BELMATT
HEALTHCARE TRAINING

Blood Result Interpretation

TIMETABLE

- AIMS AND OBJECTIVES
- NORMAL BLOOD TESTS
- QUIZ
- BLOOD RESULTS INTERPRETATION
- LFT
- VITAMIN D
- VITAMIN B12 DEFICIENCY
- TSH

SESSION AIMS

This course is for healthcare professionals working in primary care who wish to develop their knowledge and skills on the fundamentals of interpreting blood tests and provides an advanced understanding of essential blood results.

LEARNING OBJECTIVES

To understand basic blood tests terminology.

Use a case study approach in interpreting blood results in primary care and general practice

Recognise abnormal results within the context of the clinical case.

Use clinical decision-making protocols.

Review current best practice and guidelines or pathways for treatment of abnormal results.

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REFERENCE RANGES

Full blood count

- **Haemoglobin (Hb):**
- ♂ 130 – 180 g/L
- ♀ 115 – 165 g/L

White Cell Count (WCC):
- Total: 3.6 – 11.0 x 109/L
- Neutrophils: 1.8 – 7.5 x 109/L
- Lymphocytes: 1.0 – 4.0 x 109/L
- Monocytes: 0.2 – 0.8 x 109/L
- Eosinophils: 0.1 – 0.4 x 109/L
- Basophils: 0.02 – 0.10 x 109/L
- Platelet Count: 140 – 400 x109/L

- **Red Cell Count (RCC):**
- ♂ 4.5 – 6.5 x 109/L
- ♀ 3.8 – 5.8 x 109/L

- **Haematocrit:**
- ♂ 0.40 – 0.54 L/L
- ♀ 0.37 – 0.47 L/L

- **Mean Cell Volume (MCV):** 80 – 100 fL

- **Mean Corpuscular Haemoglobin (MCH):** 27 – 32 pg/cell

- **Reticulocyte count:** 0.2 – 2%

Coagulation
- **Prothrombin Time (PT):** 10 – 14 seconds

- **Activated Partial Thromboplastin Time (APTT):** 24 – 37 second

- **Fibrinogen:** 1.50 – 4.50 g/L

- **D-Dimer:** < 500 ng/mL

REFERENCE RANGES

Haematinics

Ferritin:
- ♂ 25 – 350 ng/mL
- ♀ 10 – 300 ng/mL

Vitamin B12: 180 – 1000 pg/mL

Folate: > 4.0 ng/mL

Total Serum Iron:
- ♂ 11.6 – 35.0 µmol/L
- ♀ 4.6 – 30.4 µmol/L

Transferrin: 2.0 – 3.6 g/L

Transferrin Saturation: 20 – 50%

Total Iron Binding Capacity (TIBC): 45 – 81 µmol/L

Erythrocyte Sedimentation Rate (ESR):
- ♂ ≤ 49 years: 1 – 7
- ♂ ≥ 50 years: 2 – 10
- ♀ ≤ 49 years: 3 – 9
- ♀ ≥ 50 years: 5 – 15

REFERENCE RANGES

Biochemistry

Urea & electrolytes (U&Es)

Na+: 133–146 mmol/L

K+: 3.5–5.3 mmol/L

Ca2+(adjusted): 2.2-2.6 mmol/L

Mg2+: 0.7–1.0 mmol/L

Chloride: 98-106 mmol/L

Urea: 2.5 – 7.8 mmol/L

Creatinine:

- ♂ 59–104 µmol/L
- ♀ 45–84 µmol/ L

Liver function tests (LFTs)

Alkaline phosphatase (ALP): 30–130 U/L

Alanine aminotransferase (ALT):

- ♂ <41 U/L
- ♀<33 U/L

Bilirubin: <21 µmol/L

GGT:

- ♂ <60 U/L
- ♀<40 U/L

Albumin: 35–50 g/L

REFERENCE RANGES

Inflammatory markers

CRP: < 5mg/L

Arterial blood gas results

- pH: 7.35 – 7.45
- pO2: 11 – 13 kPa (82.5 – 97.5 mmHg)
- pCO2: 4.7 – 6.0 kPa (35.2 – 45 mmHg)
- HCO3: 22 – 26 mmol/L

Base excess: (-2 to +2 mmol/L)

Metabolic tests

Serum ketones: < 0.6 mmol/L

Fasting blood glucose: 4.0 to 6.0 mmol/L

Postprandial (2 hours after eating): up to 7.8 mmol/L

HbA1c: < 42 mmol/mol (6.0%)

Cholesterol: < 5 mmol/L

Triglyceride: 0.55–1.90 mmol/L

LDL: < 3mmol/L

HDL: > 1 mmol/L

Cholesterol/HDL: < 4

REFERENCE RANGES

Endocrinology

TSH: 0.4–4.0 mU/L[2]

Free T4: 9 – 24 pmol/L

Free T3: 3.5 – 7.8 pmol/L

Parathyroid hormone: 10 – 65 ng/L

Growth hormone (random):

- ♂< 5 ng/mL
- ♀< 10 ng/mL

Cortisol (random): 137 – 429 nmol/L

Testosterone:

- Male <50: 10-45 nmol/L
- Male >50: 6.2-26 nmol/L

Triglyceride: 0.55–1.90 mmol/L

LDL: < 3mmol/L

HDL: > 1 mmol/L

Cholesterol/HDL: < 4

Other biochemistry tests

Serum Total Protein: 60 – 78 g/L

Troponin T: < 0.01 µg/L

Creatine Kinase (CK):

- ♂ 40–320 U/L
- ♀ 25–200 U/L

Lactate Dehydrogenase (LDH): 240–480 U/L

REFERENCE RANGES

Lactate (plasma): 0.5 – 2.2 mmol/L

Urate:
- ♂ 200–430 µmol/L
- ♀ 140–360 µmol/L

Amylase: 28–100 U/dL

Ammonia: 10 – 35 µmol/L

NT-proBNP:
- < 75 years: < 125 pg/mL
- > 75 years: < 450 pg/mL

Copper: 70 – 150 µg/dL

Ceruloplasmin: 15 – 60 µmol/L

Vitamin D: > 500 nmol/L

Serum Osmolality: 275 – 295 mOsmol/kg

24h Urine Osmolality: 500 – 800 mOsm/kg

Random Urine Osmolality: 300 – 900 mOsm/kg

12h Fluid Restricted Urine Osmolality: > 850 mOsm/kg

24h Urine Sodium (Na+): 100 – 260 mmol/24h

24h Urine Potassium (K+): 25 – 100 mmol/24h

24h Urine Total Protein: < 100 mg/24h

Urine pH (random): 5 – 7

REFERENCE RANGES

Tumour markers

Beta Human Chorionic Gonadotrophin (bHCG): < 5 mU/mL

Alpha Fetoprotein: < 44 ng/mL

Prostate Specific Antigen (PSA): < 4.0 ng/mL

Carcinoembryonic Antigen (CEA):

- Non-smokers at 50 years: < 3.6 µg/L
- Non-smokers at 70 years: < 4.1 µg/L

Smokers: < 5 µg/L
CA-125: < 35 U/mL

CA19-9: < 40 U/mL

Immunology

Anti-SS-A (La):

- Negative: < 3 U/mL
- Positive: > 4 U/mL

Anti-Streptolysin O Titre (ASOT):
Pre-school Age: < 100
School Age: < 250
Adults: < 125

Rheumatoid Factor (RF):

- Negative: < 20 U/mL
- Positive: > 30 U/mL

Anti-Mitochondrial Antibodies (AMA):

- Negative: < 10 U/mL
- Positive: > 10 U/mL

REFERENCE RANGES

Perinuclear Anti-Neutrophil Cytoplasmic Antibodies (p-ANCA):
- Negative: < 5 U/mL
- Positive: > 5 U/mL

Anti-Histone Antibodies:
- Negative: < 25 U/mL
- Positive: > 25 U/mL

IgA: 110 – 560 mg/dL

IgD: 0.5 – 3.0 mg/dL

IgE: 0.01 – 0.04 mg/dL

IgG: 800 – 1800 mg/dL

IgM: 54 – 200 mg/d

Anti-ds-DNA:
- Negative: < 40 U/mL
- Positive: > 60 U/mL

Anti-ss-DNA:
- Negative: < 8 U/mL
- Positive: > 10 U/mL

Cytoplasmic Anti-Neutrophil Cytoplasmic Antibodies (c-ANCA):
- Negative: < 20 U/mL
- Positive: > 30 U/mL

Anti-SS-A (Ro):
- Negative: < 15 U/mL
- Positive: > 25 U/mL

REFERENCE RANGES

Lumbar puncture results

Appearance: clear and colourless

White blood cells (WBC): 0 – 5 cells/µL

- No neutrophils present, primarily lymphocytes
- Normal cell counts do not rule out meningitis or any other pathology

