

MANAGEMENT FILE

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MEA membership costs £18 a year for people living in the UK/BFPO.
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BLOOD TESTS EXPLAINED

INTRODUCTION: WHAT DOES A BLOOD TEST MEASURE?

Human blood contains red cells, white cells, platelets and plasma.

Red blood cells carry oxygen around the body – so a deficiency or abnormality here will probably cause anaemia.

White blood cells help the body to fight off infections and respond to allergies. White cells are sub-divided into cells called basophils, eosinophils, lymphocytes and neutrophils. Each cell has a slightly different function and an increase in a specific cell type can indicate that an allergic or infective reaction is taking place.

Platelets help to form blood clots and prevent bleeding. So a platelet deficiency can cause excessive or prolonged bleeding from a wound site.

Plasma is the fluid component that contains a wide variety of substances produced by the immune system (eg antibodies, cytokines, natural killer cells) as well as enzymes, hormones and proteins that are made by or excreted by various organs and tissues in the body. The plasma also contains all the other chemicals and substances – vitamins, minerals, sugars and fats - that are carried around the body.

The use of new investigative technologies means that scientists can now also look at specific proteins (proteomics), metabolites - the remains of chemical reactions that have taken place (metabolomics) and genetic factors that may predispose people to developing



specific diseases (genomics). These tests are increasingly being employed by researchers who are looking for the cause of ME/CFS. They are also being used to try and find diagnostic blood markers (biomarkers) for ME/CFS, or markers for sub-groups, such as people with severe ME/CFS.

Laboratory analysis of a small sample of blood can, therefore, reveal a great deal of basic information about your state of health and the function of various organ systems.

IS THERE A DIAGNOSTIC BLOOD TEST FOR ME/CFS?

While minor blood test abnormalities can occur in ME/CFS, none of them are sufficiently consistent or robust enough to turn them into diagnostic markers in our current state of knowledge.

So the simple answer here is 'no' and a diagnostic 'ME blood test' seems unlikely to be made available in the near future.

THE SEARCH FOR A DIAGNOSTIC BIOMARKER FOR ME/CFS

Significant progress is however being made in the search for potential diagnostic biomarkers and a number of research groups have been reporting some interesting preliminary findings.

The UK ME/CFS Biobank (which is funded by the MEA Ramsay Research Fund) has found that some people with severe ME/CFS have a lower than normal level of a muscle enzyme called creatine kinase.

They have also published results from a big study on the immunology of ME/CFS that was funded by the National

Institutes of Health in America. This study found that some people with ME/CFS have an increased proportion of an immune system component called MAIT cells (mucosal associated invariant T cells). This is an interesting abnormality that is being linked to neurological and autoimmune conditions such as multiple sclerosis and inflammatory bowel disease, where these cells appear at sites of inflammation in the nervous system and gut lining.

The Stanford research group in America have reported on changes in the shape of red blood cells and more recently observed that when a specific type of immune cell is stressed to increase its energy requirements it reacts in a different way to immune cells from healthy controls.

Before drawing any firm conclusions about these findings they need to be repeated in larger numbers of people with ME/CFS, and by other independent research groups, and compared to findings in people with autoimmune, infective and neurological conditions, as well as people with unexplained chronic fatigue.

Summaries and reviews of all these recent research studies can be found in the news archive on the MEA website.

WHICH BLOOD TESTS SHOULD BE CHECKED BEFORE A DIAGNOSIS OF ME/CFS IS CONFIRMED?

Everyone should have a number of routine blood tests before a diagnosis of ME/CFS is confirmed. The results of all of these tests should be within normal limits. So the main purpose of arranging all these blood tests is to help the doctor to rule out medical conditions that can also produce fatigue and other ME/CFS-like symptoms.

The routine tests that make up this 'must be checked' list are:

- **Full blood count:** red cells, white cells, platelets, etc
- **Serum ferritin** – to check for iron status

- **ESR and CRP** – markers of inflammation
- **Biochemistry screen** – including electrolytes (sodium, potassium), calcium and urea
- **Blood glucose and HbA1c** – screening for diabetes
- **Coeliac disease screening** – IgA anti-tissue transglutaminase antibodies
- **Creatine kinase** – for muscle disease
- **Creatinine** – for kidney function
- **Liver function tests**
- **Thyroid function tests**
- **Adrenal gland function** – 9am cortisol

Depending on the results of these tests and/or the type of symptoms that are occurring, a number of other blood tests may be also necessary.

