Types			Drugs	Indications	Target	Notes
Lipid lowering drugs		Statins	Simvastatin			
			Atorvastatin			
		Fibrates	Bezafibrate, ciprofibrate, gemfibrozil, genofibrate			
			Exetimibe			
			Nicotinic acid derivatives			
			Alirocumab or Evolocumab			
			Inclisiran			
Fibrinolytics			Streptokinase			
			Reteplase			
			Alteplase			
			Tenecteplase			
			Urokinase			
Antiplatelets			Aspirin			
			Clopidogel			
			Prasugrel			
			Ticagrelor			
Anticoagulation			UFH			
			LMWH e.g., delteparin			
			Warfarin			
		DOACs	Dabigatran			
			Rivaroxaban			
			Apixaban			
			Edoxaban			
Antianginal		Organic Nitrates	ISMN			
			CCB			
			Beta blocker			
Anti-arrhythmic		CLASS I Na transporter blocker	///			
		CLASS II Beta blocker	Propranolol			
			Atenolol, bisoprolol, timolol			
		CLASS III Potassium channel blocker	Soltasol			
			Dronedarone			
			Amiodarone			
		CLASS IV CCB	Verapamil			
			Diltiazem			
		CLASS V	Digoxin			
			Adenosine			
			Magnesium Sulfate			

Epidemiology								
Dyslipidaemia	**CHD**	**Ischaemic Stroke**	**TIA**	**SAH**	**HF**	**AF**	**DVT**	**PE**
* 60% adults have TC>5mmol/L * TC average 5-6mmol/L for middle aged men/women * South Asian – lower HDL of <1mmol/L	*4% of UK population have symptoms *More common in males than women until menopause *124,000 AMI/year and 15-20% die *in UK S.Asians have 45% higher risk of death and black African Caribbean have 50% less risk	*2nd leading cause of death WW *100,000 annually *4th highest cause of death *Increased with age *1 in 6 men, 1 in 5 women lifetimes *Black people double likely *Black and S.Asians have stroke early in life *1.3 million stroke survivors *2/3 leave with disability	*50 in 100,000 annually * Associated with very high risk of stroke within first month to a year	*6-12 in 100,000 annually	*Increased with age *0.3-2% of overall population annually *3-5% >65yrs *8-16% >75yrs *50% dead at 5 years *5% of admissions *10% w/ HF has AF (increased thromboembolic condition)	*1 in 20 >65 yrs in UK *7% of admissions *5 times increase of stroke *More in men but men respond better to treatment	* 1 in 1000 annually *Higher incidences in hospital *1-5% fatality *More common in males * Patient over >40	* 1 in 1000 annually * 2nd most common cause of unexpected death after IHD *Increased with age * High mortality rate of 32%

Risk Factors								
Dyslipidaemia	**CHD**	**Ischaemic Stroke**	**TIA**	**SAH**	**HF**	**AF**	**DVT**	**PE**
▪ Lipid levels: LDL, HDL, VLDL, TG (TC aimed <4 mmol/L) ▪ Lipoprotein A ▪ FH of hypercholesterolaemia or hyperlipidaemia Diet and lifestyle ▪ Smoking status ▪ Alcohol consumption ▪ BMI <25	▪ Dyslipidaemia				▪ IHD ▪ Previous MI ▪ Previous smoker ▪ High alcohol intake ▪ Hypertension ▪ Overweight ▪ 65 years old ▪ Male			

Diagnosis (examination)								
Dyslipidaemia	**CHD**	**Ischaemic Stroke**	**TIA**	**SAH**	**HF**	**AF**	**DVT**	**PE**

Clinical Features								
Dyslipidaemia	**CHD**	**Ischaemic Stroke**	**TIA**	**SAH**	**HF**	**AF**	**DVT**	**PE**
* Corneal arcus (fatty ring in cornea) * Tendon xanthomas (cholesterol deposit on limbs) * Xanthelasma (cholesterol deposit on eyelids)					▪ Exercise limitation ▪ SOB ▪ Oedema (ankles, pulmonary) ▪ Orthopnoea ▪ Weight gain (fluid overload) ▪ Coughing ▪ Tiredness ▪ Left ventricular hypertrophy ▪ Ejection fraction <35%			

Dyslipidaemia Treatment Options

- 85% cholesterol from liver synthesis and 15% from gut absorption
- LDL (bad) HDL (good), VLDL, TG
- We aim for <4mmol/L TC (but no longer in NICE)
- After treatment we aim to see >40% decrease on non-HDL cholesterol

Nonpharmacological treatment:

1. Dietary modification
    a. Low saturated fat, Low trans-fat, High mono or polyunsaturated fat: to decrease LDL and increased HDL
    b. Oily fish twice weekly
    c. Plant sterols and stanols to decrease cholesterol absorption from gut
    d. High fibre intake (soluble e.g., fruit and veg) to decrease cholesterol absorption
2. Weight loss <25 BMI
3. Smoking cessation
4. Physical activity: 30 min x5 times per week
5. Reduce alcohol intake

Pharmacological Treatment:

1. Statins: inhibit HMG-CoA reductase (rate limiting enzymes in cholesterol synthesis) by competing with its substrate
    a. NOTE: not great for high TG
    b. Simvastatin is an inactive prodrug metabolised in liver to active form (fast acting
    c. Atorvastatin and rosuvastatin are long lasting
2. Fibrates: used in patient with hypertriglyceridemia where TG >10mmol/L
    a. Given if statins don't work or C/I
    b. E.g., bezafibrate, ciprofibrate, gemfibrozil, fenofibrate
3. Exetimibe: inhibits cholesterol absorption
    a. Given if statins don't work of C/I or as an addition
4. Nicotinic acid derivatives
    a. 1.5-3g a day lowers both LDL + TG by inhibiting synthesis and increase HDL
    b. No longer recommended by NICE for primary/secondary prevention of CAD, CKD or diabetes bc of vasodilatory effects leading to HT
    c. Occasional use in combination with statins
5. Alirocumab and Evolocumab: monoclonal antibodies inhibiting PCSK9, resulting in increase of LDL uptake receptors
    a. NICE approved and used in combination with statin
    b. Can develop immune tolerance
6. Inclisiran: siRNA treatment – gene slicing tool
    a. NICE approved

Before starting STATINs assess (according to NICE)

- Smoking status
- Alcohol consumption
- Blood pressure
- BMI
- HbA1c (haemoglobin levels)
- Renal function and eGFR
- Transaminase level (alanine aminotransferase or aspartate aminotransferase)
- Thyroid stimulating hormone (for hypothyroidism)

- Start with atorvastatin 20mg but after STEMI atorvastatin 80mg ON (w/I 5 drugs)

BASIC PHYSIOLOGY

Right side of the heart – deoxygenated blood from body to lungs
Superior vena cava (in) – Pulmonary arteries (out)
Tricuspid valve to separate atrium to ventricles (3 leaflet)
Pulmonary valve (in the arteries)

Left side of the heart – oxygenated blood from the lungs to the body (thicker)
Pulmonary veins (in) – Aorta (out)
Bicuspid valve to separate atrium to ventricles (2 leaflet)
Mitral valve (in the arteries)
Excitation-

CARDIAC CYCLE

Systole: contraction and emptying (top number) 120
End systolic volume – amount of blood in ventricle at end of systole

120/80 – normal patient
140/90 – hypertension under 80
150/90 – hypertension over 80
130/80 – stroke patients

Diastole: relaxing and filling (bottom number) 80
End diastolic volume – amount of blood in the ventricle at the end of the diastole

Stroke volume: end diastolic volume – end systolic volume
➔ It's the amount of blood ejected by the heart in a single beat

CARDIAC CONDUCTION

➔ Simultaneous dual pump avg. 70 BPM triggered by depolarisation
➔ Action potential generated by regions of autorhythimicity
- Sinoatrial SA node: pacemaker region, most of the action potential is generated 70/min

Takes 30ms for action potential to be passed across the right atrium to the AV node

- Atrioventricular AV node: only point of conduction between atria and the ventricle

Takes 100ms for the action potential to flow through the bundle of His

- Purkinje fibres: across the left and right ventricles

Takes 30ms for action potential to travel to the purkinje fibre branches

- Cardiomyocyte: AP travel into the ventricle cardiomyocyte

Action potential generated from the SA node:

1) There is no resting potential only depolarising or repolarising
2) Once repolarization occurs slow drift towards depolarization takes place
   a. Opening of funny sodium ion channels allows sodium into the cell + Delayed rectifier potassium ion channel close and decrease the efflux of potassium slowly increasing membrane potential
   b. Closer to the threshold potential, transient voltage gated calcium ion channels open causing influx of calcium ions until threshold is reached
3) Once threshold potential is reached all other ion channel closes and the long-lasting voltage gated ion channels opens allowing rapid depolarization
4) At peak long-lasting voltage gated ion channel closes and the delayed rectifier potassium ion channel opens allowing efflux of potassium causing rapid repolarization

Action potential carried from the cardiomyocyte:

1) Depolarization: Influx of sodium ion causes rapid depolarization from the -90 resting potential
2) Plateau phase: Opening of potassium ion channels allow efflux of potassium leading to a plateau phase where long-lasting voltage gated calcium ion channel open (slow influx of calcium)
3) Repolarization: calcium ion channel closes and potassium ion channel open causing efflux of potassium
4) Resting potential reached

Excitation – contraction coupling

1) Action potential will open the long-lasting calcium ion channel letting Ca2+ into the cell
2) Ca2+ bind to the ryanodine receptor, opening the receptor to let more Ca2+ out of the sarcoplasmic reticulum (SR)
3) Ca2+ bind to the troponin and activate crossbridge formation and contraction of the heart muscle
4) To switch this contraction off Ca2+ is reabsorbed back into the SR via the SERCA2a pump (Ca2+ ATPase pump)
5) Or removed out of the cell into the extracellular space via the Na+ Ca2+ exchanger

Refractory period

➔ During the plateau phase of the action potential, we build the contractile response (let Ca2+ in)
➔ During repolarization Ca2+ is reabsorbed into the SR or removed out of the cell
➔ Refractory period: prevent the cardiomyocytes from starting a second cycle/ contraction and let the first contraction to finish before starting a new one

Abnormal levels of K+

- Increased extracellular K+ reduce resting potential (depolarization) –> arrythmias
- Decreased extracellular K+ increases resting potential (hyperpolarization) -> bradycardia

Abnormal levels of Ca2+

- Changes in extracellular Ca2+ affects cardiac rhythm and contraction
- Ca2+ blockers reduce force of contraction
- Digoxin -> increase cytosolic Ca2+ and contractility (increase contraction of cardiomyocytes)

ECG – PQRST

P wave: atria depolarization in response to SA node
PR interval: delay of AV node to allow filling of ventricles
QRS complex: depolarization of ventricles (main pumping contraction)
ST segment (the gap between S and T): Beginning of ventricle repolarization (flat)
T wave: ventricular repolarization

ECG diagnosis examples:

- Tachycardia
- Ventricular fibrillation: cardia arrest
- Atrial fibrillation
- Heart block (bradycardia): no transmission from atria to ventricles -> deadly
- Cardiomyopathies: ischemia, infarct

Cardio Risk Assessments

Framingham Equations: based on age, gender, BP, smoking status and cholesterol (TC:HDL ratio)
Limitations:

- Does not factor in ethnicity, family history of CVD, BMI, socioeconomic status
- Reflect risks of CVD in 60-80s in north America
- Overestimate risk in current UK population by 50%, but underestimate for diabetic patients
- No longer used

ASSIGN: includes social deprivation and family history
Scores for risk factors: 1-99
If score higher than 20, high risk.

QRISK (NICE recommended)

- Based on data from 2.3 million people in England and wales between 1993 -2008
- Includes ethnicity, treated HT, social deprivation, BMI, family history of premature CVD, other conditions such as (AF, DM, CKD, RA)

QRISK3

- Includes CKD stage 3, migraines, corticosteroids, SLE (systemic lupus erythematosus)
- Drug history of atypical antipsychotic, severe mental illness, erectile dysfunction

Do not use this for these patients, as they are immediate high risk

- Type 1 DM
- Pre-existing CVD
- Risk of familial hypercholesterolaemia and other inherited lipid abnormality
- >85 years (especially if they smoke or have HT)

PEOPLE WHO NEED FULL FORMAL RISK ASSESSMENTS:

- All >40years (for primary prevention up to age 84)
- If 10-year risk CVD >10%

NICE GUIDANCE:
Lipid modification – CV risk assessment and the modification of blood lipids for the primary and secondary prevention of CVD
Underestimate in patients:

- With underlying medical conditions or treatment e.g., HIV
- Patients already treated with antihypertensives or lipid modification therapy or recently stopped smoking
- SMOKING status: if smoking stopped in previous 5 years – considered smoker
- Number of pack years = (number of cigs smoked per day x number of years smoked)/20

Speaking to patients: always present absolute risk not relative

Dysphagia

Dysphagia: physical problem causing problems with swallowing
e.g.) stroke, parkinson's (aspiration, pneumonia due to food in lungs and infection), Huntingdon's chorea (impaired with large appetite), GORD
* Aspiration: drawing breath
* Asphyxiation: lack of oxygen due to choking
Swallowing Difficulty: psychological aversion to swallowing tablets (common in child)

Interventions: patches, suppositories, IV, liquid meds (may block pharynx, if runny cause aspiration thus need gloopy consistency with thickener)

- Percutaneous Endoscopic Gastrostomy (PEG)
- Percutaneous Endoscopic Jejunostomy tube (PEJ) – small intestine tubes

Liquid medicines

- Always check change in bioavailability
- Limited availability – bc water can cause hydrolysis and loss of active ingredients and alcohol not well received by MHRA

Specials: unlicensed medicines, batch specials from special manufactures, one off specials from doctors (more expensive than batch)

Last resort: formulation tampering
Tablet crushing can be fatal – increase bioavailability, alter pharmacokinetics, alter side effect profile

- Normal tablets – crushing appropriate, but dispersing inappropriate if unstable in water

➔ Bioavailability will be increased almost 50%

- MR tablets – theophylline (keep airways open in asthma COPD, smooth peaks and troughs), nifedipine (CCB for HT, has short half-life, patient died when administered crushed from severe hypo+bradycardia), felodipine (CCB adherence difficult taken several times a day – one daily formulation), MST (slow release formula for morphine)

➔ Oxycodone death – addicts crush MR formulation and inject – now new formulation of naloxone opioid antagonist in the central reservoir for frug to pass through body not absorbed + unbreakable tablets

