Your blood profiles explained

Because we know that many patients like to be given more information about the individual blood tests undertaken as part of their health assessment, and because patients are concerned when results which appear to be abnormal are dismissed without further explanation, we have written these notes to try to make up for any shortfall in the medical report which you will receive following your health check. If despite these notes, however, you would like any further information about your results, please do not hesitate to contact the physician who carried out the assessment. Your own medical practitioner should also have received copies of your results and will be able to help explain them to you.

By convention the reference values, against which your own results are compared, are defined as being two standard deviations above and below the mean values for those particular results in a healthy population. Given that most biological results fall into a bell-shaped curve, this means that 5% of the results from normal healthy individuals, the two tails at either side of the curve, may be labelled as being 'abnormal' merely because they happen to fall above or below the so-called reference values. Since each test is independent of the others, in a profile of more than 20 tests at least one 'abnormal' result may be expected in two-thirds of perfectly healthy patients having these blood tests. You must also appreciate that the results are influenced by age, diet, medication, and even the time of day and how the blood was drawn.

It is the overall pattern of your results, normal and abnormal, taking into account your own clinical circumstances, which determines whether your particular results point to a health problem and need further investigation. Extreme values are more predictive than minimally abnormal ones, but a single extreme result in an otherwise normal pattern may well be ignorable. A set of blood results is very personal and a marked change in the result of a particular test, even within the reference range, when compared with previous results may be highly significant if it cannot be explained by changed clinical circumstances.

Your own <u>usual</u> values are often far more relevant than the <u>normal</u> values of others.

<u>Cholesterol and triglycerides</u>

The association between raised blood **cholesterol** and the development of premature vascular disease is now firmly established. A raised blood cholesterol is, of course, only one of several factors predisposing to a heart attack or a stroke: cigarette smoking, raised blood pressure and the presence of diabetes are also important factors, as is your family history, but reducing your blood cholesterol is associated with a fall in the risk of your having a heart attack, whatever your medical circumstances, and whatever your initial blood cholesterol level.

Cholesterol is an indispensable structural and metabolic component of all animal cells. In the blood stream it does not circulate in its free state but is bound to particular proteins to form macromolecular complexes, the so-called low-density and high-density lipoproteins (**LDL** and **HDL**). It is raised levels of LDL-cholesterol which predispose to coronary heart disease, while in contrast the HDL particles appear to have a beneficial and protective function. In recent years the study of heart disease worldwide has led to a progressive reduction in the level of total cholesterol which is considered to be 'safe' and the level now regarded by cardiologists as being desirable is <4.0 mmol/L (<154 mg/dL in the US). There is also increased scrutiny of the proportions of LDL and HDL in the blood and an LDL-cholesterol level consistently >3.0 mmol/L, or an HDL-cholesterol <1.0 mmol/L, ought to prompt a further review of your risk of having a heart attack.

You should note that regular exercise and a moderate alcohol consumption are known to raise HDL levels, whereas obesity and smoking lower them. Similarly, a diet rich in cholesterol and the saturated fats (animal fats and dairy products), and artificially hardened unsaturated vegetable fats, the so-called trans-fats, adversely affects the cholesterol profile, whereas the polyunsaturated fats and fish oils are more likely to improve the HDL/LDL balance. (NB: it is our practice to use random *non-fasting* blood samples for health screening purposes, but before any medical treatment is considered, with a statin, for example, blood taken after a 12-hour fast should be used to analyse the blood fats and lipoprotein concentrations.)

Triglycerides, similarly bound as lipid-protein complexes, are the principal circulating blood fats and their daily turnover greatly exceeds that of cholesterol. It is unclear, however, whether plasma triglycerides are themselves independent risk factors for coronary heart disease, but high *fasting* blood levels undoubtedly add to your vascular risk. Although not yet measured as part of this routine blood profile, there is now increasing interest being taken in the levels of the particular proteins which make up the lipoprotein complexes, and in other factors known to affect blood clotting and the risk of thrombosis, and specialist investigations in this regard may be undertaken if your risk of premature vascular disease is considered to be undue.

Blood glucose

Glucose, the body's essential fuel (and the only energy source available to the brain), is maintained within strict limits by a number of hormonal balances so as to ensure that the basic energy needs of the body are able to be met at all times. Blood glucose rises after a carbohydrate meal, but should not rise above 9.0 mmol/L (the level at which blood glucose is usually excreted by the kidneys into the urine). During fasting an adequate blood glucose level is maintained by the production of glucose from the breakdown of fat by the liver.

A blood glucose above 9.0 mmol/L, which is usually associated with the presence of glucose in the urine, may well be an indication of diabetes (inadequate insulin production by the pancreas) and demands further investigation. An abnormally low blood glucose, in a patient alert and well when the blood was taken, is likely to be a technical artefact caused by a delay in the blood being analysed.

In patients suspected of having diabetes, or to monitor blood glucose control in known diabetics, the additional **haemoglobin A_{1c}** test may be arranged. HbA_{1c} is a stable blood product which is formed at a rate that varies proportionately with blood glucose concentration and which may be used as an index of blood glucose control, and therefore of diabetic control, during the preceding 2-3 months.

