Breakspear Medical

ME/CFS
Symptoms, diagnosis & treatment

Contents

This booklet provides information on the causes of myalgic encephalomyelitis (ME) and chronic fatigue syndrome (CFS) with descriptions of the symptom, how it is diagnosed and the investigations and nutritional supplements prescribed for successful treatment.

Introduction

There is no single universal diagnostic test for myalgic encephalomyelitis (ME) and chronic fatigue syndrome (CFS). ME/CFS is characterised by profound fatigue, cognitive dysfunction, sleep abnormalities, autonomic manifestations, pain and other symptoms made worse by exertion of any sort (IOM, 2015). A recent report from the US Institute of Medicine (IOM) stated that ME/CFS is a serious, chronic, complex and systemic disease that can profoundly affect the lives of patients. The IOM committee proposed in 2015 that ME/CFS to be replaced with the name systemic exertion intolerance disease, or SEID. The committee considered that the term 'myalgic encephalomyelitis' is inappropriate because there is a lack of evidence for encephalomyelitis (brain inflammation) in ME/CFS patients, and myalgia (muscle pain) is not a core symptom of the disease. The report also propose new diagnostic criteria for the disease, which will be outlined later in the leaflet.

Conditions causing prolonged fatigue, including ME/CFS, have been shown in studies to be associated with abnormalities of immunity. The conditions often arise as a result of a viral infection which may or may not be identified at the time. The most common virus identified is the Epstein-Barr virus, which is known to cause glandular fever (infectious mononucleosis). However other infections and non-infectious agents, such as chemicals, may also cause the syndrome. Epstein-Barr virus may not be detected by standard laboratory tests. At Breakspear Medical, we use specialised tests for detecting this virus and other infectious agents which may be underlying the present condition.

Diagnosis depends on a variety of criteria, including the onset of new fatigue, causing reduction in activity for at least six months where no other cause can be identified. There may be associated mild fever, sore throat, painful lymph glands, muscle pain and weakness, prolonged exhaustion after exercise, headache, joint pains, and sleep disturbance. Blood tests show activation of the immune system and specialised brain scans can show abnormalities.

Investigation of patients attending our clinic have revealed that mental and physical functions are frequently affected by allergies to foods and chemicals. Treatment for these allergies can help dramatically. Specialised tests for nutritional status show that there are often vitamin and mineral deficiencies, abnormalities of digestive function and defects in the ability of affected patients to break down toxic chemicals and waste products for metabolism. All aspects of the syndrome must be addressed to ensure that there is appreciable improvement in the condition. Due to the multifactoral nature of the condition, single interventions are less likely to be successful.

At Breakspear Medical, an individualised programme of treatment is devised for each patient and takes into account the patient's medical history, the findings from a physical examination and the various investigations. Treatment programmes will vary from patient to patient, as different aspects of the condition may predominate. A programme of treatment will be proposed at the first consultation and an estimate of the costs involved will be provided at all stages.

There is usually an initial period of intensive treatment followed by shorter review attendances and maintenance therapy. This may include antiviral strategies, antibiotics, treatment for food and other sensitivities, improvement of immune function, intravenous vitamins, minerals and other nutrients, and detoxification.

Patients may make direct, self-referrals to consult a doctor at Breakspear Medical by simply telephoning and making an appointment. General Practitioner (GP) referrals are also welcome.

Historical fact

The term 'benign myalgic encephalomyelitis' was coined by Dr A Ramsay in relation to the Royal Free Hospital epidemics that occurred in London from 1955 to 1957 and Dr John Richardson who observed the same type of illness in his rural practice in Newcastle-upon-Tyne area during the same period. In July 1955 an epidemic of an obscured illness occurred among the staff of the Royal Free Hospital, London. Over 300 staff members had been affected. The hospital had to be closed for almost a month.

Diagnostic criteria

There is no diagnostic test for ME/CFS. The diagnosis is based on symptomatology (a specific group of symptoms) that form the basis of diagnostic criteria.

Case definitions and criteria	
Institute of Medicine 2015	Diagnosis requires that the patient has the following three symptoms: **1** A substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, educational, social or personal activities, that persist for more than six months and is accompanied by fatigue, which is often profound, is of new or definite onset (not lifelong), is not the result of ongoing excessive exertion and is not substantially alleviated by rest, and **2** Post-exertional malaise, and **3** unrefreshing sleep. At least one of the two following manifestations is also required: – Cognitive impairment, or – Orthostatic intolerance.
Myalgic encephalomyelitis: International Consensus Criteria, 2011	ME is an acquired neurological disease with complex global dysfunctions. Pathological dysregulation of the nervous, immune and endocrine systems, with impaired cellular energy metabolism and ion transport are prominent features. Although signs and symptoms are dynamically interactive and causally connected, the criteria are grouped by regions of pathophysiology to provide general focus. A patient will meet the criteria for postexertional neuroimmune exhaustion, at least one symptoms from three neurological impairment categories, at least one symptom from three immune/gastrointestinal/genitourinary impairment categories and at least one symptom from energy metabolism/transport impairments.
National Institute for Health and Care Excellence 2007	A diagnosis should be made after other possible diagnoses have been excluded and the symptoms have persisted for four months in adults and three months in children or young people. The initial assessment should include a full history, an examination of the person and an assessment of their psychological wellbeing. Symptoms that suggest ME/CFS should be investigated before attributing them to the condition. Symptoms that may indicate ME/CFS are: – fatigue, and – one or more of the following symptoms: – difficulty with sleeping – muscle and/or joint pain without evidence of inflammation – headaches – painful lymph nodes without pathological enlargement – sore throat – cognitive dysfunction – physical or mental exertion makes symptoms worse – general malaise or 'flu-like' symptoms – dizziness and/or nausea – palpitations in the absence of identified cardiac pathology.
Canadian Consensus 2003	A patient with ME/CFS will meet the criteria for fatigue, post-exertional malaise and/or fatigue, sleep dysfunction and pain; have two or more neurological/cognitive manifestations and one or more symptoms from two of the categories of autonomic, neuroendocrine and immune manifestations. The illness persists for at least six months and it usually has a distinct onset although it may be gradual. Three months is appropriate for children.
Fukuda et al., 1994	Clinically evaluated, unexplained persistent or relapsing chronic fatigue that is of new or definite onset, is not the result of ongoing exertion, is not substantially alleviated by rest and results in substantial reduction in previous levels of occupational, educational, social or personal activities. The concurrent occurrence of four or more of a group of symptoms and signs, all of which must have persisted or recurred during six or more consecutive months of illnesses and must not have predated the fatigue.

