

Lab Tests and their Interpretation

This is my interpretation of lab tests. I developed it as a reminder to myself because some of it is difficult to remember. I don't claim to be an expert in pathology but here are some tips I've picked up along the way. Regard it as a rough guide.

FULL BLOOD COUNT

RED BLOOD CELLS

Anaemia (low Hb)

Low Hb with low MCV: This usually means **iron-deficiency anaemia**. In males - **5-10% with this picture may have cancer** – so it may need investigation. Iron-deficiency anaemia is much commoner in premenopausal women (usually due heavy periods).

Low Hb with normal MCV: An important cause is blood loss. This can present with low Hb with normal (or low) MCV. Reticulocytes normally raised (>2%) as trying to produce more blood.

How much blood has been lost?

The haematocrit is a clue. A drop of 20 is equivalent to losing 2500 mls of blood.

Polycythaemia (high Hb)

If Hb raised and the haematocrit is >0.56 females >0.6 males then there is polycythaemia. This is rarely serious – **The main reason is hypoxia** (low oxygen) and hence it is often raised in smokers & COPD. But beware of carbon monoxide poisoning.

Consider **polycythaemia rubra vera** if there is also splenomegaly/pruritis in bath/when hot/thrombocytosis.

MEAN CELL VOLUME(MCV):is useful. MCHC (mean cell haemoglobin concentration) and MCH (mean cell haemoglobin) tend to follow the same pattern.

Low MCV –usually iron deficiency but if <65 consider thalassaemia. It can also be found in copper deficiency.

Raised MCV –can be B12 deficiency (also hypersegmented neutrophils) or folate deficiency –very high with the drug hydroxycarbamide –Also raised MCV with alcohol, liver disease, hypothyroid, rheumatoid drugs such as methotrexate and manganese deficiency. Sometimes found in hypothyroidism.

IRON

Iron Deficiency Findings are low MCV, **low ferritin**, low transferrin saturation, raised TIBC, **raised transferrin**.

BEWARE: *Do not give iron in pregnancy if Hb is low unless ferritin level is also low. Hb can drop due haemodilution. Giving iron unnecessarily can deplete zinc which is often already borderline and add to problems.*

Iron Overload (Haemochromatosis): raised or normal MCV, high ferritin, high iron, **high transferrin saturation**, low TIBC low transferrin and abnormality of HLA-A3 gene. (90% of haemachromatosis patients in the UK have two copies of the p.(Cys282Tyr variant and 5% have one copy).

Interpreting High Ferritin.

High ferritin is a common finding in blood tests.

It needs clarification by doing iron/transferin studies. Transferin saturation is high in haemachromatosis but this an uncommon cause of high ferritin. Check CRP (if this and ferritin high but not transferrin saturation then likely due inflammation). However, often the cause remains unclear.

Anaemia of Chronic Disease: low or normal MCV, raised or normal ferritin, low or normal TIBC (unlike iron deficiency where it is high), low iron, low or normal transferrin saturation. Often low reticulocytes (<2%) suggesting a problem producing blood. **Low transferrin** suggests iron is locked in and cannot be used normally).

BEWARE: A normal ferritin doesn't mean the iron level is normal (does not exclude iron deficiency). A low transferrin saturation and raised transferrin does confirm iron deficiency.

In iron overload (haemochromatosis) ferritin can be normal.

Samples best done fasting or in morning and not during acute illness.

Optimal Iron should be a ferritin above 50

In iron-deficiency anaemia, Hb should go up **1 gram/week** if patient given iron tablets three times daily (however usually only one tablet daily is sufficient and less likely to cause adverse effects). Because red cells live for 12 weeks – repeating the test in 12 weeks is ideal after treating anaemia

B12

Frequently misunderstood and often mismanaged

The B12 test measures **active and inactive B12** and **inactive can make up 90% of the total** -hence it is an **inaccurate test** and **22-35% of patients with low B12 have normal B12 levels**.

It is useful to measure **intrinsic factor antibodies** (virtually diagnostic of pernicious anaemia) and **parietal cell antibodies** (less diagnostic but more common in pernicious anaemia). (High eosinophils might suggest unusual cause -see B12 leaflet).

Other tests of B12 deficiency are holotranscobalamin (the active part of B12) and methylmalonic acid (MMA) (not available in many labs).

High readings of patients on treatment are of no significance (in fact **most patients taking B12 need levels of >2000 to stay well** especially if MTHFR gene variant) so no upper limit.

