

1st September, 2020

What do your blood test results mean?



Associate Professor Louis Roller



MONASH University
Pharmacy and Pharmaceutical Sciences

When you visit a GP for regular visit, it may required that you have blood tests to set parameters.



Normal physiological values

The results of laboratory tests performed on body fluids such as blood and urine are commonly used to screen for and diagnose disease, assess disease severity

Laboratory tests are performed to:

- confirm a diagnosis
- investigate symptoms
- investigate a lack of response to therapy
- investigate a toxic effect of therapy
- confirm “nothing is wrong”
- Check doses if decreased renal & liver function
- Electrolytes ? hydration status?



Examples of common monitoring tests

1. Cholesterol
2. Blood glucose
3. Thyroid
4. Fluid and electrolytes 'U & Es' or 'EUCs'
5. Renal function tests
6. Liver function tests
7. FBE (full blood examination)
8. Specialised tests

Older people:

Is there really a need?

Will this help decision making?

Will this improve QOL?



Specialist Diagnostic Services Pty Ltd, ABN 64 007 190 043 APA No. 000042, trading as Dorevitch Pathology.

3000978729

PATIENT LAST NAME/ADDRESS: **Roller, Louis**
37 Seacombe Street,
Fitzroy North. 3068

GIVEN NAME: **M**
SEX: **M**
DATE OF BIRTH: **27/Feb/1940**
TEL (HOME): **94867765**
TEL (MOB): **0448572530**

TESTS REQUESTED:
LFT + UEC + UA + Ca + Ph, serum; Total Chol + Trigs + HDL and
LDL Chol, serum; Glucose - fasting, serum; HbA1c; CPK;
FBE, ESR; TSH

CLINICAL NOTES:
On Atorvastatin

TESTS REQUESTED (checkboxes):
Fasting ☐
Non-Fasting ☐
Pregnant ☐
Horm Therapy ☐
LMP ☐
EDC ☐
Cervical Screening ☐
Cervix ☐
Vagina ☐
Self Collect ☐
Post Natal ☐
RBC ☐
PCV/Hb ☐
Abnormal Bleeding ☐
Ca Suspicious ☐
Previous AG ☐
Radiotherapy ☐
Immune deficient ☐

URGENT ☐ PRIOR ☐ RUC 3 EXEMPTION ☐ RUC (Self Determined) ☐ Confidential Reports Required? ☐

DOCTOR TO SIGN: **Dr Andrew Pattison**
REQUEST DATE: **14/01/2019**

VET AFFAIRS No: **275 Cleveland St**
REQUESTING PRACTITIONER: **Dr Andrew Pattison**
3 Beauview Parade,
Ivanhoe East. 3079
Phone: 03 9499 3184
Provider Number: 0320862A

MEDICARE ASSIGNMENT (Section 204 of the Health Insurance Act 1973): **Patient to sign** ☒

Collector to sign: **Louis Roller**
27/Feb/1940

Specimen Collected: **Louis Roller**
27/Feb/1940

Drug - Last Dose: **Louis Roller**
27/Feb/1940

COMPLETE PATIENT NAME & DATE OF BIRTH PRIOR TO ATTACHING SPECIMEN. PLACE LABEL VERTICALLY IF MORE THAN 3 SPECIMENS PLEASE WRITE PATIENT DETAILS ON ADDITIONAL SPECIMENS

PATIENT LAST NAME: **Roller, Louis**

GIVEN NAME: **M**

PATIENT ADDRESS:

Roller, Louis

TESTS REQUESTED:

**37 Seacombe Street,
Fitzroy North. 3068**

3000978729

M

DATE OF BIRTH:

27/Feb/1940

TEL (HOME):

94867765

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0448572530

69533814

LFT + UEC + UA + Ca + Ph, serum; Total Chol + Trigs + HDL and LDL Chol,
serum; Glucose - fasting, serum; HbA1c; CPK; FBE, ESR; TSH

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Interpreting data

Individual results should be interpreted using the reference ranges of the laboratory performing.

clinical signs and symptoms

- baseline pathology results
- timing of sample collection (e.g. in relation to food, medication, exercise, season)
- characteristics that differ from those of the reference population
- current medications
- diet
- tobacco and alcohol use
- levels of physical activity.

Monitoring allows

- evaluation of the disease process
- detection of adverse effects
- therapeutic efficacy of drugs eg Anti CCP, CRP, ESR in rheumatoid arthritis & other inflammatory diseases
- iron studies in anaemia
- uric acid in gout
- FEV₁ in asthma or COPD
- adverse effects eg increased CK, decreased wcc, increased LFTs.
- suboptimal levels

Treat the person not the numbers !



How do you feel?



Angry



Scared



Sad



Happy



Frustrated



Anxious



Disappointed



Calm



Lady to the doctor over the phone, "Doctor, I beg of you, please prescribes me something immediately to reduce my weight. My husband has given me a wonderful birthday present, and I can't get into it."

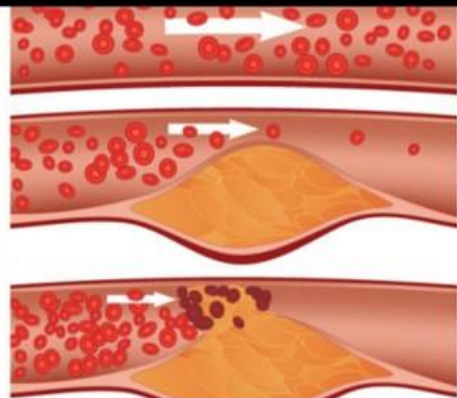
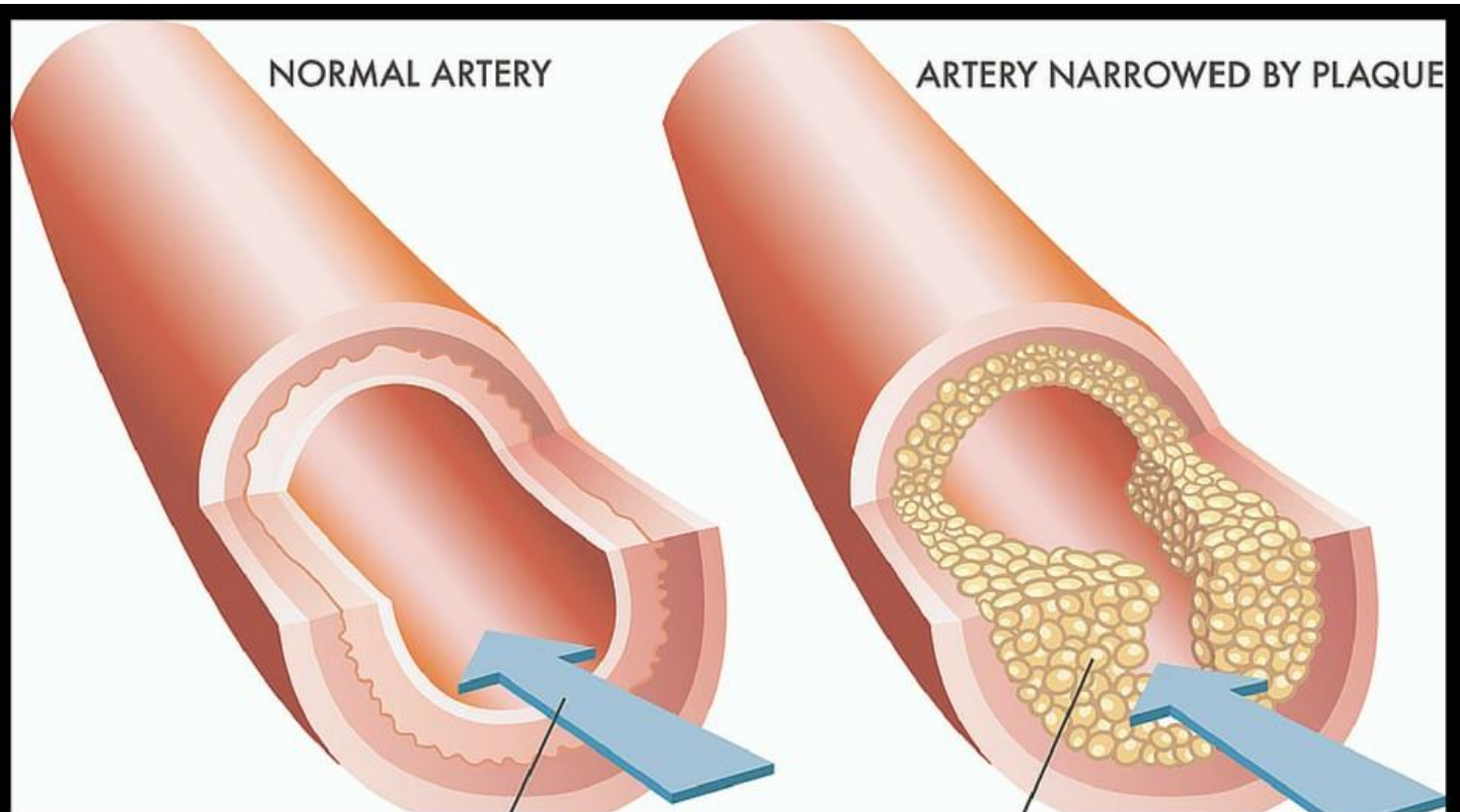
Doctor: "Just comes over here tomorrow, and I shall give you a prescription. Then you will soon be able to wear your wonderful new dress."

Lady: "Who said anything about a dress? I am talking of Car."