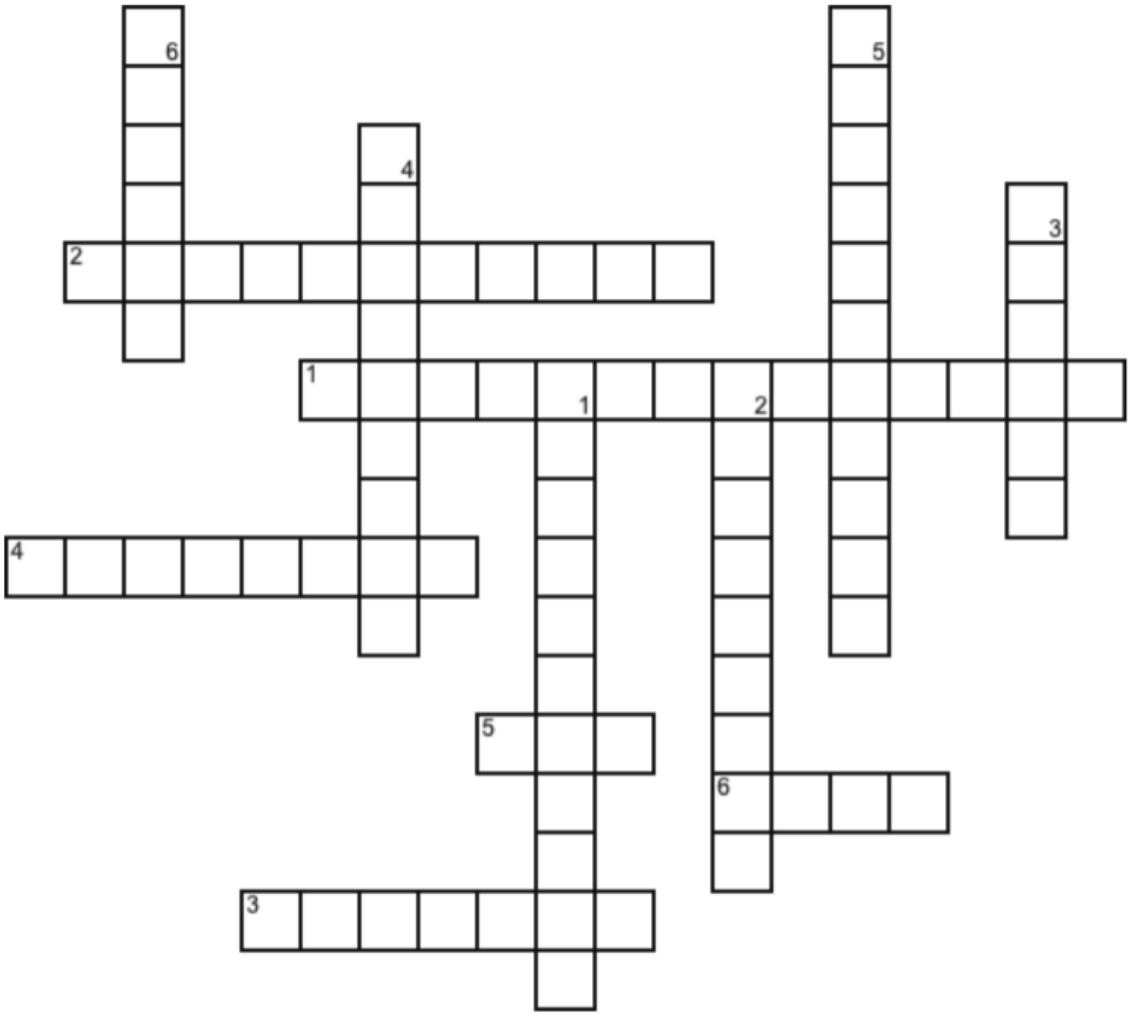
Red blood cells (RBC): 0 – 10/mm^3

Protein: 0.15 – 0.45 g/L (or <1% of the serum protein concentration)

Glucose: 2.8 – 4.2 mmol/L (or ≥ 60% plasma glucose concentration)

Opening pressure: 10 – 20 cm H2O

Blood Results



Across

1. can be given instead of a blood transfusion
2. another name for neutrophil
3. levels are reduced in primary alcohol liver disease
4. second most common protein in the blood.
5. elevated levels found in MI, kidney damage or liver disease
6. elevated levels in dehydration or heart failure

Down

1. low levels of this in anaemia
2. may be abnormal in diarrhoea and vomiting
3. indicates kidney function
4. breakdown product of haemoglobin, increased in obstructive bile conditions
5. measures amount of volume red blood cells occupy in the blood
6. this test is used to assess ph

GP Vs Secondary Care

- Reduced time constraints
- Certain bloods inappropriate for either setting eg Troponin
- Delays in results suitable in GP but not acute setting

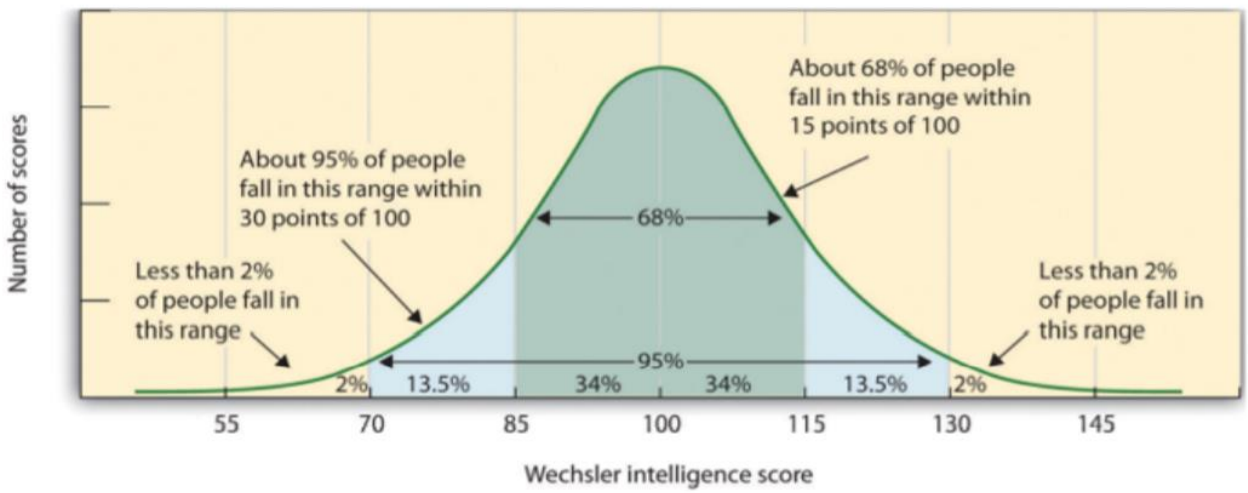
Scattergun Approach

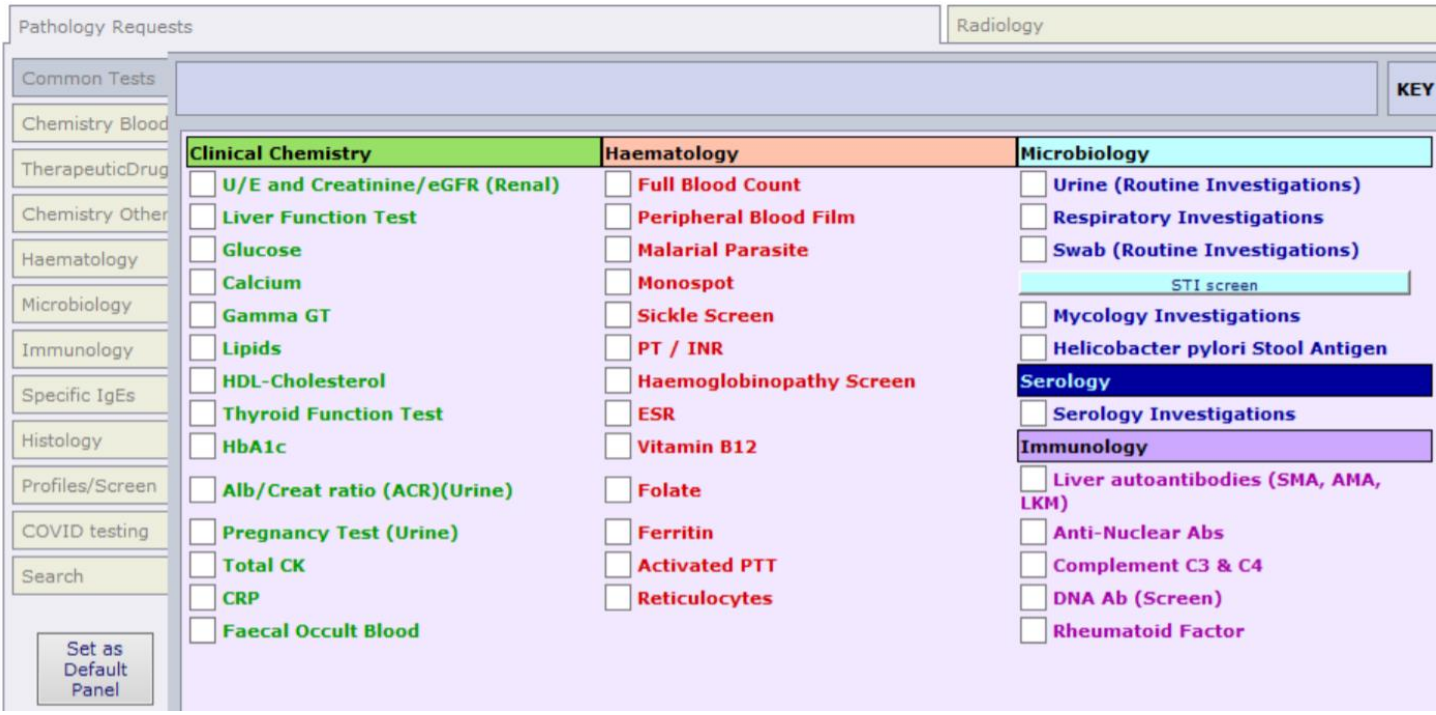
GP Vs Secondary Care

- KEY POINT: 90% OF DIAGNOSIS IS IN THE HISTORY
- Wherever you are
    - Reduce scattergun approach
    - Remember if you requested it you are responsible for chasing
    - Make requests concise to the questions you are asking

Reference ranges - 'pathology or normal?'

Following is the distribution of Intelligence among people in general.





FBC

Hb	115
MCV	76
Platelets	150
WCC	4.0
Neutrophils	2.0
Leucocytes	1.3
Monocytes	02
Eosinophils	0.04

Specimen : BLOOD Taken : 08-Jul-2020 14:24 Received : 08-Jul-2020 18:14

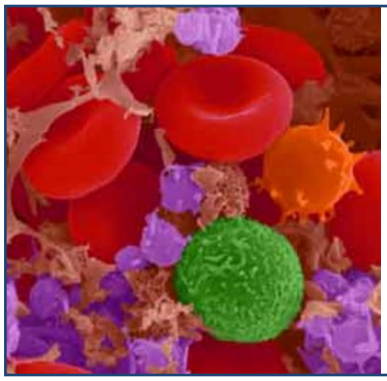
RANDOM SAMPLE

FULL BLOOD COUNT UC

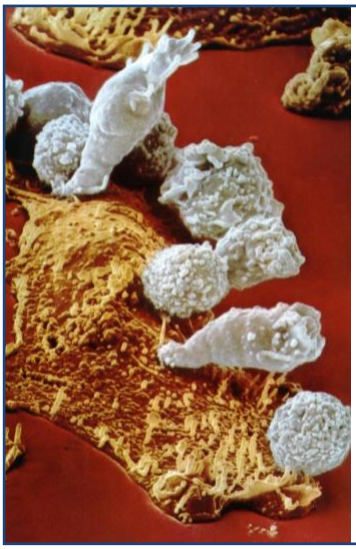
(SK) - 2 Satisfactory - no action required

Total white cell count	8.0 10*9/L	(4.0 - 11.0)	SR
Red blood cell (RBC) count	5.15 10*12/L	(3.50 - 6.50)	SR
Haemoglobin estimation	146 g/L	(125 - 180)	SR
Haematocrit	0.43 L/L	(0.38 - 0.54)	SR
Mean corpuscular volume (MCV)	84.1 fL	(79.0 - 99.0)	SR
Mean corpusc. haemoglobin(MCH)	28.3 pg	(27.0 - 34.5)	SR
Mean corpusc. Hb. conc. (MCHC)	337 g/L	(316 - 365)	SR
Platelet count	208 10*9/L	(150 - 450)	SR
Neutrophil count	3.13 10*9/L	(1.70 - 7.50)	SR
Lymphocyte count	4.28 10*9/L	(1.00 - 4.50)	SR
Monocyte count	0.37 10*9/L	(0.20 - 0.80)	SR
Eosinophil count	0.17 10*9/L	(0.00 - 0.50)	SR
Basophil count	0.03 10*9/L	(0.00 - 0.10)	SR

CONS BLOOD FILM SAND SR UC



Not all blood cells are the same….



