Two interesting and contrasting case reports in this month’s issue illustrate how precise microbiological and serological diagnoses can transform treatment decisions, even if some of the clinical features remain unexplained [1, 2].

In the first, the initial and final clinical diagnosis was sepsis. An unusual organism (Facklamia languida) is eventually grown from blood cultures, but its connection—apart from it being able to cause the physiological complications of sepsis—to the neurological features is not clear, despite the promising title [2]. During the course of the illness, the neurological catch-all term ‘stroke-like’ is used to denote a constellation of deficits even though advanced brain and vascular imaging suggests that it was not, radiologically, like a stroke. An unwitnessed seizure complicated by a Todd’s paresis is invoked as another possible explanation despite the (radiological) absence of an obvious (and irritative) cortical lesion. However, the authors clinch a peachy and precise bacteriological diagnosis, start the right treatment and suggest a decompensation of cerebral function as the most likely explanation. This is a handy concept, in the circumstances, and although difficult to verify or refute, experienced clinicians know that if an ageing brain is exposed to sepsis, hypoxia or any other systemic insult the resulting clinical problems can be asymmetrical (or focal), without an obvious imaging correlate. Whether readers think it sepsis-like or stroke-like the case serves as a very relevant cautionary tale for clinicians involved with thrombolysis: sepsis is a teratoma, plasma exchange (or intravenous immunoglobulin) and immunosuppression, are all treatment options, particularly involving the face and upper limbs and marked behavioural disturbance during recovery, investigations have to be comprehensive, and treatments, particularly when there is a low-grade temperature, have to cover the possibility of primary (e.g. viral encephalitis, Whipple’s disease), as well as the inevitable secondary (e.g. ventilator associated) infections. Neuroleptic malignant syndrome [4] and ketamine abuse [5] are just two examples of conditions which may need to be considered in the differential diagnosis. The recovery period can be prolonged and a multidisciplinary approach is often required involving intensivists and neuropsychiatrists.

The speed of developments in the understanding of the basic immunological features of the disease, and the close correlation of the antibody to a characteristic clinical presentation, has seen an account of it appear in high street book shops [6] and discussed on national radio [7] at around the time it was being presented for the first time in hospital grand rounds. The good news is that early surgery (if there is a teratoma), plasma exchange (or intravenous immunoglobulin) and immunosuppression, are all treatment options, adding to the growing list of very treatable conditions manifesting as transient or persisting changes of neurological function.

The diagnosis, prospectively, of NMDA encephalopathy is difficult. The brain imaging and CSF can be relatively (and improbably) normal at presentation and until a recognisable constellation of the (now) better known features emerges (seizures, psychosis, hyperventilation, bizarre movement disorders particularly involving the face and upper limbs and marked neurological deficit), investigations have to be comprehensive, and treatments, particularly when there is a low-grade temperature, have to cover the possibility of primary (e.g. viral encephalitis, Whipple’s disease), as well as the inevitable secondary (e.g. ventilator associated) infections. Neuroleptic malignant syndrome [4] and ketamine abuse [5] are just two examples of conditions which may need to be considered in the differential diagnosis. The recovery period can be prolonged and a multidisciplinary approach is often required involving intensivists and neuropsychiatrists.

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References
Understanding vitamin D deficiency

**Keywords:** vitamin D deficiency, vitamin D receptor, muscle and vitamin D, vitamin D deficiency threshold, vitamin D testing older people

### The production of vitamin D

Vitamin D deficiency is a global health problem caused mainly by insufficient exposure to sunlight. It is estimated that 1 billion people have vitamin D deficiency or insufficiency worldwide [1], particularly prevalent among elderly people [2]. Vitamin D exists in two forms—D2 (ergocalciferol), which is obtained from yeast and plants and D3 (cholecalciferol), obtained from the diet through the ingestion of vitamin D containing products (fatty fish and eggs), vitamin D fortified milk or margarine and/or the use of multivitamins. However, the primary source of vitamin D3 (80–90% of the body stores) is via ultraviolet irradiation of the precursor molecule 7-dehydrocholesterol in the skin. Vitamin D (D2 and D3) are then subsequently hydroxylated in the liver by 25-hydroxylase to produce 25-hydroxyvitamin D (25OHD). 25OHD is then further hydroxylated in the kidney by the 1-alpha hydroxylase to form 1,25-dihydroxyvitamin D (1,25(OH)2D) or calcitriol, which is the biologically active form of vitamin D. The 1-alpha hydroxylation can also occur in a multitude of other tissues, generating locally active vitamin D, which leads to auto and/or paracrine effects. The principal index of vitamin D status is the serum 25OHD concentration, with a half-life of 3 weeks, when compared with the biologically active form 1,25(OH)2D which has a half-life of only 4–6 h [3].

### Measurement of vitamin D

25OHD levels are measured in ng/ml or nmol/l (1 ng/ml is equivalent to 2.5 nmol/l). However, several technical problems should be recognised when measuring vitamin D levels:

- There are two main types of assays used for measuring 25OHD—the immune-based assay (commonly used in clinical practice) and the chromatography-based assay (commonly considered the gold standard for research). The utilisation of different methods among laboratories obviously leads to a great variability in test results. This has therefore led to the recent introduction of the standard reference material for vitamin D by the National Institute of Standards and Technology in the USA [4].
- Total circulating 25OHD is the sum of 25OHD2 and 25OHD3, but not all the immunoassays used in clinical practice are able to detect 25OHD2, which can lead to underestimation of 25OHD levels.
- Potential confounders of 25OHD measurement may be present, which can falsely elevate 25OHD, such as other vitamin D metabolites, which are relatively abundant and can account from 2 to 20% of the 25OHD measured.

### The function of vitamin D

The vitamin D endocrine system plays a primary role in the maintenance of extracellular fluid calcium concentration. The association between vitamin D deficiency and bone disease, such as rickets, osteomalacia and osteoporosis are well recognised; however, increasingly the relationship between vitamin D deficiency and other conditions have been identified, Table 1 [5].

In the elderly falls are a major problem, leading to significant morbidity, increased mortality and substantial consumption of healthcare resources. Vitamin D deficiency is associated with muscle weakness predominantly of the proximal muscle groups. This leads to slower walking speed, prolonged sit-to-stand time, lower quadriceps strength [6], poor