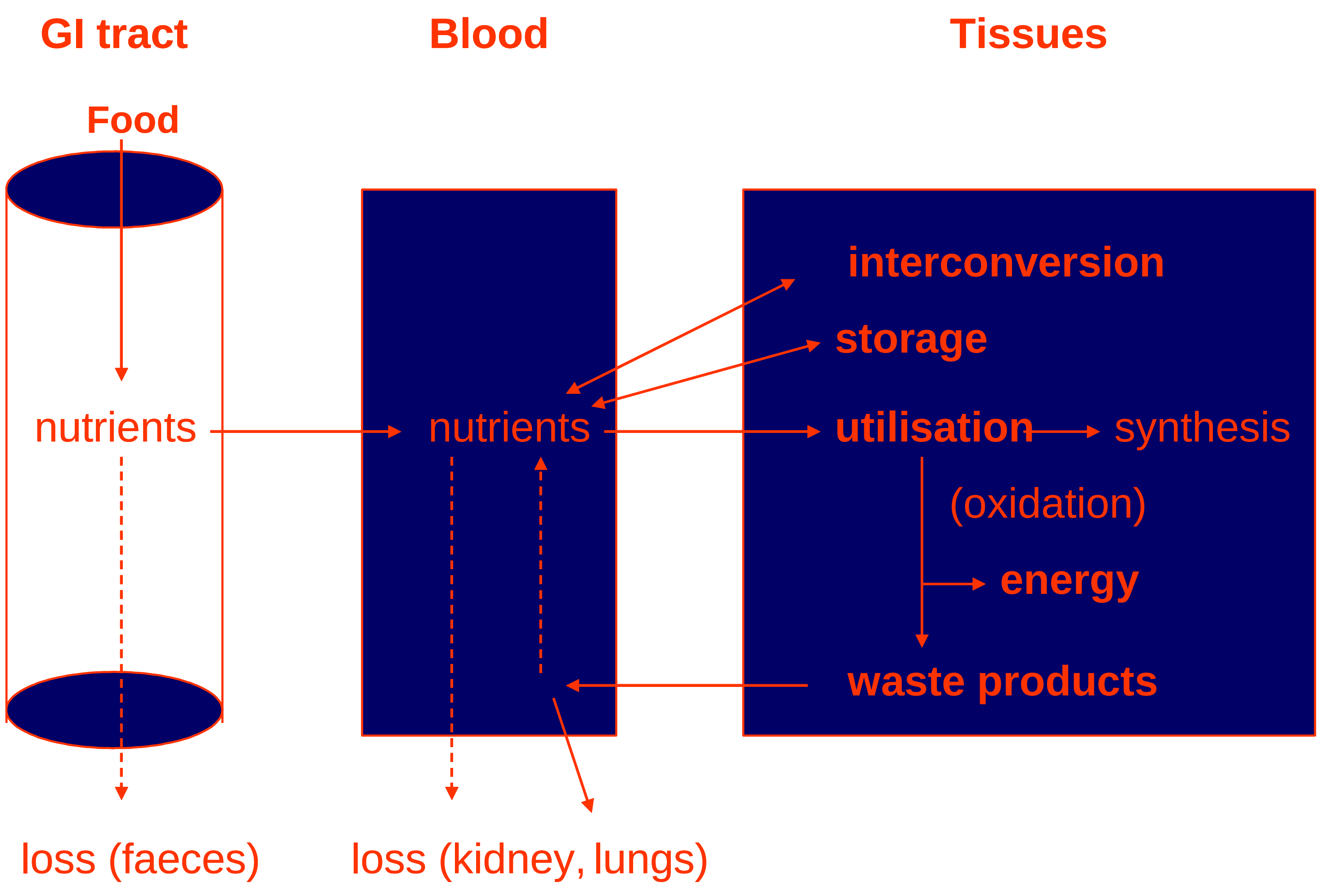
Lecture 1
Introduction of Metabolism

Dr. Abdullah Ali

Metabolism

- Is the processes which derive energy and raw materials from food stuffs and use them to support repair, growth and activity of the tissues of the body