- Enteric coated tablets: diclofenac (will irritate stomach w/o coat), omeprazole (destroyed by content of stomach w/o coat), sulfasalazine (irritate stomach w/o coat)

CASE STUDY
Use resources – NEWT guidelines, White & Bradnam

1. Check dysphagia
2. Only supply essential medications: end of life treatment e.g., simvastatin must?
3. Dipyridamole (2nd prevention of stroke) – can open capsules and flush into eating tube (unlicensed) or liquid version (unlicensed for stroke)
4. Simvastatin – atorvastatin easier to disperse in water
5. Zimovane – change to zolpidem which is easier to crush
6. Slophyllin for COPD – capsules can be opened and given by nasogastric tube 3 times a day or given in liquid dose

Definition of confusing vocabs:
*Atheroma: fatty plaque on the inside of blood vessels – atheromatous plaques
*Atherosclerosis: formation of fatty streaks on surface of endothelium
*Ischaemic: restriction in blood supply - ischaemia
*Thrombosis: blood clot – thrombus formation
*Stenosis: blockage
*Perfusion: local fluid flow through circulatory system
*Thrombus that breaks loose and travels from one location to another is embolus

CHD

Arterial thrombosis
- Acute myocardial infarction
- Transient ischaemic attacks (TIA) – mini stroke
- Cerebral vascular infarcts/accidents (CVA) – normal stroke

Inherited/Acquired
- Thrombophilia (both venous and arterial)

CHD: condition which the vascular supply to the heart is impeded by atheroma, thrombosis, or spasm – main symptoms being ischaemic chest pain
Risk factors: age, gender, FH, smoking, diet, obesity, HT, hyperlipidaemia

Stable angina – exercise induced angina
➔ DEMAND ischaemia
➔ Better with rest or GTN
Clinical symptoms:
- Central crushing chest pain that may radiate to jaw, neck, back or arms
- Described as: constricting, choking, heavy weight, stabbing, burning or like a knife
- Lack of ECG and cardiac enzyme changes

*What is a stable angina and a heart attack?
Stable angina has a narrowing of blood vessel and increase in heart demand cannot be handled. Myocardial infarction on the other hand has a formation of a blood clot at the site of rupture – thrombosis forms at the site of rupture of atheromatous plaques. Therefore, blocks blood supply

Acute coronary syndrome (ACS)
➔ SUPPLY ischaemia
➔ Not better with rest or GTN
- **Myocardial infarction** (heart attack)– complete blockage
  - **STEMI** (ST elevated on ECG)
  - **NSTEMI** (high sensitivity troponin assay repeated after 3 hrs to rule out)
- **Unstable angina** (lower troponin level than STEMI/NSTEMI) – partial blockage

Management of Stable Angina		
		NOTE
Acute angina attack	PRN S/L GTN	▪ Keep with you at all times, keep spare, can be bought OTC as well ▪ Under the tongue when get chest pain or expected chest pain ▪ If given in tablet form do not swallow, it is inactive ▪ Sit down – it may cause dizziness and rest helps with chest pain ▪ Headache may occur due to opening up of blood vessels in the head so if chest pain gone spit out or swallow ▪ If chest pain not gone after 5min take another, if no improvement take 3rd but contact GP/ambulance as well ▪ Spray – 2 years expiry date check ▪ Tablets – 8 wees expiry once opened
1st line treatment NICE guide	Beta blocker	▪ Use cardio-selective to avoid problems with beta2 receptor (bronchospasm) e.g., atenolol, bisoprolol, metoprolol ▪ + cardio-selective beta blockers are less likely to mask symptoms of hypo in DM patients ▪ Use water soluble beta blockers like atenolol rather than lipid soluble like propranolol to avoid CNS S/E such as sleep disturbance, nightmares ▪ Other Bblocker choice intrinsic sympathomimetic activity (ISA) – oxprenolol, pindolol, acebutolol, celiprolol This stimulates beta-adrenergic receptors (partial agonist effect) and to oppose the stimulating effects of catecholamines (antagonist of adrenergic receptors) in a competitive way – thus less likely to cause bradycardia and cold extremities Atenolol 100mg OD counselling points: - S/E less likely than propranolol - Do not stop abruptly – may cause angina due to rebound receptor hypersensitivity
	CCB	
	Beta blocker + CCB	
Add on MHRA guide	Long-acting nitrate Ivabradine (used in HF) Ranolazine Nicorandil	▪ Nitrate interact with sulfhydryl groups in the vascular tissues to release NO to cause vasodilation ▪ But continued use depletes sulfhydryl groups resulting in tolerance – but restoration will occur within hours of interruption ▪ NEED 4-8H of NITRATE FREE PERIOD every 24 hours ▪ Nitrate does not provide full 24 hours control of angina tf only use as add on with other antianginals ▪ When BD 2nd dose no later than 6pm ▪ Use MR, bc only have 15-20hr action (in built nitrate free period) ▪ Use patches – remove overnight ▪ Side effect of throbbing headache, but usually first few days so encouraged to use with paracetamol ▪ Other S/E flushing, dizziness, tachycardia
Secondary prevention	Lifestyle advice	
	▪ Antiplatelet – aspirin ▪ Statin – atorvastatin 20-80mg	

Diagnosis Assessments for ACS

Troponin T and Troponin I – blood test

Other causes of increased troponin levels:

Other enzyme rise:

Creatine kinase (CK)

Aspartate transaminase (AST)

Lactate dehydrogenase (LDH)

Clinical symptoms:

For NSTEMI/unstable angina patients:

Further treatment and investigation depend on prediction of 6months risk of mortality and further CV events

➔ Use GRACE scoring system

➔ If intermediate/higher risk >3% -> immediate need for PCI

➔ If low risk <3% -> conservative management

Percutaneous coronary intervention (PCI)

- Angioplasty: balloon at the tip of catheter and inserted and inflated at plaque – restenosis common
- Stenting: wire mesh inserted to keep stenosis open
    - Bare metal stent (BMS)
    - Drug eluting stent (DES)
        - Carry anti proliferative drugs e.g., tacrolimus or paclitaxel

➔ Both interventions can cause damage to vessel wall and increase risk in clotting (in-stent thrombosis) therefore need to take DAPT for 12 months and long-term aspirin afterwards

LAST RESORT:

Coronary artery by-pass grafting (CABG) – surgical intervention

- Veins grafted from leg to by-pas stenosis in coronary artery

FROM WS6 CHD

*Metformin is C/I in recent myocardial infarction due to risk of lactic acidosis increased by hypoxia but can be used once patient is stable

*Use of iodine containing x-ray contrast media used in angio is C/I in patients on metformin due to risk of renal impairment thus need to stop metformin 48 hrs before angio (but not possible with PPCI) and only restart when renal function is normal after 48hrs

*Optimise DM2 with addition of SFLT2 e.g., dapagliflozin 10mg OD

*Patient on DAPT and has history of GORD – prescribe lansoprazole 15mg OD

*Meloxicam increases risk of thrombotic event – prescribe alternative paracetamol/co-codamol or naproxen/ibuprofen if need NSAID

Management of STEMI MI		
		NOTE
Acute/immediate care	Oxygen (if indicated)	▪ Relieves ischaemia
	Diamorphine	▪ Pain relief and anxiolytic (helps with extreme anxiety) ▪ Vasodilatation – improves blood flow and oxygen supply ▪ Can be given with antiemetic e.g., cyclizine, metoclopramide
	Aspirin 300mg STAT	▪ Reperfusion: to restore blood flow
	Clopidogrel 300mg STAT Or Ticagrelor 180mg STAT Or Prasugrel 60mg STAT	▪ Antiplatelet agent ▪ To minimise infarct size
	Primary Percutaneous Coronary Intervention (PPCI)	▪ Gold standard therapy – alternative to thrombolysis ▪ Better outcome and less people with CI ▪ Patient taken straight to Angio suite for angioplasty (w/ or w/o stenting) ▪ Clot removed during procedure ▪ Call to balloon time 120min, door to balloon time 30min ▪ Challenging to achieve but very effective ▪ *if patient taking metformin for DM check renal function and restart after 48hrs of PPCI
	OR Thrombolysis + Heparin (48hrs later)	▪ Thrombosis: cause infarction due to inadequate blood supply ▪ Thrombolysis are thrombolytic agents that busts clots ▪ Fibrinolytics E.g., streptokinase, alteplase, Tenecteplase, reteplase ▪ It activates plasminogen to produce plasmin and breaks down fibrin in blood clots ▪ Call to needle time 60min, door to needle time 30min (damage after 6h irreversible) ▪ *Patient can be allergic to streptokinase (antigenic) – produce anti streptokinase antibodies and cannot have further doses as it neutralises its effects
	IN NSTEMI/unstable angina no PPCI or thrombolysis instead: Fondaparinux (if still unstable)	▪ Inhibitory factor 10A ▪ Prevents formation of new blood clots
Management of complications	Arrhythmias	
	Heart Failure	
Secondary prevention (5 drugs)	Antiplatelets Aspirin 75mg BD + clopidogrel/ticagrelor/parsugrel	▪ Dual antiplatelet therapy (DAPT) for 12 months then aspirin for life ▪ Explain increased risk of bleeding
	Beta-blocker	▪ Review after 12months and continue if HF ▪ Taken in the morning
	ACEi	▪ Continue for life ▪ Taken at night to prevent hypotension since beta blocker taken in morning ▪ Titirate dose up to 10mg daily after checking patients BP and RF ▪ E.g., ramipril 10mg
	Statin – atorvastatin 80mg	▪ Explain muscle pain rhabdomyolysis
	Lifestyle changes	▪ Smoking cessation ▪ Weight loss – diet of low sodium, low fat and take five a day ▪ Exercise – 30 mins daily five times a week ▪ Alcohol maximum 14 units

Stroke

Treatment of stroke: asses via FAST- face,arm,speech,time

Immediate Management:

Thrombolysis – alteplase within 4.5 hours of symptoms for those who show not to have intracerebral haemorrhage or other contraindications

After 24 hours: antiplatelet should be started

Antiplatelet: Aspirin 300mg OD for 2 weeks – thrombectomy patients are started on antiplatelet 24 hours after alteplase.

If not thrombectomy patient – start aspirin ASAP within 24 hours

At 2-week point – long term antithrombotic treatment should be started

If patient has had previous dyspepsia with aspirin: lansoprazole ppi

If aspirin is contraindicated: Clopidogrel

When to offer thrombectomy:

ASAP within 6 hours of symptom onset

Or

Thrombectomy should be offered to those patients with acute ischaemic stroke, have occlusion of the proximal anterior circulation and who were last known to be well between 6 hours and 24 hours previously, where:[6]

- There is the potential to salvage brain tissue (i.e. where imaging has shown a small core area and therefore the surrounding area may be able to re-perfused if the clot is removed).

Lipid Management:

Immediate initiation of statin is not recommended with acute stroke patients

If they were on a statin before then it is ok to continue this treatment

Managing other factors:

Supplemental oxygen – if oxygen saturation drops to less than 95%

Blood sugar control – aim for between 5-15mmol/L

Blood pressure – Elevated bp is normal and should resolve in most patients after 4-10 days. If bp is excessively high, it is associated with oedema or haemorrhage

Only start immediate hypertensive emergency when patient has:

- Hypertensive encephalopathy
- Hypertensive nephropathy
- Hypertensive cardiac failure/MI
- Aortic dissection
- Intracerebral haemorrhage with systolic blood pressure over 200mmHg
- Pre-eclampsia/eclampsia

When a reduction in blood pressure is required, oral (mouth/NG tube) or parenteral therapy may be used. Ex: Amlodipine or Labetolol (parenteral beta blocker)

BP target: 185/110mmHg

Blood pressure is allowed to run high for the first few days post stroke to ensure adequate perfusion

For those who are already taking antihypertensives: Treatment can be safely withheld until patients are medically and neurologically stable and have suitable oral or enteral intake.

Secondary prevention of stroke (started as soon as possible):

Blood pressure:

<table>
<tr><td colspan="5">Heart Failure</td></tr>
<tr><td rowspan="3">Aetiology</td><td>Cause 1: Pump failure</td><td colspan="2">Damage to heart muscle thus reduction in myocardial contractility</td><td></td></tr>
<tr><td rowspan="2">Cause 2: Overloading (extra workload on the heart)</td><td colspan="2">Excessive afterload - pressure the chamber of the heart must generate to pump blood (total peripheral resistance)</td><td>Pulmonary vascular resistance is high: pulmonary hypertension from chronic lung disease (right ventricular fails)

Valve dysfunction: increase the pressure the heart muscle needs to generate to push blood</td></tr>
<tr><td colspan="2">Excessive preload (uncommon) - volume of blood in the heart (filled ventricle) (left ventricular end diastolic volume)</td><td>Hypervolaemia (increased volume of blood)

Excessive demand</td></tr>
<tr><td rowspan="6">Pathophysiology</td><td>Acute Heart Failure</td><td colspan="3">- Could be caused after MI, as contractility immediately drops and cardiac output fails, initiating compensation to maintain cardiac output and peripheral perfusion -> compensated
- If MI severe with extensive damage to heart muscle, there is no cardiac reserve and CVS unable to compensate -> decompensated HF</td></tr>
<tr><td rowspan="5">Chronic Heart Failure</td><td colspan="3">Same as acute, but decline is progressive
Stress such as infection, fluid overload, exertion or anaemia can lead to decompensation</td></tr>
<tr><td rowspan="4">Compensation Process</td><td colspan="2">1. Cardiac enlargement: alteration of ventricular size, shape and function
- Cardiac muscle stretched form increased volume
- Leads to left ventricular hypertrophy (LVH)</td></tr>
<tr><td colspan="2">2. Arterial constriction: when cardiac output is reduced, arteries constrict to divert blood to essential organs but away from essential organs but away from non-essential organs e.g., skin and GI tract
- BUT raise systemic vascular resistance – increasing afterload on heart</td></tr>
<tr><td colspan="2">3. Increased sympathetic drive: failing heart and reduced tissue perfusion stimulates sympathetic nervous system (SNS)
- Exposes heart to catecholamines (neurohormones) in an attempt to maintain cardiac output to increase force and rate of heart contraction
- Promotes excessive stress on heart and widespread vasoconstriction – detrimental long term</td></tr>
<tr><td colspan="2">4. Salt & water retention: reduced cardiac output means reduced renal perfusion
- Release renin in renin angiotensin system – formation of angiotensin I and II vasoconstrictors -> adrenal aldosterone release (retains salt and water in distal renal tubule thus increasing blood volume and preload
- Promotes release of atrial natriuretic peptide (ANP)</td></tr>
<tr><td rowspan="4">Clinical Features</td><td>Exercise limitation (fatigue)</td><td colspan="2">Due to decreased cardiac output, impaired oxygenation and decreased blood flow to exercising muscle</td><td rowspan="4">CAUSE 1 Hypoperfusion (forward component) – effect independent of heart side
- Peripheral vasoconstriction
- Increase in afterload of heart and reduction of blood supply
- Fatigue, exercise intolerance, cold/pale extremities, fluid/electrolyte retention, tachycardia, and tachypnoea (breathing rate increase)

