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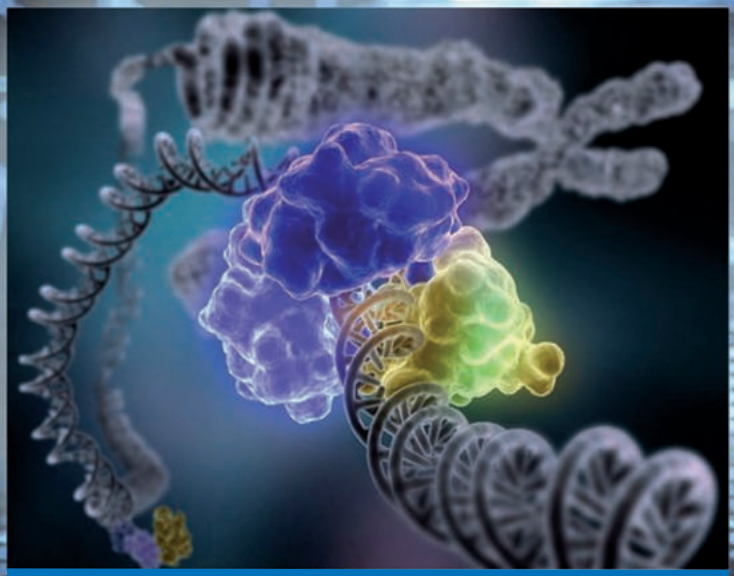
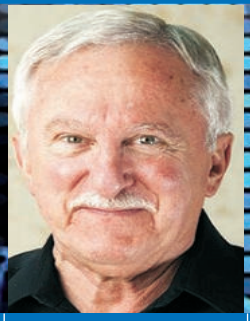
How DNA Repairs Itself

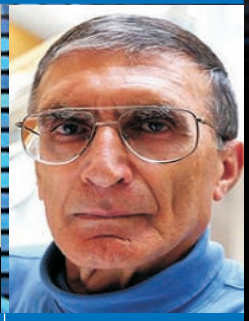


NOBEL PRIZE IN CHEMISTRY 2015

Tomas Lindahl



Paul Modrich



Aziz Sancar

... think scientifically, act scientifically... think scientifically, act scientifically... think scientifically, act...

Scientific temper for collective action: The climate cause

Dr. R. Gopichandran

We are all familiar with the talks in progress in Paris. These are related to climate change impacts management. It is well known that debates are predominantly on costs of mitigation and adaptation and differentiated responsibility of countries in meeting such costs. This creates a peculiar case of knowing the problem; yet not taking adequate and rapid action. Importantly, many people and institutions around the world have demonstrated the immediate and potential long-term benefits of preventive and remedial action. They also build capacities to sustain benefits of collective action[1, 2, 3 & 4]. Local relevance and collective benefits at the regional and global levels are also projected through many of them. India is significantly well prepared to contribute to collective action in this regard [5].

The most important take away from these deliberations is the fact that impacts alter livelihoods. This is in addition to the changes in the quantitative and qualitative profiles of resources we depend on and the consequences of extraction and consumption patterns. These consequences originate unmindful of the cause of origin. They could be natural or artificially induced or accentuated by climate change related causes. We need to however gravitate towards emphatic and clear preventive action. This is a logical extension of scientific thinking with a special emphasis on tackling problems at hand and in our vicinity. We wonder if there is any scope or justification for delays in collective action. Leadership comes with owning responsibility. These socially relevant values are steeped in scientific thinking about commonality of purpose and collective good in handling resources common to all of us.

I am inspired to refer to a snapshot on scientific temper authored by Shri Gauhar Raza in *Employment News* of 10-16 May 2014[6]. He highlights the insight that scientific temper has been at the core of our nation's development ethos. Science and technology institutions infuse and demonstrate values of scientific thinking and every one of us can play robust roles in furthering the practice of scientific temper in our own walks of life. This also reinforces the pervasiveness of science and human values steeped in truth. India has witnessed rapid progress due to the strengths of her institutions. This also means we have a duty to our country to sustain and enhance the momentum of such transitions. Importantly we should not be the reason for any backsliding on this front.

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How DNA Repairs Itself

M.S.S. Murthy
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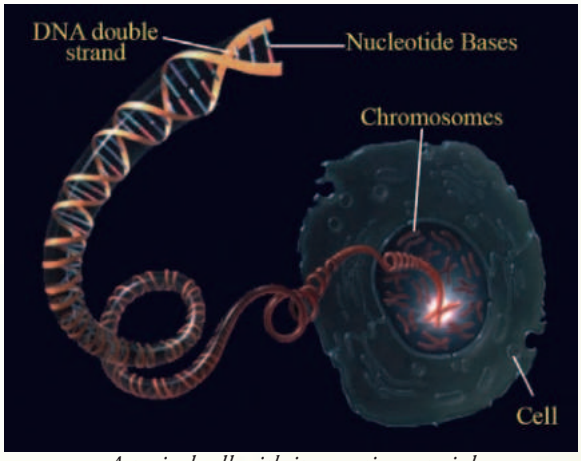
Every individual's life begins from the moment when the 23 chromosomes from a sperm combines with 23 chromosomes from an egg to form a zygote or a one-cell embryo. The chromosomes are made up of chemical strands called DNA. DNA itself is a long polymer built up with a sequence of four nucleotide bases – adenine, thymine, cytosine, and guanine. In each chromosome, DNA appears as a double-stranded molecule in which the base sequence of one strand is complimentary to the base sequence in the other. That is, adenine pairs always with thymine and guanine with cytosine in forming the double strand. Thus, the base sequence in one strand determines the base sequence in the other strand. Human genome is estimated to consist of 3 billion base pairs. The order in which the nucleotide bases are lined up in the DNA strand, in units of three bases at a time in sequence, carry the genetic information – recipes for proteins to produce a variety of traits that make us who we are.

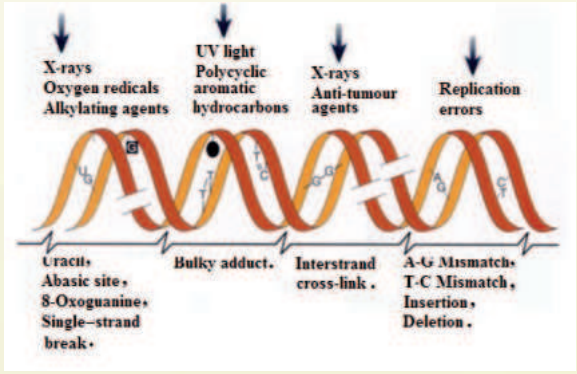


A typical cell with its genetic material

While the genetic information gets passed on from one generation to the next, it remarkably stays intact over thousands of generations, except for a few mutations that drive evolution. How does the cell maintain this level of resilience in the genetic material? The basic research carried out by the awardees of the 2015 Nobel Prize in Chemistry – Tomas Lindahl of the Francis Crick Institute, UK; Aziz Sancar of the University of North Carolina Chapel Hill, USA, and Paul Modrich of Duke University School of Medicine, USA – provides answers to this fundamental question. They were awarded "for having mapped at a molecular level, how cells repair damaged DNA and safeguard the genetic information".

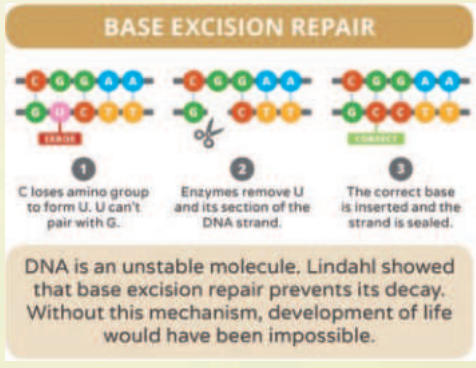
Tomas Lindahl

Until about 50 years ago scientists believed that DNA is an extremely stable molecule. For, if the genetic material were unstable, life on Earth would have been impossible. Towards the end of the 1960s, Tomas Lindahl of the Francis Crick Institute, UK, wondered how stable the DNA is. His early experiments demonstrated that DNA taken out of the cell undergoes slow but noticeable degradation. The genome is subjected to potentially devastating assaults by UV radiation from the Sun, ionising radiation from natural and man-made sources, drugs, chemical pollutants in our environment, and so on. Furthermore, defects can arise when DNA is duplicated during cell division. Even normal metabolic reactions generate reactive oxygen species like peroxides and superoxides, which attack the bases in DNA. Lindahl estimated that more than a million different types of defects such as molecular lesions-like structural damages to the DNA strands in the form of cross links within a strand, strand breaks, alterations to the chemical nature of the bases, and bulky adducts to the bases occur. These, if allowed to persist, may lead to cell death or harmful mutations causing cancer, hereditary defects, etc. He therefore, concluded that there must be some molecular machinery to repair most, if not all, of these defects before they express themselves.



Some DNA damaging agents and types of damages

Working with bacterial DNA, Lindahl found that occasionally the base cytosine loses an amino group and becomes uracil. Since uracil is similar to thymine, it pairs up with adenine in the next round of DNA replication, resulting in a change in the base sequence and possibly a mutation. Over years of study, Lindahl discovered what he called "base excision" repair process, which brings into action a series of enzymes to correct this defect. First, an enzyme known as glycosylase detects the defect and removes the altered base from the DNA strand. Then another enzyme – a nuclease – cuts the DNA strand to remove the rest of the damaged nucleotide. A third enzyme – a polymerase – now fills the gap with the correct base, and finally the broken ends are sealed by another enzyme – DNA ligase – to restore the original sequence. Similar base excision repair system exists in higher organisms, including humans.



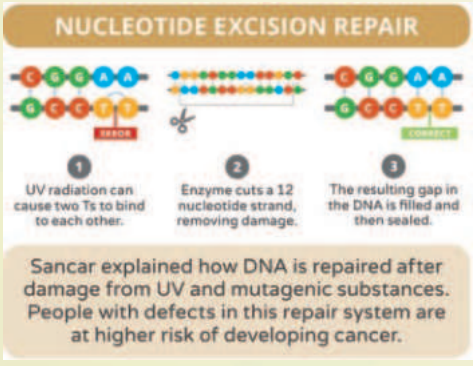
In the mid-1979s, Aziz Sancar, a physician from Turkey was piqued by a strange phenomenon concerning UV exposure. UV radiation, of which the life-supporting Sun is a natural source, is a potential mutagenic agent. When a DNA molecule is struck by

a UV photon, the energy absorbed may disrupt the chemical bonds in the pyrimidine bases (thymine and cytosine) resulting in cross linking between the adjacent thymine and cytosine. These pyrimidine dimers, being bulky, alter the DNA helical structure and inhibit its replication, leading to mutation or cell death.

