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.[5] 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 ^{18}F-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 (0·0108 ± 0·0017), patient putamen = 0·0034 (0·0099 ± 0·0011)). These findings were suggestive of a diagnosis of young onset Parkinson's disease.[3 4] 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.

K P BHATIA
N TURJANSKI
D J BROOKS
C D MARSDEN
University Department of Clinical Neurology, Institute of Neurology, Queen Square, and MRC Cyclotron Unit, Hammersmith Hospital, London UK
D THRUSH
Department of Neurology, Derriford Hospital, Plymouth, UK

Correspondence to: Professor C D Marsden, Institute of Neurology, Queen Square, London WC1N 3BG, UK.

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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 10 years before 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 33·8% (normal 37% to 47%), and 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 readmitted to hospital. She showed normal mental status and cranial nerves. A spastic paraparesis of her legs, more pronounced on the right, was found with increased muscle reflexes and bilateral 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. Schilling test (part I) gave a normal result. Gastric biopsy ruled out atrophic gastritis. Electrophysiological testing showed normal brainstem auditory evoked potentials, prolonged latency of visual evoked potentials, absent tibial derived somatosensory evoked potentials, prolonged central motor conduction time, and mild reduction in peripheral motor and sensory nerve conduction velocity. Cervical and thoracic spinal cord MRI 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 and injections 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 and her 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 malabsorption the course of subacute combined degeneration is mostly mild with only a minor neurological deficit six months after the onset of symptoms. As our patient had an interval of only two weeks between the beginning of paraesthesiae and being confined to a wheelchair a natural course of combined degeneration 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 activity of cobalamin dependent enzymes. In particular, the methionine synthase methylcobalamin complex is rendered irreversibly inactive. In healthy subjects this side effect is well compensated for by large vitamin B 12 stores 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 vitamin B 12.

Only seven patients who developed combined degeneration after a short nitrous oxide anaesthesia have been reported so far.[1–6] 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.[5] To our knowledge this is the first case of vegetarianism 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.

MARTIN RÖSENER
JOHANNES DICHGANS
Eberhard-Karls-University, Department of Neurology, Tübingen, Germany
Correspondence to: Dr Martin Rösener, Eberhard-Karls-University, Department of Neurology, Hoppe-Seyler-Strasse 3, 72076 Tübingen, Germany.

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Homozygosity for Machado-Joseph disease gene enhances phenotypic severity

Machado-Joseph disease is an autosomal dominant ataxia originally described in Portuguese emigrants to Massachusetts and California, and now described worldwide.[1] Clinical phenotypes of Machado-Joseph disease vary widely, and have been considered to correlate with the age of onset; the younger the age of onset, the greater the extent of dystonia and pyramidal signs; the older the age of onset the more pronounced the cerebellar ataxia and peripheral neuropathy. Recently, the gene responsible for