CAUSE 2 Congestion/Oedema (backward component)
- Right-sided HF
- Left-sided HF
NYHA classification: I no limitation, II mild HF ordinary activity difficult, III moderate HF comfortable at rest but walking to toilet lead to symptoms, IV severe HF even at rest discomfort</td></tr>
<tr><td>SOB</td><td colspan="2">Back pressure from failing heart causes fluid to accumulate in lung
Mostly occurs when exercising or lying down (gravitational force)
Can be accompanied by cough</td></tr>
<tr><td rowspan="2">Oedema</td><td colspan="2">Peripheral Oedema: right-sided HF (deoxygenated blood)
- Hepatomegaly (enlargement of liver)
- Peripheral cyanosis (blue skin due to lack of O2)
- Swollen ankles due to retention of salt + water</td></tr>
<tr><td colspan="2">Pulmonary Oedema: left sided HF (oxygenated blood)
- Common and serious
- Dyspnoea (SOB), orthopnoea (SOB lying down), Paroxsymal nocturnal dyspnoea (PND) SOB at night</td></tr>
<tr><td rowspan="4">Diagnosis</td><td>Symptom check</td><td colspan="3">Raised jugular vein at side of neck, lung sounds (crackles at base due to pulmonary oedema), swelling of ankles due to peripheral oedema</td></tr>
<tr><td>Natriuretic Peptides Test</td><td colspan="3">BNP (brain natriuretic peptide) and NTproBNP (N terminal brain natriuretic peptide), ANP</td></tr>
<tr><td>Echocardiography imaging</td><td colspan="3">See heart in motion and assess performance as pump
Measures ejection fraction
HF with reduce ejection fraction <40% (HFREF)
HF with preserved ejection fraction >50% (HFPEF)</td></tr>
<tr><td>Others</td><td colspan="3">Chest X-ray, HR, rhythm, sounds, Electrocardiogram – AF, BP, blood test to check underlying causes (anaemia, RF, thyroid diseases)</td></tr>
</table>

Management of CHF with reduced ejection fraction (HFREF) NICE				
	Type of Drugs	Drugs	Notes	Notes
1st line in Acute & Chronic	1. Diuretics	Thiazide e.g., Bendroflumethiazide up to 5mg OM (max 2.5mg in HT)	▪ Less potent, used in mild heart failure ▪ Not effective at eGFR <20ml/min (renal impairment)	▪ Relief of congestive symptoms and fluid retention (SOB, oedema) ▪ Lowers preload ▪ Pharmaceutical care issues due to loop diuretics: Hypotension, dehydration, renal impairment, electrolyte disturbance ▪ Rate of administration for IV furosemide:
		Loop e.g., furosemide, bumetanide	▪ MAIN IV first line ▪ Can use high dose in severe HF ▪ 40mg/80mg BD IV of furosemide	
		Metolazone	▪ Atypical thiazide diuretic, effective in poor RF ▪ Used in combination with loop (resistant HF) ▪ STAT dose of 2.5mg/5mg, short term (2-3days), long term maintenance 2.5mg/5mg 2 or 3 times a week	
1st line	2. ACEi		▪ Lowers preload and afterload ▪ Control BP at target ▪ Improves symptoms and long-term survival ▪ Start low dose then up titrate	
	3. Beta blocker (BB)	Bisoprolol Carvedilol Nebivolol	▪ Lowers preload and afterload ▪ Only 3 B blockers licensed for HF ▪ NOT ATENOLOL ▪ CAUTION: can cause worsening of symptoms initially – start low go slow (aim for target dose of 10mg OD) ▪ For stable patients only – it will slow HR down causing more problems for unstable acute HF patients	
	4. Aldosterone antagonist (MRA)	Spironolactone Eplerenone		▪ Low dose – have some diuretic effect ▪ Reduce preload ▪ For long term survival and hospital admission
Alternative to ACEi	5. ARB			▪ Evidence for improvement in long term survival but not as good as ACEi
Add on therapy	6. Hydralazine and nitrates	Hydralazine	▪ Reduce afterload	▪ Especially for African/caribbean descent ▪ For patients intolerant.CI to ACEi or ARB
		Isosorbide mononitrate (ISMN)	▪ Used to be ISDN now ISMN ▪ Reduce preload	
	7. Ivabradine		▪ Lowers heart rate – helps maintain BP ▪ Improves inotropy (heart muscle contractility) ▪ Selectively and specifically inhibit If channels in SA node ▪ Add for worsening HF in optimal first line therapy ▪ Add if sinus rhythm with a HR >75bpm and LVEF <35% in accordance with TA267	
	8. ARNI	Entresto: Sacubitril-valsartan	Stops degradation of atrial and brain natriuretic peptide	▪ Need to stop ACEi/ARB 36 hours before because it contains valsartan (an ARB) – need wash out period to prevent adverse reaction such as angioedema ▪ Replace ACEi or ARB in accordance with TA388 ▪ If LVEF <35% ▪ ESC recommends joint first line
	9. Digoxin			▪ Improves symptoms, exercise tolerance, hospital admission ▪ DOES NOT improve mortality ▪ Add for worsening HF
	10. SGLT2 Inhibitors	Dapagliflozin Empagliflozin		▪ Learnt in DM2 ▪ Improves inotropy (heart muscle contractility) ▪ ESC recommends joint first line ▪ NICE 2021 option to treat symptoms for CHF as an add on with optimised meds

From WS 9 on HF
POINT 1

Drug: furosemide IV 40mg/80mg	Indication: heart failure
Therapeutic parameter	**Toxic parameter**
Symptoms of HF improvement, weight loss aimed for 1kg loss a day, urine output – aim for negative fluid balance	BP, RF, U&Es (K+, Na+), rate of administration of maximum 4mg/min (as it can cause ototoxicity, where patient develops hearing or balance problems due to the drug)

- Initial furosemide 80mg BD
- If no response: increase to 240mg IV infusion over 24H
- If still no response, consider addition of metolazone 2.5mg STAT or 2.5mg OD for 2-3days

POINT 2
Beta blocker + bradycardia can make acute HF worse – so initial discontinuation until acute episode controlled then start low and go slow.

POINT 3
If end of life care due to condition and age – is atorvastatin necessary for 2nd prevention of MI – polypharmacy

POINT 4
Dalteparin S/C 5000IU OD or Enoxaparin S/C 40mg OD for VTE

POINT 5
Increased stroke risk score therefore needs anticoagulation
- Review ORBIT for bleeding risk
- Prescribe DOAC for stroke prevention in AF
- Stop LMWH when DOAC started because it acts as VTE as well

POINT 6
Counselling:
- Avoid OTC when treatment with HF: NSAIDs and sodium containing antacids
- Anticoagulant counselling

POINT 7
Other drugs available to add here:
- Ivabradine: must be in sinus rhythm so not appropriate here, but useful as BP maintained
- Hydralazine + nitrates

Treatment of acute heart failure:
- Offer intravenous diuretics – bolus or infusion
- Closely monitor renal function, weight, urine during diabetic therapy
- Don't offer nitrates to people with acute heart failure

Treatment of acute heart failure after stabilisation:
If already taking beta blocker treatment – continue unless that have a heart rate less than 50bpm, second- or third-degree atrioventricular block, or shock

Start or restart beta blocker treatment during hospital admission once their condition has been stabilised – ex: when iv diuretics are no longer needed – typically 48 hours after

Offer an angiotensin-converting enzyme inhibitor (or angiotensin receptor blocker if there are intolerable side effects) and an aldosterone antagonist during hospital admission to people with acute heart failure and reduced left ventricular ejection fraction. If the angiotensin-converting enzyme inhibitor (or angiotensin receptor blocker) is not tolerated an aldosterone antagonist should still be offered.

Treatment of chronic heart failure:
Diuretics:
Thiazide diuretics: Used in mild heart failure – Bendroflumethiazide – up to 5mg OM (not effective at eGFR less than 20ml/min

Loop diuretics: Mainstay treatment – furosemide, bumetanide (can use IV an high doses)
Metolazone: An atypical thiazide diuretic that is effective in patients with a reduced renal function
- It is used in combination with loop diuretics in resistant heart failure
- 5mg STAT dose
- Short term – 2.5mg/5mg OD
- Long term maintenance – 2.5mg/5mg 2 or 3 times a week

First line treatment:
- Offer ACEi – start low dose then up titrate
- Offer Beta blocker – must be licensed – bisoprolol, carvedilol, nebivolol – START LOW GO SLOW with uptitration of dose
- Offer MRA if symptoms continue – spironolactone, Eplerenone (low dose)
- If ACEi not tolerated – give ARB

If first line treatment doesn't solve symptoms:
- Consider Hydralazine and nitrate (ISMN) if intolerant of ACEi and ARB – especially if patient is of African/Caribbean descent
- Replace ACEi or ARB with Entresto (salcubitril-valsartan)
- Add ivabradine if in sinus rhythym with a heart rate of more than 75bpm and a LVEF of less than 35%

Digoxin can be used for worsening HF

Arrhythmia

➔ Abnormality in heart rate (number of beats per minute) and rhythm (irregularity)

Within ventricles or above the AV node (atrial arrythmias) or AV node junction or within the AV node

Normal Sinus Rhythm: NSR

Symptoms: dizzy/lightheaded, palpitations, chest pain, fatigue

Occasionally loss of consciousness due to sudden drop of blood pressure or blood flow

Small number of cardiac arrests – ventricular fibrillation

Managements

1. Treat underlying disease:
    1) Thyroid disease: hypo/hyperthyroidism
    2) Electrolyte imbalance
    3) Cardiac myopathy
2. Drug therapy
3. Non-pharmacological interventions
    1) Permanent Pacemaker (PPM): inserted in the skin pocket below collar bone
    - If heartbeat is below threshold (detects inappropriate rhythm) it stimulates electrical impulses – for bradycardia
    2) Cardioversion: restoration of heart rhythm for AF and A flutter
    - Type 1: chemical cardioversion – use of drugs
    - Type 2: Direct Current cardioversion (DCCV) controlled electric shock across chest wall
        - Override disordered conduction and allows SA node to regain control - NSR
        - Patient briefly anesthetised
        - DCCV increased risk of thromboembolism – needs to be anticoagulated 3 weeks before and 4 weeks after
        - If unplanned treatment anticoagulated with (LMWH) low molecular weight heparin
        - Consider amiodarone therapy starting 4 weeks before and 12months after to maintain NSR (may not be used if already on rate/symptom control therapy)
    3) Radiofrequency (RF) ablation/cryoablation (freezing)
    - Patient undergoes electrophysiological (EP) studies to identify exact location of arrhythmia
        - Catheter with electrode at tip guided to appropriate point
    - RF energy or freezing destroys the tissue and the conduction pathway
    - 90% success rate and prevent long term drug therapy for arrhythmia or thrombosis
    4) Defibrillators: delivers electric shock to the myocardium via chest wall + CPR needed to maintain cardiac output
    5) Internal cardioversion defibrillators (ICDs): implanted like pacemaker into high-risk patients with resistant VT
    - It monitors rate and rhythm
    - Electrical pulse higher than DCCV – delivers rapid rate impulses to regain control

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BRADYCARDIA: slow HR <60 bpm

1. Sinus bradycardia: SA node fires at slow rate
2. Sinus node disease: SA node fails to generate electrical impulse
   Causes:
    a. Mainly idiopathic – cause being fibrosis of myocardial conduction tissues
    b. Secondary to acute myocardial infarction (AMI) or cardiomyopathies
3. AV node disease (heart block): failure of AV node to conduct electrical impulse to ventricles
   Causes:
    a. Idiopathic
    b. Secondary to AMI, congenital defects, infection, valve surgery
    c. Drugs: beta blockers, digoxin, verapamil – slows HR

➔ ACUTE TREATMENT: Atropine (antimotility agent) STAT to increase HR
- First degree heart block: 1:1 ratio of P waves to QRS complex, but long PR interval
- Second degree heart block: 2:1 ratio
- Third degree heart block: no conduction through AV node – medical emergency
    - AV node have ability to produce automatic rhythm for a while – delay death

TACHYCARDIA: fast HR >100 bpm

Tachycardia at the atria:

1. Sinus tachycardia (ST): increased HR but normal rhythm (a normal response to exercise)
    a. Could be due to infection, lowered BP, anaemia, hypovolaemia (loss of blood), shock, pulmonary embolism (PE)
    b. Could be side effect of nicotine, beta2 agonist, salbutamol (for COPD), levothyroxine (for hypothyroidism), aminophylline

2. Atrial Fibrillation (AF)

3. Atrial flutter: like AF but less frequent
    a. Rapid atrial rhythm of 300bpm
    b. Saw tooth pattern ECG
    c. Ventricles beat once every 2 to 4 atrial flutter waves
    d. Stasis (obstruction of blood flow) in atria – need anticoagulation

Tachycardia at the AV junction:

1. Wolff-Parkinson White Syndrome: electrical pulse by-pass AV node and moves directly from atria to the ventricles
    a. Ventricular rate up to 600bpm – life threatening

Ventricular tachycardia (VT): when five or more ventricular beats occur consecutively

- Causes could be AMI, IHD, cardiomyopathies, myocarditis, valvular disease

2. Torsade de pointes: twisting of the QRS complex – ventricular depolarization
    a. QT prolongation (extension of A wave to T wave)
    b. Due to hypokalaemia and hypomagnesaemia
    c. Drug induces: antiarrhythmics IA or III, erythromycin and clarithromycin (antibiotics), tricyclic antidepressant, cisapride (for GERD), terfenadine and astemizole (antihistamine), haloperidol (antipsychotic), lithium (for bipolar), phenothiazine (antipsychotic)
3. Ventricular Fibrillation -> cardiac arrest
    a. Rapid and uncoordinated contraction of ventricular tissue
    b. Medical emergency – loss of consciousness within 10-20 sec
    c. Common cause of death due to acute myocardial infarction

CASE STUDY 1 AV Node disease bradycardia – HEART BLOCK

- Has AF, hypothyroidism, HT, glaucoma
- Third degree heart block to second degree heart block
- Action: PPM surgery, review drug therapy

