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Abbreviations and Symbols key

| Symbol/ Abbreviation | Interpretation |
|----------------------|-----------------|
| ↑ | Increased/ High |
| ↑↑ | Very high |
| ↑↑↑ | Extremely high |
| ↓ | Decreased/ Low |
| N | Normal |
| VAR | Variable |

General notes:

1. The reference ranges provided are only applicable to adults.
2. The reference ranges provided may vary according to instrument and methodology.

Part 1: BIOCHEMISTRY

ELECTROLYTES AND RENAL FUNCTION

| | Reference range | Units | Interpretation |
|--|----------------------------|----------------------------|---|
| Sodium | 136-145 | mmol/L | <p>↑ : Diabetes insipidus, dehydration (water loss in excess of salt loss)</p> <p>↓ : Drugs (e.g. diuretics, indapamide, carbamazepine), vomiting, diarrhoea, acute renal failure, congestive heart failure, Addison's disease, syndrome of inappropriate ADH secretion, etc.</p> |
| Potassium | 3.5-5.1 | mmol/L | <p>↑ : Acute renal failure, falsely elevated (haemolysed blood, aged blood, contamination with full blood count tube content), drugs (e.g. ACE inhibitors, spironolactone, amiloride)</p> <p>↓ : Vomiting, diarrhoea, drugs (e.g. Diuretics, indapamide, laxatives)</p> |
| Chloride | 98-107 | mmol/L | <p>↑ : Diuretics, vomiting</p> <p>↓ : Diarrhoea, renal tubular acidosis</p> |
| Bicarbonate (TCO ₂) | 22-29 | mmol/L | <p>↑ : Potassium depletion, vomiting, diuretics, emphysema</p> <p>↓ : Acute renal failure, diabetic ketoacidosis, diabetic hyperosmolar coma, diarrhoea, renal tubular acidosis, lactic acidosis, toxins</p> |
| Urea | 1.7-8.3 | mmol/L | <p>↑ : Acute or chronic renal failure, dehydration (due to vomiting, diarrhoea, sweating), intestinal bleeding, shock</p> <p>↓ : Hepatic failure, pregnancy, cachexia</p> |
| Creatinine | M 80-115 F 53-97 | μmol/L | <p>↑ : Acute or chronic renal failure, acromegaly, meat meals</p> <p>↓ : Pregnancy, chronic muscle wasting</p> |
| Urate | M 0.21-0.43 F 0.16-0.36 | mmol/L | <p>↑ : Gout, renal failure, insulin resistance syndrome, alcoholism, various malignancies (e.g. leukaemia, lymphoma, multiple myeloma), psoriasis, drugs (e.g. diuretics, salicylates, etc)</p> <p>↓ : Syndrome of inappropriate ADH secretion, pregnancy</p> |
| eGFR | See table below | | <p>eGFR = Estimated (calculated) glomerular filtration rate</p> <p>↓ : Renal impairment</p> |
| Osmolality | 275-295 | mOsm/kg | <p>↑ : Hyperglycemia, uremia, ethanol intoxication, hypernatraemia</p> <p>↓ : Addison's disease, water intoxication, syndrome of inappropriate ADH secretion</p> |
| Creatinine Clearance (24 hour urine & blood) | M 94-140 F 72-110 | mL/min/1.73 m ² | <p>↑ : Pregnancy, high protein diet, urine collected over > 24 hours (false increase)</p> <p>↓ : Renal insufficiency, urine collected over < 24 hours (false decrease)</p> |
| Urine protein (24 hour urine) | 0-200 | mg/day | <p>↑ : Cystitis, pyelonephritis, glomerular disease, tubular renal disease, nephrotic syndrome, diabetes mellitus, fever, strenuous exercise, orthostatic changes, rhabdomyolysis</p> |

**Estimated glomerular filtration rate (eGFR) as calculated with the MDRD
(Modification of Diet in Renal Disease) equation**

| Classification of chronic kidney disease (CKD) (Adapted from National Kidney Foundation) | | |
|---|------------|---------------------------------|
| Stage | GFR | Description |
| 1 | > 90 | Normal |
| 2 | 60-89 | Kidney damage with mildly ↓ GFR |
| 3 | 30-59 | Moderately decreased GFR |
| 4 | 15-29 | Severely decreased GFR |
| 5 | <15 | Kidney failure |

CKD: Chronic Kidney Disease

GFR: Glomerular Filtration rate

- A GFR of 60-89 only indicates CKD in the presence of other evidence of kidney damage e.g. microalbuminuria/ proteinuria and is of clinical significance for patients with hypertension or diabetes mellitus
- eGFR is unreliable at the extremes of body size and age
- eGFR underestimates GFR in cases of mildly reduced, normal and increased (e.g. DM) renal function
- eGFR is unreliable in acute renal failure
- The result should be multiplied by 1.212 for the black population

CALCIUM, MAGNESIUM AND PHOSPHATE

| | Reference range | Units | Interpretation |
|-----------|------------------------|--------------|---|
| Calcium | 2.15-2.50 | mmol/L | ↑ : Primary hyperparathyroidism, malignancy, sarcoidosis, immobilisation, Addison's disease, medication such as lithium, thiazides, loop diuretics ↓ : Renal failure, falsely decreased due to contamination with full blood count tube, hypoparathyroidism, hypomagnesaemia |
| Magnesium | 0.66-1.07 | mmol/L | ↑ : Acute and chronic renal failure, untreated diabetic ketoacidosis ↓ : Malabsorption, chronic alcoholism, diarrhoea, drugs (e.g. diuretics, laxatives) |
| Phosphate | 0.78-1.42 | mmol/L | ↑ : Renal failure, untreated diabetic ketoacidosis ↓ : Acute alcoholism, primary hyperparathyroidism, drugs (e.g. diuretics, insulin), severe diarrhoea, vomiting, treatment of diabetic ketoacidosis |

LIVER FUNCTION TESTS

| | Reference range | Units | Interpretation |
|--|------------------------|--------|---|
| Total Protein | 60-83 | g/L | <p>↑ : Multiple myeloma, autoimmune disease, chronic liver disease, chronic infection (e.g. AIDS, TB)</p> <p>↓ : Nephrotic syndrome, chronic liver failure, malnutrition, pregnancy</p> |
| Albumin | 35-52 | g/L | <p>↑ : Dehydration, prolonged tourniquet during venepuncture</p> <p>↓ : Acute and chronic liver disease, malnutrition, malabsorption, nephrotic syndrome, acute and chronic inflammation, systemic infections, autoimmune disease, congestive cardiac failure, pregnancy</p> |
| Total bilirubin | 5-21 | μmol/L | <p>↑ : Hepatocellular damage (e.g. hepatitis, toxic damage due to drugs or toxins), intrahepatic biliary tree obstruction (e.g. primary biliary cirrhosis), extrahepatic biliary tree obstruction (e.g. gallstones, carcinoma of the head of the pancreas), haemolytic diseases, neonatal physiological jaundice, Gilbert's disease</p> |
| Conjugated bilirubin | 0-5 | μmol/L | <p>↑ : Hepatocellular damage (e.g. hepatitis, toxic damage due to drugs or toxins), intrahepatic biliary tree obstruction (e.g. primary biliary cirrhosis), extrahepatic biliary tree obstruction (e.g. gallstones, carcinoma of the head of the pancreas)</p> |
| Unconjugated bilirubin | 0-18 | μmol/L | <p>↑ : Gilbert's disease, haemolytic diseases, neonatal physiological jaundice</p> |
| Alkaline Phosphatase (ALP) | M 40-130 F 35-105 | U/L | <p>↑ : Extrahepatic biliary tree obstruction (e.g. gallstones, carcinoma of the head of the pancreas), intrahepatic biliary tree obstruction (e.g. primary biliary cirrhosis), hepatocellular disease (e.g. hepatitis), space occupying lesion in the liver (e.g. liver metastases), bone metastases, children with rapid bone growth, pregnancy, Paget's disease of bone</p> |
| Gamma Glutamyl-transferase (GGT) | M < 60 F < 40 | U/L | <p>↑ : Extrahepatic biliary tree obstruction (e.g. gallstones, carcinoma of the head of the pancreas), intrahepatic biliary tree obstruction (e.g. primary biliary cirrhosis), hepatocellular disease (e.g. hepatitis), space occupying lesion in the liver (e.g. liver metastases), induction by alcohol or medication</p> |
| Alanine aminotransferase (ALT) | M < 50 F < 35 | U/L | <p>↑ : Acute hepatitis, chronic hepatitis, liver cirrhosis, liver cell necrosis (e.g. hypoxic shock, paracetamol overdose), viraemia, chronic alcohol abuse, liver cirrhosis, fatty liver</p> |
| Aspartate aminotransferase (AST) | M < 50 F < 35 | U/L | <p>↑ : Acute hepatitis, acute liver cell necrosis, chronic hepatitis, liver cirrhosis, chronic alcohol abuse, AST:ALT ratio >2, intrahepatic neoplasm, viraemia, fatty liver, haemolytic jaundice, rhabdomyolysis, vigorous exercise, muscular dystrophy</p> |
| Lactate dehydrogenase (LD) | M 100-250 F 100-250 | U/L | <p>↑ : Megaloblastic anaemia, haemolytic anaemia, leukaemia, acute hepatitis, acute liver cell necrosis, liver cirrhosis, skeletal muscular disease, neoplastic disease, myocardial infarction</p> |
| CDT (Carbohydrate Deficient Transferrin) | 0-3 | % | <p>Detects intake of > 60 gram of alcohol per day during the past 9 days.</p> <p>↑ : Chronic alcoholism, non-alcoholic liver disease, iron deficiency, pregnancy</p> |

Interpretation of Unconjugated Hyperbilirubinaemia

| | Gilbert syndrome | Haemolysis | Megaloblastic anaemia |
|------------------------|------------------|------------|-----------------------|
| Total Bilirubin | ↑ | ↑ | ↑ |
| Unconjugated Bilirubin | ↑ | ↑ | ↑ |
| ALP | N | N | N |
| GGT | N | N | N |
| ALT | N | N | N |
| AST | N | ↑ | ↑ |
| LD | N | ↑ | ↑/↑↑ |