NO/ONOO cycle in ME/CFS

Due to sufferers' symptoms varying significantly, the cost and scale of research projects, and the writing and defence of medical papers, it has taken decades for ME/CFS to become widely recognised. In 2007, a compilation of existing, accepted biomedical mechanisms was made, named the NO/ONOO cycle, which explained what may be responsible for ME/CFS, fibromyalgia and other syndromes. Ten years have passed since being published and the NO/ONOO cycle is slowly gaining recognition.

The body is like a complex machine, with parts that work by themselves and other parts which perform certain functions. Most functions are part of a chain of functions. Therefore if one function is not being completed properly, it will have a knockdown effect on the subsequent functions. To add to this, the by-products produced in a faulty function may affect how other, usually unconnected, functions are completed.

In the NO/ONOO cycle theory, there are five basic stressor elements that factor into the cycle:

1 Infections
2 Oxidative stress/pollutants
3 Energy
4 Sensitivity states
5 Chemicals

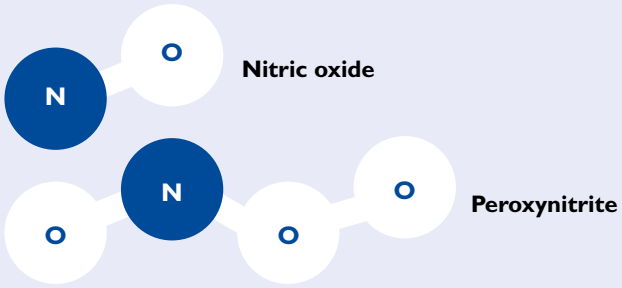
When a body is exposed to any of the stressor elements, altered functions may take place. A healthy body may be able to overcome one or more of the stressors and reregulate itself over time. However, a person with a weakened immune system may experience one or more of the stressors and not be able to re-regulate functions, causing a build-up of by-products, which may have a detrimental effect on other functions. Then, instead of the body overcoming the stressors, it then goes into a downward cyclical pattern as each of the processes of the NO/ONOO cycle is affected negatively by the others. This results in a chronic illness, which may have symptoms varying from those of frequent infections, to depleted energy when sleep is not restorative, to symptoms of oxidative stress such as fatigue, muscle/joint pain and migraine and many other symptoms.

The variation in symptoms and signs of illness has been one of the greatest puzzles of ME/CFS. One person may have certain tissues of their body impacted by the NO/ONOO biochemistry while another might have different tissues impacted, which results in the huge variation in symptoms and signs from one individual to another.

In order to treat the chronic illness, the NO/ONOO cycle needs to be re-regulated, improving the cycle's biochemistry. Each patient will require analysis of their various NO/ONOO functions and be prescribed the treatment specific to each of their failing functions, which will have an effect on their whole cycle. Using this method is treating the cause of the illness and not just the symptoms.

Simplified definition

NO/ONOO cycle: a self-perpetuating cycle that yields increasing concentrations of nitric oxide (NO), peroxynitrite (ONOO), and other elements, leading to high levels of oxidative and inflammatory stress.



Quick facts

– NO/ONOO is the abbreviation for nitric oxide/peroxynitrite.

– The NO/ONOO cycle theory was developed by Martin L. Pall, PhD, Professor of Biochemistry and Basic Medical Sciences at Washington State University and presented in his book, "Explaining 'Unexplained Illnesses': Disease Paradigm for Chronic Fatigue Syndrome, Multiple Chemical Sensitivity, Fibromyalgia, Post-Traumatic Stress Disorder, Gulf War Syndrome and Others".

– The by-products (compounds) specific to the NO/ONOO cycle theory are: nitric oxide, superoxide and peroxynitrite. These compounds all have relatively short half lives in biological tissues.

– Nitric oxide is used in the body to help the body's cells communicate with one another. It has been shown to be important to help memory and behaviour, to assist the immune system in fighting off bacteria and reduce inflammation.

– Superoxide dismutase is the enzyme involved in removing free radicals, which can cause damage at a cellular level.

– Peroxynitrite is a potent oxidant and the product of nitric oxide and superoxide, which can cause cell death.

Association with infections

There are many infectious and non-infections agents found in patients with ME/CFS and these infections may or may not be identified at the point of routine diagnosis. At Breakspear Medical, we investigate the patient's medical history thoroughly and perform vital, specialised laboratory tests to target the cause of a patient's illness.

Below are some of the infectious and non-infectious agents found in ME/CFS with an introduction to the agent, a description of the symptoms, the specific laboratory tests used to identify the agent and a brief description of our standard treatment.

Epstein-Barr virus

Epstein-Barr virus (EBV) is a member of the Herpes virus family and is common. EBV is a DNA virus responsible for glandular fever. It typically occurs during adolescence or young adulthood and causes infectious mononucleosis.

There are three principal types of Herpes virus:

- Herpes viruses which are fast-growing viruses like Herpes simplex and varicella zoster
- Herpes viruses which are latent in secretory glands and the kidneys, e.g. Cytomegalovirus (CMV)
- Herpes viruses which are latent in lymphoid tissue, e.g. Epstein-Barr virus

Symptoms

Symptoms include fever, sore throat, swollen lymph glands, sometimes a swollen spleen, or liver involvement. Heart problems or involvement of the central nervous system occur only rarely. Symptoms usually resolve in 1 or 2 months. EBV remains dormant or latent. Periodically the virus can reactivate and is commonly found in the saliva of infected persons. A late event in a very few carriers is lymphoma and nasopharyngeal carcinoma rarely. Transmission is through intimate mouth contact and not through air or blood.