On admission pharmaceutical care issues:

1. Needs to stop anticoagulants (warfarin) for PPM surgery (because anticoagulant increases risk of bleeding)
2. Stop diltiazem (rate controlling CCB) as it will make bradycardia worse
3. Review combigan eyedrop for glaucoma – contains timolol a beta blocker that lowers HR – note that for elders absorption for eyedrop can have systematic effect so held until PPM
4. Given antibiotics and pain killers before surgical procedure

Prior to discharge pharmaceutical care issues:

1. Restart anticoagulants and eye drop
2. Consider restarting rate controlling CCB depending on indication also consider alternative
- In this patient's case with a pace make in place there will be no longer a drop in HR therefore can be taken off diltiazem
- E.g., for MI patients (there are 5 drugs including beta blocker) – beta blocker will be stopped for insertion of pacemaker, but needs to be restarted to prevent secondary MI

From WS10 AF

POINT 1 WARFARIN AND DOAC

TTR = 50% - demonstrates poor INR control - Consider change from warfarin to DOAC in this case

When to start DOAC after stopping warfarin:

- Dabigatran start when INR less than 2
- Rivaroxaban start when INR less or equal to 2.5
- Apixaban start when INR less than 2
- Edoxaban start when INR less or equal to 2.5

POINT 2 Diltiazem is contraindicated in heart failure

POINT 3 Amiodarone can cause abnormal TFT – need close monitoring

TFT (thyroid function test): TSH and free T4

⇨ Alternative choice to amiodarone

⇨ Sotalol: non standard betablocker – both class II and III, tf can stop both bisoprolol and amiodarone

POINT4 Review statin therapy due to increased CV risk

QRISK3>50% - discuss with doctor and commence atorvastatin 20mg on (primary prevention)

Drug: atorvastatin 20mg	Indication: prevention of CVD
Therapeutic parameter	**Toxic parameter**
Lack of CV events, lipid profile (lowering cholesterol)	Liver function tests (LFTs), myopathy, creatine kinase (CK)

POINT 5 optimisation of HF treatment – add spironolactone 25mg om (NICE)

Drug: spironolactone 25mg	Indication: heart failure
Therapeutic parameter	**Toxic parameter**
Improvement of long-term symptoms of HF	Hyperkalaemia (K+), RF, BP, S/E e.g. gynaecomastia (여유증)

POINT 6 lifestyle counselling for CVD patients

- Diet
- Exercise
- Alcohol in moderation – 14 units over a week

POINT 7 Drug education

- Indication, dose, frequency, side effects on new drugs
- Issues associated with adherence (specifically on furosemide in this case release fluid retention and help with less load on heart – will exacerbate heart failure if not taken)
- Amiodarone: phototoxicity, night glare
- Atorvastatin: take at night, muscle (rhabdomyolysis)

Warfarin
Bisoprolol
Diltiazem
Ramipril
Carbimazole
Furosemide
Amiodarone
Digoxin

Atrial Fibrillation (AF)

- Irregular, rapid atrial rate of 300-600bpm secondary to chaotic conduction within atria
- Ventricular rate of 100-180 bpm
- 1 in 20 of >65 yrs in the UK (7% of admissions)
- Complications:
  - Increased risk of stroke x5 (25% of ischaemic stroke), HF, exacerbated angina
  - Stasis of blood w/ atria lead to cerebral and systemic thromboembolism
  - Sluggish atrial blood flow allows activation of clotting cascade
- Symptoms: SOB, dizziness, fatigue, palpitations

Management Steps

1. Stroke prevention
   First assess stroke risk – CHA2DS2VASc stroke risk score
   (if score greater than 1 in men and greater than 2 in women consider anticoagulant)
   Secondly assess bleeding risk for patients for anticoagulants – ORBIT score
   - DOAC is first line for stroke prevention for AF patients
   - Warfarin is second line if DOAC is contraindicated or not tolerated

   Last resort surgery of left atrial appendage occlusion – clots formed due to AF comes from this area so sealing it off prevents this blood clot
   - Parachute shaped watchman device inserted, it self-expands and seal off the appendage
   - Anticoagulants will be carried on up to 6 months after procedure
2. Rate control: to lower heart rate
   This is first line unless patient has a reversible cause, has HF (beta blocker will worsen HF) or has newly acute AF (electrical cardioversion first line)
   - Standard beta blocker e.g., bisoprolol 2.5mg od and titrate according to response
   - Rate limiting CCB e.g., diltiazem or verapamil
   - Digoxin – only if sedentary lifestyle, bc does not control exercise induced HR
   - If mono therapy does not control combine 2 of beta blocker, diltiazem, or digoxin (never verapamil)
3. Rhythm control: used when rate control not successful or appropriate
   First – electrical cardioversion
   Second – drug therapy
   - Standard beta blocker first line - controls both rate and rhythm
   - Dronedarone (don't use if HF because it will make it worse) – Class III antiarrhythmic
   - Amiodarone if HF – last resort drug
4. If all fail nonpharmacological intervention made
   - Left atrial ablation
   - RF ablation of AV node and PPM inserted

Paroxysmal AF (PAF) – AF that comes and goes

- Pill in the pocket (flecainide) to treat attacks
- If too frequent same treatment as AF to lower rate/rhythm (don't use digoxin)
- Abstinence from alcohol/caffeine
- Antithrombotic considered depending on frequency of paroxysm

CASE STUDY 2 Atrial Fibrillation (AF)

- Has uncontrolled AF with ventricular rate of 120 bpm
- Racing heart, angina, dizziness
- Previously failed DCCV

Drug history

- Dabigatran 150mg bd (DOAC for stroke prevention with AF)
- Bisoprolol 10mg od (max dose beta blocker for rate/rhythm control)
- Perindopril 4mg od (ACEi for HT)
- Amlodipine 5mg od (CCB for angina and HT)
- ISMN MR 30mg od (isosorbide mononitrate for angina)

New prescription of diltiazem XL 120mg od (2nd line treatment - rate controlling CCB)

- Amlodipine should be stopped because new CCB started

➔ Ventricular rate still 100bpm

Therefore:
Rhythm control new prescription – amiodarone (loading required due to long half-life of 40-50days)

- 200mg tds 1 week -> 200mg bd 1 week -> 200mg od maintenance
- Loading dose pf 400mg tds for 3 days and 200mg od for maintenance (RAPID)
  - This way patient can leave hospital with full loading dose

Rate control new prescription – Digoxin – because it takes long for amiodarone to have effect

- 500mcg x2 STAT 6 hours apart (36-51H half-life)
- 125mg od maintenance

Pharmaceutical care issues to be discussed:

1. Amiodarone monitoring and counselling
   Side effects (dirty drug but effective)
   - Bradycardia, phototoxicity, slate-grey skin (sensitivity to light develop tf need long sleeves sunscreen and stay in shade), may taste food to be metallic, corneal microdeposit (change in eyesight see glow/halo in lights)
   - Pulmonary toxicity may occur tf patient need to report SOB
   - Liver dysfunction (toxic monitoring parameter)
   - Thyroid dysfunction (toxic monitoring parameter) – baseline thyroid function needs to be measured regularly
2. Digoxin monitoring and counselling
   Has narrow therapeutic index
   - N&V, blurred vision, anorexia, bradycardia
   - If patients given antiemetics, needs to be checked bc it could be signs of toxicity
3. Management of interaction between amiodarone and digoxin
   - Amiodarone causes increased levels of digoxin (doubled)
   - Tf if used long term in combination – digoxin dose should be halved
   - Interaction takes 1-4 weeks to occur so no need to worry immediately
4. Anticoagulation – stroke risk and bleeding risk assessment

Venous Thromboembolism (VTE)

➔ Unlike MI and CVA where there are atheromatous plaques, vessels often normal

Deep vein thrombosis (DVT)

- Activation of coagulation and clotting in areas of reduced blood flow

Epidemiology	1 in 1000 people, 1-5% fatality, more common in male over 40
Causes	
Risk factors	
Clinical features	60% in calves (distal DVT) Unilateral leg swelling, tenderness, warmth, redness, superficial veins, ankle oedema, ankle pain
Diagnosis	Wells Clinical Score: high probability if 3 or up, moderate between 1 and 2 D-dimer assay – blood test - D-dimer present after fibrin breakdown - High negative predictive value but false positives in elderly bc no specific to DVT - Affected by position of clot – low sensitivity in lower calf veins Imaging: venography, duplex ultrasonography, MRI Other possible diagnosis: physical trauma, cellulitis (tissue infection), ruptured baker's cyst (fluid swelling at back of knee), oedema (swelling leg)
Management	Key aim of treatment - Prevent damage to valves of veins - Allow normal circulation to limbs - Prevent PE 1. Identify any underlying cause – the risk factors 2. Immediate management with injectable anticoagulant - Heparin 1st line choice (prevents extension of thrombosis) 3. Medicate anticoagulant - Duration usually 3 months 4. Other managements: compression stockings – assist calf muscle pump and lower venous HT, prevents venous ischemia • Unfractionated heparin (UFH) • Low molecular weight heparin (LMWH): delteparin, enoxaparin, tinzaparin (reduced frequency of dosing, less side effects than UFH) • Warfarin (VKA) • Dabigatran etexilate • DOACs (Rivaroxaban, Apixaban, Dabigatran, Edoxaban)

Treatment:
Low molecular weight heparin: Enoxaparin, Dalteparin 5000IU, Tinzaparin
Oral Anticoagulation: Warfarin, Acenocoumarol (nicoumalone), phenindione
DOACs: Apixaban, rivaroxaban,dabigatran
Oral anticoagulation duration is normally 3 months

Warfarin: Monitoring:
Baseline: Clotting screen, Hb, Platelets, LFT's
INR and signs of bleeding
Normal INR – 1-1.2

Warfarin loading dose:
Occurs as schedules:
Day 1: 10mg
Day 2: 10mg
Day 3: INR reading taken

When to give a lower dose (i.e Day 1: 10mg Day 2: INR):

- Increased prothrombin time and LFT's
- CCF
- Parental feeding
- Elderly
- Weight less than 60kg
- Other drugs that may potentiate INR

Counselling points of Warfarin:
Need to know what indication it is for
Dose and colour of tablets
Time to take it
Monitoring with the INR and warfarin booklet
Interactions with drugs (P450 metabolism) or food

Dabigatran: Doesn't require therapeutic drug monitoring, the duration depends on its indication.
Used in haemorrhages

Rivaroxaban/Apixaban/Edoxaban: Doesn't require therapeutic drug monitoring and is usedin nausea and haemorrhage. Duration dependent on indication

Management of VTE using compression stockings: Reduces venous hypertension and leg oedema.
Prevention of. Venous ischemia

Pulmonary Embolism (PE)

-

Epidemiology	1 in 1000 people, 2nd most common cause of unexpected death
Causes	
Risk factors	
Clinical features	
Diagnosis	
Management	

Treatment of Pulmonary Embolism:
Supportive therapy
Immediate anticoagulation – warfarin, DOACs
Fibrinolytics: Urokinase, Streptokinase, Alteplase, Reteplase – fibronlytic drugs are contraindicated in recent surgery, active bleeding sites, renal/liver diseases and if patient has a history of stroke.

VTE mechanical prophylaxis:
Thigh length graduated compression stockings from admission until usual levels of mobility resumes

Pharmacological prophylaxis:

- LWMH – dalteparin 5000IU S/C
    - Enoxaparin 40mg OD s/c
    - Foundaparinux
- Pre-existing anticoagulation or antiplatelet therapy

Hypertension in adults: diagnosis and treatment

NICE National Institute for Health and Care Excellence

Offer lifestyle advice and continue to offer it periodically

Clinic BP

Under 140/90 mmHg

→ Check BP at least every 5 years and more often if close to 140/90 mmHg

140/90 to 179/119 mmHg

→
- Offer ABPM (or HBPM if ABPM is declined or not tolerated)
- Investigate for target organ damage
- Assess cardiovascular risk

→ Assess for target organ damage as soon as possible:
- If target organ damage, consider starting drug treatment immediately without ABPM/HBPM
- If no target organ damage, confirm diagnosis by:
  - repeating clinic blood pressure measurement within 7 days, or
  - considering monitoring using ABPM/HBPM and ensuring a clinical review within 7 days

180/120 mmHg or more

→ Refer for same-day specialist review if:
- retinal haemorrhage or papilloedema (accelerated hypertension) or
- life-threatening symptoms or
- suspected pheochromocytoma

ABPM or HBPM

Under 135/85 mmHg

→
- Check BP at least every 5 years and more often if clinic BP close to 140/90 mmHg
- If evidence of target organ damage, consider alternative causes

135/85 to 149/94 mmHg (Stage 1)

→ **Age >80 with clinic BP >150/90 mmHg:**
- Offer lifestyle advice and consider drug treatment

Age <80 with target organ damage, CVD, renal disease, diabetes or 10-year CVD risk ≥10%:
- Offer lifestyle advice and discuss starting drug treatment

Age <60 with 10-year CVD risk <10%:
- Offer lifestyle advice and consider drug treatment

Age <40:
- Consider specialist evaluation of secondary causes and assessment long-term benefits and risks of treatment

150/95 mmHg or more (Stage 2)

→ Offer lifestyle advice and drug treatment

Age <40:
- Consider specialist evaluation of secondary causes and assessment long-term benefits and risks of treatment

Use clinical judgement for people with frailty or multimorbidity

Discuss the person's CVD risk and preferences for treatment, including no treatment.