ABOVE ALL – DO NOT STOP TREATMENT IF LEVEL HIGH

Lower limit of 197 almost certainly set too low – **Pernicious Anaemia Society think it should be set at 330**. Raised MCV gives a clue but can be normal. Raised Homocysteine is also a clue to B12 deficiency.

PLATELETS

Thrombocytosis (raised platelets) associated with a **higher incidence cancer** –consider investigation –also goes up after a bleed. However, thrombocytosis is quite a **common incidental finding**. It can be caused by a B12 deficiency.

Thrombocytopenia (low platelets) –usually **only bleeding risk if <50** and severe bleeding only if <20

Anti-phospholipid syndrome can cause of **low platelets** –may be important cause of thrombosis in younger age group.

(**Aspartame** can cause thrombocytopenia –ask about Diet Coke)

WHITE CELLS

Raised WC -11-20 abscesses >20 peritonitis >100 septicaemia

Raised neutrophils (neutrophilia) bacterial infections, inflammation –if very high consider chronic myeloid leukaemia (CML)- can be >100,000. 95% of CML have the Philadelphia chromosome present. Neutrophils are the main component of WC (40-80%)

Raised lymphocytes (lymphocytosis) –usually viral infections but also inflammation if very high (>10,000) consider Chronic Lymphocytic Leukaemia (CLL), lymphoma.

Raised lymphocytes with a low white count can occur with fungal infections.

High Monocytes –monocytes produce macrophages in tissues –raised in inflammation/ immune problems/chronic infection –also linked atherosclerotic plaques.

High Eosinophils (eosinophilia)/Basophils –usually allergy – occasionally parasites especially if high levels

Low white count: can be being used up by infection or lack of ability of marrow to produce white cells. Higher sugar intakes are associated with lower white counts.

However cause of low white count not always clear and quite a common incidental finding and can run in families.

(Herbal remedies including astragalus and echinacea may help to restore the white count).

A high neutrophil/lymphocyte ratio was a poor prognostic sign in Covid and those with high ratios had six times the mortality. The ratio should be less than three.

BLEEDING AND CLOTTING DISORDERS

Bleeding:

If bleeding do clotting screen and check platelets.

Von Willebrand Syndrome

1% of population

Symptoms may be excess bleeding, heavy periods from early age – probably **often missed**.

Prothrombin time normal, APTT variable, specialised tests usually available.

Clotting:

Antiphospholipid Syndrome (Hughes syndrome)

Auto-immune disorder, common, 2-4% population so **fairly common**, consider if early onset DVT etc

Needs specialist tests - not routinely available (see below for details)

Factor V Leiden

Genetic disorder. One copy of gene common - 3-8% population carries 4-8X risk thrombosis

Two copies gene present 1 in 5000: this carries an 80 times risk thrombosis

Needs coagulation screening tests and DNA analysis – needs specialist tests may not be routinely available.

UREA and ELECTROLYTES (U&E)

Creatinine (& hence eGFR) goes up & down with muscle mass (it is fairly constant in each person) and tends to be higher in males.

Urea goes up after a high protein meal.

If creatinine up without urea and vice-versa then less likely to be important

If in doubt check urine microalbumin & urine A/C ratio.

THE MOST COMMON ABNORMALITY IS A LOW eGFR and in the majority of cases it is of little significance

eGFR 60-90: Very common with increasing age and almost always of no practical significance. Regard as normal in over 60s.

eGFR 45-59: (Type 3a chronic kidney disease) – again extremely common and not likely to be important in older age groups unless protein in urine.

NOTE: eGFR drops 10% per decade after 35 years of age

NOTE ALSO: *People can be unnecessarily frightened by this diagnosis (they may wrongly think this means they will need dialysis) when it is mainly a feature of normal ageing.*

Symptoms usually only present if eGFR 25-30

Consider drugs as cause if eGFR unexpectedly low – **greatest risk is NSAIDs combined diuretics or ACE inhibitors.**

Proteinuria

Major reason is diabetes

If proteinuria add ACE inhibitors to treatment in diabetic males if ACR >2.5mg/mmol and for diabetic females if >3.5 mg/mmol

Proteinuria in non-diabetics is rarely important

However it comes up often as the test is overused.

For non-diabetics add ACE inhibitor if ACR >30mg/mmol if hypertensive and >70mg/mmol for others (it is rarely this high).

Test can vary from day to day so repeat if unexpectedly high.
Microalbumin is increased by standing or exercise.