Specific laboratory tests

The following laboratory tests may be used to evaluate ME/CFS:

- Paul Bunnell test, which is an early antibody test
- Chronic fatigue syndrome panel, which includes capsid and diffuse antibodies
- Tests for Epstein Barr nuclear antigen (EBNA) and capsid reactivated antibodies
- Infection screen for the following antibodies:
  - Toxoplasma IgG latex
  - CMV IgG latex
  - Toxoplasma EIA
  - Aspergillus
  - C.trachomatis/C.psittaci CFT
  - Epstein-Barr IgG and IgM
  - Legionella
  - CMV IgM EIA
  - Enterovirus
  - Coxsackie IgM
  - Borrelia burgdorferi ELISA
- Tests for the actual virus (DNA or genome) by the Polymerase Chain Reaction (PCR) technique from blood, throat swab, and saliva for the following organisms:
  - Coxsackie
  - CMV
  - Toxoplasma
  - EBV
  - Herpes
  - Brucella

The groups of antibodies involved are IgM in recurrent infection and IgG in established infection. IgM to the viral capsid antigen appears early in infection and disappears within 4-6 weeks. IgG to the viral capsid antigen appears in the acute phase, peaks at 2-4 weeks after onset, declines slightly and then persists for life. The antibody to EBNA slowly appears 2-4 months after onset and persists for life. This is not true of some EBNA enzyme immunoassays, which detect antibody within a few weeks of onset.

These tests reveal four possible profiles that help identify the current state of the virus and therefore the treatment required. These four possible profiles are:

- *Susceptibility* - No antibodies to the viral capsid antigen
- *Primary infection* - If IgM antibody to the viral capsid antigen is present and antibody to EBV nuclear antigen or EBNA is absent
- *Past infection* - If antibodies to both the viral capsid antigen and EBNA are present. Diffuse antigen can also be present
- *Reactivation* - In the presence of antibodies to EBNA, an elevation of antibodies to early antigen (capsid antigen) suggests reactivation

Treatment

At Breakspear Medical, we use high-dose Vitamin C, other anti-viral agents, injected gamma globulin and other nutrients to help patients overcome EBV. Using these methods, many of the detrimental organisms can be killed, after which immunity must be maintained and improved.

HHV-6

Human Herpesvirus 6 (HHV-6) is a common virus and its infection usually occurs in childhood and then becomes a latent infection. However, increased levels of HHV-6 antibodies and HHV-6 DNA have been found in ME/CFS patients. It has been suggested that HHV-6 reactivation could play a role in the biological mechanism that leads to ME/CFS (Ablashi et al., 2000).

Symptoms

HHV-6 is the most common cause of hospital visits in infants with fever. Other symptoms include puffy eyes and a rash that appears when the temperature normalises. In adults, fever is common with other symptoms consistent with hepatitis and encephalitis, including fatigue, weakness, aches and poor appetite.

Specific laboratory tests

A large number of adults test positive for HHV-6 therefore only the use of markers of active infection can provide useful information in postprimary infection. These markers include direct assays of virus replication (using a blood sample), such as detection of cell-free viral DNA in plasma by polymerase chain reaction (PCR) which could determine if there is a viral load present or if the body is mounting a current active response to the virus.

Treatment

Artesunate, an anti-malarial drug which also possesses antiviral activity has been shown to reduce the HHV-6 viral load and replication (Milbradt et al, 2009). Other treatments may include antivirals and nutritional supplements, such as vitamin C, lysine and epigallocatechin gallate.

Parvovirus B19

Parvovirus B19 is a small DNA virus that is spread by infected respiratory droplets after incubation of up to two weeks and most commonly affects young people. Parvoviruses are species specific and B19 is the only known pathogenic human parvovirus. It was discovered in 1975 during routine screening of blood donors.

Symptoms

Patients can develop flu-like symptoms and a rash, which may be recurrent. Those people whose immune systems are already under stress may also develop chronic anaemia.

If a woman is infected in the early stages of pregnancy, she may be at risk of miscarriage or the foetus may be at risk of hydrops foetalis, developing anaemia and heart failure.

Specific laboratory tests

Diagnosis is firstly by clinical features of rash and flu and then blood testing for the organism or antibodies to the organism. Parvovirus B19 IgM antibodies indicate recent infection and IgG antibodies latent or previous infection.

Treatment

Treatment for parvovirus is most effective by high dose gamma globulin. At Breakspear Medical, we use this in a prescribed infusion regime.

Lyme disease

Lyme borreliosis (Lyme disease) is a tick-borne infection caused by the bacterium Borrelia burgdorferi. Ticks are blood-suckers, which feed on a host daily, and can infect man as well as domestic animals.

A patient may not be aware of having had a tick bite and so initial diagnosis may be difficult. There may also be a time lapse between infection and the development of complications such as neurological or arthritic-type problems.

Symptoms

Symptoms include a rash, fever, enlargement of the lymph glands, aches and pains and fatigue. Neurological problems have also been found, including facial palsy with weakness or paralysis of muscles in parts of the face, meningitis, a burning sensation of the skin, numbness, and weakness or pain. Lyme disease can trigger arthritis, which may be prolonged or recurrent.

Specific laboratory tests

Tests used to detect Lyme disease are:

- An antibody test that measures the body's reactivity in the fluid compartment of the body of antibodies to the Lyme disease organism
- Blood test called the modified lymphocyte transformation test (LTT-MELISA) in which the T-cell immune response to recombinant, Borrelia-specific antigens can be detected. This can confirm an active infection in sero-negative, sero–ambiguous or sero– positive patients with or without clinical suspicion of Lyme borreliosis and provide an early marker for successful antibiotic therapy
- Western Blot technique for evaluating Lyme disease
- Multipeptide ELISA tests may be used, which detects antibodies created as a response to infection

Treatment

Breakspear Medical uses an antibiotic therapy, as Lyme disease is responsive to tetracycline, erythromycin, phenoxymethylpenicillin, third-generation cephalosporins and macrolides, and/or herbal remedies.

Immunological changes linked with ME/CFS

There are some other mechanisms of ill health found in ME/CFS with an immunological change in the production of cytokines. We have found that the basis of prolonged ill health in ME/CFS involves 'cytokine shift.' In this condition the protein messengers between cells (cytokines) work together to cause allergy and increased reactivity by a mechanism involving antibodies instead of the normal activity against infectious agents, such as viruses. This is a cytokine shift from a 'T_h1' to a 'T_h2' pattern.

The situation is further complicated as these two patterns interact and counteract each other; allergies are therefore perpetuated and the ability to eradicate viruses is compromised.

Treatment

It is possible to reverse the cytokine shift with a number of treatment programmes that we offer. Firstly, we stabilise allergies by using a neutralising technique that stops allergic reactions, giving respite to the body *(see page 8 – Neutralisation of food allergies, intolerances and sensitivities)*. Secondly, we then use a number of treatment programmes to stimulate the T_h1 arm of the immune system that can deal with viruses.

