CARDIOVASCULAR HOMEOSTASIS

COMPENSATIONS FOR GRAVITATIONAL EFFECTS:

- In the standing position, as a result of the effect of gravity on the blood:
  - MAP in the feet is 180-200mmHg
    - Venous pressure is 90
  - Arterial pressure at head level is 60-75mmHg
    - Venous pressure is zero
  - If the individual DOES NOT MOVE, 300-500mL of blood pools in the venous capacitance vessels of the lower limbs
    - Stroke volume decreases
    - Symptoms of cerebral ischaemia develop when the cerebral blood flow decreases to less than about 60% of the flow in the recumbent position
      - If no cardiovascular compensatory changes occurred, consciousness would be lost
  - MAJOR COMPENSATIONS ON ASSUMING UPRIGHT POSTURE:
    - Triggered by the drop in blood pressure in the CAROTID SINUS AND AORTIC ARCH
      - **HEART RATE INCREASES** to maintain cardiac output
      - Prompt increase in the circulating levels of **RENIN AND ALDOSTERONE**
      - Arterioles constrict, helping to maintain blood pressure
      - Relatively little venoconstriction occurs in the periphery
    - In the cerebral circulation:
      - Arterial pressure at head level drops 20-40mmHg, but jugular venous pressure ALSO FALLS 5-8mmHg, reducing the drop in PERFUSION PRESSURE
      - Cerebral vascular resistance is reduced because ICP falls as venous pressure falls, decreasing the pressure ON CEREBRAL VESSELS
      - The decline in cerebral blood flow increases the partial pressure of CO_2 and decreases the PO_2 and the pH in the brain tissue, further actively DILATING THE CEREBRAL VESSELS
      - Because of these measures, blood flow declines only 20% on standing
      - In addition, the amount of O_2 extracted per unit of blood increases
      - Reduced blood flow to brain on standing is mitigated by:
        - **⇓ Jug venous pressure (maintaining perfusion pressure)**
        - **⇓ ICP → ⇑CPP**

        - **Reactive hyperaemia to ⇑CO2 ⇓O2**
        - **Increased extraction of O2**

    - With prolonged standing, fainting may result
        - In a sense, fainting is a "HOMESTATIC MECHANISM"
            - Because falling to the horizontal position promptly restores venous return, cardiac output and cerebral blood flow
    - The effects of gravity on the circulation in humans depends in part UPON THE BLOOD VOLUME
        - When blood volume is low, these effects are marked, when it is high, they are minimal

- POSTURAL HYPOTENSION:
    - In some individuals, sudden standing causes:
        - Fall in blood pressure
        - Dizziness
        - Dimness of vision
        - Fainting
    - KNOWN AS ORTHOSTATIC POSTURAL HYPOTENSION
    - Causes are multiple
    - Common in patients receiving sympatholytic drugs
    - Also occurs in **diabetes and syphilis**, in which there is damage to the sympathetic nervous system
    - May also be related to PRIMARY AUTONOMIC FAILURE

- EFFECTS OF ACCELERATION:
    - Positive "g" force is due to acceleration in the long axis of the body, from head to foot
    - Negative "g" force is due to acceleration acting the opposite direction
    - During exposure to a positive g force, blood is "thrown" into the lower part of the body
        - Arterial pressure in the head is reduce, but so are venous pressure and intracranial pressure, and this reduces the decrease in arterial blood flow that would otherwise occur
        - Cardiac output is maintained for a time because blood is drawn from the pulmonary venous reservoir
        - At positive 5g, vision fails (BLACKOUT) and consciousness is lost shortly thereafter
    - Negative g causes:
        - Increased cardiac output
        - Rise in cerebral arterial pressure
        - Intense congestion of the head and neck vessels
        - Eventually mental confusion (RED OUT)

        - Vessels generally do NOT RUPTURE, because generally ICP is increased and their walls are supported
    - TOLERANCE FOR G FORCES EXERTED ACROSS THE BODY IS MUCH GREATER THAN IT IS FOR AXIAL G