Sodium

High sodium less common than low– dehydration is most likely cause (including diarrhoea and vomiting) but can be serious (combined raised urea/creatinine).

Rare causes: Diabetes insipidus, Conn's syndrome (aldosterone high, renin low) and Cushing's syndrome. (*Conn's syndrome may be underdiagnosed and is thought to affect 25% of patients with resistant hypertension*).

Low sodium –this is common and **by far the commonest cause is drugs** especially **diuretics**, SSRIs (especially citalopram), carbamazepine, PPIs, metazalone, anti-psychotics, rarely from drinking too much water.

Refer as emergency if <125 and to endocrinology if 125-129)

It can also occur in severe diarrhoea and vomiting (associated raised urea & creatinine) when it lead to syndrome of inappropriate ADH secretion (SIADH).

Clue to dehydration is raised urea.

Causes of inappropriate ADH secretion: COPD (this is a poor prognostic sign and usually associated with oedema), renal disease, advanced liver disease and heart failure.

May need to test urine sodium & urine osmolality (or refer)

Rarely due inappropriate ADH secretion from tumour, or due to Addison's disease.

Tests for SIADH: (SYNDROME of INAPPRPIATE ADH SECRETION): Check urine osmolality >100 mOs.kgH₂O & urine sodium >30, low serum osmolality (<275Mosm/kg). If urine osmolality of <100 with low Na suggests polydipsia

Note if urine Na<20mmol/l suggests low volume with hyperaldosteronism

Potassium

High Potassium – **by far the most common cause is if either using a tourniquet for a long time with difficulty getting blood or sample left too long before analysis. Repeat to confirm –ideally without tourniquet.**

Less common causes: drugs (potassium-sparing diuretics, ACE inhibitors but sometimes NSAIDs & antibiotics). Rarely a crush injury or Addison's disease. High potassium is potentially dangerous but rarely is.

Low potassium - most common cause is drugs, mainly diuretics, can occur with diarrhoea/vomiting –occasionally with laxatives/liquorice. Rarely Cushing's/Con's syndrome. Low potassium also occurs in loss of will to live and this improves after supplementation.

Low potassium nearly always associated with low magnesium and may not correct without giving magnesium first.

Bicarbonate

A measure of acid-alkali balance

A low bicarbonate suggests a metabolic acidosis (sometimes seen diabetic keto-acidosis, chronic diarrhoea, Addison's disease).

A high bicarbonate suggests metabolic alkalosis (as in hyperventilation).

Phosphate:

If high may be renal disease

If low may be Vitamin D deficiency or hyperparathyroidism

Rarely diarrhoea, malnutrition, Fanconi syndrome.

Raised phosphorus can be linked with intake of phosphoric acid and sodium phosphate. These are typically found in ultra-processed foods.

LIVER TESTS

Minor rises in liver enzymes are very common and not usually serious but need interpretation and follow-up.

The cause is unknown in 45% of cases. There is often diurnal variation (different results at different times of day).

Less than 5% with abnormal liver enzymes have liver disease

But 84% still have abnormal results 1 month with 75% abnormal at 2 yrs

Common causes: alcohol (25-40%) NAFLD (non-alcoholic fatty liver disease) (26%) unknown 45%

Clue to NAFLD is metabolic syndrome with high triglycerides and low HDL (on lipid test) and midline obesity.

Clues to Cause

AST/ALT ratio >2 suggest alcoholic liver disease >4 consider Wilson's disease

AST/ALT ratio <1 more likely non-alcoholic fatty liver but ratio raised if more severe if >1 high risk <1 low risk.

Albumin <34 high risk (2% NAFLD progress in 15yrs 12% NASH progress 8 years)
(low platelets suggest liver fibrosis or splenomegaly with liver disease)
Very high ALT/AST suggest hepatocellular disease eg hepatitis

Follow-up

if <3 times normal repeat 1-3 months with AST/ALT/GGT/Alk phos.

If >3 times normal investigate or refer
(liver scan, hepatitis screen, ?toxoplasma, glandular fever, antimitochondrial & smooth muscle AB)

ALT (SGPT) –liver (more specific for liver)

AST (SGOT) liver, heart, muscle, brain

Alk Phos - liver, bone

GGT – liver, recent alcohol exposure –can take 5 days to go down after alcohol intake, also commonly raised in fatty liver -no GGT in bone.

Can occasionally also be raised by alcohols produced by overgrowth of fungus in gut which produce alcohol.

