

I. Please tell me why Dr. Spindler said "I am confident that that day will come" based on the following paragraphs! (25%)

The study, appearing this week in the Proceedings of the National Academy of Sciences, showed that mice at the relatively advanced age of 19 months that were placed on a restricted calorie diet lived 42 percent longer than litter mates who continued to eat a standard diet.

Other studies have shown that young mice put on a low-calorie diet live much longer than mice fed the standard fare. But the new research suggests that it is never too late to enjoy a life-extension benefit by reducing calories.

Stephen R. Spindler of the University of California, Riverside, leader of a team conducting the research, said there is little evidence yet that dietary restrictions will extend human life, but in mice, at least, sensible eating even at older ages clearly has a longevity benefit. He said a 19-month-old mouse is the age equivalent of 60 to 65 years in humans.

Spindler said old mice placed on a restricted calorie diet responded quickly with better health and that eventually the animals lived up to six months longer than litter mates fed the standard diet. If such findings translate to humans, he said, "this could mean a lot more years and a lot of good years. The mice on caloric restriction lived longer and they are healthier."

Early vs late start

Spindler said that while older mice that go on a diet do live longer than those that don't, they still don't live as long as mice that have been on restricted diets for a lifetime. He said mice put on low-calorie diets just after birth have been known to live up to four years, almost twice as long as normal mice and months longer than the aged mice in the new study.

The message, he said, is that sensible eating for a lifetime is best, but there are life span benefits even if the diet is not started until old age. "This is a very important finding," said Dr. George S. Roth of the National Institute on Aging, one of the National Institutes of Health. "The dogma has always been that the earlier in life you start a restricted diet, the better it works for extending life," said Roth, a researcher studying the aging process who was not involved in

Spindler's research. "This finding suggests that you may get some of the same benefits starting late in life."

Cancer connection

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Spindler said the study also found that the restricted-calorie diets also slowed the development and advancement of cancer. Death from tumors is very common among aged mice, he said, but the researchers found that tumor growth either started later or was slowed among mice fed limited calories.

The researchers also analyzed how the action of genes changed in mice placed on restricted calorie diets. Spindler said there were changes and that these might be biomarkers of how the restricted diet works to extend life.

"People have been searching for 30 years for biomarkers of the changes that take place during the aging process," said Spindler. He said the new study in mice suggests that by measuring the amount and type of proteins made by the genes scientists could pinpoint the biomarkers of aging. Once those are known, he said, it would be possible to find drugs that have the same effect on life extension as calorie-restricted diets.

Does this mean that eventually aging could be slowed by taking a pill?

"I am confident that that day will come," said Spindler.

II. Please tell me why people are afraid to eat fish, which is a good source of protein and other nutrients and "can be important parts of a healthy and balanced diet. How can you select the good fish to eat for protecting your heart and brain! (25%)

Women who are pregnant, nursing or may become pregnant, and young children should not eat certain kinds of fish that tend to be high in mercury, said Lester Crawford, deputy commissioner of the U.S. Food and Drug Administration.

While mercury can affect almost any organ in the body, "the most sensitive organ is the brain," said Crawford. "The concern is there could be a mental effect on a young child."

At the same time, the new guidelines emphasize that fish is a good source of protein and other nutrients and "can be important parts of a healthy and balanced diet."

In recent years fish has become increasingly popular because of the omega-3 compounds it contains that can benefit the heart. The American Heart Association recommends that people eat a variety of fish at least twice a week, even more for those diagnosed with heart disease.

The problem is that mercury pollution from industry and other sources contaminates water where it is taken up by small fish, which are then eaten by larger fish, concentrating the mercury which then may affect people who eat the fish.

So, how to protect the heart and brain?

Consumer's Union and other groups have been pressing the government to come up with a consumer-friendly list of low-mercury fish, since not all fish are polluted equally.

The new guidelines, issued jointly with the Environmental Protection Agency, do that.

They say the fish most likely to contain mercury are shark, swordfish, king mackerel and tilefish. These fish should be avoided by women in the groups that may be most affected, and also by small children, the guidelines say.

On the other hand, the guidelines suggest eating up to two meals a week, totaling 12 ounces, of fish known to be low in mercury such as shrimp, canned light tuna, salmon, pollock and catfish. Albacore tuna has more mercury than light tuna, the agencies report, so it should be limited to one meal a week.

The trade association the National Fisheries Institute issued a statement stressing the health benefits of fish and expressing concern that the guidelines might alarm consumers and cause them to avoid fish.

But Crawford said that "by following these guidelines, we're confident that women and young children can safely include fish as an important part of a healthy diet."

III. The World Health Organization (WHO) has sounded a warning over the growing prevalence of drug-resistant tuberculosis (TB). Unless action is taken, these 'super-strains' of the disease could render existing therapies useless, public-health experts say.