EFFECTS OF ZERO GRAVITY:

- ON CV SYSTEM:
    - There is some disuse atrophy of the mechanisms that withstand gravity on earth, but CV function is maintained for up 14 months
    - On return to earth, astronauts have postural hypotension
        - This disappears with readaptation
- OTHER EFFECTS:
    - Muscular effort is much reduced
    - Decrease in the extensive normal proprioceptive input due to the action of gravity leads to FLACCIDITY AND ATROPHY of skeletal muscles
    - Loss of muscle mass
    - Steady loss of bone mineral
    - Increased Ca excretion
    - Loss of red cell mass

EFFECTS OF EXERCISE:

- MUSCLE BLOOD FLOW:
    - **The blood flow of resting skeletal muscle is LOW** (2-4mL/100g/min)
    - When a muscle contracts, it **compresses the vessels in it if develops more than 10% of maximal tension**
    - When it **develops more than 70% of it s maximal tension, blood flow is COMPLETELY STOPPED**
        - **Between contractions, flow is SO GREATLY INCREASED** that blood flow PER UNIT TIME is increased as much as 30-fold
    - Blood flow can sometimes increase BEFORE EXERCISE:
        - Suggests NEURALLY MEDIATED PROCESS
    - **LOCAL MECHANISMS ARE THE DOMINANT MEANS OF CONTROLLING MUSCLE BLOOD FLOW**:
        - Fall in tissue PO2
        - Rise in tissue PCO2
        - Accumulation of K, adenosine and other vasodilator metabolites
        - Increased temperature

    - Dilation of the arterioles and precapillary sphincters causes a 10-100-fold increase in the number of open capillaries:
        - I.e. **capillary recruitment**
        - The average distance between the blood and the active cells is thus GREATLY DECREASED
        - **⇑SA + ⇓diffusion distance**

- Capillary recruitment increases the cross-sectional area of the vascular bed and the **velocity of flow therefore decreases**
    - The capillary pressure increases until it EXCEEDS THE ONCOTIC PRESSURE
        - In addition, the **accumulation of osmotically active metabolites in the interstitium more rapidly than they can be carried away decreases the osmotic gradient**
            - **THUS, FLUID TRANSUDATION into the interstitial spaces is tremendously increased**
            - **Lymph flow is also increased**, greatly increasing its turnover

- **Exercising muscle → ⇑⇑fluid transudation from capillaries:**
    - **⇑SA for exudation**
    - **⇑Hydrostatic pressure**
    - **Accumilation of interstitial osmotically active metabolites**

    - **Decreased pH** and **increased temperature** shift the haemoglobin-dissociation to the right, so that more O2 is given up by the blood
    - **Concentrations of 2,3 DPG in the RBC is increased and this further decreases the O2 affinity of haemoglobin (right shift)**
    - The NET RESULT:
        - Up to three-fold increase in the arteriovenous difference
        - Transport of CO2 out of the tissue is also facilitated

- SYSTEMIC CIRCULATORY CHANGES:
    - The systemic cardiovascular response to EXERCISE depend on whether the muscle contractions are primarily ISOMETRIC (SAME LENGTH) or primarily ISOTONIC (SAME LOAD)
    - Just the thought of performing a muscle contraction increases heart rate - suggests that PSYCHIC STIMULI act on the medulla oblongata

    - With the start of an **ISOMETRIC muscle contraction** (contraction without change in length)
        - **RISE IN TPR**
        - **SYSTOLIC AND DIASTOLIC PRESSURE RISE SHARPLY**
        - Stroke volume changes relatively little and blood flow to the steadily contracting muscles is reduced due to vessel compression

    - **ISOTONIC muscle contraction**:
        - Prompt **INCREASE IN HEART RATE**
        - Marked **INCREASE IN STROKE VOLUME** (different from isometric contraction)
        - Net **FALL IN TPR** due to vasodilation in exercising muscles

        - Consequently, systolic BP rises only moderately whereas diastolic pressure usually remains unchanged