Interpretation of liver profiles

| | Hepatitis | Extrahepatic obstruction | Space occupying lesion | Alcohol |
|------------------------|-----------|--------------------------|------------------------|---------|
| Total bilirubin | N/↑ | ↑↑↑ | N | N |
| Conjugated bilirubin | N/↑ | ↑↑↑ | N | N |
| Unconjugated bilirubin | N/↑ | ↑↑↑ | N | N |
| ALP | N/↑ | ↑↑↑ | N/↑ | N |
| GGT | N/↑ | ↑↑↑ | ↑ | ↑ |
| ALT | ↑ to ↑↑↑ | N/↑ | N | N |
| AST | ↑ to ↑↑↑ | N/↑ | N/↑ | ↑ |
| LD | N/↑↑ | N/↑ | N/↑ | N |

Tests for detection of alcohol abuse: MCV, GGT, CDT

PANCREAS

| | Reference range | Units | Interpretation |
|----------------|-----------------|------------|--|
| Amylase | < 110 | U/L | ↑ : Acute pancreatitis, salpingitis, perforated duodenal ulcer, ruptured ectopic pregnancy, dissecting aortic aneurysm, small bowel obstruction, strangulated bowel, perforated hollow viscus, biliary tract disease, abdominal trauma, parotitis, mumps ↓ : Pancreatic insufficiency, advanced cystic fibrosis, severe liver disease |
| Lipase | 13-60 | U/L | ↑ : Acute pancreatitis, pancreatic duct obstruction, perforated hollow viscus, strangulated or infected bowel, peritonitis |
| Stool elastase | > 200 | μg/g stool | ↓ : Chronic pancreatitis |

INFLAMMATORY MARKERS

| | Reference range | Units | Interpretation |
|-----------------------------|-----------------|-------|---|
| CRP (C-Reactive Protein) | 0.0 – 4.9 | mg/L | ↑ : Inflammatory conditions including trauma, burns, surgery, autoimmune disease, neoplastic disease and infection. Viral infection values are usually 20 – 75. Bacterial infection values are usually > 100. |

Use of Procalcitonin (PCT) in the differential diagnosis of Community Acquired Lower Respiratory Tract Infections:

| | Value | Interpretation |
|---------------------|--------------------|--|
| PCT (Procalcitonin) | < 0.1 ng/mL | Indicates absence of bacterial infection. Use of antibiotics strongly discouraged, also in the presence of impaired pulmonary reserve in acute exacerbations of chronic obstructive pulmonary disease. |
| | 0.1 - < 0.25 ng/mL | Bacterial infection unlikely. The use of antibiotics is discouraged. |
| | 0.25 - < 0.5 ng/mL | Bacterial infection is possible. Advice to initiate antimicrobial therapy. |
| | > 0.5 ng/mL | Suggestive of the presence of bacterial infection. Antibiotic treatment strongly recommended. |

CARDIAC AND SKELETAL MUSCLE MARKERS

| | Reference range | Units | Interpretation |
|--------------|--|--------------|--|
| CK | M < 190 F < 170 | U/L | ↑ : Myocardial infarction, myocarditis, muscular dystrophies, polymyositis, seizures, muscle trauma, exercise, IM injection, post-operative |
| CB-MB (mass) | M 0-6.7 F 0-3.8 | µg/L | ↑ : Myocardial infarction, myocarditis, muscular dystrophies, polymyositis, seizures, muscle trauma, exercise, IM injection, post-operative |
| Troponin I | 0-0.06 | ng/mL | ↑ : Myocardial infarction, myocarditis, myocardial trauma, heart failure, haemodynamic compromise e.g. shock or sepsis, pulmonary embolism |
| Troponin T | 0-0.03 | ng/mL | ↑ : Myocardial infarction, myocarditis, myocardial trauma, heart failure, haemodynamic compromise e.g. shock or sepsis, pulmonary embolism |
| Myoglobin | M 28-72 F 25-58 | µg/L | ↑ : Myocardial infarction, skeletal muscle trauma, seizures, IM injection, exercise |
| Homocysteine | See table below for interpretation | µmol/L | ↑ : Homocystinuria, heterozygous cystathionine-β-synthase defect, vitamin B12 deficiency, folate deficiency, vitamin B6 deficiency, cigarette smoking, coffee consumption, renal failure, hypothyroidism, diabetes mellitus, psychiatric disorders ↓ : Pregnancy, hyperthyroidism, early diabetes mellitus |
| NT-Pro-BNP | M < 100 F < 150 See table below for interpretation | pg/mL | ↑ : Acute congestive heart failure, myocardial infarction, left ventricular hypertrophy, cardiomyopathy, valvular disease, chronic renal failure, COLS, atrial fibrillation, pulmonary embolism, severe pneumonia, primary hyperaldosteronism, hyperthyroidism, Cushing's syndrome False normal: Diuretics, vasodilators, ACE-inhibitors, Angiotensin II antagonists, hypothyroidism, obesity |

Plasma Homocysteine Interpretation

| Classification of risk for atherosclerotic vascular disease | Homocysteine concentration (µmol/L) |
|--|--|
| Moderate | 10-30 |
| Intermediate | 31-100 |
| Severe | > 100 |
| A follow up homocysteine level one month post initiation of treatment is indicated | |

NT-Pro-BNP interpretation

NT-proBNP < 300 pg/mL

Values < 300 pg/mL virtually excludes ACUTE heart failure. However, an NT-proBNP result > 150 pg/ml in females and > 100 pg/ml in males may be compatible with symptomatic heart failure in an out-patient setting

| NT-proBNP ≥ 300 pg/mL | | |
|------------------------------|---------------------------------|------------------|
| Patient age (years) | NT-proBNP values (pg/mL) | |
| < 50 | 300-450 | > 450 |
| 50-75 | 300-900 | > 900 |
| >75 | 300-1800 | > 1800 |
| Interpretation | Acute CHF less likely | Acute CHF likely |

Definition of Acute Coronary Syndrome

Typical rise and gradual fall (troponin) or more rapid rise and fall (CK-MB) of biochemical markers of myocardial necrosis

PLUS at least one of the following:

1. Ischaemic symptoms
2. Q waves on ECG
3. ECG changes indicative of ischaemia (ST segment elevation or depression)
4. Coronary artery intervention

CARBOHYDRATE METABOLISM

| | Reference range | Units | Interpretation |
|--|------------------------|--------------|--|
| Glucose fasting | 3.9 - 5.5 | mmol/L | ↑: Impaired fasting glucose, diabetes mellitus type 1 and type 2, stress, acute disease, infection, hyperthyroidism, Cushing's syndrome, acromegaly, phaeochromocytoma, corticosteroid therapy, acute and chronic pancreatitis ↓: Insulinoma, Addison's disease, reactive hypoglycaemia |
| Insulin fasting | 0.2 - 9.4 | μIU/mL | ↑: Insulin resistance syndrome, obesity, diabetes mellitus type 2, insulinoma ↓: Diabetes mellitus type 1 |
| Quicki index | ≥ 0.36 | | < 0.36 indicative of insulin resistance |
| HbA1C | 4.8-5.9 | % | Reflects the mean blood glucose concentration over the past 4-8 weeks. Target for diabetic glycaemic control: Ideal < 7%; Poor > 8% |
| Fructosamine | 0-285 | μmol/L | Reflects the mean blood glucose concentration over the past 2-3 weeks. Useful in patients with Hb variants and gestational diabetes mellitus. |
| Microalbuminuria (Albumin: Creatinine ratio) | 3-30 | mg/mmol | ↑ Risk factor for CVD progression to proteinuria and chronic renal failure in insulin-dependent and non-insulin-dependent diabetic patients |

Oral Glucose Tolerance Test

| | Fasting plasma glucose (mmol/L) | | 2 hour plasma glucose (mmol/L) |
|----------------------------|--|---------|---------------------------------------|
| Normal | < 5.6 | and | < 7.8 |
| Impaired fasting glycemia | 5.6-6.9 | and | < 7.8 |
| Impaired glucose tolerance | < 7 | and | 7.8-11 |
| Diabetes mellitus | ≥ 7 | and/ or | ≥ 11.1 |

Criteria for the diagnosis of diabetes mellitus

1. Symptoms of diabetes plus random plasma glucose ≥ 11.1 mmol/L
2. Fasting plasma glucose ≥ 7 mmol/L
3. 2 hour plasma value during the oral glucose tolerance test ≥ 11.1 mmol/L

NB: In the absence of unequivocal hyperglycaemia, the diagnosis of diabetes mellitus should be confirmed by a repeat test on a different day

Diagnostic criteria for insulin resistance syndrome/ metabolic syndrome

Presence of 3 or more criteria constitute diagnosis of metabolic syndrome

| Parameter | Categorical cut points |
|------------------------------|---|
| Elevated waist circumference | ≥ 102 cm in men ≥ 88 cm women |
| Elevated triglycerides | ≥ 1.7 mmol/L or Drug treatment for elevated TG |
| Reduced HDL -cholesterol | < 1.01 mmol/L men < 1.3 mmol/L women |
| Elevated blood pressure | ≥ 130 mm Hg systolic BP or ≥ 85 mm Hg diastolic BP or Drug treatment for hypertension |
| Elevated fasting glucose | ≥ 5.6 mmol/L |