The worst-affected areas are eastern Europe and central Asia, according to a report released by the organization's Global Project on Anti-tuberculosis Drug Resistance Surveillance. As many as 14% of new cases in these regions involve multidrug-resistant (MDR) strains of the bacterium. The project's researchers surveyed some 67,000 new TB cases in 77 countries or provinces worldwide. Six of the top ten hotspots for MDR strains are in the old Soviet Union. A collapse in the region's public-health infrastructure has left Kazakhstan, Uzbekistan, Estonia,

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Lithuania, Latvia and Russia among the countries most threatened by untreatable TB. Researchers are also worried about the potential spread of drug resistance in China, home to 485,000 new cases of TB each year. Only six of the country's 23 provinces were included in the survey. Two of them, Liaoning and Henan, are among the top ten regions worldwide.

Worldwide, TB kills 2 million people each year, and there is no vaccine that prevents infection entirely. Treatment for a patient infected with a non-resistant strain takes six months and costs around US\$10. Patients infected with an MDR strain of the bacterium do not respond to treatment with either of the two main TB drugs, isoniazid and rifampicin. Although other drugs are available, the treatment takes up to two years and can cost anything between \$500 and \$6,000. Experts think that resistance arises when patients do not complete their drug courses, or are not properly looked after. The researchers are therefore urging countries and public-health charities to invest in DOTS, a WHO scheme to standardize the detection, treatment and reporting of TB cases. The organization has now launched DOTS-Plus, an extension of the scheme that involves the use of alternative drugs to combat MDR strains. Adherence to DOTS-Plus should minimize resistance to these alternative drugs.

Q1: What are the differences in treating common TB and MDR-typed TB? (4%)

Q2: What is MDR? What are the key components to minimize drug resistance of TB? (8%)

IV. When it comes to traffic congestion, ants prefer the no-nonsense approach - they barge others out of the way, forcing them to take an alternative route. The strategy allows ants to prevent time-consuming blockages on foraging trails, say European researchers.

Foraging ants lay down scent cues that allow others to follow the route between the nest and a food source. As more ants follow the trail, the chemical signposts are reinforced and become more attractive. But problems can arise when too many ants try to use the route, says Vincent Fourcassié of the Université Paul Sabatier in Toulouse, France. His team found that ants are surprisingly good at avoiding congestion, simply by shoving each other off the main highway and on to back streets.

Fourcassié and his colleagues presented black garden ants (*Lasius niger*) with a sugar source, which was reached by a bridge divided into two branches of equal width. When branches were 10 millimetres wide, two-way traffic was much heavier over one of the two branches, showing that ants prefer to follow a well-marked route. But when the branches were narrowed to 6 millimetres or less, the flow of ants along the two routes was more even, they report in *Nature*.

This was because ants leaving the nest met returning foragers head on, and the resulting collisions caused them to take the other branch. The re-routing strategy allows ants to maintain the same flow of food back to the nest even when things start to get crowded, Fourcassié explains. He suspects that similar processes govern crowd control in the nest's network of underground tunnels. Similarly simple rules could be used to manage the flow of data through networks such as telephone systems. Many scientists rely on the behaviour of ants or other natural systems to give them clues as to how to design computer systems that avoid overcrowded networks.

Q1: What do ants do when the traffic is light, medium or extremely heavy? (6%)

Q2: Can ants' system be applied to the traffic on the road? Explain your answer. (6%)

V. Fat is bad for your heart, right? Maybe not entirely, says a group of US researchers. The team claims that cells found in fatty tissues can boost blood-vessel production. The discovery could pave the way for innovative treatments for conditions such as angina, in which narrowed arteries starve the heart of oxygen. Fat-derived cells could be injected close to the heart where they could form a new network of vessels, says Jalees Rehman of Indiana University School of Medicine, who led the study published online by the journal *Circulation*. Liposuction patients could even find a use for their own unwanted blubber, he adds. The cells could be injected wherever a patient needs them most, the researchers suggest. For someone with very poor circulation in their legs, for example, the treatment could avert the need for amputation. Rehman's team injected immature fat cells, called stromal cells, into the hind legs of mice with poor circulation. The treatment boosted their blood flow fivefold. The cells may work by secreting a nourishing cocktail of growth factors that promote blood vessel growth, explains Rehman. Cultured stromal cells release a protein called vascular endothelial growth factor. In turn this can recruit neighbouring cells to help form new veins and arteries.