White Blood Cells

- WBC's are fighter cells
- Some make antibodies
- Some fight directly
- Divided into types by how they
- ok and what they do

Anaemia

- Result of long-term negative iron balance. The iron deficiency spectrum ranges from iron depletion to iron deficiency anaemia.
- Anaemia is defined as a haemoglobin (Hb) level two standard deviations below the normal for age and sex:
- In men aged over 15 years — Hb below 130 g/L.
- In non-pregnant women aged over 15 years — Hb below 120 g/L.
- In children aged 12–14 years — Hb below 120 g/L.
- Multifactorial: dietary deficiency, malabsorption, increased loss, or increased requirements.

Findings	Hypochromic	Normal	
MCV	<80 fl (decreased)	80 to 95 fl (normal)	>95 fl (increased)
MCH	<27 pg (decreased)	> 27 pg (normal)	Increased
MCHC	Decreased	Normal	Normal
Aetiological factors	1. Iron deficiency 2. Thalassemia 3. Sideroblastic anemia 4. Chronic diseases 5. Lead	1. Haemolytic anaemias 2. After acute blood loss 3. Bone marrow failure by chemotherapy or cancer	1. Vitamin B12 deficiency 2. Folic acid deficiency 3. Aplastic anemia 4. Non – megaloblastic anemia due to: 1. Alcohol use 2. Liver diseases

Case

- Diagnosis?
  - Autoimmune ITP
- Further tests?
  - Blood film
  - TFTs and immunology screen

Vitamin B12 (187-883ng/l)

- Vitamin B12 is essential for life (needed to make new cells eg many new red blood cells which are made every day).
- Found in meat, fish, eggs and milk - but not in fruit or vegetables.
- Common symptoms: tiredness, lethargy, feeling faint, breathlessness.
- Causes: Pernicious anaemia, malabsorptive states, medicines (dmards/metformin)
- Treatment: Injections Vs Tabs

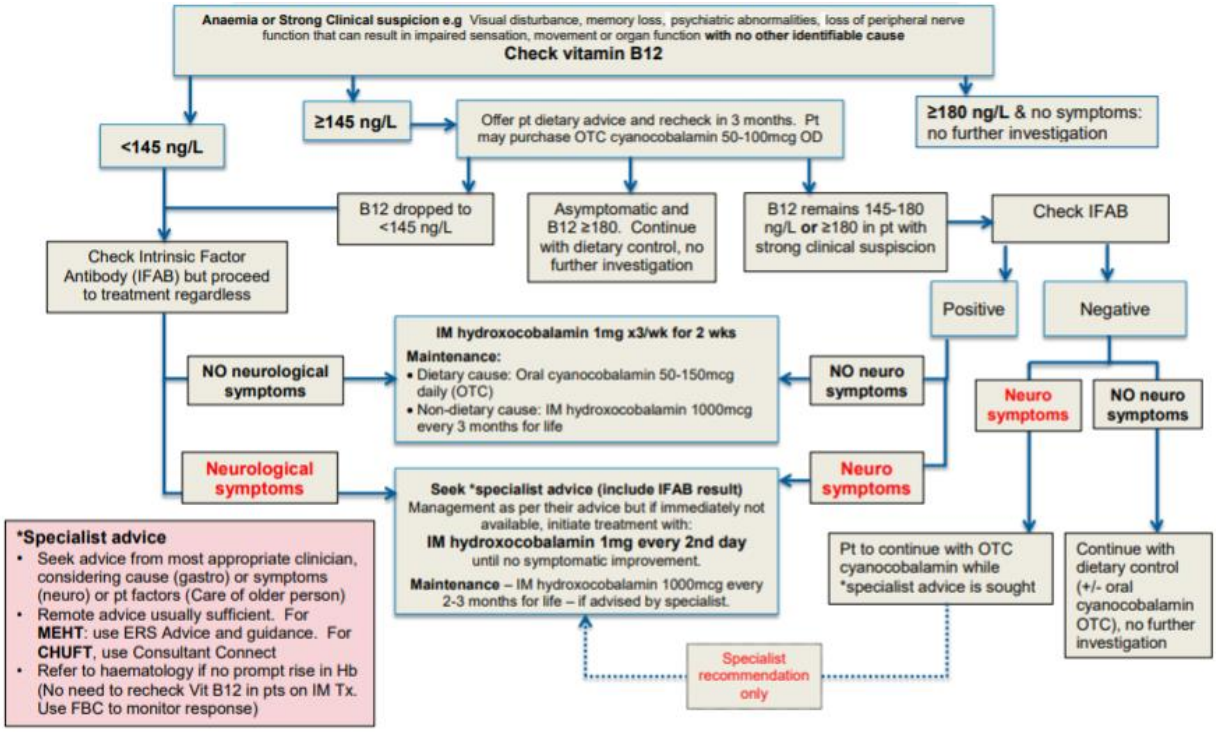
Ferritin (10-300 µg/L))

- Ferritin plays a significant role in the absorption, storage, and release of iron.
- Found in serum in low concentrations and is directly proportional to the body's iron stores.
- TO BE CHECKED IF CONCERNED ABOUT POSS 2WW!!!!

Ferritin

- Elevated in the presence of the following conditions and do not reflect actual body iron stores:
- inflammation
- significant tissue destruction
- liver disease
- malignancies such as acute leukaemia and Hodgkin's disease
- therapy with iron supplements

Guideline for the management of Vitamin B12 deficiency (For adults)



Medication/conditions that may affect levels Vitamin B12

Metformin (for longer than 12 months)

- Usually improved with dietary improvement of B12 intake
- Only assess if objective evidence of deficiency is present including peripheral neuropathy or macrocytic anaemia
- If low levels check IFAB and should be treated with a short course of OTC oral cyanocobalamin (50 micrograms orally for 4 weeks). Response should be assessed clinically and continued if benefit is shown
- No need for prophylactic B12 administration

Proton pump inhibitors and H2 antagonists

- OTC oral replacement (25-100 micrograms orally) may be appropriate if objective evidence of deficiency is found

Medication/conditions that may affect levels
Vitamin B12

Anticonvulsants

- If no objective features of B12 deficiency- no need for replacement
- OTC oral replacement (25-100 micrograms orally) may be appropriate if objective evidence of deficiency is found

Oral contraceptives and hormone replacement therapy

- Only be assessed if objective symptoms develop and this is the only indication for treatment
- OTC oral replacement (25-100 micrograms orally) may be appropriate if objective evidence of deficiency is found

Colchicine

- Low levels can easily be increased with dietary supplementation

Antibiotics

- Low levels can easily be increased with dietary supplementation

Gastrointestinal surgery

- Both gastrectomy and bariatric surgery can lead to B12 deficiency and require regular monitoring and replacement if levels are falling despite good dietary intake. Oral replacement is often **inadequate** in these patients since the cause is likely malabsorption

Pregnancy

- Not routinely measured during pregnancy therefore only identified if symptoms develop – in which case follow pathway as for non-pregnant people

Vegetarian and vegan diets

- Vegetarians and vegans are at increased risk of B12 deficiency especially during pregnancy and when breastfeeding
- Monitoring should be considered, especially at high-risk times, and OTC oral supplementation (cyanocobalamin 50mcg daily) may be required

Vitamin B12 frequently asked questions

1. If laboratory results show low (<145ng/L) vitamin B12 levels can oral supplementation be considered?

The NICE Clinical Knowledge of Summaries recommends that the intramuscular (IM) route should be used in all deficiency cases where there are neurological symptoms as an acute dose (hydroxocobalamin 1mg on alternate days for two weeks). Usually IM will then be used as maintenance. However, if the cause is dietary and the patient does not display neurological symptoms, OTC oral supplements may be used

2. What if the patient is unwilling to have the IM route?

If the deficiency is thought to be diet related and not due to lack intrinsic factor, then it is possible to use oral Cyanocobalamin. It is available as cyanocobalamin 50mcg tablets which may be purchased over the counter. Parenteral therapy is preferable for deficient symptomatic patients, as it is retained in the body for longer than oral tablets. Malabsorption is frequently a cause of deficiency, in such cases, oral supplements are unlikely to be effective. This should be explained to the patient although any decision to inject will obviously require informed patient consent. If this is not obtainable, the patient may choose to purchase OTC, but should be advised this may not be as effective as injection in their circumstances.

(Please note that Vitamin B Co strong tablets do not contain any vitamin b12 and therefore cannot be used to treat B12 deficiency)

3. How do you treat low vitamin B12 patients with Type 2 diabetes (on long term metformin longer than 12 months)?

Give patient dietary advice to increase their vitamin B12 levels, advise them to supplement with OTC oral cyanocobalamin. Monitor serum B12 every 6 months. If still low check IFAB. If positive, then treat lifelong with IM hydroxocobalamin every three months. If IFAB is negative, the reduced level may be purely as a result of metformin, increase dose of oral cyanocobalamin to 150mcg daily, if still not able to raise B12 levels, treatment with three injections of IM hydroxocobalamin with subsequent monitoring of serum B12 at 6 monthly intervals is suggested.

4. What if a person is still symptomatic despite maintenance IM vitamin B12 treatment?

If levels were borderline to begin with and only treated due to symptoms, then this suggests the B12 has not been effective. Trial withdrawal and investigate other causes of symptoms. If initially B12 deficient, retest the B12 level: if remains low, seek specialist advice. If this is corrected to normal levels, continue maintenance dose interval and investigate other causes of symptoms. If a person's symptoms recur before the next injection is due, seek specialist advice from a haematologist.

Vitamin B12 frequently asked questions

5. What dose of cyanocobalamin is recommended for purchase?
If mild deficiency is thought to be diet related, advise people to take oral cyanocobalamin tablets 50–150 micrograms daily between meals. Doses within this range are safe and sufficient to prevent dietary deficiency.

6. What foods can I advise patients to eat to increase their dietary intake of Vitamin B12?
Foods that are a good source of B12: eggs, meat, milk and other dairy products, salmon and cod; as well as foods which have been fortified with B12 (some soy products, breakfast cereals and breads)

Examples of cyanocobalamin available to purchase (other products are available)

Holland and Barrett (available on the high street or online):
- 100mcg vitamin B12 tablets x 100
- Take ONE tablet daily
- £7.49 (price at time of writing, also included in buy one get one half-price offer)

Nature's Best (online)
- 100mcg vitamin B12 tablets x 100.
- Take ONE tablet daily
- £4.99 (price at time of writing, plus £1 delivery charge)

MyProtein (suitable for vegans)
- 1000mcg vitamin B12 tablets x 60
- Take ONE tablet daily (dose is more than is necessary but will not cause harm)
- £4.49 (price at time of writing)

Folate (3.1-20.0 µg/L)

- Folate (folic acid) is one of the B group of vitamins found in small amounts in many foods.
- Absorbed through the upper part of the small intestine.
- The body's reserves of folate, unlike vitamin B12, are low and only sufficient for around four months.
- Almost half of the body folate is found in the liver.
- Sources :broccoli, Brussels sprouts, asparagus, peas, chickpeas and brown rice.