Interpreting laboratory data

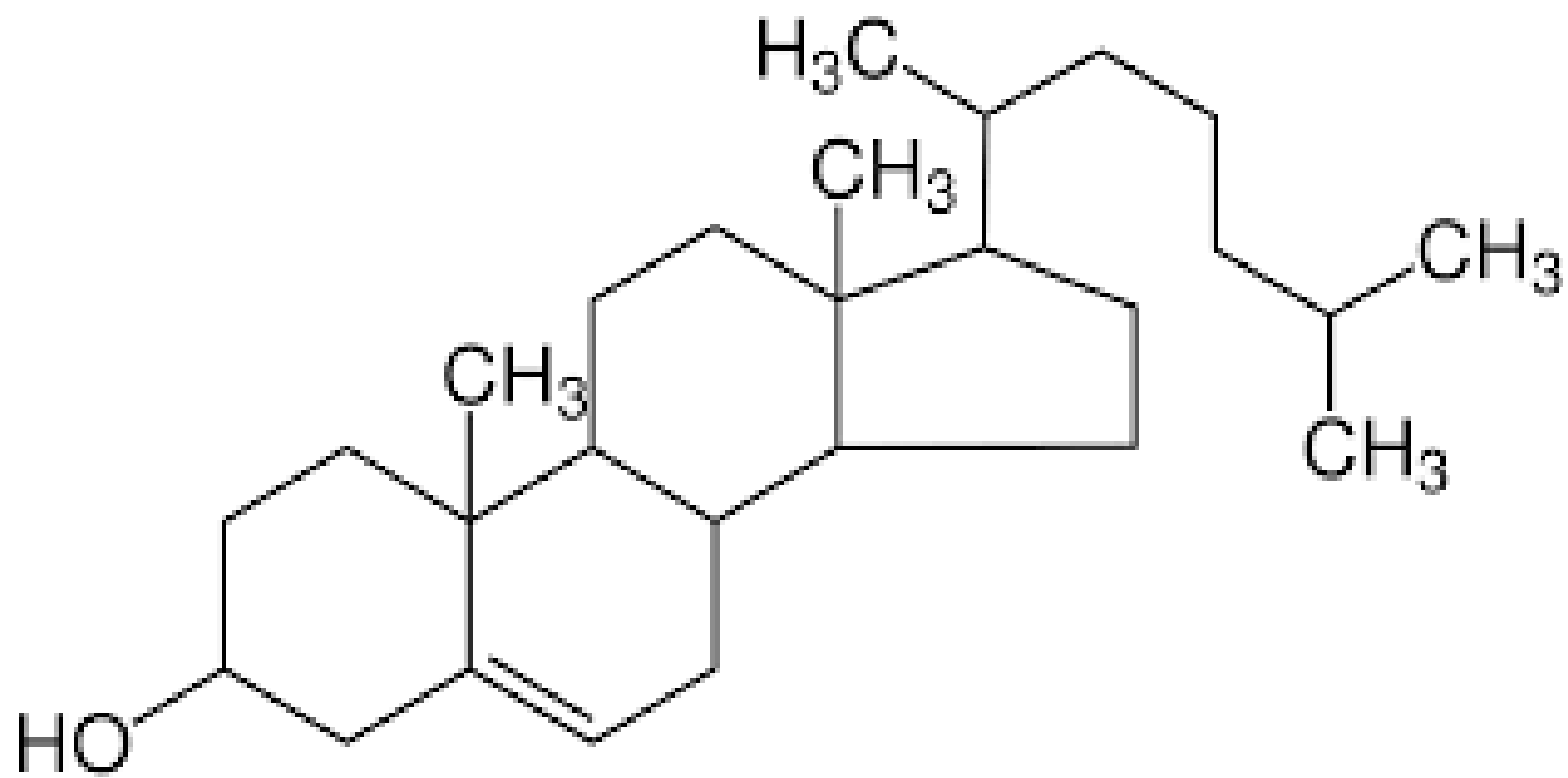
Individual results should be interpreted using the reference ranges of the laboratory performing the test. They should also be interpreted in the context of patient factors, including:

- clinical signs and symptoms
- baseline pathology results
- timing of sample collection (e.g. in relation to food, medication, exercise, season)
- characteristics that differ from those of the reference population
- current medications
- diet



High Cholesterol?

What can you do to change your levels?



1. Cholesterol



Total cholesterol- initial screening, fasting not required ($<5.5\text{mmol/L}$) : lower if CV concerns ie diabetes $<4\text{mmol/L}$. Stents $<3\text{mmol/L}$

Triglycerides- must fasting

○ ($0.3\text{--}2\text{mmol/L}$)

Lipoproteins- must fast

LDH ($<3.7\text{mmol/L}$)

HDL ($> 1.56\text{mmol/L}$)

Ratio (Total chol :HDL <3.5)



Should older people be on statins?
Risk vs benefit?

Lee JW, Choi EA , Kim YS. et al. Statin exposure and the risk of dementia in individuals with hypercholesterolaemia. Journal of Internal Medicine, 24th June, 2020.

This study aimed to examine the association between statin exposure and dementia risk in individuals with hypercholesterolaemia between 2002 and 2015.

During the follow-up period (median follow-up 11.7 years), 711 cases of dementia occurred, accounting for 11.5% of the total study population (N = 6,200) (statin exposure group, 8.2%; statin nonexposure group, 12.9%).

Compared to the statin nonexposure group HR ratios for overall dementia in the statin exposure group were 0.63 (0.43–0.91) and 0.62 (0.50–0.78) in men and women, respectively. Compared to the statin nonexposure group, the HRs for Alzheimer's disease and related dementia, vascular dementia and other types of dementia in the statin exposure group were 0.54 (0.32–0.91), 2.45 (0.69–8.68) and 0.59 (0.32–1.07), respectively, in men and 0.53 (0.38–0.73), 1.29 (0.42–3.96) and 0.70 (0.51–0.96), respectively, in women.

Conclusions: Hypercholesterolaemic individuals exposed to statin had a lower risk of overall dementia and Alzheimer's disease and related dementia in both sexes, and a lower risk of other types of dementia in women, than subjects who were not exposed to statins.

2. Glucose

Urine testing- screening

Plasma glucose

- Random testing (diabetes = $>11.1\text{mmol/L}$)
- Fasting ($3.8\text{-}5.8\text{ mmol/L}$)
- 2 hour postprandial ($<7.8\text{mmol/L}$)

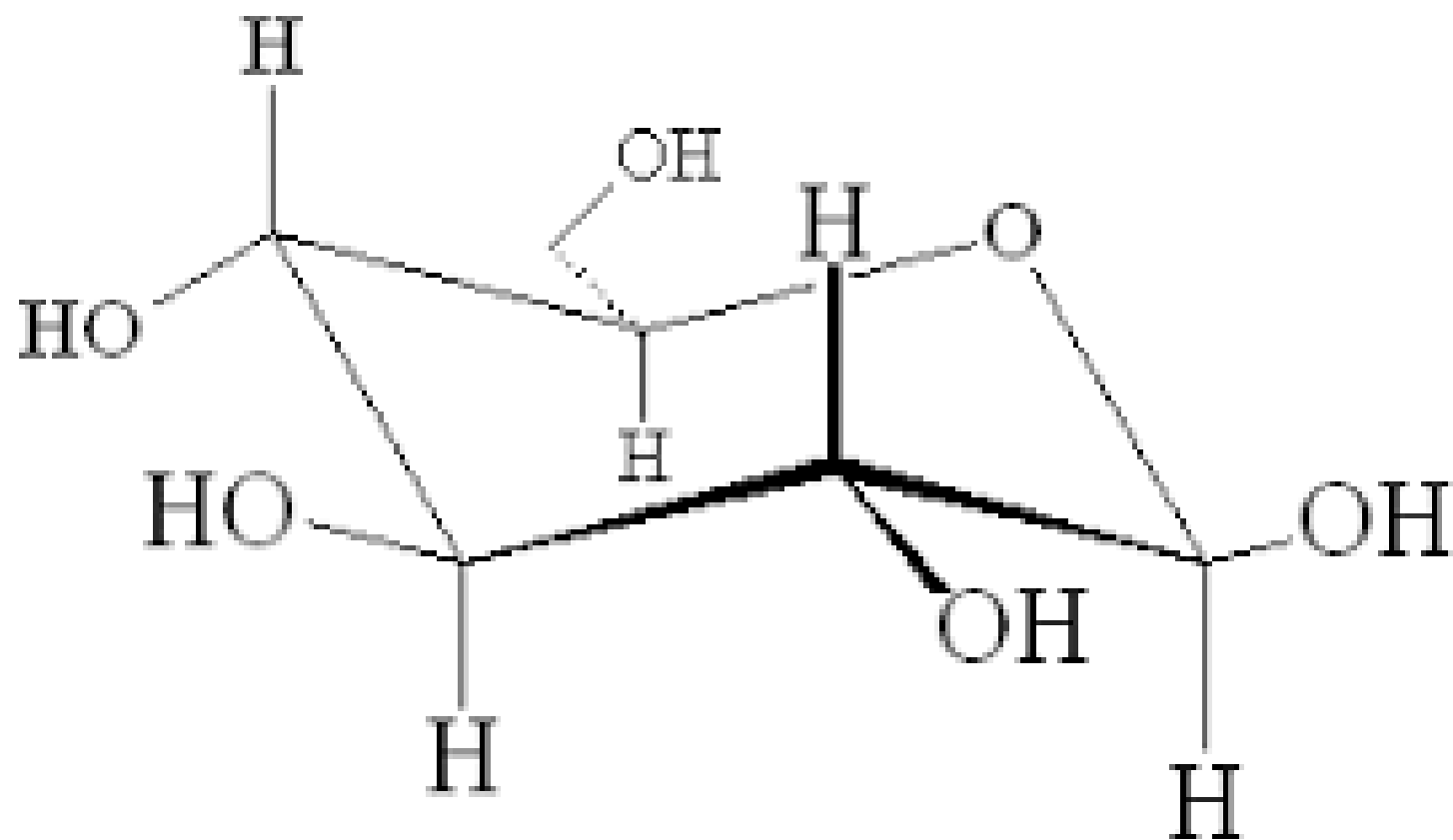
Glucose tolerance test

($>7.8\text{mmol/L}$ = IGT; $>11.1\text{mmol/L}$ = diabetes)



