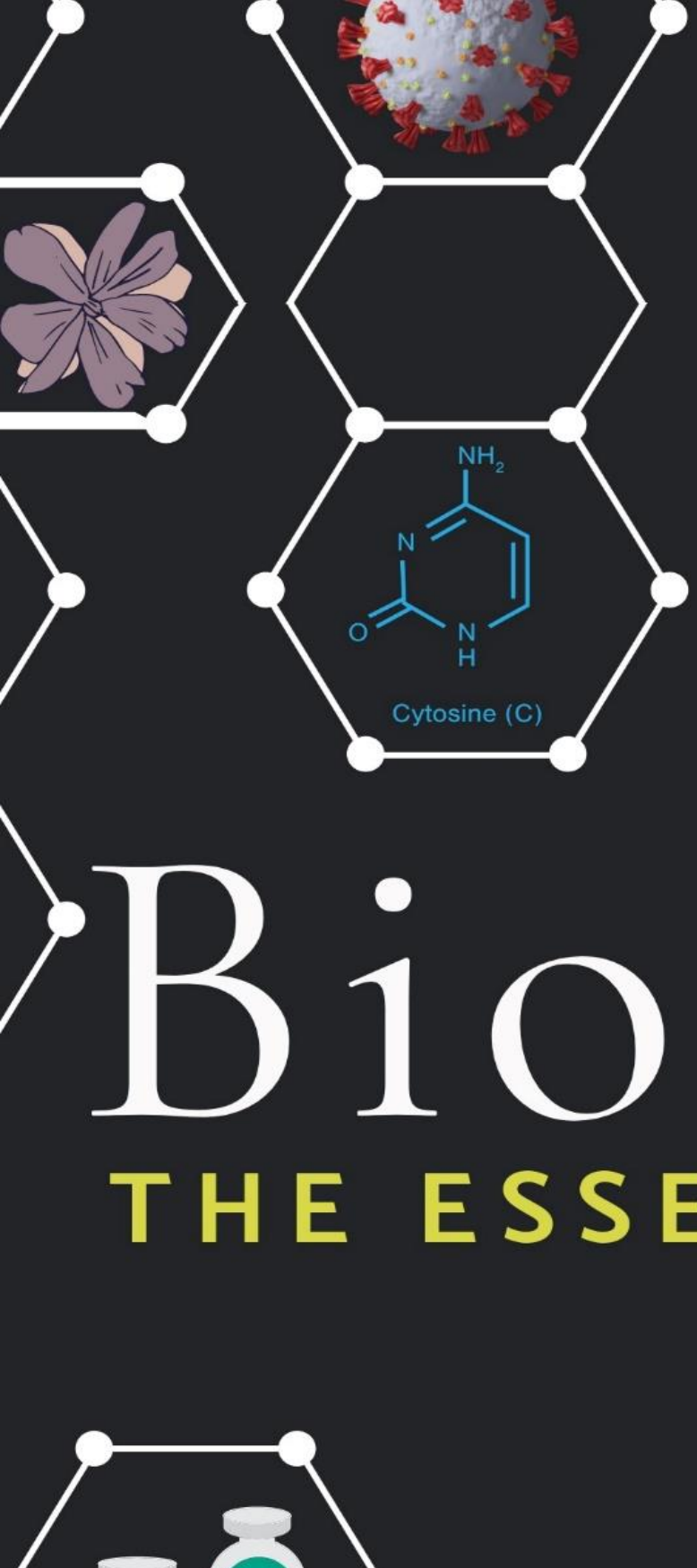
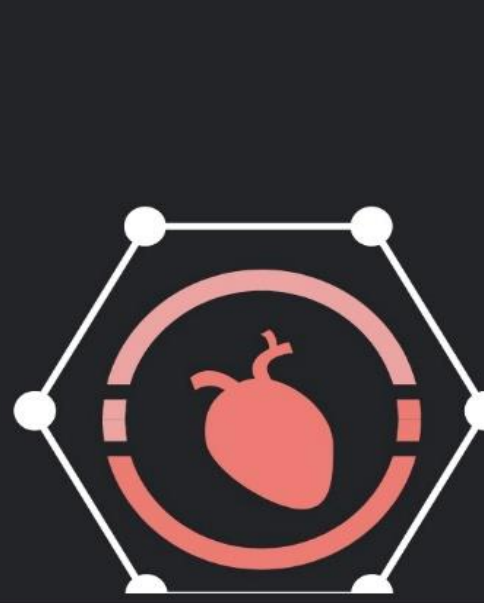
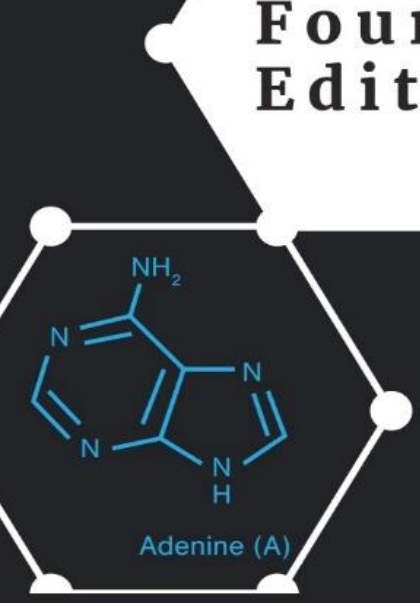
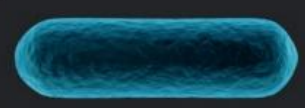


Biokemi

THE ESSENCE OF LIFE







Fourth Edition

2022

Department of Biochemistry
Shivaji College,University of Delhi

BIOKEMI 2022

Fourth Edition

Departmental Magazine

DEPARTMENT OF BIOCHEMISTRY

SHIVAJI COLLEGE

UNIVERSITY OF DELHI

DEPARTMENT OF BIOCHEMISTRY

Faculty Members

Prof. Neena R. Wadehra (Retd.), Prof. Rashmi Wardhan (Retd.), Prof. Darshan Malik, Dr. Jayita Thakur**,** Dr. Renu Baweja**,** Dr. Sunita Singh**,** Dr. Usha Yadav**,** Dr. Abhijeet Mishra**.** Dr. Kritika Raj

Non-Teaching Staff

Mr. Surender Singh, Mr. Soraj Singh, Mr. Ashok Kumar, Mr. Pawan Kumar, Mr. Jasbeer

Message from the Principal

I am pleased to know that the Department of Biochemistry is releasing the 4th edition of its annual departmental magazine BIOKEMI. We at Shivaji College, always endeavour to promote all measures that help create a nurturing domain for our students so that we produce multi-faceted trained individuals who can excel in every field. We strive to achieve an environment where teaching goes beyond the classroom and translates into knowledge.

In sync with this theme, the BIOKEMI magazine provides a great platform for students to express themselves and reach out to the scientific community by contribution of original articles, career prospect information, student progression details as well as other science-based fun compositions. I believe that this magazine has always and continues to provide students with a priceless opportunity to traverse beyond their textbook-based curriculum and study and write about the scientific phenomenon of their interest. It also provides a means to nurture and hone their writing skills and to integrate those skills with science, humor, art and photography. They learn to take responsibility while also exploiting a publishing experience. Such events not only contribute to their holistic development as students of science but also prepare them better for continuing their quest for knowledge.

I would like to extend my heartiest congratulations to the editorial board of BIOKEMI 2022 including all the faculty members as well as the student volunteers of the Biochemistry Department for marching ahead on this journey of enhancing the scientific aptitude of students with their heads proudly held high. I sincerely hope that such endeavours inspire students to dwell vigorously on the path of science and encourage them to continue to be inquisitive as well as participative. Once again, many congratulations and all the very best for all future endeavours.

Principal

Shivaji College

Message from the Keynote Speaker

A Scientist is a questioning mind with passion for the Eureka moment. This passion must be so strong that solutions come in dreams as was the case with Kekule whose mental eye saw the structure of benzene in the form of a snake which had seized hold of its own tail. There is tremendous turmoil in today's world with the pandemic of Corona on the one hand and war on the other. Both Corona and the war have been facilitated by the misuse of Science and the neglect of Scientific thought. Science should be both sweet and powerful such that it can provide a compelling sense of purpose and direction to humanity as a whole. Thus, scientists must learn a hundred other things in order to be worthy scientists. What does a Scientist know if only Science he or she knows? These other things are love for humanity, great discipline, good behaviour, joyful demeanour, tendency to be helpful and always willing to learn. Going through the thoughtful articles in BIOKEMI 2019 has made me feel delighted. The moments to cherish for any educational institution are the ones where Synergy springs from the joy of a questioning student and an alert and wise teacher who motivates the students to ask even more fascinating questions. My best wishes to Students, Teachers and the bonds of cordiality between students, between teachers and the student-teacher bond at Shivaji College for a bright future.

Dinkar Sahal *Ph.D.*
Group Leader,
Malaria Drug Discovery
ICGEB, New Delhi, India

Message from Invited Speaker

Scientific meetings are colossal platform for dissemination of knowledge and networking, Young students deserve the best future and better opportunities in the related field, and we trust that such meetings provide the multi-disciplinary exposure and shares an insight into the recent research and cutting-edge technologies. On the occasion of annual academic departmental festival "Biochaperones 2022" organized by the Department of Biochemistry I would like to congratulate the organizing committee and students at Shivaji College for compiling this scientific meet. The theme "Molecular Basis of Traditional Medicine" will give the speakers an opportunity to be able to share experiences and experimental results, discuss challenges encountered and solutions adopted while deciphering the mechanistic details of the therapeutic effects of traditional medicines. I applaud the publication of the annual magazine BIOKEMI by the Department of Biochemistry at Shivaji College. It's an excellent resource to follow recent advances in varied fields of research addressing issues directly relevant to our lives such as why is Delhi choking? And the need for sleep.

We're looking forward to an excellent meeting with great scientists sharing their new and exciting research.

I extend my best wishes for great success of the meeting.

***Saba Tabasum**, Ph.D.*
MacNaught Fellow
Harvard Medical School
Dana Farber Cancer Institute, Boston, USA

Message from Invited Speaker

Scientific meetings are an essential part of the research and academic community, such symposiums not only provide a chance to understand the current research in different areas but also for future collaborations. Discussion is key to the evolution of science with the purpose of receiving feedback at an early stage of the research. Active participation of students, young researchers, and faculty provides a highly intellectual and scientific environment that ignites new energy and ideas. Recent developments in technology have made it relatively more convenient to gather the scientific community around the world and we all should be benefitted from these advancements.

Shivaji college is making a continuous effort to contribute to science by its magazine BIOKEMI, an excellent example of student-faculty collaborative effort in bringing the science forward. It is my pleasure to be a part of academic annual function "Biochaperones 2022" with the theme "Molecular Basis of Traditional Medicine and Food", organized by the Department of Biochemistry, Shivaji College, University of Delhi. Since time immemorable natural products derived from plants and other natural sources were indispensable in traditional medicine. Modern medicine also utilizes several natural product-based medicines; thus, more discussions are needed on this topic and 'Biochaperones' should be a milestone in this important area.

I congratulate the organizing committee and all the participants and wish a great success for this meeting.

Akash Sabarwal, Ph.D.
Harvard Medical School
Boston Children's Hospital
Boston, USA

Message from the Editor's Desk

It gives me great pleasure and pride in presenting to you the fourth edition of Biokemi – the magazine of the Department of Biochemistry. It is the fruit of dedicated efforts of the faculty members and students right from its inception as an idea to finally completion as a magazine. I would like to take this opportunity to thank our Principal, Prof. Shiv Kumar Sahdev for always motivating us to reach greater heights. I also extend my heartfelt thanks to Prof. Darshan Malik for her constant guidance and support.

This magazine was conceptualized as a platform for the students to express their interests and creativity in relevance to the field of science. It is hoped that students will explore the exhilarating world of science beyond the confines of their curriculum, and come up with their own interpretations. This magazine would also provide the students with an experience of scientific writing and editing, which would stand them in good stead in the long run. The enthusiastic response of the students was overwhelming and it was delightful to see the young minds apply themselves with zest and passion into this venture.

I thank all my colleagues of the Biokemi 2022 editorial team for the team effort that made this magazine possible. The students' editorial board deserves a special mention as they led the project with dedication, hard work and enthusiasm. I would also like to acknowledge all our authors, for submitting interesting scientific articles and other content. As this was the first time for most authors in writing for a scientific magazine, their efforts are all the more commendable.

I hope you enjoy reading this magazine and look forward to the support from the readers, so that the legacy of this magazine can be continued for the years to come.

Dr. Jayita Thakur
Editor-in-Chief

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I. ARTICLES SECTION

1. CAN DEVELOPING FETUS FEEL PAIN?

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What is pain?

When we hurt our body, due to this a stimulus response is generated and the receptors particularly **Nociceptors** become active which releases chemical messenger. Nociception uses different type of neural pathways than the normal perception senses. Nociceptor neurons network travels through the peripheral sensory nerves. Their cell bodies lie in the dorsal root ganglia of peripheral nerves inside the spine.

The signals from the injured area travel into the spinal cord through the dorsal roots. There occurs formation of synapses of neurons within the dorsal horn. The spinal cord sends the pain message to the brain from its receptors, where it is processed by the thalamus and transmitted to the portion of the brain that handles the message, the cerebral cortex (Somatosensory lobe).
These descending pathways originate from the somatosensory cortex and the hypothalamus. Thalamic neurons descends down to the midbrain. There, they form synaptic networks on ascending pathways in the medulla and spinal cord and inhibit the effect of ascending nerve signals. This produces pain relief also called analgesia. This relief sensation comes from the stimulation of natural pain-relieving opiate neurotransmitters present in body called endorphins, dynorphins and enkephalins. (1, 2)

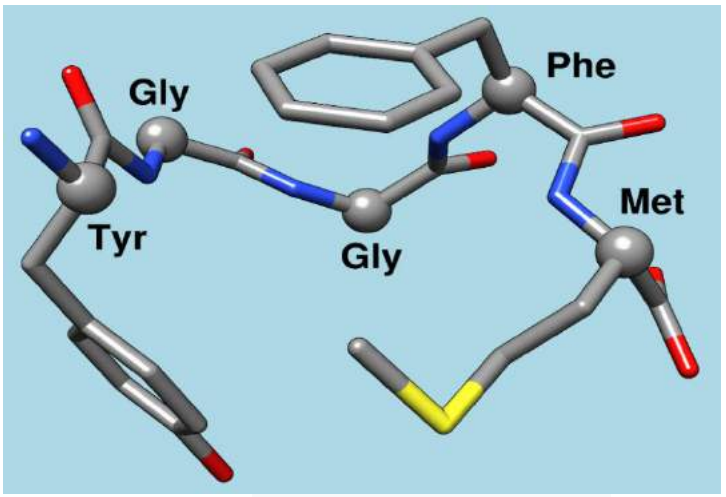

Figure 1. - Structure of Met-enkephalin

To understand whether a developing fetus has pain perception or not we must know at which trimester the neurulation does occur (2). The key characteristics a developing fetus must possess to have the perception of pain is-
1. Receptors for pain (nociceptors)
2. Neuronal network
3. Spinal cord
4. Developed brain (with thalamus and cerebral cortex

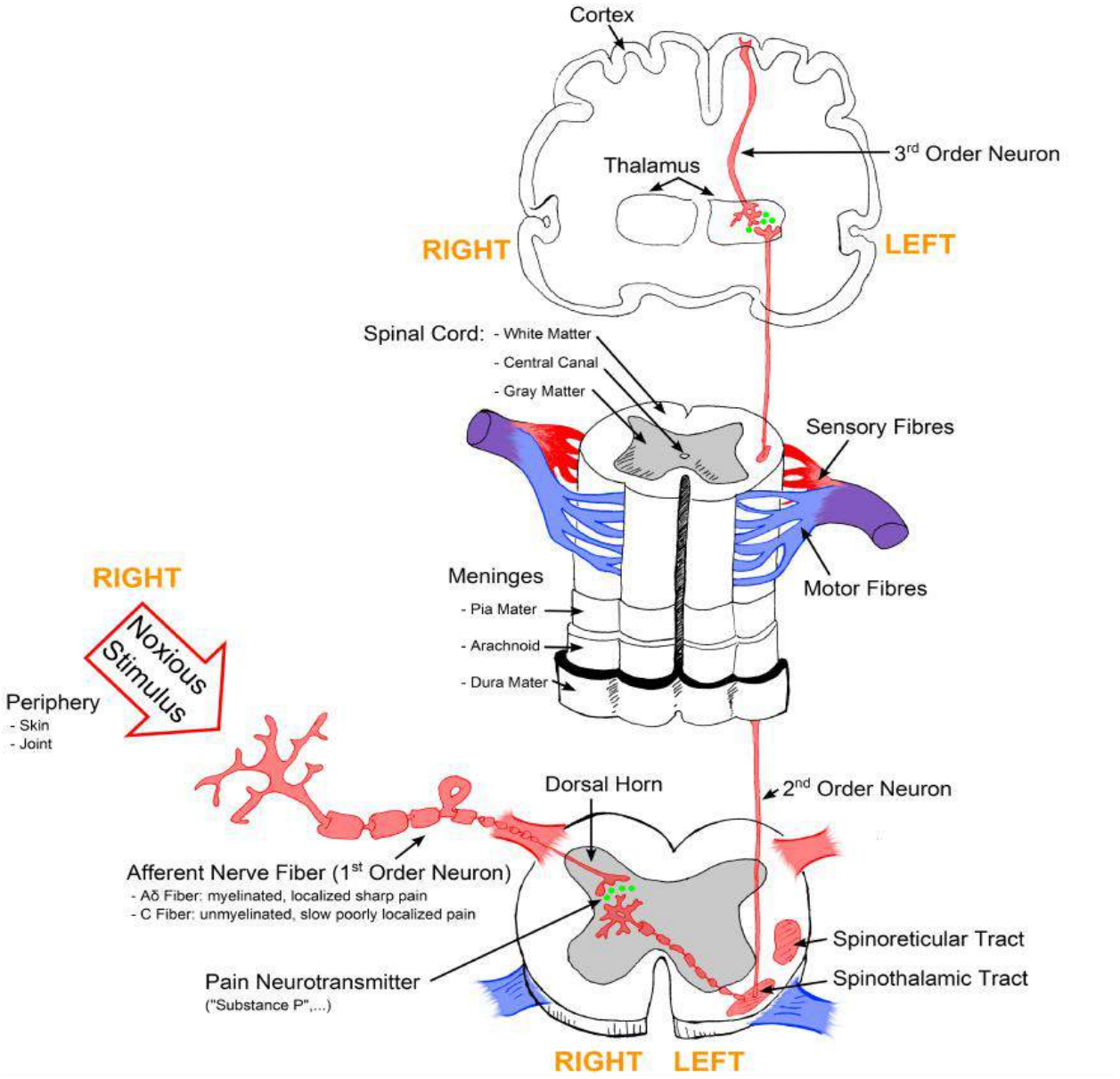

Figure 2. - Transmission of impulse from nociceptors to cerebral cortex when noxious is provided

Development of fetal pain sensation

In order to understand whether a developing fetus has pain perception or not, and at which stage of the (trimester) do they develop this sensation, recent research shows the following:

1. The development of receptors occurs between 7.5 and 15 weeks of pregnancy, and may vary depending on the location of the receptors on the body. For example, receptors in the skin and one around the mouth develops near 7.5 weeks, whereas receptors near the skin of the abdomen develop at around 15 weeks.
2. The neuronal connection present in the spinal cord that transmits the signal up to the brain must also be developed in parallel. Researchers that examined fetal tissue reported that development of this neural network occurs near around 19 weeks.

3. The neurons connecting the spinal cord to the brain need to reach all the way to the area of the brain where pain is perceived in thalamus and cerebral cortex. This neuronal network development, connecting spinal cord to various parts of brain does occur between 23 and 24 weeks.

   It has also been suggested that development of nerves is just not enough to produce the perception of pain. “These anatomical structures of the fetus must also be functional”. There is no evidence of brain activity that indicates the fetus is active near around 30 weeks. Although these time frames aren't exact — some fetuses may have these developments, a little earlier, and some fetuses may have these developments, a little later — "There isn't any science, logic to suggest that pathways for pain are complete around the 20th week of pregnancy”. (3)

   Evidences

   Electroencephalography is one of the ways for assessing general cortical function because electroencephalograms (EEGs) measure summated synaptic potentials from cortical neurons. The histological presence of thalamocortical fibers is not sufficient to give the perception of pain. These anatomical structures must be interconnected and functional. Although no such electroencephalographic “pain pattern” exists. Some researchers also proved that EEG patterns denotes wakefulness or consciousness. Wakefulness is a state of activeness mediated by the brainstem and thalamus in synchrony with the cortex. In premature fetus, the earliest EEG pattern representing consciousness is seen around 30 weeks.

   Somatosensory evoked potentials (SEPs) may also lay out an evidence of pain processing in the somatosensory cortex located in the anterior part of the parietal lobe, although this technique is not used clinically to test pain pathways. SEPs inspects the dorsal column tract of our spinal cord, which relays visceral pain sensation to the somatosensory cortex present in the parietal lobe via the thalamus. Distinct SEPs are seen to be present at 29 weeks of postconceptional age, indicating that thalamic connections with the somatosensory cortex are functional at that time. If this is so, it also raises an argument that if fetus has perception of pain from roughly around second trimester, then they must be administered anesthesia before abortions.

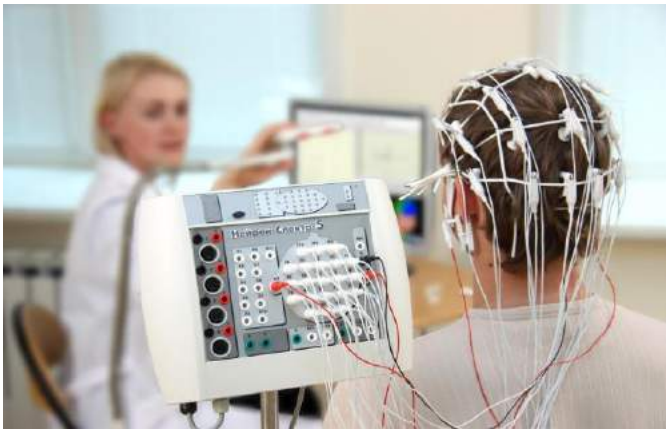

Figure 3. Patient undergoing electroencephalography

Over the last several years, many states of the United States of America, including California, Kentucky, Minnesota, Montana, New York, Oregon, and Virginia, have passed a legislation that requires physicians to inform women approaching for abortions that the fetus has the sensation of pain and to offer fetal anesthesia. Currently, many countries are considering legislation requiring physicians to inform women approaching for abortions around 20 or more weeks of gestational age. They also were advised to explain to the mother that the fetus has "physical structures necessary to experience pain," as evidence drawn by surgical instruments. The physician must also offer anesthesia or analgesia directly to the fetus. Physicians who do not obey this may be subject to substantial fines, license revocation, and civil suits for penitentiary damages. Utah recently passed a law that asks the doctors to consult the mother of fetus to give anesthesia to a fetus before performing an abortion that occurs at 20 weeks of gestation period or later (4, 5).

Arguments

An argument suggests that a fetus can experience pain before the third trimester by the facts found in research that a fetus can have a withdrawal reflex. But performing a reflex action and perceiving pain are two different aspects. For example, when a doctor uses various tests to investigate reflexes by hitting the elbow with a rubber hammer, the hand will flick out, regardless of whether one experience pain or not. "Many reflexes occur at the level of the spinal cord", and get resolved in spinal cord. They don't require the brain activity at all. But the activity of brain is essential for perceiving pain as they are processed in cerebral cortex. One more argument suggests that a developing fetus in its second trimester can display certain stress responses, such as on rising levels of stress hormones, including cortisol and endorphins. Research shows that these hormones are not specific to pain (for example, other stressful conditions may affect their levels). In addition, the hormones are not regulated by the part of the brain associated with consciousness. (4, 5)

Conclusion

Fetal consciousness and response to noxious stimuli requires functional thalamus and cortical connections. Thalamocortical fibers that connect thalamus and cortex region of brain begin appearing between the time span of 23 to 30 weeks of gestational age, while electroencephalography suggests the capacity for functional pain perception in premature fetus probably does not exist before 29 or 30 weeks. The research conducted till now are not very evident but still they clearly indicate that fetal perception of pain is not seen before the third trimester.

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2. THE MIRACLE OF FASTING

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Fasts can span a significant portion of a calendar year. Fasting may renew faith in self and God as well as one's own strength. Fasting has been a tradition in India since ancient times. It is a devotional practice performed in different religions during various types of holidays, such as in Hinduism, Islam, Christianity, Buddhism, etc. The benefits of fasting are mentioned in the Vedas, the Bible, and other sacred religious texts. Why is fasting so important in our culture since ancient times? There are many researches dealing with fasting as a treatment for many diseases such as diabetes, bacterial infections, viruses, fungi, etc. Fasting has been used successfully in the treatment of many physical ailments. Fasting also improves eating habits (1).

Benefits of fasting

The benefits of fasting are multi-pronged and recent studies have shown that apart from being a social and religious phenomenon, fasting has various physiological benefits (1, 2).

- Fasting lowers and normalizes cholesterol, homocysteine and blood pressure levels.
- Fasting calms and often relieves tension and insomnia.
- Fasting is a natural stimulant to rejuvenate growth hormone levels.
- Fasting is effectively used in the treatment of schizophrenia and other mental disorders.
- The vulnerability of the nervous system to aging is too common in neurodegenerative disorders such as Alzheimer's and Parkinson's.
- Fasting has been shown to be a potent anti-inflammatory in several previous studies and may play a role in reducing the severity of COVID-19.
- Fasting plays an important role in boosting immunity by activating autophagy, a human defense mechanism.

Fasting can cure cancer

Cancer is the one of the leading causes of death worldwide and the trend shows its rate to be increasing. Although chemotherapy has improved significantly, its efficacy in eradicating tumors is still limited and highly toxic to healthy cells. (1, 2). Chemotherapy is a mechanism that occurs before immunotherapy. Therefore, new therapeutic strategies to improve chemotherapy, radiation therapy, and targeted therapy are important targets in cancer research (3, 4). Autophagy can inhibit or promote the growth of tumors depending on the developmental stage and type of tumor, thus, the modulation of autophagy for cancer

therapy is an interesting treatment that is currently being intensively studied (1). Fasting has the ability to enhance immunotherapy which aids in cancer treatment by helping the immune system fight cancer. The immune system helps the body fight infections and other diseases (5). It consists of white blood cell, and organs and tissues of the lymphatic system. Hence, immunotherapy is a type of biological therapy (2, 6).

Nutritional restriction is a promising protocol to modulate autophagy and increase the effectiveness of anticancer therapies while protecting normal cells (7). Description and role of autophagy in tumorigenesis is summarized here. In addition, the possibility of using fasting as an adjuvant therapy for cancer treatment and the molecular mechanisms underlying this approach will be presented.

Nobel Prize was awarded in physiology and medicine in 2018 to two cancer Immunotherapy researchers James Allison and Tasuku Honjo (8). Immunotherapy is the treatment of cancer with the help of your immune system. Monoclonal antibodies, is a type of immunotherapy, in which immune system proteins were created in the lab that are designed to bind to specific targets on cancer cells. It is one of the successful treatments against cancer and has been used in many types of cancer treatment, such as breast cancer, stomach cancer and many more. Before immunotherapy, cancer cells differentiate and divide on a large scale, deactivating the working of T Cells by binding PD-L1 with PD-1 of T cells, and inhibiting the killing of tumor cells as shown in figure 1.

How immunotherapy works?

Chemotherapeutic monoclonal antibodies target cancer cells by binding to cell surface antigens. Cell surface antigens include antigens associated with growth and differentiation of cancer cells. These drugs block the growth of Cancer cells and also bind to T cells, resulting in activation of T cells against cancer cells by destroying them as shown in figure 1. Cancer cell destroyed by T-Cells after immunotherapy in which the drugs prevent the tumor cells to deactivate the T-cells

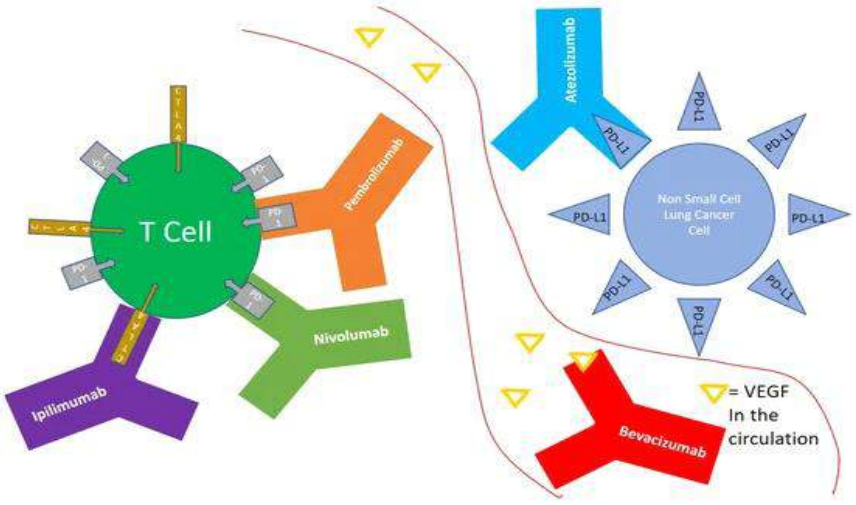

Figure 1- Cancer cell attacking T Cells by inhibiting the PD-1 by binding PD-L1. This is the mechanism happening before immunotherapy

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3. CARBON FOOTPRINT

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The total amount of carbon dioxide emitted due to the activities of a person or some entity (like a corporation) is termed their "carbon footprint (1). In addition to CO_2, the emissions also include other greenhouse gases like chlorofluorocarbons (CFCs), methane and nitrous oxide. These emissions are the result of fossil-fuel combustion while performing routine activities, including transportation, heating, and emissions from the generation of electricity from non-renewable sources for powering various electrical goods (e.g., lights, fans, geysers, microwave ovens, TVs).

The carbon footprint is an important component of the "Ecological Footprint", a concept developed in the early 1990s at the University of British Columbia by Canadian ecologist William Rees and Swiss-born regional planner Mathias Wackernagel. Footprint is defined as the total amount of an area or land (nature) required to sustain a population or an economy, such as the amount of water used by a population and the land used by them for the production of food (2). Thus, when expressed within the framework of ecological footprint, carbon footprint would help in indicating the total amount of an area that would be required to isolate those emissions, which in turn would help realise the amount of bio-capacity that would be required to cancel out the emissions from burning fossil fuels (3).

Measures of Carbon Footprint

Footprint is measured by calculating the amount of carbon dioxide and other greenhouse gases emitted per year. It is usually expressed as tonnes of carbon dioxide or carbon dioxide equivalent per year emitted. A number of tools exist for calculating the total carbon footprint of an individual, company, or major organisation. The most common tools for calculating organisational carbon footprints are the Green-House Gas Protocol, developed by the World Resources Institute and the World Business Council for Sustainable Development, and ISO 14064, developed by the International Organization for Standardization, which deals particularly with green-house gas emissions (2,3). Some organisations have developed carbon footprint calculators on the internet for calculating an individual's carbon footprint. These include ICICI Bank, TATA Power, British Petroleum, and the Nature Conservancy.

Carbon footprints are generally higher in developed countries. According to the International Emergency Agency, which calculates the carbon dioxide emissions from the combustion of coal, oil, natural gas, and other fuels, and also includes the combustion of non-renewable municipal waste and industrial wastes, China was the highest emitter of annual carbon dioxide emissions in 2018, with 10.06 GT (metric gigatons) of emissions, followed by the USA with 5.41 GT of emissions and India with 2.65 GT of emissions. These rankings change with the consideration of the population of each country, i.e., per capita emissions, with Saudi Arabia ranking at the top with 18.48 T (metric tons) of carbon dioxide emissions, followed by Kazakhstan with 17.60 T and Australia with 16.92 T (6).

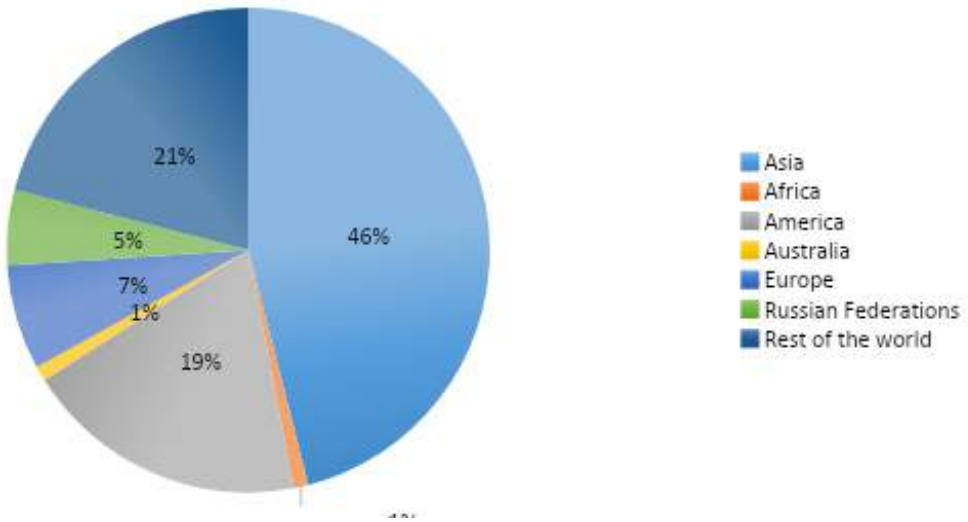

Figure 1 - Pie-chart depicting carbon emissions by each continent in 2018 modified (6)

Emissions from transportation and household energy make up a sizable portion of an individual's carbon footprint in developed nations. Emissions from such sources form a part of an individual's "primary" carbon footprint, i.e., the portion of emissions over which an individual has direct control. The remaining portion of the emissions comes under the "secondary" carbon footprint, which includes manufacturing, transportation, and consumption of goods and services (2).

Conclusion

Fortunately, there are a number of steps an individual or organization can take to reduce their carbon footprint and contribute towards a greener society. A major contributor to this can be changing one's lifestyle and purchasing habits can help to reduce one's carbon footprint. For example, creating less waste and living a low-waste lifestyle, buying goods in reusable containers, composting food scraps, walking and using public transport, shifting towards battery-powered electric vehicles, adopting a vegan diet, adding solar panels and other renewable sources for generating electricity, and insulating homes to cut down on heating and air-conditioning costs. These are some of the choices an individual can incorporate into their lifestyle to reduce their carbon footprint (5). Additionally, planting trees and introducing carbon offset taxes as a society can help reduce our carbon footprint. Individuals and companies can also purchase carbon credits to offset their carbon dioxide emissions, and the money from these credits is put into projects that invest in renewable energy or carbon-reducing technology (4).

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4. HONEY AS AN ANTIBACTERIAL AGENT

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Honey is nature's wonder. It is a sweet, viscous substance produced by bees from the nectar or from the secretion of living parts of plants. Bees collect nectar, transform and combine it with specific substances of their own, then store/leave it in the honey comb to ripen and mature (1). Honey is made by the worker bees, and all worker bees are sterile females. Males are called drones and their only job is reproduction. Honey is used as a common sweetener for foods and is a powerful medicinal tool. It is a good source of energy. It contains simple sugars that are directly absorbed into the bloodstream, without digestion process. Moisture absorbing quality of honey helps breads, cakes, cookies and candies to stay fresh longer. Its health-promoting factor comes mainly from the presence of components other than sugar: enzymes, peptides, free amino acids, vitamins, organic acids, flavonoids, phenolic acids and other phytochemicals and minerals (2). Honey has been used as a medicine for a long time, however, it has limited use in medicinal practice due to lack of scientific research. Although, in recent days it is becoming acceptable as a reputable therapeutic agent. Honey is a highly concentrated sugar solution. The three major components of honey are fructose, glucose, and water, averaging 38.2, 31.3 and 17.2% respectively (3). It also contains minor constituents such as flavoring materials, pigments, organic acids, and minerals.