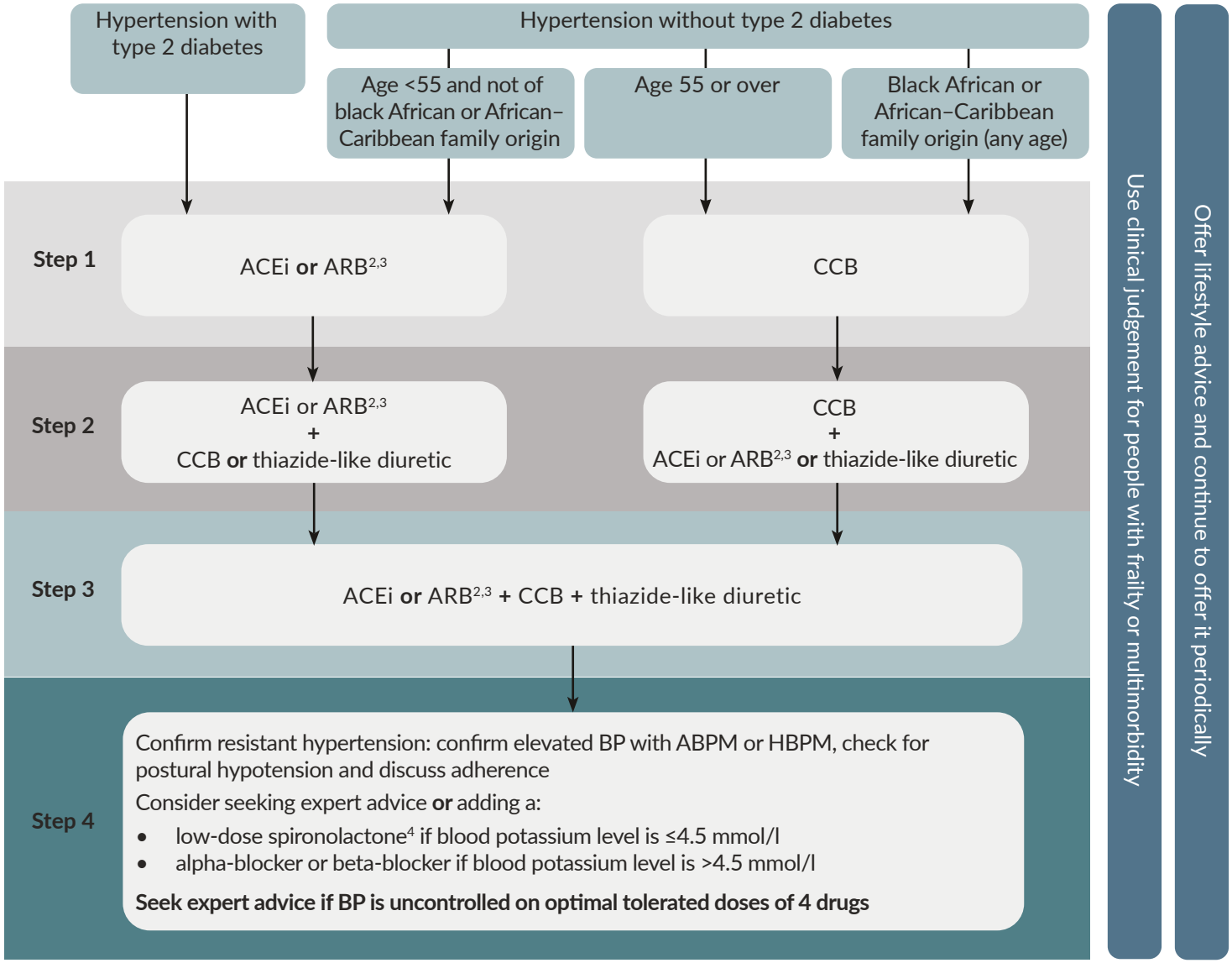
See NICE's patient decision aid for hypertension

See next page for choice of drug, monitoring and BP targets.
- Offer annual review
- Support adherence to treatment

Abbreviations: ABPM, ambulatory blood pressure monitoring; BP, blood pressure; CVD, cardiovascular disease; HBPM, home blood pressure monitoring.

This is a summary of the recommendations on diagnosis and treatment from NICE's guideline on hypertension in adults. See the original guidance at www.nice.org.uk/guidance/NG136

Choice of antihypertensive drug[1], monitoring treatment and BP targets



Monitoring treatment

Use clinic BP to monitor treatment.

Measure standing and sitting BP in people with:

- type 2 diabetes **or**
- symptoms of postural hypotension **or**
- aged 80 and over.

Advise people who want to self-monitor to use HBPM. Provide training and advice.

Consider ABPM or HBPM, in addition to clinic BP, for people with white-coat effect or masked hypertension.

BP targets

Reduce and maintain BP to the following targets:

Age <80 years:

- Clinic BP <140/90 mmHg
- ABPM/HBPM <135/85 mmHg

Age ≥80 years:

- Clinic BP <150/90 mmHg
- ABPM/HBPM <145/85 mmHg

Postural hypotension:

- Base target on standing BP

Frailty or multimorbidity:

- Use clinical judgement

[1] For women considering pregnancy or who are pregnant or breastfeeding, see NICE's guideline on hypertension in pregnancy. For people with chronic kidney disease, see NICE's guideline on chronic kidney disease. For people with heart failure, see NICE's guideline on chronic heart failure.

[2] See MHRA drug safety updates on ACE inhibitors and angiotensin-II receptor antagonists: not for use in pregnancy, which states 'Use in women who are planning pregnancy should be avoided unless absolutely necessary, in which case the potential risks and benefits should be discussed', ACE inhibitors and angiotensin II receptor antagonists: use during breastfeeding and clarification: ACE inhibitors and angiotensin II receptor antagonists. See also NICE's guideline on hypertension in pregnancy.

[3] Consider an ARB, in preference to an ACE inhibitor in adults of African and Caribbean family origin.

[4] At the time of publication (August 2019), not all preparations of spironolactone have a UK marketing authorisation for this indication.

BIHS British and Irish Hypertension Society
Committed to preventing cardiovascular disease

This visual summary builds on and updates previous work on treatment published by the BIHS (formerly BHS)

Abbreviations: ABPM, ambulatory blood pressure monitoring; ACEi, ACE inhibitor; ARB, angiotensin-II receptor blocker; BP, blood pressure; CCB, calcium-channel blocker; HBPM, home blood pressure monitoring.

Published: August 2019

Thought process (use alongside the information provided to you in the independent study pack):

- **What has the patient been diagnosed with?**

Ischaemic stroke

- **Is there any information that you need to clarify?**

Before clinically screening any drug for a patient you must ensure that the patient does not have any allergies to anything, and if they do, that you are aware of the reaction the patient suffers.

Pharmaceutical care issue (PCI) – Patient documented to be allergic to penicillin, but the reaction the patient suffers is unknown.

Action (A) – Ask the patient/patient's wife what happens when penicillin is administered. Document details of the reaction on the drug chart and in the medical notes.

Will any of the medicines the patient was on pre-admission be inappropriate (need to be put on hold/discontinued) in view of diagnosis?

Acute management of hypertension – during the early stages of a stroke, it is common for a patients BP to be elevated but this usually resolves back to the patients 'normal state'. This is seen as beneficial as it helps to increase perfusion to the brain tissue, maintaining the integrity of the penumbra and preventing further damage through ischaemia to the brain tissue. For this reason, strict control of blood pressure is **not** required in the acute phase after a stroke (unless a hypertensive crisis/for alteplase when a specific BP needs to be achieved before administration). A patients current antihypertensive medication would be held until the patient was stabilised, antihypertensive treatment in line with NICE NG 136 would be initiated if BP did not resolve (Long term secondary prevention).

Having very high blood pressure is dangerous and can increase a patient's risk of suffering with a haemorrhagic stroke, in this situation antihypertensive control would be initiated.

Pharmaceutical care issue (PCI) – Patient should not be on their antihypertensive therapy until stabilised and ongoing need established.

Action (A) - Ask Dr to stop patient's current antihypertensive treatment (bendroflumethiazide and felodipine) and monitor patients BP.

This would leave our patient with MST continus tablets and Remegel.

- **Are there any reasons why the patient cannot receive their remaining medication?**

Following a stroke, a patient is at high risk of suffering issues with their ability to swallow due to the stroke affecting areas of the brain that control that process. For this reason all stroke patients are made, 'nil by mouth' until they have had their swallow assessed by a member of the SALT or SLT – speech and language therapist. The SALT will then decide on how the patient can receive food, fluids and medication.

PCI – Determine whether the patient has had their SALT assessment and the outcome to determine how medication can be administered.

The outcome of this was that the patient had failed their SALT assessment and were going to have an NG tube inserted.

PCI – MST continus tablets are a modified release morphine tablet, due to its formulation it cannot be crushed for administration down an NG tube. Remegel is an OTC indigestion preparation which is not appropriate for administration down an NG tube.

A – Ask Dr to stop MST continus tablets and Remegel.

PCI – There is a need to determine how severe the patients back pain is/how well controlled it was with their current medication.

A - If it was well controlled, an equivalent dose of analgesic appropriate for administration down an NG tube, i.e. morphine sulphate oral solution 10mg/5mL – 5mg every 4 hours or suspension 20mg BD or opening Zomorph capsules (20mg BD). You would also provide some PRN morphine sulphate solution for any break-through pai; monitor PRN use and pain score to determine whether higher regular doses were required. Addition of regular paracetamol 1g QDS effervescent tablets via the NG tube would be appropriate as per the WHO pain ladder.

PCI - There is a need to determine how severe the dydpepsia is/how well controlled it was with the Remegel. If possible determine how often it was used and whether it was linked to food intake.

A – Speak to patient (if appropriate) or a relative or carer. Consider whether any appropriate equivalent preparation would be required. See later.

PCI – When/if antihypertensive treatment is required (if BP doesn't start to normalise especially as patient had hypertension prior to admission you would not expect it to normalise to required BP target), if the patient was still experiencing swallowing issues, it would not be appropriate to use felodipine as this is a modified release preparation. See later re. antihypertensive treatment?

A – Recommend an appropriate antihypertensive in line with NG 136 and appropriate for administration down an NG tube (if still in place), i.e. amlodipine .

- **What additional acute medication should be prescribed for this patient's stroke?**

Following diagnosis of stroke with conformation of ischaemia (through imaging), the appropriate first line treatment can be provided. Within the 4.5 hour window, it may be appropriate to give a patient thrombolysis with alteplase, however Mr GB's collapse was 6 hours previous so this treatment would not be appropriate.

The first –line treatment here would therefore be – Aspirin 300mg STAT (this had been prescribed for Mr GB).

PCI – Did the patient receive the aspirin 300mg STAT dose and was it administered appropriately.

A – Review drug chart to determine if administration correct. It is important to give the aspirin dose as quickly as possible. Even if the patient had been reviewed by SALT, it would take time for the nurses to fit an NG tube. For this reason, it would be important for the aspirin to be given via an appropriate alternative route. Aspirin exists as 300mg suppositories which would enable the dose to be given without relying on oral administration.

PCI – Patients with large disabling strokes should receive aspirin 300mg OD for 14 days before being converted onto an appropriate long–term antithrombotic (see later).

A – Ensure the aspirin 300mg OD is prescribed for 14 days, dispersible are appropriate for administration down an NG tube or the suppository is available if that route is unavailable.

PCI – Mr GB has a history of dyspepsia and has now been given a 2 week course of aspirin. NICE NG128, indicates the use of a PPI for any patient who has previously suffered with dyspepsia with aspirin.

A – Discuss with Dr and ask them to prescribe a PPI, i.e. lansoprazole 15mg OD.

Statin therapy is not indicated in the acute stages of stroke. This is because there is contradictory evidence which may indicate statins to increase the risk of haemorrhagic transformation (the patient also suffering with a cerebrovascular haemorrhage).

- **Does the patient have any other conditions that require management in the acute phases of his stroke admission?**

Mr GB is one of the 25% of people who suffer with an ischaemic stroke that is caused by AF. AF causes the stasis of blood in the heart due to the disordered pumping of the atria, which in turn allows the blood to clot and then for the clot to be pumped out of the heart to the brain. For this reason, it is important for the AF to be controlled. In line with NICE CG 196, the first line pharmacological treatment for rate or rhythm control in AF is a beta-blocker.

PCI – Patient is newly diagnosed with AF (time of onset unclear). They should be started on treatment to control their AF.

A – Ask the Dr to prescribe bisoprolol (cardioselective) 5mg OD. Monitor BP and pulse, increase dose if HR not controlled.

Additional treatment for AF, anticoagulation is not appropriate to give to a patient in the acute phase of a stroke. A stroke patient's risk of haemorrhagic transformation is increased in the acute phase and by the size of the infarct. For this reason, it is not appropriate to initiated anticoagulant therapy until the patient had received 14 days of aspirin due to the increased potential for a more severe bleed if it were to occur.

- **What stroke secondary prevention is required?**

BP control – The patients BP would be closely monitored whilst in hospital. If their BP stabilises during the acute stage of the stroke but remains high, systolic >130mmHg, antihypertensive therapy should be started in line with the NICE NG 136.

PCI – Monitor Mr GB's BP and consider initiation of treatment if systolic >130mmHg. This may or may not be required as patient has been started on a beta-blocker for control of his AF.

A – Consider initiation of felodipine 5mg MR (if swallowing issues resolved) or amlodipine 5mg OD (to be administered via the NG tube). If BP remains high, increase the dose to 10mg. If BP still not controlled below systolic 130mmHg, add an ACE-I or ARB, i.e. perindopril 2mg OD or thiazide-like diuretic, i.e. indapamide 2.5mg OM.

Statin –

PCI – Patient should be initiated on statin therapy at least 48 hours after the acute stroke for the secondary prevention of further strokes.

A – Ask the Dr to prescribe atorvastatin 80mg OD.

Anticoagulant – All patients with AF are at an increased risk of suffering with a stroke. For this reason, all AF patients should be assessed for their likelihood of suffering with a stroke. Patients who have already had a stroke are at greater risk than if they only have AF. The CHA_2DS_2-VASc assessment tool is used; male patients with a score of 1 or more and female patients with a score of 2 or more indicate that anticoagulation should be initiated.

It is also important to consider that patients risk of bleeding, this is done using the ORBIT assessment tool; here increasing points indicate that the patient is at increased risk of bleeding. Clinicians use this and their clinical judgement to determine whether the patient is still appropriate to be started on anticoagulation.

PCI – After initial 14 days of aspirin 300mg, patients should be initiated on long-term antithrombotic treatment with an anticoagulant to reduce the risk of another stroke due to the AF.

A – Ask Dr to prescribe warfarin or a DOAC (suggest name and starting dose, i.e. Warfarin 2mg OD and monitor INR).

The patient will continue to be reviewed by the SALT team and will hopefully not require an NG tube/or equivalent long–term (although some patients do). If the secondary prevention is required to go down an NG tube the following information may be helpful (remember to always use an up-to-date appropriate resource such as 'Handbook of drug administration via enteral feeding tubes' or 'The NEWT guidelines'):

Amlodipine, Lisinopril, bendroflumethiazide, atorvastatin, warfarin – can be crushed and dispersed in water.

Apixaban – Swallowed with water, with or without food. Can be crushed.

Edoxaban – Can be taken with or without food. Can be crushed.

Dabigatran – Do **not** crush. The oral bioavailability may be increased by 75% after a single dose. Can be taken with or without food.

Rivaroxaban – Should be taken with food. Tablet can be crushed.

- **What additional general interventions should you make for this patient?**

PCI – New medication started, appropriate counselling required.

A – Counselling on all new medication, name, strength, dose, frequency. Any appropriate additional information, i.e. reporting muscle pain with statin use etc.