Folate

Dietary deficiency?

- Malabsorption (eg, coeliac disease, tropical sprue, congenital specific malabsorption, jejunal resection, inflammatory bowel disease).
- Poor intake.
- Old age.
- Poor social conditions.
- Malnutrition.
- Alcohol excess (also causes impaired utilisation).
- Poor intake due to anorexia.
- Food fads.

Excessive requirements?

- Physiological (e.g, pregnancy, lactation, prematurity and infancy).
- Malignancy (e.g, leukaemia, carcinoma, lymphoma).
- Blood disorders (eg, haemolytic anaemias, sickle cell anaemia, thalassaemia major, chronic myelosclerosis).
- Inflammation (eg, tuberculosis, Crohn's disease, malaria).
- Metabolic (eg, homocystinuria).
- Haemodialysis or peritoneal dialysis.

Folate

Excessive urinary excretion?

- This includes, for example, congestive heart failure, acute liver damage and chronic dialysis.

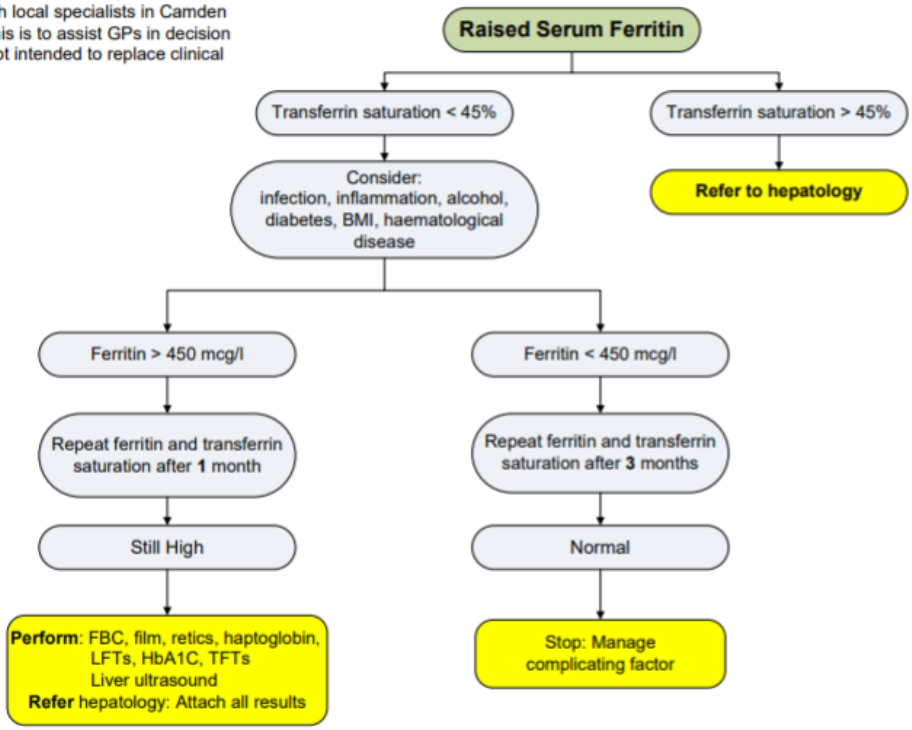
Antifolate drugs?

- With uncertain mechanism of action (eg, anticonvulsants and possibly alcohol and nitrofurantoin).
- Causing malabsorption of folate (eg, colestyramine, sulfasalazine, methotrexate).
- Trimethoprim may exacerbate pre-existing folate deficiency but does not cause megaloblastic anaemia.

Genetic disorders

- Mutations in the SLC46A1 gene, leading to proton-coupled folate transporter deficiency

Primary Care Management of raised serum Ferritin.
This guidance has been developed in collaboration with local specialists in Camden and Islington. This is to assist GPs in decision making and is not intended to replace clinical judgment.



LFTs

Bilirubin	3	17	Umol/L
ALT	5	35	U/L
Alk Phos.	30	100	U/L

Managing LFTs

- Always be systematic:
    - History and examination
    - Investigations
    - When to refer

Liver function

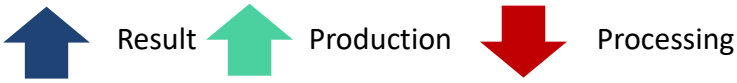
- Components?
    - Bilirubin
    - Alanine aminotransferase (ALT)
    - Alkaline Phosphatase (Alk Phos)

Common disorders

- Jaundice
- Liver damage/failure

Bilirubin

- Breakdown of haemoglobin
- Processed by the liver
- ↑Bilirubin = Jaundice



- ↑Production
  - Haemolysis
  - Hepatolysis
- ↓Processing
  - Obstruction
  - Cirrhosis

Isolated bilirubin investigations

- Split bilirubin- conjugated/ unconjugated
- Reticulocyte count
- Gilbert's syndrome

- Gilbert's syndrome
  - Jaundice
  - ↓Processing
  - Normal liver enzymes
  - Benign condition

ALT

- Liver enzyme in hepatocytes (liver cells)

- Hepatic jaundice
    - Hepatitis
    - EBV/CMV
    - Paracetamol overdose
    - Autoimmune

Isolated raised ALT
- Most likely fatty liver/ alcohol
- Needs complete liver aetiology screen
- Check AST/Gamma GT
- USS
- Biopsy if ALT >twice normal

ALK Phos.

- Liver enzyme found in bile duct cells

- Obstructive jaundice
    - Gall stones
    - Biliary obstruction
        - Pancreatic cancer

Isolated raised ALP
- Ensure origin
    - ALP isoenzymes
    - Gamma GT
- USS
- If of bony origin
    - Ca/Vitamin D/PTH

Alk Phos

- Source may be the liver/bone/gut/kidney or placenta
- Causes: cholestasis or hepatic disease; bone mets or Pagets; puberty; pregnancy
- Investigate with liver screen, ultrasound scan and auto antibody screen
- If asymptomatic, normal liver screen/USS and raised by <50% could consider observation, otherwise refer

Medication

- NSAIDs
- Flucloxacillin
- Statin
- Anti-epileptic
- TB drugs
- Co-Amoxiclav

Hepatic Jaundice

- Bili increased.
- ALT increased ++
- ALP normal or mildly elevated
- Short history
- No signs of CLD
- Causes- Hep A/B
- EBV
- CMV
- Paracetamol overdose
- Autoimmune
- Pregnancy

Case Study

After assessing GO's cardiovascular risk you decide you'd like to initiate a statin for him, but notice his last LFTs 2 years ago were slightly abnormal:

- AST 68 (8-40)
- GGT 102 (11-50)
- ALP 114 (20-130)
- Bili 14 (<21)

- What actions (if any) would you take? Would you start the statin?
- Can raise transiently due to viral infection, drugs or alcohol
- Consider Hx alcohol/recreational drug use (also penicillins/antifungals/statins/ anti-epileptics/NSAIDs/herbal medicines)
- Hepatitis screen: Hep (A)/B/C; ferritin; +/- EBV/ autoantibodies/ (alpha-1 antitrypsin/ caeruloplasmin)
- USS (?)
- Baseline reading recommended, if stronger than pravastatin/simvastatin 40mg daily repeat 3 and 12 months
    - If abnormal look for cause cirrhosis
    - Trial without statin if >3 times upper limit of normal AST/GGT
    - Consider initiation even in patients with cirrhosis as proven benefits and no confirmed risks
    - What is the most common cause of deranged LFTs in the UK?
    - Non-alcoholic fatty liver disease (though alcohol commonly implicated also!

Case Study

- TD is a 40 year old woman with a history of non- specific abdominal pain. She has been treated for IBS for the last year. When she sees you she tells you that she has felt 'fluey' and had no energy for the last 2 weeks. You notice she has not had any blood tests before and you arrange a 'tired all the time' blood screen. This is all normal except for the following LFTs:
- AST 24 (8-40)
- GGT 46 (11-50)
- ALP 160 (20-130)
- Bili 36 (<21)
- What would you do?

- You decide to repeat the test a month later. When she comes in for the result you notice that she looks a little more yellow...
- AST 40 (8-40)
- GGT 80 (11-50)
- ALP 260 (20-130)
- Bili 60 (<21)
- What would you do next?

Raised bilirubin

- Gilbert's: Raised unconjugated bilirubin; mild or no symptoms; if <3 times ULN interval retest and if no signs haemolysis or other disease no further testing required
    - Most patients without Gilbert's Disease or self limiting virus will not require referral
    - Consider haemolysis as cause of raised bilirubin, make sure you have checked FBC/reticulocytes
    - Obstructive causes: gallstones; cancer; primary biliary cirrhosis; primary sclerosing cholangitis

Case Study

- 21 Male
  - Cold symptoms for three days
  - Yellow tinge to eyes

Bilirubin	39umol/L	(3-17)
ALT	21 U/L	(5-35)
Alk Phos.	88U/L	(30-150)

- Diagnosis?
  - Gilbert's syndrome
  - Unconjugated hyperbilirubinaemia
- Further tests?
  - Repeat
  - No further tests, benign condition

Vitamin D

- Where do we get if from?
    - Sunlight, oily fish (pilchards, mackerel, eggs, red meat, liver)
- Who should we test for it?
    - Those with increased need, reduced intake, lack in diet.
    - Housebound
    - Those who cover up
    - Elderly
    - Tanned skin
    - Chronic malabsorptive states

Vitamin D insufficiency

- 30-50 nmol/L
- Do not need supplements but OTC
- Advise annual blt

Vitamin D deficiency

- <30 nmol/L
- Need oral supplements-dosage depends on local guidance
- Ideally need repeat calcium/albumin 1 month after initiation
- Risks: Digoxin, BZD, kidney stones

Cholesterol

- Serum cholesterol (2.5-5.0)
- HDL (>1.2)
- Triglycerides (<2.3)

- Eg patient
    - Serum cholesterol 5.6
    - HDL 1.0
    - Triglycerides 3.1

add statin intolerance pathway here

Treatment of Vitamin D Deficiency in Adults

Importance of vitamin D

- Vitamin D is essential for skeletal growth and bone health.
- Around 20% of adults and 8 to 24% of children may have low vitamin D status1.
- Severe deficiency can result in rickets in children and osteomalacia in adults.