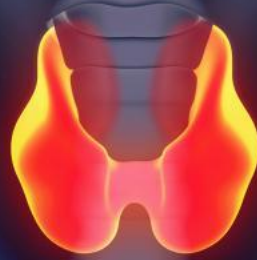
2. Glucose

- Main test now is Glycosylated haemoglobin : **HbA1c**
- Also called **glycated haemoglobin** (4.7-6.1% ; <7%)
- Listed as mmol HbA1c/mmmol haemoglobin <53mmol/mmol
- Shows last 2-3 months average
- Albumin- microalbuminuria- (UMA) measure of early reversible diabetic nephropathy





THYROID



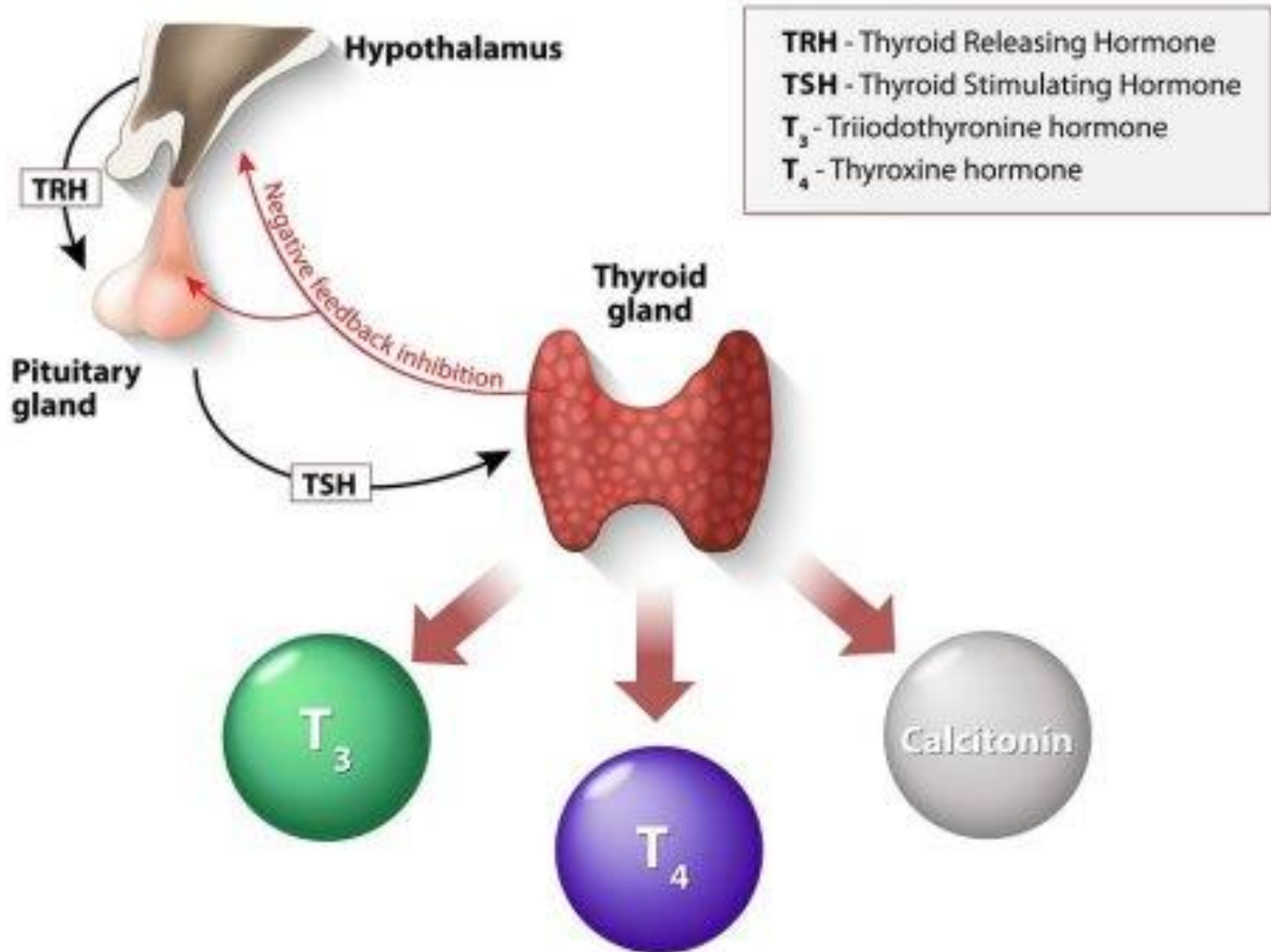
3. Thyroid function tests (TFT)

- Measure concentration of products secreted by the thyroid gland
- Free thyroxine (T4)
- Total serum thyroxine
- Total serum triiodothyronine (T3)

Evaluate the hypothalamic-pituitary thyroid axis

- Thyroid stimulating hormone (TSH)
- Thyrotropin releasing hormone
- NB: Care: amiodarone, lithium, iodine
- **Test TSH first then full TFTs if abnormal**
- **NB: If TSH is low then indicates hyperthyroidism**

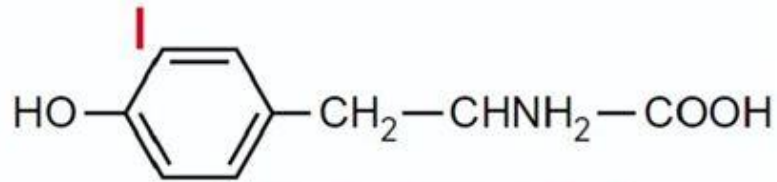
THYROID HORMONES



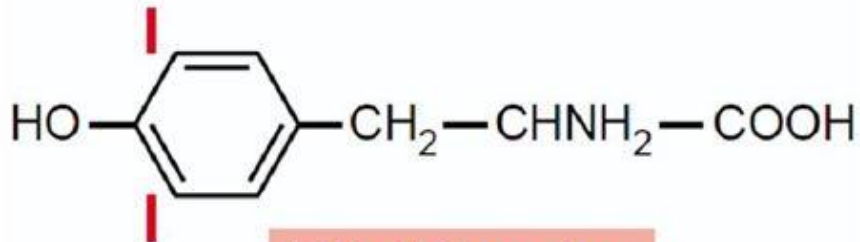
Signs and symptoms of thyroid disease

	Hypothyroidism (underactive thyroid)	Hyperthyroidism (overactive thyroid)
High suspicion	<ul style="list-style-type: none">•Goitre•Delayed reflexes	<ul style="list-style-type: none">•Goitre•Thyroid bruit•Lid lag•Bulging eye (Proptosis)
Intermediate suspicion	<ul style="list-style-type: none">•Fatigue•Weight gain/difficulty losing weight•Cold intolerance•Dry, rough, pale skin•Constipation•Family history•Hoarseness	<ul style="list-style-type: none">•Fatigue•Weight loss despite increased appetite•Heat intolerance/sweating•Fine tremor•Family history•Increased bowel movements•Fast heart rate/palpitations•Staring gaze
Low suspicion (non specific symptoms)	<ul style="list-style-type: none">•Coarse, dry hair•Hair loss•Muscle cramps/muscle aches•Depression•Irritability•Memory loss•Abnormal menstrual cycles•Decreased libido	<ul style="list-style-type: none">•Nervousness•Insomnia•Breathlessness•Light or absent menstrual periods•Weight loss•Muscle weakness•Warm moist skin•Hair loss

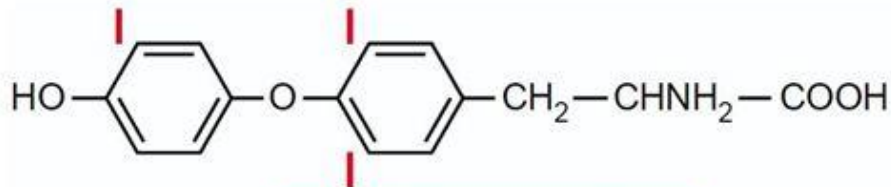
CHEMISTRY STRUCTURE OF THYROID HORMONES:



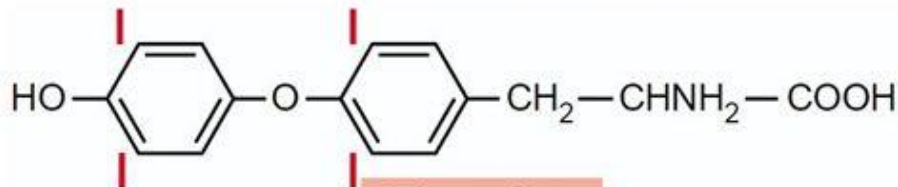
Monoiodotyrosine



Diiodotyrosine



3,5,3'-Triiodothyronine



Thyroxine

HYPERTHYROIDISM

Thyroiditis / Graves Disease

Bulging
Eyes

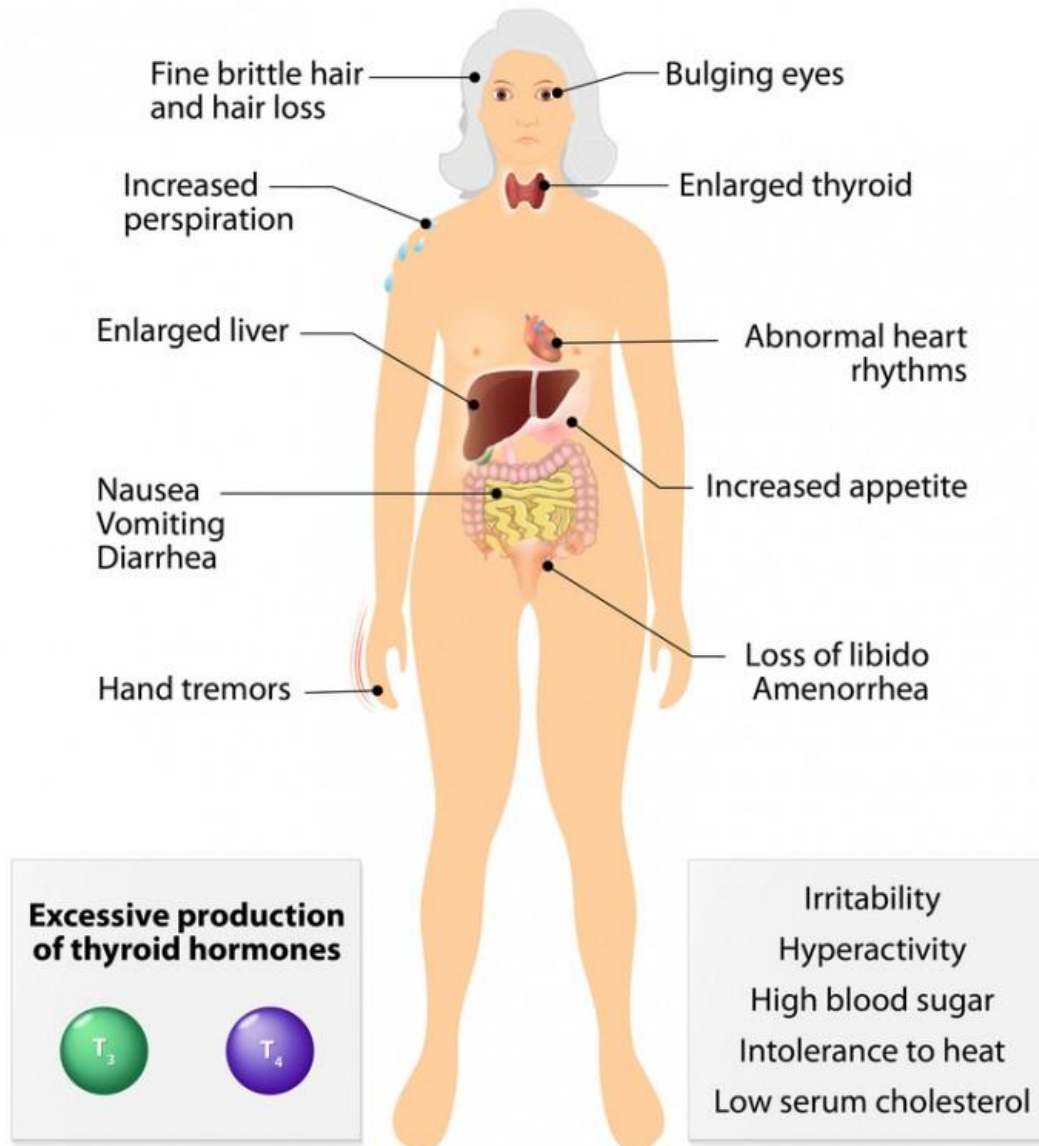
Goiter



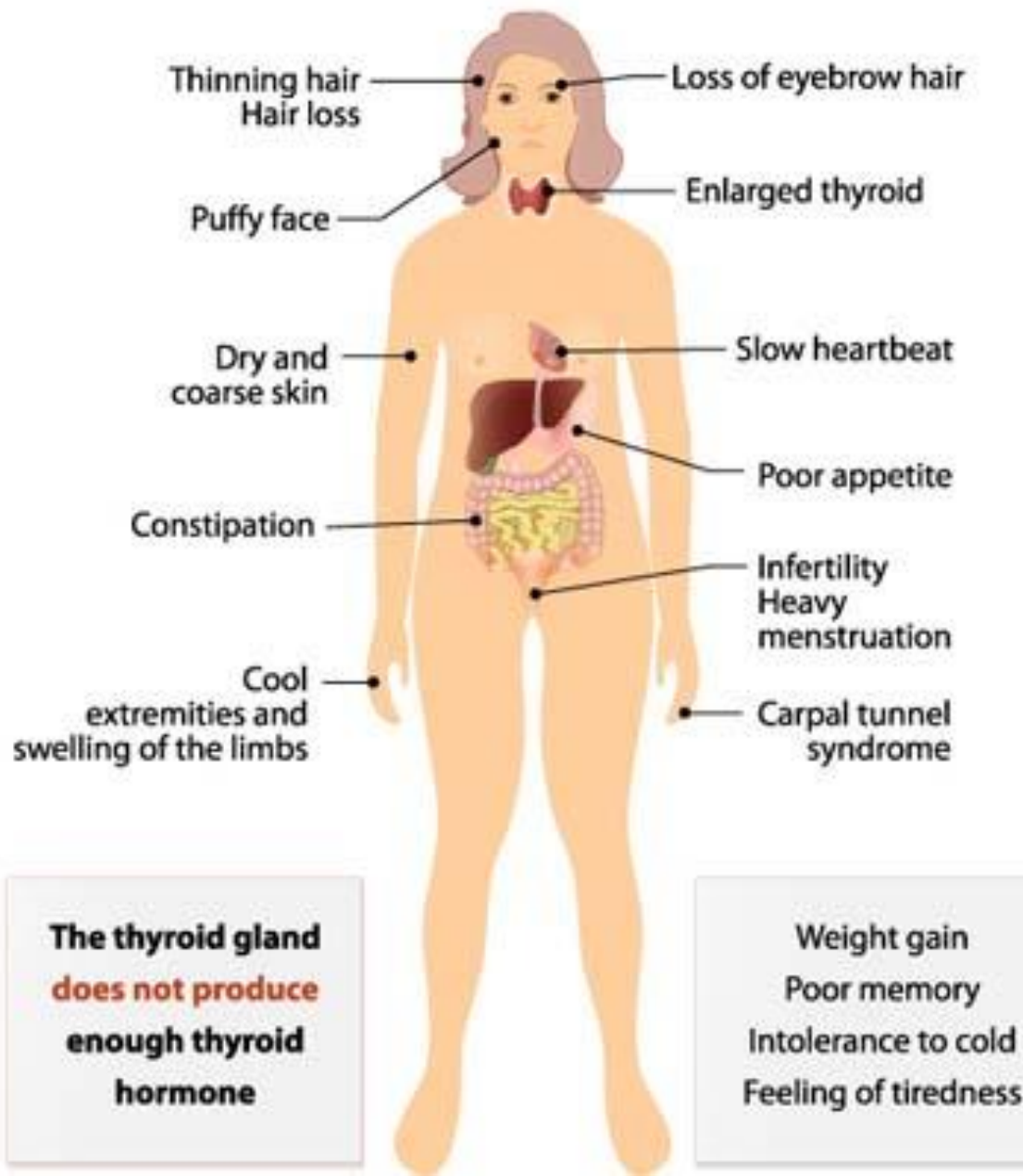
Enlarged
Thyroid



Symptoms of HYPERTHYROIDISM



Symptoms of HYPOTHYROIDISM

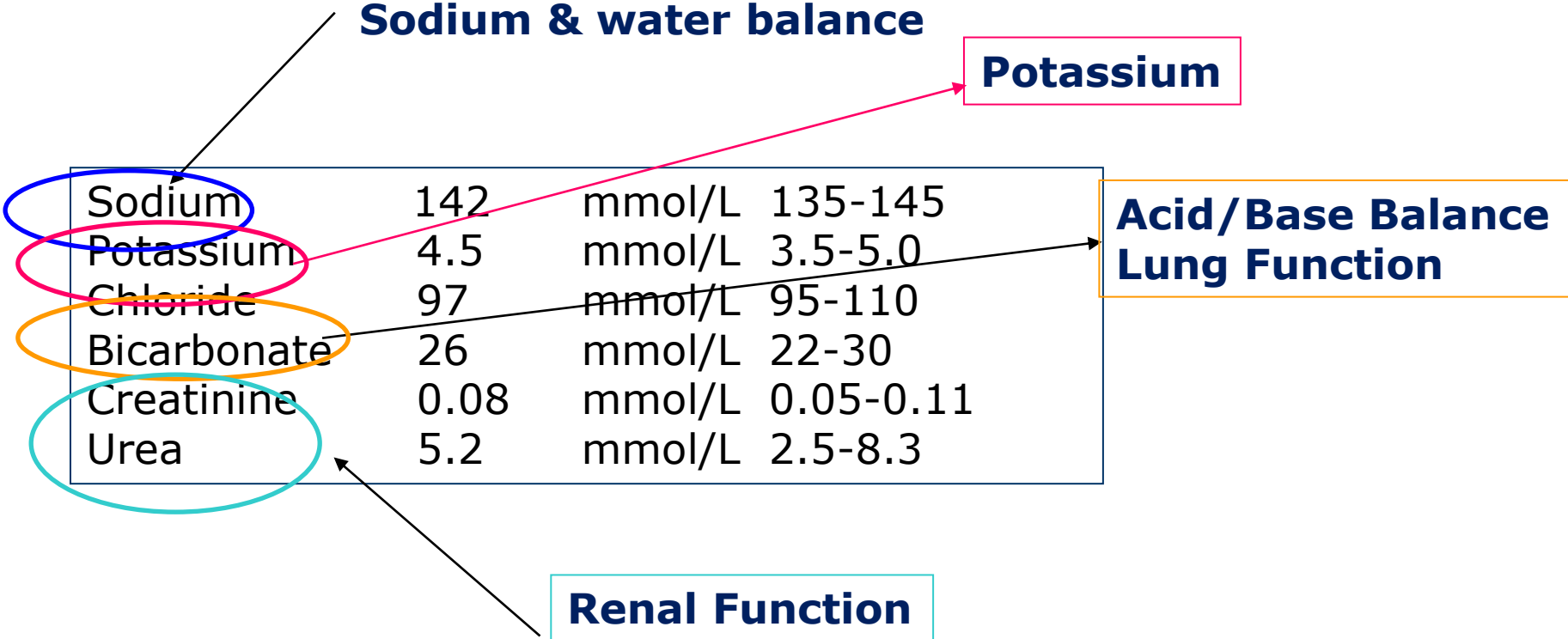


4. Urea & Electrolytes U & Es

Sodium & water balance

Potassium

**Acid/Base Balance
Lung Function**



Sodium	142	mmol/L	135-145
Potassium	4.5	mmol/L	3.5-5.0
Chloride	97	mmol/L	95-110
Bicarbonate	26	mmol/L	22-30
Creatinine	0.08	mmol/L	0.05-0.11
Urea	5.2	mmol/L	2.5-8.3