LIPID METABOLISM

| | Reference range | Units | Interpretation |
|--------------------|------------------------------|--------|--|
| Cholesterol | See table for interpretation | mmol/L | <p>↑ Primary cause: Familial hypercholesterolaemia, polygenic (sporadic) hypercholesterolaemia, familial combined hyperlipidaemia</p> <p>↑ Secondary cause: Hypothyroidism, diabetes mellitus, nephrotic syndrome, obstructive liver disease, chronic renal failure, primary biliary cirrhosis, pregnancy</p> <p>↓ : Severe acute illness, inflammation, infection, malignancy, hyperthyroidism</p> |
| LDL-cholesterol | See table for interpretation | mmol/L | <p>↑ Primary cause : Familial hypercholesterolaemia, polygenic (sporadic) hypercholesterolaemia, familial combined hyperlipidaemia</p> <p>↑ Secondary cause: Hypothyroidism, diabetes mellitus, nephrotic syndrome, obstructive liver disease, chronic renal failure, primary biliary cirrhosis, pregnancy</p> <p>↓ : Severe acute illness, inflammation, infection, malignancy, hyperthyroidism</p> |
| HDL-cholesterol | M 1-1.6 F 1.2-1.9 | mmol/L | <p>↑ : Oestrogen therapy, primary biliary cirrhosis, chronic hepatitis, alcoholism</p> <p>↓ : Several genetic disorders, type 2 diabetes mellitus, hepatocellular disorders, nephrotic syndrome, chronic renal failure, malignancy, hypertriglyceridaemia</p> |
| Triglyceride | 0.4-1.6 | mmol/L | <p>↑ Primary cause: Familial types including familial hypertriglyceridaemia, familial combined hyperlipidaemia etc.</p> <p>↑ Secondary cause: Obesity, insulin resistance syndrome, impaired glucose tolerance, type 2 diabetes mellitus, alcoholism, pregnancy, nephrotic syndrome, chronic renal failure, extrahepatic biliary obstruction, infection, inflammation</p> |
| Lipoprotein (a) | < 30 | Mg/dl | <p>↑ : Genetic. Secondary causes include uncontrolled diabetes mellitus, hypothyroidism, chronic renal failure, nephrotic syndrome</p> <p>↑ Lp(a) is associated with ↑ risk of premature coronary artery disease and stroke.</p> |
| Apolipoprotein A-I | >1.2 | g/L | ↓ : Familial causes, hepatocellular disorders, cholestasis, nephrotic syndrome, chronic renal failure, malignancy |
| Apolipoprotein B | <1.2 | g/L | ↑ : Familial hypercholesterolaemia, familial combined hyperlipidaemia, polygenic (sporadic) hypercholesterolaemia, diabetes, hypothyroidism, nephrotic syndrome, chronic renal failure, hepatic obstruction, hepatic disease |

Table to be inserted

IRON STUDIES

| | Reference range | Units | Interpretation |
|-----------------------------------|-------------------------|--------|---|
| Iron | M 11.6-31.3 F 9-30.4 | μmol/L | <p>↑ : Pernicious and haemolytic anaemia, haemochromatosis, acute hepatitis, iron therapy, repeated blood transfusions</p> <p>↓ : Iron deficiency anaemia, acute and chronic infections</p> |
| Transferrin | M 2.2-3.7 F 2.5-3.8 | g/L | <p>↑ : Iron deficiency anaemia, exogenous oestrogen intake, pregnancy</p> <p>↓ : Haemochromatosis, inflammation, hepatocellular disease, iron supplements</p> |
| Percentage transferrin saturation | 20-50 | % | <p>↑ : Haemochromatosis, secondary iron overload (liver disease, untreated pernicious anaemia, > 50 blood transfusions)</p> <p>↓ : Iron deficiency anaemia, iron depletion, acute and chronic infections, some chronic disorders, rheumatoid arthritis</p> |
| Ferritin | M 20-250 F 10-120 | ng/ml | <p>↑↑ : Haemochromatosis, HIV, non-HIV chronic infection, liver disease, malignancy, renal disease, chronic transfusions</p> <p>↑ : Infection, chronic inflammation, autoimmune disease (RA, SLE), megaloblastic anaemia</p> |
| Soluble transferrin receptors | 0.8-2.3 | mg/L | <p>Indication: Diagnosis of iron deficiency, especially in the presence of an acute phase response</p> <p>↑ : Iron deficiency, haemolysis, megaloblastic anaemia</p> <p>Normal: Acute phase response, anaemia of chronic disease</p> |

Interpretation of Iron profile

| | S-Iron | S-Transferrin | % Transferrin Saturation | S-Ferritin |
|--------------------------------------|--------|---------------|--------------------------|------------|
| Iron deficiency anaemia | ↓/N | ↑/N | ↓/N | ↓/N |
| Iron overload e.g. Haemochromatosis* | ↑ | ↓/N | ↑ | ↑ |
| Chronic disease | ↓/N | ↓/N | N/↓ | VAR |
| Acute disease | ↓ | N | ↓ | ↑ |
| Liver disease | ↑ | VAR | VAR | ↑ |
| Pernicious anaemia | ↑ | N/↓ | ↑ | ↑ |

A fasting morning specimen is preferred

*Haemochromatosis PCR is available if hemochromatosis is suspected

FOLATE AND VITAMIN B12

| | Reference range | Units | Interpretation |
|-----------------------|-----------------|--------|---|
| Serum folate | 7 - 39.7 | nmol/L | Red blood cell folate determination is the test of choice because serum folate can vary daily in response to diet For interpretation see red blood cell folate. |
| Red blood cell folate | 597 - 2334 | nmol/L | ↑ : Excess daily intake ↓ : Alcoholism, malnutrition, liver disease, vitamin B12 deficiency, adult celiac disease, Crohn's disease, malabsorption, haemolytic anaemias, carcinoma, pregnancy |
| Vitamin B12 | 145 - 637 | pmol/L | ↑ : Chronic renal failure, severe congestive heart failure, diabetes mellitus, liver disease, some leukemias, some carcinomas ↓ : Lack of intrinsic factor (pernicious anaemia, total or partial gastrectomy, atrophic gastritis, intrinsic factor antibody); malabsorption (pancreatic insufficiency, regional ileitis, celiac disease); dietary deficiency (vegetarians) |

TUMOUR MARKERS

Please note:

As a rule tumour markers should not be used for screening for malignancy. Exceptions include AFP for primary hepatocellular carcinoma, CA 125 for ovarian carcinoma and PSA for prostate carcinoma – these should not be used in isolation for screening but in conjunction with other tests.

An increased marker does not necessarily indicate the presence of a tumour, whilst a normal marker does not indicate the absence of a tumour.

| Marker | Reference range | Units | Specimen |
|--------------------|--|---------------------|-------------------------|
| AFP | 0-10 | µg/L | Blood |
| β-2-microglobulin | 0.8-2.2 | mg/L | Blood |
| CA 125 | 0-35 | U/ml | Blood |
| CA 15-3 | 0-34 | U/ml | Blood |
| CA 19-9 | 0-37 | U/ml | Blood |
| CA 72-4 | 0-6.9 | U/mL | Blood |
| Calcitonin | M 0-8.4 F 0-5 | ng/L | Blood |
| Catecholamines | Adrenaline: 0 – 109 Noradrenaline: 89-473 | nmol/d | 24 hour urine |
| CEA | 0-5 | ng/ml | Blood |
| Chromogranin A | 0-23 | U/L | Blood |
| CYFRA 21-1 | 0.1-3.3 | ng/mL | Blood |
| Ferritin | M 20-250 F 13-150 | ng/mL | Blood |
| HCG | 0-5 | IU/ml | Blood |
| HIAA | 10.4 – 41.6 0-7.2 | µmol/d µmol/mmol | 24 hour urine |
| HVA | 8-48 2-6.4 | µmol/d µmol/mmol | Random or 24 hour urine |
| Metanephrines | 160-2478 26-176 | nmol/d nmol/mmol | 24 hour urine |
| Normetanephrines | 241-3418 21-312 | nmol/d nmol/mmol | 24 hour urine |
| NSE | 0-16.3 | µg/L | Blood |
| PSA | 0-4 | ng/mL | Blood |
| PSA complexed | 0-3.75 | ng/mL | Blood |
| Free PSA/PSA ratio | See table below | | Blood |
| SCC | 0.1-2 | ng/mL | Blood |
| Thyroglobulin | 0-55 | ng/mL | Blood |
| TK | 0-6.1 | U/L | Blood |
| TPA | 0-83 | U/L | Blood |
| VMA | 11.5-34.6 0.7-4.3 | µmol/d µmol/mmol | 24 hour urine |

Interpretation of PSA Ratio (Free PSA:Total PSA)

| | | | |
|--|----------------|----------------|-----------------|
| 1. PSA Ratio is useful with total PSA values of 2.5-10 ng/mL | | | |
| 2. PSA Ratio is generally lower in carcinoma and higher in benign hyperplasia PSA ratio: > 0.25 Probability for prostate Cancer < 10% < 0.10 Probability for prostate Cancer > 80% | | | |
| 3. The probability of finding prostate Ca on needle biopsy increases with increasing age and decreasing PSA ratios: | | | |
| PSA ratio | 50-59 y | 60-69 y | >69 y |
| < 0.11 | 49% | 58% | 65% |
| 0.11-0.18 | 27% | 34% | 41% |
| 0.19-0.25 | 18% | 24% | 30% |
| > 0.25 | 9% | 12% | 16% |

Appropriate tumour markers for specific tumours

| Tumour | Tumour marker |
|-----------------------------------|--|
| Breast | CEA, CA 15-3 |
| Bladder | TPA, Cyfra 21-1 |
| Colon | Stool occult blood, CEA, CA 19-9, CA 72-4 |
| Cervix | SCC, CEA |
| Choriocarcinoma | HCG |
| Carcinoid | 24 hour urine 5HIAA, NSE, chromogranin A, Serotonin |
| Ear, nose and throat | SCC, CEA |
| Gall bladder | CA 19-9 |
| Germ cell | AFP, HCG |
| Liver | AFP, CEA |
| Lung – small cell lung cancer | NSE, CYFRA 21-1 |
| Lung – non-small cell lung cancer | CYFRA 21-1, CEA |
| Lymphoma, leukaemia | Ferritin, β -2-microglobulin, thymidine kinase, neuron specific enolase |
| Melanoma | S-100B |
| Myeloma | Serum protein electrophoresis, urine Bence Jones protein |
| Neuroblastoma | Urine HVA, NSE, Chromogranin A |
| Oesophagus | CEA, SCC |
| Ovary | CA 125, CA 72-4 |
| Pancreas | CA 19-9, CEA |
| Prostate | PSA, free PSA, complexed PSA |
| Phaeochromocytoma | Urine metanephrines and normetanephrines, urine VMA, urine catecholamines, chromogranin A, plasma catecholamines, plasma metanephrines |
| Stomach | CA 72-4, CEA, CA 19-9 |
| Testis | AFP, HCG |
| Thyroid | Thyroglobulin, CEA |
| Thyroid C-cell carcinoma | Calcitonin, CEA |
| Uterus | CEA, SCC, CA 125 |