This could include tests that check for:

- **Infections** such as HIV, hepatitis B or C, Lyme disease
- **Autoimmune and rheumatic conditions** such as lupus/SLE, Sjogren's syndrome – especially where joint pains are prominent
- **Vitamin 12 deficiency** – especially where there are neurological symptoms that are found in this condition
- **Vitamin D deficiency** – which can occur in people with ME/CFS who are largely or wholly housebound and lack regular exposure to sunlight

There are also a number of private (ie non-NHS) tests that are promoted to people with ME/CFS. These can be quite expensive and the current medical consensus is that most of these tests are unproven or unnecessary as they are not helpful in either the diagnosis or management of ME/CFS.

Two tests that fall into this group are the **RNAse-L test** for antiviral activity and the **Acumen test** for mitochondrial function – both of which have been assessed in research studies funded by The ME Association Ramsay Research

Fund. Results from the study which sought to validate the Acumen test have now been analysed and have been submitted for publication.

BLOOD TESTS AND CHILDREN

Doctors are more reluctant to carry out extensive testing on children. Even so, it is important to rule out other possible explanations for an ME/CFS like illness before the diagnosis is confirmed in a child. There are also some other blood tests that may be recommended in the case of children and adolescents.

These include:

- **Viral studies** that could help to confirm a recent or current infection with Epstein-Barr virus (glandular fever), which is a common trigger factor for ME/CFS in children and adolescents
- **Tests for other types of infection** which can sometimes cause an ME/CFS-like illness in children. Examples include Lyme disease and toxoplasmosis
- **Serum ferritin level** – a measure of iron status in the body.
- Tests for some of the rare disorders of childhood, including mitochondrial/muscle disorders, that can produce muscle weakness and fatigue.

THE RESULTS – WHAT DO THEY MEAN?

After a blood sample is taken by a GP, it is sent to the hospital laboratory for analysis in a machine. Most of these results should be back within a few days.

Each test will have a numerical result giving the level of the substance being measured in the blood. If this measurement falls within what is called the normal range, there is usually nothing to worry about.

In some cases, the result is higher than normal. If this is just outside the normal range, this may be acceptable and all that needs to be done is for the test to be repeated after an interval. Results

that are significantly higher than normal usually indicate the need for further assessment and/or investigation.

Results that are significantly lower than normal are also important – an example being a low level of thyroid hormone or haemoglobin.

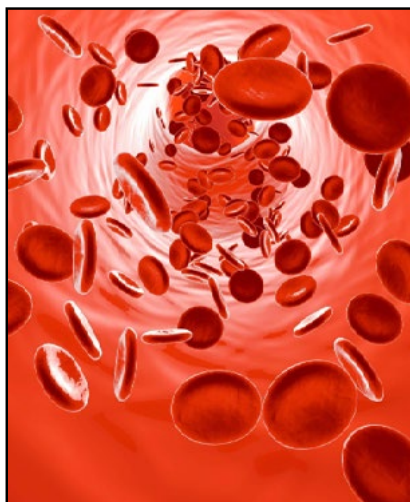
Where significant abnormalities occur, or continue to occur, it is very important to follow this up and try to find an explanation for the abnormality. Failure to do so can result in another serious medical condition, possibly in the early stages and not therefore causing any obvious symptoms, being missed.

WHEN SHOULD BLOOD TESTS BE REPEATED OR EXTENDED?

Once a diagnosis of ME/CFS has been confirmed, further investigation isn't usually necessary. But it's worth noting that new, or worsening, or unusual symptoms shouldn't just be automatically linked to ME/CFS and they may need to be investigated.

If ME/CFS persists, especially if you are over 40, there is a strong case for repeating some of the routine tests – such as thyroid function – every few years.

This is because conditions such as anaemia, diabetes and hypothyroidism (low thyroid function) become more common in older age groups and often appear very gradually – so they can be easily missed when you already have ME/CFS.



SPECIFIC TESTS

● Full blood count and differential

This checks the level of haemoglobin (the substance in red cells that carries oxygen around the body), white blood cells and platelets as well as providing information on the size of the red blood cells and breaks down the white cell count into its cellular components

Macrocytosis, where there is an increase in the size of the red blood cells, must be investigated further as it can be a marker for vitamin B12 deficiency and thyroid disease.

Anaemia is not part of ME/CFS. So if anaemia is found it must be investigated further – as it always has a cause. One fairly common cause is iron deficiency due to bleeding (sometimes menstrual). However, a number of conditions with ME/CFS-like symptoms can also cause anaemia.

These include coeliac disease (where it can cause iron deficiency anaemia) and low thyroid function (hypothyroidism). Anaemia can also be caused by dietary deficiencies, especially low iron, and is sometimes found in teenage girls with ME/CFS who do not eat enough iron-containing foods.

A rise in the overall number of **white blood cells** usually indicates the presence of infection or inflammation somewhere in the body.

A decrease in the white cell count may mean that your body isn't so good at fighting infections. Causes of low white cell count include drug side-effects and diseases of the bone marrow, where white blood cells are made.