Glucose and fructose are the only monosaccharide sugar present in honey. These sugars are combined to form di-and trisaccharide fractions of the floral honey. Simple sugars give honey its sweetness, hygroscopic properties, energy value, and other physical properties (2, 4).

Table 1- Composition of honey

Component	Average %
Fructose	38.19
Glucose	31.28
Water	17.2
Maltose	7.31
Gluconic acid	0.43
Mineral	0.2
Protein, amino acid	0.3

Honey has proven to possess antibacterial activity. It inhibits a broad spectrum of bacterial species. Methanol, ethanol, and ethyl acetate extracts of honey inhibit the growth both types of Bacteria –

- Gram-positive bacteria (Staphylococcus aureus, Bacillus subtilis, Bacillus cereus, Enterococcus faecalis, and Micrococcus luteus) and,
- Gram-negative bacteria (Escherichia coli, Pseudomonas aeruginosa, and Salmonella typhi) (5).

Table 2- List of bacterial species sensitive to honey/honey products and diseases they cause

Bacterial Species	Disease caused
Bacillus anthracis	Anthrax
Escherichia coli	diarrhoea, septicaemia, urinary infections, wound infection
Pseudomonas aeruginosa	urinary infections, wound infections
Salmonella typhi	Typhoid
Vibrio cholera	Cholera
Staphylococcus aureus	Abscesses, boils, carbuncles, impetigo, wound infections
Streptococcus faecalis	Urinary infections

Progress has been made in enhancing the antibacterial efficiency of honey by combining it with other ingredients like antimicrobial peptides, such as, synthetic Bactericidal Peptide 2 (BP2) has rapid bactericidal activity against Pseudomonas aeruginosa, Staphylococcus Epidermidis (6).

Properties that make Honey Antibacterial

- **High concentration of sugars;** (about 80% of weight of this product) Eliminates micro-organisms, mainly bacteria that are sensitive to high osmotic pressure and inhibits the development of more osmotolerant microorganisms (2, 6).
- **Low pH value;** high concentration of organic acids (e.g., gluconic acid). The average pH of most types of honey is in the range of 3.4 to 6.1, which helps in inhibition of bacterial growth.
- **Bee Defensin-1;** it is a peptide released by the honeybee's hypo-pharyngeal glands. As a component of royal jelly (it is also called royalysin), it plays a key role in the health of bee larvae. It exhibits activity against Gram-positive bacteria (3, 6).
- **Glucose Oxidase;** is an enzyme that catalyzes the oxidation of glucose to gluconic acid. The side product of this reaction, hydrogen peroxide (H2O2) is a strong antimicrobial agent (1, 7).

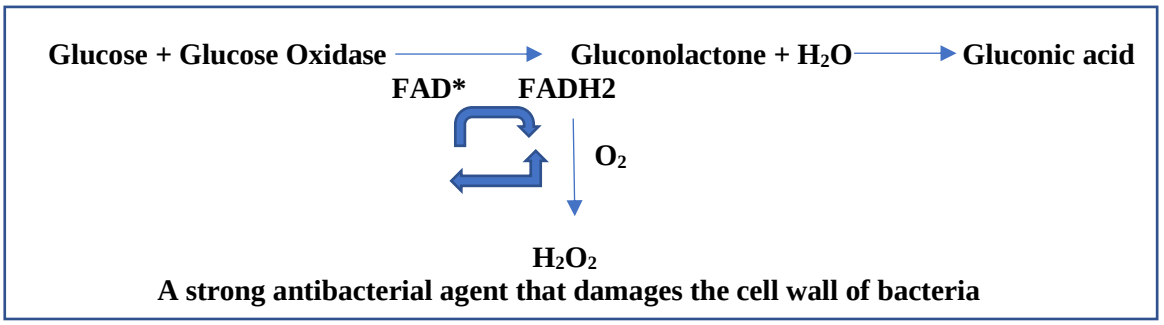

Figure 3 - The Reaction catalyze by Glucose Oxidase – Generation of Hydrogen peroxide

The enzyme (Glucose Oxidase) is produced in honeybees' salivary glands and is introduced to the collected nectar. It protects the ripening of honey due to the development of pathogenic microorganisms. H2O2 is a major antimicrobial defense factor for honey. Thus, honey can be used an alternative antibacterial agent with promising therapeutic potential in the medical setting (2, 5).

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5. EPIGENETICS: A NOVEL APPROACH TO UNDERSTANDING VIRAL INFECTIONS

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Discovery of the chemical structure of DNA by James D. Watson and Francis H. C. Crick in 1953 paved way for new opportunities and innovations which were undreamt of at the time, it was an important piece of the puzzle which would lay foundation for whole new fields of sciences and would revolutionize the way we diagnosed and treated diseases at the time, now that we knew the chemical structure of the blueprint of life, it revolutionized the way we looked at diseases but it was believed that when it comes to genetic material it's something an organism is just born with and we did not have much control over the genes once they got inherited in the offspring but studies in the last two decades have brought into light an array of factors that influence gene expression not by making changes in the nucleotide sequence but by changing the environment of the cell which made our understanding of gene expression much more complex but in an encouraging way, and the field of study that deals with these factors is called *Epigenetics* (1).

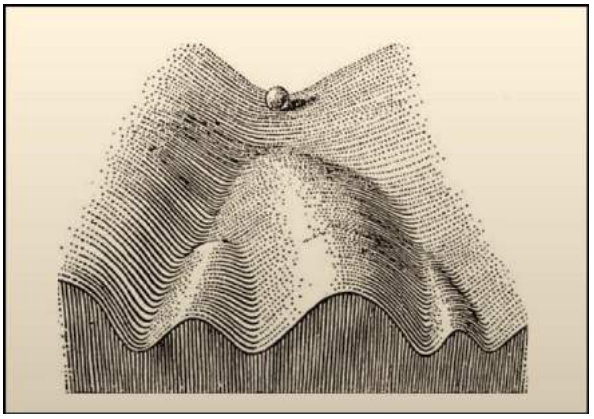

Figure 1 - Waddington's Classical Epigenetic Landscape (Source: Waddington, C. H. (2014). The strategy of the genes. Routledge)

C.H. Waddington introduced the term "Epigenetics" in 1940, he defined it as "the branch of biology which studies the causal interactions between genes and their products which bring the phenotype into being" (1). He nominated the concept of Epigenetic landscape in 1957, depicting how gene regulation modulates the unidirectional maturation of embryonic stem cells into differentiated cells. Now epigenetics is technically defined as "the study of changes in gene function that are mitotically and/or meiotically heritable and that do not entail a change in DNA sequence (2).

Epigenetic regulation constitutes 5 key components which include: DNA methylation, histone variants, histone modifications, nucleosome positioning, and regulatory RNA (3).

Among these five processes the three processes that are known to have a major influence are:

• DNA methylation	Methylation of cytosine to 5-methylcytosine through DNA methyltransferases (usually DMNTs add methyl group at a cytosine base followed by a guanine base known as CpG sites) results in silencing of the gene or activation in some cases depending upon the location of methylation.
• Histone modifications	Can result in either promotion or repression of a gene depending upon the histone proteins, for example, Histone acetylation and methylation on H3K4/H3K36 is could lead to activation of transcription, methylation on H3K9 and H3K27 is associated with repression while methylation of H4K20 could result in either activation or repression (4).
• ncRNAs (Non-coding RNAs)	These include miRNAs, siRNA, piRNA, and lncRNA. These are responsible for regulation of gene expression at the transcriptional and post-transcriptional levels.

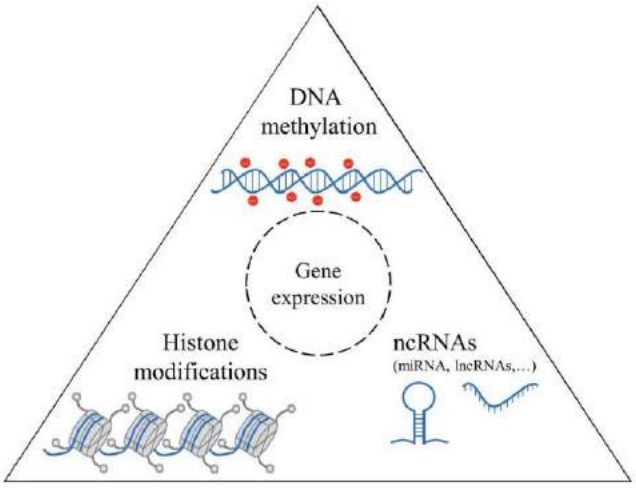

Figure 2 - Epigenetic mechanisms contributing to gene regulation (Source: Roberti, A., Valdes, A. F., Torrecillas, R., Fraga, M. F., & Fernandez, A. F. (2019). Epigenetics in cancer therapy and nanomedicine. Clinical epigenetics, 11(1), 1-18.)

Viral-Host Cell Interactions

Viral-host interactions involve complex epigenetic interactions, DNA/RNA Methylation, chromatin remodeling, and histone modifications are known to regulate and remodel host expression patterns. The different aspects in which the epigenetics of a cell is influenced upon infection are:

1. The immune system is regulated by a series of epigenetic mechanisms.
2. The invading pathogen can alter the epigenetic landscape of the cell to use the cell machinery.
3. Epigenetic changes from a previous infection tend to have consequences on future contagions.

Thus, it becomes self-evident to study the epigenetic changes that occur in virus-infected cells, Advancements in ChIP-sequencing have made it possible for us to determine the genomic location of nucleosomes and more specifically nucleosomes that contain a particular histone variant or histone modification over a complete genome. ChIP-Seq also can be used to determine the genomic location of

any proteins of interest, as studies have shown how certain viruses affect the epigenetic environment of the cell. Some of the epigenetic changes that have been seen in certain viral infections are summarized as follows:

EPSTEIN-BARR VIRUS: Through the combined action of EBNA3C and EBNA3A and their interaction with the cellular PcG protein system, EBV has evolved a very effective countermeasure to OSR/OIS that appears to be critical in its normal life cycle to establish a latent infection and therefore initiate long-term persistence in B Cells. By taking advantage of an epigenetic mode of gene regulation to tackle the problem of OSR/OIS, the target Tumor suppressing genes including INK4a and BCL2L11/BIM are repressed not only in the infected cells but also in their progeny thus making the cells more susceptible to cancer; furthermore, the genes become particularly predisposed to complete silencing by DNA modification (5).

Herpesviruses: It encodes gene products both proteins and RNAs that directly or indirectly promote epigenetic silencing and latent infection. The initiation of the herpes simplex virus infection and reactivation from latency is facilitated by two histone demethylases LSD1 and JMJD2, inhibition of either of these enzymes has been shown to result in suppression of the viral genome and blocking of infection in animal models (6, 7).

RNA Type Viruses: Epigenetic research has revealed that global DNA methylation along with ACE2 gene methylation and post-translational histone modifications may drive differences in host tissue-, biological age- and sex-biased patterns of viral infection. RNA-type viruses, such as COVID-19, have been shown to utilize RNA modifications (8). Generally, viruses from the family of coronaviruses and influenza, are not able to change genetic sequence. However, they can alter the epigenome, allowing them to overthrow a host's immune response and spread infection successfully. Noncoding RNAs are common and abundant factors expressed during the latency of a virus, many functions have been assigned to these ncRNAs, including epigenetic control of latent virus and modulation of host processes important for viral latency (9).

The Case of Spanish Flu and Encephalitis Lethargica

The Spanish Flu also known as the 1918 influenza pandemic, which was caused by the H1N1 influenza virus, was followed by another epidemic known as the "Encephalitis lethargica" which lasted for a decade more than the Spanish flu (10). The mystery behind the rise of encephalitis lethargica persists, its origin and relation with the Spanish flu are speculative, but 100 years later, with the research in epigenetics we have found that Influenza viruses tend to influence the epigenetic landscape of the cells, and as we know that the epigenetic modification is the only known mechanism for maintaining cells in a particular state for exceptionally long periods as imprinted genes get switched off at certain stages in development and stay off throughout the rest of life, So we can't deny the possibility that the epidemic of Encephalitis lethargica as a result of the change in the epigenetic landscape of the cells due to influenza virus. I have to restate that this hypothesis is speculative and limited by the amount of research and the evidence we have on this topic, but it does make for quite a fascinating explanation.

Conclusion

Epigenetic modifications play critical roles in virus replication and epigenetic changes are amenable to therapeutic intervention, the cellular factors that mediate epigenetic modifications are attractive targets

for broad-spectrum antiviral therapy (11). Understanding the epigenetic environment inside a cell in case of viral infections and identifying the heritable epigenetic changes some viruses incur inside certain cell types poses vital opportunities for making more efficient medicines and a more viable way to deal with unanticipated epidemics and pandemics in the future and when a new approach like this comes along it provides solutions not just to the problems of the present but also asks for looking at the mysteries of the past with a new perspective.

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6. NANOENZYMES IN CANCER DIAGNOSIS AND THERAPY

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The synthesis of nanoenzymes is an emerging technology that links nanoparticles to biological activity and structure (1). Nanoenzymes are a type of artificial enzyme that is made of a series of inorganic nanomaterials that mimic natural enzymes like peroxidase, catalase, oxidase, hydrolase, superoxide dismutase, etc. (2, 3) The use of natural enzymes is not pocket friendly due to high cost, unstable to environmental factors, low specificity, and non-tunability of their catalytic capabilities. Concerning that, mimic natural enzymes nanoparticles with high stability and lower cost have the best contestant for artificial enzymes. Due to the different touchable activity of nanoenzyme, they are used in the treatment of the environment, neuroprotection, antioxidation, anti-inflammatory, and antiaging (4, 5). Other than this, nanoenzymes have also played an important role in the diagnosis and treatment of cancer (5). At present, different treatment therapies for cancer are available such as radioimmunotherapy, photodynamic therapy (PDT), etc., which are minimally invasive, have low systemic toxicity, have a

fast-healing process, are portable, and are relatively low-cost technologies (3). But the hypoxic condition of cancer cells reduces the significant efficiency of these therapies.

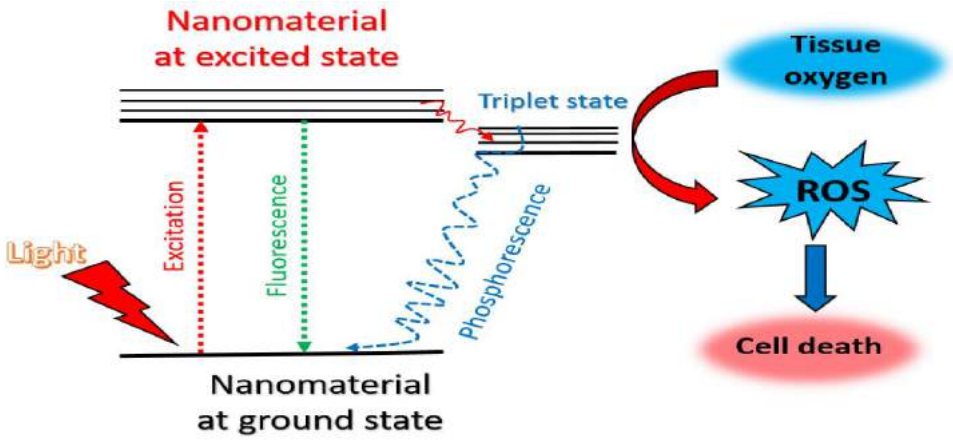

Figure 1- Mechanisms of nanoparticle mediated photodynamic therapy *(Thangudu et al., 2021)*

Nanomaterials to overcome tumor hypoxia

Subsequently, several strategies have been developed to overcome tumor hypoxia, such as oxygen-carrying nanomaterials and oxygen-generated nanomaterials. Among them, the generation of oxygen species on enzymes, especially catalase mimetic (CAT) nanozymes, convert endogenous hydrogen peroxide (H_2O_2) into oxygen (O_2) and peroxidase (POD) mimetic nanozymes convert endogenous H_2O_2 to water (H_2O) and reactive oxygen species (ROS) in a hypoxic tumor microenvironment is a fascinating approach (6). In target to improve PDT, Elizadeh et al., introduce $Co(OH)_2$/FeOOH/WO_3 ternary nanoflowers, which contain dual enzyme activity that is based on PH-switchable peroxidase and catalase like activity, due to peroxidase-like activity- detection of cancer cell and due to catalase like activity, it shows anticancer behaviour by providing O_2 to enhancing PDT efficiency which makes low cost and high stability (3).

Another study reported that a radioactive nano-oxygen generator (177Lu-APPs-PEG) with superior properties, enhances anti-tumor radio-immunotherapy by regulating the tumor microenvironment and reducing proliferation by improving the infiltration of cytotoxic T cells (CTLs) in distant tumors and reduces tumor metastasis (7). Similar to these, Huo et al. construct Zeolitic imidazolate framework (ZIF)-based nanoparticles to synergistically enhance starvation-combined chemotherapy by inhibiting the mitochondrial energy metabolism and boosting the accumulation of ROS using pristine ZIF-based nanoparticles offering a new vision of nanomedicine based on organometallic structures for alternative cancer treatments (8). This type of work is important for expanding the application of nanomaterial-based nanoenzymes for nano-sensors, and catalysts, in different molecular aspects and clinical purposes. Further insight into limitation, provide a future direction for using engineered nanozymes with enhanced biomedical and diagnostic applications.

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7. HOW NANOPARTICLES COULD CHANGE THE WAY WE TREAT CANCER

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Cancer is the second leading cause of human death worldwide with an expected 7.6 million people die every year which represents 13% of total deaths (1). In this fight against cancer, early detection is a key factor for successful treatment but the detection of cancer in the early stage has been hindered by the intrinsic limits of conventional cancer diagnostic methods (2). So, we need a change in the way cancer is diagnosed and treated because what we have been doing so far has not been working. And in medicine, the firefighters (cancer drugs) are sent, because cancer is like a big fire. But they are sent without a fire truck; so, most cancer drugs never make it to tumors, getting washed out of the body before they have time to do their job. The solution to these problems is '**nanoparticles**' – tiny particles that could be used to deliver drugs accurately to tumors. The use of nanoparticles in cancer diagnosis and monitoring has gained attention and various types of nanoparticles have been used for molecular imaging (1).

What are Nanoparticles?

The International Union of Pure and Applied Chemistry defines nanoparticles as microscopic particles with 1–100 nm in dimension. These nanoparticles (NPs) have special physical properties, like conductivity, steadiness, and optical properties, which make them an ideal selection for biology and materials science. NPs are divided into different groups based on their properties, shape, and size. These groups include fullerene, metal NPs, ceramic NPs, and polymer NPs, etc. The structure of Nanoparticles used for drug delivery is made up of several kinds of materials, such as polymers, metal particles, lipids, and so forth. NPs, recently, have been at the center of attention in DDS (Drug delivery system) (3).

Nanoparticles in Cancer Diagnosis

In cancer treatment, the most important is its early and accurate diagnosis which is in general done by Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), ultrasound, etc. but these are not so versatile to provide complete clinical information about various types and stages of tumor. In the past few decades, the use of nanoparticles in cancer diagnosis and monitoring has gained attention. Different antitumor agents including drugs and various biomolecules such as different peptides, antibodies, or other molecules can be used with nanoparticles to mark tumors with high specificity and this conjugate is useful in the early detection and screening of cancer cells.

The nanoparticle with a small size diameter has a large surface area that can easily attach to functional groups of different optical, radioisotopic, or magnetic diagnostic and therapeutic agents which makes the cancer diagnosis more convincing and efficient (1).

- NIR Quantum Dots are appropriate for in vivo imaging of cancer in tissues like the intestine, liver pancreas, and lymphatic tissue.
- Nanoshells are 10–300 nm size dielectric cores, which are usually made up of silica covered by a thin metal shell that is generally gold. Nanoshells are effective because their imaging is free from heavy metal toxicity.
- Colloidal Gold Nanoparticles act as contrast agents by scattering visible light in vitro samples and can also be used in conjugation with antibodies for biopsies and identification of cervical and pancreatic cancers. It is a priority-based diagnostic agent in different cancers.

Examples of NPs used in the diagnosis and treatment of cancer:

- *For Breast cancer* – Liposomal anthracycline with trastuzumab, Liposome, and liposomal epigolds containing doxorubicin, NPs containing paclitaxel in the central part and surrounded by albumin, Solid lipid NPs (3).
- *For Brain cancer* – The first NPs, which were used in brain tumor imaging, was a type of Fe_3O_4. They were connected to the tumor-specific L6 monoclonal antibodies. Organic NPs, like liposomes and dendrimers, work as the main diagnostic NPs for brain cancer treatment (3).
- *For Ovarian cancer*, head and neck cancer,lung cancer – Abraxane, Doxil, daunoxome, Oncaspar, and Depocyt (3).

Nanoparticles as Drug Delivery Carriers in Cancer Therapy

Various nanocarriers are used as drug delivery carriers in cancer therapy. Nanocarriers change the pharmacokinetic properties of drugs to improve their effectiveness and decrease their side effects. Their structure has some special properties, which can increase the efficiency of therapeutic drugs; these properties are controlling the releasing process of drugs in the body, protecting pharmaceutical

molecules, crossing the biological barriers to deliver the drug to the targeted place, increasing drug durability in blood flow, biocompatibility, and targeted drug delivery (3).

- Polymeric Nanoparticles usually consist of acrylates, polylactic acid, or polyglycolic acid. More than 10 polymeric nanoparticles containing anticancer drugs are under clinical development, including paclitaxel poliglumex (Xyotax), N-(2-hydroxypropyl) methacrylamide (HPMA) copolymer-camptothecin (MAG-CPT), HPMA copolymer-doxorubicin (PK1), PEG-camptothecin (Prothecan), etc.
- Dendrimer-based Nanoparticles- Dendrimers exploit malignant tumor morphology and characteristics such as leaky vasculature, specific cell surface antigen expression, and rapid proliferation.
- Liposomes- They are composed of naturally occurring phospholipids, which are biologically inert, weakly immunogenic, and generally have low intrinsic toxicity. Due to the presence of the lipid bilayer, these vesicles are considered excellent carriers for the delivery of both hydrophobic and hydrophilic drugs.
- Solid lipid nanoparticles (SLN) are colloidal nanocarriers comprising a phospholipid monolayer coating a solid hydrophobic core and encapsulating a drug in high-melting-point glycerides or waxes. Mitoxantrone-loaded SLN has been shown to lower the toxicity and improve the bioavailability of the drug.
- Silica nanoparticles-Commercially available silica nanoparticles functionalized with N- (6 – aminohexyl) – 3 – aminopropyltrimethoxysilane can efficiently result in the transfection of Cos-1 cells with minimal toxicity.
- Other nanocarriers used in cancer drug delivery are gold nanoparticles, fullerenes, calcium phosphate nanoparticles, quantum dots, magnetic nanoparticles, carbon nanotubes, iron oxide nanocrystals, cyclodextrin nanosponges.

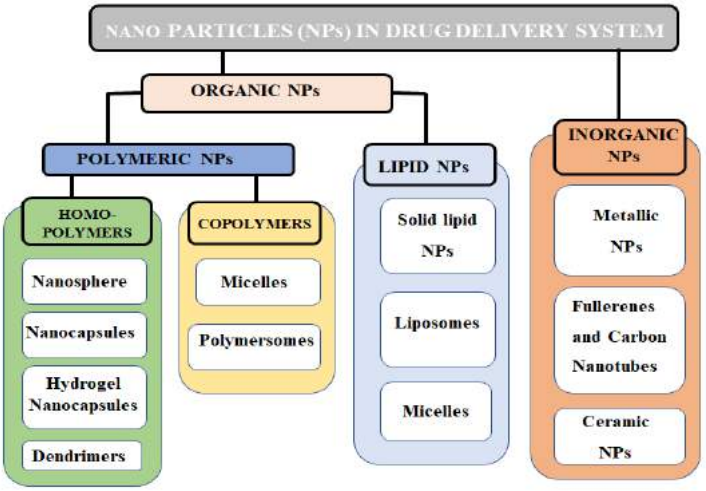

Figure 1 – Flowchart representing an overview of the classification of nanocarriers that have been used for drug delivery (3)

Mechanism of Cellular Targeting by NPs

For effective cancer therapy, the delivery system should be selective to the target cells without affecting normal cells (4). Generally, NPs carry out the drug delivery process by either active or passive mechanisms (3).

- Passive targeting of nanoparticles: In passive targeting, systems are delivered to the targeted place with the help of physical-anatomical conditions (3). Passive tumor targeting depends on the leaky tumor vasculature, tumor microenvironment, and direct local application. Non-malignant tissues are resistant to the passage of nanoparticles due to the presence of tight junctions. In cancer, the neovasculature is usually disorganized and leaky and this allows for the extravasation of nanocarriers due to the presence of fenestrations in the endothelium of tumor vessels. Passive drug targeting also depends on the drug carrier's half-life and enhanced accumulation at the target site. Hydrophilic polymer (e.g. polyethylene glycol) coating is widely used to prevent macrophage capture and to increase circulation time of nano-formulations In passive targeting, nanoparticles accumulate in the neoplastic tissues as a result of the enhanced permeability and retention effect. The transport of nanoparticles across the neoplastic tissues depends on the size, shape, and surface charge of nanoparticle and tumor microvasculature (4).

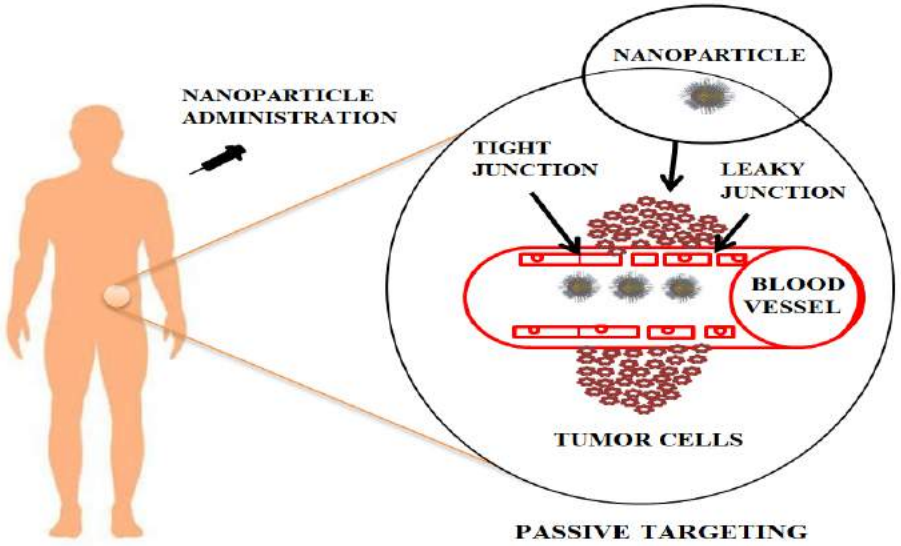

Figure 2 - Diagram illustrating the process of passive tumor targeting by nanoparticles (4)

- Active targeting of nanoparticles: In the active drug delivery method, in comparison with the passive targeting method, there is a possibility for more targeted drug delivery to cells and tissues (3). Active nanoparticle targeting of tumor cells relies on the use of specific ligands, such as transferrin and folate, which bind to molecules specifically expressed or overexpressed on target cells. This trigger infolding of the membrane and internalization of nanoparticles into the cell via receptor-mediated endocytosis. Active targeting reduces nonspecific interaction by conferring the strong ligand-receptor binding to deliver the drug in peripheral tissues. Under the acidic conditions of the endosome, nanoparticles release the drug which enters the cytoplasm after which it can act on the cellular target (4).

Classification of tumor-targeting strategies:

a. Angiogenesis-associated targeting via vascular endothelial growth factor receptors, αvβ3 integrins, matrix metalloproteinase receptors, and vascular cell adhesion molecule-1.
b. Targeting uncontrolled cell proliferation targets via human endothelial receptors, transferrin receptors, and folate receptors.

c. Tumor cell targeting for breast cancer, targeting colorectal cancer, targeting lung cancer, etc. (4).

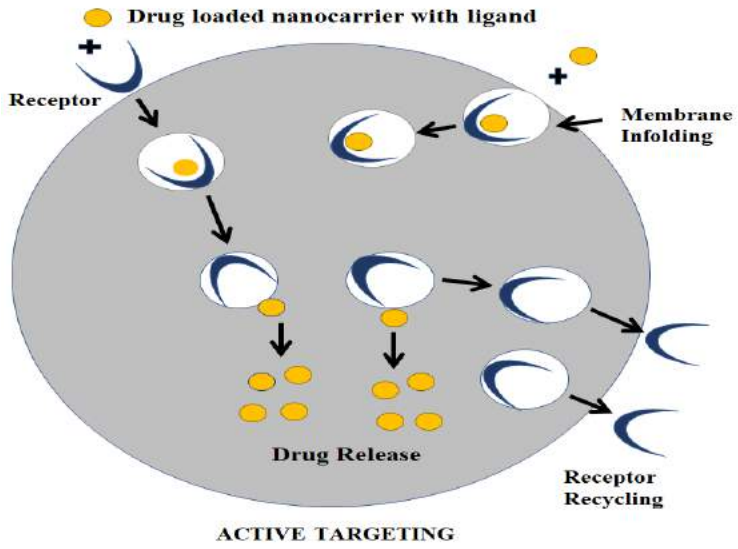

Figure 3 - Diagram illustrating the process of active tumor targeting by nanoparticles via receptor-mediated endocytosis process (4)

Nanotherapeutics Approved for Cancer Treatment

Doxil® (first nanoparticle-drug approved by the FDA in November 1995 for the treatment of HIV related Kaposi's sarcoma, metastatic ovarian cancer, metastatic breast cancer), DaunoXome®, Abraxane®, Myocet® (approved in 2000 in Europe and Canada for metastatic breast cancer), Depocyt, Genexol PM®, Oncaspar®, Endoderm (Superparamagnetic iron oxides), Feridex (Dextran is the nanoparticle carrier, used for detection of liver and spleen lesions associated with metastases, primary liver cancer, cysts, and various benign tumors, adenomas, and hyperplasia with MRI), Sinerem (Ultra-small paramagnetic iron oxides) (4).

Limitations or Challenges in using NPs for cancer treatment

- Nanoparticles are relatively unstable over prolonged periods. Manufacturing conditions like high temperatures and pressures can change the crystallinity of drugs.
- Nanotechnology is very costly. High labor costs, difficulty in the control of molecular structure and product processing are factors contributing to this (4).
- Production of nanoparticles that are highly sensitive, reproducible, and have long-term storage stability at an acceptable cost is very difficult (2).
- Factors that can affect NP-based detection signals include nonspecific binding of NP probes, aggregation, and unfit detection conditions. Obtaining reliable and quantitative detection results is a challenge (2).
- Due to the foreign compositions, nanoparticles can be cleared rapidly by the immune system, leading to undesirable tumor accumulation. Synthetic nanoparticles are easily opsonized by plasma proteins and cleared by the immune system (5).

Future Prospective

- Gene therapy offers a powerful tool for cancer therapy either by modulating the expression of tumor genes or by transferring the genes that produce therapeutic proteins. Small RNAs and genes can be attached to NPs via electrostatic interaction or conjugated onto the surface of NPs. Nanoparticles-assisted cancer gene therapy has the potential to be an effective cancer treatment approach (1).
- Cancer theragnosis is a budding concept in nanotechnology and it involves diagnostic tests and targeted therapy simultaneously in one integrated system. Various nanoparticles including gold nanoparticles, silver nanoparticles, and Chitosan-based Nanoparticles (CNPs), etc. have been developed into multimodal theranostic nanoparticles. A continuous effort in the advancement of cancer theranostic NPs would open a new avenue in cancer diagnosis and therapy (1).
- Camouflaging nanoparticles with the cell membrane, also known as a 'nanoghost' strategy, utilizes cell membranes such as red blood cell (RBC) membrane, immune cell membrane, cancer cell membrane, and platelet membrane. Such biomimetic nanoparticles create a biointerface in order to evade immune elimination, prolonged circulation time, and even target a disease region by virtue of the homing tendency of the cell membrane protein. This cell membrane biomimetic strategy has made a significant step in the field of nanomedicine (5).

Conclusion

In the last 10 years, many efforts have been made to develop assays for cancer diagnosis based on nanotechnology. Compared with the currently available cancer diagnostics in the clinic, a variety of NP-based assays showed improvement in terms of selectivity and sensitivity that could not be achieved with traditional approaches. These advances will improve the survival rate of cancer patients by enabling early detection (2). The high surface-to-volume ratio of NPs enables them to absorb, and convey small biomolecules like DNA, RNA, drugs, proteins, and other molecules to the targeted site and thus enhances the efficiency of therapeutic agents (1). The application of nanoparticles for in vivo tumors is rapidly improving (3). However, each NP has some advantages and disadvantages.

Overall, we can conclude that nanoparticles have opened an infinite way to search and design drug and drug delivery systems for the treatment of cancer. Continuous and extensive research in nanoparticles will establish it as a prominent cancer therapy approach in near future (1). Hoping that nanoparticles will shift the paradigm of cancer treatment and that the true goal of cancer nanomedicine - a dramatic improvement in patient survival will become a reality in the foreseeable future (6).

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8. AMNIOCENTESIS

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Amniocentesis is an essential tool in obstetrics. It was developed in the 1960s, and until 2007 it was offered almost exclusively to women with an identified risk for carrying a fetus with a genetic disorder that could be detected by traditional karyotyping. Amniocentesis was also offered to women who showed fetal structural irregularities on ultrasound that could be markers for chromosomal abnormalities (1). It is an invasive procedure that requires removing a sample of amniotic fluid to obtain fetal cells for chromosome analysis. Generally, not performed earlier than 15 weeks gestation, the procedure is done under ultrasound guidance (2). Although some pain is associated with amniocentesis, it is generally well-tolerated without the need for anesthesia. Five to 10 percent of pregnant women choose to have the test (3).

Uses of Amniocentesis

Amniocentesis involves using a thin needle to take a sample of amniotic fluid, the fluid that surrounds a developing fetus during pregnancy. Two to four teaspoons, or approximately 1 cc of fluid per gestational week, are removed for testing. Ultrasound technology is often used to prevent injury to the fetus or mother. The fetal cells are given a few days to multiply before a karyotype, a picture of the chromosomes to identify chromosomal abnormalities, is performed and test results can be obtained. In cases where amniocentesis is used to determine the lung maturity of a fetus the procedure is performed around or after thirty-six weeks gestation to determine if early delivery is safe, and results are available within hours (4). Tests of fetal cells found in this fluid can reveal the presence of Down syndrome or other chromosome problems in the baby. Amniocentesis can also show whether the lungs of the baby are mature enough to allow it to survive if it were delivered right away. Amniocentesis is often recommended for pregnant women over age 35, women who have an abnormal "triple screen" blood test during pregnancy, or women who have (or whose husbands have) a family history of certain diseases or birth defects. A different test that provides similar information is called chorionic villus sampling (CVS). Women can have CVS done slightly earlier in pregnancy. (5)

Case studies

Using data from a 2003 meta-analysis, the rates of adverse pregnancy outcomes in euploid pregnancies were estimated based on the positive predictive value (PPV) of increased accuracy of non-invasive prenatal testing (NIPT) and the invasive procedure used—that is, Chorionic villus sampling (CVS), early amniocentesis (EA), or termination of pregnancy (TOP). Following NIPT, it was found that the rate of

adverse fetal outcomes in euploid pregnancies was lower for CVS than for EA at all PPV levels. As the PPV of NIPT increased, the difference in risk between EA and CVS decreased. The risk to euploid pregnancies of TOP was excessive at all PPVs. CVS is the recommended diagnostic test in the first trimester because it is safer than EA for the fetus. However, EA is better than no testing when early TOP is planned. Patients should be strongly counseled against TOP without confirmatory testing (6).