THERAPEUTIC DRUGS

| | Reference range | Units | Time of sampling |
|----------------|--|--------|---|
| Carbamazepine | Therapeutic 7-51 Toxic > 63 | µmol/L | Prior to next dose |
| Digoxin | Therapeutic 1-2.6 Toxic adult > 3.2 Toxic child > 3.8 | nmol/L | Prior to next dose ideally, but at least 8 hours after dose |
| Lithium | Therapeutic 0.6-1.2 Toxic > 2 | mmol/L | 24 hours after dose ideally, but at least 12 hours |
| Paracetamol | Therapeutic 66-199 Toxic levels after overdose: 4 h after ingestion > 1324 6 h after ingestion > 927 8 h after ingestion > 662 10 h after ingestion > 463 12 h after ingestion > 331 | µmol/L | For overdose: First specimen should be taken 4 hours after paracetamol ingestion. If time of intake is unknown, 3 specimens should be taken at 4 hour intervals to determine whether the paracetamol concentration is rising or falling |
| Phenobarbitone | Therapeutic 65-172 Slowness, ataxia, nystagmus 151-345 Toxic: coma > 280 | µmol/L | Prior to next dose |
| Phenytoin | Therapeutic 40-79 Lateral nystagmus > 79 Lateral nystagmus, ataxia > 119 Depressed mental capacity > 158 Death > 396 | µmol/L | Prior to next dose |
| Salicylates | Therapeutic < 0.72 (see table below for toxicity after overdose) | mmol/L | |
| Theophylline | Therapeutic 44 -111 Toxic > 111 | µmol/L | Prior to next dose |
| Valproic acid | Therapeutic 346-693 Toxic > 693 | µmol/L | Prior to next dose |

Correlation of serum salicylate levels after acute ingestion of salicylate:

Serum salicylate levels (mmol/L)

| Hours after ingestion | Asymptomatic | Severe toxic |
|-----------------------|--------------|--------------|
| 6 | < 3.26 | > 6.52 |
| 8 | < 3.04 | > 6.19 |
| 10 | < 2.79 | > 5.79 |
| 12 | < 2.59 | > 5.18 |
| 24 | < 1.74 | > 3.48 |
| 36 | < 1.21 | > 2.27 |
| 48 | < 0.78 | > 1.45 |
| 60 | 0 | > 0.83 |

DRUGS OF ABUSE

| Drug of abuse | Street Name(s) | Type of specimen | Approximate duration of detectability |
|-------------------------------------|--|------------------|--|
| Alcohol | Booze | Blood Urine | 6 hours < 2 days |
| Urine Alcohol | | | 0.5 – 6 hours |
| Amphetamine | Speed; Crystal; Ice | Urine | 1-4 days |
| Benzodiazepines | Benzo's; Mellow; Downers | Blood Urine | 3 hours – 3 days Average 1-14 days up to 30 days |
| Cannabinoids | Dagga; Marijuana; Pot; Weed | Urine | 0-10 days (single use) 30 days-6 weeks (chronic use) |
| CAT (Methcathinone) | CAT | Urine | At least 24 hours |
| Cocaine | Crack coke; Rock; Snow; Flake; Blow | Urine | Average: 2-3 days up to 7-9 days |
| Ecstasy | "X" | Urine | At least 24 hours |
| Lysergic Acid Diethylamide (LSD) | Acid | Urine | 0-2 days |
| Opiates (codeine, morphine, heroin) | <u>Morphine</u> : Junk; White Stuff; "M" <u>Heroin</u> : Horse; White Lady; "H" | Urine | Heroin 1-2 days Codeine 9 – 25 hours Morphine 90% in 24hrs |
| Methadone | Meth; Methadose | Urine | 1-3 days |
| Methaqualone (Mandrax) | Soaps; Love Pill | Urine | 4-14 days |
| Phencyclidine (PCP) | Angel dust; PCP | Urine | Average 1-14 days up to 30 days |
| Propoxyphene | PPX, Doloxene | Urine | 1-2 days |
| Metamphetamine | Tik-Tik | Urine | At least 24 hours |

ENDOCRINOLOGY

THYROID FUNCTION TESTS

| | Reference range | Units | Interpretation |
|-------------------------------|---|--------|---|
| Free T4 | 12-22 | pmol/L | ↑ : Hyperthyroidism, thyroiditis, overtreatment of hypothyroidism, drugs (amiodarone) ↓ : Hypothyroidism, acute or chronic illness (euthyroid sick syndrome), drugs (e.g. Phenytoin) |
| Free T3 | 3.95-6.8 | pmol/L | ↑ : Hyperthyroidism, T3 thyrotoxicosis ↓ : Hypothyroidism, acute or chronic illness (euthyroid sick syndrome) |
| TSH | 0.27 – 4.2 | mIU/L | ↑ : Primary hypothyroidism, non-thyroidal illness (recovery phase), congenital hypothyroidism, undertreatment of hypothyroidism ↓ : Primary hyperthyroidism, secondary hypothyroidism (pituitary), tertiary hypothyroidism (hypothalamus), subclinical hyperthyroidism, excess thyroid hormone replacement |
| Thyroid peroxidase antibodies | 0 – 34 | IU/mL | ↑ : Autoimmune thyroid disease (Hashimoto's thyroiditis, Graves' disease) idiopathic myxedoema, found in 8-27% of the normal population |
| Thyroglobulin antibodies | 0 – 115 | IU/mL | ↑ : Hashimoto's thyroiditis, thyroid carcinoma, some cases of thyrotoxicosis, pernicious anaemia, SLE, de Quervain's subacute thyroiditis, 10% of the normal population may have low titre antibodies |
| TSH receptor antibodies | < 9 : Negative 9 – 14: Grey zone > 14: Positive | U/L | Graves' Disease |
| Thyroglobulin | 0 – 55 | ng/mL | ↑ : Hashimoto's thyroiditis, Graves' disease, thyroid adenoma, subacute thyroiditis Also used as a tumor marker for monitoring status of thyroid cancer |

Interpretation of thyroid function tests

| Parameter | Hyperthyroidism | Primary hypothyroidism | Secondary hypothyroidism |
|-----------|-----------------|------------------------|--------------------------|
| Free T4 | ↑ | ↓ | ↓ |
| Free T3 | ↑ | ↓/N | ↓/N |
| TSH | ↓ | ↑ | ↓/N |

OTHER ENDOCRINOLOGY TESTS

| | Reference range | Units | Interpretation |
|--------------------------------|---|--------|--|
| 17-hydroxy-progesterone | M 0.9 -6.7 F Follicular phase 0.3-2.4 F Luteal phase 0.8-8.8 F Oral contraceptive 0.2-2.5 F Pregnancy 6-36 F Post menopause <2.1 | nmol/L | ↑ : Congenital adrenal hyperplasia, some cases of adrenal or ovarian neoplasms |
| ACTH | 1.1 – 13.2 | pmol/L | ↑ : Adrenal insufficiency, Cushing's syndrome (pituitary origin), ectopic ACTH-producing tumour ↓ : Pituitary insufficiency, adrenal Cushing's syndrome |
| Active aldosterone:renin ratio | ≤ 62.1 | | Ratio > 62.1 with an active aldosterone of > 415 pmol/L is suggestive of primary hyperaldosteronism (Conn's syndrome) |
| Aldosterone | Resting: 0.08 – 0.44 Active: 0.19 - 0.83 | nmol/L | ↑ : Primary hyperaldosteronism (Conn's syndrome) Secondary hyperaldosteronism due to hypovolemia caused by e.g. vomiting, diarrhoea, blood loss, diuretics, cardiac failure ↓ : Addison's disease, diabetic nephropathy, renal failure, drugs (e.g. ACE inhibitors) |
| Androstenedione | M 2.8-10.5 F 1.8 – 12.9 | nmol/L | ↑ : Polycystic ovarian syndrome, congenital adrenal hyperplasia, Cushing's syndrome, hyperplasia of ovarian stroma, ovarian tumour |
| Cortisol | 8h00-10h00: 142-651 16h00-20h00: 51-424 24h00: < 50 | nmol/L | ↑ : Cushing's syndrome, oral contraceptives, oestrogen therapy, pregnancy, obesity, stress, drugs, depression, alcoholism, critical illness ↓ : Addison's disease, exogenous corticosteroids, congenital adrenal hyperplasia |
| DHEA-S | M 20-24y: 5.1-13.5 25-44y: 1.8-13.9 45-54y: 1-9.9 ≥ 55y : 1.1-8.6 F 20-24y : 3.9-11.5 25-44y: 1.5-10.8 45-54y: 0.8-8.7 ≥ 55y : 0.4-6.0 | μmol/L | ↑ : Polycystic ovarian syndrome, congenital adrenal hyperplasia, adrenal cortex adenomas and carcinomas, Cushing's syndrome associated with ↑ ACTH ↓ : Primary and secondary adrenal insufficiency |
| Free Testosterone (Calculated) | M 18-49y : 181-536 M > 49y : 146-419 F 18-49y : 2.3-41.2 F > 49y : 2.4-37.4 | pmol/L | ↑ : Polycystic ovarian disease, idiopathic hirsutism, virilising ovarian tumours, congenital adrenal hyperplasia, some adrenocortical tumours, extragonadal tumours producing gonadotropin in men ↓ : Primary and secondary hypogonadism, delayed puberty in boys, cryptorchidism, renal failure, hepatic insufficiency |
| FSH | M 1.2 – 15.8 F See ovarian profile table | mIU/mL | ↑ : Testicular absence or failure, ovarian absence or premature failure, menopause ↓ : Anterior pituitary hypofunction, hypothalamic disorders, hyperprolactinaemia, polycystic ovarian syndrome, severe illness, pregnancy |
| Growth hormone | 0-5 | μg/L | ↑ : Gigantism, acromegaly, exercise, stress, prolonged fasting, uncontrolled diabetes mellitus, renal failure, liver cirrhosis, malnutrition, anorexia nervosa ↓ : Pituitary dwarfism, hypopituitarism |
| LH | M 1.3 – 9.6 | mIU/mL | ↑ : Ovulation, testicular absence or failure, ovarian |

