Sandwell and West Birmingham Hospitals NHS
NHS Trust

LIPIDS, LIPOPROTEINS AND CVD

Clinical Biochemistry Department
City Hospital

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LIPIDS & LIPOPROTEINS

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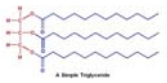
LIPIDS

- Types of lipid
- Fatty acids
  - Oxidised via ß oxidation to produce energy

- Triglycerides
  - 3 fatty acids attached to a glycerol backbone
  - Major form of dietry fat
  - Stored form of energy
  - Hydrolysed to fatty acids



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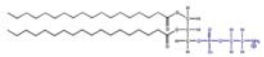
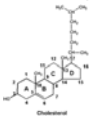
LIPIDS



- Phospholipids
  - 2 fatty acids and a phosphate group attached to a glycerol backbone
  - Present on the surface of lipoproteins and cell membranes
  - Aids solubility



- Cholesterol
  - From the diet and synthesised within the body
  - Component of cell membranes
  - Precursor for steroid hormones, vitamin D and bile acids

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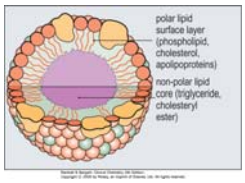
LIPOPROTEINS

- Transport of lipids
- Due to their hydrophobic nature – lipids are transported in the blood in the form of lipoproteins



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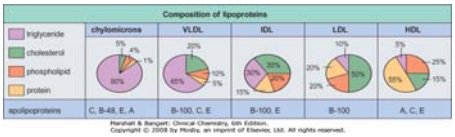
LIPOPROTEINS

- Classified on the basis of their density
  - Chylomicrons
  - Very low density lipoprotein (VLDL)
  - Intermediate density lipoprotein (IDL)
  - Low density lipoprotein (LDL)
  - High density lipoprotein (HDL)



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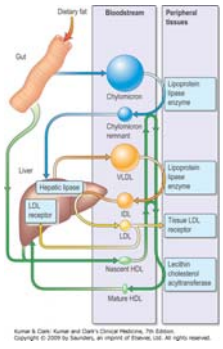
LIPOPROTEINS

- Metabolism & Function
  - Chylomicrons – transport of dietry fat
  - VLDL – transport of endogenous triglycerides
  - LDL – cholesterol transport
  - HDL – reverse cholesterol transport



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LIPOPROTEINS

- Other lipoproteins
- Lipoprotein (a)
  - LDL with apolipoprotein a
  - Independent risk factor for CVD

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HYPERLIPIDAEMIA

- Reference ranges at SWBH
  - Cholesterol 2.5 – 5.0 mmol/L
    - - the lower the better
  - Triglycerides < 2.3 mmol/L – fasting sample
  - HDL > 1.2 mmol/L
- Methods
  - Cholesterol, Triglycerides, HDL – Enzymatic colorimetric; For interferences and enzymes see kit inserts!

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HYPERLIPIDAEMIA – SECONDARY CAUSES

- Hypercholesterolemia (LDL)
  - Hypothyroidism
  - Nephrotic syndrome
  - Cholestasis of the liver
  - Anorexia
  - Drugs e.g. cyclosporin
- Hypercholesterolemia (HDL)
  - Exercise & weight loss
  - Moderate alcohol intake

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HYPERLIPIDAEMIA – SECONDARY CAUSES

- Hypertryiglyceridemia
  - Non-fasting sample
  - Diabetes mellitus
  - CKD
  - Obesity
  - Alcohol
  - Drugs e.g. oestrogens

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HYPERLIPIDAEMIA – PRIMARY CAUSES

- Hypercholesterolemia (LDL)
  - Familial hypercholesterolaemia – LDL receptor
  - Polygenic hypercholesterolaemia
- Hypertriglyceridemia
  - Familial hypertriglyceridaemia
  - Chylomicronaemia- LpL
- Mixed hyperlipidaemia
  - Remnant hyperlipoproteinaemia
  - Familial combined hyperlipidaemia

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HYPERLIPIDAEMIA

- Reasons to identify hyperlipidaemia
- Cholesterol (LDL)
  - Increased CVD risk e.g. MI, stroke
- Triglyceride
  - Increased CVD risk
  - Pancreatitis – panic list
- HDL
  - Beneficial
  - Shown to reduce CVD risk