Prenatal diagnosis of congenital toxoplasmosis (CT) influences therapeutical management in pregnant women and their offspring. In Austria, a nationwide serological healthcare program to identify potential maternal toxoplasma infections during pregnancy exists. The clinical use of amniocentesis for toxoplasma-specific polymerase chain reaction (PCR) on amniotic fluid was assessed to detect CT. Data on serology, amniocentesis, PCR, complications, treatment, and pediatric clinical outcome were collected retrospectively among the birth cohort 1992–2008. There were 1386 women with amniocentesis, but only in 707 cases (51%) was acute maternal infection confirmed serologically. A high proportion (49%) of amniocentesis with negative PCR results in women with chronic infection or seronegativity were performed without clinical justification for the women or their fetuses. The positive and negative predictive values of PCR were 94.4% and 99.3%, respectively. Thirty-nine fetuses with CT, including four deaths, were reported. The five PCR-negative but infected infants were identified by the serological and clinical follow-up program. Thirty percent of amniocentesis were performed in the third trimester, and gestational age or treatment did not influence PCR sensitivity. Amniocentesis is indicated in women with acute maternal infection, and facilitated targeted therapies in pregnant women and their offspring. In women with late toxoplasma infection, negative amniotic fluid PCR made treatment of infants unnecessary. Serological and clinical follow-up of infants is important to confirm the infection status of the infant (7).

Conclusion

Even though amniocentesis is a reliable diagnosis method, it causes certain complications. These complications are inversely proportional to the experience of the person who applies the method (8). Amniotic fluid leak, vaginal bleeding, uterine contractions, chorioamnionitis, sampling failure, fetal loss and possible fetal injuries are among the complications of amniocentesis. Fetal loss rate in amniocentesis is 0.5% or less (9). Amniocentesis is a safe, commonplace procedure for prenatal diagnosis of genetic and chromosomal disorders. The technology has advanced significantly since its inception, and with its increased use and availability, the technique is likely to improve further still (10).

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9. EPIGENETIC VIEW OF TYPE 2 DIABETES

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Diabetes is one of the chronic illnesses which leads to a variety of ailments. India leads the world in this race and is termed as the "diabetes capital of the world". According to the Diabetes Atlas 2006 published by the International Diabetes Federation, the number of people with diabetes in India currently around 40.9 million is expected to rise to 69.9 million by 2025 unless urgent preventive steps are taken. Approximately, 463 million adults (18-79) were living with diabetes in 2019. Every 1 in 5 people is suffering with this illness (1). Diabetes is linked with decreased secretion of insulin (hormone responsible for glucose metabolism) and insulin insensitivity which cause increased glucose concentration in blood. Between Type 1 and Type 2 diabetes, T2D is prevailing and around 247 million people are at increasing risk. In 2014, 8.5% of adults aged 18 years and older had diabetes. In 2016, diabetes was the direct cause of 1.6 million deaths and in 2012 high blood glucose was the cause of another 2.2 million deaths. Between 2000 and 2016, there was a 5% increase in premature mortality from diabetes (2).

Diabetes is mostly linked with obesity, junk culture, inactive lifestyle and aging. T2D is associated with hyperglycemic conditions in blood and insulin resistance. Excess lipids accumulate in tissues except adipose tissue, such as the liver, muscle, and islets which are the main cause of insulin resistance and impaired function (3). Also, factors such as Insulin secretory dysfunction, apoptosis of functional beta-cells lead to an inability to compensate for insulin resistance. It is shown that increasing age and inactive lifestyle lead to loss of pancreatic islet function which are central to development of T2D. Here comes the missing link epigenetics which acts as a bridge and connects the influence of environmental factors and aging with Diabetes. Epigenetics is the extra layer of information in addition to genetic information which regulates the expression of genes. This epigenetic pattern which has been already present since birth can be modified with certain factors and these changes can be reversed too. These reversing changes provide us a great opportunity to study and treat chronic illnesses. It has become increasingly clear that environmental factors, combined with genetic predisposition play a more important role in conferring risk for metabolic diseases.

Epigenetic View

Epigenetic modifications are considered as mitotically heritable changes. Notably, epigenetic effects may also be affected by the environment (exposure to UV light, unhealthy lifestyle, alcohol, pregnancy), making them potentially important pathogenic mechanisms in complex multifactorial diseases such as type 2 diabetes. Epigenetic factors generally include DNA methylation, histone modifications, and microRNAs, and they can help to explain how cells with identical DNA can differentiate into different

cell types with different phenotypes (4). Among all the epigenetic factors, methylation and acetylation are great choices of interest due to their wide presence.

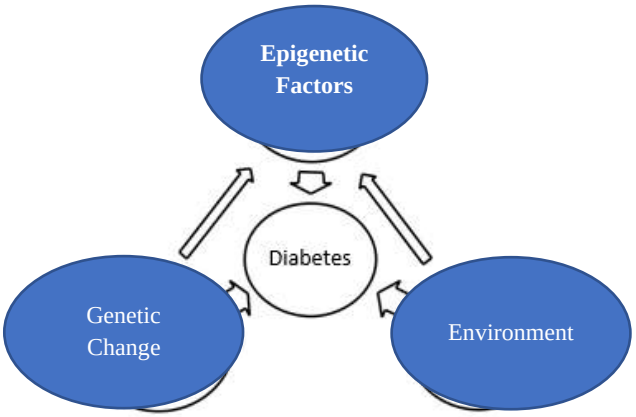

Figure1: Factors affecting Diabetes

Various common modifications:

miRNAs that are single stranded non-coding RNA present in eukaryotic cells and viruses, basically function in RNA silencing and post-transcriptional regulation of gene expression. Some of the miRNAs are involved in metabolic regulation of glucose homeostasis and in epigenetics of T2D. It has been shown that miR375 present in pancreatic islets is indirectly related to the number of beta-cells such that deletion of miR375 leads to hyperglycemia and reduction in the number of beta-cells. Scientific experiments proved that knockdown of miR375 in MIN6 cells led to enhanced glucose stimulated insulin secretion while overexpression led to 40% reduction in insulin secretion (5). This overexpression of miR375 is caused by loss of repressive histone marks and DNA methylation.

Transcription factor such as PDX1 also known as insulin promoter factor 1 which is essential for pancreatic development, beta-cell differentiation, insulin production and glucose homeostasis by regulating transcription of multiple genes such as insulin, glucose transporter (GLUT2) and glucokinase (6). Silencing via methylation at PDX-1 promoter decreases the amount of beta-cells produced which leads to insulin resistance and the inability of the beta-cells to produce an important peptide that prevents vascular deterioration and neuropathy caused by vascular inflammatory responses.

Pregnancy also plays a certain role in epigenetic modification. It has been shown that in rodents, during pregnancy islet cell mass increases due to expression of Men1, a gene that is mutated in multiple endocrine neoplasia type 1 (Men1). During pregnancy, Men1 is downregulated in pancreatic islets, leading to an increase in β-cell proliferation and total mass increment. Menin binds to the promoters of $p27^{Kip1}$ and $p18^{INK4C}$, genes that encode two cyclin-dependent kinase (CDK) inhibitors that prevent β-cell proliferation (6). Reductions in menin led to reductions in promoter occupancy at these genes and a subsequent increase in cell proliferation, providing a plausible mechanism for pregnancy-induced changes in islet expansion.

In the subsequent discussion, we will mainly focus on the most common modification which occurs in DNA i.e, methylation which is one of the reasons contributing to T2D. Methylation is known to occur at

CpG islands (CG dinucleotides) which form 5' methylcytosine. meCpG is associated with formation of repressive chromatin structure that leads to decreased transcription of DNA hence lower gene expression. DNA methylation requires the activity of methyltransferases. There are two groups of DNA methyltransferases: DNMT1, which copies the DNA methylation pattern between cell generations during replication (maintenance of methylation), and DNMT3a and DNMT3b, which are responsible for de novo methylation of DNA (7). Also, expression of insulin gene is inversely correlated with degree of methylation in CpG sites specific manner.

Regulation of insulin promoter

The insulin promoter is regulated by DNA methylation, with hypomethylation observed in beta-cells and hypermethylation in other cells. Peroxisome proliferator-activated receptor gamma coactivator 1 alpha (PGC-1α) is an important transcription coactivator regulating cellular energy metabolism. Accumulating evidence has indicated that PGC-1α is involved in the regulation of T2DM. The studies have found that PPARGC1A (encoding mitochondrial regulator PGC1-alpha) were all hypermethylated in islets from donors with T2D compared to islets from non-diabetic donors.

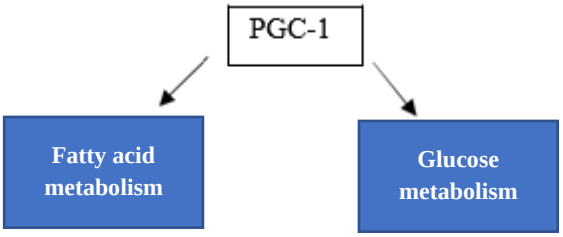

Figure2: Major effect of PGC-1

PGC-1alpha having direct impact on glucose metabolism regulates the enzyme activity of glucokinase. Glucokinase is a key enzyme in hepatic glucose utilization, and its activity is decreased in the liver of diabetic patients. Enzymes are involved in the conversion of glucose into glucose-6-phosphate in the glycolysis pathway, increasing ATP/ADP ratio in the cell. Increased ATP/ADP ratio is directly linked to increased cytoplasmic calcium concentration which results in the insulin secretion in blood. Moreover, in age compared with young rats, the liver displays reduced levels of glucokinase expression and enzyme activity in parallel with increased DNA methylation of the glucokinase promoter. When hepatocytes of aged rats were cultured in vitro and the DNA was chemically demethylated, there was a substantial increase in glucokinase expression, suggesting an important role for DNA methylation in the age-related regulation of this gene (8).

Method for Identifying DNA Methylation

Generally, there are three primary ways to identify and quantify methylation in DNA. These are sodium bisulfite sequencing, differential enzymatic cleavage and affinity capture of DNA. DNA methylation of PPARGC1A gene can be studied by Bisulfite sequencing analysis. It provides a qualitative, quantitative and efficient approach to identify 5-methylcytosine at single base-pair resolution. The methylated DNA is treated with sodium bisulfite after denaturation. Here, unmethylated cytosine residues are converted to uracil whereas 5-methylcytosine remains unaffected (9). Later PCR amplification is performed and uracil

residues are converted to thymine. In this way, DNA methylation status can be determined by direct PCR sequencing or cloning sequencing.

Table1 - Summarized expression of genes

Gene	modification	Expression
miR375	loss of repressive histone marks and DNA methylation	overexpression
Pdx1	Hypermethylation	Silenced
Men1	Binds to of $p27^{Kip1}$ and $p18^{INK4C}$	upregulation
PPARGC1A	Hypermethylated	Reduced expression

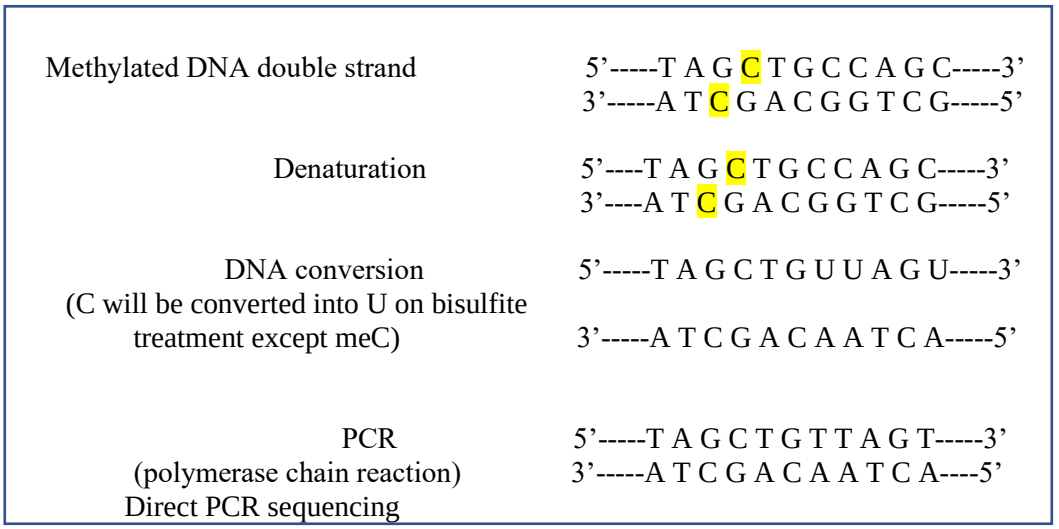

Figure3 - Model of bisulfite sequencing

Conclusion

Among all the various epigenetic modifications, DNA methylation of PPARGC1A gene is considered to be the most leading cause of Type 2 Diabetes that affects the Glucose as well as lipid metabolism. Downregulation of PPARGC1A gene leading to lower expression of PGC1-alpha and decreased glucokinase enzyme activity. This study can be used in determining the effectiveness of potential medicinal plants in pancreatic and hepatic cells. Decreased DNA methylation level of PPARGC1A gene will correspond to significantly correct regulation of this gene and increased enzymatic activity of glucokinase within physiological limit will result in lowering down glycemic level in blood and increased fatty oxidation (10).

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10. WHY THERE IS A VACCINE FOR COVID -19 BUT NOT FOR HIV-AIDS

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A novel coronavirus (CoV) disease named “2019 novel coronavirus disease” or” COVID-19” by the WHO is in charge of the current outbreak of pneumonia that began at the beginning of December 2019 in Wuhan city, China (1). It is caused by the virus SARS-CoV-2. (1) From the phylogenetic analysis carried out with obtainable genome sequences, bats occur to be the reservoir of this virus but the intermediate host has not been detected till now. COVID-19 spreads through close unsafe contact between the infected and the healthy individual. Airborn distribution has not been recorded. This disease whose outbreak started in one place became a pandemic in very less time.

COVID-19 vaccine

The S protein of the virus binds to the ACE-2 receptors of our cells. These receptors are present in many cells of our body including the brain, heart and even the reproductive organs of our body. Due to the tremendous spread of this virus and its deadly effects scientists were in a need to find its vaccine as soon as possible to develop herd immunity in the population. So, within a year, the scientists found the vaccines for COVID -19 disease in order to bring our lives back to normal (2).

Different vaccines are now available in various countries. In the U.S two vaccines have got FDA approval for use;

- The Pfizer-bioNtech COVID-19 vaccine (95% effective) and
- The Moderna COVID-19 vaccine (94% effective)

Both vaccines are made using a newer mRNA technology. These vaccines operate by encoding a fragment of the SARS-CoV-2 spike protein on its surface. As a result, antibodies against SARS-CoV-2 are made by the immune system to help fend off future illnesses. After that, both the protein and the mRNA are eliminated, while the antibodies stick around for protection. Right now, India is using two vaccines which are Covishield and Covaxin. Covishield has been developed by AstraZeneca and Oxford University and is being manufactured by Serum Institute of India So, if we can develop a vaccine for COVID -19 in such a short period of time then why haven't we developed one for HIV-AIDS even after decades have passed?

HIV-AIDS

Before reaching the answer let's explore a few aspects of HIV-AIDS. HIV (human immunodeficiency virus) is a virus that targets the immune system of an individual. It attacks the cells that help the body to fight infections making a person more prone to other infections. HIV has a long incubation period, causing symptoms of diseases and finally AIDS. HIV can damage the brain, kidney, gonad and heart directly and can cause cognitive impairment, renal insufficiency, hypogonadism and cardiomyopathy (3).

HIV is transmitted by the transfusion of body fluids (blood, seminal fluid, vaginal fluid) of an infected individual. Upon transmission, HIV gets attached to the host T cell and penetrates it via CD4+ molecules and chemokines receptors. After penetration, the viral RNA and several HIV encoded enzymes reverse transcriptase, protease, and integrase are released into the host T cell. The viral RNA is converted to DNA by enzyme reverse transcriptase before it is incorporated into host cell DNA. Once the reverse transcription is completed the viral DNA can enter the nucleus of the host cell and then be inserted into the host cell DNA by enzyme integrase. This integrated viral DNA is now replicated in the host cell, it is transcribed to viral RNA and translated to viral proteins. These viral proteins then assemble into virion at the inner membrane of the host cell and then bud off. These immature virions are matured by enzyme proteases, thousands of virions are produced by the host cell to infect other T cells. The infection causes depletion of T lymphocytes which are involved in cell-mediated immunity and humoral immunity (3). Continuous viral replication results in AIDS.

HIV is one of the deadliest viruses and also a public concern as it cannot be prevented by vaccination. It was identified in 1984, and till now it has infected millions of people worldwide.

So, what are the difficulties that we are facing in the development of vaccines for decades?

- **HIV blindfolds the immune system**
  The HIV virus attacks the immune system and weakens it in such a way that it cannot fight the diseases anymore. Even after injecting a vaccine, we need the immune system to act and produce antibodies but in AIDS the immune system is not able to produce antibodies sufficiently, which demolishes the function of a vaccine.

- **Vaccines are typically made to mimic the immune reaction of recovered people.**
  After contracting HIV, however, nearly no one has recovered. As a result, vaccinations are unable to imitate an immunological response.

- **Vaccines protect against disease, not infection.**
  Until HIV proceeds to stage 3, or AIDS, it is an infection. Vaccines give the body additional time to eradicate an infection on its own before disease develops in most infections. HIV, on the other hand, has a long period of dormancy before progressing to AIDS. During this time, the virus hides in the DNA of the virus-infected person. The body cannot find and destroy all of the hidden copies of the virus to cure itself. So, a vaccine to buy more time would not work on HIV.

- **Killed or weakened HIV viruses can't be used in a vaccine**
  The majority of vaccinations are created with viruses that have been killed or weakened. However, HIV that has been killed does not elicit an immunological response in the body. The use of any live form of the virus can be fatal.

- **Time consumed in clinical trials**
  More and more time is wasted when it comes to clinical trials of the vaccine. This could be due to a lack of volunteers and it takes a lot of time for a vaccine to get permission to get tested on people by the concerned authorities. Sometimes many years pass by and the scientists do not get the permission to experiment with the vaccine on organisms or humans but in the case of the corona, this time was saved because the people volunteered by themselves and also it got the approvals quickly for the trials.

- **Typical vaccines are effective against diseases that are rarely encountered**
  This can include Diphtheria and Hepatitis B but in the case of HIV, there is a risk factor for exposure to HIV daily. Therefore, there are more chances of infection that cannot be prevented by a vaccine.

- **A vaccine may target one form of virus and not other forms**
  HIV mutates frequently and is found in many forms which are genetically distinct. This makes it difficult for a vaccine to target HIV (4).

- **Most vaccines provide protection against viruses that enter the body via respiratory and gastrointestinal systems.** Most viruses enter the body via these two systems, unlike HIV which enters via body fluids like blood, seminal fluid and vaginal fluid. We have less experience in providing protection against viruses that enter the body in this way.

- **The animal model plays an important role in understanding the pathway of infection and how our immune system will respond to it** (4)
  There is, however, no reliable non-human animal model for HIV research. Animal HIV vaccine experiments have failed to produce a reliable prediction of how the HIV vaccine will perform in humans.

Despite these difficulties, researchers are trying many different approaches to develop an HIV vaccine. Currently, researchers are working with the following types of vaccines:

- **Peptide vaccines** use small proteins from HIV to trigger an immune response.
- **Recombinant subunit protein vaccines** use larger pieces of proteins from HIV.

- **Live vector vaccines** use non- HIV genes in the body to trigger an immune response. The smallpox vaccine uses this method.
- **Vaccine combinations,** or "prime-boost" combinations, use two vaccines one after another to create a stronger immune response.
- **Viruses like particle vaccines** use a noninfectious HIV lookalike that has some, but not all, HIV proteins.
- **DNA-based vaccines** use DNA from HIV to trigger an immune response (4).

Human immunodeficiency virus 1 (HIV-1) was the first primate virus shown to be inhibited by RNA interference (RNAi). Early studies used both synthetic and promoter expressed small interfering RNAs to demonstrate that this virus was susceptible to RNAi. In addition to targeting the virus itself, RNAi mediated down-regulation of cellular targets that encode receptors required for viral entry also proved to be effective. This has propelled the development of RNAi based gene therapy approaches for the treatment of HIV infection in humans (2).

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11. BOVINE COLOSTRUM CONSTITUENTS AND ITS HEALTH BENEFIT

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Bovine colostrum is the milky fluid produced during the first few days after parturition before original milk and it is rich in various macro and micronutrients including Immunoglobulins, lactoferrin, lysozymes, fat, casein, whey protein, growth factors, vitamin and mineral, peptides having antimicrobial activity and other bioactive molecules. (1). BC protects newborn calves from various infections and diseases. In humans, bovine colostrum supplements help in support and prevention of various diseases including cardiovascular disease, neurological disease, inflammatory bowel disease, skin disorder, gut microbial symbiosis, immune-related, and type 2 diabetes mellitus. (2) Angiotensin-converting enzyme [ACE] plays a central in the regulation of blood pressure by the central vasoconstrictor angiotensin 2. Beta-lactoglobulin is a source of peptide that helps in lowering blood pressure by inhibiting the ACE. (3) IgG affects severe and chronic gastrointestinal distributions, upper respiratory tract infection, and LPS-induced inflammation.

There are various growth factors present in bovine colostrum like Epidermal growth factor (EGF), BTC, insulin-like growth factors (IGFs), transforming growth factor (TGF-β), Fibroblast growth factors (FGF), which help in stimulating the growth of gut. In the future, antimicrobial components and growth factors can be used as potential components in clinical nutrition (4). Antimicrobial components of colostrum lactoferrin, lactoperoxidase, and lysozyme.

Lactoferrin, the iron-binding glycoprotein, has other biological functions including antibacterial, anti-inflammatory, and the iron-binding antioxidant protein present in tissues-it inhibits the growth of bacteria by providing an iron-deprived environment. Lactoperoxidase enzyme kills the bacteria by oxidative mechanism properties. The lactoperoxidase along with hydrogen peroxidase and thiocyanate generate a short-lived hypothiocyanite having antibacterial properties.

Thus antimicrobial and antibacterial properties have various applications including mastitis prevention and also improve human health (5). BC reduces the accumulation of fat, eases the motion of glucose to muscles and enhances immune function, and helps in the reduction of blood glucose levels, ketone body, cholesterol, and TGs (6). Bovine colostrum strengthens the immune system and promotes gut health but there is a gap in clinical trials.

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12. BIOCHEMICAL BASIS OF THE SUPER CROP OF OUR ANCESTORS – MILLETS

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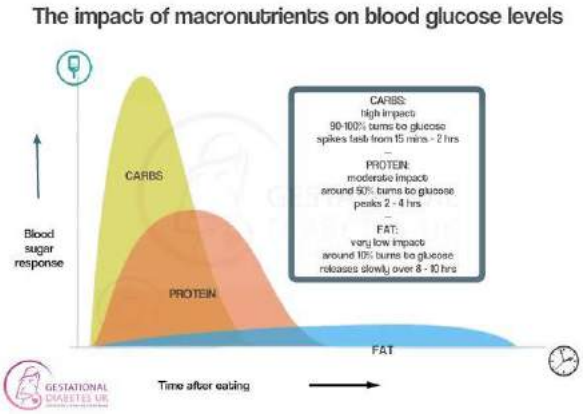
180,000,000,000. What is this no.? Yes, one hundred eighty billion. This is the total money spent in India per year on diabetic care. 1.35 billion is our population out of which approximately 20-25 percent are diabetic, up to 40 percent are suffering from hypertension, up to 40 percent are suffering from obesity and up to 30-35 percent population is diagnosed with cancer, one of the scariest diseases (1). You can go

on writing down the list. We have become so busy in our lives that we have ended up failing to understand the importance of our health.

Let us understand it through a little story of Akbar and Birbal. So, there was a competition in Akbar's Darbar and he asked a question to all the people. The question was what makes a person the happiest and the person who gave the answer which pleased Akbar would get rewards. Someone said a lot of gold, someone said a lot of food, but Birbal said that every morning when he goes and clears his bowels, it makes him very happy. Everyone started making fun of him, even Akbar started laughing at him. To prove his answer, Birbal mixed some medication in Akbar's food just before he was going in a public session. Akbar went there and started getting the urge to go to the washroom. Being the king, he could not leave the session before he finishes his duties, so he sat agitated and, in the end, he rushed and cleared his bowels. When he came back, he felt very relaxed, and then Birbal asked him if he agrees that clearing his bowels makes him the happiest. We realize the importance of clearing our bowels every day but is that happening with everybody? No, right? Constipation is one of the most prevalent conditions in the population. So, what is the solution for all of these problems? It is the food we consume. We all mostly eat rice and wheat daily. But do they satisfy the definition of food? Yes, they give us energy but they release glucose within 30mins into our blood and have no cleansing effect on the body.

Our food should contain fiber which regulates the release of glucose and is responsible for the cleansing of the blood. Hence, we need to find foods that are rich in fiber. We come across grains like ragi, jowar, bajra, corn, etc., which have 2-4 percent fiber in them, unlike rice and wheat which have just 0.2-1.2 percent of fiber. But grains like foxtail millets, Kodo millets, little millets, barnyard millets, and browntop millets are extremely rich in fiber which makes them release glucose in the blood within 5-6 hrs. These are called positive millets.



(Source: gestationaldiabetes.co.uk)

Millets (Source: healthshots.com)

Chemical basis of super food properties of millets

In India, millets have been mentioned in some of the oldest Yajurveda texts thus indicating that millet consumption was very common, pre-dating to the Indian bronze age (2). Millets were always part of the traditional Naga diet, along with rice, in Chizami village of Phek district in Nagaland. The miracle constituent of millets is fiber. Fiber is a carbohydrate, but unlike sugars and starches, it's not easily

digested in the body. Chemically, dietary fiber consists of non-starch polysaccharides such as arabinoxylans, cellulose, and many other plant components such as resistant dextrin, inulin, lignin, waxes, chitins, pectin, beta-glucans, and oligosaccharides. As soluble fiber moves through your intestines, it mixes with water and forms a gel-like substance, which prevents macronutrient (carbohydrate) absorption. This slows down digestion which helps regulate how much sugar is going into the blood (3), Kodo millets (codon) have high protein content (11%), low fat (4.2%), and very high fiber content (14.3%). They are rich in B vitamins especially niacin, pyridoxine, and folic acid as well as the minerals such as calcium, iron, potassium, magnesium, and zinc. They contain a high amount of lecithin and are excellent for strengthening the nervous system (4). Barnyard millets (Sanwa) are the richest source of crude fiber and iron. They possess other functional constituents i.e., Gamma-aminobutyric acid (GABA) and beta-glucan, used as antioxidants and in reducing blood lipid levels. Foxtail millets (kumkum) have a double quantity of protein content compared to rice. They provide a host of nutrients, have a sweet nutty flavor, and are considered to be one of the most digestible and non–allergic grains. Little millet (kutki/shaven) is high in iron content. They contain about 38% of dietary fiber.

Millets as a therapeutic agent

Millets are receiving an increasing spotlight in combating diabetes. An experiment that has used diabetic mice to test different diets has concluded that added millet protein can increase insulin sensitivities, and reduce blood glucose levels as well as triglyceride levels. A high-fiber diet is associated with response to immunotherapy for cancer. Foxtail and Pro varieties of millets are proven to inhibit the growth of cancerous cells in various tissues according to research (5). Phytochemicals in millets have an antiproliferative effect and lower the formation of cancer cells in the colon, breast, and liver without causing damage to normal cells (6). Therefore, it is now time for all of us to switch from rice and wheat to miracle grain millets.

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13. PLANTS ALTER OUR MOOD: EFFECTS OF PSYCHEDELICS

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Psychedelics are powerful psychoactive substances that alter perception and mood and affect numerous cognitive processes. Psychedelics are also known as serotonergic hallucinogens (1). Classic hallucinogens are thought to produce their perception-altering effects by acting on neural circuits in the

brain that uses the neurotransmitter serotonin. Specifically, some of their most prominent effects occur in the prefrontal cortex—an area involved in mood, cognition, and perception—as well as other regions important in regulating arousal and physiological responses to stress and panic (2). There is a consensus that psychedelics are agonists or partial agonists at brain serotonin 5-hydroxytryptamine 2A receptors 5-$HT_{2A}R$ (1). Agonists are drugs or naturally occurring substances that activate physiologic receptors, partial agonists are drugs that bind to and activate a given receptor, but have only partial efficacy at the receptor relative to a full agonist, and (3). Preclinical studies show that 5-HT_{2A}Ragonist ligands possess cognition-enhancing and hallucinogenic properties (4). Lysergic acid diethylamide (LSD), N, N-dimethyltryptamine (DMT), psilocybin, and mescaline are some of the 'classic' psychedelic drugs.

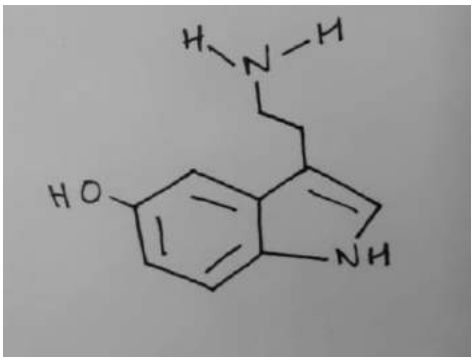

Figure 1 - Structure of serotonin

EFFECTS OF SOME CLASSIC PSYCHEDELICS

LSD (Lysergic acid diethylamide)

In a study by Schmid et al. (2015), LSD (200 μg) was administered orally to 16 healthy subjects in a double-blind, randomized, placebo-controlled, crossover study. LSD produced a pronounced alteration in waking consciousness that lasted for 12 hours and included visual hallucinations, audio-visual synesthesia, and positively experienced derealization and depersonalization phenomena. Compared with a placebo, LSD increased subjective well-being, happiness, closeness to others, openness, and trust (1).

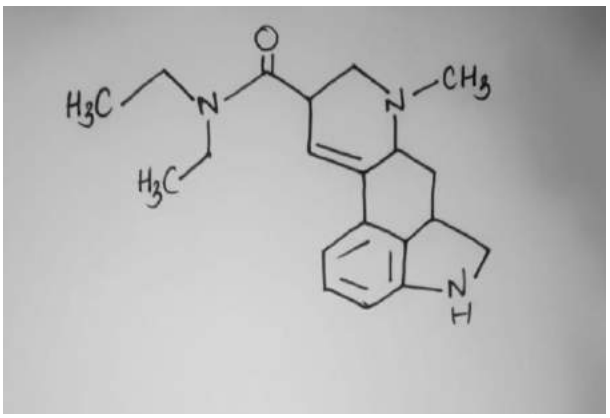

Figure 2 - Structure of LSD

DMT (N, N-dimethyltryptamine)

Oral dosing of DMT via ayahuasca produces both behavioral and neurochemical effects, such as decreases in motor activity, impairment of cognitive function, sympathomimetic effects, increased prolactin and cortisol levels, and decreased lymphocytes increased natural killer cells. Doses of ayahuasca 15 or 30-fold higher than commonly used ritual doses increased serotonergic neurotransmission. Long-term use of DMT in ayahuasca produces measurable brain changes. Long-term ayahuasca users show the difference in midline brain structures using MRI versus matched controls. Interestingly, whereas ayahuasca produced modest impairment of cognitive function in inexperienced users, little or no impairment was observed among inexperienced users (5).

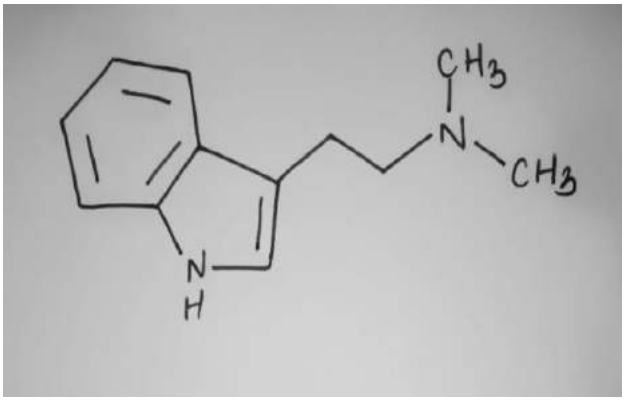

Figure 3 - Structure of DMT

Psilocybin

When psilocybin was administered under structured conditions to well-prepared volunteers, it occasioned experiences that had marked similarities to classic mystical experiences, imparting to the participants substantial personal meaning and spiritual significance. The investigators point out that the high value some subjects placed on the psilocybin experience may in part explain the long-term historical use of psychedelics within some cultures for divinatory or religious purposes (1).

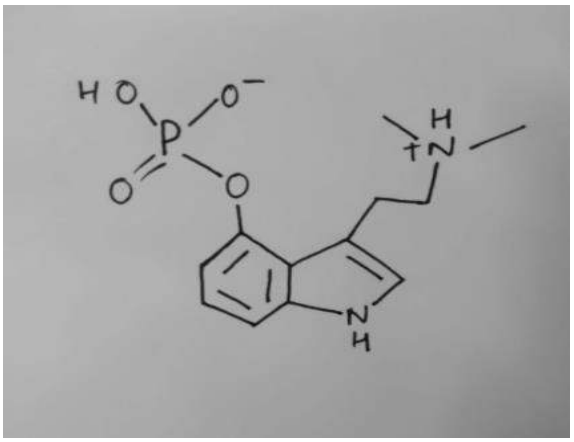

Figure 4 - Structure of psilocybin

Mescaline

Mescaline causes hallucinogenic effects by stimulating serotonin and dopamine receptors in the central nervous system (CNS). It selectively binds to and activates the serotonin 5-hydroxytryptamine (HT) 2A receptor with a high affinity as a partial agonist. It is unclear how activating the 5-HT2A receptor leads to psychedelia, but it likely involves the excitation of noradrenergic neurons in the locus coeruleus and areas of the prefrontal cortex where hallucinogens exert their most prominent effects. Mescaline is also known to bind to and activate the serotonin 5-HT2C receptors. In addition to serotonin receptor activity, mescaline also stimulates the dopamine receptors; however, it is unclear whether mescaline possesses dopamine receptor agonist properties or initiates the release of dopamine. In the peripheral nervous system, mescaline produces a sympathomimetic toxidrome consisting of mydriasis, diaphoresis, and psychomotor agitation. Changes in catecholamine metabolism and adrenal medullary function may be responsible for the agent's peripheral effects. In animals, mescaline decreases the synthesis of the cofactor nicotinamide adenine dinucleotide in the brain. Mescaline may also produce cerebral vasospasm (6).

Two long-term effects—persistent psychosis and hallucinogen persisting perception disorder (HPPD) have been associated with the use of classic hallucinogens (see text box below). Although the occurrence of either is rare, it is also unpredictable and may happen more often than previously thought, and sometimes both conditions occur together. While the exact causes are not known, both conditions are more often seen in individuals with a history of psychological problems but can happen to anyone, even after a single exposure (2).

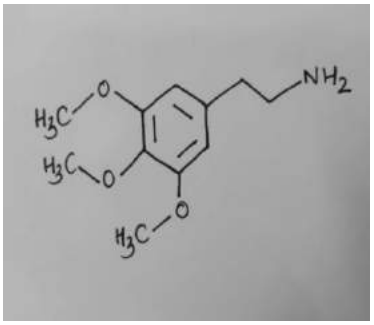

Figure 5 - Structure of mescaline

In a study seven subjects, with 130 patients, were analyzed. Three were conducted in patients with depression, two in patients with anxiety, and two in patients with both. In a supportive setting, ayahuasca, psilocybin, and LSD consistently produced immediate and significant anti-depressant and anxiolytic effects that were endured for several months. Psychedelics were well-tolerated. The most common adverse effects were transient anxiety, short-lived headaches, nausea, and mild increases in heart rate and blood pressure. Though further evidence is required, psychedelics appear to be effective in significantly reducing symptoms of depression and anxiety and are well-tolerated (7).