| | | | |
|---------------------|---|--------|--|
| | F See ovarian profile table | | absence or premature failure, polycystic ovarian syndrome, menopause ↓ : Anterior pituitary hypofunction, hypothalamic disorders, severe stress, severe illness, pregnancy |
| Oestradiol | M ≤ 207 F See ovarian profile table | pmol/L | ↑ : Exogenous oestradiol, fertility treatment, perimenopausal, liver cirrhosis, hyperthyroidism, pregnancy ↓ : Anovulation, primary and secondary hypogonadism, postmenopausal, oral contraceptives |
| Parathyroid hormone | 15-65 | pmol/L | ↑ : Primary hyperparathyroidism (calcium ↑). ↑ : Secondary hyperparathyroidism (calcium normal or ↓) due to e.g. renal disease, vitamin D deficiency, anticonvulsant therapy ↓ : With ↑ calcium - due to malignancy, sarcoidosis, immobilisation, Addison's disease, medication such as lithium, thiazides, diuretics ↓ : With ↓ calcium - due to hypoparathyroidism, hypomagnesaemia |
| Progesterone | M 0.7-4.7 F See ovarian profile table | nmol/L | ↑ : Pregnancy ↓ : Threatened abortion, primary or secondary hypogonadism, short luteal phase syndrome |
| Prolactin | M 4-15 F 6-30 | µg/L | ↑ : Prolactin-secreting pituitary tumours, hypothalamic-pituitary disease (e.g. craniopharyngioma), stress, primary hypothyroidism, polycystic ovarian disease, renal failure, adrenal insufficiency, anorexia nervosa, chest wall injury, medication (e.g. antipsychotics, monoamine oxidase inhibitors, opiates, tricyclic antidepressants), macroprolactinemia ↓ : Pituitary apoplexy (Sheehan's syndrome) |
| Renin | Resting: 2.8-39.9 Active: 4.4-46.1 | mU/L | ↑ With secondary hyperaldosteronism and hypertension: Renal artery stenosis, unilateral renal disease with severe hypertension, high-renin forms of hypertension, renal parenchymal disease, oral contraceptive-induced hypertension, pheochromocytoma ↑ With secondary hyperaldosteronism, oedema and normal BP: congestive heart failure, liver cirrhosis ↑ Without secondary hyperaldosteronism – Addison's disease, potassium depletion, ACE inhibitors ↓ With hypertension: primary hyperaldosteronism, low-renin essential hypertension, sometimes with renal parenchymal disease |
| SHBG | M 11.4 - 52.3 F 18-50y : 19.8 – 122 ≥ 51y : 14.1-68.9 | nmol/L | ↑ : Pregnancy, exogenous oestrogen, hyperthyroidism, liver cirrhosis ↓ : Hypothyroidism, excess testosterone, obesity, polycystic ovarian syndrome |

Ovarian profile:

These tests should be evaluated in conjunction with the clinical picture (prepubertal, phase of the menstrual cycle in menstruating women, menopause, etc).

To confirm ovulation a day 21 progesterone determination should be done

| Reference ranges | Oestradiol | FSH | LH | Progesterone |
|---------------------------|-------------------|------------|-----------|---------------------|
| Follicular | < 657 | 2.9-14.6 | 1.9-14.6 | 0.4-9.2 |
| Midcycle | 173-1902 | 4.7-23.2 | 12.2-118 | 2.4-9.4 |
| Luteal | 146-1045 | 1.4-8.9 | 0.7-12.9 | 4.5-110.8 |
| Post menopausal | <240 | 16-157 | 5.3-65.4 | < 2.7 |
| Oral contraceptive | <140 | | < 5.6 | |
| Pregnancy first trimester | 756 - >15781 | < 0.1 | < 0.1 | 33-140 |

PREGNANCY

| | Reference range | Units | Interpretation |
|-----|---|--------|---|
| HCG | 0-4.9 Negative 5-25 Equivocal > 25 Positive | mIU/mL | Positive 8-11 days after conception. HCG reaches 25 IU/L in 50% of pregnant women on the first day of their missed period |

First trimester Down's screening

Screening for Down's syndrome in the first trimester of pregnancy should be done between 11 weeks and 3 days and 13 weeks and 6 days. Risk calculations can only be done in this period by using an accurate crown-rump-length and nuchal thickness.

Please note: This does not include an open neural tube defect screening.

Second trimester Down's and Open Neural tube defect screening

This can be done between 15 weeks and 20 weeks 6 days gestation. An accurate estimation of gestational duration by sonar is essential

INVESTIGATION OF SPECIFIC DISORDERS

Screening tests for endocrine disorders

| Disease | Screening tests |
|----------------------------------|--|
| Addison's disease | 8-10 am ACTH and cortisol |
| Cushing's disease | 24 hour urinary cortisol excretion followed by an overnight dexamethasone suppression test (oestrogen intake should be stopped for 6 weeks before the dexamethasone suppression test) |
| Diabetes insipidus | Serum electrolytes, urea, creatinine and osmolality; 24 hour urine volume and osmolality |
| Hypercalcaemia and hypocalcaemia | PTH, phosphate, magnesium |
| Phaeochromocytoma | 24-hour urine VMA, metanephrines and normetanephrines (preferably three 24 hour specimens should be submitted for testing). Medication, which is acceptable, is diuretics, vasodilators eg. Hydralazine and minoxidil and calcium channel blockers. All other medication should be stopped for 2 weeks beforehand including paracetamol. |
| Primary hyperaldosteronism | Active aldosterone:renin ratio. Hypokalemia must be corrected before screening. Diuretics and spironolactone should be stopped for four weeks prior to screening and beta-blockers, α -methyl dopa, clonidine and dihydropyridine calcium channel blockers for at least 2 weeks. Blood pressure can be controlled with ACE inhibitors, angiotensin receptor blockers, verapamil, hydralazine and α -blockers |

Causes (with frequency) and investigation of Gynaecomastia

| Cause | Tests |
|--|--|
| A. Physiological | |
| 1. Neonatal | |
| 2. Pubertal (25%) | |
| 3. Involutional (mostly 50-80 year old men) | |
| B. Pathological | |
| 1. Neoplasms Testicular (3%) – germ cell, Sertoli cell, Leydig cell Adrenal (adenoma or carcinoma) Ectopic production of HCG (especially lung, liver and kidney cancer) | HCG Oestradiol |
| 2. Primary gonadal failure (8%) | Testosterone, LH, FSH |
| 3. Secondary hypogonadism (2%) | Testosterone, LH, FSH, prolactin |
| 4. Liver disease | Liver function tests |
| 5. Renal disease and dialysis (1%) | Urea and creatinine |
| 6. Hyperthyroidism (2%) | TSH, free T4, free T3 |
| 7. Hyperprolactinaemia | Prolactin, testosterone, oestradiol, LH, FSH |
| 8. Starvation especially during the recovery phase | |
| 9. Medication (10-20%): Amiodarone, androgens and anabolic steroids, anti-retroviral therapy (some), captopril, cimetidine, cyproterone, diazepam, digitoxin, enalapril, oestrogen and oestrogen agonists, flutamide, haloperidol, isoniazid, ketoconazole, methyldopa, metronidazole, nifedipine, omeprazole, penicillamine, phenothiazines, phenytoin, ranitidine, reserpine, verapamil, tricyclic antidepressants | |
| 10. Drugs of abuse: Alcohol, amphetamines, cannabis, heroin | |
| 11. Idiopathic (25%) | |

Secondary Causes and Investigation of osteoporosis

| Cause | Tests |
|-------------------------------|--|
| A. Endocrine disorders | |
| 1. Hyperparathyroidism | Calcium, phosphate, PTH |
| 2. Cushing's syndrome | See above |
| 3. Hypogonadism | Oestradiol, LH, FSH (females) Testosterone, LH, FSH (males) |
| 4. Hyperthyroidism | TSH, free T4, free T3 |
| 5. Prolactinoma | Prolactin |
| 6. Type I diabetes mellitus | Plasma glucose, oral glucose tolerance test |
| 7. Pregnancy and lactation | |

| | |
|---|---|
| B. Gastro-intestinal and liver disease | |
| 1. Subtotal gastrectomy | Clinical history |
| 2. Malabsorption | Serum total protein, albumin, oral fat loading test, xylose absorption test, faecal elastase, stool α -1-antitrypsin |
| 3. Hepatobiliary disease | Liver function tests |

| | |
|---------------------------------|---|
| C. Bone marrow disorders | |
| 1. Multiple myeloma | Serum protein electrophoresis, urine Bence Jones protein |
| 2. Disseminated carcinomatosis | Clinically appropriate tumour markers |
| 3. Leukaemia | Full blood count |
| 4. Lymphoma | Clinically, full blood count, ESR, β -2-microglobulin |

| | |
|--|-----------------------------------|
| D. Miscellaneous | |
| 1. Smoking | History |
| 2. Chronic alcoholism | Liver function tests, CDT |
| 3. Immobilisation | History |
| 4. Rheumatoid arthritis | Rheumatoid Factor |
| 5. Chronic obstructive pulmonary disease | X/Rays lungs, lung function tests |
| 6. Chronic renal failure | Urea, creatinine |

| | |
|-----------------------------------|--|
| E. Medication | |
| 1. Corticosteroids | |
| 2. Heparin | |
| 3. Anticonvulsants | |
| 4. Lithium | |
| 5. Excess thyroid hormone therapy | |

Osteoporosis in men

Common causes of osteoporosis in men are hypogonadism, alcohol abuse and glucocorticoid excess. In 50% of men a secondary cause is present and in the other 50% no cause may be found (idiopathic osteoporosis).

Work-up for Hypertension

Laboratory tests which are indicated after initial diagnosis of hypertension

1. Urine dipstick analysis for protein and glucose.
2. Serum urea, creatinine, glucose and total cholesterol.

Follow up visits

1. Follow up urine dipstick 3-6 monthly. If proteinuria is present, do serum electrolytes and creatinine. If glycosuria is present, investigate for diabetes mellitus.
2. Serum cholesterol and fasting glucose yearly.
3. Repeat serum creatinine and potassium after initiation of treatment, or change in dosage of medication, which could influence it.