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HYPERLIPIDAEMIA

- How to identify
  - Measure total cholesterol, HDL and triglycerides
  - Serum sample
  - Fasting for triglycerides
  - Can calculate LDL
  - [LDL] = [Total chol] - [HDL] - ([TG]/2.2)
  - The Friedewald equation should not be used under the following circumstances:
    - when chylomicrons are present
    - non-fasting sample
    - when plasma triglyceride concentration exceeds 4.5 mmol/L
    - in patients with remnant hyperlipidaemia

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CARDIOVASCULAR DISEASE

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CARDIOVASCULAR DISEASE

- Atherosclerosis
  - Inflammatory condition affecting arteries
  - Deposition of lipid in the vessel wall
  - Narrowing of the artery
  - Ischemia and necrosis of the tissue
  - Can rupture leading to thrombosis
  - Often found in the
    - Corornary (heart attack)
    - Cerebral (stroke)
    - Peripheral arteries
  - Causes approximately ⅓ of all deaths in UK – Important to treat early!!

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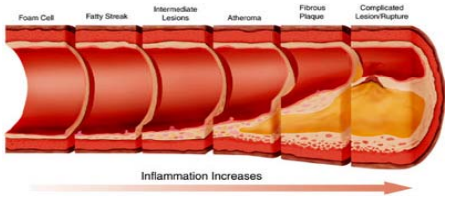
CARDIOVASCULAR DISEASE

- Atherosclerosis



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CARDIOVASCULAR DISEASE

- Modifiable risk factors
  - Hyperlipidaemia ↑TC, ↑Trigs, ↑LDL & ↓HDL
  - High blood pressure
  - Smoking
  - Diabetes
  - Physical inactivity and a poor diet
- Non-modifiable risk factors
  - Age
  - Sex
  - Ethnicity
  - Family history

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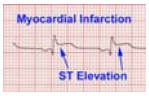
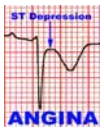
ACUTE CORONARY SYNDROME

- Atherosclerosis in coronary vessels
- **Acute** coronary syndrome (ACS)
  - ST-elevation myocardial infarction (STEMI)
  - Non-ST-elevation myocardial infarction (NSTEMI)
  - Unstable angina

  - Caused by rupture of atherosclerotic plaque
  - Thrombosis in the blood vessel
  - Myocardial ischaemia





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ACUTE CORONARY SYDROME

- Diagnosis
  - Symptoms e.g. pain in chest, arm, jaw, SOB
  - Patient history
  - Electrocardiogram (ECG)
  - Biochemical markers
    - Rule in/out MI
    - Confirm a new infarction
    - Ideally
      - Sensitive – significant levels after myocardial injury
      - Specific – released only by myocardial tissue
      - Cost effective

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ACUTE CORONARY SYDROME

- Diagnosis
  - Universal Definition of MI
  - Troponin value >99th percentile of a normal reference population
    - And at least one of
  - Symptoms of ischaemia
  - New significant ST/T wave changes on ECG
  - Development of pathological Q waves on ECG
  - Imaging evidence of new loss of viable myocardium or regional wall motion abnormality
  - Identification of intracoronary thrombus by angiography or autopsy

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ACUTE CORONARY SYDROME

- Diagnosis
  - Biochemical markers
  - CK
  - CK-MB
  - Troponin T
  - Troponin I

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ACUTE CORONARY SYDROME

- Diagnosis
  - Biochemical markers
  - Total CK – creatine kinase
  - CK catalyses the transfer of a P from ATP to creatine – used as an energy store
  - Mostly found in heart, brain and skeletal muscles
  - Released into the blood stream within 4-6 hours of injury to heart or skeletal muscles
  - Levels peak at 12-24 hours post injury

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ACUTE CORONARY SYDROME

- Diagnosis
  - Biochemical markers
  - Total CK – creatine kinase
  - UV spectroscopy – wavelength = 340 nm
  - Reference range at SWBH
    - Men <190 iU/L
    - Women <167 iU/L
  - Looking at rise in CK above the reference range
  - Not specific to heart muscle damage

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ACUTE CORONARY SYDROME

- Diagnosis
  - Biochemical markers
  - Total CK – creatine kinase
  - Causes of a raised CK include
    - Afro-Caribbean race
    - Statins
    - Skeletal muscle injury inc. seizures, exercise
    - Muscle disease e.g. polymyositis, muscular dystrophy
    - Myocardial infarction
    - Hypothyroidism