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14. SIGNIFICANCE OF MOSQUITOES IN ECOSYSTEM AND ERADICATION OF VECTOR-BORNE DISEASES

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Mosquitoes are considered one of the deadliest creatures on earth and oftentimes the most annoying. Malaria alone caused around 627,000 deaths in 2020, compared to snakes which kill around 100,000 in 2021 (1). Mosquitoes have evolved alongside us for over 100 Million years and survived many predators and environmental changes. In 1668, one of the first vector-borne viruses, causing yellow fever was recorded followed by a major epidemic in 1793 in Philadelphia causing thousands of deaths.

Today, some 3400 species of mosquitoes are recognized, which are traditionally placed in 42 genera, all categorized in the family Culicidae. Most of the disease-causing vectors belong to the genera Aedes, Anopheles, and Culex. Aedes mosquitoes carry encephalitis, yellow fever virus, dengue virus, chikungunya virus, and zika virus. The anopheles mosquitoes carry filariasis, malaria, and encephalitis. Culex mosquitoes carry filariasis, encephalitis, and the West Nile virus.

The male and female mosquitoes feed on nectar and other plant juices. However, In most species, females require a highly nutritious blood meal to mature their eggs. Interestingly, many species of mosquitoes are not good carriers of diseases. Most mosquitoes fight malaria with their immune responses to parasites. After a mosquito sucks blood from the host, a peritrophic matrix (or a barrier) forms in between the bug's lining of the midgut and the blood. This prevents the malarial parasite to enter the mosquito's circulatory system. Only the Anopheles mosquito can transmit malaria.

According to WHO reports, in 2020, there were an estimated 241 million cases of malaria worldwide with an estimated 627,000 deaths (2). Children under the age of 5 were the most vulnerable and accounted for 77% of the total deaths in 2020. Additionally, the total funding for malaria control and elimination was estimated at US$ 3.3 billion in 2020.

How are they such good transmitters of microbes? Mosquitoes have substances in their saliva that widen blood vessels, promote bleeding, and shut down the human body's natural first line of defense. The mosquitoes inject microbes in their gut directly into the host's bloodstream, bypassing a lot of immune defenses. So apart from feeding blood and creating a nuisance, do mosquitoes serve any role in our ecosystem? What is the purpose of their existence? Or are they existing just because they haven't gone extinct yet? Well, once this is clear, eliminating mosquitoes would to an extent relieve human suffering.

SIGNIFICANCE OF MOSQUITOES IN THE ECOSYSTEM

Arctic tundra, home to a large population of migratory birds is also a major breeding ground for mosquito species including *Aedes impinger* and *Aedes nigripes*. Tundra lands are covered with snow for much of the year. But they get covered with thick clouds of mosquitoes after eggs laid by the mosquitoes hatch when the snow melts (3).

What would happen if that mosquito biomass vanished? Some estimate that without mosquitoes to eat, the population of migratory birds that nest in tundra could fall by more than 50% (4). But other researchers disagree, saying that midges are a more important source of food for migratory birds.

Mosquitoes also help process detritus, decaying leaves, and microorganisms. For instance, when an insect drowns in water, mosquito larvae (*Wyeomyia smithii*) feed on their waste products, producing nitrogen which is made available for the plants. In this scenario, plant growth might be affected if the mosquitoes are eradicated. Thousands of plants and tropical crops might lose a group of their pollinators in the absence of mosquitoes.

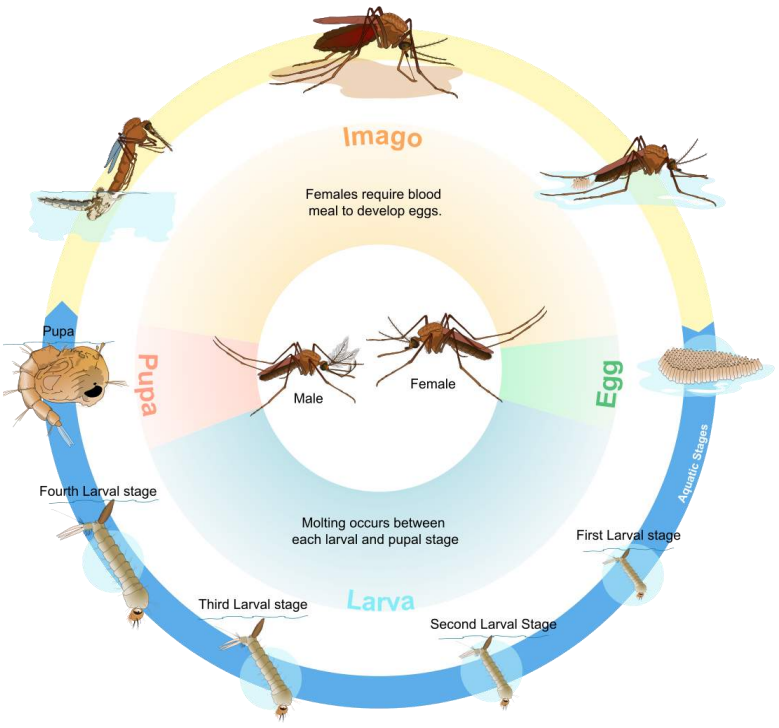

Figure 1 - The life cycle of Culex Mosquito
(Source: https://commons.wikimedia.org/wiki/File:Culex_mosquito_life_cycle_nol_text.svg)

Many species of fish, frogs, insects, salamander, spiders, bats, turtles, dragonflies, damselfly, and lizard would lose a food source. Many species of fish would have to adapt their diet without mosquito larvae. For example, *Gambusia affinis* is a specialized predator that feeds on mosquito larvae. It could have drastic effects down the food chain if these species were to go extinct.

Even though Mosquitoes are delectable things to eat and they're easy to catch, there are many other options on the table except for mosquitoes. Eradication of mosquitoes will force species to find another source of food. Given the huge number of deaths and heavy economic burden faced due to mosquito-spread diseases, it can be argued that the mosquitoes (at least the disease-spreading ones) should be completely eradicated.

METHODS TO CONTROL DISEASE-CAUSING MOSQUITO POPULATION

So mosquitoes do have some roles to play in our ecosystem but this doesn't change the fact that in the end, they are providing an ideal route for the spread of pathogenic microbes. Some scientists think that the ecosystems would heal pretty quickly if specific target vector mosquito species were removed from the food web.

So, why haven't they been dealt with yet?

One of the main reasons is their high rate of reproduction and high rate of evolution. A female mosquito can lay up to 250 eggs at a time and that is also three times during her life. With hundreds of thousands of mosquitoes hatched every day, it is nearly impossible to get rid of them entirely. Mosquitoes are insects that have been around since the Jurassic period. And during those millions of years, mosquitoes have been honing their hunting and survival skills.

Methods used to keep their population in check include the elimination of any kind of standing water near human residences like Emptying watering cans, removing old tires, covering rain barrels, etc. There are some petroleum oils that when added to water form a thin layer suffocating the mosquito eggs. Also, it is recommended to wear full covering clothes whenever temperature permits. Using Mosquito nets and window screens are some easy-to-use and inexpensive techniques to keep a check on the mosquito population in your house.

The most effective method is believed to be the use of chemical repellants on the skin, such as picaridin, DEET(NN-diethyl-meta-toluamide), and oil of lemon eucalyptus (OLE), or para-menthane-diol (PMD) (4). These repellents work by evaporating on our skin and blocking the mosquito's sense of smell which blocks it from locating its target. But Mosquito repellent must be used constantly and reapplied which may irritate the skin and may be toxic to some people and animals. Also, mosquitoes seem to obtain immunity against repellents like DEET pretty quickly.

Many pesticides (Permethrin), insecticides (pyrethroid), and chemical sprays are used to eradicate the mosquito population (5). Even though it is easy to use, it must be spread over a large area to be effective. Also, they can be toxic to many other insect species.

These methodologies, effective to some extent have their disadvantages and can only be used to keep the household mosquitoes population in check. But promising new methods to eradicate mosquitoes from a large area has emerged out to be with the use of SIT irradiated, Transgenic, and (IIT) *Wolbachia* mosquitoes.

1. In the Sterile insect technique (SIT) male mosquitoes are exposed to γ-irradiation or sterilizing chemicals, which causes large-scale damage to chromosomes or lethal mutations in the sperm (6). These SIT males are then released into the wild in large numbers where they mate with wild females

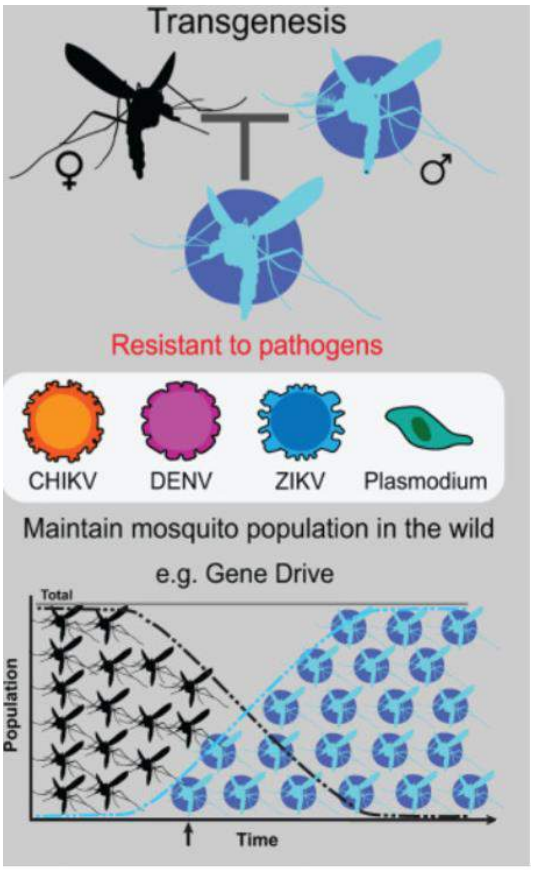

Fig 2 – Transgene based approach for mosquito population modification (Wang et al.)

and very rarely produce any viable offspring. With continuous ongoing releases of SIT males, the mosquito population competitiveness. SIT has had an unreliable success rate as some trials demonstrated reductions in target populations, whereas other trials did not (6). reduces to low levels. The drawbacks are that it requires a large amount of SIT male production and males need to be separated from females before release. Released SIT males often exhibit reduced mating

2. The approach known as the release of insects carrying a dominant lethal gene (RIDL), works somewhat the same as SIT. But instead of random mutations, males carry transgenes that if delivered to the female partner can render the offspring unviable. In one approach the expression of a gene that leads to the activation of flight muscle in female pupae is reduced (7). The daughters of the transgene males are thus unable to fly (8). In another approach, lethality genes are inserted in male mosquitoes, which causes the mosquito larvae to die unless they receive an antidote (9).

In one trial in Brazil, Scientists from the company Oxitec released about 500,000 lethality transgene mosquitoes per week, and in the second trial, they released 1.5 million per week. Continuous release of the transgene male mosquitoes for around a year reduced the population of local *Aedes aegypti* by 80% - 95% (9). But the research is arousing concern about any harmful effects on public health and the environment if they were to mutate. Another technique is using Homing endonuclease gene (HEG)-based gene drive. HEGs encode endonuclease enzymes that recognize a site, cleave a 20–30-bp sequence present on the chromosome, and insert HEGs into this site (10). HEGs could be used to dislocate genes that are essential to pathogen spread (11). Thus, HEGs serve as the vehicle for gene drive in mosquitoes. HEGs due to their aggressive self-spreading nature will require the fewest mosquitoes to be introduced.

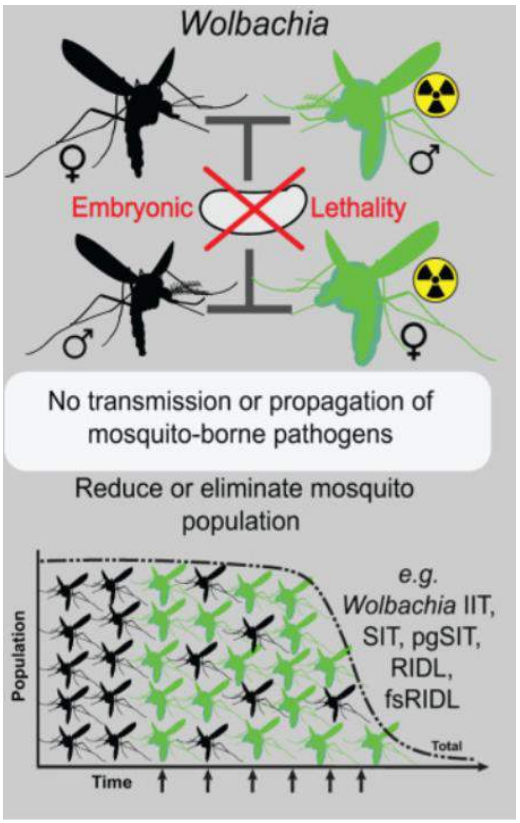

Fig 3 - *Wolbachia* based approach for mosquito population suppression (Wang et al.)

3. *Wolbachia* bacterium is found naturally in an estimated 50% of all the different species of insects. They are passed from one generation to the next through insect eggs (10).
If a male insect has *Wolbachia* and mates with a female that doesn't then the eggs won't hatch known as cytoplasmic incompatibility (11). But, if the female has *Wolbachia* and the male doesn't, she would lay her normal eggs carrying

Wolbachia strain. If the male and female insects are carrying different strains of *Wolbachia* it leads to the death of the offspring (12).

Over a few generations, the number of individuals carrying the same *Wolbachia* strain increases rapidly until nearly all the insects within a population have the bacteria. The *Aedes aegypti* mosquitoes are infected with a strain of *Wolbachia* that is resistant to plasmodium, dengue, Zika, chikungunya, mayo, and the West Nile virus. So even if the mosquitoes bite someone infected with the dengue virus, the virus wouldn't survive inside the mosquito gut long enough to be transmitted to a new person. This is referred to as incompatible insect technique (IIT). A drawback of this technique also raises concern that this could create deadly mutated viruses that are resistant to *Wolbachia*. In a study, *Wolbachia* (example *w*Mel) introgression into *Ae. aegypti* populations were efficacious in lowering the dengue rates in Yogyakarta City, Indonesia (13).

Wolbachia and transgene-based models may revolutionize vector-borne disease control. The advancements in these have led to field trials all around the world. Additional work needs to be done to optimize the efficacy and reduce the costs of these techniques. There are also ethical and regulatory issues that need to be considered before the implementation of these GM mosquitoes.

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15. DILI (DRUG-INDUCED LIVER INJURY)

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The liver is located in the upper right-hand side of the abdomen behind the rib cage. It is one of the important organs and largest glands of our body. Its main function is detoxification of chemicals and metabolizing drugs.

The primary functions of the liver include

1. Bile and albumin production
2. Blood filtration
3. Regulating amino acid and blood clotting
4. Store vitamins and minerals
5. Enzyme activation

Damage and dysfunction of the liver can lead to various liver diseases (1). The common or general symptoms of liver problems includes the following:

1. Abdominal pain
2. Dark urine/dark colored stool
3. No desire to eat
4. Fluid accumulation in legs (edema) and abdomen
5. Jaundice(yellowish skin)
6. Vomiting
7. Itching

DILI is one of the most prominent liver diseases. Drug-induced liver injury (DILI) is defined as a liver injury caused by exposure to a drug or non-infectious toxic agents, it is associated with different levels of organ dysfunction (2). DILI is a relatively rare disease but can be severe and in some cases fatal, leading to liver failure and death.

DILI is classified into two types:
Intrinsic and Idiosyncratic

- Intrinsic DILI - is a predictable dose-related type and occurs in a large proportion of individuals exposed to the drug.
- Idiosyncratic DILI - it is predictable or not usually dose-related and occurs in only a small proportion of exposed individuals.

Despite the fact that idiosyncratic DILI accords in a very small proportion of exposed patients, screening for stress in cell systems and isolated mitochondria is predictive of the risk associated with a large proportion of the drugs known to cause idiosyncratic (3).

Severe DILI symptoms:

1. Insomnia
2. Mental confusion
3. Gastrointestinal (GI) bleeding
4. Kidney failure
5. Ascites-Almost all cases of a drug can cause liver injury.

Examples of drugs associated:

- Intrinsic DILI: Acetaminophen, Antimetabolites, Cholestyramine
- Idiosyncratic DILI: Allopurinol, Amiodarone, Bosentan, Diclofenac, Fenofibrate, Isoniazid.

The commonly taken drug i.e., Paracetamol (acetaminophen) is an example of Intrinsic DILI and its hepatotoxicity is important, as according to the studies in the US and parts of Europe, Acute liver failure (ALF) is commonly caused by it. The high appreciation of this drug is due to its assumed analgesic and antipyretic properties (2). This is most common, as people consider taking overdoses of such analgesics considering more number doses will cure their pain earlier, rather overdoses of any drug is its pitfall which causes problems and severe illnesses like DILI.

DILI cases: Acute and chronic

° Acute DILI- may resolve in a few months (<3 months)
° Chronic DILI -may process for several months (more than six months)

RISK FACTOR

1. **Age**: With increasing age, the chances of liver injuries and damage also increase. Children and old groups are highly prone to liver injury mainly due to dose-related or overdose. Hepatocellular injury is more common in younger people, while older patients are more susceptible to a cholestatic pattern of injury (3).
2. **Nutritional status**: Underweight can lead to drug toxicity while overweight or fatty liver may impair liver metabolic function.
3. **Alcohol consumption**: A person with heavy alcohol consumption is usually at the highest risk of having a liver injury which maybe sometimes can be fatal too.
4. **Drug intake during pregnancy**: This poses risk for DILI eg. Antimicrobial drugs (tetracycline and antiretroviral) antihypertensive drugs (methyldopa and hydralazine) and antithyroid medicines (propyl thiouracil) are known drug that cause DILI during pregnancy.

Table 1- Common drugs, their mechanism of injury, and hepatotoxicity (3).

DRUG	*MECHANISM OF INJURY*	*HEPATOTOXICITY*
Acetaminophen	1.Mitochondrial damage 2. Nuclear DNAfragmentation	4 g daily lead to a transient elevation in serum aminotransferase level
Amiodarone	1. Damage lipid bilayers 2. Disturbance of lysosomalfunction	200-300 mg daily lead to serum enzyme elevation
Cyclosporine	1. Drug-drug interaction 2. Decreases bile flow	Mild elevation in serum bilirubin level
Allopurinol	Immunoallergic	Transient and minor level tests abnormally
Chlorpromazine	Hypersensitivity, based upon the clinical feature of a shortlatency period, fever	Elevated serum alkaline phosphate
Tetracycline	1. mitochondrial injury (inhibition of mitochondrial protein synthesis) 2. Fat metabolism inhepatocytes	Elevation in serum aminotransferase and alkaline phosphate level.

HOW DO DRUGS CAUSE LIVER DISEASE?

Most of the drugs are lipid-soluble and metabolized in the liver.

1. Dose-dependent

Drug dose plays an important role in causing intrinsic DILI. For example, in acetaminophen hepatotoxicity, 1-5 Mortality rates have been approximated at 0.4% in overdose patients, translating to 300 deaths annually in the United States (4).

2. Drug interactions

The mechanism of action of drugs changes when taken with another drug, food, or with certain medical conditions. Drug interactions may cause the drug to be more or less effective, or cause effects on the body that are not expected (5).

a. Drug-Drug interaction

These generally include over-the-counter (OTC) or non-prescribed drugs, this is the reason it is recommended to read the label and its ingredients before consumption. This occurs when two or more drugs react with each other. For example, mixing a sedative with an allergy drug (antihistamine) can slow your reactions.

b. Drug-Nutrient reaction

They are defined as a physical, chemical, physiologic or pathophysiologic relationship between a drug and a nutrient (6).

i. **Food:** Hindrance in the absorption of drugs due to the presence of food in the digestive tract often, such interactions can be avoided by taking the drug 1 hour before or 2 hours after eating.

ii. **Dietary Supplements:** These include medicinal herbs and products that contain a vitamin, mineral herb, or amino acid intended as a supplement to the normal diet.

c. Drug-Disease interaction

Sometimes, drugs that are helpful in one disease can be harmful to another disease. For example, some beta-blockers taken for heart disease or hypertension can worsen Asthma.

TYPE OF LIVER DISEASES CAUSED BY DRUGS

1. **Increase in liver enzyme in Blood (AST/ALT)**
   AST/ALT [aspartate aminotransferase /alanine transaminase] resides in cells and bile ducts. Some drugs lead to cell injury and these enzymes come out of cells into the blood and lead to elevation.
   Example: Statins

2. **Acute Liver Failure (ALF)**
   Some drugs cause ALF and it can later lead to Hepatic encephalopathy and coagulopathy and sometimes death.
   Example: Paracetamol

3. **Cholestasis**
   Drugs causing Cholestasis infer the secretion of Bile which leads to the accumulation of bile in the body and lead to Jaundice and itching.
   Example: Erythromycin, Ampicillin/clavulanic acid

4. **Steatosis (Fatty Liver)**
   Maybe excessive alcohol intake leads to the accumulation of fat in the liver and NAFLD due to obesity and diabetes.
   Some drugs cause fatty liver.
   Example: parenteral nutrition, griseofulvin.

5. **Cirrhosis**
   Liver disease like hepatitis, fatty liver, and cholestasis leads to hepatic cell death and severe scarring of the liver leads to cirrhosis. It is an irreversible condition.
   Example: Methotrexate

6. **Hepatic vein thrombosis**
   Blood is purified by the liver and from the Intestine blood is transferred to the liver through the portal vein and blood goes to the heart from the hepatic vein.
   Certain drugs cause thrombosis in the portal vein and hepatic vein which leads to liver failure.

CURRENT SCENARIO

1. **The use of anabolic steroids causing DILI**
   Anabolic steroids induce hypertoxicity which is dose-dependent, commonly it causes cholestasis, acute

cholestatic hepatitis, acute hepatocellular injury, and hepatic tumors (7).Anabolic Steroids are very common in the young generation these days. Teenagers, adults, and athletes consume Steroids for muscular strength and for improving their performance. There are many cases reported for the same causing liver damage.

Example- CASE STUDY
A 35-year-old bodybuilder, completely asymptomatic, after taking high doses of (AAS) Androgenic-anabolic steroids (oral stanozolol, oxymetholone, testosterone) for more than 15 years developed hepatic adenomas secondary to AAS abuse. The individual has been included in liver transplantation because of the severe hepatomegaly and the risk of lesions in the liver turning into malignant (8).

2. **Herbal and alternative medicines hepatotoxicity**
Herbal components and medicines are becoming more popular nowadays and are considered the best alternative and believed to be more safe, effective and without any side effects. Rather, the fact these medications have shown a number of side effects and a large spectrum of liver injury as the amount of dose to be taken for curing a particular disease is usually not mentioned. By the estimation of The US drug-induced liver injury network (DILIN), 16% of overall DILI cases have been accounted for by the Herbal preparation and dietary supplements (9). To date, more than a hundred medicinal preparations have been reported to be toxic to the liver.

Examples- Aloe vera, *Teucrium polium* (germander), *Tinospora crispa* (Giloy),

ashwagandha, green tea, cascara, Echinacea, glucosamine, Herbalife.

In Ayurvedic medicine, Giloy has a great hold in the treatment of various disorders like the reproductive system, blood, metabolism, and fat. It is considered good for the treatment of Jaundice, tuberculosis, and many others. During the Corona period, Giloy was considered an immunity booster and helped to fight Covid-19 but rather many cases were reported of liver damage as its side effect.

There are several case studies related to Giloy causing liver injury.
Examples-

- A 49-year-old male took 10 pellets per day of *T. crispa*. About 4 weeks later he experienced dark urine, pale stools, asthenia, and right hypochondrial pain. Took pallets for 2 months and was referred to the Hospital with Jaundice. He completely recovered after discontinuation of herbal medicine (10).

- A 63-year-old man was admitted to the Emergency Department suffering from altered mental stress after having consumed the juice of *T. crispa* stem for one week. He continued the consumption of *T. crispa* juice for several days and died within a few weeks (11).

DIAGNOSTIC TEST TO RULE OUT EARLY LIVER DAMAGE

Laboratory, imaging, and pathologic examination can be done to rule out initial liver injury. Common routine tests to identify the liver problem:
- liver function
- complete blood count
- ultrasonography

- liver biopsy

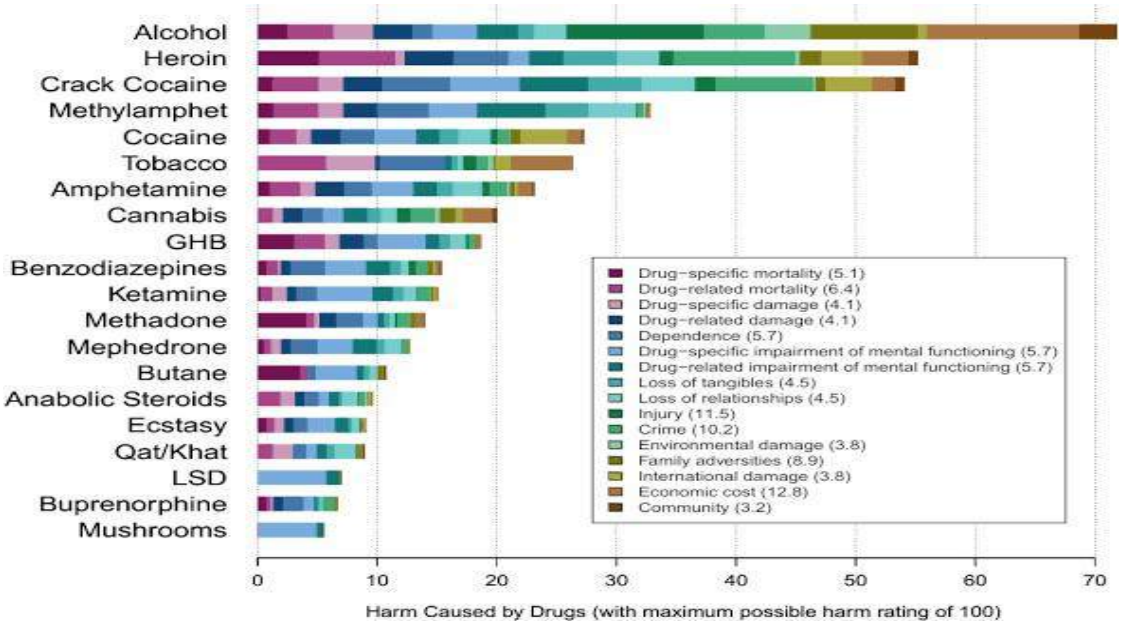

Figure 1 - Harm caused by drugs
(Source:-https://commons.m.wikimedia.org/wiki/File:HarmCausedByDrugsTableDetailed. svg)

TREATMENT

1. Early diagnosis is the pillar of treatment of DILI.
2. The main step is to stop and withdraw suspected agents/ drugs, which usually results in recovery.
3. In severe cases, like a person suffering from jaundice and impaired liver function, should consult with a specialist because these can lead to liver damage/ failure, or even sometimes fatal, liver transplantation may be required.
4. According to the clinical pattern, it can be treated with a relevant anti-inflammatory (12).
5. The treatment of DILI can also be done by using an antidote (work against drug) to drugs that causes liver injury.

Such hepatotoxin antidotes include:

a. N-acetylcysteine for acetaminophen toxicity
b. Penicillin for 'Amanita phalloides' toxicity.

PRECAUTIONS TO AVOID DILI

1. Do not perform self-medication and do not consider the counter prescription.
2. Go for regular liver test monitoring if you are on medications like antibiotics, analgesics, antiviral, antitubercular drugs, and immunosuppressants.
3. Avoid consumption of herbal and dietary supplements without any doctor's prescription.
4. Avoid taking anabolic steroids and alternative medications.
5. Always take care of special instructions mentioned on the drug, regarding- dose, temperature, etc.

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16. A LOOK INTO THE HUMAN SKIN MICROBIOME

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The Human skin microbiota is composed of a variety of bacteria, fungi, and viruses that live on our skin. Microbiome/Microbiota refers to the collection of genomes of all microorganisms inhabiting a particular environment. After the gut, there are more organisms on the skin than anywhere else in thy body (1). The skin is our body's largest organ, and it is colonized by helpful bacteria. It is the first line of defense and acts as a protective barrier against mechanical, thermal, and physical injury. In circumstances when this barrier is broken or when the balance between commensals and pathogens is disturbed that the person suffers a skin disease.

Microbial Niches

The surface of the skin is home to a sprawling and complex microbial ecosystem that varies with the anatomical state. The skin sites can be classified as follows: -

1. Oily Skin
(e.g. - Ear folds and forehead)
Sebaceous body sites contain sebaceous glands that secrete an oily substance, Sebum, allowing lipophilic bacteria like *Staphylococcus spp.* and *Cutibacterium acne* to thrive.

2. Moist Skin
(e.g.- The groin and the armpit)
Corynebacterium and *Staphylococcus* flourish in the moist skin. Sweat attracts these species contributing to body odour.

3. Dry Skin.
(e.g.-The forearms and palms)
Dry body sites are home to the greatest variety of microbes because they have high exposure to the surrounding environment. They are rich in species of *Betaproteobacteria* and *Flavobacteriales.*

4. The Feet
Feet have their distinctive ecosystem. They are rich in species of *Corynebacteriaceae*, *Micrococcaceae* and *Propionibacteriaceae*. The fungi present on the feet are much more diverse in comparison to other parts of the body. Foot sites are colonized by a more diverse combination of *Malassezia spp., Aspergillus spp., Cryptococcus spp., Rhodotorula spp.,* and others (1, 2,3).

The members of a microbial community can be studied by utilizing 2 Sequencing Strategies.

- **Amplicon Sequencing** – The segments of DNA or RNA that are targeted with primers and amplified in PCR are referred to as amplicons. The internal transcribed spacer 1 (ITS1) region of the ribosomal gene is amplified in fungi while the 16S RNA portion of the ribosomal gene is amplified in bacteria. The steps involved in performing 16S Amplicon Sequencing include the collection of cutaneous samples, isolation of bacterial DNA, annealing of selected hypervariable loop primer, and amplification of the selected bacterial region through PCR sequencing (4).

- **Shotgun Metagenomic Sequencing**
  Shotgun Metagenomic Sequencing sequences all given genomic DNA from a sample rather than just targeting the 16S RNA genes. It involves the collection of cutaneous samples followed by conversion of all the collected DNA into DNA fragments and then they are sequenced independently. The small amplified sequences produced are called Contigs. They are then arranged to recreate their respective genome and then are compared with online reference databases to determine the organism from which the DNA originated (3, 4).

  A question that could strike us is when does the skin microbiota get established? It is observed that neonates born vaginally acquire bacteria that colonize the vagina canal, whereas neonates delivered through caesarean section acquire microorganisms that are associated with the skin (3). Thus, in newborn babies, initial colonization depends upon the mode of delivery. Skin colonization during early neonatal life is essential to establish immune tolerance to commensal microorganisms. Increased hormone levels in our bodies drive the sebaceous gland to create sebum throughout puberty. Thus, the skin of postpubescent individuals favours the growth of lipophilic microorganisms like *Propionibacterium spp.*,

Corynebacterium spp., and fungal *Malassezia spp* (3). On the other hand, greater abundances of *Streptococcaceae spp*., Proteobacteria, and a more diverge fungal community inhabits the skin of pre-pubescent children. Thus, by adulthood, a final state of equilibrium is reached with a diverse microbiota, that is unique at the genus level for each individual (3, 5).

Table 1 – Various Commensal bacteria, their anatomical location, and benefits

S.No.	Commensal bacteria	Location	Benefits
1.	*Streptococcus salivarius*	Oral Cavity	It contributes to establishing immune homeostasis and regulating host inflammatory responses.
2.	*Staphylococcus epidermidis*	Human epithelial, armpits, head, and nares	They produce chemicals that help reinforce the tight junction between skin cells. Help maintain the skin's physical integrity.
3.	*Propionibacterium acnes*	Skin, in pores, Hair follicles, Sebaceous Glands	They digest oily substances from sebaceous glands thereby creating an acidic environment making it hard for pathogens to colonize.
4.	*Pseudomonas aeruginosa*	Skin, throat	Fights fungal infections thereby killing and inhibiting fungal growth.

The skin barrier and the microbiota act like a guard and are vital for human development, immunity, and nutrition. There is always a balance of host and resident /transient bacterial populations in our bodies. This balance can get disrupted by both Intrinsic (host) and Extrinsic (environmental) factors that change the composition of the human skin microbiome. This microbial imbalance is termed Dysbiosis (Dysbacteriosis). Dysbiosis results in changes in the abundance and diversity of commensal species, thereby affecting the skin barrier function and increasing the chances of chronic skin diseases. *Staphylococcus epidermidis* is an example of a skin commensal however it has the potential to act as a pathogen in immune-compromised hosts. Similarly, *Staphylococcus aureus* though a resident microbe can also act as a pathogen and over-colonize the skin (5).

Microbes are associated with skin disorders

The balance of the skin microbiome and its interaction with the host affects the state of skin health and disease. Some of the most frequent skin disorders are as follows:

A. **Acne Vulgaris** - It is the most prevalent teenage condition and is associated with the bacterium *P. acnes*. It is considered to be the most abundant organism in the microbiota of healthy individuals (3). The Highest density of *P. acnes* is found in the scalp and facial skin ($\sim 10^5$-10^6 /cm^2), followed by the upper lips and torso, and the lower limbs have the lowest density of *P. acnes* ($\sim 10^2$ /cm^2). Its relative abundance varies with age. The four main factors that contribute to acne are (6).

- hypersecretion of sebum
- abnormal proliferation and differentiation of keratinocytes in the hair follicles
- bacterial colonization
- inflammatory acne lesions.

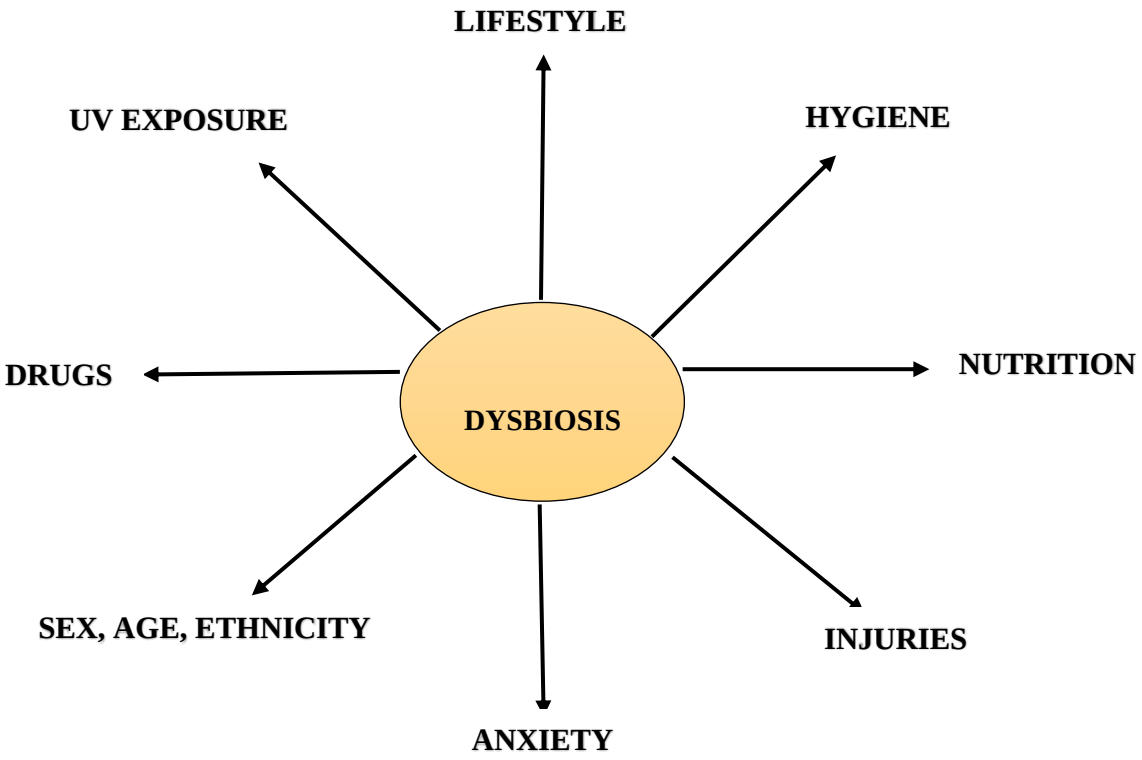

Figure 1 - Various factors affecting dysbiosis

In a study carried out to visualize *P. acnes* in follicles of skin biopsy samples (using fluorescent microscopy), it was observed that acne development was linked to the presence of *P. acnes* in the follicles and its formation of biofilms. Topical and systemic antibacterial medicines are currently used to treat acne, and they help to reduce *P. acnes* activity.