When should secondary hypertension be considered?

1. Onset of hypertension before age 20 or after age 50.
2. Very high blood pressure (>200/120 mm Hg).
3. Organ damage
 - a) Fundoscopy grade 2 or more retinopathy
 - b) Serum creatinine > 150 $\mu\text{mol/L}$
 - c) Cardiomegaly
4. Features of secondary hypertension
 - a) Spontaneous hypokalemia (primary hyperaldosteronism, Cushing's syndrome, renal artery stenosis).
 - b) Abdominal systolic bruit (renal artery stenosis).
 - c) Episodic hypertension, tachycardia, sweat, tremor (phaeochromocytoma).
 - d) Family history of renal or endocrine disease.
 - e) Hematuria, palpable kidneys.
 - f) Poor femoral pulse (coarctation of the aorta).
5. Poor response on antihypertensive therapy, which is usually effective.

Part 2: HAEMATOLOGY

BASIC COAGULATION SCREEN

| Test | What is tested | Reference range | Interpretation |
|--|---|-----------------|--|
| Prothrombin time (PT) | Efficiency of the extrinsic pathway | 12-14 seconds | <u>Prolonged</u> Warfarin therapy Liver disease Vit K deficiency DIC Clotting factor defects (FVII, V, X, II, I) |
| Activated partial thromboplastin time (aPTT) | Efficiency of the Intrinsic pathway | 22-36 seconds | <u>Prolonged</u> Heparin therapy or heparin contamination, DIC Liver disease Massive transfusion Lupus anticoagulant Clotting factor defects (other than FVII) Also moderately prolonged in patients on warfarin and in vit K deficiency |
| Thrombin time | Fibrinogen to fibrin stage | 20-30 seconds | <u>Prolonged</u> Very sensitive to unfractionated heparin (LMWH can slightly prolong it at therapeutic levels) Hypofibrinogenaemia Dysfibrinogenaemia Raised concentrations of FDP/D-dimer Hypoalbuminaemia |
| Fibrinogen | Plasma level | 2-4 g/L | ↑: Acute phase ↓: DIC, liver disease, fibrinogen deficiency or dysfibrinogenaemia |
| INR (International normalized ratio) | Standardised way of reporting the prothrombin time (To compensate for different laboratories using different reagents and instruments) Developed for the standardization of oral anticoagulant treatment. Using the INR system, the patient's INR should be the same in any laboratory worldwide | | Used for monitoring of warfarin therapy. Therapeutic target varies according to the indication for warfarin, but generally aimed at 2-3.5 INR > 4 – over anticoagulated INR < 2 – under anticoagulated |

SPECIALISED COAGULATION TESTS

| Test | What is tested | Normal values | Interpretation |
|--|---|---------------|--|
| D-dimer (XDP) (quantitative latex agglutination test) | Measures cross-linked fibrin degradation products | < 0.25 mg/L | <u>Increased</u> DIC Recent surgery Trauma DVT/ Pulmonary embolism Pregnancy (Myocardial infarction) Circulatory half-life of D-dimer is about 12 hours. Elevated D-dimer can therefore persist for some time after the active process has ceased. |
| Fibrin and fibrinogen degradation products (FDP) | Semi-quantitative detection of FDP in plasma | < 5 ug/ml | <u>Increased</u> Acute venous thromboembolism Myocardial infarction Severe pneumonia After major surgery Systemic fibrinolysis associated with DIC Thrombolytic therapy with streptokinase |
| Bleeding time (Ivy method) | Platelet function and capillary integrity Time measured for bleeding to stop after incision is made on the forearm of the patient in a standardised manner. NB: platelet count should be normal | 3-9 minutes | <u>Increased</u> Platelet dysfunction <ul style="list-style-type: none"> • Acquired e.g. aspirin, ureamia • Congenital e.g. von Willebrand disease • Vascular disorders e.g. Ehlers-Danlos's syndrome Important: a normal bleeding time does not imply normal haemostasis and it does not correlate with bleeding at other sites. |

DISSEMINATED INTRAVASCULAR COAGULATION (DIC) SCREEN

Prothrombin time (PT) ↑
 Activated partial thromboplastin time (APTT) ↑
 Thrombin time (TT) ↑
 Fibrinogen normal or ↓
 XDP (D-dimer) ↑
 Platelets ↓
 Bloodsmear: red cell fragments

TESTS USED IN THE INVESTIGATION OF A THROMBOTIC TENDENCY

| Test | What is tested | Reference range | Interpretation |
|--|---|--|--|
| Protein S | <p>Prot S function</p> <p>Prot S is a vit K dependant natural anticoagulant that potentiates the function of protein C.</p> | <p>M 77 – 143 %</p> <p>F 55 – 123 %</p> | <p><u>Decreased</u></p> <p>Congenital deficiency</p> <p>Acquired deficiencies:</p> <ul style="list-style-type: none"> • Warfarin therapy • Oral contraceptives • Pregnancy • Acute phase reaction • Liver disease • Nephrotic syndrome • L-asparaginase chemotherapy • DIC <p>The presence of a Lupus anticoagulant may interfere with the assay</p> |
| Protein C | <p>Prot C function</p> <p>Prot C is a vit K dependant anticoagulant. After activation by thrombin it forms complexes with prot S and phospholipids to degrade factors Va and VIIIa</p> | 70 – 130 % | <p><u>Decreased</u></p> <p>Congenital deficiency</p> <p>Acquired deficiencies</p> <ul style="list-style-type: none"> • Warfarin therapy • Liver disease • DIC • Early post-operative period |
| Antithrombin | <p>Antithrombin function</p> <p>It is an inhibitor of thrombin and its action is enhanced by heparin. It also inhibits factor Xa and to a lesser extent IXa, XIa, XIIa, plasmin and kallikrein.</p> | 80 – 120 % | <p><u>Decreased</u></p> <p>Congenital deficiency</p> <p>Acquired deficiency</p> <ul style="list-style-type: none"> • DIC • Nephrotic syndrome • Liver disease • L-asparaginase chemotherapy <p>Some test procedures may be affected by heparin therapy (The current method used by our laboratory is not affected by heparin).</p> |
| Activated protein C resistance (APC-R) | Resistance against activated protein C | <p>≥ 120 seconds</p> <p>If < 120 seconds sample is regarded as APC-R positive. In these cases PCR for F V Leiden is important</p> | <p>Congenital</p> <ul style="list-style-type: none"> • Factor V Leiden (mutation in factor V) • Acquired Lupus anticoagulant |
| Factor V Leiden PCR | <p>Detect a mutation Arg 506Glu in factor V. This mutation destroys the cleavage site of activated protein C.</p> | | <p>Detects heterozygotes and homozygotes for Factor V Leiden who have a higher risk of thrombosis.</p> |
| Prothrombin gene mutation PCR | <p>Detect a mutation G20210A in the 3' untranslated region of the prothrombin gene. This mutation is associated with elevated levels of prothrombin.</p> | | <p>Detects heterozygotes and homozygotes for this mutation who have a higher risk of thrombosis.</p> |
| Plasminogen | Fibrinolytic activity | 80 – 120% | <p><u>Decreased:</u></p> <ul style="list-style-type: none"> • DIC • Liver cirrhosis • During and after fibrinolytic therapy, Newborn <p><u>Increased:</u></p> <ul style="list-style-type: none"> • Acute phase and malignant disease |
| Lupus anticoagulant | See separate table | | |

TESTING FOR THE PRESENCE OF A LUPUS ANTICOAGULANT

| Test | What is tested | Reference range | Interpretation |
|------------------------------------|---|--|---|
| Dilute Russell's viper venom index | The venom activates FX directly and triggers the coagulation pathway downstream | 0.8 – 1.2 ratio If > 1.2, a confirmatory test based on the addition of phospholipids is done. | <u>Prolonged</u> <ul style="list-style-type: none"> • Lupus anticoagulant • Factor deficiency (X, V, II and fibrinogen) • Other clotting factor inhibitor The presence of a lupus anticoagulant is confirmed if the patient time is shortened by the addition of phospholipids (Screen test ratio/confirmed ratio > 1.2). If a clotting factor deficiency, correction will be obtained with addition of normal plasma and not with phospholipids. It is not recommended to perform this test on samples of patients receiving heparin (UF or LMWH). |
| Kaolin clotting time | Modified aPTT test without added phospholipid. | < 1.2 ratio | <u>Prolonged</u> <ul style="list-style-type: none"> • Lupus anticoagulant • Other clotting factor defects If correction with platelet neutralization procedure, it supports the presence of a lupus anticoagulant. |
| Lupus sensitive PTT | The reagent has been sensitized to aid the detection of lupus anticoagulants | 31.6 – 44 seconds | <u>Prolonged</u> <ul style="list-style-type: none"> • Lupus anticoagulant • Intrinsic pathway factor deficiencies or inhibitors • Dysfibrinogenemia • Presence of heparin and warfarin • Treatment with thrombin inhibitors • DIC. If correction is obtained with platelet neutralization procedure it confirms the presence of a Lupus anticoagulant, while correction with normal plasma supports a clotting factor deficiency. |

TESTS USED IN THE INVESTIGATION OF A BLEEDING DISORDER

- Start off with the basic coagulation screen (PT, aPTT, fibrinogen and thrombin time), platelet count and bleeding time.
- If PT and/or APTT are prolonged – correction studies, DIC screen and specific clotting factor assays can be done to detect the presence of a clotting factor deficiency or inhibitor.
- If platelet count is low – causes for thrombocytopenia should be investigated.
- If PT, APTT, thrombin time, fibrinogen and platelet count are normal and patient has a significant bleeding history, further investigation is needed to exclude a platelet function disorder and other rarer disorders e.g. fibrinolytic defects (tPa, PAI, antiplasmin) and von Willebrand disease.

Testing for Von Willebrand disease

- von Willebrand antigen (vWF:Ag) – normal or decreased
- von Willebrand activity (Ristocetin cofactor activity) – normal or decreased
- Factor VIII (normal or decreased)
- Von Willebrand multimeric analysis if antigen and / or activity is decreased
- Platelet aggregation study with ristocetin

NB: Testing for von Willebrand disease should be done in the absence of any acute phase responses (vWF is an acute phase protein).