Renal Function

Sodium (Na): 135-145mmol/L

- Dilutional changes reflect the hydration status of the patient
- An acute change in serum Na may cause seizures

Hyponatraemia (<125mmol/L)

Symptoms: nausea, vomiting, dizziness, muscle weakness, lethargy, confusion, delirium, high mortality in older persons

Causes : many eg CCF; Drugs eg diuretics, SSRIs, carbamazepine

HypOnatremia

Sodium	127*	(135 - 145)	mmol/L
Potassium	3.3*	(3.7 - 5.3)	mmol/L
Chloride	90*	(95 - 110)	mmol/L
Bicarb	22	(20 - 32)	mmol/L
Urea	5.1	(3.0 - 9.0)	mmol/L
Creat.	0.08	(0.05 - 0.11)	mmol/L

Hyponatraemia due to diuretics + CCF

HypErnatraemia

(> 150mmol/L: symptoms at >160mmol/L)

Symptoms:

3% loss – thirst, lethargy, muscle weakness

6% loss - poor skin turgor, dry mucous membranes

10% loss- CNS signs, altered mental state, muscle twitching, convulsions, coma, death

Causes: Increased sodium intake

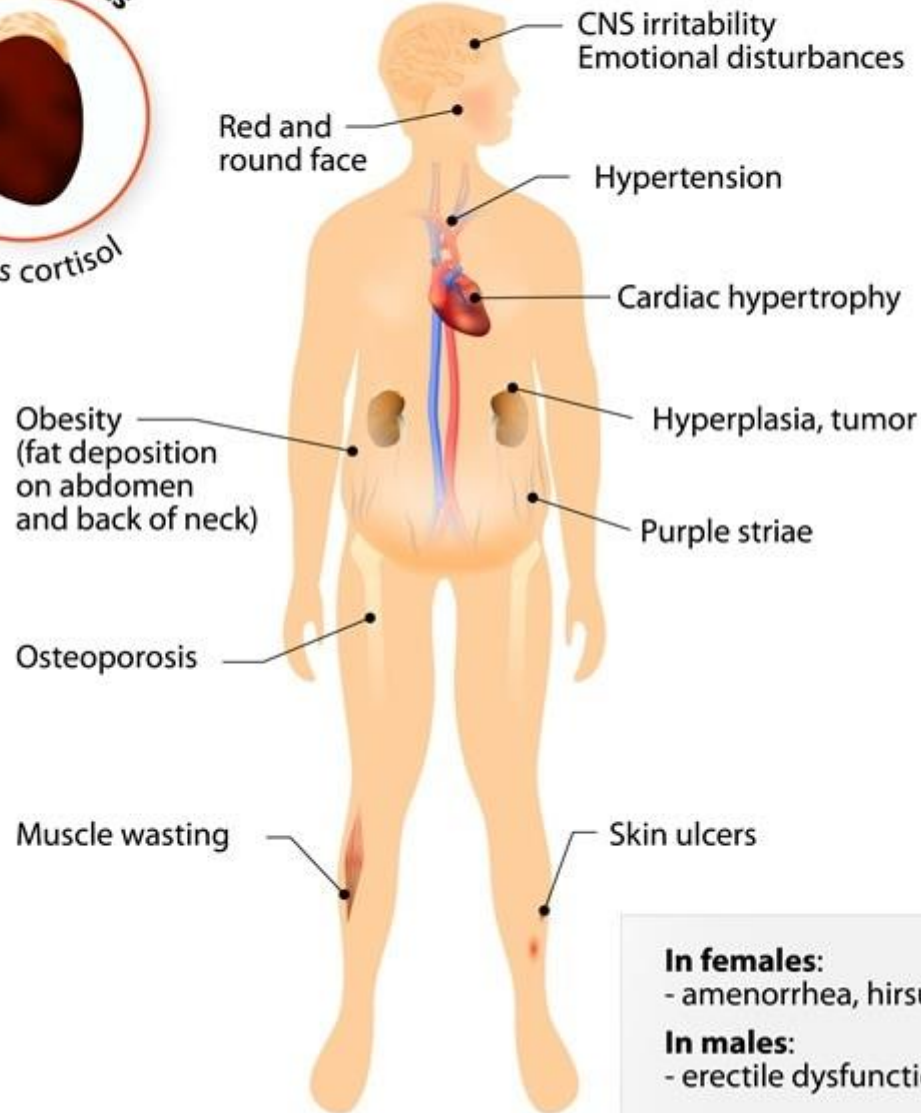
Drug eg diuretics, lithium, corticosteroids, NSAIDs

Decreased output eg increased aldosterone activity
eg. Cushing's syndrome

Water depletion: Dehydration, excess sweating, drugs, febrile illness, diabetes mellitus, gastrointestinal bleed, burns, diarrhoea, vomiting, parenteral nutrition, diabetes insipidus
from pure water loss > *Water loss > sodium loss & low water intake*

SYMPTOMS

of Cushing's syndrome



In females:

- amenorrhea, hirsutism

In males:

- erectile dysfunction

POTASSIUM

Potassium is a chemical element with symbol K and atomic number 19. It was first isolated from potash, the ashes of plants, from which its name derives. In the periodic table, potassium is one of the alkali metals.

Symbol: K

Atomic mass: 39.0983 u

Atomic number: 19

Electron configuration: [Ar] 4s¹

Melting point 63.5 °C



Potassium (3.5-5.0 mmol/L)

Hypokalaemia *Symptoms:*

- Muscle weakness, cramps to paralysis
- Fatigue & apathy
- Cardiac arrhythmia & arrest
- Hypotension
- Polyuria
- ECG changes
- Increased sensitivity to digitalis.

Causes: GIT loss eg diarrhoea, chronic laxative use/abuse; renal loss, alkalosis

Drugs eg diuretics, nebulised salbutamol, insulin, laxatives

Hyperkalaemia > 5.5mmol/L

Symptoms:

- Listless, mental confusion
- muscle weakness- myalgia, paraesthesia
- Nausea & vomiting
- Paralytic ileus
- cardiac arrhythmia & arrest, ECG changes,

Causes:

- renal failure, hyperparathyroidism, tissue damage, acidosis, drug-induced eg **spironolactone**, eplerenone. ACEI ARB, amiloride,

Hyperkalemia

Sodium	140	(135 - 145) mmol/L
Potassium	6.5*	(3.7 - 5.3) mmol/L
Chloride	99	(95 - 110) mmol/L
Bicarb	21	(20 - 32) mmol/L
Urea	2.7	(3.0 - 9.0) mmol/L
Creat.	0.08	(0.05 - 0.11)mmol/L

***Hyperkalemia due to spironolactone + K supplements**

Bicarbonate



Decreased

Metabolic Acidosis eg renal failure , diabetes

Increased

Respiratory acidosis eg COPD (as compensation)

Metabolic alkalosis eg prolonged vomiting

Magnesium (Mg) 0.7-0.95mmol/L

Hypomagnesaemia

Symptoms: Muscle weakness, confusion, cardiac arrhythmias - prolongation of QT, risk of ventricular arrhythmias

Implicated in causing: ischaemic heart disease, hypertension, glucose intolerance, non-insulin dependent diabetes mellitus, osteoporosis, stroke?,