    - The differences between these two examples lies in the fact that during ISOMETRIC contractions, muscles are tonically contracted and consequently contribute to increased TPR.
    - **Cardiac output is increased during isotonic exercise to values that may exceed 35L/minute**
    - A **great increase in venous return takes place:**
        - Venous return is increased by the great increase in the activity of the muscle and thoracic pumps:
            - Mobilisation of blood from the viscera
            - Increased pressure transmitted through dilated arterioles to the veins
            - Noradrenergically mediated venoconstriction, which decreases the volume of blood in the veins

    Isometric contraction: ⇑TPR → ⇑SBP + ⇑DBP
    Isotonic contraction: ⇑CO (⇑SVx⇑HR), ⇓TPR → Mild ⇑SBP

    Isometric contraction – tonic contraction of muscles → ⇑TPR
    Isotonic contraction - ⇑⇑capillary recruitment → ⇓TPR

SHOCK:

GENERAL CONSIDERATIONS:

- The feature common to all the entities is:
    - **INADEQUATE TISSUE PERFUSION WITH A RELATIVELY OR ABSOLUTELY INADEQUATE CARDIAC OUTPUT**
- Can occur if:
    - The amount of fluid in the vascular system is inadequate to fill it
        - Causes of HYPOVOLAEMIC SHOCK include:
            - Haemorrhage
            - Trauma
            - Surgery
            - Burns
            - Fluid loss due to vomiting or diarrhoea
    - Amount of fluid may be inadequate in a RELATIVE SENSE, because the size of the vascular system is increased by vasodilation, even though the blood volume is normal:
        - Causes of DISTRIBUTIVE SHOCK include:
            - Fainting (neurogenic shock)

            - Anaphylaxis
            - Sepsis (this also causes hypovolaemia due to increased capillary permeability with loss of fluid into tissues
    - Can also be due to inadequate pumping action of the heart due to myocardial abnormalities:
        - Causes of CARDIOGENIC SHOCK include:
            - AMI
            - CHF
            - Arrhythmias
    - Inadequate cardiac output as a result of obstruction of blood flow in the lungs or heart:
        - Causes of OBSTRUCTIVE SHOCK:
            - Tension pneumothorax
            - Pulmonary embolism
            - Cardiac tumour
            - Cardiac tamponade

HYPOVOLAEMIC SHOCK:

- COLD SHOCK
- HAEMORRHAGIC SHOCK:
    - Principal reactions include:
        - Vasoconstriction
        - Tachycardia
        - Venoconstriction
        - Tachypnoea (increased thoracic pumping)
        - Restlessness
        - Increased movement of interstitial fluid into capillaries
        - Increased secretion of:
            - Noradrenaline
            - Adrenaline
            - Vasopressin
            - Glucocorticoids
            - Renin
            - Aldosterone
            - EPO
        - Increased plasma protein synthesis
- In hypovolaemic and other forms of shock, the inadequate perfusion of the tissue leads to increased anaerobic glycolysis, with the production of large amounts of lactic acid
    - The resulting LACTIC ACIDOSIS:
        - Depresses the myocardium
        - Decreases peripheral vascular responsiveness to catecholamines
        - May be severe enough to cause coma