Fatty Liver Disease, NASH and the ELF Test:

NAFLD (non-alcoholic fatty liver disease) is a common disease affecting a quarter of the world's population. However it can develop into a more serious condition called NASH (non-alcoholic steatohepatitis) in 5-10% of cases which can go on to cirrhosis. NASH is associated with liver fibrosis.

One test used to monitor this is the **ELF test (enhanced liver fibrosis test)**. This measures three things: hyaluronic acid, procollagen III amino terminal peptide (PIIINP) and tissue inhibitor of matrix metalloproteinase (TIMP-1).

This gives a measure of liver fibrosis and hence of severity.

What it doesn't reveal is causation. **The main cause is sugar/refined carbohydrates (so testing for metabolic syndrome is crucial) and refined oils (especially soya bean oil)** –see fatty liver leaflet for more details.

Bilirubin

High BR (bilirubin) with normal/raised AST/ALT – common (5% of population) –Gilbert's syndrome or haemolysis
(Gilbert's syndrome is benign but indicates a blocked metabolic pathway (glucuronidation). People with Gilbert's syndrome have difficulty breaking down chemicals such as anaesthetics/paracetamol- commonly have fatigue –at risk of chronic fatigue syndrome).

Alkaline Phosphatase

Alk Phos 45% bone 55% liver –increases with age

Raised alk Phos with normal GGT suggest bone origin

Investigate if >200

If very high or 3 times normal consider primary biliary cirrhosis (do anti-mitochondrial AB)

Also get raised GGT and normal/slightly raised ALT & AST –raised IgM in primary biliary cirrhosis

Low Alk Phos can suggest **low zinc** (zinc dependant enzyme) –look white spots nails/stretch marks. Note zinc is crucial to wound healing.

Low albumin/globulin ratio suggests inflammation (as does high ferritin with normal transferrin saturation and high CRP). However there are other causes.

Albumin is produced by the liver and is both a transporter protein and a building block for antibodies (and globulins). Low levels suggest protein is either being lost or not being formed properly and indicates poor health. It can lead to oedema. It tends to be low in chronic disease.

Globulin is a mix of about 60 proteins including antibodies. Raised levels can be due to an inflammatory response.

IGM raised primary biliary cirrhosis **IgG** raised autoimmune hepatitis

CALCIUM

Hypercalcaemia

The most important cause is hyperparathyroidism. Check parathormone levels.

Hypocalcaemia

Vitamin D deficiency is an important cause. It can also decrease after parathyroid surgery, when albumen is low and with some drugs.

ESR and CRP

Measure of inflammation but non-specific. Usually go up together. An exception is SLE.

ESR goes up more slowly and comes down more slowly than CRP.

The CRP is usually higher in bacterial rather than viral infections.

URIC ACID

This is elevated in gout but often ignored in other diseases.

It is a risk factor for diabetes (quarter of risk of diabetes), insulin resistance, renal disease, fatty liver and hypertension. Elevated uric acid increases mortality by 16% and cardiovascular mortality by 39%.

Increased uric acid causes arterial damage by reducing nitric oxide (which dilates blood vessels).

It is also a breakdown product for fructose which has increased greatly in the food supply and uric acid has doubled over 20 years.

The ideal uric acid should be below 327.

Raised uric acid is linked with methylation difficulties (may be high homocysteine/low B12/folate).

Low urate can be linked with difficulties detoxifying using sulphate pathway (used especially for ridding body of heavy metals).

LIPIDS

Cholesterol has limited value as predictor of heart disease (*eg higher average cholesterol France/Switzerland with much lower rates CHD*) – most useful for middle-aged males

Derived measures; non-HDL cholesterol and cholesterol/HDL ratio have similar limitations but are somewhat more accurate – both should ideally be under 4.

Triglycerides and HDL: useful for diagnosis metabolic syndrome – important marker and precursor of many diseases including heart disease: Diagnose if Triglycerides >1.8 (ideal triglyceride is below 1.0) and HDL <1.0 & midline obesity (waistline measurement better marker for disease and longevity than BMI) –***treat by reducing sugar/carbs/alcohol.***

Triglycerides can be regarded as a surrogate marker for insulin resistance and for carbohydrate intake.

The Triglyceride/HDL ratio is also the best marker for small dense particles of LDL (the dangerous part of LDL).

A high triglyceride to HDL ratio is also a marker of poor ability to clear fat.

If LDL is below 2.6 then there won't be enough small dense particles to be harmful.

