

BIOLOGY OF AGING:

Introduction

- More people surviving longer than ever before. Why?
 - ➔ Sanitation
 - ➔ Improved medical treatment
 - ➔ Improved diagnosis
 - ➔ Memory and Disease changes
 - Alzheimer's
 - Cancer

BIOLOGY OF AGING:

Introduction

- What is aging?
- How long can people live?
- Is there a limit to how long people can live?
- What is life span? versus life expectancy?
- Do all living life forms age?

BIOLOGY OF AGING:

Concepts & Theories

- Definitions:
 - ▲ life span---Longest time that species is capable of living (110 years for humans)
 - ▲ life expectancy--- Average time that species lives (72-76 years for humans)
 - ▲ senescence--- The process of aging at the cell and organismal levels
 - ▲ gerontology--- The study of aging

BIOLOGY OF AGING:

Concepts & Theories

- When does aging begin and what model systems can be used to study the aging process?
- Model systems first--
 - *in vitro* vs *in vivo* systems
 - single celled vs multi-celled
 - morphological vs biochemical changes
 - animal vs other life forms (fruit flies, worms, etc....)



BIOLOGY OF AGING:

Concepts & Theories

- When does aging begin?
 - how do you measure aging?
 - are there "aging markers"?
 - do all cells age at the same rate?
 - do all people age at the same rate?
- Levels of organization
 - molecular/organelles/cells/tissues/organs



Evolution of Aging

- Why is Life Span limited?
 - all characteristics of living organisms are the result of natural selection
 - Aging and its logical outcome, death, are ubiquitous and have survived
 - therefore= implication is that aging and death confer success and are characteristics selected for during evolution. Why??
 - Remove all disease and still die at 100+



Evolution of Aging

- There is a trade-off between somatic (body) maintenance and reproduction
 - the larger the fraction of energy invested in somatic maintenance the smaller the investment in reproduction (*will see later that certain life forms live longer if they do not reproduce*)
 - if somatic maintenance is too little then the animal will die. (*Repair of soma is always less than what is required for indefinite somatic survival*) [**Disposable soma theory of aging**]
 - conflicting goals of self-long-life and greatest number of progeny, and senescence is the negative component



Definitions of Aging

- Physical changes that take place manifested as a decline of body functions
 - much variation from indiv-to-indiv
- Net effect of all these changes on the ability of the individual to survive (measured for a population)
- At the population level, the most concise def. of aging is that the overall progressive impairment of the functions of organs and tissues results in an increasing age-specific death rate (death results in greater levels the older you get!)



Theories of Aging

- ***1. Programmed Theory of Aging***
- ***2. Running out of Program Theory***
- ***3. Mutation Theory of Aging***
- ***4. Autoimmune Theory of Aging***
- ***5. Cross-linking Theory***
- ***6. Free-Radical Theory***
- ***7. Cycling/Non-Cycling Cell Theory***
- ***8. Error Catastrophe Theory***
- ***9. DNA Repair Mechanisms***
- ***10. Other Theories***



Theories of Aging

- **1. Programmed Theory & Running Out of Program Theory--**
 - **Programmed Theory--there is a genetic sequence activated at a particular time that regulates death.**
 - **Running Out Program--all events are specifically programmed into genome and are sequentially activated. After maturation genes have been activated there are no more programs to be played and as cells age there may be chance of inactivation of genes that cannot be turned on**



Theories of Aging

- **Mutation Theory**
 - random mutation hits genes and changes in proteins occur (viruses may be involved)
- **Autoimmune Theory**
 - as one gets older there is a greater incidence of autoimmune disease. Regulation of self-recognition is breaking down
- **Cross-Linking Theory**
 - of DNA and proteins- cross linking prevents the molecules from functioning properly



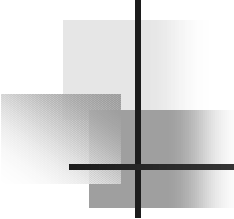
Theories of Aging

- **Free-Radical Theory**
 - highly reactive molecules that are formed during most chemical reactions. Cells can normally get rid of these but as a cell ages its ability to get rid of FR decreases (oxidation reactions)
- **Cycling/Non-Cycling Theory**
 - applies to tissues able to proliferate. Relates to whether a growing cell is blocked at a certain stage of proliferation and cannot continue to growth (i.e..., bone marrow cells)