Previous attempts to treat circulatory diseases with growth factors directly have failed. Rehman thinks that the cells, which secrete these molecules where and when they are most needed, offer a more sensitive solution. His team refers to them as "intelligent factories" for growth factors. But can these diseases really be treated with the leftovers from liposuction? The idea needs further study before it can enter doctors' therapeutic arsenal. It is already known that fat contains stem cells, which can give rise to a range of tissues including bone, muscle and cartilage. The discovery led to liposuction being hailed as an alternative source of stem cells that would sidestep ethical worries over the use of fetal material. Stromal and stem cells are both primitive cell types, but researchers are not sure whether they are the same, or subtly different. Although stromal cells may perhaps function as stem cells, Rehman says that their

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ability to recruit other cells, rather than simply dividing repeatedly to form new structures, could offer a more efficient way to build new blood vessels.

Q1: According to this article, where can you find stem cells? What are the advantages of applying stromal cells over growth factors? (8%)

VI. The concept of the cell as the fundamental structural and functional unit of a multicellular organism stems from the observations of Robert Hooke in 1665 and Nehemiah Grew in 1682, both of whom reported on the 'cells' of plant tissues. Plants have been notable and important tools in this process of cellular discovery. Paradoxically, recent advances in plant cell biology challenge the dominant position of the current version of cell theory.

Cell theory identifies the cell as the elementary unit from which all living organisms are constructed. Although this holds true for all prokaryotic and unicellular eukaryotic organisms, the supracellular structure of higher plants presents a problem. Cell-to-cell channels, called plasmodesmata, connect each plant cell to its neighbours, facilitating the exchange of large molecules (proteins and RNAs) and allowing the mass flow of smaller molecules. Thus, in contradiction with the cell theory, plant cells are neither physically separated nor structurally independent. The challenge to the cell theory does not stop with plants. There are numerous examples of supracellular assemblages known as coenocytes (which are formed by mitosis with the absence of subsequent cell division) and syncytia (which are formed by cells fusing together), both of which are found throughout the eukaryotic superkingdom. These giant cells contain multiple nuclei. Nanotubular intercellular bridges are also generated *de novo* between animal cells. These cell-to-cell connections can create complex networks of cytoplasmic continuity that facilitate cell-cell transport, of, for example, endosomal-like vesicles. It seems that algae, fungi, plants and animals have all independently developed both supracellularity and multicellularity.

To harmonize all these diverse cytological observations of eukaryotic forms, a discrete subcellular element is required that will take over from the cell as the fundamental unit, not only of eukaryotic structure, but as a propagule of life itself. One possible candidate is the 'cell body' which was proposed for animal cells by the late Daniel Mazia in 1993. The 'cell body' comprises the nucleus and a set of perinuclear radiating microtubules, and can be regarded as the basic unit of eukaryotic life, being both autonomous and self-reproducing. The 'cell body' concept is particularly suitable for supracellular plants. Plant nuclei make use of the whole of their nuclear surface to organize radiating microtubules. This feature is prominent in multinuclear coenocytes and syncytia found throughout the eukaryotic superkingdom, where the radiating microtubules determine the regular spacing of individual nuclei ('cell bodies').

Importantly, 'cell body' microtubules radiate from the organizing sites near or at the nuclear surface into the cytoplasm. This extranuclear scaffold structure provides the structural basis for the well known (but little understood) observation that the volume of the nucleus has a fixed relationship to the size of the cell (the cytonuclear ratio), a principle that underlies the organization of every eukaryotic cell.

The origin of the 'cell body' attracts further speculation. Its dual nature (nucleus and microtubules) may be the result of serial and progressive endosymbiotic events that took place during the early evolution of the eukaryotic cell. In fact, the eukaryotic cell itself is supracellular as it has been developed by the merger of several originally free-living cells. After long discussions, the endosymbiotic origin of mitochondria and plastids is now widely accepted.

Whereas 'cell bodies' cannot arise *de novo*, and are formed only by a structural splitting of pre-existing 'cell bodies' during the highly conserved process of mitosis, the plasma membrane, along with its associated structures and assemblies, can be formed *de novo* through secretory and synthetic activities organized by the 'cell body'. In plants this occurs every time a cell divides at cytokinesis! In addition, the 'cell body' is inherently motile, but is confined within the boundary structure of the plasma membrane with its associated actin cytoskeleton. The active exploration of cytoplasmic space by the 'cell bodies' is a feature that makes them appear akin to active, living organisms trapped within a protective cellular 'cage'; this exploration also underlies the cytonuclear ratio. Altogether, the 'cell body' concept represents a satisfactory and coherent conceptual framework for understanding both supracellularity and cellularity throughout the eukaryotic superkingdom.

Q1: What are supracellularity and its functional meanings? (6%)

Q2: Define "cell body" and explain the relationship between cell body and cell size (or cytonuclear ratio). (8%)

Q3: What's the role of plasma membrane in the concept of cell body? (4%)