THEME A: BLOOD PRESSURE – CAUSES & CONSEQUENCES

CORONARY RISK FACTORS

- Established risk factors are known to cause CHD
  - Age, cholesterol, BP, smoking, diabetes, BMI
- Reducing factors will ↓ risk of CHD
- Large ♥ size, clotting factors (homocysteine, fibrinogen), lipids = not established risk factors
- Risk factors aggregate ∴ present together
  - Weight gain promotes ↑ BP, insulin resistance (pre-diabetic stage)
  - Combining more factors will ↑ death rate
- Age is single most important risk factor → 80% risk in 65+ y/o
- Men have ↑ individual risk – die more frequently of CHD
- Women have reduced rates ∴ "protected" before menopause
  - Hormone therapy doesn't reduce CHD
- 4-fold ↑ in risk w familial cases → shared genes & env factors
- ***E.G:*** IRS-1 gene related to CHD w relation to insulin resistance, hypertension & impaired endothelial fctn
- Lipoproteins carry lipids
  - LDL + VLDL take lipids from liver to systemic circ. ∴ deposition in arteries
  - HDL take lipids back to liver ∴ ↑ HDL = ↓ risk
- ↑ Weight and central adiposity = ↑ risk for CHD, ↑ BP and diabetes
- **N.B:** stress is unproven factor
- ↑ alcohol = ↑ risk but 2 units/day may ↓ risk by affecting liver
- Individual graded risk is relative measure of risk comparative to individuals in society with lowest risk factors ∴ Small variation from lowest level will present as increased risk
- **N.B:** More deaths occur in the large number at modest risk – majority of the popn lies at average risk whereas only a small number is present at the highest risk
- Wealth and nutrition play key role in CHD
  - Dependent on ability to afford health care and adequate nutrition
  - Higher socio-economic groups = decline in CHD
- Low wealth correlated w infectious disease & poor life expectancy
- Adequate nutrition = adequate calories
  - Poor nutrition = excess calories → may lead to weight gain

BP VARIATION

- MAP = TPR x CO
  CO = SV x HR
- Variation b/w diff popn due to env changes
- Differences b/w individuals in a popn due to genetics but within individuals = env
  - B/w individuals = genetic changes
- Genetic variation b/w individuals w/n same popn is greater than difference b/w popn
  - Individuals differ by 1/1000 sequences whereas diff popn have the same variants
  - Effect of env more apparent b/w popn
- Unimodal distribution in popn → skewed t/w upper values
- High BP predisposes to diseases & death
  - CHD, stroke
  - Cardiac hypertrophy due to ↑ stress & atherosclerosis → causes ↓ efficiency
- ↑ BP produces physical stress on arteries → leads to atherosclerosis
  - Hardening of arteries can lead to ♥ attack or stroke
- ↑ BP can cause haemorrhage in small vessels
- Cardiac Insufficiency leads to ♥ failure → may be due to hypertrophy
- Kidney failure – damage to glomerular capillaries & replaced by non-fctn connective tissue
  - P in kidneys is normally higher than rest of body ∴ ↑ BP will significantly ↑ glomerular P
- Men have higher BP on average w ↑er individual risk of CV diseases
- BP ↑ w age – rapid incline after birth & puberty due to growth
  - At birth, both males & females have same avg. BP
  - females have ↑er avg. at puberty → perhaps b/c puberty is reached first in females

- Unacculturated individuals avoid rise in BP in adulthood
- Diastolic BP falls w age but Systolic ↑ ∴ ↑ Pulse P
  - Pulse P determined by Stroke Volume & artery compliance
  - Hardening of arteries w age = greater rise in P → lack of expansion to accommodate
  - Stiff arteries cause blood to move quickly through vessels ∴ less blood present in diastole
- Larger body size = ↑ BP – related to both height & weight → mean of BP related to mean body size
  - ↑ weight and height = ↑ vasculature ∴ ↑ resistance of flow and BP
  - Weight loss can ↓ BP
- BP varies on minute-minute, daily and seasonal basis
- Minute variation dependent of body stress & strain – changes in activity = BP fluctuation
- BP is 20mmHg lower at night w less minute-minute fluctuation
  - Greater sympathetic activation during day ∴ ↑ pulse rate
  - BP may be controlled by Renin-Angiotensin system at night
- 3mmHg difference in BP from Summer to Winter
  - Systemic vasodilation in summer may cause ↓
  - Sweating leads to ↓ blood volume ∴ ↓ SV
  - Lifestyle differences during seasons may influence weight, diet & physical activity

ENV FACTORS

- Genetic r/ships correlate to BP similarities b/w individuals
  - degree of env influence → individuals with same degree of genetic association have varying correlation
  - DZ & MZ twins share uterine env ∴ ↑ correlation but siblings have ↓er correlation
- Generation gaps, dietary diff = changes in BP correspondence despite genetic sim.
- Observational studies: watch popn overtime and examine changes in env
- Interventional studies: change env to view correspondence w BP
  - migration studies indicate BP changes w env
- *Sodium:* low salt diet ↓ BP on hypertensive subjects
  - weak correlation b/w popn (0.04 mmHg/mmol Na per day) → indistinguishable w/n popn
  - Urinary salt reflects intake → weak correlation to BP b/w popn
  - Steeper r/ship w ↑ age due to kidney insufficiency – lowered BP w diuretics
- *Alcohol:* ↑ intake ↑ BP independent of other factors
- Reversible w ↓ intake – involves sympathetic nerve stimulation & ↑ HR
- *Potassium:* ↑ intake = ↓ BP – weak correlation
  - More significant w Na/K intake ratio ∴ reflects diet
- Calcium & Mg have no proven impact on BP
- *Fats:* no r/ship b/w BP & fat intake
- Omega3 ↓ BP in hypertensives
  - May involve vasodilation & prostaglandins involved in vascular control
- Vegetarians have ↓er BPs – due to ↓ fat intake **or** alternate compounds in vegetables
- *Exercise:* BP lower w ↑ fitness – may involve sympathetic
  - ↑ fitness may mean that sympathetic NS doesn't need to be highly active
- *Smoking:* ↑ BP
  - long-term smokers have ↓ BPs – Lower BMI b/c appetite suppression ∴ ↓ weight = ↓ BP
- Popn vary in mean BP → Social, psychological, biological factors vary
  - Socio-economic status has ↑ impact in BP & CV risk → governs diet and health care

GENETIC FACTORS

- Variation in genetic sequences influence BP as phenotype
- Extremely rare coding mutations cause major genetic diseases w ↑ BP impacts
- Rare coding mutations associated w moderate effects → 5mmHg
  - Changes to coding sequences = change to protein production or fctn
- Common variants in non-coding regions have immeasurable effects → 1mmHg
- BP loci account for less than 5% of heritability & expected gene effect
  - Marker overlap & degree of gene expression not considered