Minor abnormalities in the white cell count – including the presence of what are called atypical lymphocytes – are sometimes found in ME/CFS, especially in the very early stages when the illness follows a viral infection such as glandular fever. More persistent or significant abnormalities in the white cell count will need to be investigated, especially when accompanied by physical signs

such as enlarged glands.

The **platelet count** should be normal in ME/CFS. An increase in the number of platelets (thrombocytosis) must be properly investigated as it can be an early marker for inflammatory and infectious diseases that can also cause an ME/CFS-like illness.

● Biochemistry screen

This checks the level of **salts/electrolytes** in the blood (ie sodium, potassium), **calcium** and **urea**.

An increase or decrease in the level of **calcium** suggests that there may be another cause for symptoms.

One condition that can cause a raised level of calcium is sarcoidosis and this would need to be considered if you also have a chronic cough and chest symptoms. Thyroid disease can also raise the level of calcium in the blood.

The levels of **sodium** and **potassium** provide vital clues as to how your body is dealing with fluid load and how your kidneys are functioning. An increased level of sodium could indicate lack of water intake (dehydration) or an unusual hormonal condition called diabetes insipidus.

A decreased level of sodium could indicate an excessive water intake or Addison's disease, where there is a serious fall in the output of the hormone cortisol.

A decrease in the level of potassium could be caused by drugs (including diuretics, liquorice and carbenoxalone), diabetes, kidney problems or malabsorption of potassium in the gut.

The level of blood urea gives a rough guide to kidney function.

● Blood glucose and HbA1C

A raised level of blood glucose indicates that you may have diabetes – an illness that can appear gradually with increasing fatigue and urinary symptoms. If so, more specific tests will probably need to be arranged.

● **Creatine kinase (CK)**

This is an enzyme that passes into the blood from damaged or inflamed muscle.

Although CK is usually within normal limits in ME/CFS, there are occasional reports where it is raised, possibly due to muscle inflammation in the early post infection stage of ME/CFS.

A significant increase in the level of CK will need to be investigated, possibly with a muscle biopsy (where a small sample of muscle is removed for examination under the microscope) to exclude a primary muscle disease.

As noted earlier, a study from the UK ME/CFS Biobank has found that CK levels are reduced in some people with ME/CFS. The explanation is uncertain – it could be related to muscle inactivity and disease activity.

● **ESR and/or CRP (C-reactive protein)**

These are two tests that simply pick up whether there is inflammation or infection somewhere in the body. Results of these tests should be normal in people with ME/CFS. If significantly raised, further investigations are likely to be necessary.

● **Hormone function tests**

The only hormone levels that need to be routinely checked in people with ME/CFS are **thyroid** and **adrenal gland** function.

The thyroid gland produces a vital hormone called thyroxine; the adrenal glands are where cortisol is produced.

If symptoms, or electrolyte results, are suggestive of Addison's disease – a very rare condition where the adrenal glands produce dangerously low levels of cortisol – this will require further hospital-based tests.

The basic screening test for Addison's involves checking the morning level of cortisol. If the level is low then further investigation, including what is called a synacthen test to measure cortisol output when the adrenal glands are stimulated by another hormone called

ACTH, will be arranged.

In some circumstances, other hormones may need investigation. One possible example is **serum oestradiol** and **FSH levels** in women who have a significant exacerbation of symptoms at period time. This is because they may benefit from treatment with hormonal supplementation if oestrogen levels are low. Reference: Studd J and Panay M. (1996) Chronic fatigue syndrome. *Lancet*, 348, 1384.

● **Immune function tests**

The white blood count gives a rough idea of how your immune system is functioning.

There are also specialised tests of immune system function that show how the various different components are functioning.

Although abnormalities do quite often occur in ME/CFS involving all the different components of the immune system orchestra – eg autoantibodies, cytokines, immunoglobulin levels, natural killer cells – the changes are not consistent enough to help with diagnosis and so are of research interest rather than clinical use.

And, in most situations, the results are not going to affect the management of your illness. So a more comprehensive investigation of the immune system is not normally indicated.

Autoantibodies are antibodies that the body sometimes produces against its own tissues and this type of abnormal immune system response can sometimes follow an infection. This may explain why low levels of autoantibodies are sometimes found in people with ME/CFS.

● **Liver function tests(LFTs)**

These measure the level of various chemicals, proteins and enzymes that are produced in the liver.

Minor abnormalities in LFTs can occur in ME/CFS for a number of reasons. These include the type of infection that triggered the illness and drugs (eg antidepressants) or herbal remedies that

affect liver function.

A benign condition of the liver called **Gilbert's syndrome** is more common in ME/CFS and this can cause an intermittent rise in the level of bilirubin – a pigment that causes jaundice.

