

Testing for fatigue

How pathology testing can help identify the cause of patient fatigue



Fatigue is a symptom which can have debilitating effects on patients, posing a negative impact on their overall quality of life including work, family life and general social relationships. Patients experiencing chronic, ongoing fatigue often find it difficult to convey their symptoms to their healthcare professionals. What if there was a way to test for conditions associated with fatigue, giving practitioners and their patients a clearer more targeted treatment approach? Studies have confirmed that without treatment the prognosis of patients with idiopathic fatigue is poor.

Pathology testing is the first step in identifying the cause of patients' fatigue. The most common conditions associated with fatigue are usually anaemia, thyroid disorders and vitamin D deficiency. These disorders have a known pathophysiological association with fatigue, therefore testing for these first will provide practitioners with a baseline for potential underlying causes of fatigue.

Stress and poor sleep can also have direct influence in elevated levels of fatigue. Testing patients' salivary cortisol and melatonin levels can provide further insight into potential contributors to fatigue symptoms.

Gut health and genetics can also be implicated in the development of fatigue symptoms. Testing for intestinal permeability (leaky gut) or identifying a polymorphisms on the MTHFR gene methylation pathway, may be useful particularly with patients presenting with idiopathic symptoms of fatigue.

Detailed below are pathology tests which may prove to be beneficial in establishing underlying causes of fatigue and may assist in monitoring treatment progress.

Anaemia



One of the most common conditions associated with fatigue, is anaemia. Anaemia can be caused by a reduced number of red blood cells or impaired haemoglobin production, which is responsible for transporting oxygen in peripheral blood.

As the levels of haemoglobin drop, the ability of the blood to deliver oxygen to organs, muscles and tissues declines. This means that less energy is available to these

organs resulting in symptoms perceived as fatigue. This is particularly evident when there is a reduction in cerebral oxygenation. Some studies have suggested that fatigue may in fact be due to deficiency of iron at a cellular level rather than anaemia, as iron plays a major role in the formation of red blood cells.

The varied causes of anaemia require different treatment, therefore it is essential to identify the type of anaemia before any treatment can be initiated.

Available Tests

Identification of anaemia is based on a Full Blood Examination (FBE) and reticulocyte count. This test will clarify the type of anaemia the patient may be presenting with. Too much iron, in conditions such as thalassemia can also be problematic causing similar symptoms of fatigue.

The full iron studies test will also help in identifying whether there may be iron deficiency or excess. Pathology testing is essential to identify the underlying cause of symptoms as the treatment for these conditions would be

Thyroid Insufficiency



Fatigue is a common symptom of thyroid disease. The adrenal and the thyroid systems are closely involved with direct cross regulation between the hypothalamic-pituitary-adrenal (HPA) axis and the hypothalamic-pituitary-thyroid (HPT) axis. Increased stress can cause a reduction in the production of thyroid hormones. Glucocorticoids can inhibit conversion of T4 to T3 resulting in a reduction of serum T3 levels. Studies have also confirmed that prolonged stress can cause a decrease in peripheral thyroid hormone levels.

Thyroid hormone is required in several energy producing processes, namely, the Krebs' citric acid cycle and in oxidative phosphorylation. A thyroid problem can in fact have a direct impact on ATP producing mechanisms thereby resulting in fatigue.

Thyroid hormone Testing

Monitoring thyroid levels in patients presenting with fatigue can provide insight into symptoms that may be stemming from thyroid insufficiency.

Vitamin D deficiency

Low levels of vitamin D have been seen in patients presenting with fatigue. More so, it has been found that normalization of low vitamin D levels in patients with fatigue significantly improves symptoms.

There are a number of mechanisms by which vitamin D is believed to ameliorate symptoms of fatigue. Vitamin D is involved in the process of energy production in the body. Research has shown that low levels of vitamin D are associated with suboptimal mitochondrial function and therefore reduced energy levels. Mitochondria are part of the cell involved in ATP production, the body's main energy production mechanism.