High LDL –suggest free radicals –may be high in gall bladder disease – limited correlation with coronary heart disease

HDL: If it's over 1.55 this is a sign of cardiovascular health whatever the other fractions show. If it is <1.0 in men or under 1.2 in women then heart disease is more likely.

HDL/Cholesterol Ratio: This is more useful –should be at least 20% but the higher the better for heart health.

LDL/HDL ratio: should be <2

NOTE: Lipid test are normally not done fasting as this makes little difference to cholesterol, HDL and LDL levels but a meal can increase triglyceride levels.

But oxidised LDL may be a more important marker of cardiac disease than LDL.

Note HbA1C correlates oxidised LDL making HbA1C important risk factor for heart disease

Beware of high strength statins and bringing down cholesterol too much in over 65s as:

- 1) Direct correlation between cholesterol and cognitive function (numerous studies) –cholesterol is brain food and LDL carries it to the neurons
- 2) Both cholesterol & LDL protect against cancer (11 studies)
- 3) 50% increase in cataracts on statins (85% if diabetic and on statins)
- 4) Cholesterol is building block for all hormones which often decline with age
- 5) Higher cholesterol and LDL linked lower rates of infectious disease

Note no benefit in using higher (as opposed to lower) dose statins in trials.

Three trials investigating this (A to Z, SEARCH and TNT trials) found no difference in mortality from heart disease between those using the highest and lowest dose of statin. But higher doses greatly increased the risk of adverse effects.

HbA1C (Glycosolated Haemoglobin)

Measure of sugar control **>48mol/mol is used to diagnose diabetes.**

Problems: HbA1C is a measure of the control of sugar in the blood – this is only a tiny fraction of the sugar in the body so the test is unsatisfactory as a measure of sugar load.

Note: some drugs (sulphonylureas, glitazones, insulin) push sugar out of the blood into the body increasing the sugar load but giving a reassuringly lower HbA1c.

This means the test gets better but the patient gets worse (see diabetes leaflet for more info). **Normal is** <41 with ideal being below 34.

HOMOCYSTEINE

This is an excellent measure of general health. It measures methylating capacity of body – the key orchestrator of the body's biochemistry -dependent on many nutrients including B12.

For every 5 point rise in homocysteine the risk of a wide variety of health problems is doubled, notably cardiovascular disease.

Lab normal range is poor guide.

Interpreting Result:

<6 very healthy,

6-9 – better than average health

9-12 health less than ideal –risk of premature disease

12-15 poor health with higher risk premature disease

15-20 poor health with very high risk premature disease >20 health at high risk

Samples for homocysteine need to be taken at path lab as need putting in ice –they prefer fasting samples.

Faecal Calprotectin

Useful for distinguishing between IBS where levels usually normal (but occasionally above 50) and inflammatory bowel disease (nearly always above 50). But can be up to 150 in bowel infection, diverticulitis and celiac disease.

Faecal Elastase

Raised levels linked to poor pancreatic function.

THYROID TESTS

Thyroid tests are a minefield and should be regarded as only a guide to true diagnosis.

Unfortunately, they are often regarded as gospel.

The clinical findings are just as important, if not more important. Always treat the patient not the test.

TSH unreliable on its own - hypothyroidism can be pituitary origin with low TSH –so always measure T4 as well.

Ideally if symptoms of hypothyroidism, need to do all four thyroid tests to make a diagnosis (TSH, T4, T3 and thyroid antibodies) as may get an abnormality in only one of these.

Typically the T4 is low and TSH high in hypothyroidism and the T4 high and, TSH low in hyperthyroidism.

When treating hypothyroidism aim to get the T4 in the upper range and the TSH below 2 (1.5 in pregnancy).

If T4 in upper range but TSH also high then consider a conversion problem (T4 not converting to T3). Check T3.

Difficulty converting T4 to T3 becomes commoner as we age and through a common genetic variation (but T3 fluctuates a lot so difficult to interpret)–*need zinc & selenium to convert T4 to T3*

Note the normal range has been decreasing for T4 is almost certainly set too low. It measures the average in the population. (This is like saying there has been no increase in obesity in recent decades because the normal range has changed and the normal is now 1 stone heavier than it used to be).

If clear clinical signs of hypothyroidism and either TSH >3 (bizarrely the American normal range goes up to 3, UK to 5) or T4 below 14 consider a therapeutic trial of thyroxine.

Doctors are told in medical school to treat the patient not the lab result but this rule is frequently ignored in thyroid disease.

It is possible (though rare) to have hypothyroidism with completely normal tests due to receptor resistance (when gender-bender chemicals or halogens block thyroid receptors).