To stop *P. acnes* from growing, a probiotic treatment with *Staphylococcus epidermidis* is employed. When applied topically, *Lactobacillus plantarum* has been demonstrated to be anti-inflammatory and improve the antibacterial characteristics of the skin.

B. **Atopic Dermatitis -** Eczema, or atopic dermatitis, is a chronic, recurrent inflammatory condition. The population of *Staphylococcus aureus* in both lesional and non-lesional skin has increased in people with atopic dermatitis. Mutations in approximately 30 host gene loci have been linked to atopic dermatitis susceptibility, including the gene encoding the skin barrier protein filaggrin and genes related to the immune system (3). Apart from *S. aureus* cultured from the skin of individuals suffering from atopic dermatitis, additional factors have been observed that hypothesize that microbiota has an influential role in disease pathogenesis. Topical and systemic antibiotics, corticosteroids, and diluted bleach baths are all used to treat atopic dermatitis. The use of commensal skin bacteria, *S. epidermidis*, to suppress the growth of *S. aureus* could be a potential probiotic treatment.

Conclusion

The skin microbiota is of high importance as it contributes to the protective functions of human skin in many ways. Many studies are currently focused on the manipulation of the skin microbiome to explore its therapeutic potential (7). With the increasing understanding that the skin microbiome plays a major role in maintaining human health, the interest of researchers in the effect of cosmetics on the skin is rapidly growing. Soaps, fragrances, and personal care products alter the skin microbiome. Products containing harsh preservatives and synthetic ingredients change the pH of the skin and change the skin microbiota. The need to maintain a healthy skin microbiome has to lead to the development of microbe-related products (Prebiotic, Probiotic, and Post biotic skincare products). Therefore, it becomes imperative to take care of our skin to protect this community of microorganisms to prevent microbial imbalance which could lead to several skin diseases (7).

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17. *PANAX GINSENG* IN TREATMENT OF ALZHEIMER'S?

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Alzheimer's disease (AD) is a neurodegenerative disorder that disintegrates memory and thinking skills and, therefore the ability to perform simple day-to-day chores. It is characterized by amyloid β-protein (Aβ) plaques and tangles, and the weak/lost connection between the neurons in the brain. The parts of the brain that associate with memory are affected, that is the entorhinal cortex and the Hippocampus (1,2). The unusual metabolism of amyloid precursor protein (APP) is directly correlated with the disease and is considered a cause. Aβ clearance capability, mitochondrial function, dysfunction of the synapse, down-rate of anti-oxidants, an increase of oxidative stress, and inflammatory response are modified in the Alzheimer's brain (3,4).

Panax ginseng (Korean Red Ginseng) or "Miracle root" is a traditional medicine of the Far East countries of Asia. It has been used for over 2000 years and it is known to treat a variety of ailments and has several beneficiary properties (5).

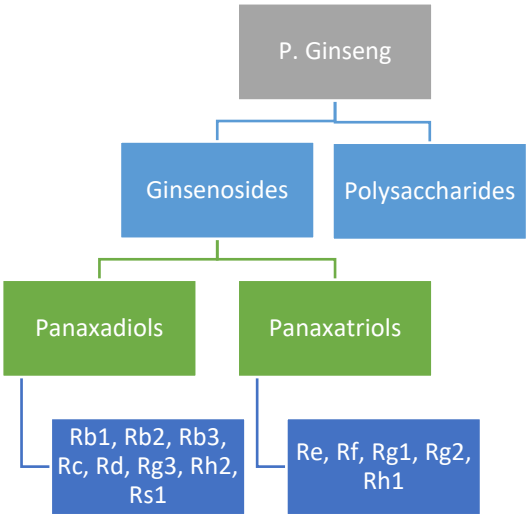

Fig 1: Composition of Ginseng

Roles and components of Ginseng

Being Anticarcinogenic, immunomodulatory, anti-inflammatory, anti-allergic, Anti-atherosclerotic, Anti-hypertensive, Anti-stress, positively effective on CNS and various metabolic processes, and Anti-diabetic, it is a clinically important medicinal herb in research (3, 6).
Panax ginseng constitutes of the active compounds- ginsenosides and polysaccharides. The saponins ginsenosides are of two classes being- panaxadiols and panaxatriols. There are more than 40 ginsenosides that have been isolated and identified from *P.Ginseng* (7,8).

Observed Effects of Ginseng

Recent studies have shown that Korean Red ginseng extract has shown noticeable improvement in Alzheimer's disease. In mice, consumption of ginseng for 7 months demonstrated a decrease in oxidative stress and upraising plasticity-related proteins, thus leading to the prevention of memory loss in aged mice with Alzheimer's.

Figure 2 - Ginseng Root
Source:www.healthline.com/nutrition/ginsengbenefits#TOC_TITLE_HDR_2

P. ginseng exerts neuroprotection properties by regulating the phosphatase activity of purified calcineurin. It also regulates tau phosphorylation in SY5Y human neuroblastoma cells as hyperphosphorylation is one of the neuropathologic features in the brains of AD patients. Here are some positive effects of ginsenosides on treating Alzheimer's Disease:
Rb1- Rb1 is responsible for the reversal of several direct or indirect neuroinflammation at many Alzheimer-related sites in primary cortical neurons through antioxidant pathways

Rg1- Alzheimer's disease is associated with cell death due to cell stress and chronic inflammation. Rg1, inhibiting the expression of caspase-3, prevents apoptosis in the brain cells of rats. It prevents memory and learning impairment by stopping the cortical and hippocampal choline acetyltransferase activity decline induced by Aβ25-35.

Rg2 - It prevents memory impairment by anti-apoptosis, through a range of mechanisms via the expression of various protein levels.

Rg3 - It promotes the phagocytosis of Aβ, and as Aβ are the major constituents of plague, Rg3 has therapeutic potential in the treatment of Alzheimer's.

Re and Rh2 - Aβ bring about reactive astrocytes that contribute to Alzheimer's disease progression. Rh2 stimulates the expression of pituitary adenylate cyclase-activating polypeptide, encouraging cell proliferation and survival, while Re helps in reducing Aβ levels in mice**.** Hence, they are active participants in slowing down the progress of the disease (4).

Conclusion

Alzheimer's Disease is a prevailing neurodegenerative disorder in the world and hence a major concern. However, if it is possible to treat it with economical and easily available herbs or simple medicines, it could save the lives of many. Ginseng has been considered to treat all kinds of ailments and scientists have been working to prove this statement. Hence, we can conclude from mentioned studies that ginseng can be used to treat/ reduce symptoms of Alzheimer's disease.

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18. FERTILITY PRESERVATION IN CANCER PATIENT

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Why there is pressing need of fertility preservation?

Fertility preservation means saving or protecting sperm and eggs for the future. Fertility preservation is done in many individuals who have endometriosis, uterine fibroids or who are about to be treated for autoimmune diseases (such as lupsus, rheumatoid arthritis *etc*), endocrine disorders (like thyroid, adrenal

disorders, diabetes, etc,) or for people who have sexual transmitted disorders like Chlamydia, Syphilis, Gonorrhea, Genital herpes, HIV, Hepatitis, Mycoplasma genitalium, etc, and even for those who wish for a delayed parenthood or have genetic diseases that affects future fertility, or about treated for cancer (1).

Cancer is a disease where abnormal cells grow in an uncontrolled manner anywhere in our body. There are over 200 types of cancers including breast cancer, prostate cancer, uterus cancer, ovary cancer, cervical cancer, colorectal cancer, bladder cancer, testicular cancer, etc to name a few.
Cancer treatment affects the fertility of many individuals directly or indirectly. Indirectly by the techniques used to treat the cancer such as radiation therapy, chemotherapy, hormone therapy, immunotherapy, stem cell transplant whereas by directly affecting the reproductive organ by surgery such as hysterectomy, oophorectomy. Approximately, 40-80% females and 35% males face possible infertility owing to their cancer treatments, i.e., surgery, chemotherapy and radiation therapy. Even 70-75% of young cancer survivors are interested in parenthood but fertility preservation methods are lower. Fertility preservation allows many cancer survivors to achieve their goals of a happy family (1, 2).

Fertility preservation techniques available for females
Fertility preservation can be carried out by several techniques (2, 3). In females following methods can be carried out:

Radical Trachelectomy: In this technique the lower part of cervix is removed mainly in cervical cancer. This surgery allows the cancer patients to remain fertile. To achieve great success, cervical lesions should be <2-2.5 cm with limited endocervical extension, and have no lymph node metastases.
Germplasma Cryopreservation: it includes two techniques that are slow freezing and vitrification (flash freezing). Both these techniques are used to freeze the eggs to -196°C to stop the processes that are going on within the eggs. Slow freezing takes hours to process whereas flash freezing technique takes some minutes to complete this process. It includes both the embryo and oocyte cryopreservation. In oocyte cryopreservation, the eggs are preserved at low temperature and later sperms are injected in the eggs by ICSI. A major risk factor involved is usage of various drugs such as follitropin alpha or beta, (Follistim AQ, Gonal-f) or menotropins (Menopur) are given for ovarian stimulation and to prevent ovulation. Embryo cryopreservation is a more successful technique than the oocyte cryopreservation. In this technique, the embryo (fusion of female egg and male sperm) is preserved and in vitro fertilization (IVF) is involved. Processes that involve embryo preservation are ovarian stimulation, oocyte retrieval and fertilization.

Cryopreservation and transplantation of ovarian tissues: Ovarian tissue cryopreservation seems a feasible option for prepubertal girls post cancer diagnosis. Ovarian tissue is removed via laparoscopy and frozen. After cancer treatment, the ovarian tissue can be reimplanted. Cryopreservation shows up to 65% of survival of follicles. Oophoropexy/ovarian transposition is a surgical operation in which one or both ovaries are either disconnected from the uterus or fastened to the abdominal wall. Patients undergoing radiation therapy may have their ovaries moved in the abdominal cavity away from the radiation field via laparoscopy prior to the first radiation treatment, minimising radiation exposure.

Fertility preservation techniques available for males
In males, sperm cryopreservation is the method to preserve fertility in males. In this method, the semen is collected and morphology, motility and sperm count are observed. The semen can be collected by

many ways such as ejaculation, electroejaculation, urine, sperms extraction and aspiration procedures (4). Apart from this, testicular shielding, is also used to limit the exposure of testicles to radiation used in radiation therapy, shield is placed over the scrotum sac. Clampshell-like shields are made and used each day of treatment with pelvic or inguinal radiation therapy (4, 5).

These methods are of immense help for the cancer patients but they also have limitations such as women with ovarian hyperstimulation syndrome and venous thromboembolism are not advised for fertility preservation, due to controlled ovarian hyperstimulation and oocyte retrieval causes stroke, myocardial infarction, etc. (5, 6).

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19. WHERE ARTIFICIAL INTELLIGENCE AND BIOLOGY COLLIDE

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Proteins are the major workforce of the cell from catalyzing almost every single biochemical reaction to providing the structural support to the cell almost everywhere. But it all starts from the molecule which stores all the information of the cell, also called as master molecule – DNA, which after getting transcribed generates mRNAs which ultimately serves as the code for the protein (1). Proteins are made with the combination of 20 different amino acids connected with an amide bond called peptide bond. The chemistry of protein is dependent on the nature of the side chain present in the amino acids constituting the protein. On the basis of side chain, amino acids are classified as non-polar, and polar which includes uncharged and charged: positive and negative (1,2).

Protein structure

The primary structure of polypeptide is the linear sequence of amino acids and also the driving force and instruction for the native folded conformation of protein. Further folding is characterized by hydrogen bonds within and between the chains namely as alpha (α) helix and beta (β) sheet respectively. The assembly of different folds and formations in a single chain of polypeptide forms the tertiary protein. Lastly, the quaternary structure of protein is mediated by interactions between multiple polypeptide chains or subunits (1).

Deciphering the complexity of protein folding is beyond understanding. Levinthal's paradox questioned the amount of time required for the folding of protein because to attain native conformation to function

with many possible combinations would take years to achieve but the proteins can fold in seconds or less in vivo (3).

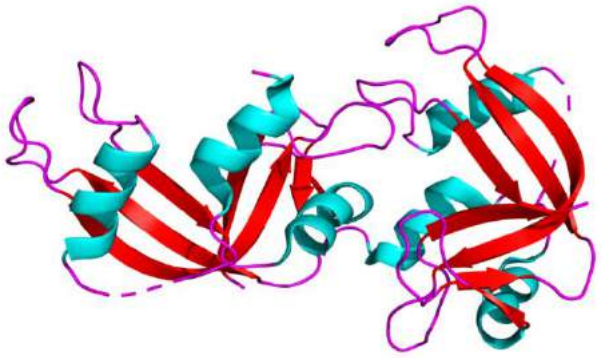

Figure 1 - Human pancreatic ribonuclease (representation- blue: alpha (α) helix, Red: anti parallel beta (β) sheet and Pink: loop)

Protein folding

Protein folding plays a crucial role in the function of various enzymes and proteins. X-ray diffraction is a very common method used to determine the 3D structure of the protein. The study of protein folding has opened frontiers in the field of protein engineering and de Novo design of proteins with new functions (4).

Computational biology has been actively employed for the prediction of the 3D native structure of a protein from its amino acid sequence (5). This is important in the discovery of new drugs much faster and annotation of protein functions from the genomic sequences (5, 6).

The concept of using the computers began with the prediction of secondary structures for the proteins by Chou and Fasman in the 1970s. They employed a simple and direct method, lacking any complex computer calculations, and used the empirical rules to predict the alpha helices and beta regions in a protein (7).

In the 1980s, computational physics was used in the structure prediction of a five residue protein named Metenkephalin. A combination of the Metropolis Monte Carlo minimization approach along with an atomic force field to generate a Markov walk on the energy minima of the Boltzmann transition probabilities corresponding to the native structure of the protein (8).

Modeling Databases

During the 1990s, many databases and algorithms were used for the automatic modeling for proteins. Majority of them worked by recognizing folds by threading unknown sequences onto the 3D structure from a database (9,10).

CASP : Critical Assessment of Techniques for Protein Structure Prediction (CASP) was invented by John Moult in 1994. It is a blind test for the prediction of the structure of a protein (5, 11). CASP had been held every two years since 1964 to determine the structures of unknown proteins. It is an experiment which aims to establish the current state of protein structure prediction, to identify the progress made in the field, and to identify the areas where more research can yield successful results(12). In this, the amino acid sequence of target protein is provided to the participants and the participants then build up a three-dimensional structure corresponding to the protein. The structures are compared to the experiment one by independent assessors in a double-blind manner, i.e., the participants do not have access to the experimental structures and the assessors do not know the identity of the participants making the submission (13).

In the CASP13 held in 2018, the DeepMind team developed a new system called AlfaFold based on Artificial Intelligence to effectively predict the structure of a protein, and went in to score the highest points in the experiment (14).

AlphaFold is a protein structure prediction system which uses a simple gradient descent algorithm for the generation of structures bypassing the need for complex sampling procedures. AlphaFold uses a free modeling (where new structure is made without referring to any previously known structure) instead of template-based modeling (where a known structure is used to make a new stucture) to yield results (14,15). AlphaFold uses neural networks to determine the probability of the distance between different pairs of residues in a protein and the angle between these pairs. These probabilities were then combined into a score that gives estimation on the accuracy of the resultant structure. To attain this accuracy, the database was trained on a public dataset of more than 170,000 proteins of known structure and then with many protein sequences with unknown structure (14,15).

AlphaFold 2 is the 2020 version of the 2018 AlphaFold 1 version and official information about this is yet to be released by deep mind.

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20. TOURETTE'S SYNDROME: A NEUROPSYCHIATRIC DISORDER

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Tourette syndrome (TS) is a medical specialty disorder that's characterized by persistent motor and vocal (also referred to as phonic) tics. Excessive eye blinking, nose vellication, head jerks, shoulder shrugging and lip biting are some examples of motor tics whereas examples of vocal tics embody throat clearing, whistling or hissing, sniffing or snorting etc. Its onset happens in early childhood *i.e.,* juvenile stage. As the age of the sufferer increases, its symptoms decrease in intensity and show less variation over time relating to each severity and kinds of tics (1). It is more prevalent in males than in females, with magnitude relation being 3-4:1. Youngsters and adults suffering from tourette's syndrome often have other psychiatric behavioral disorders like attention deficit hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), self-injurious behavior, depression, or specific learning disabilities (2).

History

Tourette's Syndrome has been named after Gilles de la Tourette, a French neurologist. In 1884, Gilles de la Tourette began training under Dr. Charcot's (Father of Modern Neurology) guidance at the Salpêtrière hospital. Before he discovered Tourette's Syndrome, he studied various medical conditions such as hysteria, hypnosis and ataxia. Gilles de la Tourette, in his most celebrated article, printed within the January 1885 issue of the medical journal *Archives de Neurologie* described tourette's syndrome as a bizarre psychiatric condition that he cited as *'maladie des tics'*. He observed 9 people with a condition that had varied characteristics such as hereditability, waxing and waning, stereotypic movements, premonitory sensation, echolalia and coprolalia. Dr. Charcot later renamed the disorder in his student honor, thus named Tourette's Syndrome (3).

Prevalence

CDC supports a nationally representative survey that gives information on health conditions among children in the United States, referred to as the National Survey of Children's Health. The information from 2011-12 showed that roughly 1 out of every 360 children 6-17 years of age in the United States had been diagnosed with TS; this delineated about 138,000 children (4). As per the findings of 2007 National Survey of Children's Health data, it was observed that among US children aged 6-17 years,0.28% (representing more or less 138,000 US children) had ever diagnosed with the syndrome. Similar findings were obtained from 2011-2012 survey data. According to the report, 0.19% (representing approximately 95,000 children) had current TS. Additionally, it had been observed that current TS was more prevalent in boys and among children with ever-diagnosed TS, the average age of identification was 8.1 years (5).

Clinical Characteristics

Various behavioral and psychological conditions that are associated with TS are referred to as co-occurring conditions. Individuals suffering with TS and other associated conditions are at additional risk for learning, behavioral and social problems. These conditions embody attention-deficit/hyperactivity disorders (ADHD), obsessive-compulsive disorder (OCD), and different behavioral or conduct issues.

- Attention-deficit/hyperactivity disorder (ADHD) - It is the foremost usually occurring co-morbid condition. Children with ADHD face hassle focusing and behaving at one time or another. This sort of neurodevelopmental condition is usually diagnosed at an early age and lasts till adulthood.

- Obsessive Compulsive Disorder (OCD) or Obsessive-Compulsive Behavior (OCB) - The obsessive–compulsive behaviors in individuals with Tourette syndrome embody thoughts (obsessions) of violence, sex and aggression, and actions (compulsions) regarding touching of the self and/or others, symmetry and ordering. This differs from many folks with OCD, who are often more preoccupied with dirt, germs and contamination.
- Behavior or Conduct Problems - It includes Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD). Children with ODD show hostile behaviors towards adults and authority figures whereas children with CD act aggressive toward others and break rules, laws, and social norms and might have additional injuries and issues with friends.
- Autism Spectrum Disorder (ASD) - It impairs the ability to communicate and interact. ASD impacts the nervous system and affects the general psychological feature, emotional, social and physical health of the affected individual.
- Anxiety - These include generalized mental disturbance, OCD, anxiety disorder, post-traumatic stress disorder, separation anxiety, and differing kinds of phobias.
- Depression - The aetiology of depression is usually complex and includes genetic factors and also psychosocial variables like recent adverse life events, adverse childhood circumstances (e.g., parental loss, stress or abuse), adverse current social circumstances and physical illness.
- Other clinical conditions such as echo phenomena, coprolalia (the involuntary and repetitive use of obscene language), copropraxia (the inappropriate making of obscene gestures) and premoitory sensations are also discovered in patients laid low with TS.

Aetiological aspects

- GENETICS – More than one gene is assumed to be concerned within the development of TS. The genetic science of GTS is complicated and not well understood. The Genome Wide Association Study (GWAS) design can hopefully overcome the restrictions of linkage and candidate gene studies. However, large-scale collaborations are required to produce sufficient power to utilize the GWAS design for discovery of causative mutations (6).
- NEUROIMMUNOLOGY - In genetically susceptible individuals, tics and associated phenomena are thought to arise as a consequence of the immunologic response to infections with Group A beta hemolytic Streptococci (GABHS). Antibodies directed against the streptococci are hypothesized to cross-react with structures of the central nervous system, subsequently resulting in the damage of these structures, which eventually leads to the emergence of tics and associated features.

  Researchers of the National Institute of Mental Health (NIMH) subsequently projected criteria to spot a putatively distinctive subgroup of patients from the spectrum of illness encompassing Tourette's syndrome and obsessive-compulsive disorder (OCD), whose tics and obsessive-compulsive symptoms are shown to arise in response to beta-hemolytic streptococcal infections. They designated it by the term pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS), implicitly suggesting that in non-PANDAS cases auto immunity would not be involved (1, 7, 8).
- PERINATAL FACTORS – A stress-diathesis model for the pathologic process of TS, in keeping with that the clinical expression of TS could be a product of the interaction of an inheritable vulnerability with environmental factors; these could embody Central Nervous System stimulants or intermittent, uncontrollable stress throughout an essential period of brain development. Thus, it’s been projected those prenatal events or exposures like maternal life stress throughout pregnancy, severe nausea and puking throughout pregnancy, and antiemetic medication could cause changes within the sensitivity of some dopaminergic receptors and this might partly confirm the ultimate severity of expression of the sensitivity to TS (7).

Treatment

According to international pointers the medical aid consists of medicine, psychotherapeutic and neurosurgical approaches. Antipsychotics are the foremost effective pharmacotherapy. Psychotherapeutic approaches play an additional subordinated role. Deep brain stimulation is experimentally applied in untamed TS (9).

- Neuropsychological Interventions- The proof based and the most typical treatments are-
- Habit reversal training (HRT) - It consists of 5 key techniques: awareness coaching, development of a competitory response, contingency management, relaxation coaching, and generalization of skills.
- Exposure and response prevention (ER) - ER is a methodology of psychological feature BT and type of exposure therapy within which the people confront their fears and discontinue their escape response.
- Comprehensive behavioral intervention (CBIT) - It is a typical structured medical aid, which trains patients to become conscious of their tics and teaches them specific behavioral ways that scale back tics.
- Pharmacology- The essential cluster of medication for TS medical aid is antipsychotics (especially dopamine receptor antagonists). However, some physicians are reluctant to inflict them because they concern their extrapyramidal facet effects, particularly dyskinesia. The foremost effective medicine appears to be antipsychotics haloperidol, pimozide, and risperidone. Within the theory of GABAergic and cholinergic transmission, clonazepam and baclofen perceived to be the foremost potent. The impact of glutamate as an excitant neurotransmitter was included in the studies with riluzole (inhibitor), D-serine (stimulant), *N*-acetylcysteine, and acamprosate. The most recently studied neurotransmitter system is that the histamine system, that has been influenced by the pitolisant within the studies (2).
- Neurosurgical- Multiple targets are investigated for DBS, GPi DBS as a surgical approach for rising medication-refractory TS: neural structure (thalamus), globus pallidus-internal section, anterior limb internal capsule/nucleus accumbens, and multiple targets. Some patients could expertise sedation, abulia, fatigue, apathy, sexual pathology, and visual disturbances (2).

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21. SLEEPLESS NIGHTS: JOINING ENDS OF REM SLEEP WITH OBSTRUCTIVE SLEEP APNEA

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"Feel the vibe, when you sleep because
It will give you the power for not to weep"

Sleep is a natural phenomenon of recurrent states of mind and body characterized by changes in consciousness, inhibition of sensory activity, decreased muscle activity, and almost all voluntary muscle inhibition during rapid eye movement (REM) sleep. It has a reduced ability to respond to environmental stimuli, but is more sensitive than lethargy or confusion, along with other active brain patterns that appear during sleep. Sleep is coupled with a state of muscle relaxation and decreased awareness of environmental stimuli (1).

What is actually a REM sleep?

REM sleep is a specific stage of sleep, featuring muscular tones, fast eyes and dream movements. It has a unique physiological characteristic that exists in all mammals and is distinct from nerve sleep.
This sleeping phase is also called "paradoxical sleep" or "asynchronous sleep" due to its waking human physiological similarity. This includes low and quickly brain waves. The chemical and electrically active way to regulate this step of this sleep occurs in the brain head, which is the abundance of acetylcholine (Neurotransmitters) and serotonin, histamine and ninepine. (Monoamine neurotransmitter) (2).

Figure 1 - REM sleep behavior disorder involves unusual actions or behaviors during the rapid eye movement sleep phase. (Source:https://www.medicalnewstoday.com/articles/247730)

Disorders associated with sleep

People suffer from a variety of sleep disorders, including insomnia, hypersomnia, narcolepsy, and sleep apnea. parasomnia, such as sleepwalking and rapid eye movement sleep disorder; bruising; circadian sleep disorder. The use of artificial light has significantly altered human sleep characteristics. A common source of artificial light is the screens of electronic devices such as smartphones and TVs, which emit large amounts of blue light, a form of light usually associated with daylight. This interferes with the release of the hormone melatonin, which is needed to regulate the sleep cycle (1, 2).

Obstructive Sleep Apnea Syndrome (OSAS) is a potentially serious disease that affects millions of people worldwide. Many of these patients are not diagnosed, and even after being diagnosed, they are often unable to maintain positive airway pressure at night, so it is a very effective non-surgical treatment. Various surgical procedures have been proposed for the management and treatment of OSA. This article provides insight into the assessment of occlusion sites and the various surgical procedures designed to treat OSA (3, 4).

Figure 2 - Comparison of normal airway passage v/s Obstructive sleep apnea air passage during sleep (https://www.leporedentistry.com/obstructive-sleep-apnea/)

Major accidents that are happening at night on the national highways are caused by the truck drivers due to lack of good sleep. They get struck by the sleep disorder like the obstructive sleep apnea, which is more or less associated with REM Sleep they undergo. Numerous studies have been conducted to show that OSA during REM sleep is a common disorder which is being found in various case studies of Truck Drivers carrying Dangerous Goods (TDDGs). Due to lack of sleep, the sense to focus and paying attention reduces drastically, leading to a number of accidents like crashing into trees, petroleum and gas stations, dividers and also tumbling of the vehicle, causing damage to the driver as well as the passers-by (5).

Studies Associated with Obstructive Sleep Apnea and Rem Sleep Correlation

Accidents of truck drivers at night due to obstructive sleep Apnea: The study investigated the association between OSAS and global endpoints of CVD during REM sleep in a community sample with and without advanced CVD (6). A homogeneous sample of truck drivers transporting goods was evaluated to estimate the prevalence of obstructive sleep apnea syndrome (OSA), secondary risk of road traffic accidents, and prevention of accidents in this population.

Method: A full home polysomnography was performed as part of a sleep health study. The study group was followed for an average of 9.5 years when sleep events were assessed. Only participants with a non-REM apnea-hypopnea index (AHI) of less than 5 breaths per hour were added. A composite cardiovascular endpoint was transcribed as the occurrence of a nonfatal or fatal event, including myocardial infarction, coronary revascularization, congestive heart failure, and stroke (6, 7).

Measurements and Key Results: The sample consisted of 3265 subjects with AHI in the non-REM sleep phase of less than 5.0 events/hour. Using REM AHI < 5.0 events/hour as a control (n = 1758), the adjusted hazard ratio for the composite CV endpoint in patients with severe REM OSA (≥30 events/hour, n = 180) was 1. 35 (95% confidence interval, 0.981.85). Stratified analysis showed that the association was strongest in individuals with advanced CVD and severe OSA during REM sleep, with an adjusted risk ratio of 2.56 (95% CI, 1.464.47) (6, 7).

Conclusion: This study showed an unexpectedly high prevalence of OSA in with significantly increased risk of accidents in the population. For professional drivers, OSAS inspection, treatment and monitoring are essential to reduce the risk of road traffic accidents and improve road safety (6, 7).

Remedies for curing Sleep Apnea (8)

1.Maintaining a Healthy Weight: Doctors generally recommend weight loss for people with sleep apnea. Obesity, especially in the upper body, may increase the risk of airway obstruction and nasal stenosis. These disorders can cause sudden or prolonged cessation of breathing during sleep.

2.Try Yoga: Regular exercise can increase energy levels, strengthen your heart, and reduce sleep apnea. Yoga can especially improve breathing and stimulate oxygen flow.

3.Changing Your Sleep Position: Small changes in your sleeping position may reduce symptoms of sleep apnea and improve nighttime rest. A 2006 study found that over half of cases of obstructive sleep apnea depended on body posture.

4.Use A Humidifier: The humidifier is a device that humidifies air. Dry air can irritate the body and respiratory system. Using a humidifier can open the airways, reduce nasal congestion and clearer breathing.

5.Avoid Alcohol and Tobacco: Lifestyle changes can improve health and sleep habits. Consider quitting smoking and limiting your alcohol intake to reduce the complications of sleep apnea.

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22. NANO ARTIFICIAL NOSE/ E-NOSE: EARLY DETECTION OF LUNG CANCER

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Lung Cancer is the second most common type of cancer (12.3% of all the cancers) with an estimated 2.09 million cases in 2018 (1). It is extremely lethal and accounts for around 28% of cancer-related deaths worldwide. According to the recent projection of global mortality, by 2030 lung cancer will emerge as the third and the fifth leading cause of death (2,11). At the early stages, it cannot be detected as the patient remains asymptomatic until the advanced stages due to which the chances of survival are less. Patients diagnosed during their initial phase of lung cancer can live for a period of 5 years (2,3,6). One cannot be rely on the symptoms to indicate the presence of lung cancer as they often do not appear until the cancer is relatively advanced (4,5). The major contributors of developing lung cancer include tobacco smoking and use of tobacco products, airborne environmental pollution exposure and epigenetic changes. Lung cancer causes the neoplastic metamorphosis of epithelial cells in the lung (2-5). It is categorised into two broad categories based on histological assessment,

i) Small-cell lung cancer (SCLC) and ii) Non-small cell lung cancer (NSCLC) (5).

Small Cell Lung Cancer: SCLC records 14% of all the lung cancer cases. This type is generally considered as the "Smoker's Disease". It is characterized as a neuroendocrine malignancy with histological features including nuclear moulding, high number of mitoses, necrosis and crush artefacts (3,6).

Non-Small Cell Lung Cancer: NSCLC records 85% of all the lung cancer cases. Risk factors include second-hand cigarette smoke, certain foods (cured and barbequed meats, deep-fried consumables), alcohol, a sedentary lifestyle, air pollutants, and genetic susceptibility and mutations in the proto-oncogene epidermal growth factor receptor (EGFR) (3,7). The major subtypes of NSCLC are adenocarcinoma and squamous carcinoma and large-cell carcinoma (2).

Detection Techniques

Treatment of any cancer aims to remove or destroy the cancerous cells without killing normal cells. Traditional methods used for treatment include surgery, radiation, and chemotherapy which can be used either alone or in combination with each other. The most effective option to treat patients suffering from lung cancer is surgical removal (resection) of the lobe of the lung affected by lung cancer (5). Symptoms like persistent cough, pain in the chest, change in the voice pattern, blood filled sputum, and recurrent pneumonia or bronchitis are usually observed in the last stage of lung cancer (6). The lung cancer is diagnosed through a physical exam of blood, urine samples, and atypical physiology detected through techniques such as X-rays, computed tomography (CT), fibre-optic endoscopy, magnetic resonance imaging (MRI) and ultrasound (7,8).

Nanotechnology in Cancer Treatment:

Nanotechnology can be broadly defined as fabrication and application of man-made materials, devices and systems that fall within the size range of 1-100 nm in at least one dimension (3,8). Includes the use of man-made nanoparticles (NPs) and novel nano-devices and nano-materials at the molecular and atomic levels (2,9). This field gives a way of detecting the presence of a disease in the body at an early stage such as a tumour. Nanomedicine used in cancer therapy include injectable drugs such as liposomes for treatment of breast cancer; nanoparticles for detection of nucleic acids and proteins, and for brain cancer imaging using nanoparticles as contrast reagents in magnetic resonance imaging (MRI) (2,10). Nanoparticles are of great ease because of their high surface area to volume ratio compared with their

macromolecular counterparts, tuneable thermal, magnetic, optical and electrical properties and the diversity of shapes and sizes that can be synthesised, either hollow or solid, with desirable chemical composition and surface chemistry that can be manipulated with exogenous and endogenous stimulus. They have the potential to overcome the biological and chemical barriers within the human body which allows them for augmented therapeutic and diagnostic localisation and efficacy with lower invasiveness and higher biocompatibility (10).

What is a Nano-Nose/E-Nose?

Nano Artificial Nose is an instrument which comprises an array of electronic chemical sensors with partial specificity and appropriate pattern recognition system, capable of recognizing simple, or complex odours. It works as a chemical-array sensor system that mimics the mammalian olfactory system (11-13). It is a cheap, non-invasive tool that would sniff out traces of early lung cancer based on people's breath (7,12). In the diseased conditions, the biochemical processes of organs get altered which results in the production of new chemicals or altered consumption of existing chemicals. These abnormal changes in the metabolism of the body alter the composition of the body fluids resulting in presence of complex gas mixture of volatile organic compounds (VOCs) in the exhaled breath. These breath signatures can serve as a biomarker for specific diseases and can be a potential candidate for early detection of certain diseases (8,13).

Electronic Nose (E-nose) consists of an array of gas/VOC sensors integrated with artificial neural networks which have shown a promising non-invasive technology for detecting targeted VOCs from the exhaled breath resulting in early diagnosis of several diseases (8). The surface of cancerous tissue emits chemicals in the form of Volatile organic compounds (VOCs) which can be detected by sensors on a Nano-sensor array. These sensors are used to differentiate between the breath of a healthy and cancerous individual. This allows fast, accurate method for detection of cancer (6). More than 3000 different volatile organic compounds (VOCs) have been observed in exhaled breath and the list is continually growing (10,13).

Exhaled organic compounds originate from two main sources: exogenous volatiles that are inhaled (or absorbed through the skin) and then exhaled and those endogenously produced by different biochemical processes. Regardless of the distance of the organ, VOCs can be transported by the blood to the lungs and exhaled during breathing. The origin of exhaled VOCs is assumed to be mainly alveolar; however, direct comparison of VOC profiles from different parts of the lung and the airways is lacking. The use of an electronic nose for detection of lung cancer offers several advantages of high sensitivity, ease of administration of the test and portability of the detector (11).

VOCs coming out through lung, kidney, sweat or skin provide vital information of metabolic alterations or malfunctions happening inside our bodies (8,11).

Around 42 VOCs help in detection of lung cancer biomarkers namely (6):

- Acetaldehyde (below 2-10 ppb)
- Formaldehyde (below 2-10 ppb)
- Undecane (24+4 ppb)
- Isopropene (72.9- 81.5 ppb)
- Methanol (below 118.5 ppb)
- Ethylbenzene (145+35 ppb)
- Acetone (below 458.7 ppb)

Origin of exhaled VOC's

Cells in their normal state produce reactive oxygen species (ROS) at a definite rate owing to the oxidative stress that results from daily routine cell activities. The ROS leaks from the mitochondria or the fatty acids in the cell membrane to the cytoplasm. The leaked ROS then acts on the organic material in the cytoplasm and produces different volatile alkanes which are exhaled through the breath as VOCs. During cancer, the cells are proliferating and survive in a condition of hypoxia and through impaired mitochondrial respiration there is a higher rate of glycolysis (Warburg effect) leading to an acidic microenvironment. This environment breaks the basement membrane, while keeping the immune cells at bay and increases the metastatic potential of the malignant transformation at the site. Simultaneously, there are genetic mutations also happening. For instance, the increased expression of mixed oxidase enzymes such as Cytochrome p450, known to be associated with tobacco smoking and lung cancer. The over activation of p450 through genetic and microenvironment changes during malignant transformation, accelerates the catabolism of the oxidative stress products that normally creates VOCs thereby leading to their increased abundance and hence modified ratios in the exhaled breath which help in detection (8,3,12).