PCI – Warfarin/DOAC started; appropriate counselling required.

A – Warfarin/DOAC counselling (see workshop 5). Provide patient with completed yellow book/specific drug information book.

PCI – Dependent on the patient's condition at the time of discharge appropriate discharge planning is required to ensure Mr GB can received his required treatment when he is discharged from hospital.

A - Discharge planning – Ensure you know where the patient is being discharged to and what care is in place. Provide the relevant carer and patient information regarding medications.

- **What lifestyle intervention should you make for this patient?**

PCI – Patient smokes 20 cigarettes a day. Smoking increases your risk of stroke.

A - Discuss reduction/cessation of smoking. Determine the patient's stage of change and respond appropriately to this. If indicated discuss assistance to smoking cessation in the form of NRT.

PCI – Patient is obese. Obesity increases your risk of stroke and MI.

A – Discuss healthy diet – 5+ fruit and vegetables per day, decreased saturated fat and cholesterol intake, appropriate exercise – mobilisation around the house, gardening, cleaning as appropriate to the patient's ability. Discuss weight loss.

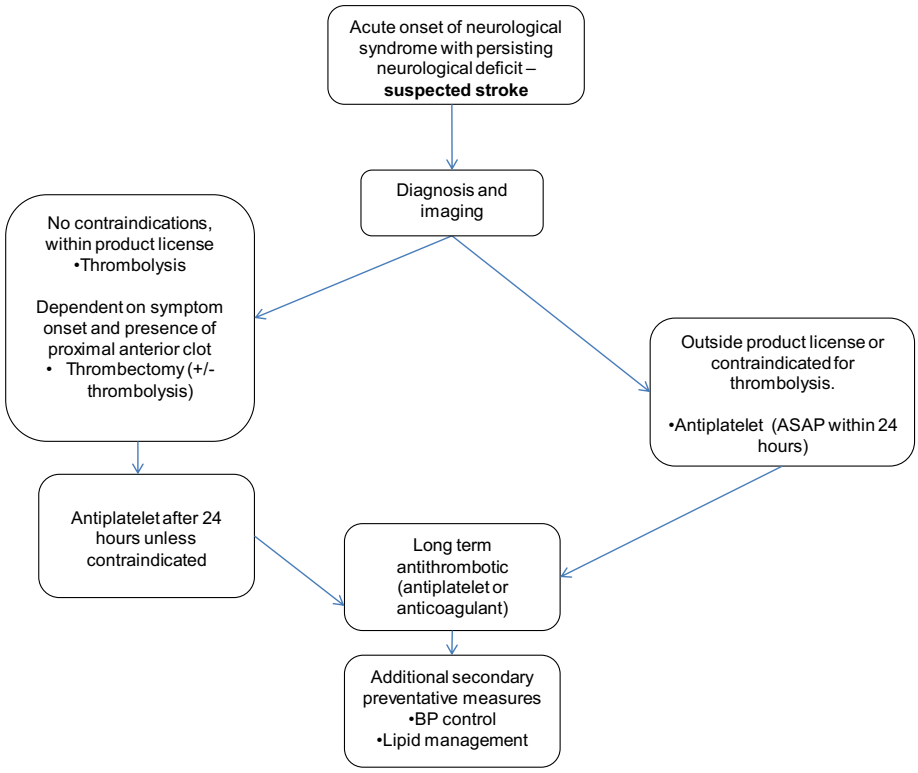
Clinical features	Clinical features depend on: a. Area of the brain affected b. Extent of the damage c. Patients underlying health **Symptoms alone are not specific enough to distinguish ischaemic stroke from haemorrhagic stroke.** Generalised symptoms such as: nausea, vomiting, sudden onset headache and altered level of consciousness (non-focal neurological symptoms) may indicate increased intracranial pressure and are therefore more common in haemorrhagic or large ischemic strokes.[2, 10] Seizures are more common in haemorrhagic stroke occurring in up to 28% of patients either at the onset or within 24 hours of the event.[10] Focal symptoms of ischaemic stroke include:[10] ▪ **Weakness or paresis** that may affect a single extremity (monoparesis), one half of the body (hemiparesis) or (rarely) all four extremities (quadraparesis) ▪ **Hemisensory deficit** – loss of sensation in one side of the body ▪ **Facial droop** – unilateral sagging of the face which indicates paralysis of facial muscle or effect on the facial nerve ▪ **Monocular or binocular blindness** - affecting the sight in one or both eyes ▪ **Blurred vision and/or visual field deficits** – loss of some aspects of sight ▪ **Dysarthria** – difficulty in articulating words due to difficulty in coordinating the muscles used in speech. ▪ **Vertigo** – Sensation of rotation or movement of oneself or surroundings ▪ **Ataxia** – failure of muscular coordination or irregularity of muscular action ▪ **Aphasia** – partial or total loss of the ability to communicate verbally or using written words. The patient may have difficulty speaking, reading, writing, recognising the names of objects or understanding what people have said. People with aphasia make mistakes in the words they use, sometimes using the wrong sounds in a word, choosing the wrong word or putting words together incorrectly. **Aphasia**: Watch the following video of a young stroke patient with aphasia: http://www.youtube.com/watch?v=1aplTvEQ6ew – accessed 14/11/2022 ▪ **Gazing** – looking steadily in one direction for a period of time ▪ **Nystagmus** – rhythmic oscillating motions of the eyes more usually horizontal ▪ **Diplopia** – perception of two images of the same object (double vision) ▪ **Dysphagia** – paralysis of the throat muscles disrupting swallowing ▪ **Decreased consciousness** ▪ **Confusion** ▪ **Severe headache** Patients who have had a stroke often have significant disturbance of physiological homeostasis (greater disturbance with increasing size of infarct) with raised temperature, raised blood pressure, raised blood glucose and hypoxia.

Patient journey / Diagnosis	**Stroke is a medical emergency**
1. FAST recognition 2. Specialist stroke unit 3. Physical examination / Imaging / blood tests **TASK**	95% of patients suffer their first symptoms outside the hospital setting. It is vital for everyone to be able to recognise this early to facilitate appropriate care.[2, 19] **Screening tools – Clinical guidance**[2, 6, 19] **FAST – Face, Arm, Speech, Time** This is the tool of choice for pre-hospital clinicians (i.e. ambulance service and GPs). However, not all symptoms are covered by this, therefore pre-hospital clinicians may treat patients who have a negative-FAST but are suspected of having a stroke (i.e. suffering symptoms such as visual disturbance).[2, 6, 19] This has also been part of a wider public health campaign encouraging members of the public to respond appropriately if symptoms are recognised. Those with ongoing neurological symptoms who have a positive FAST (or negative FAST but where stroke is strongly suspected) should be **transferred to a hospital with a specialist acute stroke unit**.[5, 19] There is strong evidence in favour of specialist stroke unit care to deliver effective acute treatment that reduces long term brain damage and disability if given within a few hours.[2, 19] From the recognition of neurological symptoms patients should be made 'Nil By Mouth' (NBM). Screening of a patient's swallow will occur during admission (within 4 hours of arrival[19]) to hospital by a specifically trained member of staff, usually a speech and language therapist (SALT) – patients are termed as having a 'SALT' assessment. No fluid, food or medication should be given **orally** until this has occurred.[6, 19] Until a safe swallowing method is established, patients should be: a) considered for alternative fluids, b) be considered for a nasogastric tube feeding within 24 hours, c) be referred to a dietician for assessment, advice and monitoring, d) have a comprehensive specialist assessment of their swallow, e) receive hydration, nutrition and medication by alternative means.[19]
TASK	Any person with an acute onset of neurological syndrome with persisting symptoms requires a full diagnosis to differentiate between an acute cerebrovascular cause and other causes. In A&E, determination of a provisional diagnosis should be made by a stroke specialist or by using additional validated tools, i.e. ROSIER (Recognition of Stroke in the Emergency Room – a scale used to establish the diagnosis of stroke or TIA. Factors assessed include: demographic details, blood pressure and blood glucose concentration; items on loss of consciousness and seizure activity; and physical assessment including facial weakness, arm weakness, leg weakness, speech disturbance and visual field defects).[6] **Brain Imaging (Magnetic Resonance Imaging (MRI) or Computerised Tomography (CT))**: Immediate scanning is the most cost-effective strategy.[2,19] Imaging enables identification of the presence of a haemorrhage or ischaemic infarct, the extent of the cerebral damage (core and penumbra) and aetiology as this will dictate the treatment. NICE[6] recommends: Brain imaging immediately if any of the following applies: ▪ Indications for thrombolysis or thrombectomy ▪ On anticoagulation treatment ▪ Known bleeding tendency ▪ Depressed level of consciousness (Glasgow Coma Scale (GCS) below 13)

	▪ Unexplained progressive or fluctuating symptoms ▪ Papilloedema, neck stiffness or fever ▪ Severe headache at onset of symptoms For all other circumstances, imaging should be carried out as soon as possible but within 24 hours.[6] **Carotid doppler:** This is a non-invasive test using sound waves to measure the flow of blood through the carotid arteries which supply blood to the brain. It is used to identify narrowing of these arteries. In some specialist stroke units this will be performed after the MRI/CT to decide whether surgery is appropriate. **Additional tests** (underlying causes of stroke, i.e. heart disease, diabetes and hypertension require determination/diagnosis/exclusion as the cause of the symptoms): Blood glucose (BM) – to determine whether the symptoms are related to a hypoglycaemic episode, this can present with similar symptoms and requires specific treatment. Clotting (APTT, PT and INR) – to determine whether there is any underlying bleed risk which may be a causative factor in the presentation or dictate treatment. ECG – to determine whether the patient is suffering with any type of arrhythmia which could be the cause of the stroke. Fasting lipids – to determine the likelihood of atherosclerosis. Blood culture – to determine the presence of an infective cause. Full blood count (FBC) – may reveal a cause for the stroke, (i.e. thrombocytosis, polycythaemia, leukaemia, thrombocytopenia). Urea and electrolytes (U&E) – baseline study to determine whether there are any other likely causes of the symptoms (i.e. hyponatraemia) or evidence of concurrent illness (i.e. renal impairment). **Physical examination:** Potential examinations used to determine the area and extent of damage to the brain and includes: Cranial nerve examination Motor function examination Sensory function Cerebellar function Gait Deep tendon reflex Language (expressive and receptive capabilities) Lumbar puncture – (removal and examination of cerebral spinal fluid to rule out meningitis or SAH). **TIA** For patients whose symptoms resolve quickly, (i.e. **TIA patients**), there is an increased risk that these patients will develop a stroke. CT brain scanning should not be used unless there is a clinical suspicion (symptoms or history that indicate it is not a TIA) of an alternative diagnosis.

	These patients will be assessed by a specialist physician who will make the decision of whether any imaging is required; scans will be carried out on those patients if the area of the brain affected is unknown, the cause of the symptoms is unknown (not typical symptoms etc.), to detect haemorrhage (i.e. for those on anticoagulation – when scanning should be immediate) or if these factors will influence treatment (i.e. dependent on the area of the brain affected, may dictate a patients treatment i.e. carotid surgery).
Treatment guidance (covering ischaemic stroke and TIA only – you are not required to know the treatment of haemorrhagic stroke)	**Aims of stroke treatment:** ▪ **To maintain/improve vascular perfusion of the brain** ▪ **To prevent further deterioration of neurological symptoms by preventing the advancement of the penumbra.** **Patient-centred care**[6, 18] – treatment and care should take into account peoples' needs and preferences, where possible, patients should have the opportunity to make informed decisions about their care and treatment. Good communication between healthcare professionals, people with acute stroke or TIA and their families and carers, is essential. It should be supported by evidence-based recommendations tailored to the person's needs. All patients, following initial assessment should be admitted to a specialist stroke unit.[6] **Acute phase care** – i.e. from the time of onset of symptoms and covers the first 24 hours and up to 7 days depending on the severity of the disease; for most people this stage is over in approximately 3 days.[2] **Immediate management**:[6] Urgent treatment has been shown to improve the outcome in stroke. Once the patient has a diagnosis of ischaemic stroke, the most appropriate urgent treatment for that patient can be decided: **Thrombolysis**[2, 6, 19] – use of drugs, such as alteplase, to break up a clot. Unless contraindicated or outside of its marketing authorisation, alteplase is the recommended for treating ischaemic stroke. Its use should only be undertaken in units/A&E where staff are trained and experienced in its provision and monitoring and where imaging has occurred to confirm the differential diagnosis of ischaemic rather than haemorrhagic stroke. Treatment should be given as soon as possible after the onset of stoke. The benefits of treatment quickly diminish with time and beyond 4.5 hours are unproven. The licensing[15] for use of thrombolysis (alteplase) reflects this: ▪ Treat as early as possible **within 4.5 hours** of known symptom onset for those who have been shown to **NOT** to have an intracerebral haemorrhage or other contraindications. ▪ After 24 hours, all patients who have undergone thrombolysis should be started on an **antiplatelet** (unless contraindicated), see below.

TASK	Note – the decision to thrombolyse a patient will be a clinical decision based on the individual patient characteristics (i.e. co-morbidities). If you refer to the RCP guidance[18] you will see that they provide additional research into the time for use of alteplase which varies from the SPC and NICE 2019 – please be aware that use outside of the 4.5 hours is unlicensed. **Thrombectomy for people with acute ischaemic stroke[6]** To find out more about thrombectomy, please watch this video: https://www.youtube.com/watch?v=C2oxyIZR4xo – accessed 14/11/2022 Thrombectomy should be offered to patients with acute ischaemic stroke and have occlusion of the proximal anterior circulation:[6] - As soon as possible and within 6 hours of symptom onset, - with intravenous thrombolysis (if not contraindicated and within the licensed time window). Or Thrombectomy should be offered to those patients with acute ischaemic stroke, have occlusion of the proximal anterior circulation and who were last known to be well between 6 hours and 24 hours previously, where:[6] - There is the potential to salvage brain tissue (i.e. where imaging has shown a small core area and therefore the surrounding area may be able to re-perfused if the clot is removed). When clinicians are determining the most appropriate treatment options for patients, they must take into account a patient's co-morbidities and functional status prior to the stroke. **Antiplatelets**:[5, 19] **All** patients with acute stroke, where primary intracerebral haemorrhage has been excluded by brain imaging, should receive: ▪ **Aspirin 300mg OD for 2 weeks.** ▪ For patients that have been thrombolysed, the aspirin should be started 24 hours after alteplase treatment unless contraindicated. ▪ For patients that have NOT been thrombolysed, aspirin should be started ASAP, but within 24 hours. ▪ Aspirin should be given orally if the patient is not dysphagic and swallow has been assessed or rectally/via NG tube if the patient is dysphagic. ▪ At the two-week point, long term antithrombotic treatment should begin. If patients are discharged prior to completion of the initial two-week therapy, their long-term treatment can be started earlier at the time of discharge. (See below for details of long-term treatment). ▪ For patients in whom previous dyspepsia associated with aspirin has been reported, a **proton pump inhibitor (e.g. lansoprazole)** should be given in addition to aspirin. ▪ Patients with ischaemic stroke who are allergic or genuinely intolerant of aspirin should be given an alternative antiplatelet agent, **e.g. clopidogrel.**



Lipid management:[2]

- Immediate initiation of statin treatment is **NOT** recommended in people with acute stroke. However, those who were already receiving statins should continue their statin treatment.[2, 5]

Maintenance of homeostasis: [5, 19]

A key element of care for people with acute stroke is the maintenance of cerebral blood flow and oxygenation to prevent further brain damage. Supplemental oxygen, maintenance of normoglycaemia and blood pressure manipulation are considered below:

- **Supplemental oxygen**: stroke patients should only receive supplemental oxygen if their oxygen saturation drops below 95%.