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ACUTE CORONARY SYDROME

- Diagnosis
  - Biochemical markers
  - CK – isoenzymes
  - Isoenzymes = enzymes with different AA sequences but they catalyse the same chemical reaction
  - 3 different isoenzymes
    - CK-MM – located in striated muscle
    - CK-MB – located in cardiac muscle
    - CK-BB – located in brain, colon, bladder

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ACUTE CORONARY SYDROME

- Diagnosis
  - Biochemical markers
  - CK – isoenzymes
  - CK-MB more specific than total CK for heart muscle damage
  - Reference range at SWBH
    - <25 iU/L
    - CKMB/CK usually 6-30% if specimen taken within 24hr of an MI
  - Good to detect early changes post MI
  - But not 100% specific and levels fall to 0 within 3 days

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ACUTE CORONARY SYDROME

- Diagnosis
  - Biochemical markers
  - Troponins
  - Regulatory proteins found in skeletal & heart muscle
  - Released into blood during cell necrosis
  - 3 subunits
    - T – different isoforms in skeletal & cardiac muscle
    - C – isoforms the same in skeletal & cardiac muscle
    - I – different isoforms in skeletal & cardiac muscle

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ACUTE CORONARY SYDROME

- Diagnosis
  - Biochemical markers
  - Troponins
  - More specific than CK
  - Cardiac isoforms of Troponin T and I are not usually detectable
  - Looking at rise in Troponin above detection limit
  - Sensitive to small muscle damage
  - Rise 4-10 hours post onset, peak at 12-48 hours and remain elevated for several days

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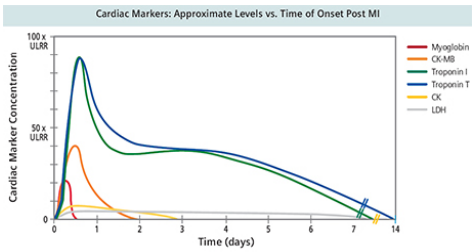
ACUTE CORONARY SYDROME

- Diagnosis
  - Biochemical markers



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ACUTE CORONARY SYDROME

- Diagnosis
  - Biochemical markers
  - Troponins – not completely specific
  - Other causes of a raised Troponin – Acute & Chronic
    - Inflammation
    - Myocardial trauma
    - Drugs e.g. Cocaine
    - Heart failure
    - Pulmonary embolism
    - Kidney disease
    - Stroke

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ACUTE CORONARY SYDROME

- Diagnosis
  - Biochemical markers
  - Troponins – T or I?
  - Depends on manufacturer
    - Roche owns the patent on the TnT method
  - Currently recommend 2 samples
    - One at presentation
    - One six hours later
  - Sandwich immunoassay method
  - Interference from haemolysis

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ACUTE CORONARY SYDROME

- Diagnosis
  - Biochemical markers
  - hs-Troponin T
  - One hs-Troponin T ≥14 ng/L
    - AND
  - 100% increase in hs-Troponin T after 6 hours
  - Indicates myocyte damage

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ACUTE CORONARY SYDROME

- Diagnosis
  - Biochemical markers
  - hs-Troponin T
  - Two hs-troponin T <14 ng/L
    - AND
  - Taken 6 hours apart excludes myocardial infarction
  - If rise in hs-Troponin T <100% over six hours
  - Grey area!
  - Further evaluation e.g. ECG, history
    - Distinguish between acute and chronic rise

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ACUTE CORONARY SYDROME

- Diagnosis
  - Other markers
  - Myoglobin – present in skeletal & myocardial muscle, rises 2-3 hours before other markers but non-specific and not used much now
  - Troponin, CK, CKMB and myoglobin can be used in combination to increase sensitivity
  - PoCT options available for acute wards and GP surgeries

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ACUTE CORONARY SYDROME

- Diagnosis
  - Newer markers
  - Markers of ischaemia
    - Ischaemia modified albumin
  - Markers of inflammation
    - hsCRP

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CARDIOVASCULAR DISEASE

- Treatment
  - NICE Clinical Guideline No.94: Unstable angina and NSTEMI
  - NICE Clinical Guideline: STEMI – In development
  - NICE Clinical Guideline No.68: Stroke
  - NICE Clinical Guideline No.48: MI – secondary prevention
  - NICE Clinical Guideline No.67: Lipid Modification