Aziz Sancar

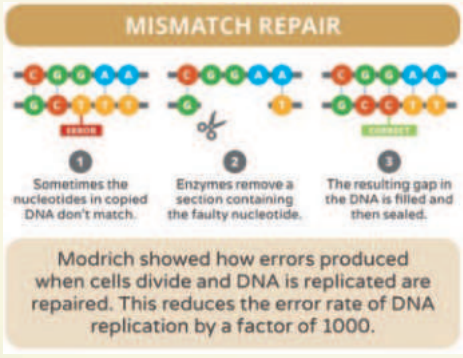
Sancar found that bacteria exposed to lethal doses of UV radiation suddenly recover if illuminated by blue light. To find out the answer to the basis of this 'photoreactivation', he took to biochemistry. Working at the University of Dallas, Texas, USA, he succeeded in cloning an enzyme called 'photolyase' responsible for photoreactivation. In the presence of blue light it could remove the pyrimidine dimers formed by exposure to UV light and restore the DNA structure.

In the next few years it became clear that bacteria has another system for repairing UV damages, independent of photolyase – a "dark repair" system. Sancar managed to identify, isolate, and characterise the various enzymes involved in this repair process. While one of the enzymes identifies the UV damage such as pyrimidine dimers, another makes two incisions in the damaged strand, one on each side of the damage to remove about 12 to 13 nucleotides. As in the case of base excision repair, a DNA polymerase fills up the gap and a DNA ligase stitches the loose ends. This process came to be known as "nucleotide excision repair". Later he worked out that a similar, but more complex system functioned in all higher organisms, including humans. Persons deficient with this type of repair system are prone to skin cancer.



Paul Modrich's work concerned a series of enzymes that affect DNA. Cell division is a basic process in all living systems, wherein the entire genome is copied and distributed equally between the two daughter cells. In humans, each time a cell divides 3 billion base-pairs are copied. During replication the double-stranded DNA opens up and with each strand as a template a new strand is synthesised. The exactness of this copying is based on the principle of complementarity that adenine pairs with thymine, and cytosine pairs with guanine. However, mispairing can occur thousands of times during each cell division. In the face of this infidelity how does the genome guard its integrity?

Paul Modrich

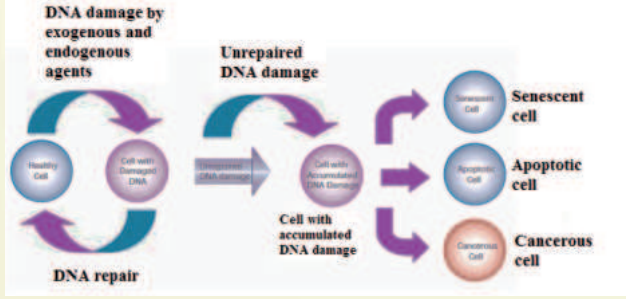


In the late 1970s Matthew Meselson, a molecular biologist at Harvard University in USA had created viruses with several mismatched bases. When these infected bacteria, Meselson found that the bacteria corrected the viral mismatches. How does bacteria accomplish this "mismatch repair" and how does it know which strand of DNA is mismatched?

In the late 1960s, Modrich, then a doctoral student at Stanford University, was examining a series of enzymes that affect DNA, namely DNA ligase, DNA polymerase, and restriction enzyme EcoRI (an enzyme that cuts DNA strands). During this work he stumbled on another enzyme called 'Dam methylase'. In the later years, he systematically cloned and mapped all the enzymes involved in the mismatch repair system in bacteria. His work revealed that during replication, Dam methylase attaches a methyl group (-CH_3) to the template DNA, while the newly synthesised strand would have none. While an enzyme called Mut H recognised the methyl group on the template DNA, two other enzymes Mut L and Mut S attach themselves at the mismatched sites in the newly synthesised strand (lacking methyl group). The faulty DNA is cut and the mismatch is removed. From then on DNA polymerase and DNA ligase take over to fill the gap and seal the loose ends.

Besides the base excision repair, nucleotide excision, repair and mismatch repair, there are several other repair mechanisms like SOS repair and recombinational repair. They all continuously monitor and counter damage to the genetic material. However, not all damages may be repaired if the cells are overwhelmed with damages or the repair genes themselves are damaged. In such cases, as cells accumulate damage, they become senescent (dormant), apoptotic (programmed cell death), or malignant (cancer). For example, persons with deficiency in nucleotide excision repair are prone to skin cancer if they are exposed to sunlight; unrepaired mismatches may lead to a form of colon cancer. Defective germ cells will cause several hereditary diseases.

In announcing the Prize, the Royal Swedish Academy of Sciences stated that the basic research carried out by the 2015 laureates make a "decisive contribution to the understanding of how the living cells function, as well as providing knowledge about causes of several hereditary diseases and about mechanism behind both cancer and aging".



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Are We Alone?

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Are we alone in the Universe? Is there someone watching us from space? Is there life beyond Earth? To explore answers to these questions, we first need to understand three mysteries: what defines life, what the pre-requisites for life are, and finally, how life has evolved and survived on Earth in the first place.

What really are the defining features of 'life'? Looking around, we can identify several characteristics of life – life grows, life replicates, life metabolises, life manipulates the environment for energy and sustenance, life displays a level of complexity that distinguishes it from non-life. Life has a sophisticated system for storing, processing and transmitting information to the next generation. Life adapts and evolves. But there is hardly any characteristic that is not shared by non-life. Crystals of salt grow on their own, computer programs can replicate and evolve, and computers possess highly sophisticated system of storage and sharing of information. Fire metabolises, releasing energy by burning. Weather exhibits incredibly complex behaviour. So, none of these characteristics can be said to be unique to life.

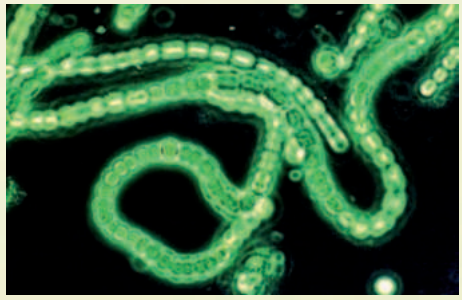
Gerald Joyce, a NASA scientist, gave a simple definition of life as a self-sustaining chemical system capable of Darwinian evolution. But as Carol Cleland, a philosophy professor, said, we are perhaps yet to develop a proper language of natural sciences to be able to define life, just like a proper definition of water needed our understanding of molecular chemistry. However, the 'most accepted working definition of life' is that living forms are those that use energy to build molecular structures and replicate themselves following a specific set of instructions embedded within themselves.

Scientists generally agree that for 'Earth-like' life to evolve and thrive anywhere, there are certain pre-requisites, the most important of which is the presence of water. Further, there has to be a 'habitable zone' conducive to life; that is, a planet at an appropriate distance from the parent star on which water can exist in liquid state under ordinary temperatures and pressures. (This habitable zone called the circumstellar habitable zone (CHZ) is also known as Goldilocks zone, from the fairy tale of 'Goldilocks and the Three Bears', in which a little girl chooses one that is "just right" from various items, ignoring the ones too large or too small or too extreme.)

There also has to be abundance of organic elements necessary for making the complex organic molecules required to capture and reflect the complexity of life. Ninety-nine percent of all living materials on Earth are composed of only six elements – carbon, hydrogen, nitrogen, oxygen, phosphorus and sulphur (CHNOPS). All metabolising organisms contain organic molecules made up of these elements dispersed in water, which provides an ideal environment in which chemical interaction between these molecules can take place.

Water has some unique properties unlike any other liquid. Due to the strong chemical bond between hydrogen and oxygen, liquid water remains stable over a wide range of temperatures. Further, ice, being less dense, floats on water – it also implies that oceans that harbour life freeze from the top when temperature drops and the top layer of white ice insulates the bottom layers of water protecting living forms below. Ammonia, in contrast, which remains a liquid from −78° to −33° Celsius, would solidify upwards from the ocean floor, freezing all living forms to death. Other liquids may not be as conducive to life as water.

Apart from the presence of liquid water, other conditions necessary for life include a steady source of energy, like sunlight, for metabolism, which a star can supply. Such energy could also come from chemical reactions that make it possible, at least in theory, for life to evolve in sub-surface environments. A renewable supply of organic elements along with a stable interface between solids, liquids and gases as on land or ocean-surface are other prerequisites for life.



Cyanobacteria were the initial source of oxygen in Earth's atmosphere.

How did life evolve on Earth? As J.E. Lovelock said in his book "*Gaia: A New Look at Life on Earth*": Life was "an utterly improbable event with almost infinite opportunities of happening." Life on Earth evolved probably as an accident, a random event that was the result of sundry combinations of chemicals taking place in the primeval oceans over billions of years of change and transformation that ultimately resulted in the formation of a molecule capable of replicating itself. From its cradle in the blue-green waters of the primeval ocean where life probably evolved, it grew most luxuriantly through billions of years of trials and tribulations, taking myriad shapes and forms through endless chains of transformations.

The same process could also have happened in the interstellar clouds of gas and dust where the simple molecules and elements were present and chemical reactions among them could have been triggered by the energy of a nearby star. Indeed, ammonia and water vapour were discovered in interstellar space in 1968 through radio-astronomical observations in microwaves. In 1969, formaldehyde, another organic molecule, was discovered in the interstellar clouds of gas and dust. Obviously, if life processes could start on Earth out of chemical reactions after only 800 million years of its existence, the same processes would have a greater probability of occurring in the interstellar clouds, which are several billion years older. These processes could also have been triggered inside the nucleus of a comet, where heat provided by the decay of radioactive elements could have easily formed the 'warm little ponds' as on Earth.

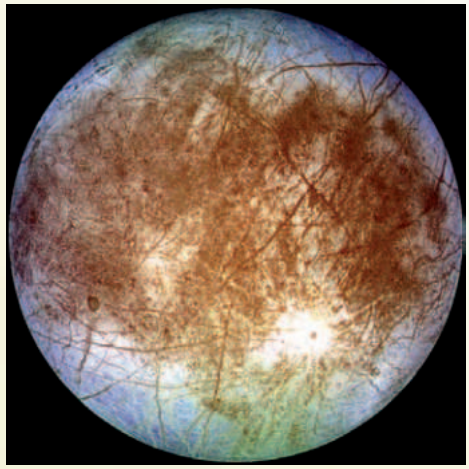
On 28 September 1969, a large meteorite struck at a place called Murchinson in Australia. Among the debris were traces

Murchison meteorite was a large meteorite that struck at a place called Murchinson in Australia. Among the debris were traces of five amino acids, which were not of biogenic origin.

of five amino acids – glycine, alanine, glutamine, valine and proline, which were not of biogenic origin. In fact, they could be direct chemical precursors to organic evolution. Seeds of life could thus have been carried to Earth from the outer space, an extra-terrestrial planet, by meteorites or other objects that bombarded the Earth incessantly during its initial formative eons; they could also have come to Earth through solar or stellar winds. But in whatever form the original living molecules existed in the beginning and wherever they came from, they were still far from becoming the kind of life we are familiar with. That would still take billion years of evolution. Consciousness and intelligence would still take many more million years to evolve.