Amongst the treatments we use are mushroom products (primarily coriolus-based supplements) and Transfer Factor. Other agents which can stimulate T_h1 include some hormone products and bacterial agents, including Bacille Calmette-Guérin (BCG), normally used in protection against tuberculosis.

Bacterial product which can improve intestinal biome is known to help modulate the immune system. Some probiotic preparations can induce a T_h2 response. Lactobacillus, Escherichia coli, Bifidobacteria and others have a local effect protecting against gut mucosal injury through both T_h1 and T_h2 responses.

Combination therapies are more effective than single agents.

Evaluation of hormonal status

A patient's medical history must be examined thoroughly and this may include analysis of hormonal status. This is important because it affects the basal metabolic rate at which we function.

With ME/CFS, the following are often found, which shows that hormonal status plays a key part in these conditions:

- Low DHEA and cortisol. This is because of adrenal atrophy from hypothalamic under-stimulation or chronic excessive sympathetic activity which can cause down-regulation by biological feedback
- Thyroid function may be impaired
- Deficiency of antidiuretic hormone (ADH), causing urinary frequency
- Deficiency of aldosterone, causing hypotension

Symptoms

If the DHEA is low, there may be muscular weakness and hypotrophy, macromastia, abdominal and hip obesity, lack of emotional dominance and weak libido. Indications of cortisol deficiency are general weakness and recurrent infections.

Thyroid deficiencies may be indicated by any or all of the following: hoarse voice, constipation, loss of hair, particularly the outer third of the eyebrows, weight increase, and rough skin.

Aldosterone impairment may cause low blood pressure, leading to fainting, light-headedness and general weakness.

If albumin levels are low, there is probably a low protein reserve and higher likelihood of liver failure.

Treatment

To overcome irregularities in hormonal status, we occasionally use adrenocortisol hormone (ACTH) to increase pituitary drive to the adrenals. Nutritional support and detoxification may ensure that the thyroid is not polluted. In some cases, thyroid supplements may be required as well. Prescription salts, such as fludrocortisone, are sometimes needed to increase albumin levels.

Neutralisation of food allergies, intolerances & sensitivities

Food allergies are very common. The immediately recognisable form of food allergies is called IgE mediated hypersensitivity reaction. This results in swift responses such as diarrhoea, vomiting, anaphylaxis, and sometimes rashes, eczema or asthma.

Protection from this type of food allergy is primarily the avoidance of the food. If the individual is sensitive to many foods by this mechanism, sodium cromoglycate, which is a mast cell stabiliser, can be used prophylactically. Treatment for the ingestion of food may include the utilisation of antihistamines, or if anaphylaxis occurs, adrenaline to combat shock and perhaps resuscitation might be required.

The majority of food allergy reactions are, however, not due to IgE mediated reactions but to IgG reactions. IgG antibodies are formed when food has gained access to the tissues in large enough amounts for an antibody response to be marked. Normally food is broken down adequately by digestion in the gastrointestinal tract and then absorbed and then enters the blood stream in small particles, often attached to IgA. IgA antibodies are the protective antibodies in the gut lumen. They also have the function of protecting the gut lining from being attacked by bacteria, stopping bacterial adhesion to gastrointestinal cells.

IgA antibodies can also attach to food particles and transport them into the portal circulation. When transported to the liver they become detached from the food particles, which are further metabolised by the liver and are then disseminated through the systemic circulation as nutrients. However, if large food particles without IgA antibody adhesion enter the systemic circulation, IgG antibodies are formed. The complexes that are produced (IgG antibodies plus antigen) have to be broken down and in this process a cascade of chemical reactions occur which cause the disintegration of the antigen. If complexes latch on to tissue cells in sufficient numbers an inflammatory reaction at that site occurs. Tissue can then be destroyed by cytokine responses and disease at that location can ensue. IgG antibodies also inhibit the formation of IgA antibodies by Peyer's patches in the gastrointestinal tract wall. Hence, food-mediated responses can be perpetuated.

Symptoms

Food allergies, intolerances and sensitivities may be indicated by a wide range of symptoms, including but not limited to mood swings, upset stomach, lack of concentration, lethargy, depression, forgetfulness, ringing, popping or fullness in the ears, watery eyes, sore throat, dark circles under the eyes, difficulty in sleeping, diarrhoea, vomiting, rashes, eczema, asthma, headaches, migraine and many other symptoms.

Treatment

Food intolerances and sensitivities must be addressed to protect the gastrointestinal lining from triggering foods. Food avoidance is not usually possible as a large number of IgG food reactions may occur once there has been increased intestinal permeability and simple avoidance may limit the diet so much that it leads to malnutrition.

Breakspear Medical uses neutralising vaccines to help patients deal with a variety of foods and also uses other supportive management. Our vaccines are formulated on weak dilution principles but are isopathic. In addition, we consider the role of yeasts, candida, parasites and digestion in gastro-intestinal health.

Fibromyalgia

Fibromyalgia primarily affects women. Symptoms develop at any age and progress in cycles, perhaps mild with remissions between attacks, but the symptoms may worsen and become continuous.

There may be either cellular or matrix problems in fibromyalgia. Half the components of the body are cellular and the other half intercellular in the connective tissue or matrix. In the matrix are embedded the capillaries and the terminations of autonomic nerves. There are fibres of collagen and fibroblasts in this system, and the whole is distributed through a 3-dimensional network of tightly coiled glycoprotein fibrils. The function of the matrix and connective tissue is to allow buffering, so that pressure can be exerted on tissues without destruction of cells, and also as a medium in which there is accumulation of fluids and a chemical buffering within the tissues. Often the chemical buffering is between an acid and an alkaline balance. When acids accumulate, there also tends to be an accumulation of fluids to dilute the acids to equilibrate and balance the pH. Excessive water accumulation under pressure will cause pain and lumpiness in the tissues. Intercellular dilution of fluid will inhibit many of the energy-releasing processes.

Intracellular swelling can occur also. Excessive phosphate entering the mitochondria will block adenosine triphosphate (ATP) formation. In the intercellular spaces there is no discrimination between what is necessary for health in the tissues and what is a pollutant. Many accumulations of pollutants can occur in the matrix, and can dissolve in cell walls, if fat-soluble.