Risk factors for vitamin D insufficiency and deficiency

- Infants and children under 5
- Pigmented skin (non-white ethnicity)
- Pregnant and breastfeeding women, particularly teenagers and young women
- Lack of sunlight exposure
- People over 65
- Skin concealing garments or strict sunscreen use
- Multiple, short interval pregnancies
- Elderly or housebound or confined indoors for long periods.
- Vegan / vegetarian or high phytate consumption such as in chapatis
- Malabsorption (e.g., inflammatory bowel disease, coeliac disease, pancreatic insufficiency)
- Use of anticonvulsants, rifampicin, cholestyramine, anti-retrovirals, glucocorticoids
- Certain conditions e.g. liver or renal disease, cystic fibrosis
- Obesity (BMI > 30)

Sources of vitamin D

- It is recommended that everyone over one year of age should consume 10 micrograms of vitamin D daily1 .It is essential that everyone, especially those people most at risk (see list above), are aware of the implications of vitamin D deficiency and what they can do to prevent it
- From March to October ultraviolet B (UVB) rays help people produce vitamin D. Increasing regular UVB sunlight exposure (to forearms, hands & lower legs) , without sunscreen, for 10 to 15 minutes, between 11am to 3pm (people with darker skin will need longer) helps maintain levels.
- From October to March, sunlight contains very little UVB wavelength the skin needs to make vitamin D so people rely on body stores from sunlight exposure in the summer and dietary sources to maintain vitamin D levels. Food sources include oily fish, cod liver oil, red meat, egg yolks and foods fortified with vitamin D: All infant & toddler formula milk, some breakfast cereals, soya products, dairy products, powdered milks and fat spreads e.g. margarine. Note: Increasing the dietary intake of vitamin D alone will not avoid the need for supplementation in patients with vitamin D deficiency.
- Pregnant women especially need to ensure their own requirement for vitamin D is met and that their baby is born with enough vitamin D for early infancy.

Prevention of vitamin D deficiency and insufficiency

It is important that people who find it hard to get enough vitamin D from the sun and their diet take a vitamin D supplement. Specific groups who may benefit from vitamin D supplementation are listed in the table below (Department of Health recommendations):

People at risk of vitamin D deficiency	**Daily vitamin D supplement**
All pregnant and breastfeeding women	400 International Units (10 micrograms) / day
People who are not exposed to much sun (e.g., people confined indoors for long periods and those who cover their skin for cultural reasons)	400 International Units (10 micrograms) / day
People aged 65 years and over (see elderly patients section)	400 International Units (10 micrograms) / day

Patients can be advised to buy over the counter vitamin D supplements or signposted to Healthy Start Clinics where Healthy Start Women's vitamins are available. These contain folic acid 400 micrograms, vitamin D 10 micrograms [400 International Units] and vitamin C 70 mg, and are suitable for vegetarians, free from milk, egg, gluten, soya and peanut residues. For more details of the scheme see:
www.healthystart.nhs.uk

Clinical features of vitamin D deficiency

- Muscle pain
- Proximal muscle weakness
- Rib, hip, pelvis, thigh and foot pain are typical
- Fractures

Prevention of vitamin D deficiency and insufficiency

Assessing the patient

Patient characteristics	Advice and management
Healthy, no risk factors, symptom free	No investigations required Lifestyle advice
Risk factors only	Lifestyle advice Consider long term preventative therapies
Risk factors AND clinical features	Lifestyle advice Investigations Therapeutic intervention Long term preventative treatment

Investigations

Test	Reason
Renal function tests (U&E, eGFR)	To exclude renal failure. See note below on renal patients.
Liver function tests (including ALP)	To exclude hepatic failure
FBC	Anaemia may be present if there is malabsorption.
PTH	To exclude primary hyperparathyroidism.
Calcium	To exclude hypercalcaemia and provide a baseline for monitoring. Hypocalcaemia may indicate long standing vitamin D deficiency.
Phosphate	Hypophosphataemia may indicate long standing vitamin D deficiency.
25-OH Vitamin D levels*	To determine vitamin D status

* Only measure if patient is symptomatic and has risk factors for Vitamin D deficiency.

Prevention of vitamin D deficiency and insufficiency

Measurement, status and management

Vitamin D level	Vitamin D status	Health effect	Management
<30 nmol/L	Deficient	Rickets, Osteomalacia	High dose cholecalciferol then maintenance treatment
30-50 nmol/L	Insufficient	Associated with disease risk	Maintenance vitamin D supplements
50-75 nmol/L	Adequate	Healthy	Lifestyle advice
>75 nmol/L	Optimal	Healthy	None

Primary Care Only - Diagnosis and coding

If deficiency diagnosed use the Read code C28 Vitamin D deficiency (for audit purposes)

Contraindications for vitamin D

Patients with hypercalcaemia or metastatic calcification.

When to refer to secondary care

Atypical biochemistry Renal stones
Atypical clinical manifestations or biochemistry Sarcoidosis
Deficiency due to malabsorption Short stature and skeletal deformity
Failure to respond to treatment after 3 months Tuberculosis
Focal bone pain Unexplained deficiency
Liver disease Unexplained weight loss
Lymphoma Parathyroid disorders
Metastatic cancer

Prevention of vitamin D deficiency and insufficiency

Treatment regimes

1. Treatment of deficiency (25-OHD <30 nmol/L) - loading regime of colecalciferol followed by long term maintenance treatment

Used where rapid correction of vitamin D deficiency is required, e.g., symptomatic disease or before starting treatment with a potent antiresorptive agent (zoledronic acid, denosumab).

	Colecalciferol dose – licensed products only	Route	Length of course	Total loading dose	Preparation
First line	40,000 International Units, weekly (two capsules)	Oral	7 weeks	280,000 International Units	Colecalciferol 20,000 International Unit capsules (preferably after food)
First line	50,000 International Units, weekly (one 1ml plastic snap & squeeze ampoule)	Oral	6 weeks	300,000 International Units	Colecalciferol oral solution 50,000 International Units /ml
Second line - option for patients with compliance issues	3,200 International Units, daily (one capsule daily)	Oral	12-13 weeks	280,000 International Units	Colecalciferol 3,200 International Unit capsule

Prevention of vitamin D deficiency and insufficiency

2. Treatment of insufficiency (25-OHD: 30-50 nmol/L) or long term maintenance after deficiency

	Colecalciferol dose – licensed products only	Route	Total loading dose	Preparation
First line	20,000 International Units, every four weeks	Oral	Indefinite	Colecalciferol 20,000 International Unit capsules (preferably after food)
First line	25,000 International Units, (one 1ml plastic snap & squeeze ampoule)	Oral	Indefinite	Colecalciferol oral solution 25,000 International Units /ml
Second line - option for patients with compliance issues	800 – 2000 International Units, daily (occasionally up to 4,000 International Units daily)	Oral	Indefinite	Colecalciferol 800 International Unit capsule OR advise to purchase over the counter vitamin D treatments

A wide range of vitamin D preparations, in varying strengths are available to buy over the counter from pharmacies and health food shops. For patients not exempt from prescription charges these supplements are generally less expensive to purchase than to obtain on prescription. These products do not have a UK marketing authorisation and are marketed as nutritional supplements.

When prescribing please ensure that licensed products are used. For Primary Care - please follow advice provided by ScriptSwitch as recommendations are reviewed and amended periodically, indicating the most cost effective licensed products.

Prevention of vitamin D deficiency and insufficiency

Special patient groups

Elderly Patients

The elderly are at increased risk of vitamin D deficiency due to a combination of factors including lower sun exposure and reduced capacity to generate vitamin D. The joint formulary for the management of osteoporosis recommends that calcium and vitamin D supplements should be prescribed routinely for mobile frail, elderly individuals who are housebound or care home patients. The recommended daily dose is Calcium 1 – 1.2g and vitamin D3 800 International Units. Secondary care clinicians should prescribe the formulary choices as indicated on Cerner.

Primary care clinicians should follow ScriptSwitch messages to prescribe the most cost-effective brand.

Calcium and Vitamin D Preparations

Generally (apart from elderly patients, as above) clinicians should avoid giving combined calcium and vitamin D preparations in the long term because the calcium component is unnecessary and unpalatable, reducing concordance. There may be an increased risk of some cardiovascular events in postmenopausal women who use calcium and vitamin D supplements to prevent osteoporotic fractures but no change to prescribing practice is currently recommended.8 Prescribers should provide calcium and vitamin D treatment for osteoporotic fractures in line with NICE guidance and should consider offering these supplements to patients who receive treatment for osteoporosis (e.g., with bisphosphonates), unless they are confident that the patient has an adequate calcium intake and is vitamin D replete.

Renal Patients

Patients with CKD should have their native Vitamin D replaced as per these guidelines, the exception being when they are also taking Vitamin D analogues (such as alfacalcidol) and in end stage renal failure, where advice should be sought from a renal consultant regarding replacement and monitoring requirements.

For further information please see - NICE clinical guideline CG182 on chronic kidney disease, published in 2014, which advises on which vitamin D preparations should be used and when, according to the stage of renal impairment. Available at http://www.nice.org.uk/guidance/CG182

Intestinal Malabsorption

Vitamin D deficiency caused by intestinal malabsorption or chronic liver disease usually requires vitamin D in pharmacological doses. A suggested regime for adult patients would be to use Ergocalciferol 300,000 IU by intramuscular injection, rechecking levels again after 3 months and repeating if required. Sometimes patients have been reversed at this stage so monthly injections for 3 months are not prescribed but repeat levels would always be checked before giving another injection.

Prevention of vitamin D deficiency and insufficiency

Patients on Anti-epileptic medication

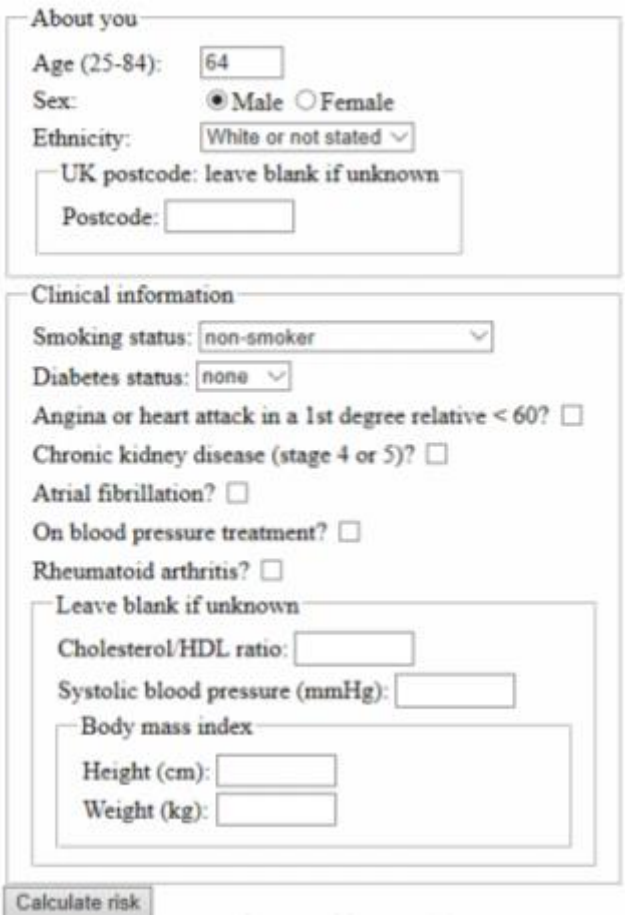
Long-term use of anti-epileptic drugs (in particular carbamazepine, phenytoin, phenobarbital, primidone and sodium valproate) is associated with decreased bone mineral density that may lead to osteopenia, osteoporosis, and increased fractures in at-risk patients. Vitamin D status should be assessed and patients treated according to their level (see Appendix 1). NICE clinical guideline CG137 on epilepsy, published in 2012, advises full blood count, electrolytes, liver enzymes, vitamin D levels, and other tests of bone metabolism (e.g., serum calcium and alkaline phosphatase) every 2–5 years for adults taking enzymeinducing drugs. Available at http://www.nice.org.uk/guidance/CG137

Other Drugs

In addition to anti-epileptic medication, there is an increased breakdown of vitamin D with other drugs including rifampicin, highly active antiretroviral treatment and glucocorticoids.