By all accounts, life was an early feature of Earth – primitive life appeared almost as soon as the Earth's crust had solidified. The strip of land stretching from Greenland to Canada called the North Atlantic Craton has some of the most ancient rocks formed on this planet, dating back to nearly 3.8 billion years ago. Isua supracrustal belt is one such place in the interior of Greenland, where sedimentary rocks have been buried long and become metamorphosed. These rocks have been found to contain mineral graphite – a form of carbon which can come only from two sources: primordial inorganic carbon released during volcanic eruptions or organic carbon from buried remains of organic matter on the ocean floor. Carbon has two stable isotopes, with atomic weights 12 and 13 (^{12}C and ^{13}C). Living organisms tend to contain a little more ^{12}C than ^{13}Cin their tissues, as ^{12}C is more reactive than ^{13}C. The graphite in Isua was found to be richer in ^{12}C by about 2 percent, indicating its organic origin from marine microbes which must have died and got buried in the sediments, subsequently becoming compressed and metamorphosed into graphite as old as these sediments. The origin of life thus dates almost back to the unremembered beginning of this planet, less than 800 million years since this rocky planet had come into existence.

The Sun was about a quarter less luminous then as its fusion reactions were far from consummate. It produced less energy and consequently the Earth also received less. But for the greenhouse gases carbon-di-oxide and methane, which were abundant in the atmosphere of the nascent Earth and partly neutralised the faint young Sun, the Earth would have been a frozen planet, with its surface transformed into permafrost conditions unsuitable for evolution of life. The dark oceans that covered most of the Earth's surface absorbed sunlight, while the few icecaps on mountains reflected little sunlight back into space. A temperature balance was thus maintained which was crucial to the evolution of life.



Scientists have identified nine bodies within the solar system including Jupiter's moon Europa where life might exist in subsurface oceans of water or other organic liquids like methane or ammonia.

By 2.8 billion years ago, most of Earth's crust had already been formed and continents had started to emerge along with the development of large shelf areas around them. Weathering of these areas led to concentration of nutrients in the oceans, resulting in significant increases in the population of microscopic organisms. Till late in the Archean era, around 2.5 billion years ago, the atmosphere was primarily composed of methane, with less than one part per million of molecular oxygen. Oxygenation of its atmosphere – the so-called Great Oxidation Event – would occur in steps; first 2.4 billion years ago, taking the oxygen level to about 2 percent; then 750 million years ago, increasing the level of atmospheric oxygen to 3 percent; and finally about 580 million years ago, raising the oxygen content in the atmosphere to above 10 percent. This oxygenation was caused primarily by the evolution of photosynthetic oxygen-producing bacteria in the surface of oceans, an ancestor to the blue-green 'cyanobacteria' that today swarm in the lakes and oceans of Earth. The surge in oxygen would naturally lead to development of complex 'aerobic' or oxygen-breathing organisms.

Till then, life forms could only exist by breaking the complex substances and using the energy released. These complex substances, food for the primitive micro-organisms, were rebuilt from their simpler constituents by the action of ultraviolet light on oceans. But once oxygen is formed in the atmosphere, oxygen molecules split by sunlight into oxygen atoms combined with other molecules of oxygen to yield ozone. The released ozone formed the ozone layer above the atmosphere, shielding the Earth from ultraviolet rays from the Sun. While the ozone layer protected life from the destructive ultraviolet rays which it still does, it also hastened the pace of evolution of life by cutting off ultraviolet light that was making food for the molecules of life. Replenishment of the chemical food supply no longer being possible in absence of ultraviolet, an acute competition now set off among the living molecules for food. As the primordial chemical soup was nearing exhaustion in the oceans, organisms capable of synthesising their own food had to evolve, and the only energy available was that from sunlight. Organisms that could use this low-energy light to manufacture their own food had to learn to trap this energy. They were some mitochondria-like substances containing chlorophyll – the blue-green algae. These sea-dwelling microbes were probably the first cells, very simple 'prokaryotes', the ancestors to modern 'chloroplasts' – the sub-cellular bodies containing chlorophyll within plant cells where photosynthesis takes place.

As chloroplasts multiplied in the ancient seas, the blue green algae started using carbon dioxide in the atmosphere to produce molecular oxygen through the process of

photosynthesis, gradually transforming the terrestrial atmosphere. Lime secreted by these algae would collect in the shallow oceans that received sunlight, forming the first life-created structures called stromatolites. Bubbles containing oxygen would form on these stromatolites by photosynthesis, then rise slowly to the surface of the sun-blanched oceans and detach themselves from water, freeing their oxygen into the atmosphere. Once the atmosphere was oxygenated and ozone layer was completely formed, it was safe for organisms to dwell on the surface of oceans and eventually to come to land from their watery abode, heralding the evolution of aerobic creatures. From now on, the evolution of life forms would proceed along two distinct directions – one developing into the oxygen-breathers and rapid-movers, evolved from the aerobic living forms, and the other evolving into the immobile plant kingdom, the breathers of carbon dioxide. These two forms would have a complementary and symbiotic relationship with each other. The change in environment brought about by the release of oxygen was thus the most significant event in the history of life. Gradually, from the simple prokaryotes, 'eukaryotes'- organisms with cell-nuclei would evolve. Subsequent advent of sexual reproduction would accelerate the pace of biological evolution manifold, making the process of evolution of life almost uncontrollable and leading to speciation, formation of new species, bringing myriads of forms and irrepressible diversity of life on Earth.

Fossil and other evidences establish that life had been remarkably resilient on Earth, holding onto the most extreme environments. In 2013, a microbe was retrieved from Lake Whillans, almost a kilometre underneath the Antarctic ice. Colony of microbes has thrived even in toxic environments of carbon monoxide and hydrogen sulphide 15 metres underground in a cave in Mexico. Superheated hydrothermal vents on ocean floors have been found to harbour a rich ecosystem of bacteria. Life, in fact, has been found to survive and proliferate in almost every extreme environment, in hot springs and frigid lakes deep below the Earth's surface, in highly acidic, alkaline or radioactive sites – almost everywhere in every inconceivable environment. This only confirms that it can evolve and grow anywhere in the galaxies.

Let us now look beyond our planet. There may be any number of Earth-like rocky planets within the habitable zone in other stellar systems within and outside our galaxy that may nurture life. Scientists have discovered nearly 3,400 planets, called 'exoplanets', beyond our Solar System, but so far, haven't had any evidence of extra-terrestrial life. Exoplanets are detected indirectly from stellar properties, which are affected by the presence of planets – by tracking the wobbling motion of a distant star, by measuring Doppler shift in the stellar spectra or periodical decrease in starlight due to the movement of a planet across its face, or by a technique called micro-lensing, using the bending of light beams by the star's gravity. They can also be detected by direct observations made by telescopes in space, like Hubble Space Telescope (2001), Spitzer Space Telescope (2003), Corot (2006), and Kepler Space Telescope (2009). In January 2015, Kepler had discovered an Earth-like exoplanet in our Galaxy which has since been named as Kepler 452b, also known as 'Earth 2.0'. Three more Earth-like rocky exoplanets were discovered in July 2015 in the constellation Cassiopeia, only 21 light-years away from Earth.

Once an exoplanet is discovered, scientists look for bio-signatures of life in it. The planet's visible or infrared spectrum may reveal the presence of oxygen or methane, two gases produced by life through photosynthetic or other biological processes. They may look for the evidence of liquid water which is essential for life. Ozone will provide another bio-signature as also compounds of organic sulphur or carbon-di-oxide. However, some of these gases and compounds may also be produced by abiotic processes; there also remains the possibility that even when no bio-signature is detected, some form of life may still be ebbing and flowing beneath the surface of some planets – in subsurface oceans of water or organic compounds like methane or ammonia.

Scientists have identified nine bodies within the solar system where life might exist in subsurface oceans of water or other organic liquids like methane or ammonia: Mars, Ceres (the largest asteroid), Europa, Ganymede and Calisto (all moons of Jupiter), Enceladus and Titan (moons of Saturn), Triton (the largest moon of Neptune), and Pluto. Mars once had free flowing water on its surface – some of it may still be flowing underground. Europa has a cracked surface covered with vast ice sheets covering oceans of liquid water underground – due to the internal heat generated by tidal forces of Jupiter's other moons; it may also have hydrothermal vents in its ocean floor like Earth. Enceladus contains underground water, and Titan has huge oceans and lakes of methane and ethane. Right now, Pluto is under close observation by the *New Horizons* spacecraft of NASA that has detected vast frozen, craterless, young plains in the northern icy mountainous region of Pluto, named "Tombaugh Region", after Clyde Tombaugh, who discovered the planet in 1930. But so far there was nothing to suggest that life did or could exist on the dwarf planet.

It is understood that our best chances of detecting extra-terrestrial life would come from an alien civilisation that is intelligent – at least as intelligent as we are – and communicative too. In 1961, Frank Drake, a young radio astronomer, had formulated an equation that has since been known as the Drake Equation for estimating the number of active, communicative extra-terrestrial civilisations in the Milky Way galaxy. The Drake equation runs like this:

$N = R^*. f_p. n_e. f_l. f_i. f_c. L$, where

N = number of civilisations in the Milky Way Galaxy whose electromagnetic emissions are detectable;

R^* = rate of formation of stars suitable for the development of intelligent life;

f_p = fraction of those stars with planetary systems;

n_e = number of planets, per solar system, with an environment suitable for life;

f_l = fraction of suitable planets on which life actually appears;

f_i = fraction of life bearing planets on which intelligent life emerges;

f_c = fraction of civilisations that develop a technology that releases detectable signs of their existence into space; and finally

L = life time of such civilisations.

Except the rate of formation of stars suitable for life, all other factors still remain highly speculative. Even then, in 1961, Drake had estimated about 10,000 such communicative civilisations in our Galaxy. The Drake equation is a simple, fascinating

Continued on page 26

Leukoderma: No Longer Incurable

Rajni Arora
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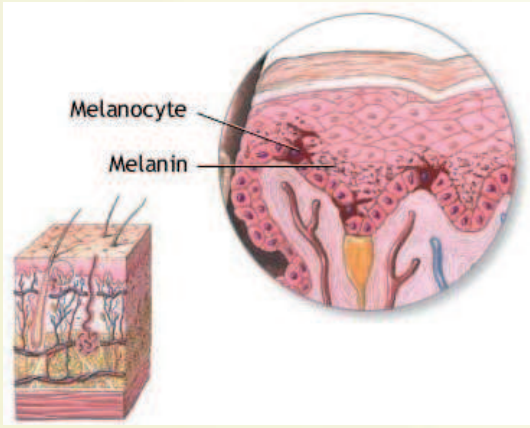
Spots not only make our skin livid or colourless; it also reduce its beauty. White spots on the skin are known as leukoderma or vitiligo. Statistics show that about 2% of the total world population is affected by leukoderma. In India about 4-5% of the population suffer from leukoderma.



Hollywood pop-star Michael Jackson suffered from this skin disorder and to hide it he took the help of surgery to make whole of his skin look white.