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CARDIOVASCULAR DISEASE

- Primary Treatment
- CVD risk calculations
  - Use one of a number of calculators to determine your 10 year CVD risk and whether treatment is required
  - Framingham Risk Score
  - JBS Cardiovascular risk assessor
  - QRisk calculator
  - NICE guidelines used to recommend Framingham but this has since been withdrawn.
  - Not to be used for people who have already suffered a CVD event, have a primary hyperlipidaemia or who have diabetes

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CARDIOVASCULAR DISEASE

- Treatment of modifiable factors
- Life style choices
  - Stop smoking!!
  - More exercise – 30 mins a day, 5 days a week
  - Diet <30% fat, 5 portions of fruit and veg and ↓alcohol
  - Lower blood pressure
  - Lower blood lipids
  - Lower body weight

  } Lifestyle changes 1st before medication!

- Prevention is cheaper than cure!

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CARDIOVASCULAR DISEASE

- Medication
- If an individual has a 10 year CVD risk >20%, has diabetes or has a primary lipid disorder
  - Treatment
    - Statins
    - Ezetimibe
- Prevention is cheaper than cure!

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CARDIOVASCULAR DISEASE

- Secondary treatment
  - Thrombolytic drugs
  - Angioplasty
  - Analgesia e.g. Morphine
  - Anti-platelet therapy e.g. Aspirin
  - Anti-hypertensives e.g. Beta blockers, ACE inhibitors
  - Vasodilators e.g. Nitrates
  - Lipid modification e.g. Statins
  - Life style advice

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CHRONIC HEART FAILURE

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CHRONIC HEART FAILURE

- Structural or functional cardiac disorder
- Impairs the ability of the heart to act as a pump
- Compromises the circulation
- Causes
  - Ischaemic heart disease e.g. atherosclerosis
  - Cardiomyopathy e.g. infection, drugs
  - Hypertension
  - Atrial fibrillation

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CHRONIC HEART FAILURE

- Diagnosis
  - Presentation – SOB, fatigue, oedema
  - X-ray – exclude chest infection
  - ECG – signs of ischemic changes
  - Blood tests – natriuretic peptides
  - Echocardiogram

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CHRONIC HEART FAILURE

- Diagnosis
  - NICE Clinical Guideline No.108: Chronic heart failure
  - Previous MI – ECHO 1st
    - Abnormality consistent with CHF
    - If no abnormality measure serum natriuretic peptides
  - No previous MI – measure serum natriuretic peptides 1st
    - If raised send for ECHO
    - If normal CHF is unlikely

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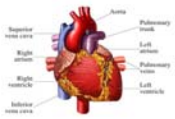
CHRONIC HEART FAILURE

- Diagnosis
  - Natriuretic peptides
  - Cardiac hormones with diuretic, natriuretic and vasorelaxant properties
  - Released by the heart in response to expansion of
    - The atria – Atrial Natriuretic peptide (ANP)
    - The ventricles – Brain (B-Type) Natriuretic peptide (BNP)



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CHRONIC HEART FAILURE

- Diagnosis
  - BNP
  - Synthesised as ProBNP
  - Then cleaved releasing
    - BNP (active)
    - N-terminal – ProBNP
  - High correlation between BNP and NT-ProBNP
  - Both can be used as effective markers of ventricular distension and overload
  - Used to rule out heart failure and in prognosis of patients with CHF

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CHRONIC HEART FAILURE

- Diagnosis
  - BNP
  - Normal values from NICE guidelines – vary by lab
    - BNP <100 pg/ml
    - NT-ProBNP <400 pg/ml
  - Which to use
    - Manufacturer dependent
    - PoCT available
    - EDTA sample
  - Things to consider
    - NT-ProBNP affected by renal function
    - BNP stability at room temp <24 hrs
    - ?Age/gender related reference ranges required
    - Not offered at SWBH!!

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CHRONIC HEART FAILURE

- Diagnosis
  - BNP
  - Not completely specific for heart failure hence it is used to rule-out CHF rather than diagnosis
  - Other causes of a raised BNP and NT-ProBNP
    - Previous heart failure
    - Advanced age
    - Renal dysfunction
    - ACS
    - Pulmonary disease
    - Atrial fibrillation

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CHRONIC HEART FAILURE

- Treatment
  - Similar to CVD
  - Lifestyle choices
  - Anti-hypertensives
    - ACE inhibitors
    - Beta-blockers
    - ARBs
  - Diuretics
  - Vasodilators
  - Cardiac glycosides e.g. Digoxin