Hypermagnesia

Causes: Drug-induced eg laxatives, mineral supplements, antacids

NB As phosphate levels fall Mg levels fall

Calcium (Ca) 2.2-2.6 mmol/L

Only about 0.0005% of body calcium is found in the serum

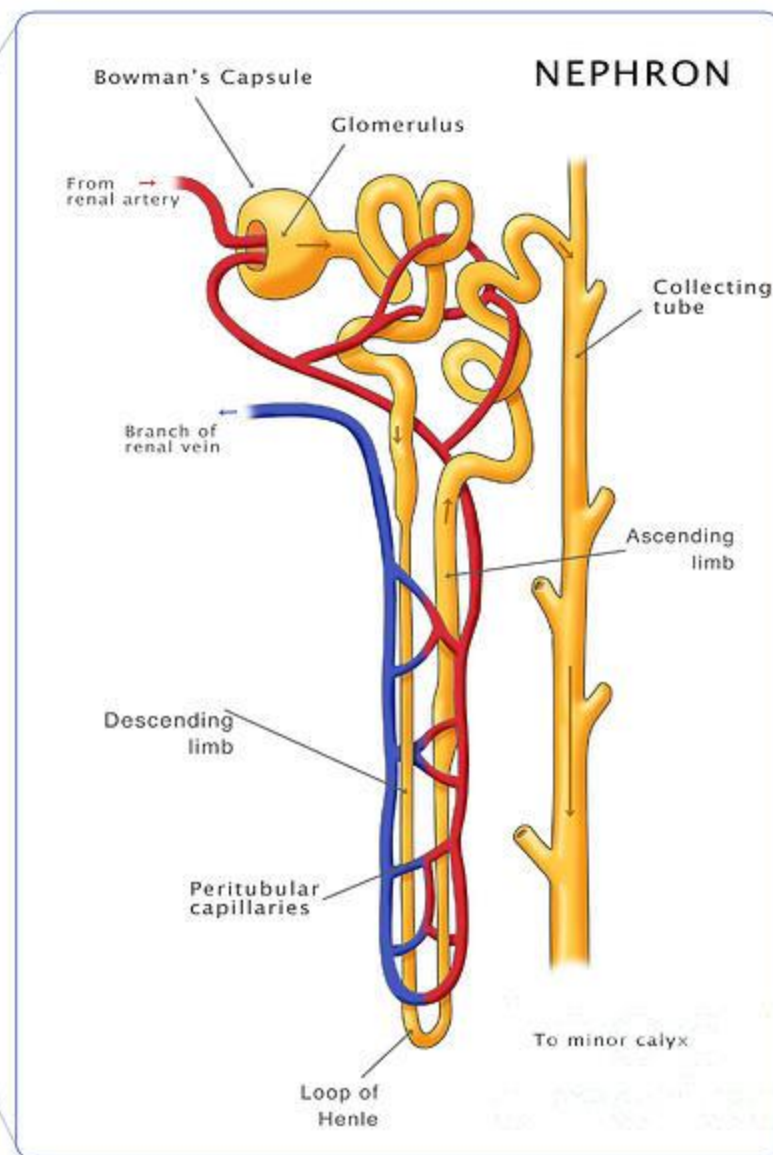
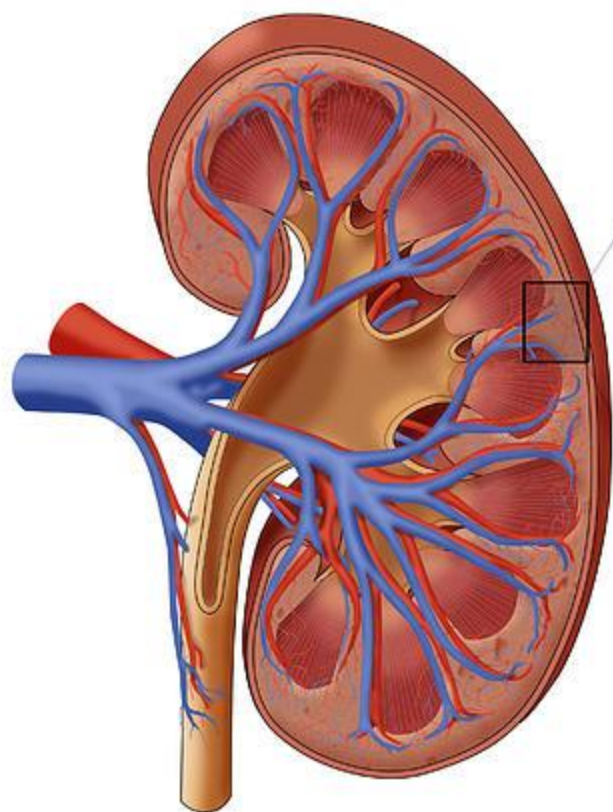
Calcium is present in the serum bound mainly to the albumin component of protein (46%), complexed with citrate and phosphate (7%), and as free ions (47%).

Only the free ions of calcium Ca^{++} are physiologically active.

Hypocalcaemia: Vit D deficiency, chronic renal disease, denosumab (Prolia[®])

Hypercalcaemia: malignancy, lithium tamoxifen, oestrogen, progesterone

Check phosphate and parathyroid hormone at same time



5. Renal function tests

- Estimates of glomerular filtration rate (eGFR): rate (volume/unit of time) at which ultrafiltrate is formed by the glomerulus)
- Pharmacists calculate CrCl taking age, sex and weight into account - reduced dosing

Check for

- a) renally cleared drugs eg digoxin, cyclosporin, methotrexate, lithium, gentamicin, theophylline, vancomycin
- b) drugs with renal toxicity eg cyclosporin, gentamicin, methotrexate, vancomycin
- c) Others eg allopurinol, bisphosphonates, calcium, H2RA, flozins, gliptins, furosemide, metformin, colecalciferol, NSAIDs

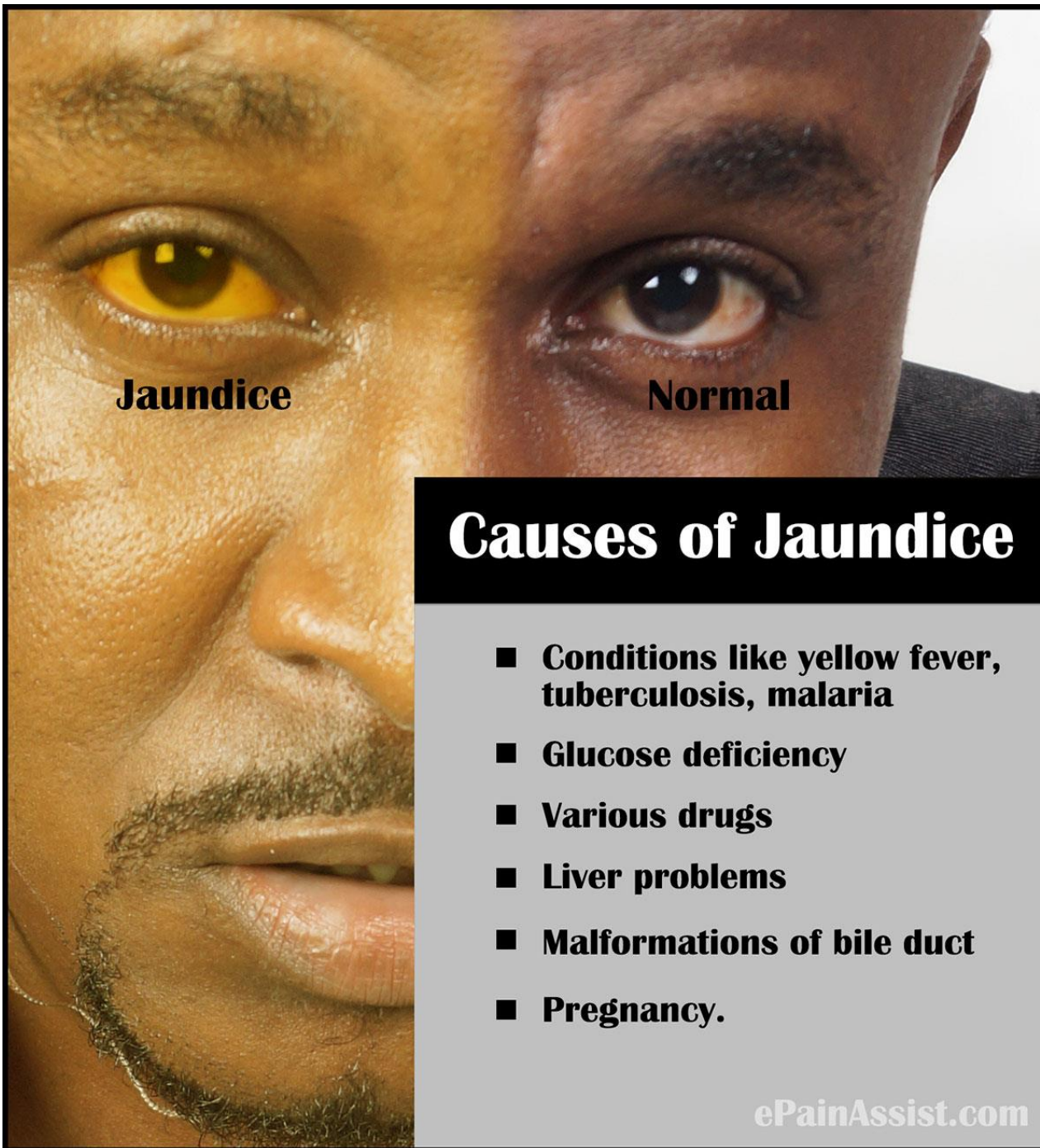
6. Liver Function Tests

Synthetic function

"Obstructive" parameters

T.Prot.	75	(60 - 81)	g/L
Albumin	43	(35 - 50)	g/L
ALP	90	(50 - 140)	U/L
GGT	45	(< 51)	U/L
Bili.	10	(< 25)	umol/L
AST	13	(< 41)	U/L
ALT	11	(< 51)	U/L

Hepatic Enzymes



Jaundice

Normal

Causes of Jaundice

- **Conditions like yellow fever, tuberculosis, malaria**
- **Glucose deficiency**
- **Various drugs**
- **Liver problems**
- **Malformations of bile duct**
- **Pregnancy.**

Drugs commonly implicated in jaundice-

Damage to hepatocytes

- alcohol
- Amiodarone
- methyldopa
- paracetamol-OD
- phenytoin

Cholestasis*

- antimicrobials-
erythromycin, flucloxacillin
- tricyclics, benzodiazepines
- oestrogens, androgens
- carbimazole,
propylthiouracil

*Cholestasis: Interference with metabolism or secretion of bilirubin

7. Full blood examination (FBE)

HAEMOGLOBIN	130 g/L	(115 - 165)
RBC	$4.36 \times 10^{12} /L$	(3.80 - 5.50)
PCV	0.40	(0.35 - 0.47)
MCV	92 fL	(78 - 99)
MCH	30 pg	(27 - 32)