Overview


GI tract
Blood
Tissues
Food
nutrients
nutrients
interconversion
storage
utilisation
synthesis
(oxidation)
energy
waste products
loss (faeces)
loss (kidney, lungs)

Cell metabolism

- A great deal of metabolic activity goes on
- Some things happen in virtually all cells
- Other things in only some cells
- Reactions organised into distinct, but integrated metabolic pathways

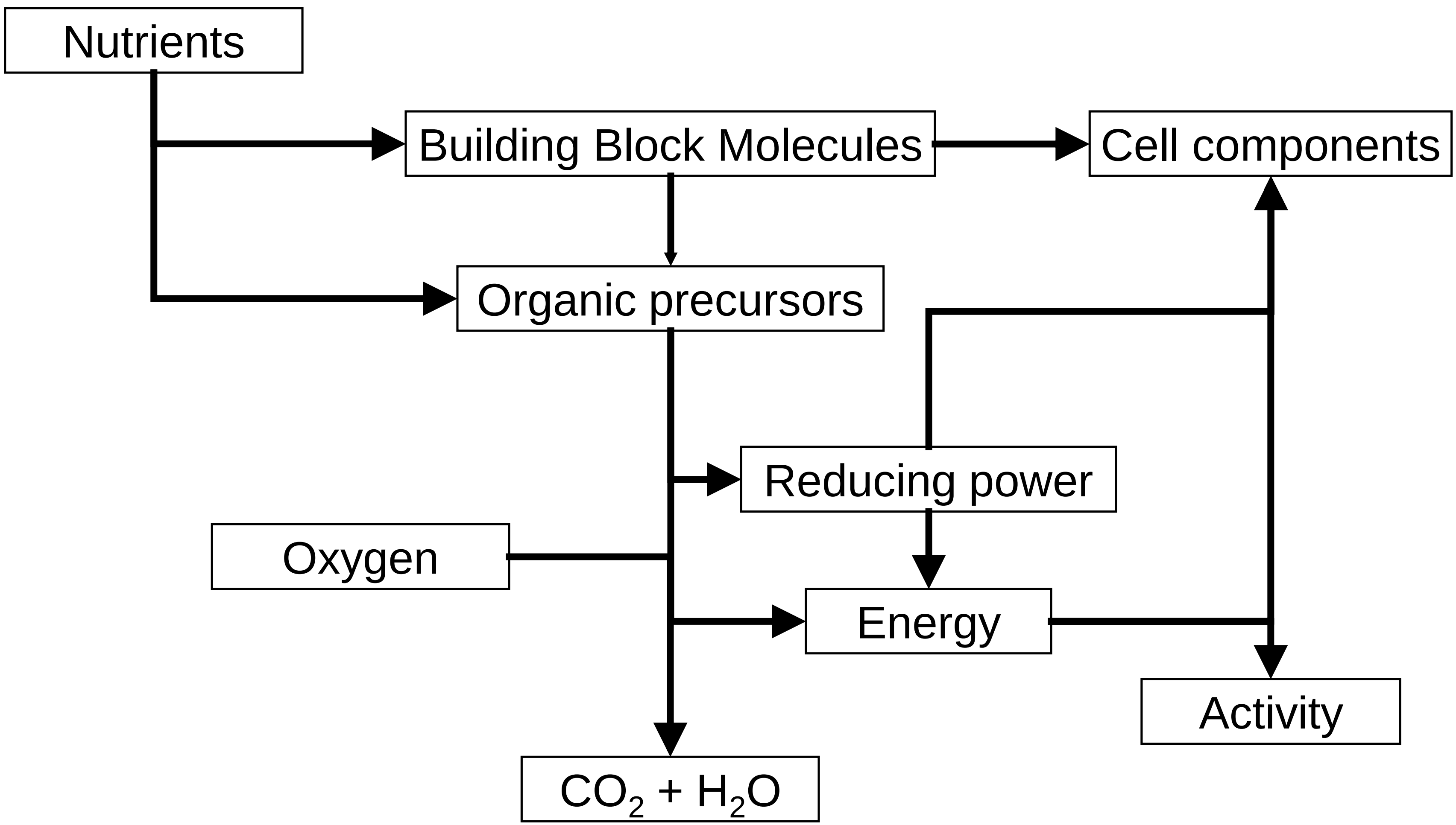
Metabolic pathways

- Chemicals involved in pathways
  - Metabolites
- Lots of different reactions
  - Few reaction types
  - Small number of molecules in central role
  - Pathways often localised to particular cell compartments
- Pathways are described using metabolic maps
  - Starting points & end points
  - Intermediates
  - Connections