Sometimes **reverse T3** needs to be measured (not available NHS) if patient appears hypothyroid but tests normal. This indicates when these hormones which are being stored in an inactive form or receptor is blocked.

If start on levothyroxine retest after 6-8 weeks (takes this long for TSH to reset).

A major problem in thyroid testing and management is that most labs do not test **iodine**, a very common deficiency (some think up to 80% deficient in iodine in hypothyroidism).

Dr Brownstein, an authority on iodine, comments: ***"I can state that it is impossible to treat thyroid illness if there is an inadequate level of iodine in the body and this includes auto-immune thyroid disorders"***. (Urine iodine can be tested Biolab).

In pregnancy if on treatment test 4, 16 & 28 wks & post-partum. Note guidelines suggest TSH should be <1.5 in pregnancy.

Note levothyroxine absorption affected PPI drugs.

If start treatment with levothyroxine and get worse consider an adrenal problem as well

A useful test of thyroid function is the temperature. Measure the underarm temperature. Use an analogue or digital thermometer (measuring 0.1C increments) on waking. Leave thermometer 10 minutes (for underarm reading) before getting out of bed (2nd or 3rd day cycle in premenopausal women).

Underarm temperature below 97.3 F (36.2C) suggests low thyroid (Dr Broda Barnes, an American thyroid specialist).

Alternatively an oral temperature on waking of below 97.8 (36.6C) suggests hypothyroidism.

I find a combination of clinical assessment, thyroid tests and temperature all combine nicely to help with the diagnosis and to judge the results of a therapeutic trial.

If get normal T3 and T4 with raised TSH - consider increasingly common problem of blocking of thyroid receptors by toxicity from bromides (teflon pans, pesticides, plastics, fire-resistant chemicals) or fluorides (toothpaste, some water) –can add iodine to treatment as displaces other halogens.

OTHER HORMONES

If check **testosterone**, then check SHBG as well (as SHBG gets higher then less free testosterone and vice versa) – typically SHBG goes up in males with age and down in women after menopause. Consider checking prolactin as well.

PCOS (Polycystic ovary syndrome): Free Androgen Index (key test with testosterone for PCOS) factors in SHBG also LH to FSH ratio (normal ratio 1:1 goes up to 2 or 3:1 in PCOS as have higher LH however this ratio is an unreliable guide if obese)

If testosterone >5 in women could be virilising tumour

VITAMIN D

Optimal	>125 nmol/l (see below)
Normal	75-150 nmol/l
Suboptimal	50-75 nmol/l
Low	<40 nmol/l.

Vitamin D is the best available guide to immunity.

T cells and B lymphocytes need adequate Vitamin D to function.

Immunity decreases in winter. This is due to lack of sunlight and hence Vitamin D. Hence we get more infections in winter.

There is now strong evidence that Vitamin D reduces the incidence and severity of infections.

This has become more evident during the Covid 19 pandemic where numerous papers have shown that as Vitamin D levels go down then the incidence, severity, risk of hospitalisation and mortality from Covid 19 go up.

For example:

A meta-analysis of 8 studies below found a negative correlation between covid mortality and Vitamin D levels and suggested a very low if non-existent risk at Vitamin D levels of 50ng/ml (125 nmol/l).

COVID-19 Mortality Risk Correlates Inversely with Vitamin D3 Status, and a Mortality Rate Close to Zero Could Theoretically Be Achieved at 50 ng/mL 25(OH)D3: Results of a Systematic Review and Meta-Analysis
Nutrients, 2021; Oct 14;13(10):3596.

A large study in the US by Kaufman of 190,000 people again found the lower the Vitamin D level the higher the mortality.
Doi.org/10.1371/journal.pone.0239252

A similar conclusion came from this recent paper from Israel.

They looked at Vitamin D levels in 1176 admitted with Covid 19 and found:

Those with levels below 50nmol/l: 68% had severe disease or critical disease

Those with levels of 50-75nmol/l: 12% had severe disease or critical disease

Those with levels of 75 to 100nmol/l 7% had severe or critical disease

Those with levels >100nmol/l 0% had severe or critical disease.

doi: <https://doi.org/10.1101/2021.06.04.21258358>

Having Vitamin D levels in the upper part of the normal range (as opposed to low normal levels) also gives much greater protection against breast and colon (and probably most) cancers (See leaflets Breast and Bowel cancer: Reducing the Risks).