Theories of Aging

- **Error Catastrophe Theory**
 - postulates that nothing is perfect. There is a chance for a mistake to occur. The more occurrences that happen the greater is the chance that a mistake will happen. i.e..., live long enough, enough mistakes happen, death occurs
- **DNA Repair Mechanisms**
 - DNA constantly needs repairs (mutations, radiation, chemicals, polymerase, etc...). Repair mechanisms decrease with age



Normal and Successful Aging

- **Do not know why people become more debilitated with age. People of the same chronological age can have vastly different aging responses**
- **More people are retaining vitality, an interest in life, and the ability to be active in some way physically and/or mentally.**
- **SOME PEOPLE CAN AGE WELL!!**
- **Most studies done on the aged are done in clinics where only “sick” people come. These people are eager to contribute to studies, but healthy older people are not seen by doctors or researchers.**



Normal and Successful Aging

- No way to characterize what a “normal aging” process is.
- Many changes that have been associated with aging are no longer unavoidable (inc blood pressure, inc in body weight, inc in serum cholesterol, inc in cancer)
- Rural areas exhibit different age-linked changes than urban: Industrial countries are different than un-developed nations

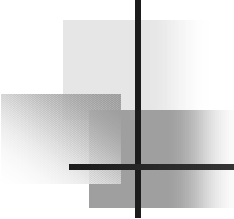


Normal and Successful Aging

- **Diseases such as Osteoporosis have other contributing factors other than just age that cause loss of calcium from bones:**
 - cigarette smoking
 - heavy alcohol intake
 - inadequate calcium intake
 - inadequate exercise
- **Mental faculties decrease with age?**
 - always exceptions to the rule. Some older people may be sharper than when they were younger
 - when one compares old to young to show a difference and then look at young when they are older, not much difference will be seen

Normal and Successful Aging

- **Cohort studies and studies between young and old show that 50 & 60 year olds exhibit a differences in aging responses**
 - in 10 yrs the 50 yr olds do not show the same decline in function as did the 60 yr olds had 10 yrs previously???
 - Due to differences in time of growing up (i.e., depression era teens vs children, war years vs fun yrs,...). They faced different challenges and stresses which could affect future mental and physiological health
- To determine if intelligence drops with age the best study would be to test 20 year olds and then 20 years later to test the same group again, NOT to compare 20 year olds with different 40 year olds.



Normal and Successful Aging

- **Exercise may be one of the major factors involved in increasing the numbers of the elderly who do not display so many debilitating aging symptoms.**
 - decreases osteoporosis
 - enhances cardiovascular ability
 - restores lung capacity
 - prevents loss of muscle tone
- **Diet is very important in slowing aging changes:**
 - not one proper diet for all people
 - high fat diets lead to inc heart attacks
 - colon cancer is inc by red meats and decreased by complex carbohydrates and by fiber



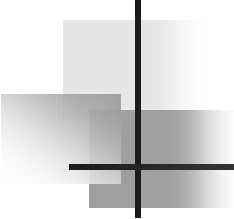
Normal and Successful Aging

- While it seems that some people die young no matter how healthy they try to keep themselves (diet, exercise, ...) they probably outlive what they would have otherwise
- (Science, Jan 1993) Shows that low cholesterol can lead to depression (low cholesterol levels inhibit serotonin, a neurotransmitter) and there is a higher suicide rate (balancing lowered risk of heart attack)
- No real connection between life styles of centenarians except for "intellectual curiosity" that is retained by all.



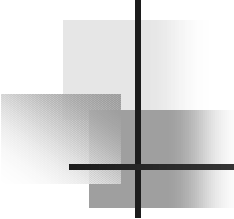
Normal and Successful Aging

- People who lose interest in life age more quickly
- Does successful aging lead to intellectual curiosity, or does intellectual curiosity lead to successful aging?
- Intellectual activity in old age has shown that there is an increase in the number of dendrites and synapses (put rats in a stimulating environment in old age and study brain)
- Early life diseases and trauma and experiences may shape aging processes (chicken pox-->shingles, athletic injuries-->arthritis, ...)