Qrisk2

- The QRISK®2 algorithm has been developed by doctors and academics
- Based on routinely collected data from many thousands of GPs across the country who have freely contributed data for medical research.
- Updated annually each April, refitted to the latest data to remain as accurate as possible.



To treat or not to treat….

- Qrisk >10% start on statins
- Qrisk < 10% diet/lifestyle advice
- Needs annual review
- Document….

Kidney Function

Sodium	135	145	mmol/L
Potassium	3.5	5.0	mmol/L
Urea	2.5	6.7	mmol/L
Creatinine	70	150	µmol/L
eGFR	>90		ml/min

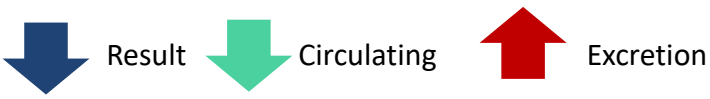
- Role
  - Electrolyte balance
  - Measure of kidney function
- Components?
  - Sodium (Na)
  - Potassium (K)
  - Urea
  - Creatinine/GFR

Sodium

- Physiology
  - Blood volume
  - Cell membrane reactions
- Pathology
  - Depends on how much water is circulating in plasma
  - Neurological and cardiac effects

Hypokalaemia

- High Potassium (K)



- ↓Excretion
    - Kidney failure
    - Diuretics – ACE-i, spironolactone
    - Addison's disease

- Low Potassium (K)
- ↓Circulating
    - Intestinal absorption disorders (rare)
- • K<2.5 – 999

Management:

- Admit if K+ <2.5
- Cushings syndrome/ steroids Renal tubular failure
- Consider oral potassium supplement if <3 (but poorly tolerated due to nausea)
- If >3 and on thiazidediuretic rarely needs treatment (Oxford GP Handbook)

Urea

- Physiology
- Waste product
- Broken down protiens

- ↑ Pathology
- ↓ Excretion

Kidney injury/failure

- Creatinine
  - ↑Rise
  - > 150 µmol/L
- GFR
  - ↓Fall
  - < 90 ml/min

Case Study

DR is a 72 year old man with a past history of: hypertension; an MI 3 years ago; COPD . He is a smoker and you notice he has a long list of medications. He came in as the receptionist said that his salt level was low. His U&Es were:

◦ Na 128	◦ K 4.8
◦ Creat 105	
(135-145)	(3.5-5.2)
(60-120)	

How would you manage this result?

_____

_____

You repeat the test a month later and his sodium is now 124. What further investigations would you like to arrange?

_____

_____

_____

_____

Case Study

You are the duty doctor at the surgery and a fax comes in from the biochemistry lab.
JF is a 60 year old diabetic who had routine blood test at the surgery:

- Na 137 (135-145)
- K 6.2 (3.5-5.2)
- Creat 122 (60-120)

What would you do?

_____
_____
_____
_____

Case Study

A few minutes later you receive another fax from the lab, results for BK, a 67 year old lady with heart failure who was seen last week with diarrhea and vomiting:

Na 132 (135-145)
K 2.4 (3.5-5.2)
Creat 70 (60-120)

What action would you take?

_____
_____
_____
_____

Case Study

A few minutes later you receive another fax from the lab, results for BK, a 67 year old lady with heart failure who was seen last week with diarrhea and vomiting:

Na 132	(135-145)
K 2.4	(3.5-5.2)
Creat 70	(60-120)

What action would you take?

_____
_____
_____
_____

- PB sees you again after some repeat tests.
- The second eGFR was 37, his creatinine was 142, and you also notice from his blood results that he was slightly anaemic (normocytic) with a haemoglobin of 12.3.
- His albumin/creatinine ratio on the urine sample was 32 mg/mmol.

What would you do in the consultation and what follow up would you arrange?

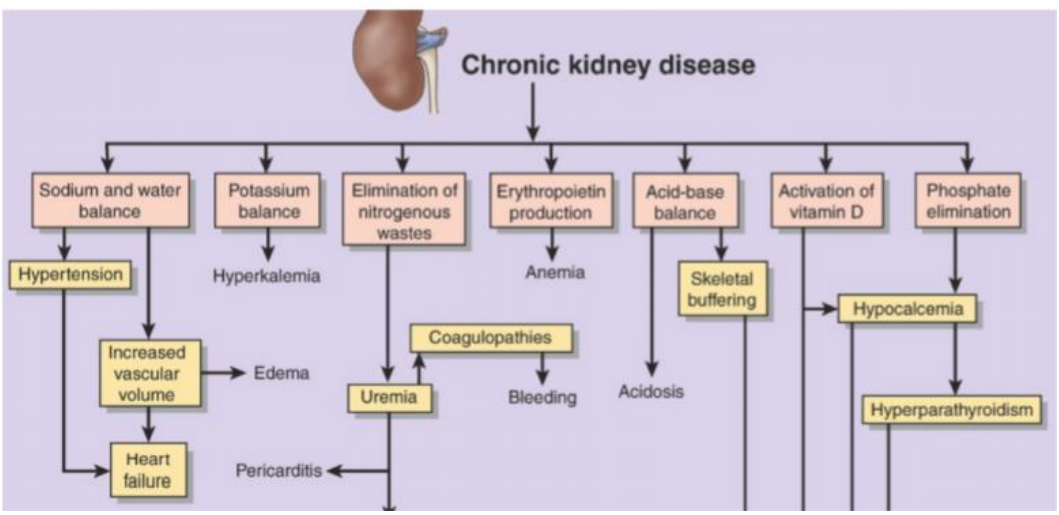
_____
_____
_____
_____

Chronic Kidney Disease

- DIAGNOSIS:
- At diagnosis: First eGFR <60 you should re- test within 2 weeks, and obtain an ACR, confirmed on an early morning ACR after first abnormal result (if not early morning sample)
- ACR >30 indicates proteinuria. In diabetics microabluminuria considered significant (ACR>2.5 in men, >3.5 in women)
- Test for haematuria using reagent strips. Investigate appropriately if persistent

Stages of CKD

Stage	Description	eGFR (mL/min)	Potential complications of reduced GFR (in alphabetical order)
1	Kidney damage with normal or ↑ GFR	≥90	• Anemia, including functional iron deficiency • Blood pressure increases • Calcium absorption decreases • Dyslipidemia /heart failure/volume overload • Hyperkalemia • Hyperparathyroidism • Hyperphosphatemia • Left ventricular hypertrophy • Metabolic acidosis
2	Kidney damage with mild ↓ GFR	60–89	
3	Moderate ↓ GFR	30–59	
4	Severe ↓ GFR	15–29	
5	Kidney failure	<15 or dialysis	



Chronic Kidney Disease

- Education and lifestyle advice
- Monitor progression (6 monthly in CKD stage
- Offer renal ultrasound in stage 3 CKD if:
    - Haematuria present
    - Progressive CKD (>5/year or >10/5 yrs)
    - FHx polycystic kidneys
    - Outflow obstruction
- Aim to keep BP <140/90 (<130/80 if diabetic and ACR >70)
- Check Hb in stage 3B (eGFR<45

- Diabetics:
    - Offer ACEi/ARB to all diabetics with microalbuminuria

- Non-diabetics:
    - Offer ACEi/ARB to patients with hypertension and

- ACR>30
    - Offer ACEi/ARB to all patients with ACR>70
    - Otherwise treat according to normal hypertension guidan

- Refer to a specialist for:
- Stage 4 and 5 CKD
- Higher levels of proteinuria (ACR ≥ 70 mg/mmol) unless known to be due to diabetes and already appropriately treated

Case Study

- 52 female
  - Weakness, fall
  - PMH: Hypertension

Sodium	126 mmol/L	(135-145)
Potassium	3.2 mmol/L	(3.5-5.5)
Urea	7.5 mmol/L	(70-150)
Creatinine	98 µmol/L	(70-150)

Case Study

Diagnosis?

Hyponatraemia

Diuretics

Further tests?

Magnesium

Postural BP

Case Study

- 66 Male
  - PMH: Type 2 diabetes, hypertension

Sodium	126 mmol/L	(135-145)
Potassium	3.2 mmol/L	(3.5-5.5)
Urea	7.5 mmol/L	(70-150)
Creatinine	98 µmol/L	(70-150)
eGFR	48ml/min	(>90)

- Diagnosis?
  - Renal impairment
  - Diabetes

- Further tests?
  - HbA1C
  - Ultrasound
  - Bone profile

Diabetes

- Diabetes is diagnosed on the basis of history (ie polyuria, polydipsia and unexplained weight loss) PLUS
  - a random venous plasma glucose concentration >= 11.1 mmol/l
  - OR a fasting plasma glucose concentration >= 7.0 mmol/l
  - OR 2 hour plasma glucose concentration >= 11.1 mmol/l 2 hours after 75g anhydrous glucose in an oral glucose tolerance test (OGTT)

- In the absence of symptoms 2 results from different days are required

Impaired fasting glycaemia

- Fasting plasma glucose >=6.1 but <7.0 mmol/L
- British Dietetic Association recommends all should have glucose tolerance test
- 2.2% relative annual risk progression to diabetes (?higher), remember gestational.
- Manage risk factors and arrange annual follow up

Impaired fasting glycaemia

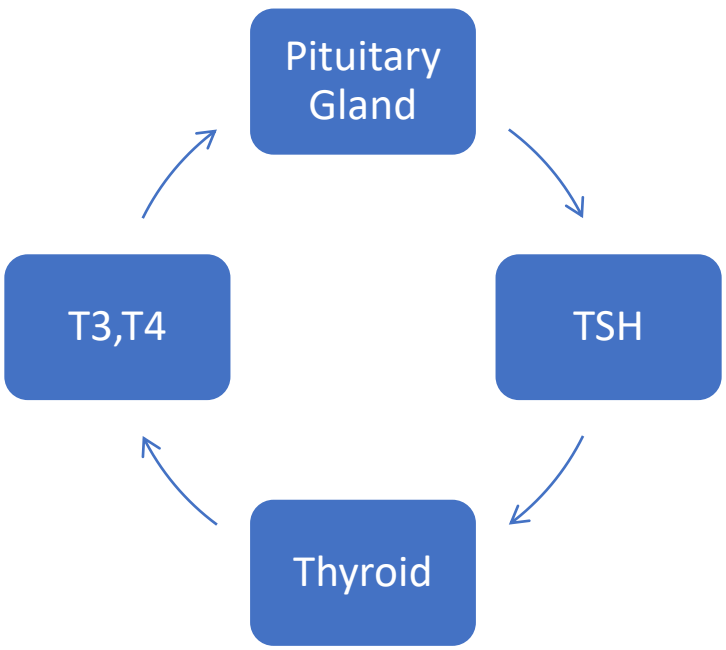
- Refined marker of sugar control over 3 months
- High risk of DM 42-48
- Diabetic 48+ on more than 1 reading
- Diabetic control should be 48-58
- Beware of variants

TFTs

- TSH (0.4 – 4 mU/L)
- Free T4 (9 – 25 pmol/L)
- Free T3 (3.5 – 7.8 nmol/L)

- Whilst free T3 (fT3) is measured, it is less relevant than free T4 (ft4),because the thyroid releases T4 and T3 at a ratio of about 20:1 respectively, with T3 mainly being produced by peripheral conversion of T4. As a result, T4 is a much better marker of thyroid function.
- Free T4 (fT4) is roughly 1% of the total T4, with the rest being bound to thyroid binding globulin.
- T4 has a half-life of about one week, therefore to monitor the impact of an intervention (e.g. increasing a patient's levothyroxine dose) you need to wait several weeks before repeating TFTs.