People at high risk of Vitamin D Deficiency: Elderly (older skin produces much less Vitamin D, people with darker skin, obesity, many chronic diseases.

Most people need supplements – these are cheap over counter – suggest at least 2000 IU/daily during winter and 1000 IU daily during summer (?for everyone).

Lying in sun 1-2hrs until slight redness will produce 10-20,000 IU Vitamin D

If level very low start higher dose eg 5000iu daily (no toxicity observed in doses up to 10,000 IU daily).

A useful guide to treatment is to subtract the patient's level from the lower limit of normal (75). So if the level is 35nmol/l the 75-35 would be 40 so the patient would need 4000 iu daily until stable.

Ideally take a magnesium supplement as well as magnesium activates Vitamin D

For MS and auto-immune disease: Aim for Vitamin D levels 150-250 (ideally at least 200)

Each 12 nmol/l reduces relapse rate in MS by 16%

(4x risk auto-immune disease if Vitamin D <75)

MISSING INFORMATION

A major blind spot in conventional medicine is its inability to check for adrenal function.

The conventional test is called the short synacthen test but this is a complex hospital test. It involves injecting ACTH and is used to diagnose Addison's disease (complete adrenal failure).

However there is no NHS test to check for milder forms of adrenal deficiency which are common and occur in chronic disease and chronic stress. This can cause fatigue, muscle weakness, reduced libido and poor temperature control.

The **salivary adrenal stress profile** is a useful test and is available privately (from Genova Diagnostics or Biolab) as it measures cortisol and DHEA over the course of a day.

A clue to poor adrenal function is a variation of temperature of >0.6C over the course of the day.

CANCER MARKERS

CA125 – mainly marker for ovarian cancer

CEA -mainly for colon and rectal cancer

CA15-3 – breast cancer

CA19-9 – pancreatic, gallbladder, bile duct cancer

AFP (alphafetoprotein) – liver cancer also cirrhosis

All these are non-specific and can be raised in other cancers and other diseases.

ALLERGY

Raised IgE suggest allergy

IgE (RAST) tests can be done for specific allergens (eg house dust mite) but these have limited usefulness as **negative test doesn't exclude allergy** and doesn't pick up common type B allergens such as most food intolerance. Some non NHS tests are available –see separate leaflet – or you can use an exclusion diet (see food intolerance leaflet).

SPECIFIC INFECTIONS

Lyme disease: due to *Borrelia burgdorferi* –**negative AB tests do not exclude** (because gets in cells and hides in biofilm).

Most reliable test is **Elispot** through Armin labs –high specificity and sensitivity.

Can get tested without seeing doctor through **naturalhealthworldwide.com**.

Tick bites can also cause other similar illnesses such as Bartonellosis, Babesia and Ehrlichia.

COELIAC DISEASES

Transglutaminase –unreliable if low IgA and 10% of coeliac patients have low IgA so routinely do immunoglobulins with transglutaminase.

This test greatly underestimates gluten sensitivity (see gluten leaflet on other tests)

HELICOBACTER

This is a bacteria that lives in the stomach and is a treatable cause of peptic ulcer. It is also linked with gastric cancer.

A stool test for helicobacter is 90% accurate.

However there is an important exception. If you are taking a PPI (an acid-blocking drug) the accuracy of the stool test diminishes by 20% in one week and 72% at 2 weeks. In other words it's a waste of time doing it if you are taking these drugs. However stopping the drugs for 2 weeks will resolve the situation.

MAGNESIUM

Most people are borderline deficient. **Intake has gone down from 500 grams daily a century ago to 200 grams daily now.** This is due to the use of fertilizers (with progressive depletion of magnesium), binding by glyphosphate and fluoride-containing pesticides and refining of food. **Drugs also decrease magnesium** notably **diuretics and PPIs** but also fluoride-containing drugs.

Serum magnesium is a very poor test. (Body will keep magnesium in blood up at all costs otherwise heart may stop beating).

So we only get drop in serum magnesium when there is a a major deficiency so **A NORMAL SERUM MAGNESIUM DOES NOT EXCLUDE SERIOUS MAGNESIUM DEFICIENCY.**

Can do red cell magnesium at Biolab which is more accurate and not expensive.

Note PPIs can cause major magnesium deficiency (as magnesium absorbed in the duodenum only when combined with acid).

PH

Urine pH: if less than 6.5 then body is too acid –need more alkaline diet (more fruit & vegetables).

Acidity is not good for general health.