E-Nose Technology

The human olfactory system consists of nose and brain which are interlinked and trained to detect and distinguish several chemicals which in turn provide necessary information such as the freshness of food, pungent smell, perfumes, and gas leakage. Complex volatile compounds interact with neuron cell receptors and then signals are sent through nerve impulse to the brain for processing. In the end signals are stored and analysed with help of hypothalamus and olfactory cortex in the brain (2,8,12).

Nano-Nose analyses the gases present in the breath and identifies those gases which stipulate the presence of lung cancer. It works by binding gases to specific chemiresistors coated with gold nanomaterials, aiding in the detection of volatile organic compounds (VOC) of the exhaled breath.

Components of e- nose:

(i) Multiple sensor array
(ii) Data acquisition system
(iii) Pattern recognition algorithm

Classification of E-Nose

E-NOSE are generally classified based on the detection principle involved or the type of sensor used. These includes the following:

1. Optical Sensor Systems
2. Mass and Ion Mobility Spectrometry
3. Gas Chromatography
4. Infrared Spectrometry
5. Chemical Sensors

E-Noses based on various Nanomaterials:

The primary innovation in nanomedicine has largely centred on the development of NPs as the delivery vehicle for a plethora of therapeutic molecules including small molecules, nucleic acids, proteins, peptides and hormones (3,5,12). Approximately, 33 lung cancer biomarker VOCs are produced in exhaled breath (4,12). Advances in technology have helped produce small, portable array type devices to

detect and identify chemicals in gaseous samples which are designed to respond to the mix of compounds in the sample rather than identify individual compounds. The principle behind this device is that the VOCs adsorb onto a sensor producing a change in conductivity, color or oscillation of a crystal. Output is usually a pattern representing the mix of VOCs (9,12).

Types of Nanostructures used:

1. *Isolated and Single Nanostructures*: One-dimensional structures are particularly important as they can be effectively utilized for developing EN based on single structures. In particular, a simple and excellent performing EN based on single SnO2 nanobelt (NB) was realized using a combination of bottom-up fabrication protocols with the state-of-the art microfabrication methods (12).
2. *Multiple Nanomaterials*: Decorating the NWs surface with different metal nanoparticles is akin to functionalizing them with chemically specific moieties. The EN could unequivocally discriminate three gases, namely, H2, CO, and C2H4 when the sensor responses were classified using linear discriminant analysis (LDA) (12).
3. *Nanomaterials Film*: include drop casting, air brushing, spin-coating, inkjet printing, micro dispensing, immersion, microcontact printing, place-exchange cross-linking precipitation, and liquid phase cross-linking (12).
4. *Conductive Polymer Nanocomposites*: Nanomaterial incorporated polymer nanocomposites are one of the attractive class of materials for developing a room temperature sensors. five different polymer matrices (polymer nanocomposites [PNC]), namely, poly(caprolactone) (PCL), poly (lactic acid) (PLA), poly(carbonate) (PC), poly(methyl methacrylate) (PMMA), and a biobased polyester (BPR) (12).

Conclusion

Lung cancer identification by breath test is a rapidly growing area of research that could provide novel improvements in molecule-oriented screening and monitoring of lung cancer (11,12). For the early detection of lung cancer, standard diagnostic techniques cannot be used as they detect abnormalities at the later stages. A portable technique/device is required for the early detection (6,12). Nanotechnology can be used in the development of a simple, portable and effective screening device for lung cancer, as the surface area of the nanoparticles is high, making them more suitable as breath biomarkers (6,12). In future the E-tongue can be used to confirm E-Nose and liquid biopsy findings, thus enhancing the overall diagnostic ability in the “no touch” diagnostic lung cancer diagnosis. The E-Nose with its non-invasive modality of obtaining histological diagnosis of a pulmonary nodule is of great benefit (12).

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23. LUNG CANCER

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Lung cancer is a type of cancer that occurs when tumors start inside the bronchioles or alveoli sacs. Our lungs are two sponges like organs in the thorax region of the body. The right lung has three sections, called lobes. The left lung consists of two lobes. The left lung tends to smaller than the right lung because the heart takes up more space on that side of the body. When we breathe in, air enters through our mouth or nose and goes into the lungs through the **trachea** (windpipe). Trachea further divides into tubes called **bronchi**, which enter the lungs and divide into smaller bronchi. These divide to form small branches called **bronchioles** (1). At the end of these bronchioles are small sacs known as alveoli. These alveoli help in exchange of O_2 into the blood and helps in removal of Co_2 from the blood when we exhale (1).

TYPES OF LUNG CANCER

There are two main types of lung cancer and the treatment of both is very different.

Non-small cell lung cancer (NSCLC)

About 80 to 85 % of lung cancers are NSCLC. Some main subtypes of NSCLC are Adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. These subtypes generally start when different types of lung cells are grouped together as NSCLC because their prognoses (outlook) and treatment are often similar (1, 2).

Adenocarcinoma starts in those cells that normally would secrete substances such as mucus. This type of cancer mainly occurs in current or former smokers, but it is the most common type of lung cancer seen in non-smokers. It is generally seen more in women than in men. This type of cancer is most likely to occur in younger people. Adenocarcinoma is usually found in the outer parts of the lung and is more likely to be detected before it spread (1).

Squamous Cell Carcinoma starts in squamous cells; these are flat cells that line the inside of the airways in the lungs. They are often linked to a history of smoking and tend to be found in the central part of the lungs, near main airway (bronchus).

Large cell (undifferentiated) carcinoma can arise in any part of the lung. These tend to grow and spread quickly, which makes it harder to treat. A subtype of large cell carcinoma, known as large cell neuroendocrine carcinoma, is a very fast growing cancer that is very much similar to small cell lung cancer.

There are few subtypes of NSCLC, such as adenoaquamous carcinoma and sarcomatoid carcinoma, are much less common.

Small cell lung cancer (SCLC)

About 10 to 15 % of all lung cancer are SCLC and it is sometimes referred as **oat cell cancer.** This type of lung cancer tends to grow and spread much faster than NSCLC. About 70 % of people with SCLC type cancer will have tumor cells that have already spread at the time they are diagnosed. Since this type of cancer grows quickly, it tends to respond well to radiation therapy and chemotherapy. But, mostly this cancer will return at some point (1, 2).

Other types of lung tumors

Along the main types of lung cancer, there are other types of tumors that occur in the lungs.

Lung carcinoid tumors account for fewer than 5 % of long tumors. Most of these grow slowly. Other types of lung cancer such as adenoid cystic carcinomas, lymphomas, and sarcomas, as well as benign lung tumors such as hamartoma are rare.

Sometimes cancer from other organs such as breast, pancreas, kidney, or skin can sometime metastasize to the lungs, but these are not lung cancers.

CAUSES AND RISK FACTORS OF LUNG CANCER

Some of the causes which and risk factors which give rise to cancer in early or later stage are as follows:

Age: Lung cancer is more common in men and women in the age of 70 years or more than 70 years.

Gender: Lung cancer generally is not seen in a particular genders both men and women are affected by lung cancer.

Tobacco smoking: Smoking is the leading risk factor for lung cancer. About 80 % of total lung cancer deaths occur because of smoking.

Breathing in the smoke of others also causes lung cancer even if you don’t smoke this is called as “Secondhand smoke”.

Smoking marijuana: Marijuana smoke contains tar and many of the cancer causing substances that are found in tobacco smoke. Marijuana is inhaled very deeply and the smoke is held inside the lung for longer duration, which gives these cancers causing substances more time to deposit inside the lungs (2).

Exposure to radon: Radon is a naturally occurring radioactive gas which comes from the breakdown of uranium and thorium in soil and rocks. You can't see, smell or taste it. Breathing radon gas in your lungs exposes it to small amounts of radiation. This may increase a person's risk of getting lung cancer.

Exposure to Asbestos: Asbestos is a natural mineral and carcinogen (such as in mills, textile plants, mines). People who are exposed to asbestos are at greater risk of getting lung cancer. People exposed high amount of asbestos is at greater risk of developing mesothelioma (type of cancer that starts in pleura).

Air pollution: In metropolitan cities where heavily trafficked roads are common appear to raise the risk of the lung cancer slightly. This is very less in comparison to the risk caused by smoking, but air pollution adds up to the effect of smoking which increases the chance of developing lung cancer (2).

SYMPTOMS OF LUNG CANCER

Symptoms of lung cancer varies depending upon where and how much the cancer has spread; in some cases it may occur without cause any pain. These are some most common symptoms of person suffering from lung cancer (3):

- Chest pain
- Coughing up blood or phlegm
- Persistent cough and wheezing
- Shortness of breath
- Persistent bronchitis or respiratory infections like pneumonia
- Loss of appetite
- Fatigue
- Unexplained weight loss

STAGES OF LUNG CANCER

By knowing the exact stage in which the cancerous tumors are in helps knowing how severe it is and how wide it has spread to the neighboring tissues (4).

Stage 1: Cancer in this stage is found in lung, but it has not spread outside the lung.

Stage 2: Cancer in this stage is found in the lung and it has spread to nearby lymph nodes.

Stage 3: Cancer is in the lung and lymph nodes and also in the middle of the chest.

- **Stage 3A:** Cancer is found in this stage in lymph nodes, but only on the same side of the chest where cancer cells first started growing.
- **Stage 3B:** Cancer has spread to lymph nodes in this stage on the opposite side of the chest or to lymph nodes above the collarbone.

Stage 4: Cancer has spread to both lungs, into nearby area of the lungs, or to distant organs.

DIAGNOSIS OF LUNG CANCER

To determine the presence of cancerous tumors, there are numbers of tests that are to make sure that the person is having lung cancer or not, are:

- **Biopsy:** Tissue sample or abnormal cells will be taken from patient and then it will be carefully analyzed inside the lab to find out the type of lung cancer (3).
- **Imaging tests:** X-ray helps to find abnormal cell mass or nodules inside the lungs. CT scan also helps to find out small lesions inside the lungs that might not get detected by X-ray (3, 4).
- **Sputum cytology:** If the patient is coughing and producing sputum, this sputum will be collected and will be analyzed under a microscope this helps to find the presence of lung cancerous cells (4).

TREATMENT OF LUNG CANCER

After the diagnosis of the patient treatments are planned on the basis of the stage of lung cancer and how far it has spread to the neighboring tissues, the different types of treatment are:

SURGERY

For removing the part of lung which is affected with cancerous cells surgery is performed:

- **Wedge resection** is used to remove a small section of lung that contains the cancerous cells along the margin of the healthy lung tissue.
- **Segmental resection** is used to remove a larger portion of the lung where cancerous cells are present, but not the entire lobe.
- **Lobectomy** is used to remove the entire lobe of lung.
- **Pneumonectomy** is the used to remove the entire lung from the chest region.

Surgery may be an option when the cancer is only confined to the lungs and has not spread outside to neighboring tissues (5).

RADIATION THERAPY

Radiation therapy uses high powered energy beams from sources such as X-rays and protons to kill cancerous cells. During radiation therapy, the patient lie on the table while machine moves around you, directing radiation to the precise where the tumors are located on the body.

For people with advanced lung cancer, radiation may be used before or after the surgery. It is often combined with chemotherapy treatments to get rid of tumors. For advanced lung cancers and those that have spread to the neighboring or distant areas of the body radiation therapy may help in relieving symptoms such as pain (5, 6).

CHEMOTHERAPY

Chemotherapy uses drugs to destroy cancerous cells. One or more chemotherapy drugs may be given to the patient through a vein in arm (intravenously) or given orally. Combination of drugs is usually given

in series of treatments over a period of weeks or months, with breaks in between so that the patient can recover.

Chemotherapy is often used after surgery to kill any cancerous cells that may remain after surgery. It can also be used alone or in combination with radiation therapy. It can be used before surgery to shrink the tumors and make them easy to remove (6).

STEREOTACTIC BODY RADIOTHERAPY

Stereotactic body radiotherapy, also called as radiosurgery, is an intense radiation treatment that aims many high powered energy beams of radiation from many angles at the tumor location. Radiosurgery is an option for people with small lung cancers who can't undergo surgery. It can also be used to remove cancer that spreads to other parts of body, including the brain (5, 6).

IMMUNOTHERAPY

Immunotherapy uses the person's immune system to fight cancer. Body's disease fighting immune system may not attack the cancer cells because these cells produce a protein that helps them to hide from the immune system cells. Immunotherapy works by interfering with this process. It is majorly used for people with advanced lung cancers and cancers that have spread to the other parts of body (5, 6).

TARGETED DRUG DELIVERY

Targeted drug treatments focuses on the specific abnormalities present within cancer cells. By blocking these abnormalities, targeted drug delivery can cause these cancer cells to die. These are mostly used for people with advanced lung cancer or recurrent cancer. Some targeted therapies only work in those who have cancer cells because of certain genetic mutations. These cancer cells may be tested inside a laboratory to make sure if these drugs might work for the person having cancer (6).

CONCLUSION

Lung cancer causes the highest amount of deaths out of all the cancer that affects humans. From the above we can conclude that lung cancer has many factors which affect us from our day to day life and out of those there are certain factors that we can control. As far as treatment goes it has many ways to diagnose but it is totally dependent on which stage the cancer is at currently inside the lungs. So people who are chronic smokers or works at places where they are exposed to asbestos or some kind of radiation is at high risk of getting lung cancer. As of now cancer is an incurable disease but it can be cured if it's diagnosed at perfect time.

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24. SEPTICEMIA: DID YOU KNOW ABOUT THAT?

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Septicemia is another term that is used to describe blood poisoning. It is very serious caused by the presence of large amounts of bacteria in the bloodstream. It is a potentially life-threatening infection that affects the lives of thousands of people every year all over the world (1). Septicemia occurs when infection elsewhere in the body, such as the lungs, gastrointestinal system, and skin enters the bloodstream. Bacteria usually drain from the primary infection rapidly to the various systems of the body. The immune system of a person affected with septicemia shows an immediate response to the function in the bloodstream.

The onset of this disease is signaled by a high fever, chills, weakness, and excessive sweating, which is followed by a decrease in blood pressure. The microorganism which causes septicemia is usually gram-negative bacteria, which releases the toxic products which trigger an immune response and blood clotting within the blood vessels, which reduces the flow of blood to tissues and organs. Bacteria from the infection, if it enters the bloodstream spread the infection throughout the body (2,3).

CAUSES OF SEPTICEMIA

It is caused by an infection in some other part of the body, this infection is typically very severe. Bacteria in these types of infections enter the bloodstream and then multiply rapidly,which causes immediate symptoms. Blood, in which millions of WBCs are present fights off the infection. As these cells are effective in fighting the infection will help to keep this infection in control. E.g., when a wound becomes infected with some infection, WBCs will fight off that infection and helps to heal the wound. But sometimes infection grows at much rapidly so that these cells cannot control the infection. This is maybe because the infection reaches a severe stage and also may be that the immune system because of some other disease. When this situation occurs, bacteria that cause this infection enter the bloodstream. Once the bacteria enter the bloodstream, bacteria carry this to other tissues and organs of the body which may lead to serious complications (1, 4).

WHO IS MORE PRONE TO GET SEPTICEMIA?

It can develop from a normal wound or a simple burn or a serious illness. Older people and young children are more prone to septicemia because of their weak immune systems. Those who recently had surgery or have a weak immune system are at high risk to get this infection. Those who are already in the hospital for some other illness such as surgery are also at high risk of getting this. This type of infection becomes more dangerous because the bacteria which cause this infection are resistant to antibiotics. You are also prone if you:

- Have some severe wounds or burns in which infection develops
- Very old or very young
- Have a weak immune system

We cannot catch this from some other person because it happens only when we overreact to this infection (3, 4).

SIGNS AND SYMPTOMS OF SEPTICEMIA

Usually, symptoms of septicemia start very quickly. Even in the initial stages, a person having this infection looks very sick. When this infection occurs, the Immune system tries tofight the infection in the stream of blood. This will bring several symptoms because the body fights with the bacteria. some of the symptoms are:

- The feeling of extreme tiredness
- Shivering and chills
- Pale skin
- Rapid breathing
- A high temperature of the body

The skin develops some bruises (called petechiae) or large purple areas (called purpura). This is a common sign of meningococcal septicemia, a type of septicemia which is caused by meningococcus bacteria, which also causes meningitis. In some severe cases of septicemia, the proteins and chemicals released in the bloodstream to fight the bacteria cancause blood vessels to become leaky and loss of fluid which affects the flow of blood. When the blood flow is affected, it reduces the blood pressure which causes damage to some organs like the brain and kidneys, which is called septic shock. This infection has more severe types of symptoms which will emerge as septicemia, which increases without proper treatment. Some of the symptoms are:

- Inability to think clearly
- Vomiting
- Red dots appear on the skin
- Urine volume reduced
- Inadequate supply of blood

It is very crucial to go to the hospital right away if you or someone else showing the symptoms of septicemia. We don't have to wait or don't try to treat this problem at home (6).

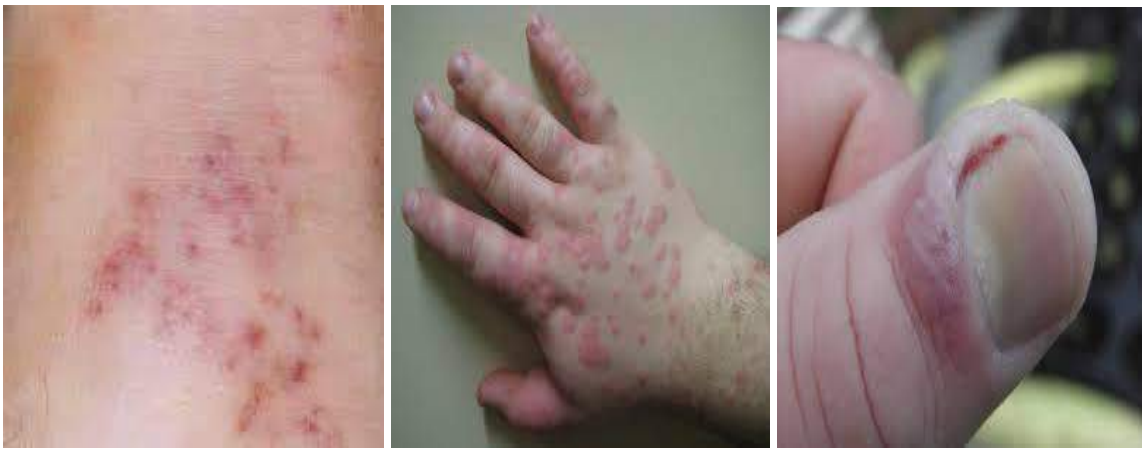

Figure 1 - Signs and symptoms of septicemia (Source: Google images)

COMPLICATIONS OF SEPTICEMIA

Septicemia [blood poisoning] has caused several serious complications. These complications become

fatal if they are left untreated or if delay too long in treatment. SEPSIS – it occurs when the body shows a strong immune response to this infection. it may lead to widespread inflammation throughout the body. It is called severe sepsis, and it may lead to organ failure.

SEPTIC SHOCK – in this complication, a serious drop in blood pressure is observed. This is called septic shock. Bacteria release toxins in the blood which cause extremely low blood pressure it may result in organ or title damage. It is a medical emergency.

ACUTE RESPIRATORY DISTRESS SYNDROME [ARDS] – it is a life-threatening conditionthat prevents enough oxygen from reaching your lungs and blood. It may lead to permanent lung damage. It also damages our brain which leads to memory problems (1, 6).

HOW SEPTICEMIA IS NORMALLY DIAGNOSED?

Diagnosing septicemia is one of the biggest challenges which doctors face. It will involve a wide range of tests. septicemia can be life-threatening and the person will need to be admitted to the hospital as soon as possible, firstly, the doctors aim to discover: what infection originally caused the blood poisoning, what type of infection is in the bloodstream, how badly the body has been affected. It may lead to performing many tests on multiple fluids which help to confirm the infection. Some of the tests are urine tests, blood tests, etc. Doctors may also check cell and platelets counts and may perform tests to analyze blood clotting. Doctors may also check oxygen and carbon dioxide levels in the blood. if septicemia cause breathing issues, and the signs of this infection aren't obvious, doctor may also ordera test to look more closely at specific organs and tissues such as X-ray, MRI, CT scan, ultrasound, etc. (2, 5, 6).

TREATMENT OF SEPTICEMIA

Septicemia when start to affect our organs and tissues' function is a medical emergency. Itmust be treated at the hospital. If this infection is diagnosed early when it has not started to affect the organ and tissues function or the function of any other internal organ, it can be treated with the help of antibiotics. But in severe cases, patient will stay in the hospital and be put on antibiotics intravenously. But this happens only when antibiotics are delivered straight into the blood in a vein. In some serious cases, children also need medication for low blood pressure and are supported by machines so that their organs function properly. Treatment will also depend on some factors like

- age of the patient
- the overall health of the patient
- the extent of the condition of the patient
- tolerance level for certain medications of the patient

Antibiotics are also used to treat the infection. It's typically very hard to determine the type of bacteria, initially, treatment will use usually broad-spectrum antibiotics, which are designed to work against a wide range of bacteria. A more focused antibiotic is used, when the specific bacteria is identified. The patient may also get fluids and other types of medications intravenously to maintain the blood pressure, mainly to prevent forming blood clots. The patient may also get oxygen through a mask or ventilator if breathing issues are detected as a result of septicemia (4, 6).

IS THERE ANY WAY TO PREVENT SEPTICEMIA?

Bacterial infections are the cause of septicemia. If the infection is treated effectively with antibiotics in the early stages, it is possible to prevent bacteria from entering the blood. Children can be protected by

ensuring that they stay up to date with their vaccinations. Some precautions also help to prevent septicemia: (2)

- avoid smoking
- avoid taking illegal drugs
- take healthy diet
- do exercise regularly
- wash your hands regularly
- stay away from people who are sick

Conclusion

From the above article, it can be concluded that septicemia has many factors which can affect us in our day-to-day life. As discussed in the article that it has many ways to diagnosebut it is dependent on the stage at which is affected and treatment is also dependent on the affected area including tissues or organs. As it affects mostly babies, people over 75, peoplewith diabetes, and people with a weak immune system. Cancer is an incurable disease but it can be cured until it is diagnosed at the perfect time, so it's better to go for check-ups if something is uneasy it's better to stay alert rather than regretting later.

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25. *IDEONELLA SAKAIENSIS*: A BACTERIUM THAT FEEDS ON PLASTIC

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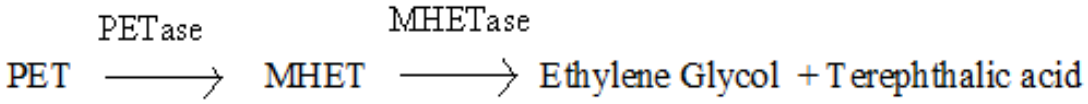
Polyethylene terephthalate (PET), one of the most extensively applied synthetic polymers, is composed of ester bond linked terephthalic acid (TPA) and ethylene glycol (EG). The majority of the world's PET production is for synthetic fibres (in excess of 60%), with bottle production accounting for about 30% of global demand. This huge demand is due to its transparency, malleability, and resistance to natural degradation processes. The annual production of PET is estimated to exceed 50 million tons. Large amounts of this plastic accumulate as waste in landfills and oceans, and have caused a severe environmental burden. Using enzymes to decompose PET into its building blocks is an eco-friendly

strategy to reduce plastic waste and recover the petroleum based starting materials TPA and EG, closing the loop of PET production and recycling (1-3).

Polyethylene Terephthalate

PET is produced by the polymerization of ethylene glycol and terephthalic acid. When heated together under the influence of chemical catalysts, ethylene glycol and terephthalic acid produce PET. Under the influence of heat and catalysts, the hydroxyl and carboxyl groups react to form ester (CO-O) groups, which serve as the chemical links that join multiple PET units together into long-chain polymers. Water is also produced as a by-product. The aerobic bacterium Ideonella sakaiensis uses the enzyme PETase to break down PET into mono (2-hydroxyethyl) terephthalate (MHET). Minor amounts of Bis-(2-hydroxyethyl) terephthalate (BHET) are also produced, but they are converted to MHET by further action of PETase. Another enzyme, MHETase, subsequently breaks down the MHET into ethylene glycol (EG) and terephthalic acid (TPA). The optimum pH is 7 and the optimum temperature range is 30–37 °C for this reaction (1, 2, 5).



Description about the Bacteria

Ideonella sakaiensis

Order: Burkholderiales **Family**: Comamonadaceae **Genus**: Ideonella **Species: Ideonella sakaiensis**

Ideonella sakaiensis is a bacterium from the genus Ideonella capable of breaking down and consuming the plastic poly (ethylene terephthalate) (PET) as a sole carbon and energy source. Ideonella sakaiensis was first identified in 2016 by a team of researchers led by Kohei Oda and Kenji Miyamoto after collecting a sample of PET-contaminated sediment near a plastic bottle recycling facility in Japan. These were also found to contain Cytochrome oxidase and catalase enzymes. Growth was observed by the scientists within the pH range 5.5-9 and temperature 15–42 degree Celsius. Optimum pH and temperature range were found to be pH 7-7.5 and 30–37 degree Celsius respectively (1).

Structure of PETase

The PETase enzyme has an alpha/beta hydrolase fold that has a twisted central beta sheet made up of 9 beta strands sandwiched by 6 alpha helices. The location of the catalytic triad could be elucidated easily by the scientists due to the similarity of PETase and cutinases (upto 47% sequence identity to homologous cutinases). The triad comprises Ser131-His242-Glu177. A superficial groove located above the nucleophilic serine is the putative substrate-binding pocket. Interestingly, the active site of PETase seems to be wider than the other cutinases. The wider substrate-binding space may be one of the causes due to which PETase could accommodate a bulkier substrate like PET. However, residues that comprise the

substrate-binding pocket are conserved or semi conserved in PETase and other homologous enzymes. The Trp156 wobbling in PETase plays an important role in the catalytic reaction. Austin et al. introduced two mutations in the adjacent region of the catalytic site to make the secondary substrate-binding cleft narrower; and this resulted in higher efficiency of the enzyme in reducing PET crystallinity (4).

Mechanism of action of PETase (3.1.1.101)

A number of enzymes from plastic-degrading microbes which can cleave ester linkages are lipases, esterases, carboxylesterases, and cutinases. Among these, cutinases (EC 3.1.1.74) are the most efficient PET hydrolysing biocatalysts as they lack the lid structure. Lipases, on the other hand, are known to require activation at the lipid water interface in order to function. Astonishingly, PET and cutin share minimal structural features other than the ester bond, which is attacked and cleaved by the enzyme. It has been found that PETase and other PET hydrolysing cutinases share high sequence identity, which indicates that there are critical structural features responsible for substrate binding to the enzymes. PETase prefers PET over p-nitrophenol (pNP)-linked aliphatic esters as a substrate. Also, PETase shows between 5 and 120 times higher depolymerisation activity against PET films at 30°C than thermophilic PET-degrading enzymes tested to date. For the mechanism of action shown below, the scientists used substrate analogue HEMT [(1(2hydroxyethyl) 4methyl terephthalate] and product analogue pNP of PET, and this helped them to discover the mechanism of action of PETase.

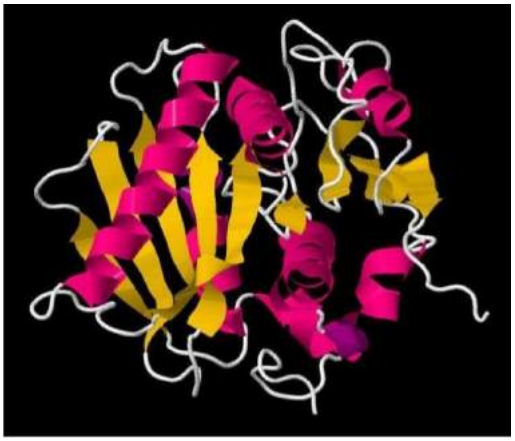


Figure 1 - Structure of PETase from PDB(A)

HEMT contains an ester bond moiety and so is considered a substrate analog. In the complex structure, its carbonyl group lies adjacent to Ala131, facilitating nucleophilic attack by Ser131 in the wildtype enzyme. The carbonyl O atom is within the H bond distance of the oxyanion hole formed by the main chain NH groups of Met132 and Tyr158. Ile179 and Met132 provide hydrophobic contacts, and the Trp156 indole ring appears to provide a T stacking (face to edge) force to the aromatic moiety of HEMT. pNP is an analogue of a leaving product of PETase as it is structurally similar to TPA. pNP binds to the same position as HEMT and is in contact with Trp156, Ile179, and Met132 via hydrophobic interactions. When the bound ligands in the two complex structures are compared, pNP is rotated by about 36° and shifted away from the catalytic centre by 2.3, so that the benzene ring is stacked (face to edge) by the Trp156 indole ring (4). It would not be considered an exaggeration to say that the invention of plastics was the biggest invention of the 20th century.

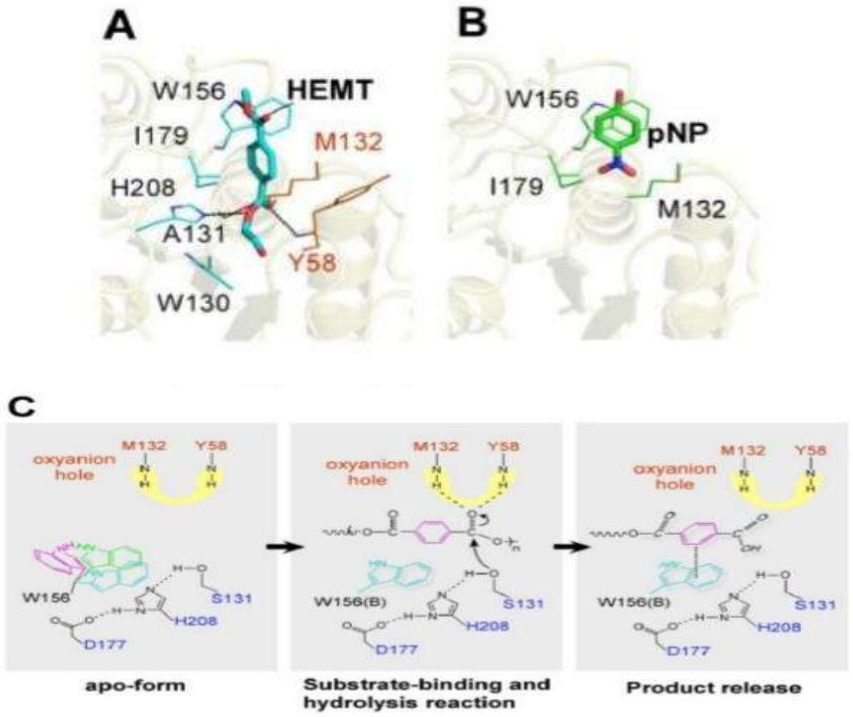


Figure 2 - Mechanism of action of PETase (B)

However, now it has become one of the biggest burdens on the environment (6). With the discovery of the unique plastic-eating bacteria, *Ideonella sakaiensis*, the major environmental issue of plastic waste management can be resolved. There is a dire need for a way to combat the severe environmental burden posed by plastic waste. As we know, enzymes are the best and most efficient catalysts in nature, so they can be utilized to transform useless plastic waste into useful and innocuous products.

Conclusion

It would not be considered an exaggeration to say that the invention of plastics was the biggest invention of the 20th century. However, now it has become one of the biggest burdens on the environment (6). With the discovery of the unique plastic-eating bacteria, *Ideonella sakaiensis*, the major environmental issue of plastic waste management can be resolved. There is a dire need for a way to combat the severe environmental burden posed by plastic waste. As we know, enzymes are the best and most efficient catalysts in nature, so they can be utilized to transform useless plastic waste into useful and innocuous products.

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II. Nobel HALL OF FAME

2021-22

John B. Goodenough

M. Stanley Whittingham

Akira Yoshino

The Nobel Price In Chemistry (2019) has been awarded for the development of the lithium-ion battery. This lightweight, rechargeable and powerful battery is now used in everything from mobile phones to laptops and electric vehicles. It can also store significant amounts of energy from solar and wind power, making possible a fossil fuel-free society.

William G. Kaelin Jr

Sir Peter J. Ratcliffe

Gregg L. Semenza

The Nobel Prize in Physiology or Medicine (2019) has been awarded jointly "for their discoveries of how cells sense and adapt to oxygen availability."

Jennifer A. Doudna

Emmanuelle Charpentier

The Nobel Price For Chemistry(2020) has been awarded for discovering one of gene technology's sharpest tools: the CRISPR/Cas9 genetic scissors.

Harvey J. Alter

Michael Houghton

Charles M. Rice

The Nobel Prize in Physiology or Medicine (2020) has been awarded to three scientists who have made a decisive contribution to the fight against blood-borne hepatitis, a major global health problem that causes cirrhosis and liver cancer in people around the world.

Benjamin List

David W.C. MacMillan

The Nobel Prize in Chemistry (2021) has been awarded jointly for the development of a precise new tool for molecular construction: organocatalysis. This has had a great impact on pharmaceutical research, and has made chemistry greener.