- RAPID COMPENSATORY REACTIONS:
  - When blood volume is reduced and venous return is decreased, the arterial baroreceptors are stretched LESS and sympathetic output is thus INCREASED
  - **Even if there is no drop in MAP, the drop in pulse pressure decreases the rate of discharge in the arterial baroreceptors and reflex tachycardia and vasoconstriction result**
  - Vasoconstriction is generalised, sparing only the vessels of the brain and heart
    - Most marked in the skin, where it accounts for the COOLNESS AND PALLOR
    - Also marked in the kidneys and viscera
  - Haemorrhage evokes a widespread venoconstriction that helps maintain the filling pressure of the heart
    - SPLANCHNIC AND SPLENIC constriction shifts blood form the visceral reservoir into the systemic circulation
  - In the kidneys:
    - BOTH afferent and efferent arterioles are constricted, but the efferent vessels are constricted to a greater degree
    - The GFR is depressed, but renal plasma flow is decreased to GREATER extent, so that the **filtration fraction INCREASES**
    - Especially when the hypotension is prolonged, renal tubular damage may be severe (ARF)
  - Haemorrhage is also a potent stimulus to adrenal medullary secretion
    - Increased circulating catecholamines probably contributes relatively little to the generalised venoconstriction, but it may lead to stimulation of the reticular formation => restlessness and apprehensive
  - Loss of red cells decreases the O2 carrying power of the blood
    - The blood flow in the carotid and aortic bodies is reduced
    - The resultant anaemia, stagnant hypoxia, as well as the acidosis **STIMULATE THE CHEMORECEPTORS**
      - Probably the main cause of RESPIRATORY STIMULATION IN SHOCK
    - **Chemoreceptor activation also excites vasomotor areas in the medulla, increasing vasoconstrictor discharge**
  - Increases in the level of circulating angiotensin II produced by the increase in plasma renin activity during haemorrhage:
    - **Causes thirst by an action on the subfornical organ**
  - When the arterioles constrict and the venous pressure falls because of the decrease in blood volume, a drop in capillary pressure takes place
    - **⇓Hydrostatic pressure → influx of fluid into capillaries along most of their course helping to maintain the circulating blood volume**

- LONG-TERM COMPENSATORY REACTIONS:
    - After a moderate haemorrhage, the circulating plasma volume is restored in 12-72 hours
    - When whole blood is lost, the haematocrit may not fall for several hours after the onset of bleeding
    - **EPO appears in the circulation and the reticulocyte count increases, reaching a peak in 10 days**
        - Red cell mass is restored in 4-8 weeks
        - **Increased production of 2,3 DPG, which causes haemoglobin to give more O2 to the tissues**

- **REFRACTORY SHOCK**:
    - In this condition, shock persists for hours and gradually progresses to a state in which no response to vasopressor drugs takes place and in which, even if the blood volume is returned to normal, **cardiac output remains depressed**
    - Various positive feedback mechanisms contribute to the production of refractory shock:
        - **Severe cerebral ischaemia leads eventually to depression of the vasomotor and cardiac areas of the brain**
            - Causes vasodilation and reduction of the heart rate, both of which DROP BLOOD PRESSURE FURTHER, leading to further reduction in cerebral blood flow
        - In severe shock, **coronary blood flow is reduced** because of the hypotension and tachycardia, even though the coronary vessels are dilated
            - The myocardial failure makes the shock and acidosis worse
            - This in turn leads to further depression of myocardial function
    - A late complication of shock that can be fatal is pulmonary damage with the production of **ARDS**
        - This syndrome is characterised by acute respiratory failure with a high mortality
        - Can be triggered not only by shock but by:
            - Sepsis
            - Lung contusion
            - Other forms of trauma

- OTHER FORMS OF HYPOVOLAEMIC SHOCK:
    - Breakdown of skeletal muscle (RHABDOMYOLYSIS) is a serious additional problem when shock is accompanied by extensive muscle crushing (CRUSH SYNDROME)
        - Kidney damage is also common in this syndrome

        - It is due to accumulation of myoglobin and other products from reperfused tissue in kidneys in which glomerular filtration is already reduced by shock
        - The products damage and clog the tubules, frequently causing anuria
    - **BURN SHOCK:**
        - Loss of plasma as exudate from the burned surfaces
        - Since the loss is plasma and not haemoglobin, haematocrit may actually RISE due to **haemoconcentration**
        - Also causes **increases in metabolic rate**
        - High mortality rates still persist
    - OTHER CAUSES:
        - Adrenal insufficiency
        - DKA
        - Severe diarrhoea

DISTRIBUTIVE SHOCK:

- Blood volume is normal but the capacity of the circulation is increased by marked vasodilation
- Also known as "WARM SHOCK"
    - Because the skin is not cold and clammy
- Good example is anaphylactic shock
    - Large quantities of histamine cause increased capillary permeability and widespread dilation of arterioles and capillaries
- SEPTIC SHOCK:
    - Usually due to gram-negative bacteria
    - Has both distributive and hypovolaemic properties
    - ENDOTOXINS cause vasodilation and increased capillary permeability, with loss of plasma in the tissues

FAINTING:

- A third type of distributive shock is NEUROGENIC SHOCK
    - A sudden burst of autonomic activity produces vasodilation, pooling of blood in the extremities and loss of consciousness
        - These are called VASOVAGAL ATTACKS
        - Short lived and benign
    - About 25% of syncopal episodes are of cardiac origin and are due to either transient obstruction of blood flow through the heart or sudden decreases in cardiac output owing to various cardiac arrhythmias
    - Syncope is the presenting symptoms in 7% of patients with AMI

CARDIOGENIC AND OBSTRUCTIVE SHOCK:

- The pumping function of the heart is impaired to the point that blood flow to the tissues is no longer adequate to meet resting metabolic demands
    - CARDIOGENIC SHOCK
    - Most often due to extensive infarction of the left ventricle, but it can also be caused by other diseases that severely compromise ventricular function
- The symptoms are those of shock PLUS congestion of the lungs and viscera because the heart fails to put out all the venous blood returned to it
- A picture of congested shock is seen in obstructive shock

TREATMENT OF SHOCK:

- Should be aimed at correcting the cause and helping the physiologic compensatory mechanisms to restore an adequate level of tissue perfusion
- In haemorrhagic shock, treatment should include:
    - Early and rapid transfusion of adequate amounts of compatible whole blood
    - Saline is of limited temporary value
    - The immediate goal is restoration of an adequate circulating blood volume

HEART FAILURE:

PATHOGENESIS:

- **Failure of cardiac output to meet the metabolic demands of the body in the context of normal filling pressures.**
- Can be acute and associated with sudden death or chronic
- May involve primarily the right ventricle (COR PULMONALE)
    - Much more commonly it involves the larger, thicker left ventricle or BOTH VENTRICLES
- In chronic heart failure, cardiac output is initially inadequate during exercise but adequate at rest
- There are two type of failure:
    - SYSTOLIC:
        - Stroke volume is reduced because ventricular contraction is weak
        - Causes an increase in the end-systolic ventricular volume
        - EJECTION FRACTION (fraction of blood in the ventricle that is ejected during systole) FALLS
        - The initial response to failure is HYPERTROPHY of cardiac myocytes and thickening of the ventricular wall (CARDIAC REMODELLING)
        - The incomplete filling of the arterial system lead to increased discharge of the sympathetic nervous system and increased

secretion of renin and aldosterone =>sodium and water retention =>worsening of heart failure

- DIASTOLIC:
  - Ejection fraction is initially maintained but THE ELASTICITY OF THE MYOCARDIUM is reduced so filling during diastole is reduced
  - This leads to inadequate stroke volume and the same cardiac remodelling and sodium and water retention that occur in systolic failure

- It needs to be noted that inadequate cardiac output in failure may be RELATIVE rather than absolute:
  - Large arteriovenous fistula
  - Thyrotoxicosis
  - Thiamine deficiency
    - In the above examples cardiac output may be ELEVATED in absolute terms but still be inadequate to meet the needs of the tissues
      - HIGH OUTPUT FAILURE

TREATMENT:

- Aimed at:
  - Improving cardiac contractility
  - Treating the symptoms
  - Decreasing the load on the heart
- Currently most effective treatment is INHIBITION OF ANGIOTENSIN II
  - Reduces circulating aldosterone level
  - Decreases blood pressure
  - Reduces the afterload
  - Thought also to have a direct effect on the heart
- Diuretics reduce the fluid overload
- Beta blockers improve mortality
- Reducing venous tone with nitrates increases venous capacity so that the amount of blood returned to the heart is decreased, thus decreasing PRELOAD