National Hospital for Neurology and
16 Neurosurgery, Queen Square, London W1C 1BG, UK.

Correspondence to: Dr M Prevett, National Hospital for Neurology and Neurosurgery, Queen Square, London WC1N 3BG, UK.


The usefulness of functional imaging in movement disorders: an illustrative case

The clinical utility of functional imaging for movement disorders has been well pointed out in a review by Sawle it can be a valuable tool in the subset of patients where a diagnosis of dopa-responsive dystonia versus young onset Parkinson’s disease is suspected. These two conditions can be clearly differentiated by a [18F]-dopa scan.4 The distinction between the two conditions is crucial with regard to therapy and prognos-
sis. Because of the problems associated with levodopa therapy in young-onset Parkinson’s disease,1 an early diagnosis is helpful so that alternate treatment, such as the use of agonists, can be initiated keeping levodopa in reserve for as long as possible to delay the emergence of motor fluctuations and dyskinesiae. We report an illustrative case.

This 26 year old woman had normal birth and milestones. She first noticed problems at the age of 11 years when she began to walk on the outside of her feet with knock knees. At the age of 12 she developed a tremor of both arms and occasionally of her legs. As she was thought to have a spastic paraparesis, a myelogram was performed which was normal as was examination of the CSF. She had only a mild deterioration between the ages of 12 to 25 years, but then the tremor and her gait markedly worsened over a year. Her maternal grandfather and a maternal aunt were said to have had a sim-
ilar tremor but further details were unknown. On examination she had parkin-
sonian features with an expiratory phase, a stooped posture, pronounced bradykinesia, and rigidity. Her tendon reflexes were very brisk but the plantar responses were flexor. The rest of the neurological examination disclosed no other abnormality. Routine and special investigations including blood counts, serum biochemistry, and tests to exclude Wilson’s disease were all normal. Head CT was normal.

1 J Neurol Neurosurg Psychiatry: first published as 10.1136/jnnp.60.3.353 on 1 March 1996. Downloaded from http://jnnp.bmj.com/ on May 28, 2022 by guest. Protected by copyright.
Six months before she was seen by us, the referring physician started her on treatment with Sinemet-plus 125 mg (carbidopa 25 mg, levodopa 100 mg) four times a day with a dramatic initial benefit. Within a few months, however, she noticed wearing off problems with each dose lasting only three hours and the dose was increased to six Sinemet plus a day with one Sinemet CR (carbidopa 50 mg, levodopa 200 mg) at night.

The differential diagnosis in this patient was between dopa responsive dystonia and young onset Parkinson’s disease. The initial presentation with what seemed to be a spastic paraparesis and the positive family history suggested dopa responsive dystonia. Later evaluation suggested the possibility of young onset Parkinson’s disease as she had developed wearing off dose responses early after initiation of treatment with Sinemet.1

By contrast, patients with dopa responsive dystonia are known to have a sustained long term benefit without complications on small doses of levodopa. For purposes of prognosis and further management it was important to distinguish between the two conditions. This was achieved with 18F-dopa PET which showed significantly reduced tracer uptake in the putamen (averaged side to side, Ki values using an occipital reference; patient caudate = 0.0080 ± 0.0017, patient putamen = 0.0034 ± 0.0011). These findings were suggestive of a diagnosis of young onset Parkinson’s disease.1

With a diagnosis of young onset Parkinson’s disease established the drug therapy was modified by giving her levodopa sparing drugs such as amantadine, dopamine agonists, and anticholinergic drugs to avoid the levodopa induced motor fluctuations for as long as possible.

This case shows the part functional imaging can play in selected cases and the prognostic and therapeutic implications made possible by this technique.


### Severe combined degeneration of the spinal cord after nitrous oxide anaesthesia in a vegetarian

Nitrous oxide has been extensively used as an anaesthetic agent and is regarded as an ideal drug with few side effects. We report a female vegetarian who developed subacute combined degeneration of the spinal cord due to lack of vitamin B 12 one month after nitrous oxide anaesthesia.