David Julius

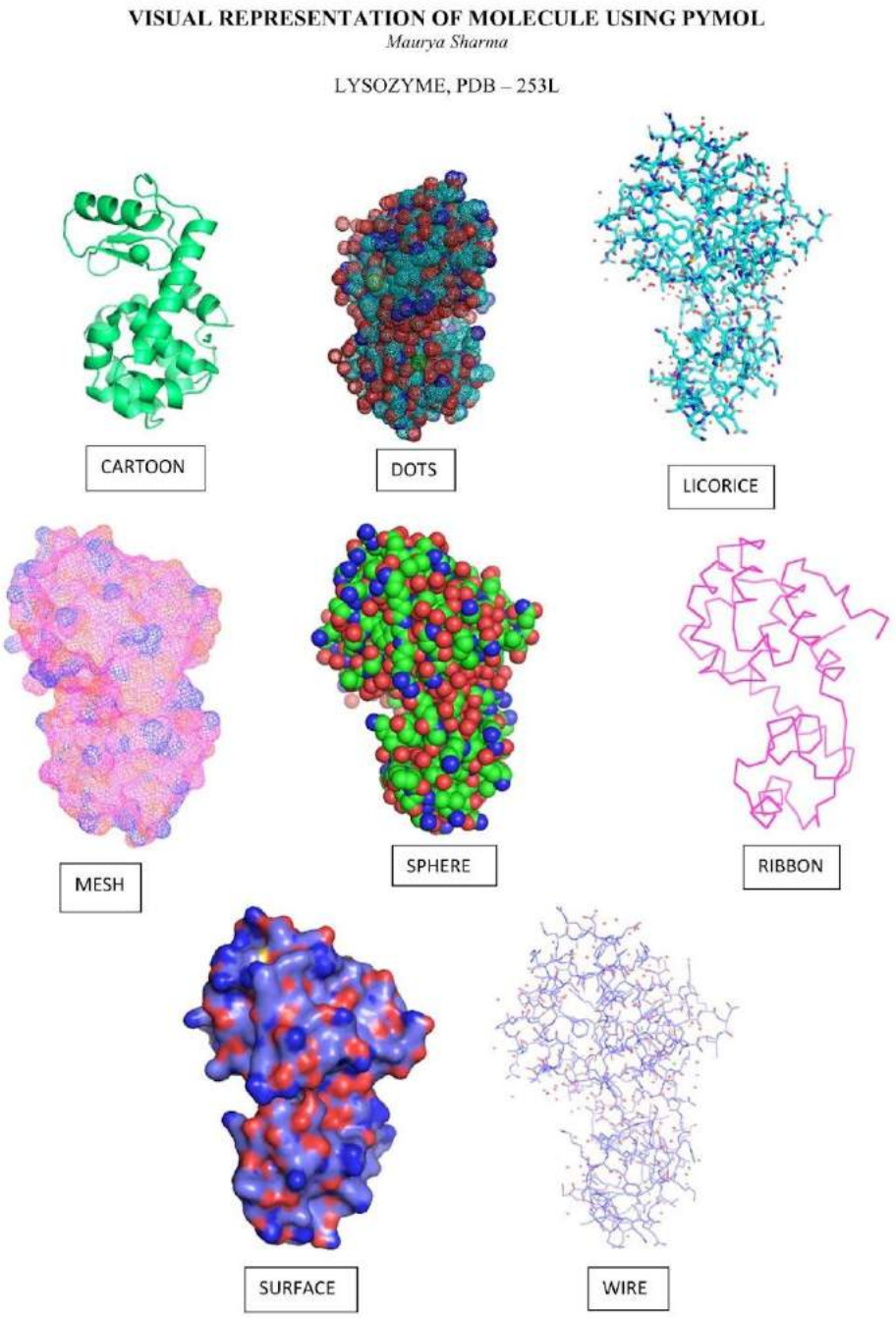
Ardem Patapoutian

The Nobel Prize in Physiology or Medicine (2021) has been awarded jointly to David Julius and Ardem Patapoutian for their discoveries of receptors for temperature and touch

III. Fun with Science

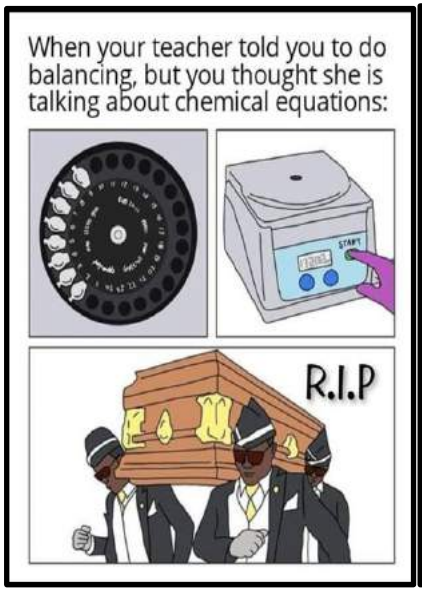
Can you see what I can see?

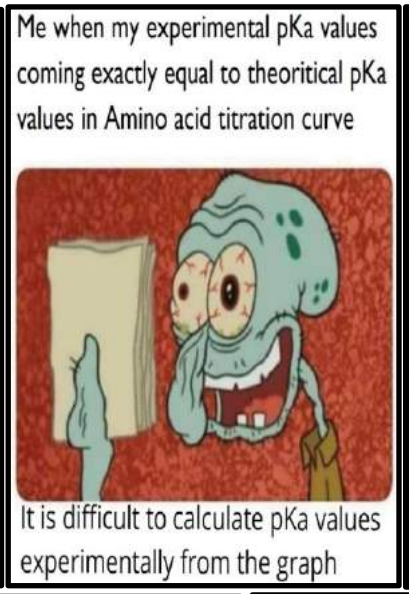
Maurya Sharma, 3rd Year, Bsc (H) Biochemistry, Shivaji College, DU

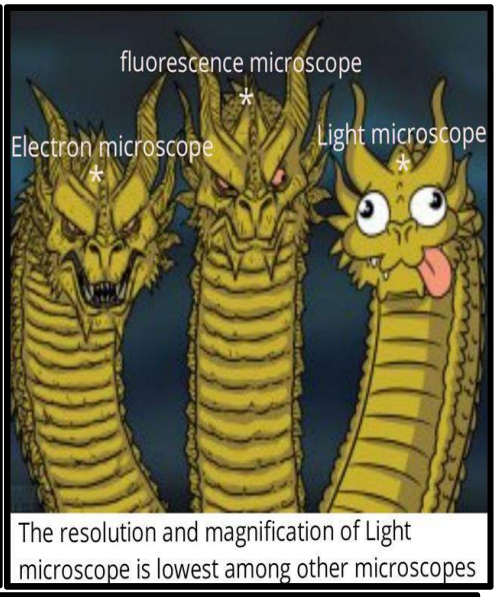


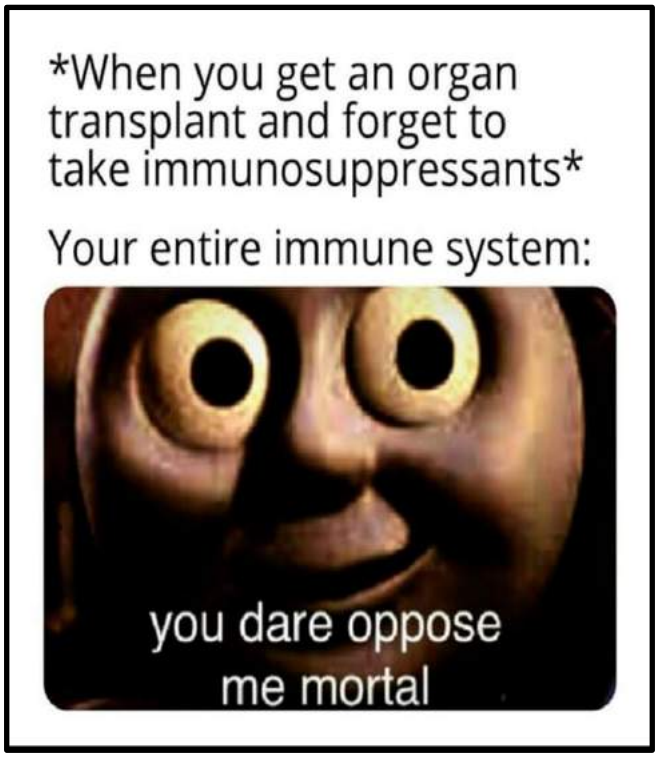
Meme Zone

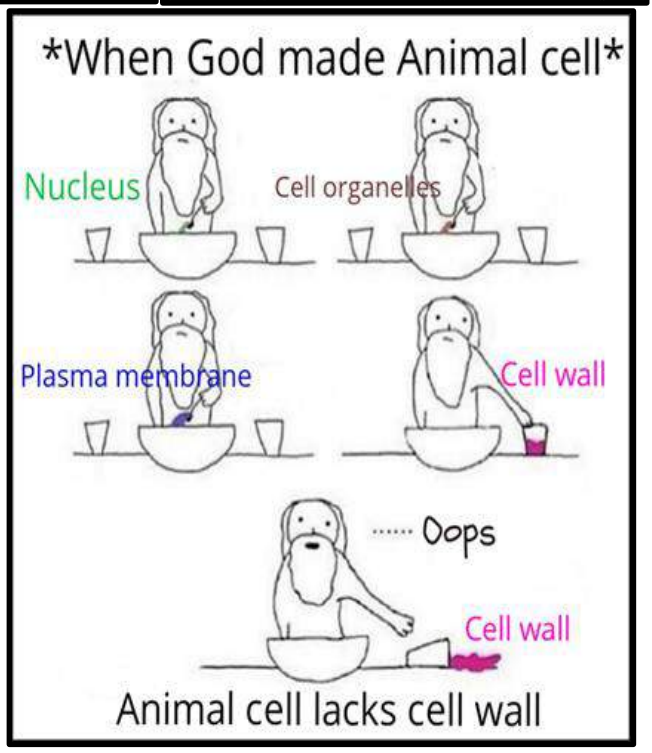
Vinayak Joshi (Batch of 2018-21), Aditi Rattan, Riya (Batch of 2019-22)
Naman Gupta (Batch of 2020-23)
Department of Biochemistry, Shivaji College, University of Delhi











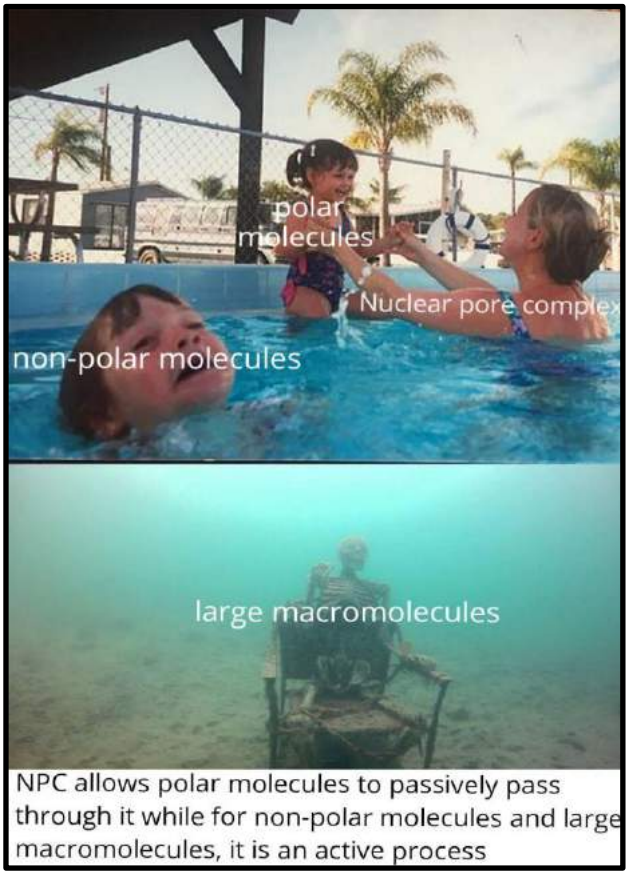

Me: writing a review article
PubMed

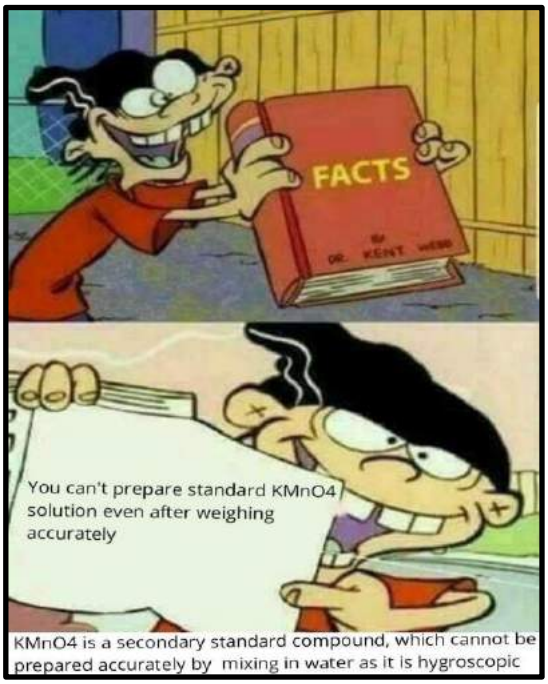

TRANSCRIBED DNA
REPLICATED DNA
WAITING FOR TRANSCRIPTION

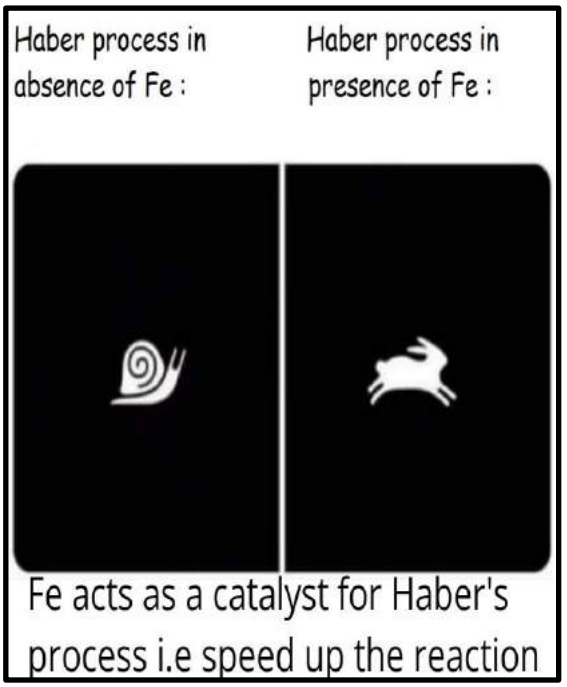

DNA Polymerase when there is a mutation after proofreading


Producing ROS
Getting killed by ROS


Cancer cell


polar molecules
Nuclear pore complex
non-polar molecules
large macromolecules
NPC allows polar molecules to passively pass through it while for non-polar molecules and large macromolecules, it is an active process


FACTS
You can't prepare standard KMnO4 solution even after weighing accurately
KMnO4 is a secondary standard compound, which cannot be prepared accurately by mixing in water as it is hygroscopic

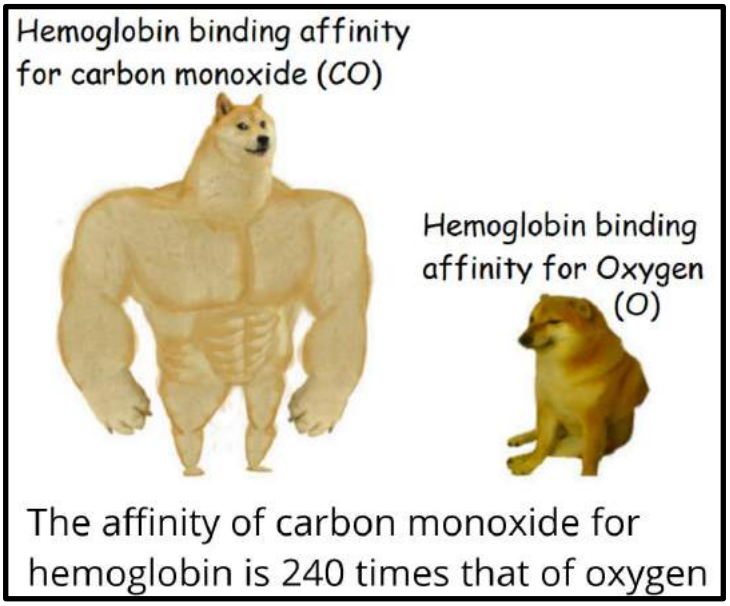

Haber process in absence of Fe :
Haber process in presence of Fe :
Fe acts as a catalyst for Haber's process i.e speed up the reaction

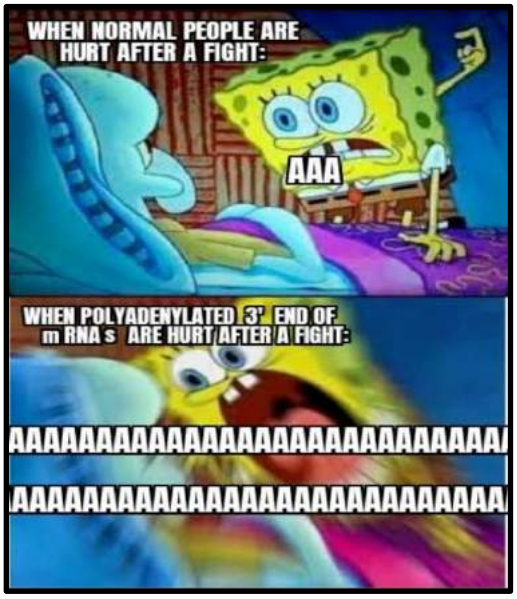

WHEN YOU CONSUME ACETIC ACID WHILE PIPETTING
LAB PARTNER
FRIEND

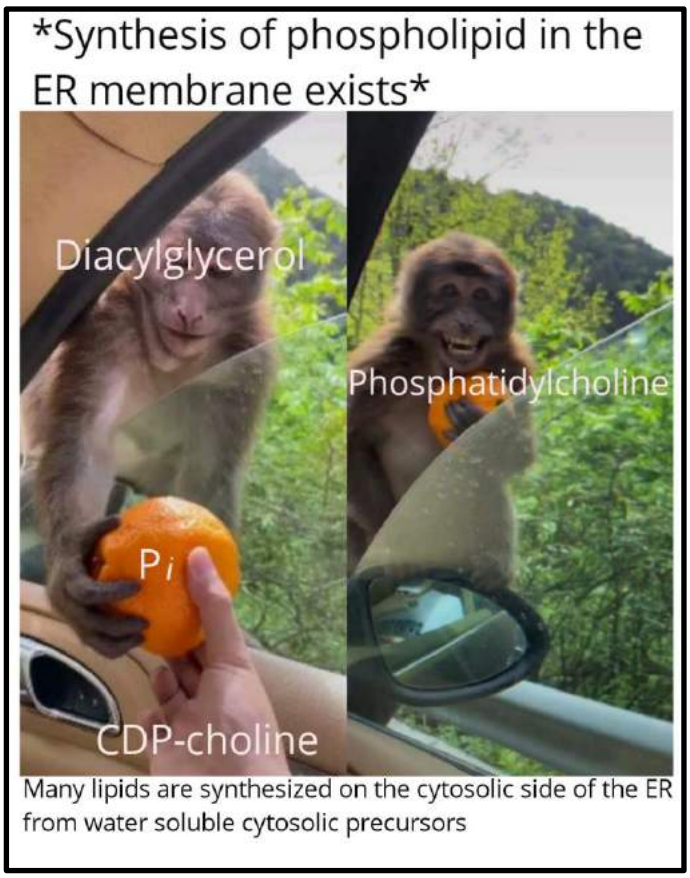

What does this mirror do, professor?
It shows us nothing more or less than the deepest, most desperate desire of our hearts
Perfect pink colour in KMnO4 titration
It is difficult to get light pink colour, just 1 more drop of KMnO4 makes it dark pink


Astronaut : Living in space
Circadian rhythm :
(confused unga bunga)
circadian rhythm regulates the sleep-wake cycle. It depends on sunlight, therefore inspace, it gets disturbed

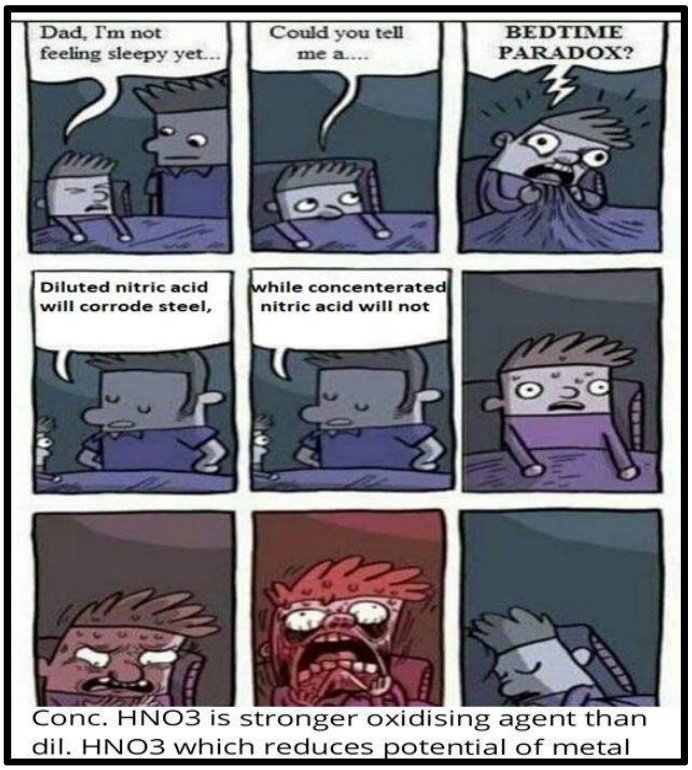

IS THAT YOU?
YEAH... BUT THAT'S AN OLD PHOTO...
Frog's larvae do not resemble the adult
Fun Fact : Frogs lay around 2500-6000 eggs at a time


Hemoglobin binding affinity for carbon monoxide (CO)
Hemoglobin binding affinity for Oxygen (O)
The affinity of carbon monoxide for hemoglobin is 240 times that of oxygen


WHEN NORMAL PEOPLE ARE HURT AFTER A FIGHT:
AAA
WHEN POLYADENYLATED 3' END OF m RNA s ARE HURT AFTER A FIGHT:
AAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAA



Many lipids are synthesized on the cytosolic side of the ER from water soluble cytosolic precursors



Conc. HNO3 is stronger oxidising agent than dil. HNO3 which reduces potential of metal

Unscramble

Maurya Sharma, Ishita Jha (Batch of 2019-22)
Department of Biochemistry, Shivaji College, University of Delhi

1. It is a homology and similarity tool.

L	T	S	B	A

2. It is a multiple sequence alignment tool.

U	A	C	L	W	L	S	T

3. It is a sequence database.

E	K	B	G	N	A	N

4. It is a metabolic database.

G	E	G	K

5. It is a protein sequence database.

W	O	P	S	S	R	I	T	S

6. It is a tool used for discovering motifs.

A	O	I	P	C

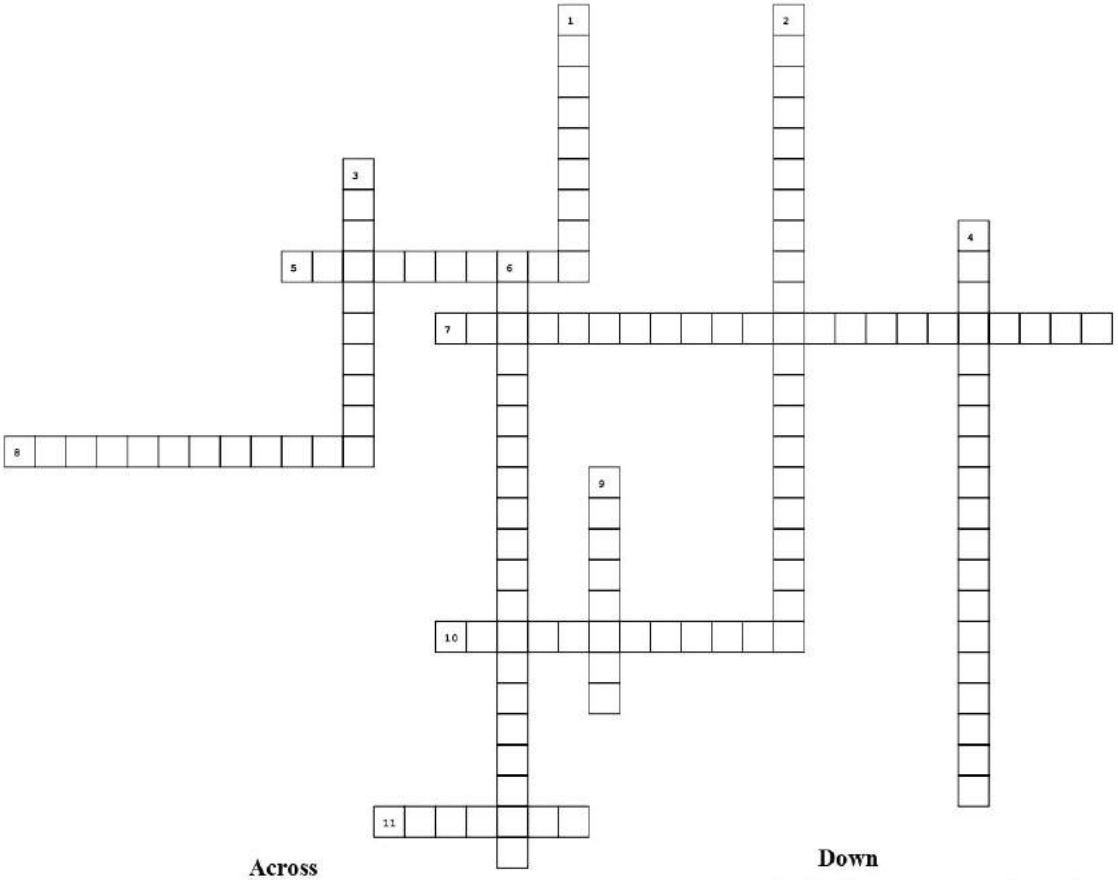
7. It is a Literature database.

E	L	I	M	N	D	E

ANSWERS: 1. BLAST, 2. CLUSTALW, 3. GENBANK, 4. KEGG, 5. SWISS PROT, 6. COPIA, 7. MEDLINE

CROSSWORD

Shashank Kumar Gupta (Batch of 2018-21)
Department of Biochemistry, Shivaji College, University of Delhi



Across

5. A protein responsible for the bidirectional translocation of phospholipids between the two monolayers of a lipid bilayer of a cell membrane, without utilizing any ATP.

7. Catalyzes the conversion of succinate to fumarate.

8. A digestive enzyme that breaks down. proteins. It is naturally produced by the pancreas in the human body.

10. A serine/threonine kinases, with phosphotransferase activity, that help the dividing cell dispense its genetic materials to its daughter cells.

11. An acronym for Ribulose-1,5-bisphosphate

Down

1. An enzyme involved in the conversion of the male sex hormone to estrogen.

2. A metalloenzyme extracted from Horseradish, used extensively in biochemistry, also, catalyzes the oxidation of various organic substrates by hydrogen peroxide

3. A soluble blood protein involved in clotting and wound healing which could form a suitable provisional matrix for supporting the development of new tissues.

4. Superoxide dismutases are a group of enzymes that catalyze the dismutation of superoxide radicals to molecular oxygen and hydrogen peroxide, providing cellular defense against reactive oxygen species.

6. It is our primary defense against alcohol, a toxic molecule that compromises the function of our nervous system.

9. A marker enzyme for Peroxisomes.

Answers: 1. Aromatase 2. HorseRadishPeroxidase 3. Fibrinogen 4. SuperoxideDismutase 5. Scramblase 6. Alcohol dehydrogenase 7. succinate dehydrogenase 8. Chymotrypsin 9. Catalase 10. AuroraKinases 11. RuBisCo

Pallavi Dutta (Batch of 2018-21), Aditi Rattan (3rd year)

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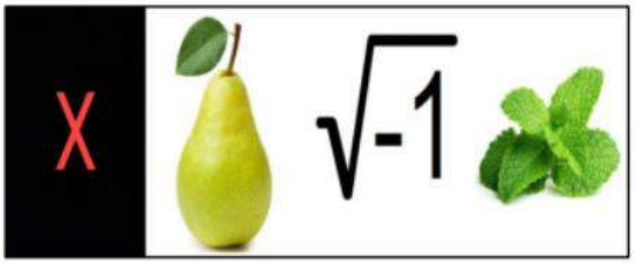
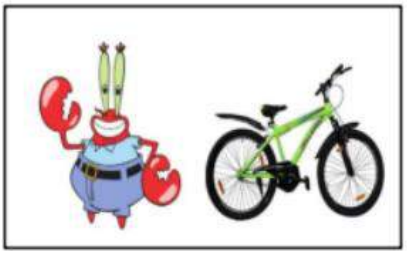
1)



2)

3)

4)



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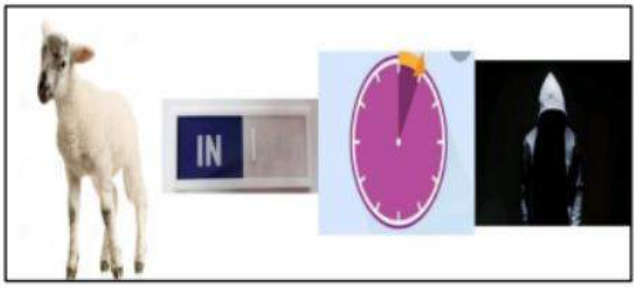

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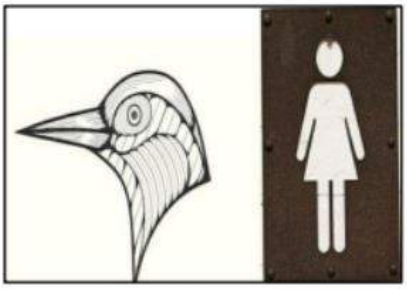

7)

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10)

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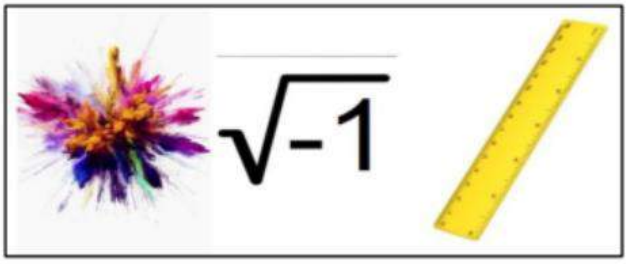
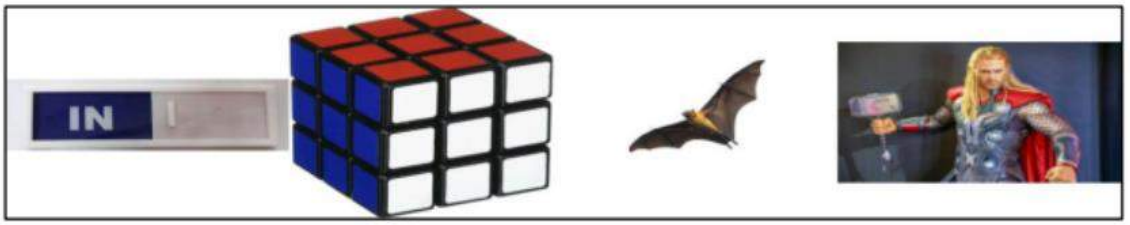
13)



14)

15)



Answers: **1)** Experiment. **2)** Nobel Prize. **3)** Calmodulin. **4)** Krebs cycle. **5)** Laminar hood. **6)** Beaker. **7)** Fermentation. **8)** Protein. **9)** Histology. **10)** Active site. **11)** Thermodynamics. **12)** Daughter cell. **13)** Calorimeter. **14)** Autoclave. **15)** Incubator.

Did You know?

Riya Thomas, Aditi Rattan (Batch of 2019-22)

Department of Biochemistry, Shivaji College, University of Delhi

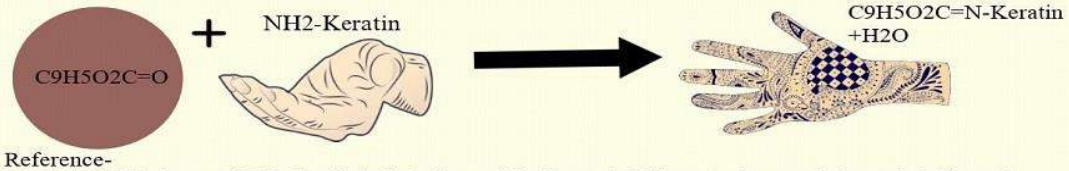
- Human saliva contains a painkiller called opiorphin that is six times more powerful than morphine.
- White clothes including lab coats are preferred while working in the labs as they glow under UV light in the presence of a special compound class called FWA (fluorescent whitening agent). FWA is added to all laundry detergents. These compounds adsorb to fabric during washing and eventually brighten clothing by making clothes optically whiter, they reflect light in the blue spectrum while absorbing UV light.
- Geosmin produced by Actinomycetes has a distinct earthly flavour and aroma, and is responsible for the earthly taste of beets and a contributor to the scent in the air when rain falls after a dry spell of weather.
- Bees communicate through 'waggle dance. The waggle dance is a set of very precise movements. The direction the bee moves in relation to the hive indicates direction; if it moves vertically the direction to the source is directly towards the sun.
- There isn't enough water in honey for microorganisms to live on, which is why honey never goes bad.
- Scent of bread: Bread contains over 500 volatile compounds, but only about 20 contribute to its aroma. Bread smells slightly sweet due to maltol and isomaltol (resulting from caramelization during baking). Other compounds result from mailard reaction: 2-acetyl-1-pyrroline responsible for the roasty aroma; 2-nonenal and diacetyl.
- Your gut bacteria communicates with your brain, and has a profound impact on making you feel happy or sad.
- The killer fungus (Entomophthora muscae) turns flies into the zombies! After a fly picks up the fungal spore, it stops flying. It starts summiting and then some liquid drips out its mouth that glues the fly to the surface it's standing on. Then, the fly's wings ascent until they're pointing upwards and it dies frozen in this lifelike pose. Soon after, white spongy fungus oozes out of its abdomen.
- Jellyfish and lobsters are considered biologically immortal. They don't age and never die unless they are killed.
- Butterflies drink turtle tears in search of nutrients. As herbivores, they have naturally lower levels of sodium in their diets, they have to seek out alternative sources.
- The color which we see when we close our eyes is called Eigengrau which is different from black.

Biochemistry in Everyday Life

Pallavi Dutta, Vinayak Joshi (Batch of 2018-21)
Department of Biochemistry, Shivaji College, University of Delhi

Chemistry behind Henna tattoos

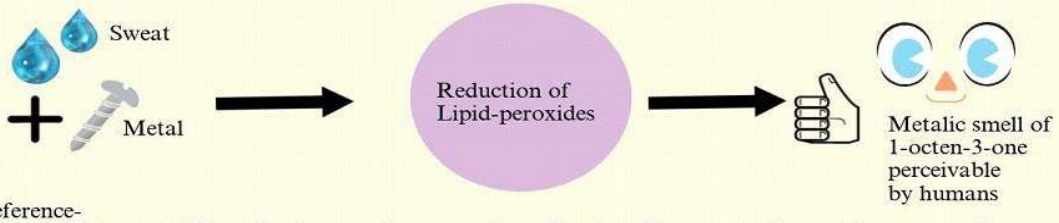
Ever wondered how does Henna produce such a rich color on your skin? Henna (*Lawsonia inermis*) leaves contain a chemical called Lawsone(0.5-2% concentration in dried & powdered henna leaves). Lawsone is the main compound that stains & gives characteristic color. Lawsone does not stain unless it is released from dried Henna powder. For application, a thick henna slurry is made and a slightly acidic liquid (Lemonjuice) is added to prevent its oxidation . The slurry is left for a few hours (for proper soaking of henna and release of Lawsone).This product is called Mehndi, and is applied on skin and hair. Lawsone penetrates through and binds and binds to keratin protein (present in skin, hair, nails). This binding of Lawsone to Keratin gives characteristic color of mehndi. Oils with high monoterpene alcohols levels improve this staining. Therefore, it is advised to apply a little oil after sraping off mehndi. After binding with Keratin, Lawsone initially darkens with time due to oxidation. The color lasts for 3-4 weeks, gradually fading away.



Reference-
1. Semwal RB, Semwal DK, Combrinck S, Cartwright-Jones C, Viljoen A. Lawsonia inermis L.(henna): Ethnobotanical, phytochemical and pharmacological aspects. Journal of Ethnopharmacology. 2014 Aug 8;155(1):80-103.
2. Bhuiyan MR, Islam A, Ali A, Islam MN. Color and chemical constitution of natural dye henna (Lawsonia inermis L) and its application in the coloration of textiles. Journal of Cleaner Production. 2017 Nov 20;167:14-22.

The "Ironic" smell of Iron

Have you ever wondered about the origins of the metallic smell that comes from the coins? Can we really smell iron? Well, the answer is "no". The chemical that causes the metals to impart a metallic smell is ironically a compound produced by our own bodies!!
Metals in their native, non-ionic forms are non-volatile thus rendering them unable to trigger olfaction. The smell that is emitted by iron metal (and copper) is attributed to mixture of lipid-peroxides that are released when the skin comes in contact with the metal. The sweat in human skin reacts with metallic iron (Fe) oxidizes it to Fe2+ ions which in turn get oxidized to Fe3+ ions and this is combined with the reduction and of lipid peroxides present on skin and release of odorant carbonyl hydrocarbons, majorly 1-octen-3-one which is perceived by humans as "metallic smell".



Reference-
1. Block, Eric, et al. "The role of metals in mammalian olfaction of low molecular weight organosulfur compounds." Natural product reports 34.5 (2017): 529-557.
2. Glindemann, Dietmar, et al. "The two odors of iron when touched or pickled:(skin) carbonyl compounds and organophosphines." Angewandte Chemie International Edition 45.42 (2006): 7006-7009.

