Q4 Explain how a normal, healthy adult regulates their body temperature (70% of marks). Explain how paracetamol exerts an antipyretic effect in a febrile patient (30% of marks). (March 2009)

Temperature – average kinetic energy of the atoms and molecules that make up a substance
Thermoregulatory responses maintain ideal body temperature between 36-38 degrees
Thermoneutral zone – the range of environmental temperatures (27-31 degrees for a 70kg naked male) across which metabolic heat production is minimal and thermoregulation is maintained via vasomotor action.

Body temperature afferent sensors:

- Cold receptors – bulbs of Krause located in dermis, innervated by Aδ fibres, discharges increase below 24-25°C
- Heat receptors – bulbs of Ruffini located in dermis, innervated by C fibres, static discharge 30-40°C, maximal output at 44°C
- Temperature sensors may also be present in the spinal cord and intestinal walls
- Impulses travel via lateral spinothalamic tract and synapse in the reticular tract of the medulla before travelling to hypothalamus

Central processing unit:

- Hypothalamus is the main body temperature regulatory centre
- Posterior hypothalamus responds to cold (inputs from peripheral afferents) and is responsible for the temperature set point. ACh is the major neurotransmitter here.
- Anterior hypothalamus responds to heat (both peripheral input and change in blood temperature). Major neurotransmitters are Nad, 5HT, dopamine and prostaglandins.

Efferent responses:

- Responses to cold:
    - Major response is shivering – uncoordinated involuntary contraction of skeletal muscles increases heat production 5 fold
    - Peripheral vasoconstriction via sympathetic control – reduces heat loss via skin. Cutaneous blood flow can decrease by 10-fold in cold situations
    - Increase in metabolic rate – below 27°C, metabolic rate rises linearly to produce heat. Enhanced by thyroxine and adrenaline
    - Non shivering thermogenesis – occurs in brown fat via uncoupling of oxidative phosphorylation. Important in neonates, can increase heat production 3 fold
    - Behavioural changes – seeking heat, warm clothing etc

- Responses to heat:
    - Peripheral vasodilatation via decrease in alpha-adrenergic activity to peripheral vasculature, resulting in opening of A-V anastomoses (enhanced by bradykinin released from sweat glands). Skin blood flow can increase by up to 30-fold in heat stress
    - Sweating – latent heat of evaporation of water at 37°C is 2.4kJ/ml of water, the majority of which comes from the body
    - Heat loss also occurs via radiation, conduction and convection

PARACETAMOL:

- Fever is thought to be induced by cytokines and other inflammatory and infectious pyrogens (interleukins, TNF, IFN) acting on the circumventricular organs which activate the supraoptic nucleus of the hypothalamus, likely producing prostaglandins which cause fever
- Paracetamol is thought to inhibit prostaglandin E2 production in the hypothalamus via inhibition of COX3 (a central COX variant), thus preventing pyrexia