BLOOD DISORDERS

Monoclonal bands

These usually occur in the gamma globulin region on **electrophoresis** and indicate a monoclonal gammopathy. **Unlike a polyclonal band, a monoclonal band usually indicates malignancy.**

The commonest cause is **multiple myeloma** (a cancer of the plasma cells) but sometimes it can be caused by rare conditions like Waldentrom's macroglobulinaemia, plasma cell leukaemia, amyloidosis and solitary plasmacytoma (multiple myeloma is a malignancy of plasma cells in multiple areas).

In myeloma a band happens in 80% of cases. These bands are made up of abnormal antibodies but sometimes fragments of the antibodies, light chains, will be present which may not form a band. Normally there should be equal amounts of lambda and kappa chains in light chains.

Light Chains: increased kappa free light chains and abnormal kappa/lambda ratio suggest a monoclonal gammopathy, usually myeloma.

However a monoclonal protein is not always due to myeloma. It can be a monoclonal gammopathy of uncertain significance (MGUS). However the levels of monoclonal protein are lower in MGUS.

MGUS is quite common, occurring in 3% of those over 50 years. However it can develop into myeloma (at the rate of 1% per year).

Other features of myeloma include raised ESR (often very high) and high CRP (slightly less frequent), raised calcium (later in course of illness) and Bence Jones proteins (light chains) in the urine.

Beta2 Microglobulin: Very high levels can suggest myeloma, CLL or lymphoma, but elevations can occur with infections and inflammation. High levels are usually a poor prognostic sign.

NOTE: there is not a diagnostic blood test for lymphoma.

Immunoglobulins (rough guide as quite variable)

Increased Globulin: Inflammation

IgM up with acute infections IgG with past infections

Raised IgA with normal IgG and IgM

Acute infections, Ulcerative colitis, Crohn's disease, Guillain Barre

Raised IgG normal IgA and IgM

SLE, auto-immune hepatitis, sarcoidosis

Raised IgM and raised or normal IgG normal IgA

Acute viral infections, primary biliary cirrhosis, SLE, lymphoma. Lyme disease, sclerosing cholangitis

Raised IgM, IgG and IGA

Chronic bacterial infections, polyarteritis nodosa, sometimes rheumatoid arthritis

Raised IgG raised IgA normal IgM

Chronic resp infections, alcoholic cirrhosis, TB, Wegners granulomatosis

Normal IgA and IgM, low IgG

Nephritic syndrome

Normal IgA Low IgM low IgG

Lymphoma, vasculitis, immune suppression

Rheumatology –Not all tests available at all labs

Rheumatoid Arthritis: RF+ve 80% (sensitivity 75% low specificity – present 3-5% population and 30% of elderly), anticitrulline (anti-CCP) AB (assoc erosive disease) sensitivity 75% specificity 98%, raised ESR/CRP when active, hypergammaglobulinaemia, low albumin, mild anaemia

Systemic vasculitis: – raised pANCA (anti-neutrophil cytoplasmic antibodies,

Wegner's granulomatosis: raised inflammatory markers, hypergammaglobulinaemia, neutrophilia and thrombocytosis, **raised cANCA which is specific for Wegner's granulomatosis.**

SLE: ANA positive 95% but also pos other disorders (present 5% population –SLE only 0.2% population, **levels over 1 in 80 suggest SLE**), anti-double-stranded DNA (dsDNA) is highly specific but present in only 65%, also can get ENA, **ESR usually high but CRP often normal.** Can be thrombocytopenia or low WC.

Systemic sclerosis: FBC often anaemia ESR often elevated, ANA positive 70% RF positive 30% SCL-70 antibody assoc progressive systemic sclerosis and ACA (anti-centromere antibody) assoc CREST variant

Osteomalacia: raised alk phos, low serum phosphate, calcium low or normal

Haemochromatosis: elevated ferritin and serum iron, reduced TIBC, almost complete transferrin saturation, abnormality of HLA-A3 gene

Sarcoidosis: elevated ESR/CRP, serum ACE (angiotensin-converting enzyme) can be elevated and RF elevated 15%

Polymyositis: raised CK, RF +ve 50%, ANA +ve 30% -including Jo-1 antibody if lung involvement.

Antiphospholipid syndrome: low platelets raised APTT, anti-phospholipid antibodies. Tests include anticardiolipin, lupus anticoagulant and anti-beta 2 glycoprotein tests.

Ankylosing spondylitis: assoc HLA-B27 antigen 90% (psoriatic & Reiter's 60%) HLA-B27 also raised in reactive arthritis and polymyalgia.