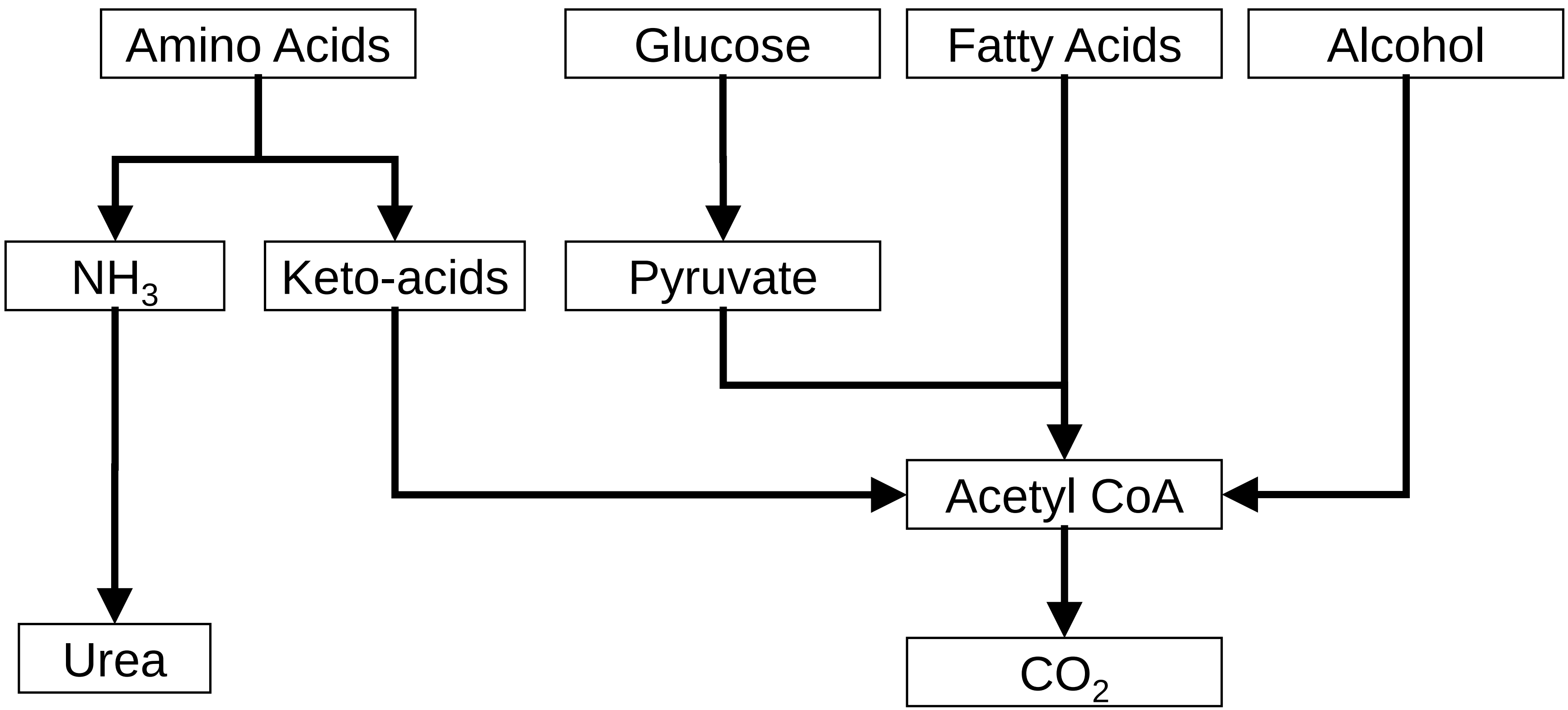
Breaking things and making things

- Catabolic pathways
  - Break down larger molecules into smaller
  - Oxidative (release H - “reducing power”)
  - Release energy
- Anabolic pathways
  - Build up large molecules from small ones
  - Reductive (use H)
  - Use energy released from catabolism

Overview


Nutrients
Building Block Molecules
Cell components
Organic precursors
Reducing power
Oxygen
Energy
Activity
CO_2 + H_2O

Simple Metabolic Map



Catabolic reactions

- Are oxidative
- Release energy

Biological oxidation

- Oxidative reactions
  - Oxidation is removal of electrons
  - In biological reactions removal of hydrogen atoms ($H^+ + e^-$)