A 50 year old white woman had become a vegetarian patient six years after admission. Over the past five years, she had increasingly restricted her diet to include only apples, nuts, and raw vegetables; intentionally avoiding legumes. Six weeks before admission she underwent surgery for a right hip fracture acquired while ice skating. Her preoperative blood count showed a mild macrocytic anaemia with a packed cell volume of 33.3% (normal 45% ± 2%), a mean corpuscular volume of 101:2 (normal 80 to 93) fl. During combined anaesthesia with isoflurane, she was ventilated with 66% nitrous oxide for two hours. She continued her diet without any supplementation of vitamins or folate. Four weeks later, she rapidly developed increasing unsteadiness of gait and sensory impairment of her legs. Six weeks after anaesthesia, she was unable to walk and was transferred to the hospital. She showed normal mental status and cranial nerves. A spastic paraparesis of her legs, more pronounced on the right, was found with incoordination of the hands and delayed extensor plantar responses. She had severe impairment of position and vibration sense up to the iliac crest. Laboratory results showed a macrocytic anaemia with a packed cell volume of 28% and a mean corpuscular volume of 108:3 fl. Blood vitamin B 12 concentrations were decreased to 29-6 (normal 48-443) pmol/l with normal folate concentrations. Sculling test (part 1) gave a normal result. Gastroscopy showed atrophic gastritis. Electrophysiological testing showed normal brainstem auditory evoked potentials, prolonged latency of visual evoked potentials, absent tibial somatosensory evoked potentials, prolonged central motor conduction time, and mild reduction in peripheral motor and sensory nerve conduction velocity. Cervical and thoracic spinal cord MNCV showed increased signal intensity within the dorsal columns on T2 weighted images. Brain MRI was normal. A diagnosis of subacute combined degeneration of the spinal cord secondary to vitamin B 12 deficiency was made after injection of cyanocobalamin were begun. After five months her clinical status was much improved. She was able to walk on crutches and had only mild spastic paraparesis of the legs, but still severe impairment in position and vibration sense. The tibial derived somatosensory evoked potentials continued to improve at one year after anaesthesia.

Vitamin B 12 deficiency in vegetarians is rare as only 5 μg of vitamin B 12 is needed per day and an adequate amount is usually available in legumes. Because our patient intentionally avoided legumes in her strictly vegetarian diet, the preoperative mean corpuscular volume was raised, it is likely that she had a pre-existing vitamin B 12 deficiency due to malnutrition. In patients with a vitamin B 12 absorption deficiency, the course of subacute combined degeneration is mostly mild with only a minor neurologi- cal deficit six months after the onset of symptoms. In our patient an interval of only two weeks from the beginning of paraparesis and being confined to a wheelchair a natural course of combined degener- ation is highly unlikely.

Nitrous oxide is known to oxidise the cobalt (Co) atom of vitamin B 12 from an active Co (I) to an inactive Co (II) or Co (III) state, which in turn reduces the neurotoxicity of cobalamin dependent enzymes. In particu- lar, the methionine synthase methylcobalamin complex is rendered irreversibly inactive. In healthy subjects this side effect is well compensated for, but in patients with vitamin B 12 deficiency the anaesthetic is no longer available in the liver and bone marrow for up to 24 hours during nitrous oxide anaesthesia. For patients with a preexisting vitamin B 12 deficiency, even a short nitrous oxide anaesthesia may deplete the few remaining stores. Furthermore, the inactivation of methionine synthase by nitrous oxide may be more rapid in patients with low concentrations of vita- min B 12.

Only seven patients who developed combined degenera- tion after a short nitrous oxide anaesthesia have been reported so far.1 They were five women and two men with an age range from 25 to 70 years. The duration of nitrous oxide application ranged from 90 minutes to 235 minutes and the elapsed time between anaesthesia and onset of symptoms was between 14 days and eight weeks. The cause of vitamin B 12 deficiency was resection of the terminal ileum for Crohn’s disease in one patient, pernicious anaemia in four, and not stated in one. One patient had pernicious anaemia and was a vegetarian, but not a very strict one.2 To our knowledge this is the first case of vegetarian- ism alone leading to subacute combined degeneration of the spinal cord secondary to vitamin B 12 deficiency after short term nitrous oxide anaesthesia.

In summary, our patient shows that for strict vegetarians nitrous oxide might be a harmful anaesthetic and should draw the attention of physicians to the eating habits of their patients scheduled for anaesthesia.