PLATELET AGGREGATION STUDIES

| Platelet aggregation response to different agonists are measured. It detects congenital and acquired abnormalities of platelet function. | | |
|---|-----------------|---|
| Agonist | Reference range | Interpretation/causes |
| ADP (10 uM/ml) | 50 – 100% | ↓ Drugs e.g. Clopidogrel ; storage pool defect; aspirin |
| Collagen (10 ug/ml) | 50 – 100% | ↓ Storage pool defect; aspirin; cyclo-oxygenase and thromboxane synthetase deficiency |
| Arachidonic acid (1.5 mM/ml) | 50 – 100% | Aspirin ; storage pool defect; cyclo-oxygenase and thromboxane synthetase deficiency |
| Ristocetin high concentration (1.25 mg/ml) | 50 – 100% | ↓ Bernard Soulier syndrome; Von Willebrand disease |
| Ristocetin low concentration (0.5 mg/ml) | < 10% | ↑ Von Willebrand disease type 2 b (functional defect) |
| If ↓ with all 4 agonists | | Glanzman thrombasthenia |

THROMBO- ELASTOGRAM (TEG)

What is tested:

The rate of clot formation, the kinetics of clot formation, the strength and stability of the clot.

Indication:

Investigation of patients with abnormal bleeding during and after surgery. It can guide in the specific treatment needed.

It is also requested by some physicians as part of pre-operative work-up. Its usefulness to predict bleeding or thrombosis is however debatable.

| Different aspects of TEG | Reference range | Interpretation |
|--|-----------------|---|
| R-time (reaction time) Measures the time between the start of the test until the first sign of fibrin formation | 3-8 min | If prolonged, it indicates a longer time for fibrin to form and may be due to a clotting factor defect or anticoagulant therapy. |
| K-time Measures the speed to reach a certain level of clot strength. | 1-3 min | Dependant on the availability of fibrinogen and FXIII and to a lesser extent platelets. |
| Alpha angle Measures the rapidity of fibrin build-up and cross-linking (clot strengthening) | 55-78 | Dependant on the availability of fibrinogen and FXIII and to a lesser extent platelets. |
| Maximum amplitude (MA) Direct function of the maximum dynamic properties of fibrin and platelet bonding via GPIIb/IIIa and represents the ultimate strength/stability of the fibrin clot | 51-69 | Affected by platelet function and to a lesser extent by fibrinogen concentration. A small MA usually indicates a thrombocytopenia or platelet dysfunction. |
| Thromboelastogram index (mathematic product of the netto effect of the R-time, K, alpha angel and MA measurements) | -3 to +3 | < -3: hypocoagulable > 3+: hypercoagulable especially if > 5 |

FULL BLOOD COUNT (FBC)

| Test | Reference range | Interpretation |
|--|--|--|
| Haemoglobin | M 13.5 – 18.0 g/dl F 11.8 – 16.3 g/dl | ↑ Polycythaemia ↓ Anaemia (bleeding, dietary deficiencies, malabsorption, chronic illness, haemolysis and bone marrow failure (inherited or acquired)). |
| Red cell count | M 4.5 - 6.4 x 10 ¹² /litre F 4.0 - 5.6 x 10 ¹² /litre | ↑ Polycythaemia, thalassaemia ↓ Anaemia |
| Haematocrit | M 40-54 % F 37-46.5% | ↑ Polycythaemia ↓ Anaemia |
| MCV (mean corpuscular volume) | 80 -100 fl | ↑ Macrocytic red cells Vit B12/folate deficiency, liver disease, hypothyroidism, antiretroviral therapy, alcohol, chemotherapy, reticulocytosis and myelodysplasia Check peripheral blood smear for round or oval macrocytes. Oval macrocytes are associated with megaloblastic anaemia (vit B12/folate deficiency) ↓ Microcytic red cells Iron deficiency, thalassaemia, other hemoglobin defects, anaemia of chronic disease, lead poisoning, sideroblastic anaemia |
| MCH (mean corpuscular haemoglobin) | 27 - 32 pg | ↓ - Hypochromic (pale) red cells Causes as for microcytic red cells ↑ - Hyperchromatic red cells e.g. spherocytes |
| MCHC (mean corpuscular haemoglobin concentration) | 32-35 g/dl | ↑ - Spherocytes, bilirubinaemia, auto-agglutination, lipaemic sample |
| Red cell distribution width (RDW) | | If raised it means there are red cells of different sizes (e.g. anaemia). Often the earliest sign of iron deficiency. |
| Platelet count | 140 – 450 x 10 ⁹ /L | ↑ <u>Thrombocytosis</u> Reactive causes should firstly be excluded e.g. iron deficiency, trauma, infection, and malignancy. If no reason is found and platelets remain increased, a chronic myeloproliferative disorder should be excluded. ↓ <u>Thrombocytopenia</u> Production defect - bone marrow infiltration/failure or peripheral loss mechanism e.g. immune (ITP), hypersplenism, DIC, TTP, etc. |
| White cell count | 4 -10 x 10 ⁹ /L | If abnormal look at the differential white cell count |
| Neutrophils | 1.9 – 7.4 x 10 ⁹ /L | <u>Neutrophil leucocytosis</u> Bacterial infection, inflammation, trauma/surgery, neoplasia, haemorrhage, haemolysis, pregnancy, metabolic e.g. diabetic ketoacidosis, drugs e.g. steroids, GCSF <u>Neutropenia</u> Decreased production <ul style="list-style-type: none"> • General bone marrow failure • Specific failure of neutrophil production e.g. congenital, cyclical, drug induced, Increased destruction e.g. hypersplenism, autoimmune, severe infection |
| Lymphocytes | 1.0 – 4.5 x 10 ⁹ /L | <u>Lymphocytosis</u> Viral infections, certain bacterial infection (e.g. pertussis) and lymphoid neoplasia. <u>Lymphopenia</u> Viral infection, lymphoma, connective tissue disorders and severe bone marrow failure |
| Monocytes | 0.2 – 1.0 x 10 ⁹ /L | Monocytosis Chronic bacterial infections, malignancy and myelodysplasia (CMML). |
| Eosinophils | 0.0 – 0.5 x 10 ⁹ /L | <u>Eosinophilia</u> Allergy e.g. asthma, parasites, skin disease, drug sensitivity, Connective tissue disease, Hodgkin lymphoma, chronic myeloproliferative disorders, hypereosinophilic syndrome |
| Basophils | 0.0 - .01 x 10 ⁹ /L | Usually increased in chronic myeloproliferative disorders e.g. chronic myeloid leukaemia. |

ESR (erythrocyte sedimentation rate)

It measures the rate of fall of a column of red cells in plasma during 1 hour.

Largely determined by the concentration of plasma proteins e.g. fibrinogen and globulins.

Raised ESR is a non-specific indicator of an acute phase response and is of value in monitoring disease activity e.g. rheumatoid arthritis.

Normal value: Male 1-15 mm/hour and female 1-20 mm/hour (we use the Wintrobe method)

Causes of raised ESR include:

- * Inflammatory disorders
- * Infections
- * Malignancy
- * Myeloma
- * Anaemia
- * Pregnancy

BONE MARROW INVESTIGATION

Bone marrow aspirate and trephine biopsy can be done to assess bone marrow status.

It is usually done under local anaesthetic from the posterior iliac crest.

Aspirated cells and bone marrow particles are spread onto slides, which allow evaluation of cytological detail, and iron stores while the trephine biopsy is fixed in formalin and processed for histology assessment.

Indications for bone marrow investigation

- Unexplained cytopenias e.g. anaemia, thrombocytopenia, neutropenia and pancytopenia
- Suspected bone marrow infiltration e.g. leukaemia, myelodysplasia, chronic myeloproliferative disease, myeloma, storage disease.
- As part of a staging procedure in lymphoma.
- Suspected infection e.g. TB.

Special investigations that can be done on bone marrow aspirate

- a) Chromosome analysis (cytogenetics), FISH (fluorescent in situ hybridization) for specific molecular abnormalities and PCR analysis.
- b) Immunophenotyping of abnormal populations of cells with flow cytometry.

These tests are used to aid in the diagnosis, sub-classification and prognostification of haematological malignancies. Also used to detect evidence of residual disease after treatment.

- c) Microbiological cultures e.g. tuberculosis.

FLOW CYTOMETRY

Automated technique where cells are incubated with different monoclonal antibodies that are conjugated to different fluorochromes. The labeled cells are then passed in a fluid stream past a laser light source, which allows quantification of antigen expression on the population of interest.

Various panels of antibodies can be used depending on the underlying pathology.

This technique is very important in the classification of leukaemias and lymphomas and to detect residual disease during follow up.

Flow cytometry can be performed on blood samples, bone marrow aspirate and body fluids e.g. pleural effusions and ascites fluid.

Sample needed: EDTA (purple top) or heparin (green top).

TESTS USED IN THE INVESTIGATION OF A HAEMOLYTIC PROCESS

Reticulocyte count

Reticulocytes are young red cells, which contain remnants of RNA.

Normal range: 0.5 – 2.5 % (absolute count $50 - 100 \times 10^9/L$)

Increase with increased erythropoietic activity e.g. blood loss, haemolysis and response on hematinic replacement therapy.

Decreased: red cell production defect e.g. bone marrow disorders and dietary deficiencies.

Direct coombs test

Detect the coating of red cells by immunoglobulins and/or complement.

Causes for a positive direct coombs include:

- Auto-immune haemolytic anaemia (warm type and cold type)
- Allo-immune haemolytic anaemia (mismatched transfusion, haemolytic disease of the newborn and following solid organ or bone marrow transplantation)
- Drug induced immune hemolytic anaemia
- False adsorption of antibodies to the surface of the red cells (occurs in some cases of HIV)

Osmotic fragility

Red cells are suspended in different concentrations of saline and the degree of haemolysis is assessed by spectrophotometry. Spherocytes have an increased volume/surface area ratio and are therefore more susceptible to lysis than normal red blood cells.

If blood smear shows a picture of spherocytic haemolysis, it is usual practice to start off with a direct coombs test. If negative, an osmotic fragility is done and if that is increased, a sample should be send for red cell membrane protein electrophoresis to confirm a possible congenital spherocytosis.

