K. Nutrition and Metabolism

a. Define basal metabolic rate and describe its measurement.

The rate of energy expended by the body at rest at room temperature 12 hours after a meal. Normal value is expressed divided by surface area: 40 kcal/m²/hr (50 W/m²)

Measured directly using an Atwater-Benedict chamber (calorimeter).

Measured indirectly using O₂ consumption at rest and assuming 4.82 kcal/O₂ (20 kJ/O₂). A more accurate measure can be obtained from measuring CO₂ production concurrently and calculating R or allowing for dietary constituents.

b. Describe the factors that influence basal metabolic rate.

sex 
- males 10-15% more than females

age 
- BMR double adult value per unit bodyweight at birth
- falls to a plateau through adulthood and falls further in old age

increased
- fever, hyperthyroidism, ↑ GH, sympathetic stimulation
- ingestion of food, especially protein
- activity

decreased
- sleep (by 10-15%)
- starvation

c. Describe relevant cellular biochemical pathways and the control of fat, carbohydrate and protein metabolism including the role of vitamins and trace elements.
yield
- acetyl-CoA: 12 ATP per turn of the TCAC
- glucose: 2 ATP anaerobic, 38 ATP aerobic
- G-6-P: 3 ATP anaerobic, 39 ATP aerobic
- fats: 17 ATP per 2 C unit less 7 ATP overhead

energy value
- carbohydrate: 4 kcal/g
- protein: 4 kcal/g
- ethanol: 7 kcal/g
- fat: 9 kcal/g

d. Explain the physiological principles of parenteral nutrition.

acute stress
- responses below
- TPN will not help as excess energy substrate is already being mobilized
- just increases CO₂ load, urinary N load and risk of fatty liver
- after several days
- benefits from providing energy substrates to reduce protein catabolism
- fat up to 1 g/kg/day as Intralipid (omega-6-fa → immunosupression)
- carbohydrate up to 4 g/kg/day
- monitored with metabolic cart
- measures RER
- normal 0.85
- >1 suggests fat synthesis (→ ↓ carbohydrate intake)
- nitrogen around 0.2 g/kg/day (= a.a. 1.3 g/kg/day)
- depends on nitrogen balance
  = ureaₚₘᵋᵣᵲₑᵋₑ / 28/60 - Δureaₚₘᵋᵲₐₙₑ x 0.6 x weight
- increased N increases urinary solute load
- some units tie caloric input to N input (possibly obsolete)
- total energy intake typically 1700 kcal/day (usage ≈ 2500 kcal/day)
- hypocaloric nutrition is practised in some units
- electrolytes must be monitored separately
  - tendency to loss of K⁺ and Cl⁻ resulting in alkalosis
  - intracellular K⁺ deficit reflected in ↓ [Na⁺]ₚₘᵋᵲᵲₐᵲₑ due to osmolarity effect

starved patients
- small glucose load in first few days until ketosis resolves
- then fat
- trace element and vitamin deficiencies are unmasked by nutrition

e. Describe the consequences of anaerobic metabolism.

- glucose → 2 pyruvate → 2 lactate yields net 2 ATP per glucose molecule
- does not require O₂ or NAD⁺ or mitochondrial e⁻ transport function
- does not produce CO₂
- results in ↑ lactate ↓ pH
- subsequent metabolism of lactate to glucose (Cori cycle) requires O₂ (oxygen debt)

f. Describe the physiological consequences of starvation.

reserves
- fat: 15 kg 141,000 kcal
- protein: 6 kg 24,000 kcal (available)
- glycogen: 75 g 300 kcal
muscle glycogen cannot be liberated as glucose

liver glycogen provides for a few hours of metabolism
some tissues are glucose-dependent
  RBC, marrow, renal medulla, peripheral nerves
the brain requires some glucose, but can also use ketones
during starvation, adaptation gradually reduces the glucose requirement to a minimum
obligatory glucose use requires protein breakdown and nitrogen loss
  initial rapid protein breakdown until adaptation occurs
  nitrogen loss falls after two days
  ketone bodies rise for two to three weeks
    renal ketone excretion is titrated with NH\textsubscript{4}\textsuperscript{+}
    ↑ glutamine use by the kidney
  supplemental glucose or glycerol (in fat) reduces protein breakdown

gluconeogenesis
  transamination of pyruvate yields alanine and α-ketoglutarate yields glutamate and glutamine (mainly from muscle)
  brached-chain amino-acids are used to provide amine groups and their keto-acids enter the TCAC
  alanine and glutamine enter the gluconeogenic pathway in liver and kidney, yielding glucose and urea
  glycerol from triglyceride breakdown also provides a substrate for gluconeogenesis
  capacity: 85 g/day (20 g from protein, 15 g from glycerol, rest from recycling lactate etc.)
ketosis
  low intracellular glucose → low pyruvate, oxaloacetate (carrier for TCAC)
  acetyl-CoA cannot enter the TCAC (lack of oxaloacetate)
  → acetoacetyl-CoA → acetoacetate, β-hydroxybutyrate (in liver)
  circulating ketone bodies can be taken up by other cells and enter the TCAC

g. Describe the metabolic consequences of sepsis, burns and trauma, as well as the effects of anaesthesia in this setting.

stress response
local mediators
  tissue damage
    inflammatory mediators: PGs, bradykinin, substance P, serotonin, histamine, cytokines
    nociceptive afferents (A\textsubscript{∂} and C fibres) → anterolateral and dorsal columns
central mediators
  ↑ ACTH, GH, prolactin, ADH
  ↑ sympathetic outflow
    produces endocrine and metabolic responses
endocrine
  steroid response
    ↑ cortisol, aldosterone
    ↑ renin-angiotensin
    ↑ insulin, ↑ glucagon
  inflammatory mediators
    NO, 20-HETE, PG\textsubscript{F\textsubscript{2α}}, TX\textsubscript{A\textsubscript{2}}, PAF, LTs, ILs
    expression of cellular iNOS
metabolic
  ↑ MR, T, O\textsubscript{2} consumption, CO\textsubscript{2} output
  mediators alter distribution of blood flow: ↓ α response, vasodilation
  catabolism of protein, fats and carbohydrate stores
↑ plasma glucose, rapid glucose turnover in anaerobic metabolism
catabolism of muscle protein for gluconeogenesis and synthesis of protein
inflammatory mediators
does not fall after a few days if stress continues (unlike starvation)
↓ synthesis of albumin, prealbumin, transferrin
rapid cycling of triglycerides to fatty acids and back again in the liver
inadequate VLDL production causes fatty liver
excess exogenous glucose worsens futile cycling and fatty liver
modification by anaesthesia
volutiles: little effect
intravenous: only etomidate has any effect (↓ cortisol)
opioids: ablate response in very high dose
regional
  spinal, epidural LA
    ablate the response from lower body surgery
    attenuate response to upper abdominal & thoracic surgery
spinal opioids
  no effect despite analgesia