Normal and Successful Aging

- **Women and Aging**:: Women live longer than men. Why? Very little research done on women (Why?)
- Menopause (climacteric) involves major change in hormonal balance affecting the immune and nervous systems.
- Changes in behavior and attitude occur. Is not a disease
- **Aging and Sex**:: changes in vaginal lubrication, ability to attain and maintain an erection, and in abilities and desires to be stimulated. Sex and old age do go together! (Parents and GP do it!!)



Normal and Successful Aging

- **Nursing homes do not cater to old age and sex and intimacy for couples. This can lead to a variety of social and personal problems. Important to recognize for self-esteem issues and happiness**
- **Older people can hold hands, engage in sex, and even get married and should not be looked at in disbelief or disgust.**
- **sex at any age between compatible partners bolsters emotional health, elevates self-esteem and helps to keep one aware of the world and interested in keeping in good health (like intellectual curiosity?)**

Goals & Responsibilities of Aging Research

- ✂ **Those who took Biology 20 years ago know almost nothing of the new discoveries. Technology has made incredible advances**
- ✂ **Goals of aging research::**
 - * extension of human life span beyond the present apparent limit of 110 years
 - * the ability to guarantee a full and healthy life up to the last moment of allotted span
- ✂ **These goals raise ethical questions:**
 - * extension of life assumes that all faculties will be functional (do not want to be dependent for 200(?) years {read "Steel Beach" nanobots?})

Goals & Responsibilities of Aging Research

- ✂ Live life healthy until you die (if you are healthy then why die? paradox)
- ✂ Through use of medicine, technology, etc... can extend "life expectancy" for those who have access to this technology (developed vs undeveloped countries)
- ✂ Elimination of one cause of death may lead to a different cause of death (i.e., from cancer to Alzheimer's)
- ✂ In developing countries, smoking and carcinogens may be very low on priority list of needs to improve health

Goals & Responsibilities of Aging Research

- ✂ If life is to be extended to use our 110 years then there must be a limit put on birth rates!!
Controversial to say the least
- ✂ Concerns over euthanasia and the right to die (living wills) but State may decide who lives and dies in certain situations of health and disease
- ✂ Keeping people alive may be very expensive. Who pays? Taxpayer ultimately. Are we willing? Who should decide? (Kevorkian)
- ✂ Implantation of fetal tissues can help in Parkinson's and Alzheimer's diseases.
Controversy

Goals & Responsibilities of Aging Research

- ✂ **Study of aging is a multi-discipline process**
- ✂ **What are the models for studying aging??**
- ✂ **Any theory of aging must encompass ALL organisms, from single cells to complex humans. The question is: What do all aging organisms have in common??**
- ✂ **All aging organisms are able to undergo differentiation. A cell that does not differentiate does not age. Cells that do not differentiate only take in food, grow and divide. Can change food requirements by changing active genes and enzymes**

Goals & Responsibilities of Aging Research

- ✂ **What cells “live” like this?**
- ✂ **Bacteria and cancer cells do not age (they are immortal. as long as there is a food supply and wastes are taken away they will continue to grow and divide)**
- ✂ **As cells differentiate they need to be able to respond to external stimuli. Do this by receptors. Need to remove waste products and toxic substances and these processes require a lot of energy. The use of energy for these processes takes away energy for reproduction. Sexual reproduction takes a lot of energy from individual cells**

Goals & Responsibilities of Aging Research

- ✂ Aging is species specific (mice live 20 X shorter than humans). It is not the failure of individual cells that causes aging, but a breakdown in communication and response processes between cells so that the system is no longer controlled.
- ✂ Mice and people have different metabolic rates. Does this create the difference in life span?
- ✂ Many studies needed and many things need to be found out to fully understand aging and how to delay the overall effects of aging in humans