  - Often remove two hydrogen atoms
- Redox
  - Hydrogen atom reacts immediately with something else
- Carriers
  - When fuel molecules are oxidised hydrogen atoms are transferred to carrier molecules
  - Which carry reducing power to other reactions

Major H-carrier molecules

	Oxidised form
• Nicotinamide adenine dinucleotide	• NAD^+
• Nicotinamide adenine dinucleotide phosphate	• $NADP^+$
• Flavin adenine dinucleotide	• FAD^+

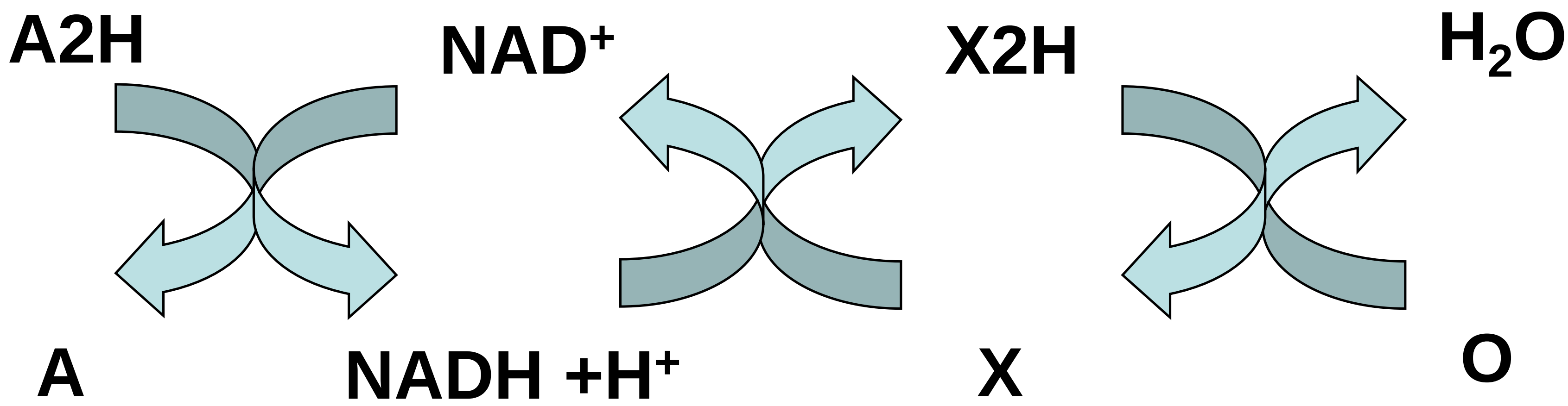
H-carrier molecules

- Complex molecules
  - Contain components from vitamins (B vitamins)
- Converted to reduced form by adding two H atoms ($H^+ + e^-$)
- H^+ dissociates into solution

