Lecture 2 – Cardiovascular Response to Stress

Course objectives:

- Understand that the cardiovascular responses to physiological stressors are diverse and depend on the stimulus
- Understand that these adjustments involve intrinsic, neural and hormonal mechanisms
- Understand the basic principles underlying cardiovascular control
- Understand how intrinsic mechanisms such as autoregulation and reactive hyperaemia operate

Summary:

- Challenges to cardiovascular homeostasis by changes to blood/central blood volume
    - Reductions
        - Haemorrhage: need to maintain adequate arterial pressure and perfusion of the brain and heart while cardiac output falls, due to loss of blood volume
        - Head-up tilt: pooling of blood → lower central blood volume → decreased CO
    - Increased
        - Blood or plasma transfusion: increased blood volume → cardiac output increases
        - Head-out water immersion: increase pressure → increased venous return → increased central blood volume → increased CO
    - Changes in energy/organ blood flow requirements
        - Exercise: increased O2 and nutrient delivery to muscles via increased blood flow
        - Diving: conservation of oxygen by limiting blood flow to non-essential organs
        - Alerting responses
    - Similarities and differences that need to be considered
        - Control of cardiac output
        - Organ-specific control of vascular resistance
    - Control mechanism
        - Intrinsic, neural and hormonal → Gain, latency and duration of these control mechanisms
- Basic principles
    - Key formulae
        - Arterial pressure **(AP) = CO x TPR** or AP = CO/total peripheral conductance
        - **Local blood flow = AP/Organ vascular resistance** or AP x organ vascular conductance
        - Cardiac output **(CO) = HR x SV**
        - Poiseulle's Equation: Resistance = [Constant (K) x Length (L) x Viscosity (n)]/Radius $(r)^4$
            - Flow is proportional to length of tube, proportional to viscosity but inversely proportional to *diameter* → the main factor given the 4 fold change
    - Control of cardiac output
        - **CO** is controlled by HR and SV
        - **HR** is controlled by neural (symp. and parasymp. NS) and hormonal (Adr + NA) factors
            - Sympathetic nerves → NA → SA node + atrium (contractility) → increase HR
                - Adrenaline from the adrenal medulla → beta-adrenoceptors → HR ↑
            - Parasympathetic (vagal) nerves → Ach → SA node → decrease HR
        - **SV** is controlled by *contractility* (neural and hormonal influence) and intrinsic factors (e.g. end-diastolic volume [Frank-Starling law])
    - Control of blood pressure and vascular resistance
        - At large arteries → little fall in pressure BUT steep fall at arterioles given they are the critical blood vessels in the control of vascular resistance
            - Arterioles are the most important due to **TWO** critical properties
                - Small diameter + smooth muscle (change diameter → change resistance)
        - NOTE: venous vascular tone does play a role in the control of venous return → CO
- Factors that alter the diameter of resistance vessels
    - Local/metabolic/intrinsic factors
    - Nerves → mainly sympathetic
    - Hormones → endocrine, paracrine and autocrine
    - Structural properties, e.g. thickness of smooth muscle
    - Pathology, e.g. artherosclerosis, endothelial damage (NO?)
- Myogenic/intrinsic mechanisms
    - **Local control** of blood flow (NOT arterial pressure)
    - Matching blood flow to **metabolic demand**

        - Active hyperaemia: blood flow ↑ with increasing metabolic need (response to activity)
        - Reactive hyperaemia: repayment of blood flow debt (after starvation)
    - Matching blood flow to **organ function** → autoregulation of blood flow to the kidney and brain
- Metabolic demand
    - *Active hyperaemia:* Linear relationship between O2 consumption and (coronary) blood flow → increased diameter
    - *Reactive hyperaemia:* After occluding blood flow for 2 or 4 minutes → debt, then blood returned → big overshoot → arterioles dilate → increased blood flow
        - More time occluded → more debt → more dilation → more blood flow
    - Factors contributing to active and reactive hyperaemia are essentially the same
        - Carbon dioxide (potent vasodilator); Hypoxia; Lactic acid (severe exercise + ischaemia); reduced pH (acidic; due to lactate and increase CO2); adenosine (= ATP consumption); endothelial derived nitric oxide
        - BUT, these are paracrine and autocrine hormones acting in proximity, not *really* intrinsic
- Autoregulation → truly intrinsic
    - Particularly important in organs requiring right control of blood flow, e.g. brain, kidney, heart
    - Increased blood flow (and/or pressure) → stretch tissue → stretch smooth muscle → release of calcium from within cells → increased cross-bridges → increased contraction → decrease flow to within desired/normal limits
        - Counterintuitive, increased BP → constrict → increase resistance; decrease BP → dilation
    - Local mechanisms tightly control the level of blood flow in response to perfusion pressure
- Acute blood loss (AP = CO x TPR)
    - Cardiac output falls as blood is lost
        - To maintain AP → TPR must increase
    - Blood flow/AP must be maintained to some critical organs (e.g. brain + kidneys), this cannot be achieved by the arterioles in these organs by more peripherally
    - Mechanisms: local (metabolic/myogenic; short-term), neural (short) and hormonal (long-term)
- Response to haemorrhage (Barcroft et al. 1945)
    - **Phase 1** = Early in the bleeding
        - Vasoconstriction → blood pressure maintained
        - BUT was associated with decreased CO, increased HR and TPR
    - **Phase 2** = Once ~1/3 of blood volume is removed (decompensation + circulatory shock)
        - Vasodilation → blood pressure plummets
        - The body is no longer able to increase TPR or HR any more → syncope to lie down
        - Massive drop in MAP, TPR, HR, associated with vasovagal syncope (paras. involvement)
- Long-term recovery from acute blood loss (restoring CO to normal) is mediated by;
    - Increased salt and fluid intake → increase blood volume
    - Reduced salt and fluid output (urination) → retain blood volume
    - Fluid shifts into vascular compartment from extracellularly
    - Hormone-induced vasoconstriction → longer lasting ↑ TPR → ↑ BP
- Cardiovascular response to changes in central blood volume
    - Reduced (e.g. haemorrhage) → reduced venous return → reduced cardiac output
        - Increase HR; vasoconstriction (except brain and heart); increased salt appetite and thirst; reduced urinary salt and water excretion; movement of ECF → plasma
    - Increased (e.g. water immersion) → increased venous return → increased cardiac output
        - Reduced HR; vasodilation (except brain and heart); reduced salt appetite and thirst; increased urinary salt and water excretion; movement from plasma → ECF
- Cardiovascular response to exercise and diving
    - Exercise → increased demands from muscle for oxygen and nutrients → increased CO; vasoconstriction to gut, kidneys and skin; vasodilation in skeletal muscle
    - Diving → conservation of oxygen while maintaining blood flow to vital organs → reduced CO; vasoconstriction everywhere but the brain