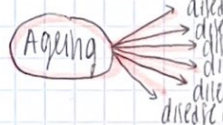


LECTURE 1 : Theories of ageing

- Disease in the past $\Rightarrow$ main causes $\Rightarrow$ microbial pathogens (ex: tuberculosis / cholera), viruses (small pox), parasites (hookworm), malnutrition (rickets) & violence (warfare)
- Nowadays $\Rightarrow$ major progress in identification of disease aetiology, immunisation, antibiotics, $\uparrow$ sanitation & hygiene, control of environmental toxins & $\downarrow$ violence
- $\Rightarrow$ result $\Rightarrow$ we live longer BUT experience diseases that didn't live long enough in the past to experience
- Leading causes of death in UK:
 - $\Rightarrow$ cardiovascular disease (atherosclerosis)
 - $\Rightarrow$ cerebrovascular diseases (stroke)
 - $\Rightarrow$ late-life cancers (prostate, breast & colon)
 - $\Rightarrow$ dementia (AD)
 - $\Rightarrow$ chronic obstructive pulmonary disease (COPD)
 - $\Rightarrow$ macular degeneration of the eyes
- cancer $\Rightarrow$ 'ageing is the greatest carcinogen'
- $\Rightarrow$ AGEING now main cause of disease worldwide
- $\Rightarrow$ infection due to immune senescence, $\uparrow$ accidents & lethal falls, $\uparrow$ suicide due to depression / chronic illness / terminal condition
- diseases of ageing $\Rightarrow$ aetiology unknown + largely incurable $\Rightarrow$ new challenge of biomedical research

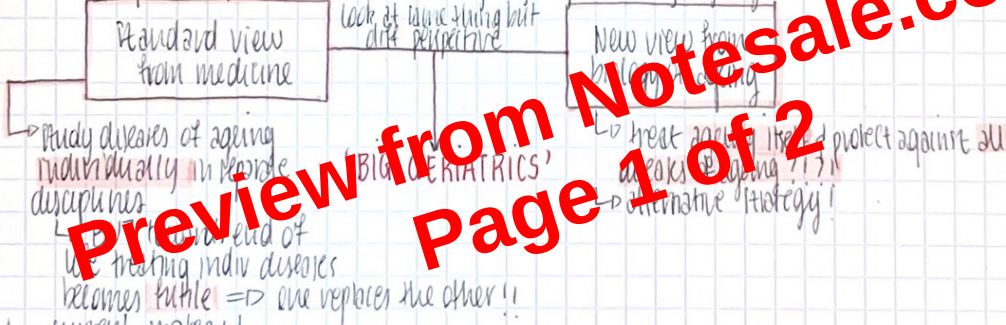
- key?
 - $\Rightarrow$ what are the aetiologies of diseases of ageing?
 - $\Rightarrow$ what is ageing?
 - $\Rightarrow$ how does ageing give rise to diseases of ageing?
 - $\Rightarrow$ are they preventable?
 - $\Rightarrow$ is ageing one or many disease?

AGEING as central cause



"White of Healthy Ageing" expression??

- Radical proposal: prevent diseases of ageing by treating ageing itself!



- current strategy!
- Dietary restriction!
 - $\Rightarrow$ in rodents $\Rightarrow$ postpones multiple diseases of ageing + confers 20-40% $\uparrow$ in lifespan & extension of 'health-span'
 - $\Rightarrow$ McClay et al. 1994
 - $\Rightarrow$ autoimmune disorders, cancer, osteoarthritis, T2D, hypertension & kidney failure
- Comparative biology of ageing:
 - $\Rightarrow$ ageing rates varied greatly b/w even closely related species $\Rightarrow$ evolve rapidly
 - $\Rightarrow$ ex: human lifespan 2x longer than higher primates
 - $\Rightarrow$ some species age very slowly / not at all $\Rightarrow$ ex: *Phew longeva* (~5000yrs), *Artemia felina* (not ageing)
- single genes mutations $\Rightarrow$ influence ageing rate!
 - $\Rightarrow$ can extend lifespan $\Rightarrow$ ex: *C. elegans* age-1 PI-3 kinase mutants can live up to 10x longer than WT
 - $\Rightarrow$ Aravamudan et al. 2009
- Geriatrics = late-life health
 - $\Rightarrow$ need to integrate fragmented study of diseases of ageing into unified discipline!
- Conclusion:
 - $\Rightarrow$ ageing is plastic
 - $\Rightarrow$ appears to be a central aetiology of senescence
 - $\Rightarrow$ potential targets for anti-ageing therapies
 - $\Rightarrow$ seek unified understanding of diseases of ageing
 - $\Rightarrow$ bring together fields of geriatric medicine + biogerontology $\Rightarrow$ BIG GERIATRICS!
- What does 'ageing' mean?
 - $\Rightarrow$ several meanings $\Rightarrow$ calendar ageing (the passing of time) $\Rightarrow$ senescence (deteriorative change)
 - $\Rightarrow$ age changes (only time dependent changes)