H-carrier molecules

- Total of oxidised and reduced form in cells constant
- Pathways which convert oxidised to reduced form must be matched by other pathways converting reduced to oxidised form
- Otherwise reactions will stop

H-carriers



Catabolic reactions

- Are oxidative
- Release energy

Energy

- Exergonic reactions release energy
- Cannot all be used by the cell
  - Some lost by decrease in entropy
- Rest available to do work
  - Free energy or Gibbs Free Energy (ΔG)
- When energy is released ΔG is negative

Coupling

- Metabolism is all about coupling the energy released by exergonic reactions to that needed for endergonic reactions
- Needs an intermediate process
  - The ADP/ATP cycle

Adenosine triphosphate

- Adenine-ribose-phosphate-phosphate-phosphate
- Phosphate-phosphate bond high energy of hydrolysis
- Can give up lots of energy to drive other reactions
- $ATP^{4-} + H_2O \leftrightarrow ADP^{3-} + HPO_4^{2-} + H^+$

Standard free energy change

- Under standard conditions
  - Temperature 25 deg C
  - Pressure 101 kPa
  - pH 7.0
  - Concentrations of reactants and products 1mol.l^{-1}
- Standard free energy change (ΔG^{o}’)
- Conditions in cells not standard

$\Delta G^{o'}$ for ATP ADP hydrolysis

- $ATP + H_2O \rightarrow ADP + Pi$
  - $\Delta G = -31\ kJ.mol^{-1}$
- $ADP + H_2O \rightarrow AMP + Pi$
  - $\Delta G = -31\ kJ.mol^{-1}$
- This energy can drive endergonic reactions

Phosphorylated compounds

- Many phosphorylated compounds have high energies of hydrolysis (large negative ΔG)
- Can form a hierarchy
  - Phosphoenolpyruvate – ΔG -62 $kJ.mol^{-1}$
  - Creatine phosphate – ΔG -43 $kJ.mol^{-1}$
  - ATP ΔG -31 $kJ.mol^{-1}$

Balancing catabolism and anabolism

- Catabolic pathways increase intra-cellular concentrations of
  - Reduced H carriers (eg NADH)
  - Phosphorylated high energy carriers (ATP)
- Anabolic pathways increase intra-cellular concentrations of
  - Oxidised H carriers (egNAD+)
  - Hydrolysed high energy carriers (ADP)

Oxidative phosphorylation

- Reducing power can be converted to high energy bonds in ATP by
  - Oxidative phosphorylation
  - Protons transferred to oxygen
  - Energy to ATP
  - Occurs in mitochondria

Energy signals

- Cell must respond to ‘low energy signals’
  - Increased oxidised H carriers
  - Increased hydrolysed energy carriers
- By increasing catabolism
- And vice versa for ‘high energy signals’
  - Increased reduced H carriers
  - Increased phosphorylated energy carriers

Energy stores in cells

- Some cell types need to increase metabolic activity very quickly (eg muscle)
- Need a reserve of high energy stores
  - Can be called on immediately
- Use creatine phosphate

Creatine Phosphate

- Creatine + ATP ⟷ Creatine Phosphate + ADP
- Catalysed by creatine kinase
- When ATP plentiful reaction goes forward
- If ATP concentration falls suddenly, reaction reverses providing short term boost to [ATP]

Creatine Kinase

- In different forms in different muscles
  - Different sub-units in molecule
- One specific to heart muscle
- Released from cells if they are damaged, in myocardial infarction (heart attack)
- Appears in blood after a few hours
- Diagnostic of MI

Creatinine

- Breakdown product of creatine
- Produced at very constant rate
  - Unless muscle is wasting
- Excreted via kidneys
- Urine concentration a marker of urine dilution
- Can be used to estimate true urinary loss of many substances
  - Eg hormones in pregnancy

Clinical importance of creatine phosphate

- Amount in body determined by to muscle mass