Sources of some of the acids that can cause imbalances include yeast and bacterial by-products absorbed from gastrointestinal micro-organisms. It is thought that gastrointestinal tract micro-organisms number as many as the total number of cells in the human body itself. Of approximately 500 species of bacteria, 30-40 species predominate and most are anaerobic. Yeast and fungal species and clostridia often follow the use of antibiotics. Amongst the acidic products of yeast species is tartaric acid, which can be toxic (large amounts can produce gastrointestinal symptoms, diarrhoea and vomiting, abdominal pain, thirst, muscular pain and weakness, and can, in very large amounts, cause a nephropathy).

Tartaric acid is an analogue of malic acid which is an intermediate in the Krebs cycle. Tartaric acid inhibits the Krebs cycle enzyme fumarase, which produces malic acid from fumaric acid. Other by-products mimic substances in the Krebs cycle, for example, 3-oxoglutaric acid resembles alpha-ketoglutaric acid. Citramalic acid can be high from yeast products. Arabinose produced in the liver from arabitol, a yeast toxic product, can cross-link proteins and make them unavailable for function. This is carried on the lysine residue site on proteins, and biotin, B6 and lipoic acid which can be carried at these sites, are made unavailable for use. A DHPPA-like compound is produced from anaerobic bacteria, and can have neurological consequences. An enzyme called 2,3-diphosphoglycerate (2,3-DPG) has been found to be low in some patients and thiamine deficiency can cause this. Hypoxia results from low 2,3-DPG.

Symptoms

Some people have muscle pain as their predominant symptom. Other symptoms may include but are not limited to:

- Hypoglycaemia or carbohydrate intolerance with tiredness, panic, palpitations and light-headedness after eating sugar or starch
- Pain and stiffness in the muscles, tendons and ligaments
- Fatigue, irritability, depression, poor memory and lack of concentration
- Some patients have irritable bowel syndrome/ allergic colitis, irritable bladder/allergic cystitis, and sometimes recurrent vaginitis, headaches, burning hands and feet

Treatment

We offer treatments including nutritional support, pain management and neutralisation of food and other sensitivities *(see page 9 – Neutralisation of food allergies, intolerances and sensitivities)*.

Mitochondrial dysfunction

Mitochondria generate most of the cell's supply of adenosine triphosphate (ATP), used as a source of chemical energy. ATP is the principal source of energy for muscles and other tissues.

Mitochondrial dysfunction may be caused by mutations, acquired or inherited, in mitochondrial DNA or in the nuclear genes that code for mitochondrial components. They might also be the result of adverse effects of infections, drugs or other environmental causes. There are many conditions associated with mitochondrial dysfunction such as anaemia, diabetes, dementia, hypertension, lymphoma seizures and neurodevelopmental disorders, and ME/CFS.

To determine if mitochondria dysfunction is present, tests of molecular biology are used to evaluate if there are any blockages in the mitochondrial function.

If this condition is diagnosed at Breakspear Medical, a mitochondrial dysfunction treatment programme of both oral and intravenous nutrients may be advised and individualised. This is most often in conjunction with detoxification, as the mitochondria are easily affected by environmental pollutants.

Boosting immune system with antioxidants

All the evidence suggests that the healthy body is continually exposed to potential damage by free radicals, which, as a result of their reactivity, eagerly combine with other chemicals in the body. Free radicals have been implicated in cancer causation, liver damage by toxins like carbon tetrachloride, lung damage by nitrogen dioxides, ozone and paraquat ultraviolet light, radiation damage and inflammatory processes.

Free radicals are formed when pollutants enter the body and the greater the exposure to the solvent or smoke, for example, the more free radicals will be produced. The most common free radicals are *superoxide* (O_2-), *peroxide* (HO_2-) and *hydroxyl* (OH-) and a similarly reactive atom, though not strictly a free radical, is called *singlet oxygen* (O-). These free radicals are produced in the course of normal function of the body processes and within the body there exist systems that mop them up to prevent damage (quenching). However, these protective systems are sometimes overwhelmed and may be inadequate to check free radical amplifying cascade reactions.

Symptoms

There are not many definable symptoms though some patients may feel unwell, malaise and may experience accelerated ageing.

Treatment

It is possible to help the body to prevent free radical damage either by prevention of free radical formation (avoidance of pollutants, toxins and drugs where possible) or by maximising ability to quench radicals nutritionally, once they are formed.

There are two main nutritional approaches to preventing free radical damage. The first approach is to provide the micronutrients necessary to the body's own protection mechanisms. These nutrients include: zinc and manganese for *superoxide dismutase*, a protective enzyme discovered in 1969 by McCord and Fridovich; selenium for *glutathione peroxidase*, an enzyme which can destroy hydrogen peroxide and organic peroxides; and zinc is also an essential component of several DNA repair enzymes. The second approach is to take supplements of substances which have an intrinsic antioxidant activity. The main dietary antioxidants are vitamins, in particular vitamins C and E (which have long been known to act as free radical scavengers, able to inhibit peroxidation damage of fats), vitamin A and beta carotene, cysteine and glutathione. Other supplements also have powerful antioxidant activity (e.g. coenzyme Q10, OPC pine bark extract). It has also been shown that vitamin C can enhance the effects of vitamin E, having the capacity to regenerate it. It is thought that the protective effect may help in prevention of many diseases and so a diet rich in antioxidants, supplemented where necessary, may have a role in the prevention of disease.

Treatment with antioxidants is mandatory for immune disorders, which occur in ME/CFS and fibromyalgia, as well as many other illnesses. We use intravenous and oral supplements in antioxidant treatment programmes.

Detoxification

In environmental medicine, it is very well known that taking into consideration workplace encounters is imperative.

Between 1965 and 1978, over 4 million distinct chemical compounds were reported in the scientific literature. Of approximately 6,000 reported per week, about 55% are now in use and in commercial production. The toxicology of the majority of these compounds has not been completely understood.

Many thousands of these compounds have been released into the environment and the interactions of these are not known, and the effects on flora and fauna are only now being established. In environmental and occupational health, the chief principle involved is preventing exposure. Should this fail, it is necessary to try to alleviate adverse effects by limiting the use of chemical compounds known to be harmful or potentially harmful and also by reducing contamination and release, so as not to endanger the environment. Equally these similar compounds should not be used in such a fashion as to cause contamination of the human body. Where such contamination has occurred, the compounds should be safely removed from the body.