WHITE CELL COUNT	$7.4 \times 10^9 /L$	(4.0 - 11.0)
Neutrophils	57 % $4.2 \times 10^9 /L$	(2.0 - 8.0)
Lymphocytes	32 % $2.4 \times 10^9 /L$	(1.0 - 4.0)
Monocytes	5 % $0.4 \times 10^9 /L$	(< 1.0)
Eosinophils	6 % $0.4 \times 10^9 /L$	(< 0.6)

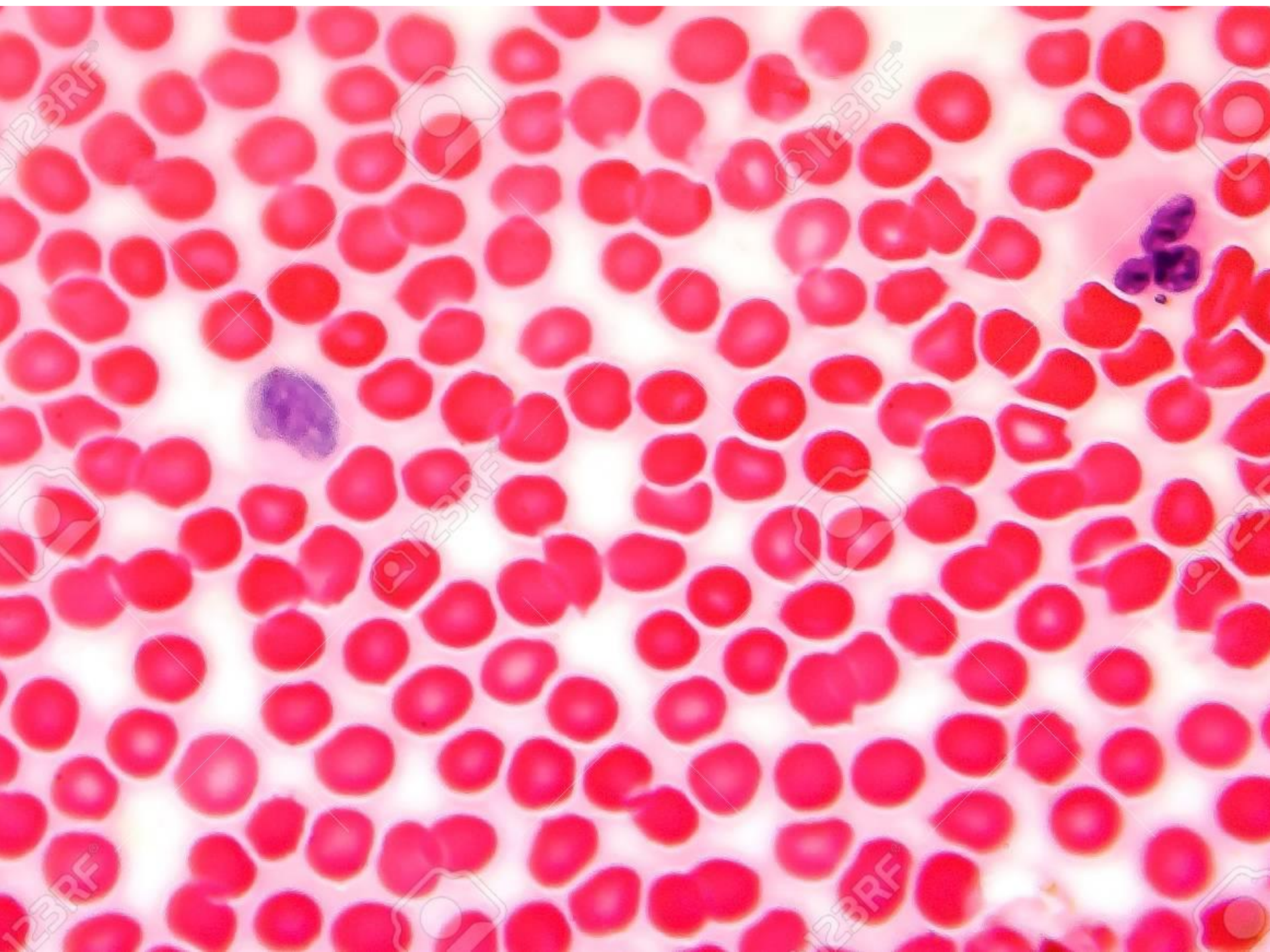
PLATELETS	$201 \times 10^9 /L$	(150 - 450)
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ESR	20 mm/h	(< 21)
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COMMENT:

Red cells are normocytic and normochromic. Leucocytes are mature and normal in distribution. Platelets adequate.

WITHIN NORMAL LIMITS.



Haematology monitoring

(a) Red cells, white cells, platelets

Drugs which may cause anaemias

eg anti-TB drugs, cefalosporins, cytotoxics,
methyldopa, nitrofurantoin

Drugs which may cause neutropenia/ agranulocytosis

eg antithyroid drugs, azathioprine, clozapine, co-
trimoxazole, indometacin

b) Coagulation tests

Prothrombin time (PT) expressed as International Normalised Ratio (INR) is the internationally recognised standard for monitoring warfarin therapy.

$$\text{INR} = \frac{(\text{patient's PT})^{\text{ISI}}}{(\text{control PT})}$$

ISI = international sensitivity index

Low intensity therapy: INR 2.0- 3.0 prevention and treatment of thromboembolic disease.

High intensity therapy INR of 2.5-3.5. valve replacement etc

- INR of 3-4 for thrombosis assoc with antiphospholipid antibodies

Assessment of anaemia:

Decrease in rbc or haemoglobin concentration

Changes in red blood cell indices

Iron studies

- serum iron
- total iron binding capacity (TIBC)
- transferrin saturation
- ferritin

Vitamin B12 & folic acid levels

- Care: anaemia may be due to iron deficiency, chronic disease, or vitB12 or folic acid deficiency
- B12: Consider PPIs, metformin, vegetarian diet
- Folate: Phenytoin, methotrexate

Specialised investigations

- Blood gases, arterial
- BMD
- Cardiac enzymes
- CRP, ESR
- CK
- PSA
- Immunoglobulin
- Malabsorption
- Uric acid
- Spirometry
- Tumour markers- PSA, CEA, AFP etc ,
- Vit D : 25-OH D
- Urine- leucocytes, erythrocytes, etc
- Swabs/Cultures
- Sensitivities
- S = sensitive; R = resistant

And many more!!

Clinical aspects of laboratory data

View data with clinical context of

- **patient**
- disease state
- therapy

Check when monitoring required

Consider all laboratory data together instead of isolated results

Get the whole picture



Therapeutic drug monitoring (TDM)



TDM : Introduction

- Therapeutic drug monitoring (TDM) is the clinical practice of measuring specific drugs at designated intervals to maintain a constant concentration in a patient's bloodstream, thereby optimizing individual dosage regimens.
- In other words, TDM refers to the individualization of drug dosage by maintaining plasma or blood drug concentrations within a targeted therapeutic range or window.

Purpose of TDM

- To confirm/establish 'effective' concentrations
 - Maximizing efficacy
- To avoid or anticipate toxic concentrations
 - Consider also function of excretory organs and drug interactions
- To investigate unexpected lack of efficacy
 - To check compliance
 - Before increasing to unusually large doses
- Limited role in toxicology - drug screen

Clinical significance of TDM

1. Maximizes efficacy
2. Avoids toxicity
3. Identifies therapeutic failure
 - Non compliance, subtherapeutic dose
4. Facilitates adjustment of dosage

New dose = Old dose X Desired C_{ss} / Old C_{ss}
5. Facilitates the therapeutic effect of drug by achieving target drug concentration
6. Identify poisoning, drug toxicity and drug abuse

Therapeutic range

- The therapeutic range is a drug concentration range associated with a high likelihood of treatment success and an acceptable risk of drug-related harm in the majority of patients.
- For most drugs, concentrations above the upper limit of the range are likely to be associated with an increased risk of toxicity.
- Concentrations below the range will be associated with inadequate benefits or treatment failure.

The **optimal therapeutic range** can vary depending on several factors, including:

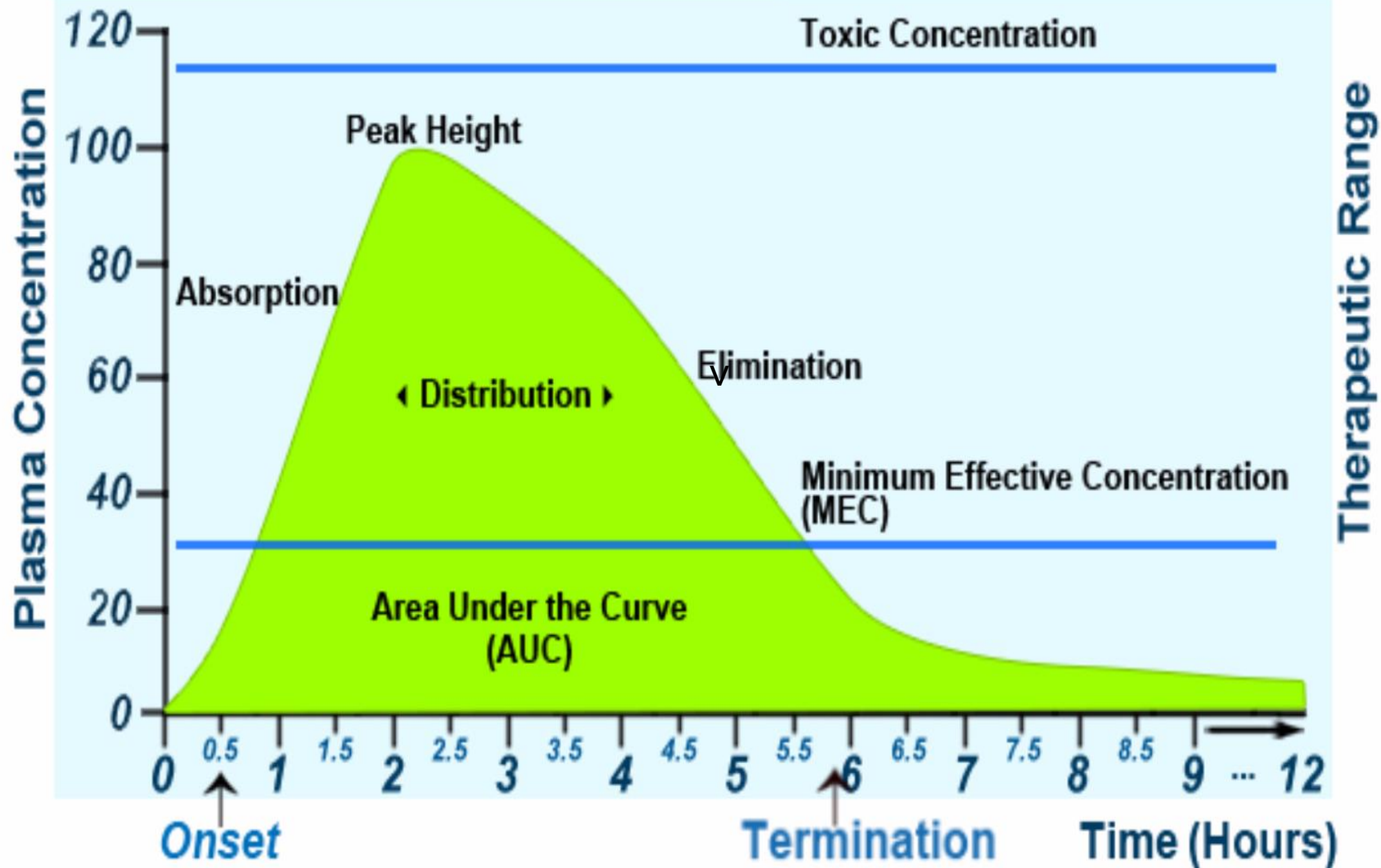
- the stage or severity of the condition being treated
- alterations in tissue or receptor responsiveness (pharmacodynamic changes)
- the extent of plasma protein binding and the amount of unbound (free) drug
- electrolyte concentrations.

Common medicines which need therapeutic drug monitoring

- **Carbamazepine**
 - Cyclosporin
 - **Digoxin**
 - Gentamicin
 - Lignocaine
 - **Lithium**
 - Mexiletine
 - Perhexiline
 - **Phenytoin**
 - Tacrolimus
 - Theophylline
 - Valproate?
 - Vancomycin
- and more!!!

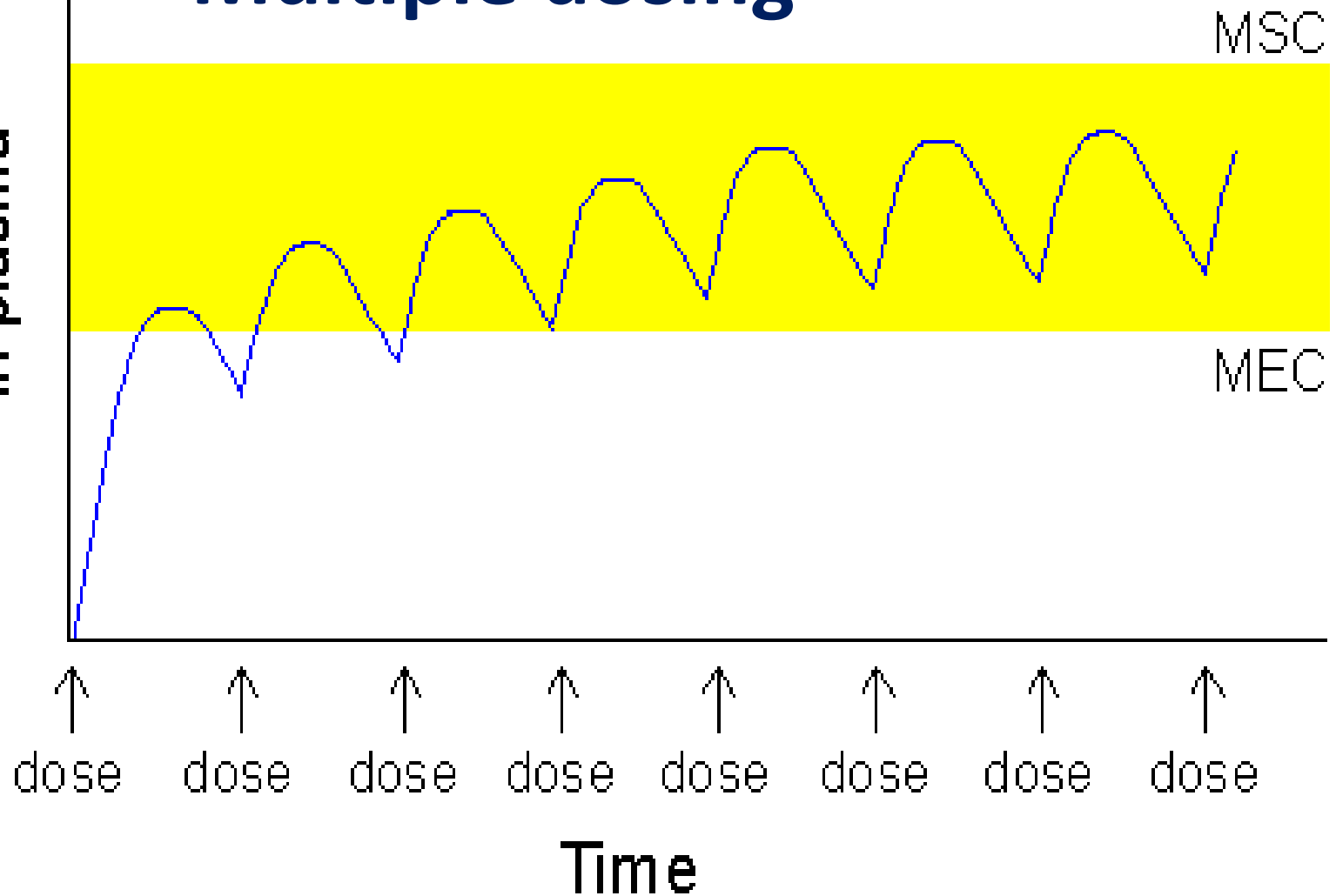
Toxic or sub-therapeutic?

Pharmacokinetics



Multiple dosing

Concentration of drug
in plasma



Common medicines requiring monitoring protocols

Drug therapy/monitoring Standard review time

- Antiarrhythmics 6/12
eg amiodarone
- Anticonvulsants 6/12
eg carbamazepine, phenytoin
- Antidiabetic therapy
Type 1 (& type 2 insulin) BG prior to inj
Type 2 if no insulin Weekly/monthly
(change times of day)
- Hypertension 6/12 BP & Pulse,

Common medicines requiring monitoring protocols cont

Drug therapy/monitoring Standard review time

- Biologicals 3-6/12
- Digoxin 6/12
- Diuretics 3-6/12
- DMARDs eg MTX FBE, LFTs etc
- Iron therapy FBE 6/12
- Lithium therapy 3/12
- Theophylline therapy 6/12
- Thyroid replacement TSH levels 6/12
- Warfarin INR 1/52 – 4/52

Monitoring- what needs to be checked

- Alendronate?
- Amiodarone?
- Apixaban?
- Denosumab
- Furosemide
- Gliclazide?
- Hydroxychloroquine?
- Insulin
- Methotrexate? (Also Hep B prior to starting)
- Metformin?
- Phenytoin?
- Ramipril?
- Spironolactone

Blood pressure monitoring



Blood pressure is expressed as a measurement with two numbers, with one number on top (***systolic***) and one on the bottom (***diastolic***), like a fraction.

For example, 120/80.

The top number (***systolic pressure***) refers to the amount of pressure in the arteries during contraction of the heart muscle.

The bottom number (***diastolic***) refers to the blood pressure when the heart muscle is between beats.

Both numbers are important in determining the state of heart health.

Numbers greater than the ideal range indicate that the heart is working too hard to pump blood to the rest of the body.

Definitions and classification of blood pressure levels

Category	Systolic (mmHg)	Diastolic (mmHg)
Optimal	<120	<80
Normal	<130	<86
High-normal	130-139	85-89
Mild hypertension	140-159	90-99
Moderate hypertension	160-170	100-109
Severe hypertension	180+	110+
Isolated systolic hypertension	140+	<90

Temperature

The average body temperatures based on age are estimated as:

Babies and children, the average body temperature ranges from 36.6°C to 37.2°C.

Adults, the average body temperature ranges from 36.1°C to 37.2°C.

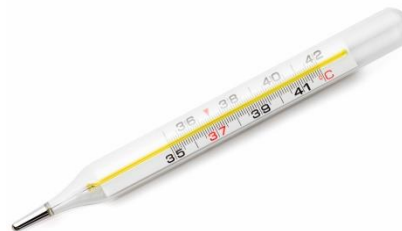
Adults over age 65, the average body temperature is lower than 37.0°C).

Normal body temperature varies from person to person.

Body temperature might be up to 0.6°C higher or lower than the guidelines above.

Identifying ones' own normal range can make it easier to know if there is a fever.

Thermometers



THANK YOU

A group of hands holding up large red letters spelling 'THANK YOU'. The letters are thick and three-dimensional. The word 'THANK' is in all caps, and 'YOU' is in title case. The hands are of various skin tones and are positioned below the letters, holding them up. The background is plain white.