- **Blood sugar control**: stroke patients should be treated to maintain a blood glucose concentration between 5 and 15 mmol/L (tight control has not been shown to improve outcome in stroke patients).

Blood pressure control:[2, 5, 19, 9]

Blood pressure control post stroke remains an area where there is little evidence to guide care.[2, 19] Excessive or too rapid reduction of blood pressure may compromise cerebral blood flow and lead to development of the penumbra (i.e. death of brain tissue).

Elevated BP in the acute phase following ischaemic injury is common, however in most patients this resolves on its own after 4-10 days. However, continued or excessively high blood pressure is associated with the development of oedema and haemorrhage.

- Immediate treatment of hypertension following an acute stroke is only recommended if there is a **'hypertensive emergency'** with one or more of the following medical issues:
    - Hypertensive encephalopathy
    - Hypertensive nephropathy
    - Hypertensive cardiac failure/MI
    - Aortic dissection
    - Intracerebral haemorrhage with systolic blood pressure over 200mmHg
    - Pre-eclampsia/eclampsia

Where a reduction in blood pressure is required (as above, plus prior to thrombolysis (where the target BP is = 185/110mmHg)) **oral** (either by mouth or NG tube) or **parenteral** therapy may be used.

For example:

- Calcium channel blockers, e.g. amlodipine (safe for administration down NG tubes, always check reference sources)
- Parenteral beta blocker, e.g. Labetolol

In practice blood pressure is allowed to 'run high' (be slightly raised) for at least the first few days to ensure adequate perfusion.

For stroke patients:[2]

- Those admitted already taking antihypertensive therapy - treatment can be safely withheld until patients are medically and neurologically stable and have suitable oral or enteral intake.[19]

Secondary prevention of stroke:

'The risk of a patient having a recurrent stroke is 26% within 5 years of the first stroke and 39% by 10 years'[2, 18,]

- The greatest risk of a vascular event is highest after a TIA or stroke and may be as high as **25% in the first 3-months**, half of which are within the first 4-days.[19]
- There are also additional risks of about the same magnitude of other vascular events, i.e. myocardial infarction.[2, 19]
- Secondary prevention should be started **as soon as possible***, registry data indicates this can significantly reduce the risk of recurrent events.[19]
- All people with stroke or TIA should receive a **comprehensive and personalised strategy for vascular prevention** including medication and lifestyle factors, this should be implemented as soon as possible and continue long term (with review and monitoring occurring in primary care at least once a year).[19]

*Once appropriate to do so.

Blood pressure:

This is a known treatable risk factor of stroke and is estimated to cause about 50% of ischaemic strokes. The relationship between blood pressure and cerebral perfusion pressure means that changes to BP in acute stroke may influence the extent of brain damage. **Treatment recommendations differ when considering the acute setting and long-term secondary prevention.**

The PROGRESS study demonstrated that blood pressure reduction after stroke or TIA (using two different anti-hypertensives) prevented further vascular events. It showed that even in normotensive patients, a reduction in blood pressure (of 12/5mmHg) resulted in a 42% reduction in recurrent stroke and 35% fewer major coronary events.[19]

Meta-analysis found BP lowering treatment significantly reduced cardiovascular events and death in proportion to the magnitude of the BP reduction achieved with no differences in the proportional benefits between trials with lower (below 130 mmHg) or higher systolic BP at baseline.[19] Overall, a 10 mmHg reduction in systolic BP reduced the risk of cardiovascular disease by 20% and stroke by 27%.[19]

There remains uncertainty of when to initiate BP therapy. There is no evidence to show that early intervention results in long term benefits.[19] **For those admitted already taking antihypertensive therapy, treatment can be safely withheld until patients are medically and neurologically stable and have suitable oral or enteral intake.**[19]

- **Recommended target blood pressure <130mmHg** [19] – patients with TIA or stroke should have their BP checked, and treatment should be started and/or increased to consistently achieve a clinic systolic of <130mmHg. (For those with bilateral carotid stenosis this should be increased to 140-150mmHg).[19]
- **Initiation**[19] - BP lowering treatment for stroke and TIA patients should be initiated prior to the transfer of care out of hospital or at 2 weeks, whichever is soonest (or the first clinic visit for non-hospitalised patients).[19]
- **Control/monitoring**[19] – monitoring should occur frequently, and the dose increased to achieve a target BP as quickly as tolerated and safe.
- **Treatment choices**[19]**:**

Patient group	Treatment option
55 years or over, African or Caribbean patients of any age	First choice: ▪ Dihydropyridine calcium channel blocker, or Where this is ineffective, add: ▪ Angiotensin-converting enzyme inhibitor, or ▪ Angiotensin-II receptor blocker, or ▪ Thiazide–like diuretic
Not of African or Caribbean origin or younger than 55 years, or Diabetic of any age	First choice: ▪ Angiotensin-converting enzyme inhibitor, or ▪ Angiotensin-II receptor blocker Where this is ineffective, add: ▪ Dihydropyridine calcium channel blocker, or ▪ Thiazide-like diuretic

The PROGRESS trial[16] demonstrated the benefit of two antihypertensive drugs, an ACE-inhibitor and thiazide diuretic (**perindopril and indapamide**).In practice this combination is still occasionally seen.

Refer to your screencasts and workshop material on hypertension. See Bb 'Independent study for week 8 – CVD clinical workshop – Hypertension'.

RCP noted[19]: 'There should be a move away from concept of treatment of hypertension and towards the concept of modifying BP as a risk factor. It is appropriate to modify the BP in patients that would previously have been considered normotensive'[19]

Long term use of antiplatelets:[19]

For long term vascular prevention in people with ischaemic stroke or TIA **without atrial fibrillation.**

The Antithrombotics Trialists' Collaboration demonstrated 36 fewer serious vascular events (25 fewer stroke) per 1000 patients for patients treated for 29 months with

antiplatelet drugs.[2] The CAPRIE, ESPIRIT and PRoFESS comparative studies show that aspirin plus modified release dipyridomole and clopidogrel monotherapy are equally effective and both SUPERIOR to aspirin monotherapy.[19]

Recommendation for stroke:

Treatment	Type of antiplatelet
First line	***Clopidogrel 75mg OD***
Second line (when clopidogrel contraindicated)	**Aspirin 75mg OD plus modified release dipyridamole 200mg BD**
Third line (when clopidogrel and aspirin or dipyridamole are contraindicated)	**Aspirin or modified release dipyridamole monotherapy.**

Use of aspirin plus clopidogrel has been compared and was not superior to clopidogrel monotherapy with some evidence of increased side effects.[2, 19]

See NICE technology appraisal guidance 210 at:

https://www.nice.org.uk/guidance/ta210?unlid - accessed 14/11/2022

- Patients with previous dyspepsia associated with antiplatelet use should be given a **proton pump inhibitor.**

Lipid management:[2]

Raised lipid levels, especially hypercholesterolaemia is a well-known risk factor for atherothrombotic events (especially MI). Lowering these levels is effective in primary and secondary treatment of vascular events, including stroke.[19]

The Heart Protection Study **(HPS)** looked at the effect of Simvastatin 40mg OD in individuals at high risk of cardiovascular events and showed a relative risk reduction of 17% in vascular death, 27% in major coronary events and 25% in stroke. Long term follow-up showed persisting benefits.[2]

SPARCL investigated the effect of atorvastatin 80mg OD in individuals with previous TIA or stroke within the previous 6 months and demonstrated a relative risk reduction of 15% in stroke and 35% in major coronary events. [2, 19]

Lowering low density lipoprotein (LDL) cholesterol by 1mmol/L reduces the relative risk of major vascular events by 21%, total mortality by 9% and stroke by 15% irrespective of baseline cholesterol or gender. Therefore, the decision to initiate treatment should be determined by their cardiovascular risk rather than their cholesterol level.[19]

NICE CG181 for lipid modification, provides guidance in line with these studies and the recommendations of the RCP 2016 guideline[19] match the recommendations for stroke and TIA patients.

Note: Risk with statin – A number of studies have shown an increase in the risk of **haemorrhagic stroke** with the initiation of statin therapy in the acute setting. More prospective studies are required to determine this association.[2] This helps to explain why **statins are not introduced in the immediate acute period (first 48 hrs).**[5]

Recommendations:

- Patients should be offered advice on lifestyle factors that may modify lipid levels (diet, physical activity, weight, alcohol and smoking).[19]
- Patients who have had a stroke should be offered treatment with a statin unless contraindicated.[19]

- Begin with a high intensity statin (**atorvastatin 80mg**), change to an alternative statin at maximum tolerated dose if a high intensity statin is unsuitable or not tolerated.
- NICE 181[17], Lipid modification advises a target of >40% reduction in non-HDL cholesterol.[17, 19]

Anticoagulation:[2, 17, 19]

Anticoagulation should be started for patients with confirmed ischaemic stroke who have had a cardioembolic stroke, particularly in **atrial fibrillation**, **AF.** Anticoagulation is not more effective than antiplatelet therapy in people with non-cardioembolic ischaemic stroke or TIA and carries a greater risk of bleeding.[19]

There is a 12% attributable risk of recurrent stroke per year associated with AF which for most patients tips the risk-benefit balance in favour of anticoagulation.[19]

The **CHA_2 DS_2-VASc** assessment tool is used to assess stroke risk in patients with AF.

One or two points are awarded to the patient based on each of the characteristics of this tool. The value is then used to guide whether the risk is high and therefore if anticoagulation should be started. A value of **1 for a man** and **2 for a woman** indicates anticoagulation should be started.[19]

Components	
C	Congestive heart failure
H	Hypertension
A_2	Age >75 (2 points)
D	Diabetes mellitus
S_2	Prior stroke or TIA (2 points)
V	Vascular disease
A	Age >65
Sc	Sex (female 1 point)

The **ORBIT** assessment tool is used in conjunction with **CHA_2 DS_2-VASc** to estimate the risk of major bleeding for patients on anticoagulation for AF. Dependent upon the number of points awarded the risk of bleeds per year can be estimated. This helps guide the decision on whether anticoagulation should be started.

Components	
Hb	<13g/dL male <12g/dl female (2 pts)
Age	>74 (1 point)
Bleeding history	GI/intracranial/haem stroke (2 points)
Renal function	eGFR<60ml/min/1.73m^2 (1 point)
Antiplatelet treatment	(1 point)

Using the values from ORBIT a clinical decision must be made as to whether anticoagulation should be used or not (unlike the CHA_2 DS_2-VASc score there are no threshold values to guide this decision, however an ORBIT score of 0-2 is considered low risk, 3 medium risk and 4-7 high risk of bleeding).

If, despite addressing modifiable risk factors for bleeding the risk of bleeding is still considered too high; aspirin is not regarded as a safer option.[18] In the only randomised control trial to compare aspirin to placebo, aspirin was not shown to be more effective than placebo in the prevention of disabling stroke or thromboembolic events.[2, 19]

When to start anticoagulation:

The medical team must make their decision based on the risk of haemorrhagic transformation (the risk is increased with increasing size of infarct and occurs in around 6% of stroke patients[2, 19]) and the risk of further infarcts as a result of the AF.

- Patients with severe disabling strokes should be **deferred from anticoagulant treatment until at least an arbitrary 14 days post onset.** They should receive aspirin 300mg until this time.[2, 19] (This is because, the larger the infarct, the greater the risk of haemorrhagic transformation).
- Patients with less significant, non-disabling infarcts should be deferred for an interval at the discretion of the prescriber, but no later than 14 days.[2, 19]

Available anticoagulants:

- **Warfarin**
- **Direct Oral Anti-Coagulants (DOAC)**

Factor Xa inhibitor or direct thrombin inhibitor (see appendix for pharmacology):

- **Dabigatran**
- **Rivaroxaban**
- **Apixaban**
- **Edoxaban**

NICE NG196, Atrial Fibrillation: Diagnosis and Management[17], last updated April 2021 recommends the use of a DOAC as first-line for secondary stroke prevention for people with non-valvular AF. Warfarin is second-line when DOACs are contraindicated, not tolerated or not suitable.

Research continues to distinguish between the different DOACs and therefore current recommendation is dependent upon their specific characteristics, i.e. side effect profile, cautions etc.

The DOACs have a rapid onset of action, have fewer interactions with other drugs and foodstuffs and do not require regular coagulation monitoring.[18] Three studies – RE-LY, ROCKET-AF and ARISTOTLE have demonstrated a more effective stroke prevention with reduced intracranial bleeding compared to warfarin. No significant differences have been seen in relation to major and gastrointestinal bleeding risk (however this does not provide evidence of safety or efficacy of the DOACs in whom the bleeding risk is considered to be too high for warfarin).[19]

The **RE-LY study** compared the use of warfarin to dabigatran in cardioembolic events. The benefit of dabigatran over warfarin was greatly reduced in patients where the quality of anticoagulation control was high. 'Quality' of warfarin anticoagulation is determined by the 'time in therapeutic range' (TTR)[2], i.e. the time that a patient on warfarin is maintained at the desired therapeutic range; the average for UK centres was documented as 72%.[2] For warfarin, we are able to monitor the INR (International Normalised Ratio) by taking and analysing a blood sample from the patient. INR is a measure of the time taken for blood to clot (expressed as a ratio against population data), the higher the number the greater time blood will take to clot. So, the blood of a patient on warfarin with an INR of 2.5 will take approximately 2.5 times longer to clot than someone not on warfarin with normal clotting.