Vitamin D is also required for calcium homeostasis, supporting bone density and turnover. A deficiency in Vitamin D results in skeletal demineralisation and muscle weakness. Fatigue is believed to be the end result of the underlying muscle fatigue, which is more commonly encountered than muscle weakness.

Additionally, Vitamin D is also involved in supporting immune function by down regulating cytokine, T helper cell and NF-κB activation, therefore reducing pro-inflammatory immune responses, and enhancing immune function.

Testing for Vitamin D

Testing serum vitamin D is a reliable and effective way of monitoring potential vitamin D deficiency. Supplementation can readily rectify deficient vitamin D levels.

Adrenal Hormone

Adrenal hormones, predominantly cortisol has been found to have a direct relationship with fatigue. Studies show reduced function of the hypothalamic-pituitary-adrenal (HPA) axis as well as hypocortisolism (reduced cortisol levels, seen via reduced salivary cortisol levels), in people suffering with fatigue.

Available Tests

Testing cortisol levels in saliva is an effective way of monitoring adrenal levels. Saliva is the most reliable way to measure free bioavailable hormone levels at a cellular level, as it reflects the non-protein bound 'free' fraction of hormones at a given point in time. Our tests are able to be performed in the privacy and comfort of the patients' home, therefore allowing for testing at multiple time points throughout the day. Studies have confirmed that fatigue has a diurnal pattern similar to that of cortisol, therefore this method of testing provides an effective way of monitoring cortisol levels throughout the day.

Melatonin dysregulation



A common complaint of patients with fatigue is sleep impairment. The hormone melatonin is significant in the regulation of the circadian rhythm, regulating the sleep-wake cycle.

Ideally in humans melatonin levels should start to increase with the onset of darkness, and reduce again during the second half of the night. This pattern may be altered in patients suffering with fatigue. Studies have found that Melatonin levels are in fact elevated in some people suffering from fatigue. It has been hypothesised that this elevation in melatonin levels may be due to the dysregulation of the hypothalamus-pituitary-adrenal (HPA) axis, however this is yet to be confirmed.

Saliva Melatonin Testing

A simple saliva melatonin test performed at night prior to sleep and again on waking can demonstrate the fluctuations of an individual's melatonin hormone levels.

Gastrointestinal Tract- Leaky Gut



Ongoing fatigue, in particular chronic fatigue syndrome (CFS), can be associated with an immune disorder due to the induction of pro-inflammatory cytokine levels and increased oxidative stress seen in patients with this condition.

Patients with chronic fatigue syndrome are more likely to present with increased levels of IgA where the levels of serum IgA, identified directly correlated with the severity of symptoms. Levels of enterobacteria are also significantly higher in patients with CFS. It is believed that enterobacteria is involved in the aetiology of CFS.

Increased intestinal permeability or 'leaky gut' allows the enterobacteria to cross the gut epithelium, increasing pro-inflammatory cytokine production and oxidative stress, resulting in the induction of central neuro-inflammation. Leaky gut can be the underlying cause of CFS allowing enterobacteria species to infiltrate the gut, or may develop as a result of CFS where the activation of pro-inflammatory pathways such as increased cytokine and NF- κ B production may facilitate loosening of tight junctions in the epithelial lining.

It has been shown that fatigue and other symptoms of CFS are reduced with gut permeability treatment.

Digestive Analysis

Patients presenting with fatigue would benefit from monitoring levels of IgA as well as evaluating potential leaky gut through urinary Intestinal Permeability testing, a simple challenge test.

MTHFR

Genetic factors and compromised methylation pathways can play a significant role in the predisposition and development of fatigue. Methylation is a process in the body where a methyl group is donated to a molecule, to ensure proper functioning of metabolic pathways. One important methylation process is that of homocysteine. Homocysteine is remethylated to methionine utilising the enzyme MTHFR (methyltetrahydrofolate reductase). The MTHFR enzymatic pathway utilizes folate to convert to its active form, folinic acid, which is required to facilitate the remethylation of homocysteine to methionine.