Thyroid Axis

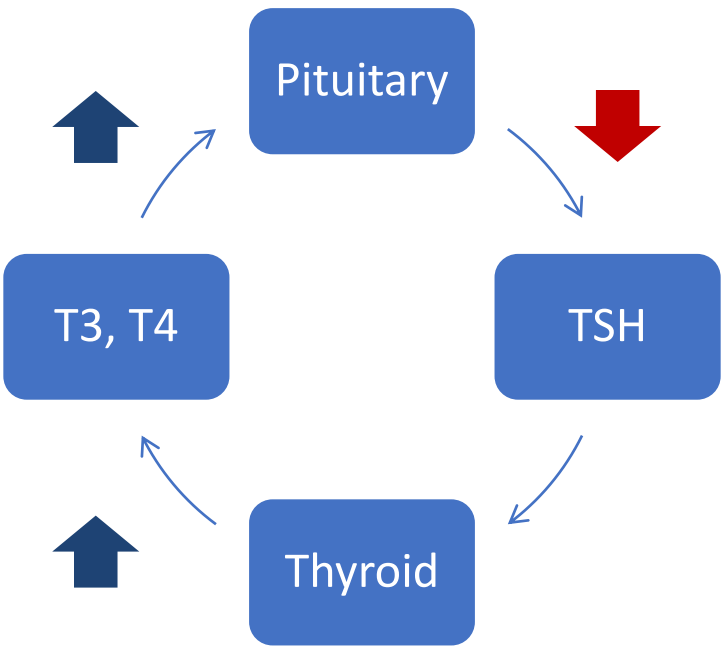


Thyroid Hormonal axis overview

- The paraventricular nuclei in the hypothalamus release thyroid releasing hormone (TRH).
- This causes thyrotrope cells in the anterior pituitary to release thyroid stimulating hormone (TSH).
- The thyroid responds to the TSH by releasing T4 and T3.
- T4 inhibits the pituitary and hypothalamus in a negative feedback loop. This is the 'brake system' which aims to maintain a state of homeostasis.

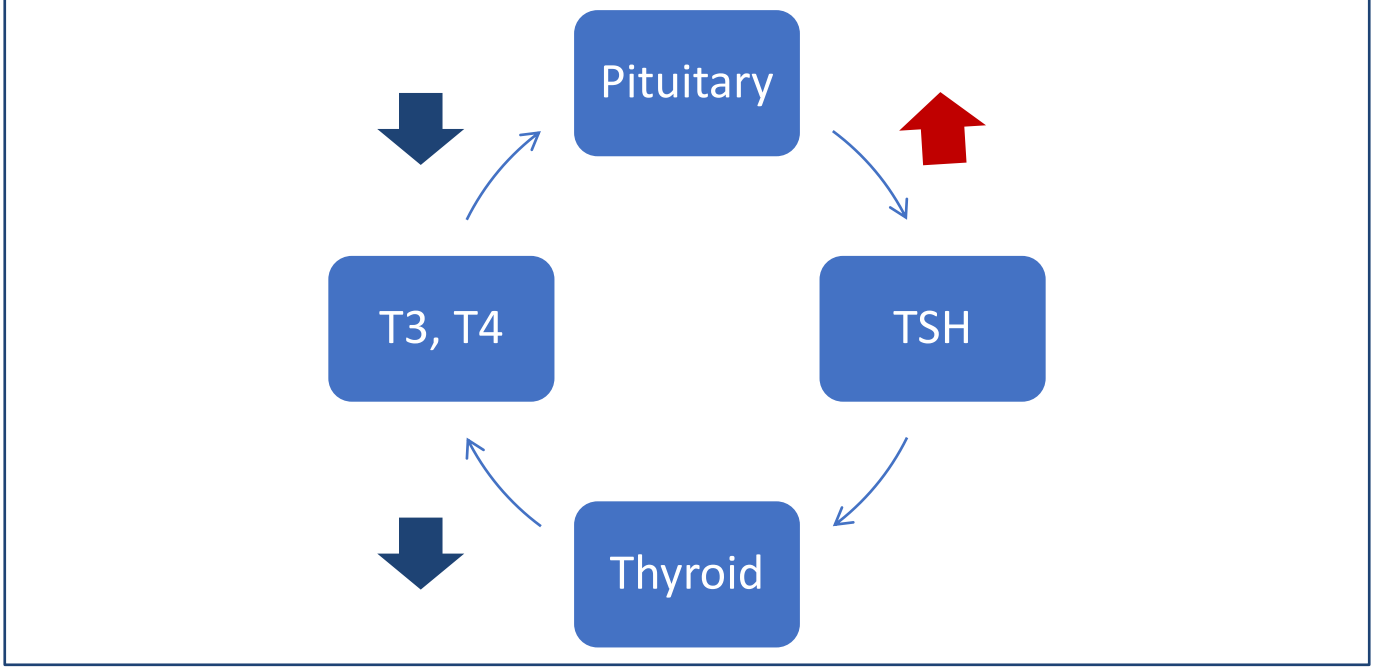
Hyperthyroidism

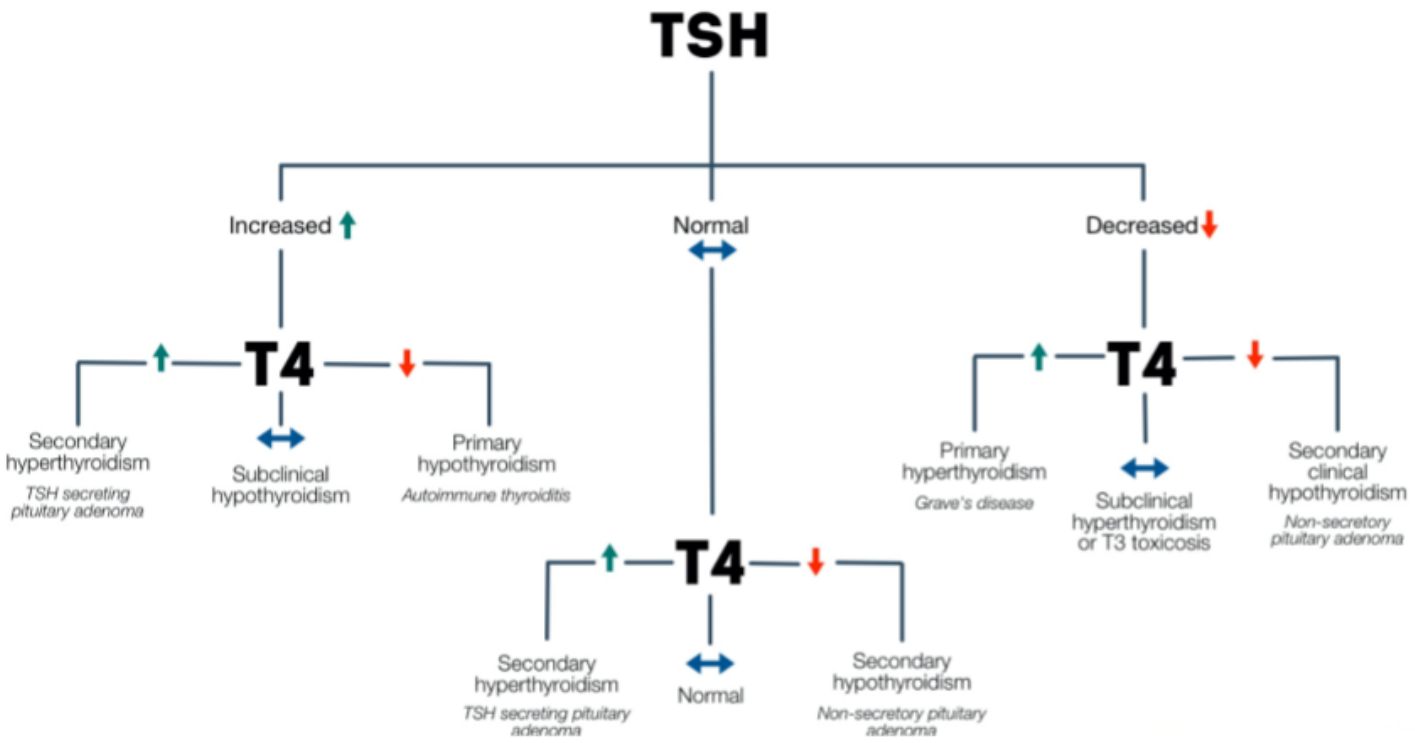
- Excess secretion of T3 & T4
- Negative feedback on pituitary gland
- Decreased production of TSH



- Reduced secretion of T3 & T4
- Reduced response to TSH
- Positive feedback on pituitary gland
- Increased production of TSH

Hyperthyroidism





HYPOTHYROIDISM GUIDELINES

Abnormal Thyroid Function Tests

TSH high	T4 normal	T3 normal	Subclinical hypothyroidism
TSH high	T4 low	T3 low or normal	Hypothyroidism
TSH low	T4 normal	T3 normal	Subclinical hyperthyroidism
TSH low	T4 high/normal	T3 high/normal	Hyperthyroidism (unless on T4 treatment)
TSH low	T4 low/normal	T3 low/normal	Non-thyroidal illness (rarely secondary hypothyroidism)

Thyroid dysfunction in pregnancy / postpartum

TSH

Pulsatile release, peaks during night
Takes 4-6wks for TSH to reflect circulating thyroid hormone levels