Advantages of warfarin*	Disadvantages of warfarin*
Been used for many years - experience	Many food and drug interactions

Antidote available	Requires loading to be therapeutic
Requires regular INR monitoring – efficacy/compliance monitoring	Requires INR monitoring – time and resource consuming

Advantages of DOACS*	Disadvantages of DOACs*
Rapid onset – no loading required	Relatively new to the market, little experience of use
Coagulation monitoring not required	Unable to monitor efficacy/compliance
Predictable anticoagulant effect	Short half-life meaning missed doses could leave patient un-protected
Fewer interactions with drugs and no known food interactions compared to warfarin	Only for use in patients with creatinine clearance greater than 30ml/min
Fixed dosing	Idarucizumab antidote for dabigatran – limited use Andexanet antidote for apixaban, edoxaban, rivaroxaban. Other antidotes in trials.
	Increased cost
	Long term adverse effects unknown

*These lists are not exhaustive but give you an idea of the considerations required when initiating different forms of anticoagulation.

Recommendations:[19]

- For patients with ischaemic stroke or TIA **and AF** anticoagulation should be the standard long-term antithrombotic treatment.
    - It should not be given until haemorrhage has been excluded by imaging.
    - It should not be given to those with uncontrolled hypertension.
    - For those with disabling ischaemic stroke, initiation should be deferred until at least 14 days from onset – aspirin 300mg should be used in the meantime.
    - For those with non-disabling ischaemic stroke, initiation should be deferred for an interval at the discretion of the prescriber, but no later than 14 days from onset.
    - Anticoagulation for those with TIA or ischaemic stroke should be with either:

(i) A direct thrombin or factor Xa inhibitor
OR
(ii) Warfarin adjusted to an INR of 2.5 (range 2-3) with a target time in the therapeutic range greater than 72%.

TASK

Aims of TIA management:

- **To reduce the risk of having a stroke.**

Initial management of <u>suspected</u> TIA:

- **Give Aspirin 300mg[5] OD immediately, unless contraindicated.**
- **Refer for specialist investigation/assessment <u>within 24 hours</u> of the onset of symptoms.**[5] The risk of subsequent stroke after a TIA is high and additional risks may be conferred by: the presence of AF, use of anticoagulant therapy or recurrent attacks.

TASK	Those whose symptoms occurred more than a week ago should be assessed by a specialist physician as soon as possible but within 7 days.[18] These patients are considered at lower risk of subsequent stroke.
	
	Once diagnosis is confirmed:
	
	▪ **With confirmed diagnosis - clopidogrel 75mg OD monotherapy.** [2, 19]
	
	▪ **Additional measures for secondary prevention should be introduced:**[5, 18]
	  ▪ **Hypertension control (if indicated),**
	  ▪ **High intensity statin therapy (atorvastatin 80mg),**
	  ▪ **Discussion of individual risk factor management**
	
	[Although **clopidogrel** does not have a license for use in TIA and is not recommended in the NICE guidance[5]; the RCP 2012[2] and 2016[18] guidance recommends its use to bring TIA treatment in line with that of stroke. Clopidogrel is the more cost effective, and better tolerated option, thus the benefits are seen to outweigh the risks.][2, 19]
	
	Surgery
	Patients with suspected TIA assessed by the medical team may undergo carotid imaging to determine the amount of stenosis in the carotid vessels if indicated. Following this, for those in which it is indicated a carotid endarterectomy may be carried out.
	
	Those with symptomatic carotid stenosis – 50 to 99% → Referred for urgent endarterectomy plus best medical treatment (BP control, cholesterol lowering, lifestyle advice)
	Those with symptomatic stenosis of less than 50% → No surgery. Best medical treatment.
	
	Additional considerations
	
	Where **AF** is identified to be the cause of the TIA, **anticoagulation therapy**, with an agent with rapid onset should be given immediately once haemorrhage is excluded.[2, 19] Refer to section above on anticoagulant therapy.
	
	Other management strategies for stroke and TIA patients:
	
	Lifestyle measure:[2, 19]
	
	Evidence for lifestyle interventions comes from studies for primary prevention with little high-quality research for secondary prevention. It would seem that lifestyle changes are as important in secondary prevention as they are in primary prevention. They require a change in behaviour of the patient, (HCP responsible for providing information, advice and support), for example:
	
	▪ **Smoking cessation**[19] – Around 1 in 5 adults in the UK smoke with an estimated 454,700 hospital admissions being attributable to smoking, including 1 in 4 strokes. Smokers have up to 3 times the risk of stroke and double the risk of recurrent stroke compared to non-smokers, but if they stop the risk decreases significantly and is at the level of a non-smokers by around 5 years. **Stroke and TIA patients should be advised to stop immediately using appropriate individualised interventions.**
	
	▪ **Physical activity**[19] – tailored to the patient. General principles: at least 150 minutes of moderate intensity exercise over a week and strength activities at least twice a week, older people at risk of falls should activities which incorporate balance and coordination, patients should be active every day and minimise the

	amount of time sitting for long periods. This will need to be individualised to the patient ▪ **Improved dietary intake**[19] – There is evidence that cardioprotective diets can favourably modify cardiovascular risk factors but there is limited evidence that this translates into a reduction in stroke recurrence and mortality. Patients should be advised to: eat an optimum diet: 5 or more portions of fruit and vegetables/day, two portions of oily fish/week, replace saturated fats with poly- and mono- unsaturated fats, overweight/obese patients should be offered advice and support to aid weight loss, reduce their salt intake, reduce alcohol intake to a maximum of 14 unit/week over at least 3 days **Rehabilitation services**[19]**:** Pharmacological treatment is only a small part of the treatment required to improve a patient's condition and quality of life after a stroke. Many services are involved in the rehabilitation of patients to help them regain some/all of their normal functions. This process is started soon (within a week) after the event with the involvement of the inpatient rehabilitation team (designated specialist multidisciplinary team) in the patients care. There are a number of other elements that are needed to enable the whole process to occur, they include: ▪ Complete and relevant information transfer from secondary care back to primary care, ▪ Early supported discharge to deliver stroke specialist rehabilitation at home or in a care home, ▪ Services in outpatient and community settings in liaison with inpatient services to continue rehabilitation, ▪ Specialist follow-up at 6-months and annually after a stroke (including a review and monitoring of risk factors), ▪ Further therapies if goals for specific function and activities are identified and a change is likely, ▪ Practical and emotional support (i.e. housing and employment), ▪ GP support, ▪ Social services. **Mental health**: After stroke all patients should be screened to identify mood disturbances and cognitive impairment. For this reason, there may be the introduction of pharmacological treatment, for example: for depression. **End of life care**[19]: Around 1 in 20 acute stroke patients will receive EOL care within 72 hours onset and 1 in 7 die in hospital. Providing high quality EOL care is therefore a core activity for any stroke MDT. Stroke may cause pain, distress, depression, confusion, agitation, and issues relating to nutrition and hydration; appropriate MDT management of these reduce the distress of EOL care for both the patient and those around them.
<u>Pharmacology</u> [18]	To understand the pharmacology of the drugs you are required to understand the mechanism of blood clotting: Haemostasis – The arrest of blood loss from damaged blood vessels, a process which is essential to life.

Damage to a blood vessel causes vasoconstriction plus adhesion and activation of platelets (to form a plug) and formation of fibrin (a reinforcing network) to stop the bleeding.

Thrombosis is the formation of a haemostatic plug in the vasculature without the presence of bleeding, i.e. it is occurring at the wrong place. **Arterial thrombus** consist mainly of platelets and is usually the result of atherosclerosis. **Venous thrombus** consist of a small white head (platelets) and a large red tail (red blood cells).

A thrombus (or part of it) can break away from the primary site and travel to a secondary site, in which case it is termed an **embolus**. Venous embolus usually lodge in the lungs, whereas arterial emboli affect other organs such as the brain or heart.

Blood coagulation is a complex process involving many different factors working together, these include the clotting factors, vessel endothelium and blood components such as platelets.

Coagulation cascade: Appendix 1

This process sees the formation a gel/solid form of blood. Each of the components of the clotting cascade (in the black boxes) are called factors and are found in the blood as inactive precursors of proteolytic enzymes and co-factors (active forms are denoted by 'a'). Each factor in tern activates another down the cascade (starting at the top of the page) and amplifies the downstream effects.

There are two potential mechanisms which could lead to the downstream effects of fibrin formation and stabilisation and they are the **extrinsic** (as some of the components come from outside the blood vessels) and **intrinsic** (as all components are present within the blood vessel wall) pathways. In vivo the whole system functions as a single pathway with complex interplay and feedback loops between the different factors.

If you refer to appendix 1 and 2 you can see that following an atherosclerotic plaque rupture you have several complex processes occurring together which culminates in the formation of a thrombus. Adhered and activated platelets provide co-factors and expose phospholipids important in activating the clotting cascade. Pro-thrombotic factors are synthesised and stored in the endothelium, for example, tissue factor is also responsible for activating the cascade.

Both pathways converge on the activation of factor X and have a shared final course ending with the last enzyme thrombin, derived from prothrombin (II), converting soluble fibrinogen to an insoluble meshwork of fibrin in which cells and platelets become trapped.

Platelet activation:

When platelets are activated, they undergo a sequence of reactions essential for haemostasis, healing and inflammation. For example:

Adhesion – to areas of vascular damage via the glycoprotein 1b receptors on the platelets.
Shape change – the smooth disc structure changes to spiny spheres to enable entrapment within the fibrin mesh.
Secretion – of platelet agonists (i.e. ADP) and coagulation factors to further activate other platelets and the clotting cascade.
Biosynthesis – of factors such as TXA_2 and platelet-activating factor responsible for platelet aggregation and vasoconstriction.
Aggregation – aggregation agonists lead to expression of GPIIb/IIIa receptors that bind fibrinogen linking adjacent platelets.
Phospholipid exposure – promote thrombin formation.

TASK	However, this pathway may be inappropriately activated, for example when an artery wall is diseased (i.e. atherosclerosis) resulting in the inappropriate thrombosis There are also physiological mechanisms for inhibition/reversal of the clotting system, the fibrinolytic system - see appendix 2. Endogenous plasminogen activators, for example, tissue plasminogen activator (t-PA) is released and diffuses into a thrombus where plasminogen is deposited on the fibrin strands. The t-PA activates plasminogen to form active plasmin which cleaves fibrin and a number of clotting factors. It acts locally to lyse the thrombus and halt further clotting action. Please refer to appendices 1, 2 and 3 for graphical representation and you pharmacology text books for the pharmacology of the following drugs. **Thrombolytics** – Appendix 2 purple box– i.e. alteplase, a recombinant t-PA. **Aspirin** – Appendix 1, 2 and 3 red box – Irreversible inhibition of COX-I in platelets preventing the formation of Thromboxane A2 (TXA_2) preventing the downstream steps needed for platelet aggregation. **Clopidogrel** – Appendix 3 blue box- $P2Y_{qw}$ receptor antagonist on platelets responsible for promoting aggregation. **Dipyridamole** – Appendix 3 purple box – Inhibits platelet aggregation by several mechanisms. **Warfarin** – Appendix 1 see factors in red, these are the factors whose formation relies upon the presence of vitamin K. Vitamin K must be in the reduced form to do this; warfarin inhibits the enzyme vitamin K reductase allowing formation of the active form of vitamin K and therefore preventing formation of the clotting factors. **DOACs** – Appendix 1 Rivaroxaban – Direct factor Xa inhibitor. Apixaban – Direct factor Xa inhibitor. Dabigatran etexilate– Is a prodrug which is converted to dabigatran by hydrolysis in the plasma and liver. In this form it is a potent, competitive, reversible direct thrombin inhibitor. Edoxaban – Direct and reversible inhibitor of factor Xa. For any of the drugs above that you have not already looked up in the BNF, remind yourself and make a note of the important cautions, contraindications and side effects as appropriate. **Refer to screencasts and workshops on antiplatelets and anticoagulants. See Bb 'Independent study for week 9 – Antiplatelets, Coagulation Introduction, Anticoagulation Pharmacology, Fibrinolytics'.**
Multidisciplinary team (MDT)	**Ongoing care:** Stroke patients are at high risk of developing dehydration, malnutrition, infections, hypoxia and hyperglycaemia. There is a body of evidence for the management of stroke patients on specialist stroke units rather than in non-specialist care settings with improved patient outcomes. The patients physiological state should be closely monitored to include:

	▪ Blood glucose – should be maintained between 5 and 15 mmol/L[19] ▪ Blood pressure – see above ▪ Oxygenation – supplemental oxygen should be given if saturation drops to below 95% ▪ Nourishment and hydration – food and fluid chart completion ▪ Temperature ▪ Early mobilisation and positioning – sitting will help maintain oxygen saturation and reduce the risk of pneumonia. Patients should be helped to sit up and mobilised as soon as their condition permits. The care and long-term outcome for a patient with stroke relies on the co-ordinated work of the multidisciplinary team (MDT). This will include: consultants, registrars, senior and junior doctors, nurses, speech and language therapists, occupational therapists, physiotherapists, dieticians, pharmacists, healthcare assistants, psychologist, social workers.
Swallowing difficulties / Enteral feeding tubes / Formulation ***ESSENTIAL - TASK*** **TASK**	▪ You are expected to be able to: ▪ Describe the issues surrounding administration of medicines to patients with swallowing difficulties ▪ Outline the issues surrounding tablet crushing ▪ Describe the role of pharmacists in managing medicines for patients with swallowing difficulties ▪ Enteral feeding tubes are routinely used in patients with dysphagia and those unable to take adequate nutrition and fluids orally to administer nutritional support. ▪ The most common type of feeding tube used in the acute treatment of patients with dysphagia is the nasogastric (NG) tube **Essential** – To develop your understanding of swallowing difficulties, please watch the 2019 'Dysphagia' lecture (uploaded in the same folder as this pack). Please note that although the title page/date/course code do not match your module - 'From bench to bedside', all material in this recording is relevant to you understanding of the care of a stoke patient. ▪ There are several different information resources that pharmacists use in practice to help ascertain the most appropriate methods of drug administration. These include: ▪ Handbook of drug administration via enteral feeding tubes. Rebecca White and Vicky Bradnam. ▪ The NEWT guidelines for the administration of medication to patients with enteral feeding tubes and swallowing difficulties. J. A. Smyth. ▪ http://www.swallowingdifficulties.com/ - accessed 14/11/2022 ▪ First principles – interpretation of formulation pharmacokinetics. ▪ Please refer to - http://www.swallowingdifficulties.com/ - and read the information on 'How to prescribe for patients with dysphagia'