A polymorphism in this gene can reduce the efficacy of the MTHFR enzyme, causing reduced conversion of homocysteine to methionine, resulting in elevated levels of homocysteine and reduced activation of folate to its active form.

Vitamin B12 and folate are essential for brain development and function, a deficiency in these nutrients has been linked to an increase in neurological symptoms such as fatigue. Furthermore, this methylation pathway is involved in activation and production of SAMe, an important methyl donor, especially in the brain, which is required for neurotransmitter synthesis. Elevated levels of homocysteine also have a direct adverse effect on neurons and blood vessels including those that are in the brain, contributing to symptoms.

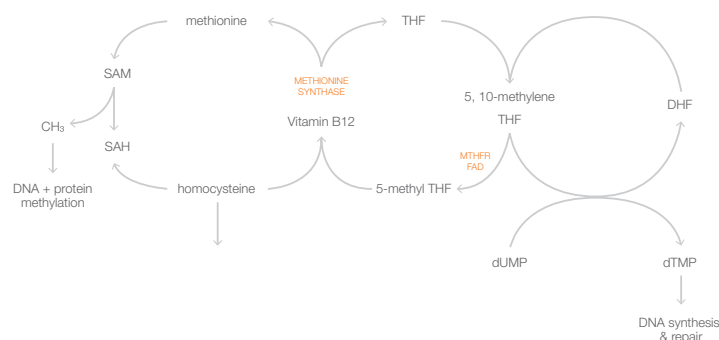
Another common finding associated with a defect of MTHFR is an increase in copper levels. Elevated copper levels have been linked to conditions such as hyperactivity, headaches, depression, increased adrenal stress, fatigue and can also be responsible for a lowered immune system. Elevated copper levels may also make it difficult to raise iron levels, another contributing factor to symptoms of fatigue.

Vitamin B12 and folate are essential for brain development and function, a deficiency in these nutrients has been

linked to an increase in neurological symptoms such as fatigue. Furthermore, this methylation pathway is involved in activation and production of SAMe, an important methyl donor, especially in the brain, which is required for neurotransmitter synthesis. Elevated levels of homocysteine also have a direct adverse effect on neurons and blood vessels including those that are in the brain, contributing to symptoms.

Another common finding associated with a defect of MTHFR is an increase in copper levels. Elevated copper levels have been linked to conditions such as hyperactivity, headaches, depression, increased adrenal stress, fatigue and can also be responsible for a lowered immune system. Elevated copper levels may also make it difficult to raise iron levels, another contributing factor to symptoms of fatigue.

Diagram: MTHFR Methylation pathway



Testing for MTHFR

A simple swab or blood test can determine whether an individual has a mutation on either the C677T and/ or the A498C variants. This test can provide vital information into potential causes of fatigue which may be readily rectified should the MTHFR polymorphism be involved.

Testing for serum B12, folate and homocysteine levels show whether the MTHFR polymorphism is affecting the patient. Red Cell copper levels can also be useful in monitoring copper toxicity levels.

There are many reasons patients present to their healthcare professional with fatigue. Pathology testing provides key insights into potential causes so that appropriate and effective treatment can be considered.

BeFunctional prides itself on providing our referrers with the highest levels of scientific expertise and integrity. All of our tests are performed by a highly skilled team of scientific and technical staff. We are committed to providing superior technical support to our practitioners to discuss appropriate test selection, interpretation of test results, review and discussion individual cases and any other related clinical issues.

Contact us today to get your free starter pack, and start referring your patients for pathology testing to get a clearer insight into the underlying causes of their presenting conditions.

For a list of references please visit:
www.befunctional.com.au/testing-for-fatigue