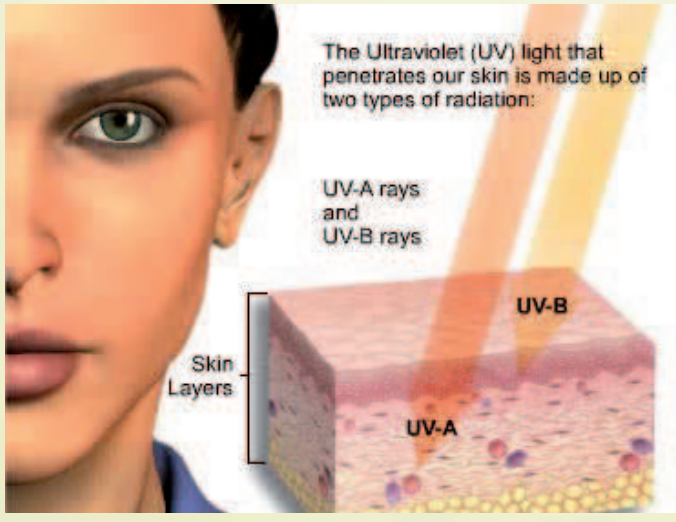
What is leukoderma?

In today's scientific age, it is utterly wrong to relate leukoderma as an infectious disease like leprosy. Actually it is a type of skin disease. Leukoderma ("*leuko*" meaning white and "*derma*" meaning skin) means whitening of skin. Leukoderma is an auto-immune disorder and is closely linked with a pigment present in our skin called "melanin" produced by cells called melanocytes. The colour of our skin depends upon the concentration of melanin. Higher the concentration of melanin, darker is the complexion and lesser the concentration, lighter is the complexion of the skin. Auto-immune disorder arises from an abnormal immune response of the body against substances and tissues normally present in the body and it start to harm our body. This disorder destroys the melanocytes, which leads to the depletion of melanin pigment in the skin. This creates white spots or patch in the epidermis, which is the upper layer of our skin. The size of the spots can be of varying size. Many times, these spots stop on its own without any treatment, but in most cases they tend to spread over time. These spots can also affect a person's eyes, nose, and mouth. Even the colour of mucous membranes in mouth and the retina in eyes can also get damaged, and hair on head, eyelashes and eyebrow can become white. Scientists have given different names to leukoderma happening in different parts of the body, for example, lip-eyes-tip leukoderma (on lips, eyes, and hands); focal leukoderma (small spots on one or two places in the body); segmental leukoderma (on one full body part; for instance, arm or leg), and general leukoderma (on many body parts).

Symptoms of leukoderma

Leukoderma can occur at any age, but mostly it happens to people between 10-30 years of age. Due to their more soft and sensitive skin, women are affected more affected by leukoderma. These spots are much more visible on a dark skin. Though these spots are not harmful to the health but reduce the individual's beauty. Leukoderma can be recognised from the following symptoms:

- When colour of skin and hair at any part of the body become light/white.
- A place gets white spots and becomes itchy.
- The part becoming white after a scratch or injury.
- Change in colour of the mucous membrane in the mouth or the retina in eyes.
- Premature greying of the hairs all over the body.



What causes leukoderma?

It is very difficult to tell the root causes of leukoderma. However, scientists have found some factors that may cause it, which include the following:

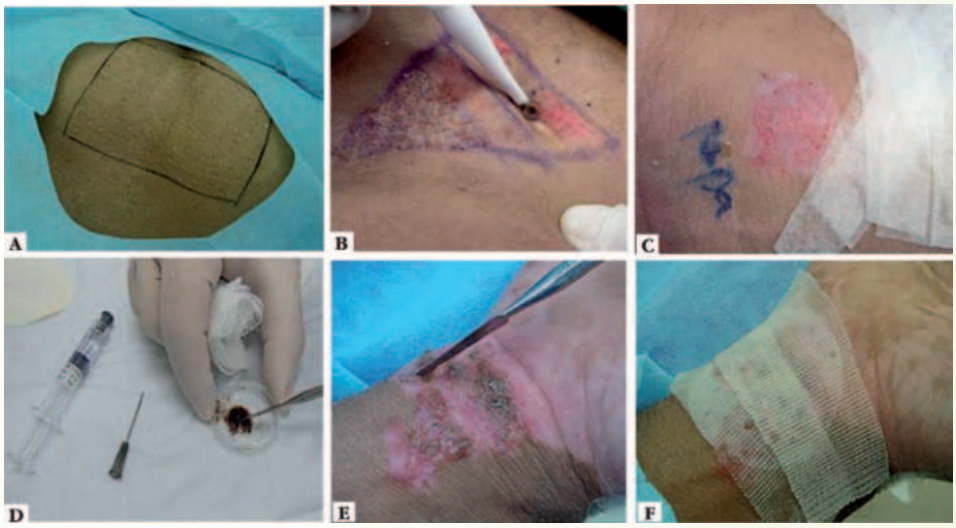
- Lack of melanin pigment tissues in the body.
- Excessive stress or anxiety, acute gastric disorder, severe jaundice, anaemia, liver infection and digestive system malfunction, thyroid disease, which lead to acute immune disorder.
- Using inferior quality cosmetic products, which damage the skin (such as due to the monobenzyl esters of hydroquinone in *bindis* that creates white spots on the forehead)

Treatment is possible

Today leukoderma is not an incurable disease. There are many treatments for leukoderma available in medical science. If treated properly, it is possible to come out of this serious disease within 1-2 years. One just needs awareness, initiative and patience.

Ultraviolet ray treatment

Dermatologists try to determine the immunity efficiency and health of the leukoderma patient by his/her case- history and biopsy check-up. The ultraviolet ray treatment is done on this basis of these reports. According to medical experts, the treatment of leukoderma with ultraviolet rays is the safest and effective way worldwide. Through this, the skin gets back its original

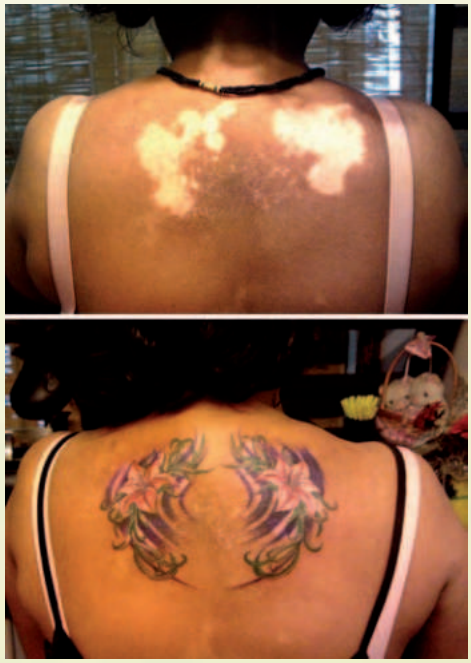


colour and remains in that way. Some of these techniques are:

- **Corticosteroid** – After applying medicated cream containing vitamin D, the skin is fomented by UV-A rays.
- **Psoralen photo-chemotherapy** – This process is done on a person with less than 20% of the skin affected by leukoderma. A thin layer of psoralen lotion or cream is applied on the person's affected areas and the person is made seated. He is then exposed and fomented with UV-A rays. This makes the skin pink and it slowly and steadily comes to its original colour.
- **Narrowband ultraviolet B (UV-B) phototherapy**– In this process, the affected person is exposed to UV-B radiations of a specific wavelength.
- **Surgical treatment of leukoderma** – This method is chosen by dermatologists for those people, whose spots stop growing. In this process, patches of the person's normal skin are grafted over the affected areas when melanocytes in the normal skin start producing the pigment and restore the skin colour.
- **Melanocyte suspension formed from epidermal cells** – In this method, a large area affected by leukoderma is covered, without any dissection. Melanocyte cells are taken from outer layer of skin and made into suspension. This liquid suspension is then injected into the affected area. The skin slowly recovers after that.
- **Platelet-rich plasma** – In this process, platelet-rich plasma from blood is injected into the affected skin. This improves the chances of formation of melanocytes.
- **Depigmentation**–Whenmorethan 60% of the skin of a person is discoloured due to leukoderma, dermatologists suggest this treatment. In this process monobenzylether of hydroquinone is applied to skin two times in a day, until the whole skin becomes of the same colour.

Cosmetology: Hiding white spots by tattoo

Experts believe that although treatment of leukoderma is possible, the patient is often depressed. In such situations, cosmetology can be a better option. According to beauty experts, until these white spots on skin are not treated, they can be hidden by colouring and making tattoos on the skin. However, these tattoos are not permanent, although they may give some relief to the leukoderma patient. Beauty experts first test these colours on any one spot of the patient. If there is no problem of itching or irritation, then the colour can be used safely. These colours reach the epidermis layer of the skin, where they remain for a long time.



Myths and facts_

Sometimes people have many misconceptions about leukoderma. For example, leukoderma is not leprosy or cancer. The white spots neither spread by touching, nor by any physical contact. They are also not a threat to the victim's life. Some people think of leukoderma as psoriasis, when red spots appear on the skin. The skin becomes dry and white particles start falling from it.

Some people are born with less melanocyte tissues in their body so the colour of their skin is white from the birth. This disease is hereditary and incurable and is called albinism, while this is not the case with leukoderma.

Precautions to be taken

Avoid emotional stress and depression because of white spots on the skin. Remember, leukoderma is not a curse but only a disorder of the skin, which can be cured and overcome.

- Do not fall prey to charlatans; instead consult a doctor or a dermatologist. Do not ignore changes in colour of skin. Contact a doctor immediately and give full support in investigation. Leukoderma takes a long time to be cured. So be patient, complete the course and take medicines in proper dosage as well as make routine check-ups.
- Use SPF 30 percent sunscreen lotion. It protects your skin from harmful UVA and UVB rays of the Sun.

Take care of diet

Take a balanced diet rich in calcium and nutrients. Have a higher intake of vegetables. Eat foods rich in beta carotene (carrot), lycopene (tomato), vitamin E (grapes), and mineral-rich foods (meat, whole grains, legumes, pulses, and green-leafy vegetables). Include green tea, olive oil, black pepper, ginger, and garlic in your daily diet.

(Based on conversation with consultants of Sir Ganga Ram Hospital and Dermatologist Dr. Rohit Batra, Dr. Suruchi Puri, and Beauty Expert Bharti Taneja)

Mitochondrial Diseases and Three-Parent Babies

Dr. Jayanti Dutta
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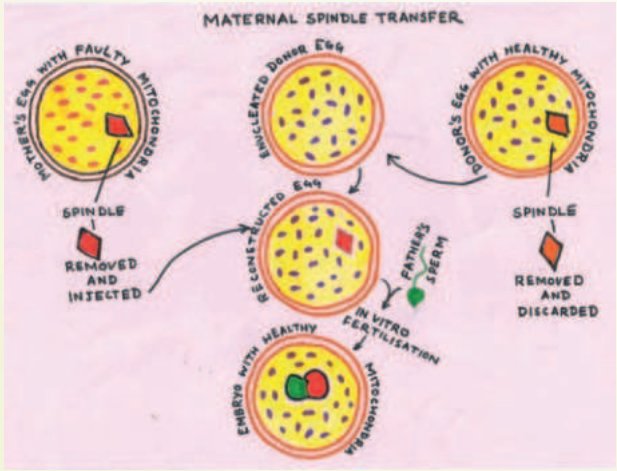
Mitochondria, also known as 'powerhouses of the cell', are organelles (specialised parts) present in the cell which are extremely important and crucial for life. The function of the mitochondria is to convert chemical energy from food into energy molecules called adenosine triphosphate (ATP). This energy is then utilised by the cell for performing different activities of core functioning, growth and maintenance. If mitochondria do not work properly, less and less energy is generated; the cells get damaged and ultimately die leading to organ and system failure.