Abnormal TSH can persist for several months after achieving clinical euthyroid

Following thyroxine replacement wait 6-8wks before measuring TSH
After treating hyperthyroid wait 3mths

If on thyroxine treatment,
↓TSH, ↑T4 can also be:
Over replacement in 1° hypothyroidism

Expected in 2° hypothyroidism
(after surgery, radiotherapy) - discuss

British Thyroid Foundation Patient Information

Who to test

Symptoms? Suspected goitre?
AF, Dyslipidaemia, Osteoporosis,
Subfertility, Type 1 Diabetes

Check TFT annually:
Down / Turner syndrome
Previous postpartum thyroiditis
Previous neck irradiation

Healthy populations – no evidence for screening
Target case-finding in individuals with symptoms

NB Congenital hypothyroidism
Incidence 1:4000
Commonest treatable cause mental retardation
UK national screening programme but not done worldwide

Drugs affecting thyroid hormones:

Lithium ↓ 6mthly TSH

Amiodarone can ↑ or ↓ 6mthly TSH, T3, T4

Estrogens can ↓ T4 (by ↑TBG)
Androgens, Corticosteroids can ↑ T4 (↓TBG)
Methadone can ↑ T3,T4

Nodules & Multinodular Goitre

Patients with a thyroid nodule or a multinodular goitre who have normal TFTs may have thyroid cancer and must be referred to a specialist for further evaluation / consideration of FNA

Hypothyroidism

Prevalence 1-2%
10:1 female:male

Indications for T4 replacement	
Asymptomatic	TSH > 10
Symptomatic	TSH > 5
Pregnant /TTC	TSH >5
Goitre	TSH >5

TSH 5 - 10 | TSH > 10

No symptoms | Symptoms | FT4 Normal or Low

Subclinical hypothyroidism
Prevalence 1.3-17.5%
Asymptomatic
Normal T3,T4

Repeat 3 - 6mths after excluding non-thyroidal illness or drug effect

Treat if any cardiac disease, >60 or osteoporosis

Otherwise, could consider trial of treatment on individual patient basis

Check TPO Antibodies

TPO Antibodies Raised | TPO Antibodies Normal

5% per year become hypothyroid
Monitor TSH annually

Monitor TSH every 3 years

Treat with Levothyroxine

Start at 50-100mcg OD
then in 25-50mcg increments increasing every 3-4 weeks
Maintenance dose 100-200mcg OD

If older (eg. >50) or IHD consider commencing at 25mcg OD to avoid cardiac complications
Maintenance dose 50-200mcg OD

Titrate Levothyroxine against TSH whilst assessing clinical wellbeing
Monitor TSH & FT4 every 8wks until within reference range
(FT4 may be slightly above ref range)

Then annually or if develops symptoms

Symptoms non-specific
Dry skin
Brittle hair
Weight gain
Tiredness
Constipation
Muscle aches
Bradycardia
Cold intolerance
Depression
Memory Loss
Menorrhagia
Hoarseness

Results in hypothyroidism

↑TSH, ↓fT4
TPO Antibody -/+

↓B12 so ↑MCV
↑LDL, Cholesterol
↓Na

Causes of Hypothyroidism
99% Primary, <1% deficiency
Chronic autoimmune
Eg. Hashimoto's thyroiditis
Most common, Goitre,
Anti TPO abs 90%,
Anti thyroglobulin abs 20-55%

Destructive treatment for hyperthyroidism

Postpartum

Secondary hypothyroidism
Low T4
TSH low, normal or slightly raised

Refer these patients

Can differentiate from non-thyroid causes by history, TSH/FT4/FT3 + other anterior pituitary tests

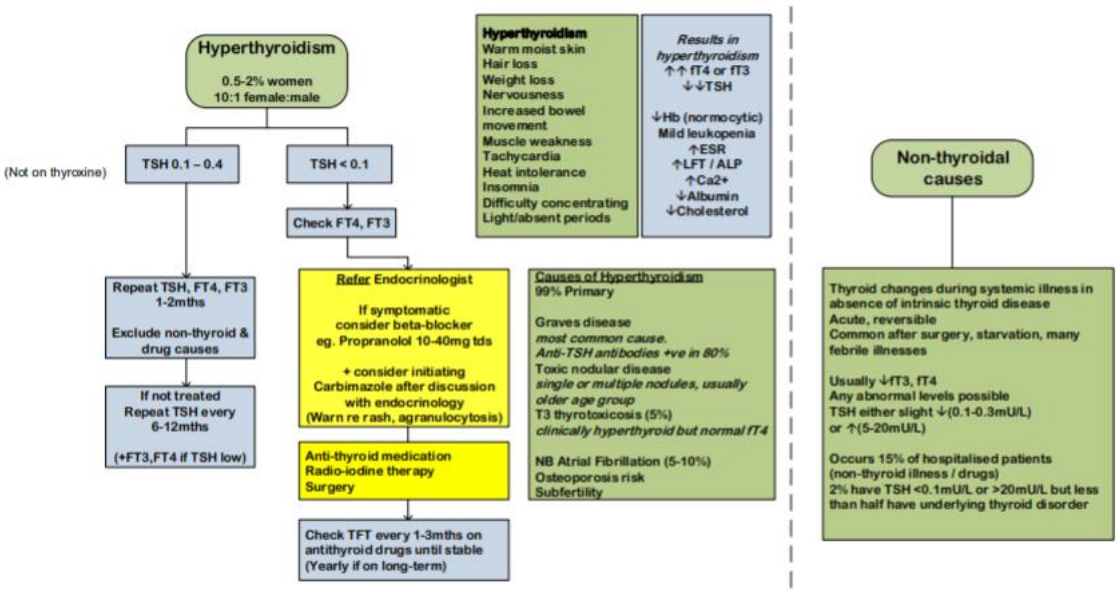
9am cortisol needs to be >200nmol/l before thyroxine replacement

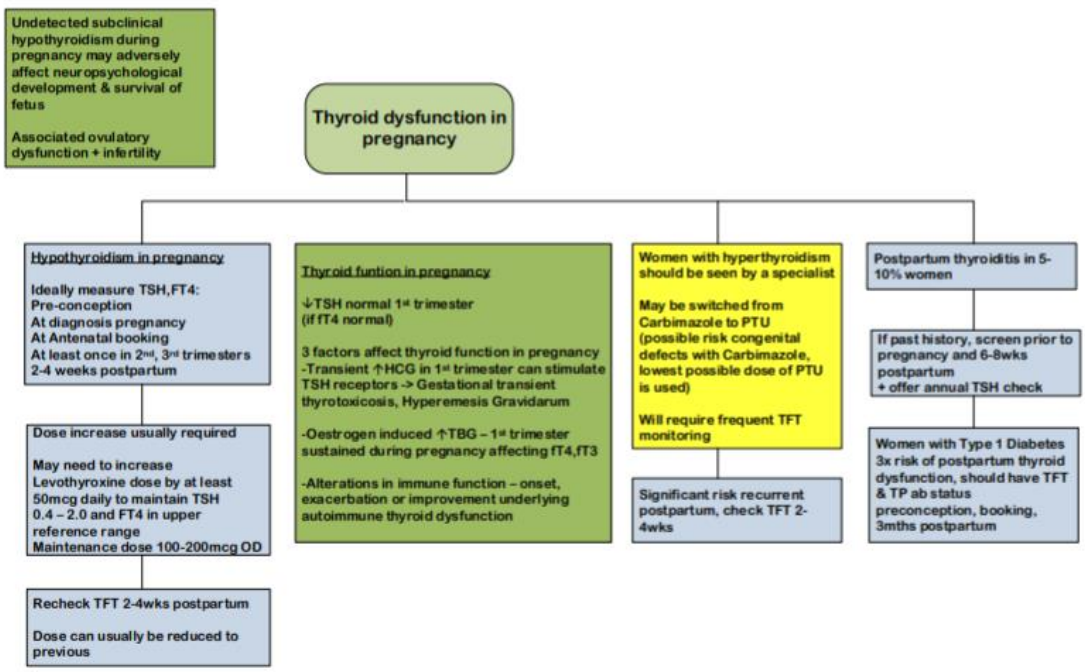
Hypothyroidism - Who to refer?

Unresponsive to therapy
TSH not in normal range despite ≥ 200mcg of Levothyroxine *and* compliant with treatment,
or Symptoms continue despite apparently adequate thyroid replacement

Age under 16yrs, Pregnant or postpartum
Undergoing fertility investigation / treatment
Presence of nodular goitre, Other pituitary disease,
Others where specialist input on management helpful
Eg. IHD, drug treatment with Amiodarone, Lithium

HYPERTHYROIDISM GUIDANCE





Case Study

- 35 Male
  - Anxious
  - Palpitations
  - Tremor

TSH	<0.01 mU/L	(0.4-4.5)
T4	55 pmol/L	(10-24)

- Diagnosis?
  - Primary hyperthyroidism (Grave's disease)
- Further tests?
  - ECG

Case Study

- 66 Female
  - Tired
  - Cold
  - Confusion

TSH	<10.2 mU/L	(0.4-4.5)
T4	8.9 pmol/L	(10-24)

- Diagnosis?
  - Primary hypothyroidism (Autoimmune thyroiditis)
- Further tests?
  - Immune screen

Prostate Specific Antigen

When you have a PSA test, you should not have:

- An active urine infection.
- Produced semen during sex or masturbation (ejaculated) in the previous 48 hours.
- Exercised heavily in the previous 48 hours.
- Had a prostate biopsy in the previous six weeks.
- Had an examination of the back passage with a gloved finger (a digital rectal examination) in the previous week.
- Gay, bisexual, and other men who have sex with men should avoid receptive anal intercourse for 48 hours before a PSA test.
- Each of these may produce an unusually high PSA result

PSA Cut off Values	
Age (years)	**PSA Cut-off**
40-49	2.0 nanogram/mL or higher
50-59	3.0 nanogram/mL or higher
60-69	4.0 nanogram/mL or higher
70 or older	5.0 nanogram/mL or higher
There are no age-specific reference limits for men older than 80 years of age.	

- **If your PSA level is not raised**
- You are unlikely to have cancer. No immediate further action is needed but you may need further tests to confirm the result.
- **If your PSA level is slightly raised**
- You probably do not have cancer. You might need further tests, including more PSA tests.
- **If your PSA level is definitely raised**
- Your GP will refer you to see a doctor who is a specialist for you to have further tests to find out if you have prostate cancer.

Prostate Specific Antigen

- The higher the level of PSA, the more likely it is to be a sign of cancer.
- The PSA test can also miss cancer.
- ~ 15 /100 men who have prostate cancer will have had a normal PSA level.
- A one-off test is not reliable and repeating the test may provide important information.

PSA dilemma

- • Around 2/3 of men with a raised PSA do not have prostate cancer
- • One study found 1 in 6 men with a ‘normal’ PSA may have prostate cancer

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REFERENCES

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