A condition called **primary biliary cirrhosis**, which can cause debilitating fatigue, should be considered when liver function is abnormal – especially where someone also complains of generalised skin itching without the presence of a skin rash.

A condition called **non -alcoholic fatty liver disease (NAFLD)** is becoming increasingly common, often as a result of sedentary lifestyles and obesity, and can cause fatigue and ME/CFS-like symptoms. NAFLD causes an increase in the level of liver enzymes called serum transaminases.

An abnormal LFT result normally indicates that something is wrong with the liver, and the spread of results can provide clues to the nature of the problem. However, normal LFTs do not always mean that the liver is normal. People with cirrhosis can still have normal LFTs.

● **Screening for coeliac disease**

Anyone with irritable bowel-type symptoms – ie abdominal pain, bloating, changes in bowel habit, mouth ulcers – must be properly checked for coeliac disease as this is a fairly common disorder that shares a number of symptoms with ME/CFS. An antibody screening test – the IgA anti-tissue transglutaminase – is commonly used.

If the result suggests coeliac disease, a biopsy of the gut lining will probably be arranged. Coeliac disease symptoms, including the fatigue, often respond very well to a gluten-free diet.

● **Screening for infection**

Antibodies, which are part of the body's immune system response to infection, often remain in the blood for a long period of time after the acute infection has disappeared. But their presence does not necessarily indicate that

the infection is still present or active. So looking for antibodies to specific infections can normally only provide clues as to what triggered your ME/CFS.

Unfortunately, this sort of information isn't usually of any help in either diagnosing or managing ME/CFS. So most doctors believe that looking for antibodies to past infections isn't normally of any practical value. These type of antibodies can also be present in perfectly healthy people.

Even so, there are a number of specific and treatable infections that do sometimes need to be checked for if your clinical history suggests that one of them could be involved. Examples include hepatitis B and C, HIV, Lyme disease and Q fever.

● **Screening for rheumatic conditions**

ME/CFS can produce joint pain. If this is severe, or accompanied by inflammation, swelling or deformity, you will need to be checked for some of the rheumatic diseases that can produce fatigue. This will involve immunological tests that are positive in conditions like lupus/SLE and Sjogren's syndrome.

● **Thyroid function tests**

As both underactivity (hypothyroidism) and overactivity (hyperthyroidism) of the thyroid gland can produce an ME/CFS-like illness, testing thyroid function is essential before a diagnosis can be confirmed.

The most sensitive test of thyroid function involves measuring TSH – thyroid stimulating hormone. As the name suggests, this is a hormone whose function is to stimulate thyroid hormone (thyroxine) production.

If thyroxine output is low then the TSH level rises to stimulate the gland. If too much thyroxine is being produced, the TSH level falls to compensate. Thyroid hormones that are measured in the blood are T3 (occasionally) and T4.

Some private doctors prescribe thyroid hormones to patients with ME/CFS who have normal thyroid function

test results. This is inappropriate and potentially dangerous as even small unnecessary amounts of thyroxine can trigger serious heart rhythm disturbances.

● **Other blood tests that may be helpful**

The above tests are all used during the process of making a diagnosis of ME/CFS. However, once a diagnosis has been confirmed, there are other tests that may be useful when it comes to on-going management.

For example, testing for vitamin D levels is useful in people who are largely or totally housebound and are not therefore producing vitamin D following exposure of the skin to sunlight – which is where 90% of the body's vitamin D is made. Vitamin D status is best determined by a blood test that measures 25-hydroxyvitamin D levels.

A deficiency of vitamin D should be

queried in people who have a level of less than 30 nmol/litre (nanograms/millilitre). Below 12 nmol/Litre indicates a significant deficiency. A level between 30 and 50 nmol/L may indicate a degree of deficiency. For most people, a satisfactory level of vitamin D is around 50nmol/L

The MEA has an information leaflet covering all aspects of vitamin D and ME/CFS, including the blood test.

FURTHER INFORMATION

More information about all these blood tests can be found in the Investigation section of the MEA purple book.

We have an MEA information leaflet that covers thyroid disease and thyroid function tests in ME/CFS.

A new paper from the UK ME/CFS Biobank, which reports on their analysis of routine blood tests in people with ME/CFS, can be downloaded from the MEA website. Click on the following link to find it: <https://tinyurl.com/y63zryd5>

Drug and medical information contained in this leaflet is not intended to be a substitute for medical advice or treatment from your doctor. The ME Association recommends that you always consult your doctor or healthcare professional about any specific problem. We also recommend that any medical information provided by The MEA is, where appropriate, shown to and discussed with your doctor.



ME CONNECT

The Support and Information Service for people affected by ME/CFS/PVFS and Long Covid



Freephone
0800 538 5200

Monday to Friday 10am - 6pm
(Late night until 9pm on Thursdays)

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