Mitochondrial functions are conducted through more than 1,500 different types of proteins. These proteins are coded by two types of DNA – the nuclear DNA (nDNA) and the mitochondrial DNA (mtDNA, or mDNA). The mitochondrion is the only organelle in the cell, besides the nucleus, which contains a small DNA fragment consisting of 16,000 base pairs comprising 37 genes. These genes code for 13 proteins, which play different roles in the functioning of the mitochondria.

While the nuclear DNA is passed on to the child from both father and mother, the mitochondrial DNA can be inherited only from the mother. This is because the sperm contains mitochondria at the base of its tail and when the sperm enters the egg, its tail along with the mitochondria is shed outside and the father's mitochondria never pass on to the child. On the other hand the egg from the mother retains its mitochondria, which after fertilisation, become the part of the growing embryo. Therefore, each child inherits the mitochondrial DNA exclusively from its mother.

Unfortunately, the mitochondrial DNA has a rapid mutation rate, and when it mutates the functioning of the mitochondria is disturbed; it may become partly or fully disabled causing the cell to lose its ability to generate energy, which may be manifested as any of the mitochondrial diseases numbering more than 150. In addition to energy generation, mitochondria are also involved with other functions related to major metabolic pathways of the cell such as detoxification of ammonia, metabolism of cholesterol, functioning of neurotransmitters, and breaking down of fats, proteins and carbohydrates. Mitochondrial diseases impact these functions too. Since the mitochondria are inherited through maternal inheritance, if the mother's mitochondrial DNA carries even a small proportion of mutation, it can blow up to a large number in the growing embryo as the faulty mitochondria divide and get into each daughter cell of the embryo leading to the birth of a baby with mitochondrial disease. Incidence of mitochondrial disease ranges from about 1 in 2,000 to 1 in 5,000 live births in Western countries. Figures for exact incidence in India are not known



Although there are only 13 mitochondrial genes, these are carriers of many significant diseases such as Leigh Syndrome, mitochondrial myopathy, maternally inherited diabetes and deafness (MIDD), Leber's hereditary optic neuropathy (LHON) or Leber optic atrophy, neuropathy, ataxia and retinitis pigmentosa (NARP) syndrome, and many others. The symptoms of mitochondrial diseases range from developmental delays in children, seizures, muscle weakness, poor balance, and low endurance to chronic fatigue, vision and hearing problems, learning disabilities, droopy eye lids, etc. Organs affected are muscles, kidney, heart, brain and eyes. Persons with mitochondrial disease are affected differently and there is a range of variation in the symptoms also. Symptoms can range from extremely mild to severe and can fluctuate over the course of the disease between no symptoms to several symptoms. This happens because of various reasons.

For these reasons mitochondrial diseases are difficult to understand, study and research and hence difficult to treat and the whole range of mitochondrial diseases are not yet discovered and even their total number is not known. Although, one thing is true for all mitochondrial diseases – these are severely debilitating, often fatal and complex in nature and that there is no cure for these diseases

It is quite clear that diseases contracted through maternal inheritance can be prevented if we can altogether prevent the passing on of the faulty mitochondrial DNA from the mother to the offspring; for example, if we can somehow bypass the process of transfer of the mother's cell organelles into the foetus. Scientists have figured out a method to execute this process. In this process, the nucleus of the egg of a woman with healthy mitochondria is taken out and replaced by the nucleus from the egg of the mother with faulty mitochondria. The composite egg cell has the nucleus of the mother but mitochondria of another woman so that the child inherits its mother's nucleus and hence most of the genetic traits of its natural mother, but not the faulty mitochondrial DNA. Babies born out of such arrangement are called three-parent babies because they have three parents – the father, the mother and another female who contributes the enucleated egg.

The process of three-parent babies has come to the rescue of women who have mitochondrial diseases themselves and also those who have affected family members and therefore are at great risk of having a child who could be similarly affected. Here, the

faulty mitochondria of the mother can be prevented from entering the unborn baby's cell while the contribution of the nuclear DNA of the mother would ensure that she can pass on her other traits to the child and be a parent in the true sense. In such cases, only 0.1% of the child's DNA will be inherited from the third parent.

This technique can be implemented in two ways known as pronuclear transfer (PNT) and maternal spindle transfer (MST)

In pronuclear transfer, egg of the mother is fertilised with the sperm of the father using *in-vitro* fertilisation to form two pronuclei (pronucleus is the nucleus of the ovum or sperm after fertilisation). The donor egg (with healthy mitochondria) is also fertilised with the sperm of the father using *in-vitro* fertilisation to form two pronuclei, which are then discarded, leaving the enucleated embryo ready to receive the pronuclei from the mother's fertilised egg.

The two pronuclei are removed from the mother's fertilised egg (with faulty mitochondria) and injected into the enucleated donor fertilised egg. After removal of the nucleus, the fertilised mother's egg is discarded. When implanted in the mother's womb, the reconstructed embryo develops into a baby with maternal and paternal nuclear DNA and healthy mitochondrial DNA from the donor.

Maternal spindle transfer is a technique similar to pronuclear transfer in its effort to prevent the transmission of mitochondrial disease. However, the main difference between these two techniques is that maternal spindle transfer uses unfertilised eggs instead of the fertilised eggs used in pronuclear transfer. The technique is still at the research stage in laboratories of UK and USA. While there could be ethical questions related to the issue where the traditional notion of parenthood is being challenged, it is also an opportunity where science can come to the rescue and mitigate the impact of devastating diseases. The new techniques could give a boost to the struggle to fight mitochondrial diseases in addition to other strategies of developing better diagnostic tools, finding better treatments, and discovering more gene mutations and searching for their cure.

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Are We Alone? *(Continued from page 30)*

equation that suggests that life being the end product of a natural, cosmic evolution, may not be unique and that we may not occupy any special position in this Universe in that sense, even though so far ours is the only kind of life known.

The Search for Extra-terrestrial Intelligence (SETI) is the name for collective scientific investigations undertaken to search for intelligent extra-terrestrial life. The search began in 1957 with the Lovell Radio Telescope in Manchester, UK, to detect radio signals from intelligent alien civilisations. The SETI Institute was established in 1984

The Search for Extra-terrestrial Intelligence (SETI) began in 1957 with the Lovell Radio Telescope in Manchester, UK, to detect radio signals from intelligent alien civilisations.

to "explore, understand and explain the origin, nature and prevalence of life in the Universe" and which today comprises the largest distributed array of radio telescopes across the world. With increasingly high-powered of radio-telescopes now being deployed, searches have become much broader and deeper, but we have not yet succeeded in detecting any intelligent life elsewhere. And that is an enigma.

After all, our Earth is only a 4.6-billion-year-old planet orbiting a star that is too young in the Universe; there are stars in our Galaxy that are twice as old. If life was a random event, it must have arisen on other planets in the Galaxy long before it did on Earth. By now, those civilisations would have mastered the technology of space travel or even time travel, and possibly even to travel at superluminal speeds. They should have colonised the Galaxy by now. Such colonisation would have been a necessity for their survival, because energy is the driver of all civilisations and they would have exhausted their planetary or even stellar supply of energy long back and thus would be forced to seek it elsewhere. Then why haven't we found any of them so far? Why haven't they discovered us? Why haven't they intercepted and responded to the several radio messages we have sent into space? This is the fundamental question Enrico Fermi asked in 1950, known as the Fermi Paradox.

Maybe, we are truly alone in this vast Universe, making us a rarity and our Earth a 'Rare Earth' that shelters the only life in this Universe, in which case at least one factor in Drake's equation will have to be vanishingly small. Or maybe, the advanced civilisations do not need to colonise the Galaxy, having solved the energy problem by the use of advanced technology. But these answers look rather improbable, given that vastness of the Universe and the deepness of time through which it has evolved. Another possibility is that they have already destroyed themselves through an Armageddon-type nuclear war; in fact, we on Earth had come very close to this in the last century.

There is of course another possibility – maybe they have indeed found us and are just watching us from space, refusing to communicate. A civilisation that has the technological prowess to explore the galaxies must be a very mature civilisation, and must have already conquered hunger, poverty, sickness, maybe even physical death. Conflicts and wars between their people must have been a thing of antiquity, as must have been hatred and jealousy, bigotry and social cleavage, while we are as yet far from conquering these evils. Our ways on this Earth, where we constantly fight, bleed, kill and inflict unspeakable atrocities upon our fellow beings must seem extremely repulsive to an advanced, intelligent and sophisticated intergalactic civilisation. We cannot blame them for hiding from us; rather we should be ashamed of ourselves.

Govind Bhattacharjee is a civil servant and a popular science writer. His book, "Story of Evolution", has been published by Vigyan Prasar.

Neglected Parasitic Diseases

Yogesh Kumar
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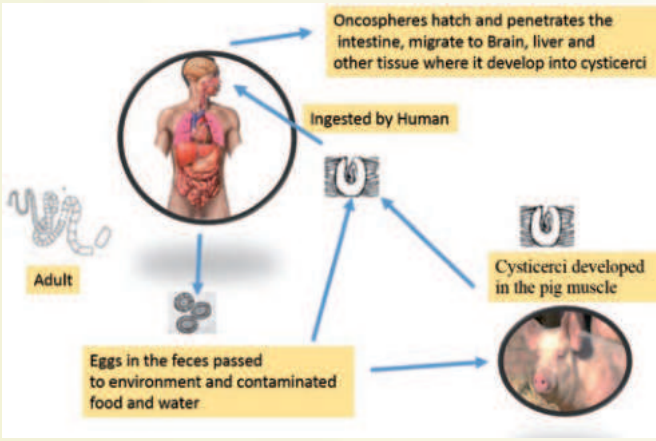
A parasitic disease is an infectious disease caused or transmitted by a parasite. But not all parasites cause diseases; some can even be beneficial. It is known that some kinds of worm infection can reduce incidences of autoimmune and other allergic/inflammatory-type conditions. Many diseases caused by parasites, especially those that inflicts health burden on the world's poorest people, rarely attract attention of health authorities or pharmaceutical companies because they kill people very slowly, over a period of time, unlike an epidemic. These diseases are infectious and prevalent in tropical climates, especially in areas where hygiene and sanitation is not maintained properly or where health care is not accessible. According to World Health Organisation (WHO), one-sixth of the world's population suffers from neglected parasitic diseases. These diseases are prevalent in low-income countries and many developing countries. Some of the common neglected parasitic diseases include Chagas disease, Cysticercosis, Toxocariasis, and Schistosomiasis, which are described here.