Thyroid function tests

The thyroid gland, which produces the essential thyroid hormones responsible for metabolic control, is itself controlled by the master hormone regulator, the pituitary gland, by the release from the pituitary of a thyroid activator, **thyroid stimulating hormone** (TSH). A change in thyroid gland activity, which may occur for a number of reasons, including in response to stress or because of a familial 'autoimmune' illness, may be recognised by an increase or decrease in the level of TSH as the pituitary gland tries to correct for under- or overproduction of the thyroid hormones.

If your TSH result is abnormal, we may have arranged for a specific measure of the principal thyroid hormone, **thyroxine** (free T_4), so as to obtain confirmation of a thyroid imbalance. Slight degrees of thyroid imbalance are not uncommon, however, particularly at times of stress, and do not necessarily imply a need for further investigation or treatment. Nonetheless, thyroid disease is very often under-diagnosed and the correction of a thyroid imbalance often restores to good health a patient who has been inexplicably below par for some time.

Renal function tests: blood urea and creatinine

Urea is the principal breakdown product of protein metabolism and is excreted from the body in the urine. The blood urea concentration is dependent on the amount of protein in your diet, as well as the normal breakdown of your body tissue proteins. It is low in patients with a low protein diet, but rises above normal if kidney (renal) function is impaired - especially if this occurs in conjunction with a high protein diet. **Creatinine**, a product of the regular turnover of muscle protein in the body, is independent of dietary protein intake and, being excreted by the kidneys, may also be used as a guide to renal function. Although independent of diet, it is, however, dependent on body weight (i.e. muscle mass).

Total plasma bilirubin

Bilirubin, a bile pigment formed when haemoglobin from effete red cells is broken down, passes with bile from the liver through the bile ducts and, via the gallbladder, into the small bowel where it is further metabolised. In normal circumstances only a small amount of bilirubin enters the blood stream (to be excreted by the kidneys in the urine as the yellow pigment urobilinogen), most remains in the gut to be converted to stercobilin which is responsible for colouring the faeces brown. Excessive bilirubin in the blood stream is manifest clinically as yellow jaundice, often an important sign of liver disease.

A rise in circulating bilirubin may occur if the production of bilirubin is excessive (for example with the increased breakdown of haemoglobin seen in haemolytic anaemia), if its passage through the liver cells is disturbed (e.g. in viral hepatitis), or if bile excretion is impaired (e.g. in the obstructive jaundice caused by gallstones). A rise in plasma bilirubin is also seen in a benign familial condition known as Gilbert's syndrome, the cause of which is uncertain but which affects up to 7% of the population. The syndrome is readily differentiated from liver disease by the normal values for the remaining liver function tests, and sufferers may be reassured that they do not have hepatitis or any serious liver problem.

Liver enzyme tests: alkaline phosphatase, aspartate transaminase, alanine transaminase and gamma GT

These cellular enzymes, normally present in the circulation in trace amounts, are released in greater quantities when tissue cell damage occurs. All are released in liver disease, but a raised **alkaline phosphatase** is also associated with metabolic bone disease and, in children, with normal bone growth, while **aspartate transaminase** is also released in cardiac and other muscle cell damage. **Gamma GT** is often the most sensitive of the liver enzyme results and may be an important marker for alcohol liver damage. Slightly elevated enzyme results may be permanent legacies of previous liver disease, especially the recurring bouts of malaria or hepatitis which may occur in those living or brought up in, for example, tropical Africa.

Plasma proteins

Measurement of the **total plasma protein** concentration is a crude method for determining either deficiency or excess of these circulating proteins. It is of limited value but remains one of the tests included in a standard profile and may provide complimentary support for other results. While the single protein, **albumin**, accounts for 60% of the total, the remaining plasma proteins are **globulins**, the antibody proteins responsible for providing an immune response to any foreign protein invasion. The total globulin concentration, however, indicates very little about precise antibody activity.

Tests for bone disease: calcium and phosphorus

While 99% of the body's total **calcium** is locked into the bony skeleton, free calcium has an important part to play in muscle contraction, nerve conduction and hormone activity. Because of this plasma concentrations are closely controlled by parathyroid hormone and vitamin D activity. A raised serum calcium occurs with abnormal parathyroid hormone activity, or diseases which cause bone destruction, but may also occur in patients with sarcoidosis (or similar lung diseases) or, artificially, if the blood sample is particularly slow being drawn. A low serum calcium is an infrequent finding, but occurs as a result of vitamin D or parathyroid hormone deficiency or ineffectiveness.

It should be noted that whereas localised bone destruction releases calcium, which then goes into the plasma calcium pool and may cause a rise in the serum calcium level, the bone thinning disease, osteoporosis, does not affect calcium metabolism, and a diagnosis of osteoporosis cannot be inferred from any change in serum calcium, phosphorus or alkaline phosphatase (see above). Many factors affect the plasma **phosphorus** concentration and its relevance in the blood profiles is limited. In disease, serum phosphorus often varies inversely with serum calcium and so it may be used to check the validity of a plasma calcium level.