Symptoms

Indications of the need for detoxification are:

- Multiple chemical sensitivity
- Presence of lipophilic
- Xenobiotics in blood or fat biopsies
- History of exposure to lipophilic xenobiotics
- History of heavy metal intoxication
- Presence of excess heavy metal residues in tissues

Treatment

Aims and objectives of biodetoxification are the reduction of the lipophilic xenobiotic and heavy metal body burden by:

- Fat mobilisation
- Enhancement of the body's natural detoxification pathways (respiratory, renal, gastrointestinal and cutaneous)

Our detoxification programme is designed to mobilise fat, increase sweat and sebum secretion, prevent gastrointestinal re-absorption of xenobiotics excreted in the bile and to maximise the detoxifying systems by provision of optimal amounts of nutrients. The programme may use either the IRATHERM® whole-body hyperthermia treatment or sauna treatments.

Dental materials & the immune system

The amalgam used in dental fillings contains more than 50% mercury with other amounts of silver, tin, copper and zinc.

In the past it had been thought that the mercury was locked into the filling and could not escape. Recently, however, it has been proved that mercury is constantly leaked from the fillings, the amount increasing up to fifteen-fold when especially hot, salty or acidic foods are chewed.

Mercury is one of the most toxic substances known to mankind. It can affect many of the regulatory systems of the body. Primarily it targets the central nervous system, thyroid and pituitary glands, the kidneys, circulatory, digestive and respiratory systems.

Symptoms

Recent research has shown that mercury from fillings can reduce the effectiveness of the body's immune system resulting in increased susceptibility to bacterial and viral infections. In addition, it has been associated with arthritis, migraine, epilepsy, food, chemical and inhalant allergies, candida and other yeast overgrowths and neurological disturbances such as multiple sclerosis, which it can mimic or exacerbate.

Treatment

We can coordinate a detoxification programme with your dentist's removal of toxic fillings and replacement with preferable materials.

Nutritional assessment

In order to ensure that a patient is properly nourished and their digestive system is functioning optimally, we look at their intake, digestion, absorption, utilisation and excretion of products.

This involves examining the patient's dietary history, from foods that are never or rarely eaten to ones consumed nearly daily. The quantity and quality of the foods is also taken into consideration and an assessment of alactasia, which is the absence of the enzyme needed to degrade milk sugar. This particular assessment entails taking lactose and doing a breath test for products. Stool and/or urine tests may also be performed to determine immunity status, analyse the absorption of digestive enzymes, and evaluate how the enzymes breakdown commonly consumed foods such as wheat, milk and yeast products. Urine tests may also be conducted to evaluate degradation of carbohydrate, protein and fat. Blood tests may be given to assess minerals, antioxidants, vitamins and enzymes.

Symptoms

The symptoms of poor nutrition, lagging digestion and insufficient gut flora are widely varied.

Treatment

A thorough assessment of nutritional state is undertaken and all the implications and deficiencies are rectified. Supplements often include essential fatty acids, magnesium and other supplements either by oral or intravenous infusions. Evaluating and addressing a patient's nutritional status will help build immunity.

Autonomic dysfunction & postural hypotension

The autonomic nervous system (ANS) is often disturbed by ME/CFS. People develop postural hypotension, which can be due to abnormal hormonal states or poor function of the hypothalamic pituitary adrenal axis (HPA). This axis requires appropriate feedback information to function properly, which is sometimes lacking in ME/CFS.

Symptoms

Symptoms of autonomic dysregulasion (also known as dysautonomia) include dizziness associated with weakness or rapid heartbeats called palpitations, which comes during or accompany changes in posture. There may be dry mouth or dry eyes, poor regulation of body temperature, irregular sweating that can be meagre or profuse. Bowel movements may be disturbed, usually unpredictably causing both diarrhoea and constipation alternately and sometimes causing pain in the abdomen. Bladder function can also be affected in dysautonomia, often causing frequent and uneasy visits in the toilet with the feeling of urgency to pass urine. People with ANS dysregulation often have abnormal tissue oxygen or carbon dioxide or both due to poor tissue respiration. This can cause unexplained air hunger when there is actually normal lung function and normal level of oxygen in the arterial blood.

In dysautonomia, a patient's blood pressure may drop when they lie down flat in the supine posture and this is called supine hypotension or when they stand up straight in the erect posture, which is called postural hypotension. This is because the blood drains to the legs and feet in the erect posture or can be confined in the abdomen in the supine posture due to dysautonomia.

In both conditions, there will not be enough blood getting to the brain and this can cause the person to faint or feel faint. Arterial baroreceptors or pressure sensors are embedded in the walls of the enlarged sections of the carotid arteries in the neck known as the carotid sinus. These baroreceptors control blood flow by maintaining blood pressure to a functional level as required by the body. Carotid bodies or chemoreceptor, which are small swellings embedded in the junctions where the carotid arteries divide into two in the neck do sense the saturation of oxygen in the blood and adjust breathing accordingly. The two types of carotid organs are therefore involved in the adjustments of blood pressure and breathing to meet the body requirements, but they are both vulnerable to pollutants and toxins in the bloodstream. They also do not work well in the stagnancy caused by reduced blood pressure.

Detection and treatment of dysautonomia in ME/CFS

Transcutaneous measurements of blood gases can be done to analyse proportions and deficits of oxygen and carbon dioxide coming through the tissues.

This procedure is completely non-invasive but provides vital information about tissue respiration. Tissue hypoxia can be treated by facilitation of oxygen delivery, which we do by increasing the level of dissolved oxygen in the blood using an oxygen concentrator. This is a delicate procedure and requires specialised medical equipments and appropriate expertise. Low level of transcutaneous carbon dioxide signifies chronic respiratory alkalosis caused by long-term over-breathing, which is in turn caused by chemoreceptor over-drive of breathing. This can be treated using a re-breathing mask fitted with appropriate dead space. Again, this is another very delicate procedure that requires the right equipment, appropriate set up and the right expertise.

Sometimes the level of carbon dioxide in the tissues does not justify the use of the re-breathing mask, so we have our own experts in Butyeko type of breathing who work with patients to try and overcome the chemoreceptor drive of breathing and voluntarily correct the level of carbon dioxide in the tissues. Correction of tissue respiration requires patience because it takes several weeks for the body to acclimatise and adjust to the new levels of blood gases.