Hb electrophoresis

A lysate of red cells is applied to a gel and an electronic current is applied at an acid and alkaline pH. Different hemoglobins show different migration patterns.

Indication: to detect the presence of inherited haemoglobin defects e.g. Hb S (sickle cell disorders), Hb E, Hb C, HbD, Hb H and thalassaemia.

Our laboratory has changed to a new method using ion exchange high-performance liquid chromatography (HPLC) to detect abnormal hemoglobins in whole blood and to determine the percentages of Hb A2 and HbF.

PNH screen (paroxysmal nocturnal haemoglobinuria)

Haemosiderin in the urine – confirms the presence of intravascular haemolysis.

Immunophenotyping of neutrophils and/or red cells for the expression of CD55 and CD59 using flow cytometry. In PNH, there is a decreased expression of one or both of these antigens.

Testing for inherited enzyme abnormalities

- Glucose-6-phosphate dehydrogenase deficiency (G6PD)
A screening test is done and if positive, a quantitative test should be done for confirmation. Reticulocytes have higher G-6PDH levels and therefore false negative results may be obtained if testing is done during a reticulocytosis.
- Pyruvate kinase deficiency screen (test available at Wits NHLS).

Malaria testing

- Thin smear – used for species identification and quantification of parasite load
- Thick smear – higher detection rate, but cannot be used for species identification or quantification
- Fluorescent microscopy (malaria parasites fluoresce after staining with acridine orange).
Increases the detection rate and is more sensitive than the thick smear.
- Malaria antigen testing based on the presence of certain malaria antigens (pLDH and HRP-2). It aids in the detection and identification of malaria and is usually used in conjunction with the thin smear.

Part 3: SEROLOGY

Immunoglobulins

| | Reference range | Units |
|-----|-----------------|-------|
| IgA | 0.70-4.00 | g/L |
| IgM | 0.40-2.30 | g/L |
| IgG | 7.00-16.00 | g/L |

Complement

| | Reference range | Units |
|----|-----------------|-------|
| C3 | 0.90-1.80 | g/L |
| C4 | 0.10-0.40 | g/L |

Interpretation of IgE values

| Atopic disease not likely | Atopic disease possible | Atopic disease Highly probable |
|---------------------------|-------------------------|--------------------------------|
| 0 – 22 | 22 - 85 | > 85 |

Normal values in Rheumatology

| | Reference range | Units |
|--|-----------------|-------|
| Rheumatoid factor (RF) | 0.00-15.00 | IU/ml |
| Rose Waaler (RF by sheep agglutination test) | <1:10 | |
| Antinuclear antibodies | <1:40 | |

Interpretation of Antinuclear Antibodies

| Antibody | Disease association |
|---|--|
| ANA pattern: | |
| Homogenous | SLE |
| Speckled | Sjogrens syndrome, SLE |
| Nucleolar | Scleroderma, Polymiositis-Scleroderma overlap, SLE |
| Centromere | CREST syndrome |
| Rim | SLE |
| Multiple nuclear dots | Various autoimmune diseases, especially Sjogrens syndrome, SLE and Primary Biliary Cirrhosis (PBC) |
| Few nuclear dots | Auto-immune and viral liver disease |
| Golgi | SLE, Sjogrens, other undefined rheumatic diseases |
| Lysosomal | SLE |
| Centriole | Viral infection, Raynaud's, scleroderma, hyperthyroidism, non-specific rheumatic disease. |
| Mibbody | SLE, Scleroderma, Raynaud's. |
| Mitotic spindle | Unknown significance; associated with respiratory tract tumours |
| PCNA (Proliferating cell nuclear antigen) | SLE |
| Ds DNA antibodies: | |
| Total dsDNA antibodies | SLE; autoimmune hepatitis |
| High avidity dsDNA antibodies | Highly specific for SLE; associated with renal involvement. |
| ENA (extractable nuclear antigens) | |
| Sm | SLE |
| RNP | Mixed connective tissue disease; SLE |
| SSA | Sjogrens, SLE, PBC, autoimmune hepatitis |
| SSB | Sjogrens, SLE |
| Scl-70 | Scleroderma |
| PM-Scl | Polymiositis, dermatomyositis and Scleroderma overlap syndrome, Scleroderma, dermatomyositis and Polymyositis. |
| Jo-1 | Polymyositis, often associated with interstitial lung fibrosis. |
| Nucleosome | SLE |
| Histone | Drug-induced SLE; SLE; Rheumatoid arthritis. |
| Ribosomal-P | SLE |
| Antimitochondrial M2 | Primary Biliary Cirrhosis |

Guidelines for commencing antiretroviral therapy in HIV infected individuals:

| Symptoms | CD4 count | Recommendation |
|---|-----------|---|
| Acute primary infection | Any | Treatment recommended |
| AIDS defining illness (except TB), unexplained weight loss >10% body weight, unexplained diarrhoea lasting > 1 month, oral candidiasis or oral hairy leukoplakia. | Any | Treatment recommended |
| No AIDS-defining illness | >350 | Defer treatment |
| No AIDS-defining illness | 200-350 | Monitor CD4 count; Consider treatment if annual decline is more than 50 / if CD4 count approaches 200. |
| Any | <200 | Treatment recommended |

Criteria indicative of treatment failure for patients on antiretroviral therapy:

1. A sustained increase in viral load >5 000 copies/ml
2. A decline in viral load of LESS than 1 log 6-8 weeks after commencement of therapy.
3. A sustained increase in viral load of >0,8 log from its lowest point or a return to 50% of pre-treatment value.

Please note that several factors can cause fluctuation in viral loads and decisions to change therapy should only be made on 2 consecutive viral load measurements 1-2 weeks apart. The most common cause of treatment failure is inadequate patient adherence.

Interpretation of Hepatitis B virus serology

| Surface antigen | Surface antibody | Core Antibody | Core IgM | E antigen | E antibody | Interpretation of results |
|-----------------|------------------|---------------|----------|-----------|------------|---|
| - | - | - | - | - | - | There is no serological evidence of recent or past exposure to Hepatitis B virus. Consider immunisation. |
| + | - | - | - | - | - | The serological findings are indicative of an early acute phase Hepatitis B infection or a false positive Hepatitis Bs antigen titre. Depending on the clinical findings, Hepatitis B serology can be repeated in 1-2 weeks' time or a Hepatitis B PCR can be requested to confirm the diagnosis. |
| + | - | + | + | + | - | The serological findings are indicative of a recent Hepatitis B infection. If the patient has been ill for longer than 2 months, the positive Hepatitis B e antigen suggests a poor prognosis. The patient has a high infectious potential. We suggest that the patient be monitored for at least a year / until Hepatitis B e and s antigen seroconversion has taken place. Therapy is recommended for patients with chronic Hepatitis B (Hepatitis B s antigen positive for longer than 6 months) and persistent Hepatitis B e antigen positivity |
| + | - | + | + | - | + | The serological findings are indicative of a recent Hepatitis B infection with a good prognosis, as seroconversion of Hepatitis B e antigen to an antibody has already occurred. The patient is, however, still infectious. We suggest that the patient be monitored for at least a year / until Hepatitis B s antigen seroconversion has taken place. Therapy may be recommended for patients with chronic Hepatitis B (Hepatitis B s antigen positive for longer than 6 months) |
| - | + | + | - | - | - | The serological findings indicate past exposure and recovery from Hepatitis B virus infection |
| + | - | + | - | + | - | The serological findings indicate a chronic hepatitis B virus infection (please note the negative Hepatitis core IgM result). The positive test for the Hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg) indicates that the patient is highly infectious and may have a poor prognosis. We suggest that a Hepatitis B viral load be performed, as it can be used in conjunction with liver function tests to evaluate the need for therapy. |
| + | - | + | - | - | + | The serological findings indicate a chronic hepatitis b virus infection (please note the negative Hepatitis core IgM result). The positive test for the Hepatitis B surface antigen (HBsAg) and a negative test for hepatitis B e antigen (HBeAg) indicate that the patient is probably a healthy carrier with a good prognosis. The patient is, however, still infectious. A Hepatitis B viral load and liver function tests should be done to evaluate a possible need for therapy. |
| + | + | + | + | + | + | The serological results are indicative of a late acute phase Hepatitis B infection and seroconversion from s antigen to s antibody and e antigen to e-antibody is taking place. The patient has a high infectious potential. We suggest that the patient be monitored until seroconversion has been complete. |
| - | + | - | - | - | - | The serological findings indicate immunity to Hepatitis B probably due to Hepatitis B vaccine. |
| - | - | + | - | - | - | This serological profile may occur in the following instances: <ul style="list-style-type: none"> • Most commonly patients with remote past Hepatitis B infections may have "lost" their |

| | | | | | | |
|---|---|---|---|-----|-----|--|
| | | | | | | <p>Hepatitis B s antibodies.</p> <ul style="list-style-type: none"> • During late acute phase convalescence “convalescence window” the Hepatitis B s antigen is below detectable levels and Hepatitis B s antibodies have not yet been formed • Silent carriers of Hepatitis B with Hepatitis B s antigen below detectable levels. <p>We suggest that a Hepatitis B core IgM and a Hepatitis B PCR be done to distinguish between these possibilities.</p> |
| - | - | + | + | +/- | +/- | The serological findings suggest recent hepatitis b virus infection - the patient may be in the immediate recovery phase of acute Hepatitis B virus infection with undetectable Hepatitis B s antigen levels and Hepatitis B s antibodies not yet formed. |
| + | + | + | + | +/- | -/+ | The serological findings are indicative of a late acute phase Hepatitis B infection and seroconversion from s antigen to s antibody is taking place. We suggest that the patient be monitored until seroconversion has been completed. |
| + | - | + | + | + | + | The serological findings are indicative of a late acute phase Hepatitis B infection and seroconversion from e antigen to e antibody is taking place. The patient has a high infectious potential. We suggest that the patient be monitored until seroconversion has been completed. |
| + | - | - | - | + | - | The serological findings are indicative of an active Hepatitis B infection in an immunocompromised patient. The patient is highly infectious. Should there be any doubt regarding the diagnosis of Hepatitis B, this result can be confirmed by a Hepatitis B PCR. |