Chagas disease

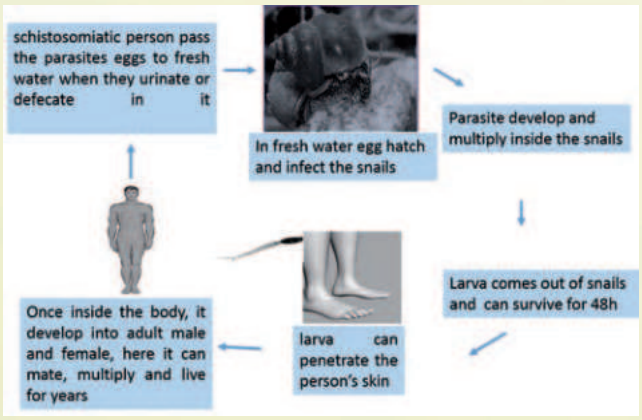
Chagas disease is caused by the parasite *Trypanosoma cruzi* named after Brazilian physician Carlos Chagas, who is credited with discovering the disease. It is also referred to as American trypanosomiasis. *T. cruzi* is transmitted to animals and people by blood-sucking insects commonly known as 'kissing bugs' of subfamily Triatominae and is prevalent in mostly poverty-stricken regions. The bug is found in the cracks or holes in wooden walls and roofs and beneath tree bark. The Triatomine bug is nocturnal and feeds on the blood of mammals, birds and reptiles. The parasite *T. cruzi* is spread by faeces of the bug. The bug generally defecates near the site where it bites while it is feeding on blood, generally when the person is sleeping. Scratching the site of the bite causes the faeces to rub into the wound, allowing the parasite to enter the host's body through the wound, or through intact mucous membranes, such as the conjunctiva of the eye.

Chagas disease is an acute and chronic and the infection that remains lifelong if untreated. In the acute phase of the disease following the infection, parasites may be found in the circulating blood. Infection may be mild or asymptomatic. There may be fever or swelling at the site where parasite enters the skin. If undiagnosed, most of the infected people go into the chronic phase of the disease. The condition creates life threatening problem for 20-30 % of the infected people; otherwise it remains asymptomatic and never developing Chagas-related symptoms. Complications associated with the chronic Chagas disease include heart rhythm abnormalities, dilation of the digestive tract including the oesophagus or colon, leading to difficulties with eating or passing stool.

The diagnosis of Chagas disease can be made by observation of the parasite in a blood smear by microscopic examination. The disease can be controlled by effective spraying of insecticide to eliminate the carrier triatomine bugs that help spread of *T. cruzi* parasite. Treatments of the patients depend on the anomalies development due to the disease.

Cysticercosis

Cysticercosis is a parasitic infection caused by larval cysts of the pork tapeworm *Taenia solium*. These larval cysts infect brain, muscle, or other tissue, and are a major cause of adult onset seizures in most low-income countries. The infection is found mostly in rural areas where pigs are allowed to roam freely and have access to human faeces. Cysticercosis is usually acquired by eating food or drinking water that has tapeworm eggs in it. Among foods, uncooked vegetables are the major source. Pigs become infected by eating tapeworm eggs in the faces of human infected with a tapeworm. The highest rate of cysticercosis is found in Latin America, Asia, and Africa. Sign and symptoms depend on the location and number of cysts in the body. Symptoms can appear a month to a year after infection and starts with death of cysts. When cysts die, the brain or other tissue surrounding get swollen and that develops symptoms of the infection.



Cysts in muscles: In this condition people do not develop symptoms but sometimes they may feel a lump under the skin. The lump sometimes becomes tender.

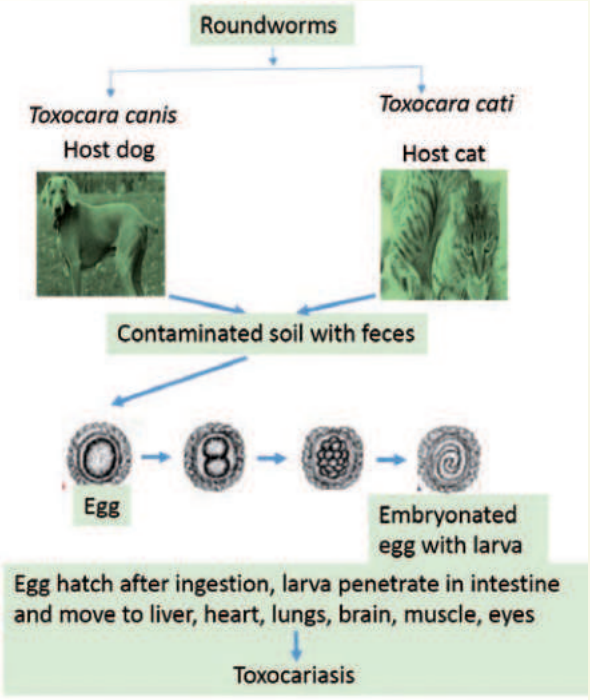
Cysts in the eyes: Cysts in the eye can blur or cause disturbed vision. It may also cause swelling or detachment of the retina.

Neurocysticercosis: In this

condition, cysts are found in the brain. Seizure and headache are the most common symptoms. Other manifestations include lack of attention to people and the surrounding, and difficulty with balance. Excess fluid around the brain (hydrocephalus) may also occur and the disease can even lead to death.

Patients are generally treated with anti-parasitic drugs, but in case of drugs not responding sometimes surgery is required to treat cysts or to reduce brain swelling. Diagnosis may require testing of blood or imaging studies. Blood tests are not always accurate and MRI or CT scan usually are required for diagnosis of neurocysticercosis.

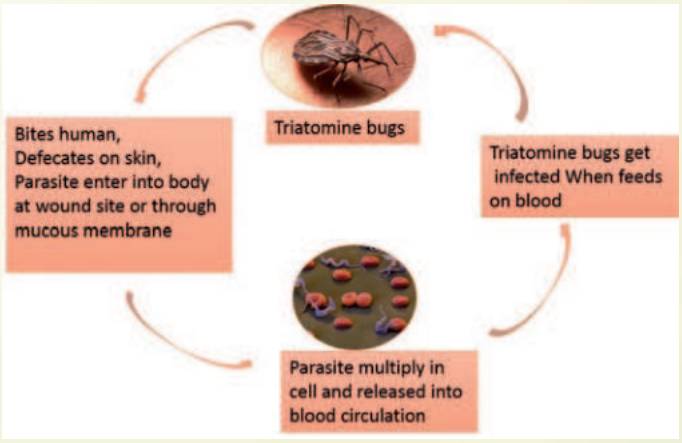
Cysticercosis can be prevented by simple hygiene such as washing hands with soap and water after using the toilet, washing and peeling all raw vegetables and fruits before use, especially in those areas where the disease is prevalent, and eating hygienic food and clean uncontaminated water.



Toxocariasis

Toxocariasis is an infection transmitted from animals to humans. It is caused by the larvae of parasitic roundworms commonly found in the intestine of dogs and cats. Dogs and cats infected with Toxocara can shed eggs of the parasite in their faeces and can infect children who accidently swallow dirt contaminated with toxocara eggs. Many people do not have any symptoms or sickness after infection, but in some cases symptoms appear.

Ocular toxocariasis occur when toxocara larvae migrate to the eye. Symptoms include vision loss, eye inflammation or damage to the retina; typically, one eye is affected. Visceral toxocariasis occur when toxocara larvae migrate to various body organs such as liver or central nervous system. Symptoms include fever, fatigue, and coughing, wheezing or abdominal pain. After ingestion, the eggs hatch and larvae penetrate the intestinal wall and from there it carried to different organs/tissues. The larvae do not undergo any further development and cause severe local reaction that forms the basis of toxocariasis symptoms. There are mainly two clinical symptoms of toxocariasis, called 'visceral larvae migran' and 'ocular larvae migran'. Visceral toxocariasis can be treated with anti-parasitic drugs such as Albendazole or Aebendazole. Treatment of ocular toxocariasis is more difficult and usually consists of measures to prevent progressive damage to the eye.



Schistosomiasis

Schistosomiasis – also known as bilharzia, snail fever and Katayama fever – is a chronic disease caused by parasitic worms that dwells in certain freshwater snails. Farmers, fishermen and laundry people who wash clothes in contaminated water are mainly at risk of infection. It is considered second most dangerous parasitic disease after malaria. The parasites are released into water by the host snails and the disease is spread by contact with water contaminated with the parasites. Schistosomiasis causes liver damage, renal and bladder dysfunction, and intestinal problems. It may cause poor growth, anaemia and learning difficulty in children. Schistosomiasis affects people worldwide and according to one estimate, 12,000 to 2, 00,000 people die every year from the disease. The disease is mostly found in Africa, Asia and South America.

Species of Schistosoma that can infect humans are *Schistosoma mansoni* and *Schistosoma intercalatum*, which cause intestinal schistosomiasis, and *Schistosoma haematobium*, which causes urinary schistosomiasis. The infected person may develop rash on the skin after a few days of infection. After one or two months of infection, flu-like symptoms may develop. Chronic infection develops due to the body reaction to the parasites eggs which become lodged in the intestine or bladder, causing inflammation. Urinary schistosomiasis causes bladder and kidney damage leading to painful urination and sometimes blood in the urine. It also can increase the risk of bladder cancer. In women, urogenital schistosomiasis may cause genital lesions, vaginal bleeding, pain during sexual intercourse, and nodules in the vulva. In men, urogenital schistosomiasis can induce pathology of the seminal vesicles, prostate, and other organs. The major intervention used to control the disease is treatment with praziquantel, accompanied by the provision of safe water, adequate sanitation, and where possible, snail control. The gold standard for schistosomiasis diagnostic is the examination of stool and urine specimens by microscopy to detect the presence of parasite eggs. Urinary schistosomiasis also can be detected based on the presence of blood in the urine. Children with *S. haematobium* almost always have microscopic blood in their urine that can be detected by chemical reagent strips.

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Pica: the Eating Disorder
All You Want to Know About

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Pica (pronounced as 'paika') is an eating disorder. More frequently found in young children, and in some pregnant mothers, it is a malady wherein the victim gets into the habit of eating a variety of non-food items. Such substances may include soil, sand, clay, chalk, stones, pebbles, hair, lead, plastic, pencil erasers, ice, fingernails, paper, paint chips, coal, wood, plaster, light bulbs, needles, string, cigarette butts, wire, laundry starch, vinyl gloves, faeces, and burnt matches.

The condition is unremitting. In fact, doctors tend to take notice only if somebody continues with eating non-nutritive, non-food substances for a continuous period of at least 1 month.

Who may develop pica?

Pica is observed more commonly during the second and third years of life. Under the age of two years, however, if a child has pica, it is often nothing to worry about. That's simply because in children aged 18 months to two years, the ingestion and mouthing of non-nutritive substances is common and is not considered abnormal.

As a child grows, the chances of his developing pica decrease. It may occasionally extend into adolescence but is rarely observed in adults. Among individuals with intellectual disability, pica occurs most often in those aged 10-20 years.