Sometimes we detect poor vascular endothelial function in peripheral tissues. We have special procedures in our autonomic examination to diagnose vascular endothelial dysfunctions. This means the lining of the walls of very small blood vessels are not facilitating proper exchange of nutrients including blood gases. In this case, we would recommend a

cell repair protocol, including antioxidants in our treatment regime to rejuvenate the lining of blood vessels and open up more vascular bed to improve circulation.

We may also recommend an exercise programme to improve muscle tone and circulation. We have a number of other manoeuvres for proper examination of the autonomic nervous system. For example, we can detect weaknesses in the pumping strength of the heart. This is known as the inotropic function of the heart. Inotropic fatigability can be treated using dietary supplements that boost energy production in the mitochondria. It requires a proper diagnosis for this treatment to work properly in patients with ME/CFS. When we detect supine hypotension, we try to prevent any deleterious stagnancy during sleep by advising patients to increase their total blood volume by consuming more than the usual amount of water and minerals in their diet and to increase the amount of high quality proteins. Our nutritional therapists are trained to give this sort of advice. We may in some occasions recommend pharmacological interventions like fludrocortisone for postural hypotension.

Brief summary of ME/CFS conditions, investigations & treatments

Condition	Investigation	Treatment
Toxic overload	Blood and urine tests for pollutants	IV vitamins Oral nutrients Glutathione IRATHERM® whole-body hyperthermia Sauna
ANS dysfunction	Quantitative inotropic fatigue test Transcutaneous measurements of blood gases	Intropoic support and repiratory regulation Appropriate breathing tools, which may include exercises, re-breathing masks or an oxygen concentrator
Epstein-Barr virus infection and glandular fever	Blood tests	IV vitamin C Antivirals IRATHERM® whole-body hyperthermia Gamma globulin
Lyme disease	Antibody MELISA Western Blot	Antibiotics Herbal remedies Biofilm breakers
T_h1 to T_h2 shift	Lymphocyte subsets	Transfer factor Coriolus BCG DHEA
Parovirus	Blood tests	High-dose Gamma globulin
Food allergy	Blood tests Skin tests Elimination and challenge Stool test	Neutralisation Diets Supplements
Thyroid problems	Blood tests Scan	Iodine Tyrosine Glutathione Thyroid replacement
Nutritional deficiencies	Lymphocyte proliferation tests Cellular mineral tests	IV/oral treatment
Oxidative stress	Blood tests Urine tests	Antioxidants
Fibromyalgia	Blood tests Urine tests	IV Lignocaine
Dental problems	24-hour urine test for metals	Detoxification

Conclusion

Chronic fatigue syndrome (CFS) and myalgic encephalomyelitis (ME) are debilitating and distressing conditions, which affect people of all ages.

CFS is defined by Fukuda *et al* by the presence of the following:

- Clinically evaluated, unexplained persistent or relapsing chronic fatigue that is of new or definite onset, is not the result of ongoing exertion, is not substantially alleviated by rest and results in substantial reduction in previous levels of occupational, educational, social or personal activities
- The concurrent occurrence of four or more of a group of symptoms and signs, all of which must have persisted or recurred during six or more consecutive months of illness and must not have predated the fatigue

It has been shown in studies that these conditions are associated with abnormalities of immunity.

Breakspear Medical uses a multidisciplinary approach to help those with ME/CFS. We use specialised independent laboratory tests for detecting the commonly affiliated viruses and other infectious agents, and we use an individualised programme of treatment for each patient to address different aspects of a patient's illness, taking into account the patient's medical history, the findings from a physical examination, and the results of the various investigations. A programme of treatment will be proposed at the first consultation and an estimate of the costs involved will be provided at this stage.

The Centre for Reviews and Dissemination, based at the University of York, produced a series of bulletins 'on the effectiveness of health service interventions for decision makers' and summarises the effectiveness of treatments for the management of ME/CFS. This publication gives guidance to health care providers. It describes treatments which the Centre for Reviews and Dissemination has deemed effective; amongst them are those used at Breakspear Medical. Full copies of the articles which the Centre uses to validate the effectiveness of the treatments are available from Breakspear Medical and also from the Centre for Reviews and Dissemination.

Breakspear Medical has the facilities to provide services for children, young people, adults, disabled and the elderly. We offer support for coping and adjusting to the illness and appropriate care packages.

Breakspear Medical is a private clinic in operation since 1982. All new patients, or their guardians, can make an appointment to see a doctor directly. It is recommended that patients seek a referral from their General Practitioner where possible as we regularly correspond with local Primary Care Teams.

An analysis, conducted by independent statistical audit, of over 1,000 symptom scoring charts completed by Breakspear Medical patients, demonstrated a highly significant difference in overall score between the first symptom scoring chart and the final completed questionnaires. This implies a reducing of the symptom effects over time amongst our patients.

Our patients' many success stories are testimony to the effectiveness of the treatment we provide for ME/CFS sufferers.

You can find such testimonials on our website **breakspearmedical.com/testimonials**

Definitions

Definition of fatigue

Fatigue, also referred to as tiredness, exhaustion and lethargy, described a physical and/or mental state of being tired and weak (Nordqvist, 2015).

Some of the possible causes include:

- anaemia (not including iron-deficiency anaemia)
- iron-deficiency anaemia
- Coeliac disease
- endocrine/metabolic, such as in hypothyroidism
- as an adverse effect of drugs/medication. For example, statins has been shown to cause fatigue
- sleep problems
- infectious diseases and infections, i.e. EBV, HHV-6, cytomegalovirus, etc
- secondary to vitamin and mineral deficiencies
- secondary to chemical and substance exposure.

Aldosterone
The main sodium-retaining hormone which keeps salt and water in the system. Part of the complex mechanism used by the body to regulate blood pressure.

Antidiuretic hormone (ADH)
A peptide hormone which controls reabsorption in the kidneys by affecting the tissue's permeability.

Antioxidant
A substance that quenches free radicals.

ATP
Adenosine triphosphate is able to store and transport chemical energy within cells and plays an important role in the synthesis of nucleic acids.

Autonomic nervous system (ANS)
Controls all the involuntary body functions, such as respiration, perspiration, heart rate and rhythm, digestion, bladder control, circulatory control, blood pressure and emotion.

Chronic excessive sympathetic drive
Fight or flight response in overdrive without an outlet provoking anxiety.

Collagen
Main structure protein found in animal connective tissue.

