## HUMAN AGEING AND HUMAN LIFESPAN. By William Reville, University College, Cork.

I often receive invitations to subscribe to American health magazines. The advertising blurb accompanying a typical offer confidently exclaims - 'three minutes a day to a 120-year lifespan'. You are advised to consume large amounts of vitamin and mineral dietary supplements during these vital daily minutes. You are also promised that this daily three-minute munch will ensure robust health, including a vigorous sex life - you can literally become 'the oldest swinger in town'.

Such advertising inevitably prompts many questions. Is the process of gradually declining vigour in old age, culminating in death, inevitable? If so, is it nevertheless feasible to significantly extend human lifespan beyond the current familiar limit? How much biomedical research should be invested in this area?

Is death inevitable for humans? In so far as present knowledge goes, the answer is yes. For some simple organisms, things are different. In a certain sense, many single-celled organisms neither age nor die. For example, an amoeba, under optimum environmental conditions, grows, and, when it is ready, simply divides in two. In turn, the progeny also grow and divide in two. In this way the first amoeba attains a sort of immortality - at no stage can you say it has passed away. On the other hand, more complicated biological organisms go through the irreversible sequence of birth, growth, senescence, and death.

The death of the body seems to be as natural as birth. Death within a limited period after birth ensures turnover of the species and allows evolution by natural selection to proceed with some efficiency. If, on the other hand, organisms didn't die, and continued to procreate, those species with no, or few, natural predators would quickly grow in numbers and crowd out most other species.

Turnover is a basic characteristic of life. Whenever nature presents a face of apparent constancy, this invariably masks an underlying dynamic equilibrium. Thus, the molecules in our cells are continually being broken down and replaced. In many of our tissues, whole cells are continually dying off and being replaced. For example, every second, two and a half million worn-out red blood cells are removed from your circulation and broken down. At the whole population level, constant species numbers simply reflects a balance between birth rate and death rate. Death is part of life.

Different animal species have different lifespans. A mayfly lives for 1 day. A spider lives for 1 year. A mouse lives for 3 years. A squid lives for 4 years. A rat lives for 6 years. A cat or dog can live for 25 years. A horse can live for 40 years. An elephant can live for 70 years. A human being can live for 120 years. Some tortoises can live for 150 years. Plants easily hold the record. Some trees can live for more than 4,000 years.

As a general rule, among mammals, larger species live longer than smaller ones. This may be due in part to the slower metabolism (body chemistry) of the larger animals. The metabolic theory of ageing holds that small mammals tick over faster, burn rapidly and live for a shorter time than large mammals which live longer at a more sedate pace. To use a mechanical analogy, if you take two engines and constantly run one fast and hot and the other one at a slower rate, the faster-running engine will grow smokey and will burn itself out well before the slower-running engine.

There are exceptions to the simple rule that lifespan is proportional to rate of metabolism. For example, some birds with high metabolic rates live longer than mammals three times their size. Consequently there are several other theories of ageing. The oldest theory holds that senescence results simply from wear and tear. Cells taken from old animals and examined under the electron microscope show obvious signs of 'wear and tear' compared to the cells from a young animal.

But the wear and tear theory doesn't explain everything either. In some third world countries, where life is hard and medicine a luxury, death rates in infancy and youth are high, but, once a person reaches mature adulthood, life expectancy can be as good as in developed countries. There appears to be an inner biological clock which determines the rate at which we age, and sets a limit on our lifespan.

But it might be argued that, if we live long enough we will each develop a disease, e.g. heart disease, and this is what eventually terminates most lifespans. In other words, if medicine could abolish disease, would people live indefinitely? I'm afraid not. It appears that there is such a thing as a 'natural death'. One American study reported that 30% of autopsies, carried out on people who were at least 85 when they died, could identify no cause of death. These people seemed to have simply died of old age.

To return to the analogy of the two motor cars. The heavily used car wears out faster and dies sooner than the lightly used car. But, consider an alternative scenario in which the heavily used car is regularly treated to comprehensive repair and maintenance. This would obviously greatly extend its lifespan. Living cells also have a repair mechanism whereby the essential genetic material that controls day to day activities in the cell is maintained in good working order. However, the repair mechanism itself becomes less reliable as the organism ages and this results in the gradual accumulation of genetic mistakes. Eventually it can be envisaged that the cumulative effects of genetic mistakes, mechanical wear and tear, and metabolic burn out conspire to end the life of the organism.

Until recent times, most people everywhere died young. On average, ancient Romans lived no more than 20 or 30 years. 200 years ago, the average person would hope to live to 40. Average life expectancy in Ireland today is about 75 years. One must distinguish between life expectancy and maximum lifespan. In ages past, average life expectancy was much lower because of uncontrollable disease, high infant mortality, and powerful psychological factors (see previous article). But I am not aware of any evidence that the maximum lifespan attainable by humans in past ages, in those people fortunate enough to escape disease and to be equipped with robust psychological health, was much less than presently attainable lifespans. Over the past 200 years, average life expectancy has been slowly rising towards a maximum lifespan ceiling, which is probably genetically determined and no greater than about 120 years.

Future advances in molecular biology may make it possible to extend human lifespan. Much research effort is afoot, particularly in the USA, aimed at slowing down the ageing process. Supplementing the diet with large amounts of Vitamin E is widely promoted as a way to slow down metabolic burnout. It is extremely unlikely that it will ever become possible to broaden human lifespan indefinitely, i.e. to achieve immortality. Even if this could ever be achieved, it is doubtful if it would be desirable, either biologically, medically, ethically or psychologically.

In any event, there are several uncomplicated ways presently available to us to achieve at least a measure of immortality. First of all if you are a religious person you may have no problem at all with the concept of immortality, since you will believe that you have an immortal soul. But even if you are not religious you can still aspire to achieving a measure of immortality, either by having some of your characteristics transmitted to future generations through your descendants, or even by having a memory of your existence preserved by posterity as a result of making a major contribution during your life time. But, of course, there will always be people who feel like Woody Allen when he was asked - 'Mr. Allen, how would you like to achieve immortality?' He replied - 'By living forever'.

(This article first appeared in The Irish Times, January 13, 1997.)