Infants and children commonly ingest paint, plaster, string, hair, and cloth. Older children tend to ingest animal droppings, sand, insects, leaves, pebbles, and cigarette butts. Adolescents and adults most often ingest clay or soil. In young pregnant women, the onset of pica frequently occurs during their first pregnancy in late adolescence or early adulthood. Although the pica usually diminishes at the end of the pregnancy, it may continue intermittently for years.-

Pica typically occurs with equal frequency in boys and girls; however, it is rare in adolescent and adult males. Some people with developmental disabilities also may develop pica. The strongest association is with autism spectrum disorder, intellectual disability, and, to a lesser degree, schizophrenia and obsessive-compulsive disorder (OCD). When pica coexists with trichotillomania (impulsive hair pulling disorder) or excoriation (scratching of skin), the hair or skin is typically ingested. Pica may also coexist with avoidant or restrictive food intake disorder.

What causes pica?

Nobody quite knows why some people develop pica. However, a number of hypotheses have been put forward to explain the malady. These range from psychosocial causes to causes of purely biochemical origin. Possible causes include the following:

Nutritional deficiencies

Deficiencies of iron, calcium, zinc, and other nutrients, for example, thiamine, niacin, and vitamins C and D have been associated with pica. In some patients with malnutrition who eat clay, iron deficiencies have been diagnosed, but the direction of this causal association is unclear. Whether the iron deficiency prompts the eating of clay or whether the inhibition of iron absorption caused by the ingestion of clay produced the iron deficiency is anybody's guess.

Current methodologies for the physical, mineralogical, and chemical characterisation of pica substances, particularly clay and soil, may be useful for determining the bioavailability of nutrients and other bioactive components and for generating data to support or negate these nutritional hypotheses.

Cultural and familial factors

Ingestion of clay, soil, or starch may be culturally acceptable in certain social groups. Clay eating and starch eating are seen in some areas and is prevalent in some communities, primarily among women and children. Starch eating, in particular, is frequently started in pregnancy as a treatment for morning sickness and may be continued into the postpartum period. Parents may proactively teach their children to eat these and other substances. Pica behaviour may also be learned via modelling and reinforcement.

Stress and low socio-economic status

Maternal deprivation, parental separation, parental neglect, child abuse, and insufficient amounts of parent-child interaction have been associated with pica. Ingestion of paint is most common in children from families of low socioeconomic status and is associated with lack of parental supervision. Malnutrition and hunger may also result in pica.

Non-discriminating oral behaviour

It has been suggested that in individuals with intellectual disability, pica may result from an inability to discriminate between food and non-food items; however, the findings that individuals select pica items and that they often search aggressively search for non-food items of choice do not support this theory.

Learned behaviour

In individuals with intellectual and developmental disabilities in particular, the traditional view is that the occurrence of pica is a learned behaviour maintained by the consequences of that behaviour.

Underlying biochemical disorder

The association of pica, iron deficiency, and a number of pathophysiologic states with decreased activity of the dopamine system suggests the possibility of a correlation between diminished transmission of nerve impulses related to the chemical dopamine and the expression and maintenance of pica.

To date, however, no specific pathogenesis resulting from any underlying biochemical disorders has been identified empirically.

Risk factors

A number of factors may increase the risk for pica. These include the following:

- Parent-child stress
- Family disorganisation
- Environmental deprivation
- Pregnancy
- Epilepsy
- Brain damage
- Intellectual disability
- Developmental disorders

Signs and symptoms

Pica is a serious behavioural problem because it can result in significant medical sequel, which is determined by the nature and amount of the ingested substance.

The clinical presentation of pica is highly variable. It is associated with the specific ingested substances and the nature of the resulting medical conditions. In poisoning or exposure to infectious agents, the reported symptoms are extremely variable and are related to the type of toxin or infectious agent ingested.

The physical signs and symptoms may include the following:

Nutritional effects

A child with pica may develop iron and zinc deficiency syndromes.

Lead toxicity and other poisonings

Pica has been shown to be a predisposing factor in accidental ingestion of poisons. Many paints, toys and other artefacts have a high lead content. This can lead to lead poisoning and produce neurologic, hematologic, endocrine, cardiovascular, and kidney related complications.

The ingestion of bizarre or unusual substances can result in other potentially life threatening toxicities, such as high potassium (hyperkalaemia) after ingestion of burnt match heads.

Worm infestations and infections

Soil or clay ingestion can result in soil-borne parasitic infections, for example, roundworm infestation (ascariasis) and infestation by roundworm larvae (toxocariasis).

Gastro-intestinal complications

Eating objects that cannot be digested, such as stones, can cause constipation or obstructions in the digestive tract, including the intestines and bowels. Hard or sharp objects such as paperclips or metal scraps can cause tears in the lining of the food pipe or intestines, ulcerations, perforations, and haemorrhage.

Dental ill health

A child with pica may suffer severe tooth abrasion, partial loss of tooth, and surface tooth loss

Diagnosis

No specific laboratory tests are needed for the evaluation of pica. However, certain laboratory studies may be indicated to assess the consequences of the condition.

Some children may require screening of blood lead concentrations, stool examination, blood tests to see for the fall outs. Some may rarely need abdominal radiograph, ultrasound or endoscopy.

How is pica treated?

Given the grave risk of such complications as lead poisoning, a close monitoring is necessary. Some complex cases may require a multidisciplinary approach. The treatment team may include psychologists, counsellors, and physicians for effective remedy.

Pills

No medical treatment is specific for pica. Some evidence suggests that pills that enhance dopamine-related functioning, for example, olanzapine may provide treatment alternatives in individuals with pica that is refractory to behavioural intervention.

If a nutritional deficiency like iron or zinc deficit is identified, it must be corrected with vitamin or mineral supplementation.

Behaviour therapy

Currently, behavioural treatments are considered the most effective strategy in the treatment of pica. Such strategies include antecedent manipulation, training in discrimination between edible and non-edible items, self-protection devices that prohibit placement of objects in the mouth, sensory reinforcement, and differential reinforcement of other or incompatible behaviours.

Consultation with a dentist

A child with pica who has suffered severe tooth abrasion, a partial loss of tooth, or surface tooth loss requires the help of a dental surgeon.

What is the outlook for people with pica?

Pica often remits by itself in most young children and pregnant women. However, it may persist for years if untreated, especially in people with intellectual and developmental disabilities.

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Recent Developments in Science and Technology

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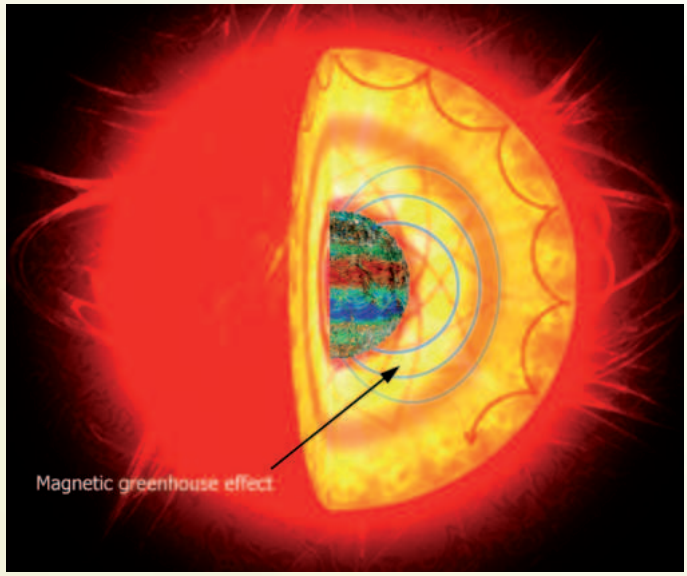
Strong internal magnetic fields of stars discovered

Scientists use ingenious techniques to probe deep inside objects including stars that lay trillions of kilometres away. An international team of researchers used a technique called 'astroseismology' to calculate the magnetic field strengths inside dozens of red giant stars – stars that are evolved versions of our Sun. This is the first time astronomers have been able to measure the internal magnetic field of stars directly. Until now, they were able to study the magnetic fields of stars only on their surfaces and had to use supercomputer models to simulate the fields near the cores, where the nuclear-fusion process takes place.

Asteroseismology is the science that studies the internal structure of stars by the interpretation of their pulsations. It is well known that certain stars, including our Sun, pulsate and the waves that propagate through the star can bring to surface precious information about the internal regions they crossed. This is similar to what seismologists do with our planet Earth. By studying the characteristics of seismic waves created by earthquakes they can learn a lot about the structure and properties of the Earth's inner regions. This is also analogous to medical ultrasonography, which uses ultrasound waves to image otherwise invisible parts of the human body.

Structurally, red giants are quite different from so-called main-sequence stars such as our Sun, which makes them ideal for asteroseismology. The cores of red-giant stars, which are the later stages of stars like our Sun, are much denser than those of younger stars. As a consequence, sound waves do not reflect off their cores, as they do in stars like our Sun. Instead, the sound waves are transformed into gravity waves. This conversion from sound waves to gravity waves has major consequences for the tiny shape changes, or pulsations, that red giants undergo.

The outer regions of red giants, which are more evolved than our Sun and with larger radii, are characterised by turbulent motions that excite sound waves. According to the researchers, sound waves generated by pulsation of a red giant star propagate in the outer layers of the star, while gravity waves propagate in the inner layers where a magnetic field is present. If the magnetic field is strong enough, the gravity waves become trapped in the star's core, which the researchers have termed as the 'magnetic greenhouse effect'. When the gravity waves become trapped, some of the wave energy is lost in the core, which makes the amplitude of the observable surface pulsation smaller compared to a star with weak magnetic field, where no trapping occurs (*Science*, 23 October 2015 | DOI: 10.1126/science.aac6933).



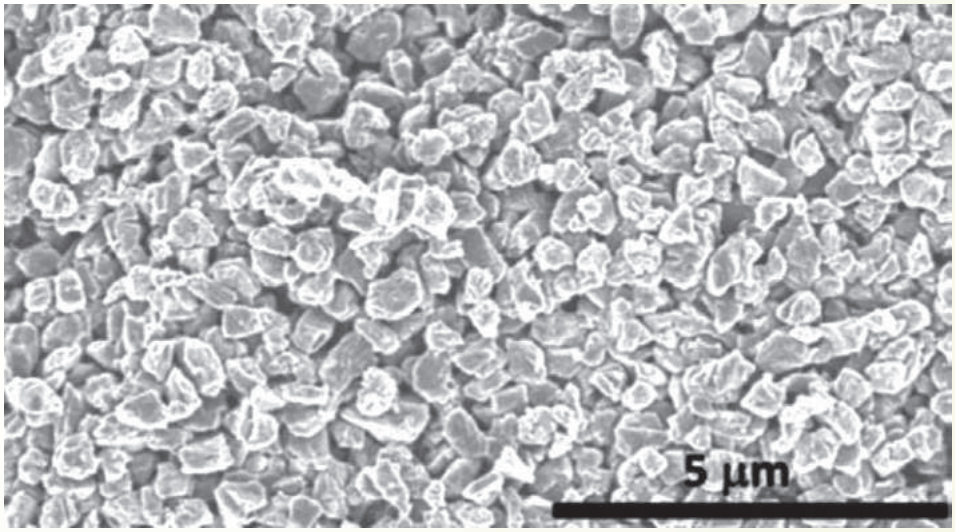
Artist's representation of a red giant star with a strong internal magnetic field shows sound waves (red) propagating in the stellar outer layers, while gravity waves (blue) propagate in the inner layers where a magnetic field is present. (Credit: www.news.ucsb.edu)

Stars pulsate in different patterns depending on their size and internal structure. In one form of pulsation pattern, known as the dipole mode, one hemisphere of the star becomes brighter while the other becomes dimmer. Astronomers observe these tiny pulsations in a star by measuring how its light varies over time. In 2013, NASA's *Kepler* space telescope, which can measure stellar brightness variations with incredibly high precision, detected such variations in several red giants. Analysis of the data showed that the magnetic greenhouse effect was the most likely explanation for the slowing down of pulsation in the red giants. Calculations further revealed that the internal magnetic fields of the red giants were as much as 10 million times stronger than Earth's magnetic field.