Cortisol
Critical steroid hormone made in the adrenal glands, which are above the kidneys.

Cytokines
Mediators of immune activity. Chemicals which carry messages from one cell group to another.

Cytokine shift
The shift where T_h1 cytokines are lessened and T_h2 cytokines are increased in an allergic state.

DHEA
Dehydroepiandrosterone is a precursor hormone for steroid hormones. When levels are low, there is lack of emotional dominance and weak libido. There is no reason for concern when levels are high.

DHPPA
Dihydroxyphenyl propionic acid is a chemical degradation product from bacteria.

Fibroblast
Cell in connective tissue that produces collagen and other fibres.

Fibromyalgia
Condition in which there are knots in the connective tissue in muscles.

Free radicals
Reactive oxygen-containing compounds, formed when pollutants enter the body.

Glycoprotein fibrils
Protein core carbohydrate fringe.

Hypoglycaemia
Deficiency of glucose in the blood stream.

IgA antibodies
The protective antibodies in the gut lumen. They also have the function of protecting the gut lining from being attacked by bacteria.

IgE reactions
Acute allergic reactions. IgE is measured to detect allergic conditions.

IgG reactions
Antibody response. IgG is produced in subsequent exposure to an antigen.

IgG antibodies
Antibodies that are produced to 'remember' a previous antigen.

IRATHERM® hyperthermia treatment
Water filtered infrared-A bed used to raise body core temperature.

Krebs cycle
A term used to describe the citric acid cycle which accounts for the production of energy in most higher animals.

Lipophilic xenobiotics
Foreign chemicals which dissolve in fat.

Mast cells
Release histamine. If the cell wall is stabilised, then reaction is less likely.

Mitochondria
Intracellular packets for energy production. sometimes referred to as 'cellular power plants', mitochondria generate cellular energy from food and are involved in other processes, such as processing oxygen signalling, cell growth and death as well as cellular differentiation.

Nephropathy
A kidney disease.

Peyer's patches
Gastrointestinal germinal lining centres, which produce IgA (the policing antibody of the gut) and which consequently play a central role in the induction of mucosal immune responses in the gut. They protect from bacterial infections and link with food, 'tagging' it so that when it is absorbed there is no acute reaction.

Postural hypotension
Low blood pressure when assuming an upright posture.

Quench
System body uses to 'mop up' free radicals and prevent them from causing damage.

Thyroid function
To take iodine, found in many foods, and convert it into thyroid hormones, which are transported throughout the body where they control metabolism (conversion of oxygen and calories to energy).

T_h1
T-helper type 1, required for cell-mediated immune responses. They are essential for controlling such intracellular pathogens as viruses and certain bacteria.

T_h2
T-helper type 2. These provide help for B cells and, in so doing, are essential for antibody-mediated immunity. Antibodies are needed to control extracellular pathogens.

Transfer factor
Products derived from colostrum to provide immune factors to enhance immunity.

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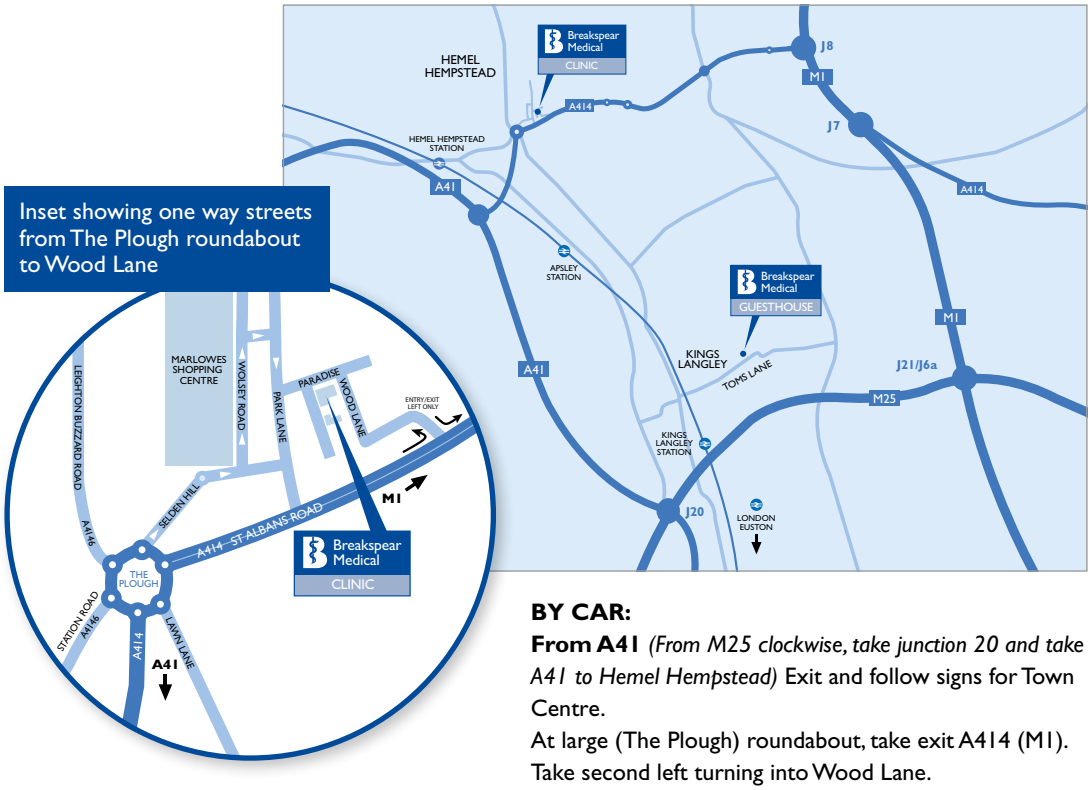

BY CAR:

From A41 *(From M25 clockwise, take junction 20 and take A41 to Hemel Hempstead)* Exit and follow signs for Town Centre.
At large (The Plough) roundabout, take exit A414 (M1). Take second left turning into Wood Lane.

From M1 *(From M25 anti-clockwise, take junction 21 and take M1 Northbound)* Exit at junction 8, Hemel Hempstead. Follow dual carriageway towards Town Centre across four roundabouts. At fifth roundabout (The Plough) U-turn back up the dual carriageway. Take the second left turning into Wood Lane.

BY RAIL:

Hemel Hempstead is on the Euston/Northampton line, about 25 minutes from London Euston. A taxi rank is present at the station.

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