Uric acid

Uric acid is formed by the body's metabolism of compounds known as purines, which are derived from the breakdown of body proteins but are also taken in when we eat purine-rich foods. Uric acid is excreted from the blood stream via the kidneys, and body fluids may become saturated with uric acid if the plasma concentration rises above 450 µmol/L. When this occurs needle-shaped crystals of monosodium urate are formed and may then be deposited in the peripheral joints and tendons, causing an acute attack of gout (typically in the big toe joint). Not all patients with a raised uric acid level will develop gout, but the greater the degree and duration of hyperuricaemia, the greater the chance of crystal deposition.

While a family history is often paramount, anything which increases purine metabolism (a purine-rich diet or increased protein turnover), or which decreases uric acid excretion (illnesses or drugs which affect renal function), may predispose to the development of gout. Patients who, while not suffering acute episodes of gout, nonetheless have consistently raised uric acid levels, may suffer a low-grade painful arthritis often affecting the knees. Those most at risk of developing gout are the overweight; those enjoying purine-rich foods (offal, game, anchovies, shellfish, blue cheese, yeast extracts, pulses, *et al*), especially if there is also a degree of alcohol abuse; and men very much more so than women.

Red blood cells and haemoglobin

The concentration of **haemoglobin**, the oxygen-carrying protein contained in red blood cells, is the usual index used to measure the integrity of your blood volume and capacity. A fall in haemoglobin concentration, anaemia, occurs after a sudden haemorrhage or when slow continuous bleeding exhausts the body's ability to make good the loss, or when red cell or haemoglobin production is in some way inadequate. Because of monthly blood loss, women tend to have lower haemoglobin concentrations than men, and to try to correct for mild but repeated carbon monoxide poisoning, smokers tend to have higher haemoglobin concentrations than non-smokers. While even slight degrees of anaemia, especially if inconsistent with previous results, may be highly significant and deserve further investigation, many patients do have consistently low levels of haemoglobin despite perfectly normal health - particularly those who have genetically-determined haemoglobin variants (thalassaemia, sickle-cell anaemia, etc.).

As well as haemoglobin concentration, the other red cell indices measured or calculated are your **red cell count**; the proportion of packed red blood cells (the so-called **haematocrit**); the mean corpuscular (red cell) volume (**MCV**); the mean corpuscular haemoglobin (**MCH**); and the mean corpuscular haemoglobin concentration (**MCHC**). It is variations in these parameters which help to indicate which type of anaemia may be present, and the need for further investigation. For example: the iron-deficiency anaemia of chronic blood loss is characterised by small red cells (low MCV) with a low haemoglobin content (low MCHC); and the 'pernicious anaemia' of vitamin B_{12} deficiency is characterised by large red cells (high MCV). Alcohol abuse may also lead to swollen red blood cells, macrocytosis, (high MCV), but usually without anaemia, and this may be a more sensitive sign of alcohol abuse than abnormal liver function tests (see above).

White blood cell and platelet counts

An abnormal **white cell count** is one of the cardinal signs of infection. With the advent of specific antibody tests for so many infectious diseases, however, the total WBC count and the concentrations of the constituent cell types, the so-called differential count, although still recorded, have lost much of their earlier diagnostic significance. **Platelets**, the smallest of the blood cell elements, are essential in the initial stages of blood clot formation. Within seconds of a break in a blood vessel wall, platelets aggregate to form a thrombus so as to plug vascular leakage. Red cell, white cell and platelet counts taken together also provide evidence of bone marrow integrity and function - it is in the bone marrow where these blood cell elements are formed.

Erythrocyte sedimentation rate (ESR)

The **ESR**, the rate at which red cells (erythrocytes) settle in a column of blood, is a non-specific index of the body's inflammatory processes and almost any infection or inflammatory disease may produce an often dramatic rise in its value. In the absence of physical signs or symptoms, and with otherwise normal blood results, a raised ESR is most likely to be a legacy of a recent mild viral infection which may have passed unnoticed, but an unexplained result usually warrants a further test after a suitable interval to confirm that it has returned to a normal level.

Prostate-specific antigen

Prostate-specific antigen (PSA), a specific protein produced by prostatic cells, is normally present in the circulation in trace amounts, but is released in greater quantity by active, inflamed or damaged prostate cells. 'Normal' values increase with age: ≤ 2.5 µg/L at 50 years; ≤ 3.5 µg/L at 60 years; ≤ 4.5 µg/L at 70 years; and ≤ 6.5 µg/L at 80 years - in line with the physiological growth of the prostate gland with age.

PSA blood levels are moderately elevated in those patients with significant benign enlargement of their prostate gland. Sudden rises in PSA are usually associated with an infection in the gland - a prostatitis, and levels up to 40 or 50 µg/L may be reached. Any significant rise in PSA, however, particularly if out of line with the clinically-determined size of the prostate, demands further investigation to rule out malignant activity.

A low PSA suggests a quiet benign prostate - but whenever possible, the result should be judged against a clinical assessment of the gland, by digital rectal examination, and the circumstances of each patient.