According to the researchers, the findings will help astronomers better understand the life and death of stars because magnetic fields likely determine the interior rotation rates of stars and such rates have dramatic effects on how the stars evolve. A better understanding of the interior magnetic fields of stars could also help settle a debate about the origin of powerful magnetic fields on the surfaces of certain neutron stars and white dwarfs, two classes of stellar remnants that form when stars die.

Diamond created at room temperature from Q-carbon

Carbon is a unique element that is capable of forming many allotropes or structurally different forms. Well-known forms of carbon include diamond and graphite. In graphite, which is soft and flaky, the carbon atoms line up to form thin sheets. In diamond, which is the hardest substance known, the carbon atoms form a rigid crystal lattice. In recent decades many more forms of carbon have been discovered that include ball-shaped fullerenes and sheets such as graphene. The latest is a brand new phase of solid carbon, which is termed as 'Q-carbon', discovered by researchers at the North Carolina State University in USA. What is



An image of microdiamonds created using the same technique that researchers used to create Q-carbon using laser pulse. (Credit: NC State University)

more exciting is that the researchers have also developed a technique of utilising this new (and extremely rare) phase of carbon to create cheap tiny diamonds for industrial use at room temperature and at normal atmospheric pressure. Previously, lab-grown diamonds required incredibly high temperatures and pressures to be created (*Journal of Applied Physics*, 30 November 2015 | DOI: 10.1063/1.4936595).

Q-carbon is a rare material and is not found in nature. According to Jagdish Narayan, the John C. Fan Distinguished Chair Professor of Materials Science and Engineering at NC State University, who led the research team, "The only place it may be found in the natural world would be possibly in the core of some planets". The team uses an ingenious technique to convert amorphous carbon to the new form. They start with a substrate, such as sapphire, glass, or plastic and coat it with amorphous carbon – elemental carbon that does not have a regular, well-defined crystalline structure like graphite or diamond. The carbon layer is then blasted with a single laser pulse lasting approximately 200 nanoseconds. The laser pulse causes the temperature of the carbon to rise momentarily to 4,000 kelvins (about 3,730° Celsius), which fuses the amorphous carbon. The end result is a film of Q-carbon. The researchers can control the process to make films between 20 nanometres and 500 nanometres thick. This operation takes place at one atmosphere – the same pressure as the surrounding air. By using different substrates and changing the duration of the laser pulse, it is possible to control how quickly the carbon layer cools and creates diamond structures within the Q-carbon layer. And, if researchers want to convert more of the Q-carbon to diamond, they can simply repeat the laser-pulse/cooling process.

Q-carbon has some unusual characteristics. It is ferromagnetic; that is, it can be magnetised in a magnetic field and retains its magnetism when the field is removed. Other solid forms of carbon do not have this property. Also, Q-carbon is harder than diamond and glows when exposed to even low levels of energy. According to Narayan, its unique properties make it a very promising material for developing new electronic display technologies. Eventually this material could lead to new super-thin yet durable displays or screens.

"Using the process, it is possible to create diamond nano-needles or microneedles, nano-dots, or large-area diamond films, with applications for drug delivery, industrial processes and for creating high-temperature switches and power electronics. The diamond objects produced from Q-carbon have a single-crystalline structure, making them stronger than polycrystalline materials. And it is all done at room temperature and at ambient atmosphere – using a laser like the ones used for laser eye surgery. So, the process itself is relatively inexpensive," says Narayan.

'Electronic' plants

Scientists in a Swedish lab have woven electronics into the circulatory system of living plants for the first time in a breakthrough which they say could allow them to convert photosynthesis into power. The researchers achieved the four key components of an electronic circuit using the xylem, leaves, veins, and signals of the plant as the template and integral part of the circuit elements and functions. The team led by Magnus Berggren of Linköping University in Sweden 'wired up' a garden rose by setting cut flowers in a basin of water containing a soluble polymer called poly(3,4-ethylenedioxythiophene) or PEDOT, which conducts electricity. As the rose sucked up the water it also took in the polymer, in the same way that allows flowers to be coloured by dipping the stems in dyed water. Once inside the plant, the polymer formed a conductive film that behaved like a wire inside the plant's xylem, allowing electric signals to be transmitted, but still letting the plant get the nutrients and water it needs. By connecting external wires to the conductive electrolyte film in the xylem, the researchers were able to create a working transistor and a digital logic gate – the basic building block of a computer system (*Science Advances*, 20 November 2015 | DOI: 10.1126/sciadv.1501136)

In another experiment, the researchers used a method common in plant biology called 'vacuum infiltration' to infuse a variant of PEDOT into the leaves of the rose plant. In this method, leaves, or whole plants are submerged in a beaker containing the solution, and the beaker is placed in a vacuum chamber. When the vacuum is applied, air is forced out of the stomata of

Semi-conductive polymers have allowed scientists to form electronic circuits inside a rose plant (Credit: Laboratory of Organic Electronics, Linköping University)

the leaves, which then takes up and gets impregnated with the polymer. The team was then able to create a coloured display on the leaves, making the polymer inside the leaves light up and change colour in a display-like device.

It is well known that the roots, stems, leaves, and vascular circuitry of higher plants are responsible for conveying the chemical signals that regulate growth and functions. From a certain perspective, these features are analogous to the contacts, interconnections, devices, and wires of discrete and integrated electronic circuits. According to the researchers, by growing circuits inside plants, it could be possible to get an unprecedented look into how plants function, and monitor their health on an amazingly close level. By controlling the chemical pathways in plants it may become possible to produce photosynthesis-based fuel cells and devices that modulate the internal functions of plants so that they could produce important molecules more quickly, such as those needed for medicines. Besides, it may also be possible to measure and also to influence the concentration of the various substances that regulate growth and development in a living plant.

According to the researchers, the present study is a proof-of-concept that primarily utilised plant cuttings; its applications to living plants remain to be seen. Says Berggren, "These results are early steps to merge the diverse fields of organic electronics and plant science. The aim is to develop applications for energy, environmental sustainability and new ways of interacting with plants. Now we can really start talking about 'power plants' – we can place sensors in plants and use the energy formed in the chlorophyll, or produce new materials. Everything occurs naturally, and we use the plants' own very advanced, unique systems".

How snakes lost their legs

There are nearly 500 genera comprising almost 3,000 named species of snakes. Yet, till recently, surprisingly little was known about the ultimate origin of snakes. It was once believed that snakes evolved from marine reptiles with a slender body and lack of legs serving as adaptations to move through a watery home. However, recent fossil discoveries point to a probable origin of snakes from land-dwelling, burrowing reptiles. Sometime ago, the discovery of a four-legged fossil snake dubbed *Tetrapodophis amplectus* (literally, four-legged snake) in Brazil gave the first clue to how snakes may have evolved from lizards. Estimated to be 113 million years old, it was the oldest snake fossil on record and looked almost like a modern snake, except for one glaring difference; it had four tiny limbs, each with five digits (*Dream 2047*, October 2015).

Now, based on a new analysis of a 90 million-year-old reptile fossil skull, scientists are beginning to believe that snakes may have lost their limbs when their ancestors evolved to wriggle through burrows, and not in order to swim in the sea. A team of researchers, led by Hongyu Yi, of the University of Edinburgh's School of Geosciences in UK, arrived at this conclusion after studying 3-D virtual models of the skulls created from CT scans of 44 fossil and modern reptile species. Comparisons of CT scans of the fossils with the skulls of modern reptiles indicate that snakes lost their legs when their ancestors evolved to live and hunt in burrows, which many snakes still do today (*Science Advances*, 27 November 2015 | DOI: 10.1126/sciadv.1500743).

The researchers concentrated on the structure of the inner ear in the fossil skulls, a tiny structure within the skull, which snakes use for balance and hearing. The researchers found that the inner ears of snakes living in different environments have tell-tale shapes. The researchers found a distinctive structure within the inner ear of animals that actively burrow, which may be helping them detect prey and predators. The inner ears of burrowers appear more inflated than those of other reptiles – like a "balloon wrapped with a piece of cord". Such a structure, the researchers say, has been linked with low-frequency hearing, and would have helped snakes underground to detect the rumbling vibrations of predators or prey, but would not be of much use on the ground. This shape was not present in modern snakes that live in water or above ground. One of the fossil species that was found to have the balloon-shaped inner ear cavity of a burrower was a 90 million-year-old fossil skull of *Dinilysia patagonica*, a 2-metre long reptile closely linked to modern snakes.

The new findings are expected to help scientists fill gaps in the story of snake evolution, and confirm *Dinilysia patagonica* as the largest burrowing snake ever known. They also offer clues about a hypothetical ancestral species from which all modern snakes descended, which was likely a burrower.

According to Mark Norell of the American Museum of Natural History, New York, USA, who took part in the study, "This discovery would not have been possible a decade ago – CT scanning has revolutionised how we can study ancient animals. We hope similar studies can shed light on the evolution of more species, including lizards, crocodiles and turtles".

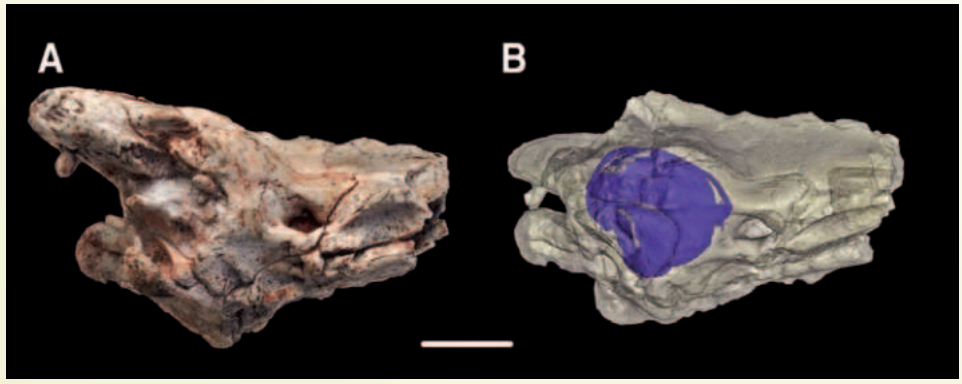


Image (A), and representation of brain case and inner ear (B), of Dinilysia patagonica fossil, which scientists at the University of Edinburgh and American Museum of Natural History have used to show that modern snakes lost their legs when their ancestors became expert burrowers. (Credit: Hongyu Yi)

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