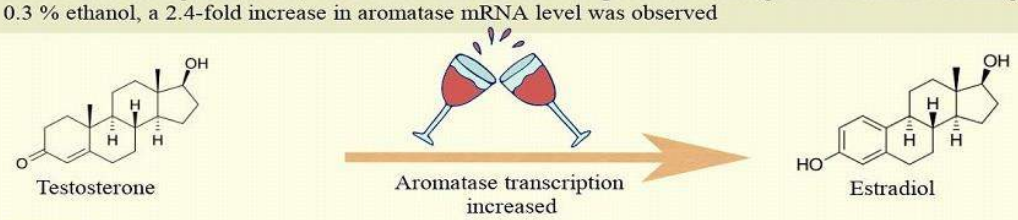
Shashank Kumar Gupta (Batch of 2018-21), Aditi Rattan (Batch of 2019-22)
Department of Biochemistry, Shivaji College, University of Delhi

Alcoholism and estrogen production in males!

Did you know that alcoholic men, may be utilising wine and beer as a way to treat depression, are at more risk to breast cancer and ironically to depression.

Aromatase enzyme belongs to the cytochrome P450 superfamily and is characterized by the presence of a heme group. Humans only have one aromatase protein; naturally, it is a key enzyme involved in the production of estradiol-E2 and estrone-E1 from testosterone and androstenedione respectively

It has been reported that consumption of alcohol increased the transcription of the Aromatase enzyme, naturally, this will lead to a higher rate of conversion of the male sex hormone testosterone to the female sex hormone estrogen. In vitro, when breast cancer cells were proliferated in a growth medium containing 0.3 % ethanol, a 2.4-fold increase in aromatase mRNA level was observed

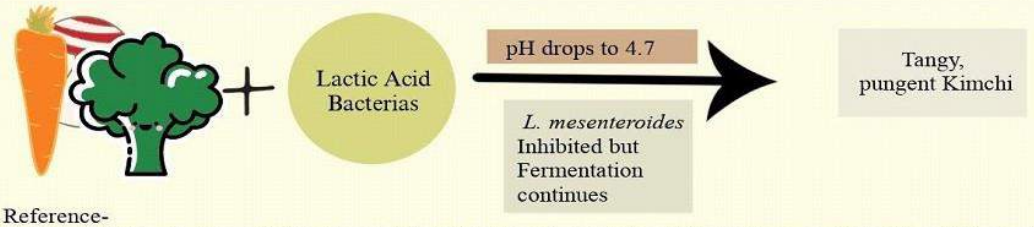


Reference-
1. Subramanian, Ashok et al. "Oestrogen producing enzymes and mammary carcinogenesis: a review." Breast cancer research and treatment vol. 111,2 (2008): 191-202. doi:10.1007/s10549-007-9788-0.
2. Etique, N., Chardard, D., Chesnel, A., Merlin, J., Flament, S., Grillier-Vuissoz, I."Ethanol stimulates proliferation, ERα and aromatase expression in MCF-7 human breast cancer cells". International Journal of Molecular Medicine 13.1 (2004): 149-155.

Fermentation in Kimchi

Have you ever wondered about what else Koreans are crazy about apart from K-pop? Well, it is a spicy, pungent vegetable dish called Kimchi. It is prepared by fermenting the baechu cabbage together with other vegetables and lactic acid bacteria (LAB).

Fermentation is initiated by lactic acid bacteria such as *L. mesenteroides* under normal anaerobic conditions, where lactic acid, acetic acid, carbon dioxide, and ethanol are produced as major end products. As the pH drops to 4.6-4.9 with organic acid accumulation *L. mesenteroides* activity is inhibited, but fermentation continues with other lactic acid bacteria such as *Streptococcus faecalis, Lactobacillus brevis, Pediococcus cerevisiae,* and *L. plantarum*. *L. plantarum* gives the maximum acidity at the later stages. Metabolites produced by lactic acid bacteria like lactic acid and mannitol, determine the flavor the quality of kimchi. Lactic acid creates a tangy, pungent flavor.



Reference-
1. Patra JK, Das G, Paramithiotis S and Shin H-S. Kimchi and Other Widely Consumed Traditional Fermented Foods of korea: A Review (2016) Front. Microbial. 7:1493.
2. Cheigh H-S, Park K-Y and Lee C.Y. Biochemical, microbiological, and nutritional aspects of kimchi(Korean fermented vegetable products) (1994) Critical Reviews in Food Science and Nutrition, 34:2, 175-203.

Simran (Batch of 2018-21), Riya Thomas (Batch of 2019-22)
Department of Biochemistry, Shivaji College, University of Delhi

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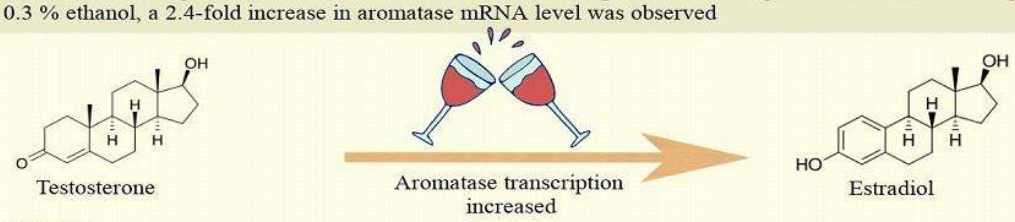

Reference-
1. Subramanian, Ashok et al. "Oestrogen producing enzymes and mammary carcinogenesis: a review." Breast cancer research and treatment vol. 111,2 (2008): 191-202. doi:10.1007/s10549-007-9788-0.
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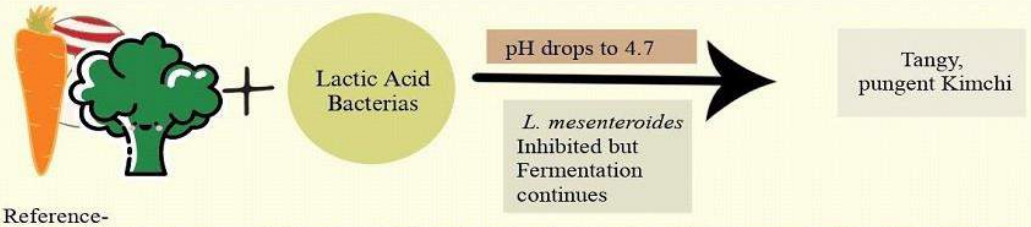

Reference-
1. Patra JK, Das G, Paramithiotis S and Shin H-S. Kimchi and Other Widely Consumed Traditional Fermented Foods of korea: A Review (2016) Front. Microbial. 7:1493.
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IV. Scientific Gallery

DAHLIA

PARVANA P *(Batch of 2019-22)*
Department of Biochemistry, Shivaji College, University of Delhi

Dahlia pinnata is a perennial herbaceous plant with rhizome and tuberous roots, reaching a height of 70 to 120, rarely 160 centimeters. The stem is erect being branched only in the inflorescence. The leaves are usually simple, with leaflets that are ovate and 5–10 cm long. The plant is slightly shaggy. The two to eight flower heads have a diameter of 6 to 10 centimeters on 5 to 15 centimeters long stems. The eight florets have a length of 3 to 5 centimeters, are ovate and coloured pink to deep purple. Dahlias are mid-year to late-year season flowers that grow in a lot of various colors

- Scientific Name: *Dahlia Pinnata*
- Camera: Iphone Xr
- Location: Sir Syed College Botanical Garden, Kannur, Kerala
- Date:6th February 2021
- Captured By: Parvana P
- Reference: https://davesgarden.com/sitewidesearch.php?q=Dahlia+pinnata

THE SHRUB FROM A DISTANT LAND

MERLIN MATHEW *(Batch of 2019-22)*
Department of Biochemistry, Shivaji College, University of Delhi

The shrub *Medinilla speciosa* is easily recognized for its bright pink clusters of flowers and berries. In summer months, tiny flowers grow in panicles with matching pink stems, and they are followed by hot pink berries that mature to purple. These fruits give the plant the common name "**Showy Asian Grapes**", though they are not edible. *Medinilla speciosa* is native to the mountain forests of Borneo, Java, and the Philippines. It is a woody, evergreen shrub which grows to about 2 m (7 ft) and has large, leathery leaves. Though semi-epiphytic in the wild, the species can grow surprisingly well as a houseplant, or in an outdoor pot in tropical or subtropical climates. It is widely used as a traditional medicine, by boiling, brewing or consuming it directly. The fruits are used for diarrhea, mouth sores, anti-inflammatory, anticancer, and antibacterial treatment.

- Scientific Name: *Medinilla speciosa*
- Camera: OnePlus 5T
- Location: KBC Gardens, Kottayam, Kerala
- Date: 6th February 2021
- Captured by: Merlin Mathew
- Reference: https://www.theseedybusiness.com/seeds/medinilla-speciosa

BEAUTY OF NATURE: HONEY BEE SUCKING NECTAR FROM POT MARIGOLD

RIYA THOMAS, *(Batch of 2019-22)*
Department of Biochemistry, Shivaji College, University of Delhi

Calendula (*Calendula officinalis*), also called Pot marigold or English marigold, offers a wealth of culinary and herbal medicine uses that set this lovely flowering annual apart from other garden plants and is native to Eurasia. Calendula grows from 8 inches to one or two feet high, depending on the variety. The flowers are available in orange, yellow and white. These plants do need full sun, defined as six or more hours a day of bright, direct sunshine. They can tolerate partial sun easily. It is Deer resistant; deer generally don't munch on calendula flowers. The flowers are used to make topical preparations to treat skin conditions. Burns, cuts and bruises may all be helped by a cream infused with calendula. The flower has tubular disk flowers in the center and ray flowers, which are often strap shaped, around the periphery

- Scientific Name: *Calendula officinalis*
- Camera: Samsung A20
- Location: St. Paul's Sr. Sec. School, Mala Road, Kota, Rajasthan
- Date: 7th February 2021
- Captured by: Riya Thomas

- Reference: https://gobotany.nativeplanttrust.org/species/calendula/officinalis/
https://davesgarden.com/guides/articles/growing-harvest-and-using-calendula

THE MEDICINAL 'POT MARIGOLD'

ADITI RATTAN, *(Batch of 2019-22)*
Department of Biochemistry, Shivaji College, University of Delhi

Calendula officinalis is a short-lived aromatic herbaceous perennial, growing to 80cm (31in) tall, with sparsely branched lax or erect stems. It belongs to the family of Asteraceae, commonly known as English Marigold or Pot Marigold is an aromatic herb which is used in the traditional system of medicine for treating wounds, ulcers, herpes, scars, skin damage, frost-bite and blood purification. It is mainly used because of its various biological activities to treat diseases like analgesic, anti–diabetic, anti-ulcer and anti-inflammatory. It is also used in gastro-intestinal, gynecological, eye disease, skin injuries and in some cases of burns. Studies have suggested that Calendula extracts have antiviral, anti-genotoxic properties in-vitro. In herbalism, Calendula in suspension or in tincture is used topically for treating acne, reducing inflammation, controlling bleeding, and soothing irritated tissue.

- Scientific Name: *Calendula officinalis*
- Camera: Realme XT
- Location: Shivaji College, Raja Garden, New Delhi
- Date: 11th February 2020
- Captured by: Aditi Rattan
- Reference: AshwlayanVD, Kumar A, Verma M, et al. Therapeutic Potential of Calendula officinalis. Pharm Pharmacol Int J. 2018;6(2):149-155

THE SYMBOL OF LOYALTY AND DEVOTED LOVE

ADITI RATTAN, *(Batch of 2019-22)*
Department of Biochemistry, Shivaji College, University of Delhi

Chrysanthemum x morifolium is an herbaceous perennial which adds a pop of colour to the garden when the leaves start to fall and the colder days start to come. The leaves have a curved edge which adds to the

attractiveness of this plant. It can multiply very fast in garden beds, making it more than just a potted plant for the autumn. A white chrysanthemum is a symbol of loyalty and devoted love. In general, chrysanthemums are believed to represent happiness, love, longevity and joy. Family roots: Member of the Asteraceae or Compositae (aster or sunflower) family. Native to China.

- Scientific Name: *Chrysanthemum x morifolium*
- Camera: Realme XT
- Location: Shivaji College, Raja Garden, New Delhi
- Date: 26th November, 2019
- Captured by: Aditi Rattan
- Reference: https://plants.ces.ncsu.edu/plants/chrysanthemum-x-morifolium/
  https://www.calyxflowers.com/floral-library/chrysanthemum/
  https://www.easternfloral.com/blog/meaning-chrysanthemum-flower/

MEDICINAL PLANT: PINK PERIWINKLE

SUNIDHI BISHT, *(Batch of 2019-22)*
Department of Biochemistry, Shivaji College, University of Delhi

Catharanthus roseus is an evergreen subshrub or herbaceous plant growing 1 m tall. The leaves are oval to oblong, glossy green, hairless, with a pale midrib and a short petiole; they are arranged in opposite pairs. It is a medicinal plant belonging to the dogbane family, Apocynaceae and is one of the most explored short-lived medicinal plant species popularly called “Sadabahar” in some Asian countries such as India. This plant species is native to Madagascar and is usually grown as a medicinal and ornamental plant in parks, gardens and farms. The different plant parts of *C. roseus* are used traditionally in the Indian

system of medicine such as Ayurveda, Unani, and Traditional Chinese Medicine (TCM). It is known to exhibit antimicrobial, antioxidant, anticancer, anthelmintic, antisterility, antidiarrheal, and antidiabetic properties. The plant is used in herbal medicines as it contains anticancer bisindole/monoterpene indole alkaloids (MIAs) such as vinblastine, vincristine, vindesine, and vinorelbine, that have been permitted for clinical use in the U.S. Food and Drug Administration for chemotherapy and other medicinal uses in the pharma sectors. Both extracts and isolated compounds are safe to use for a certain limit, beyond that they can cause adverse effects. Hence, necessary precautions should be taken before consumption.

- Scientific name: *Catharanthus roseus*
- Camera: Vivo V15 Pro
- Location: Shivaji College, Rajouri Garden, New Delhi
- Date: 11th April, 2022
- Captured by: Sunidhi Bisht
- Reference: https://pubmed.ncbi.nlm.nih.gov/34562562

AS PATIENT AS MULBERRIES

SPARSH AGGARWAL, *(Batch of 2021-24)*
Department of Biochemistry, Shivaji College, University of Delhi

Mulberry, belongs to genus Morus, which is a genus of around ten species of small to medium-sized trees, under the family Moraceae comprising of sweet edible fruits. Mulberries of various kinds are native to temperate Asia and North America, and several species are cultivated for their fruits and as ornamentals. Mulberry flowers can be monoecious or dioecious and are deciduous having toothed, sometimes lobed leaves which are alternately arranged along its stemEach fruit develops from an entire flower cluster and is formally known as a multiple. The fruits somewhat resemble blackberries which ripen to white, pink, red, or purple. Red mulberry i.e. Morus rubra found mostly eastern North

America and western Asia is the largest of the genus, often attaining a height of 21 metres (70 feet). It has red and dark purple edible fruits.

- Scientific Name: *Morus rubra*
- Camera: Realme 8s 5g
- Location: Lajpat Nagar Market, New Delhi, India
- Date: 24th March 2022
- Captured by: Sparsh Aggarwal
- Reference: https://www.britannica.com/plant/mulberry-plant#ref9200

MONARCH BUTTERFLY

RAJAT MAURYA, *(Batch of 2019-22)*
Department of Biochemistry, Shivaji College, University of Delhi

Common Name- Monarch Butterfly
Scientific Name- *Danaus plexippus*
During migration, Monarch Butterflies may travel 250 or more miles each day.
The monarch butterfly exhibits the most highly evolved migration pattern of any known species of butterfly or moth and perhaps any known insect.

- Date of Capture- 08/02/2021
- Dimensions- 4096 x 1848 pixels
- Place- Home Garden
- Device- Mobile Camera
- Reference: national geographic.com

PUNY PULCHRITUDINOUS PEST: MEALYBUG

SPARSH AGGARWAL, *(Batch of 2021-24)*
Department of Biochemistry, Shivaji College, University of Delhi

Mealybugs are small, unarmored, scaly, sap-sucking insects belonging to the family *Pseudococcidae*, that are found worldwide, mostly in moist and warm habitats. These are considered as pests that attack citrus trees and ornamental plants, specifically in the interior plantscapes and greenhouses establishments. The name 'mealybugs' is a clear description of the insects' body that is covered wholely with a cornmeal like white sticky powder. The males of this species are mostly two-winged active fliers while the females and the young active members, called the 'crawlers' are present on the underside of the leaves, forming clusters along the veins. Some of the common members of the *Pseudococcidae* family are the 'citrophilus mealybug' (*Pseudococcus calceolariae*) and the 'citrus mealybug' (*Planococcus citri*). Some traditional insecticides, insecticidal soaps, horticultural oils and biological control have proven to be effective against these pests.

- Scientific Name: *Pseudococcidae*
- Camera: Realme 8s 5g
- Location: Shivaji College, University of Delhi, New Delhi, India
- Date: 13th April 2022
- Captured by: Sparsh Aggarwal
- Reference**:** https://www.britannica.com/animal/mealybug

THE THIRSTY OSTRICH

VANSHIKA BANSAL, *(Batch of 2020-23)*
Department of Biochemistry, Shivaji College, University of Delhi

The ostrich is most commonly found in Africa, in various colors like black, brown, pink and white.

Their size is around 210 to 300 cm and weight is around 60 to 150 kg. Incubation period is around 35 to 45 days.Their average clutch size is 20 to 30 eggs.

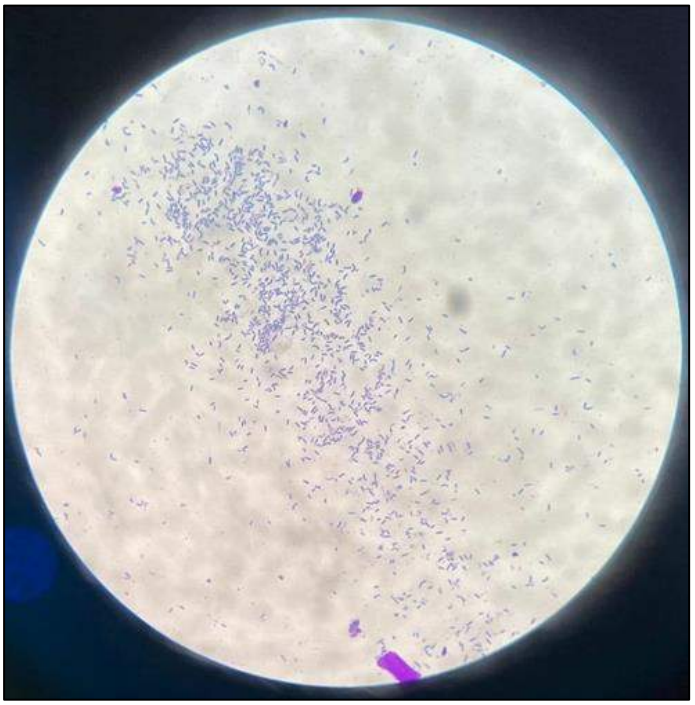



- Scientific name: *Struthio camelus*
- Camera: motoe7 power
- Date: 15 April 2022
- Captured by: Vanshika Bansal
- Location: National zoological park, Delhi
- Reference:https://en.wikipedia.org/wiki/Ostrich

***ESCHERICHIA COLI* STAINED BY METHYLENE BLUE**

AFREEN SHAMSI, *(Batch of 2019-22)*
Department of Biochemistry, Shivaji College, University of Delhi

E. coli is a bacterium commonly found in the intestines of humans and other animals. It is a Gram-negative, rod-shaped, facultative anaerobic, coliform bacteria of the genus Escherichia. Methylene Blue is recognized as a simple stain used for determining bacterial morphology. Is recommended for use in the staining of gram-negative bacteria.



- Bacteria: *Escherichia Coli* (*E. coli*)
- Stain used: Eosin Methylene Blue
- Instrument: Light Microscope
- Magnification: 40x
- Date: 27th October 2021
- Camera: iPhone 11
- Captured by: Afreen Shamsi
- Location: Biochemistry Lab, Shivaji College, University of Delhi

HIBISCUS

RAJAT MAURYA, *(Batch of 2019-22)*
Department of Biochemistry, Shivaji College, University of Delhi

The flowers of Hibiscus rosa-sinensis are edible and are used in salads in the Pacific Islands.

- Common Name- Hibiscus
- Scientific Name- *Hibiscus rosa-sinensis*
- Date of Capture- 16/12/2020
- Dimensions- 2080 × 4068 pixels
- Place- My Home Garden
- Device- Mobile Camera

V. Students' Progression

2016-19

Total strength of class: 26			
S. No.	**Name of student**	**Name of Institute/University**	**Name of programme**
1	Shivani Dixit	Dr. B.R. Ambedkar Center for Biomedical Research, University of Delhi	M. Sc. Biomedical Science
2	Nasrin Naz	Jiwaji University, Gwalior, MP	M. Sc. Biochemistry
3	Somoshri Banerji	Pondicherry University Pondicherry	M. Sc. Biochemistry and Molecular Biology
4	Nisha Pandey	Jamia Millia Islamia	M.Sc. Biotechnology
5	Palak Khandelwal	Utkal University, Bhubaneswar	M. Sc. Biotechnology
6	Anisha Grover	Jamia Millia Islamia, Delhi	M. Sc. Biochemistry
7	Chaithanya Joshy	Pondicherry University, Pondicherry	M. Sc. Biochemistry and Molecular Biology
8	Ayush Kumar Ganguli	JIPMER, Puducherry	M. Sc. Medical Biochemistry
9	Nitya Sharma	Dr. B.R. Ambedkar Center for Biomedical Research, University of Delhi	M. Sc. Biomedical Science
10	Bhoomika Arora	Jamia Millia Islamia, Delhi	M. Sc. Biochemistry
11	Rohit Soni	Banaras Hindu University, Banaras	M. Sc. Biochemistry
12	Nibedita Roy	Department of Biochemistry, South Campus (UDSC), University of Delhi	M. Sc. Biochemistry
13	Maneshwar Dixit	Department of Biochemistry, South Campus (UDSC), University of Delhi	M. Sc. Biochemistry

Student Progression
2017-20

Total strength of class: 33			
S. No.	**Name of student**	**Name of Institute/University**	**Name of programme**
1	Niharika Jain	Dr. B.R. Ambedkar Center for Biomedical Research, University of Delhi	M. Sc. Biomedical Science
2	Sparsh Singh	Dr. B.R. Ambedkar Center for Biomedical Research, University of Delhi	M.Sc. Biomedical Sciences
3	Aayush Srivastava	University of Delhi, Delhi	M.Sc. Biophysics
4	Juhi Bhan	Panjab University, Punjab	M.Sc. Microbial Biotechnology
5	Shruti Khandelwal	Guru Gobind Singh Indraprastha University	B. Ed
6	Shivani Mishra	Central University of Haryana, Haryana	M.Sc. Biochemistry
7	Mansi Tanwar	University of Delhi, South Campus	M.Sc. Biochemistry
8	Ankita	Central University of Haryana, Haryana	M.Sc. Microbiology
9	Kiran	Central University of Haryana, Haryana	M.Sc. Biochemistry
10	Anuj	ICAR- National Dairy Research Institute	M.Sc. Animal Biochemistry
11	Nisha	ICAR- National Dairy Research Institute	M.Sc. Animal Biochemistry
12	Vikram Aditya	Bharathiar University, Coimbatore	M.Sc. Medical Biotechnology
13	Hardik Singhal	Alagappa University, Tamil Nadu	M.Sc. Biotechnology
14	Harsh Mahawar	Bioinformatics and Computational Biology, IBAB, Bangalore	M.Sc. in Biomathematics

15	Harshita	Welingkar Institute of Management Development and Research, Mumbai	MBA
16	Devika Maggo	Panjab University Punjab	M.Sc. Microbial Biotechnology
17	Damini	Welingkar Institute of Management Development and Research, Mumbai	MBA
18	Harsh Raheja	AIIMS, Delhi	M. Sc Biotechnology
19	Jyoti	Lalit Narayan Mithila University, Darbhanga	B. Ed
20.	Muskaan	Jiwaji University, Gwalior	M.Sc. Biochemistry

Student Progression
2018-21*

Total strength of class: 24			
S. No.	**Name of student**	**Name of Institute/University**	**Name of programme**
1	Pallavi	Jawaharlal Nehru University	M. Sc Biotechnology
2	Vinayak	University of Delhi	M. Sc Biochemistry
3	Ritika	Jamia Hamdard University	M. Sc Biochemistry
4	Deepika Gola	Dresden University of Technology, Germany	M. Sc Biochemistry

*Data collection ongoing

VI. Career Notifications

Aditi Rattan and Vaibhav Sharma (Batch of 2019-22)
Department of Biochemistry, Shivaji College, University of Delhi

Competitive Examinations

Tentative dates of some important competitive examinations for students pursuing biological sciences

S. No.	EXAMINATION NAME	REGISTRATION STARTS FROM (Tentative)	MONTH OF EXAMINATION (Tentative)
1.	TIFR (Tata Institute of Fundamental Research Graduate School Admissions)	January 2023	March 2023
2.	IIT JAM (Indian Institute of Technology Joint Admissions Test for M.Sc.)	September 2022	February 2023
3.	GAT-B (Graduate Aptitude Test Biotechnology)	March 2023	April 2023
4.	AIIMS Biotechnology Entrance Exam	March 2023	July 2023
6.	Alagappa University M.Sc. Biotechnology Entrance Exam	July 2023	August 2023
7.	GATE(Graduate Aptitude Test Examination)	September 2022	February 2023
8.	IBAB (Institute of Bioinformatics and Applied Biotechnology Entrance Exam)	January 2023	May 2023
9.	CUCET (Central Universities Common Entrance Test)	March 2023	May 2023
11.	KIITEE (Kalinga Institute of Industrial technology Entrance Exam), M.Sc. Biotechnology	November 2022	April 2023

12.	University of Madras M.Sc. Entrance Exam	April 2023	June 2023
13.	ICAR (Indian Institute of Agricultural Research All India Entrance Examination)	March 2023	September 2023
14.	Punjab University CET-PG	April 2023	July 2023
15.	JNTU M.Sc. Biotech Entrance Exam	June 2023	July 2023
16.	DUET (Delhi University Entrance Test)	April 2023	June 2023
17.	Hyderabad University, M.Sc. Biochemistry	April 2023	June 2023
18.	HPU Shimla, M.Sc. Biotechnology	June 2023	July 2023
19.	MSU (Maharaja Sayajirao), Baroda, M. Sc. Biochemistry and Medical Biotechnology	June 2023	September 2023
20.	Osmania University, Hyderabad, M.Sc. Entrance	April 2023	July 2023

Internships

Tentative Dates of some important internships/training programs for students pursuing Biological sciences:

S. No	Internship/ training program title	Organizing institution	Duration	Eligibility (BSc bio-science courses)
1.	Visiting Students Research Program (VSRP)	Tata Institute of Fundamental Research	8 weeks	BSc (2nd year completed)

2.	Summer Undergraduate Research Program (SURP)	Dr. B.R Ambedkar Center for Biomedical Research	6-8 Weeks	BSc. in Biomedical Science, Life Science or related subjects
3.	Science Academies' Summer Research Fellowship Programme for Students and Teachers	●Indian Academy of Sciences, Bengaluru ●Indian National Science Academy, New Delhi ●The National Academy of Sciences, India, Prayagraj	8 Weeks	BSc (2nd year only)
4.	Project Oriented Biology Education (POBE)	Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR)	6 to 8 weeks over 3 consecutive summers	BSc (1st year of 3 year B. Sc programme only)
5.	Summer Research Fellowship Programme (SRFP)	Indian Academy of Science	8 weeks (renewable for a second year for selected students)	BSc (1st and 2nd year)
6.	Summer Student Programme (SSP)	IISER Pune	4 to 8 weeks	BSc (2nd year onwards)
7.	Summer Research Program	IISER Mohali	4 to 8 weeks	BSc(2nd year onwards)
8.	Summer Student Research Programme	IISER Kolkata	4 to 8 weeks	BSc
9.	Summer Visiting Programme	IISER Thiruvananthapuram	8 weeks	Bsc (preferably 2nd year)
10.	IARI internship training	Indian Agricultural Research Institute (IARI)	1 to 6 months	BSc
11.	Summer Internship Programme	NIT, Durgapur	4 weeks or more	BSc

12.	Bose Institute Summer Training	Bose Institute	8 weeks	BSc (Only if recipient of KVPY, INSPIRE, JBNSTS, NTSE or other similar awards)
13.	Annual Summer school program	School of Life Sciences, Jawaharlal Nehru University	8 weeks	BSc
14.	Summer Research Internship	Regional Centre for Biotechnology, RCB	7 weeks	BSc (3rd year)
15.	Summer Research Internship Program (SRIP)	IIT Gandhinagar	8 weeks	BSc (any year)
16.	CRG Summer Internship Program	The Centre for Genomic Regulation, Barcelona, Spain	8 weeks	BSc (2 full years i.e 4 semesters completed) MSc students not eligible
17.	Max Planck Summer Internship	International Max Planck Research Schools (IMPRS), Germany	10 weeks	BSc (or MSc) IELTS or TOEFL required

Scholarships

Tentative dates of some important scholarships for students pursuing biological sciences:

S. No.	NAME	BENEFITS	ELIGIBILITY CRITERIA
1.	**Kishore Vaigyanik Protsahan Yojana (KVPY)**	INR 5000 monthly fellowship and 20000 annual contingency grant during B.Sc. and 7000 monthly fellowship and 28000 annual contingency grant during M.Sc.	Students enrolled in XI Standard (Science Subjects) during the academic year 2021-22 and having secured a minimum of 75% (65% for SC/ST/PWD) marks in aggregate in MATHEMATICS and SCIENCE subjects in the

			X Standard Board examination immediately in the preceding academic year, Students enrolled in XII Standard/ (+2) (Science subjects) during the academic year 2020–21 and aspiring to join undergraduate program in Basic Sciences namely Physics/Chemistry/Mathematics and Students enrolled in the 1st year of undergraduate program in Basic Sciences
2.	**Dr. B.R. Ambedkar State Award to SC/ST/OBC/Minorities Students, Delhi 2021**	INR 25,000 to students who top among the SC/ST/OBC/Minorities in each discipline of the professional/technical degree course	Must be pursuing graduation in recognized college/institutions and Belonging to SC/ST/OBC/Minority community
3.	**Sardar Patel Scholarship for Students Pursuing Graduation**	INR 15,000	Must be studying in the 1st/2nd year of a 3-year graduation programme in regular full-time mode and the annual family income should be less than INR 6,00,000 (6 lakhs) per annum.
4.	**INSPIRE Programme**	INR 5000 to one million young learners of the age group 10-15 years, ranging from Class VI to Class X standards, INR 80,000 per year is offered to talented youths in the age group 17-22 years, for undertaking Bachelor and Masters level education in natural sciences.	Candidates are eligible to apply for INSPIRE programme if they are a part of the top 1% students in their Class 12 board exams and are studying Natural and Basic Sciences at BSc level or Integrated MSc level or are among top 10,000 rank holders in JEE or NEET and have also opted to study Natural and Basic sciences in any institute or university leading to BSc and MSc degrees or have studied at any of the below-mentioned colleges and have opted to study Natural and Basic sciences at the BSc or MSc level are eligible for SHE Scholarship: IISERs, NISER, Department of Atomic Centres for Basic Sciences, KVPY, NTSE, JBNSTS scholars and International Olympiad Medalists.

5.	**Narotam Sekhsaria Scholarship Programme**	Maximum INR 20 lakhs	Final year graduate student or have completed graduation from a recognised university, below 30 years of age who want to pursue PG courses in fields like Applied Sciences, Pure Sciences, Social Sciences and Humanities, Architecture Law, and Management at good Indian as well as international universities.
6.	**HDFC Educational Crisis Scholarship Support (ECSS)**	INR 10,000 to INR 25,000 per annum	Aspirants who are pursuing a Diploma, Graduation Degree or Postgraduate degree and whose annual family income is equal to or less than INR 3,00,000 are eligible to apply for this scholarship.
7.	**Post-Graduate Merit Scholarship for University Rank Holders**	INR 3,100 per month for the duration of two years.	Rank holders of each university at UG level are eligible to apply for this scholarship.
8.	**Indira Gandhi Scholarship for Single Girl Child**	INR 36,200 per month for maximum two years	Any girl below 30 years of age who is the only girl/twin daughter/fraternal daughter of a family and has secured admission in full-time (regular) Master's degree programme from a recognised university/college.
9.	**Women Scientist Scheme (WOS-A)**	PhD holders or equivalent candidates get a maximum grant amount of INR 30 lakh and for MSc or equivalent the maximum grant amount is INR 20 lakh. The amount is awarded for a maximum duration of three years.	Women candidates who are pursuing M.Sc. or **PhD** are eligible to apply for this scheme. The minimum age limit under WOS-A is 27 years and maximum age for MSc or equivalent category is 35 years and for PhD and equivalent category is 57 years.

VII. Toppers

First Year (Batch of 2020-23)

Aantra Rao
Ist Position
CGPA-9.27

Naman Gupta
IInd Position
CGPA-9.18

Karishma
IIIrd Position
CGPA-9.05

Second Year (Batch of 2019-22)

Aditi Rattan
Ist Position
CGPA-9.64

Merlin Mathew
IInd Position
CGPA-9.57

Takhellambam Malemnganba
IIIrd Position
CGPA-9.18

Third Year (Batch of 2018-21)

Utsav Kapoor
Ist Position
CGPA – 9.70

Pallavi Dutta
IInd Position
CGPA – 9.68

Vinayak Joshi
IIIrd Position
CGPA – 9.60

VIII. Memory Lane – Alumni Messages

It's been around 16 years since my first day in Biochemistry dept. and I still clearly remember that day and many more for the whole graduation. - the classes, labs and the discussion with teachers. It was full of experiences of every kind. To this day, I feel nostalgic of my time of the graduation days. Everyone was so helpful - all the faculty, fellow mates, juniors, lab staff. I have utilized every experience I gained from those 3 years, where ever I could for the years to follow. I would like to thank the coordinators for this opportunity to express my gratitude to the whole biochemistry department.

Nagendra Singh (Batch of 2006-09), Assistant Consultant, Tata Consultancy Services

It is my privilege to say few words for the department of biochemistry, Shivaji college. I had an excellent experience during my bachelor's study (2009-2012) to study the essence of biochemistry from highly skilled professors. Indeed, this period was evidently a foundation for my career to serve as today's scientist.

Dr. Ankit Tanwar (Batch of 2009-12), Post-Doctoral Scientist, Department of Cell Biology Albert Einstein College of Medicine, New York, USA

I would like to say, that in anything we do or we opt for, our intention matters a lot. If we go by that. Everything that will happen, will happen for our best. Then no matter what the result would be. I really believe in this punjabi saying,
"Jitthe chah, uthhe rah"
Where there's a will, there's a way.
So, we should remember that, and keep doing our job. That's all this small person could say. Wish you and team, a very best of luck.

Sahil Mehta (Batch of 2015-18), Actor

It was a great journey at Biochemistry Department, Shivaji College. 3 years in this department gave me a great exposure towards biochemistry and created many more opportunities ahead in my life. The teachers and all the lab members put enormous effort in teaching all the concepts practically and theoretically. I am thankful to be part of this great department. Also, I will be happy if I can be of any help to teachers and students of this department in future.

Subhasis Sahoo (Batch of 2014-17), PhD Scholar, NCCS, Pune

Three years in Biochemistry Dept came with a lot of experiences academic and non-academic. Long lab hours to the first ever outstation trip to Chail, International Conference, Departmental fest, being part of editorial team of Biokemi. Well, the list goes on. Truly those were the best days of my life. Thankyou teachers for making it all so easy. All the best to all my juniors.

Shivani Mishra (Batch of 2017-20), Intern at Cellular Biochemistry Lab, DIPAS DRDO

The Department of Biochemistry, Shivaji College has been like a second home to me. The three years spent in Shivaji College have been the best three years in which I got exposure to so many new opportunities. This department provided me the opportunity to grow academically and socially. I'm really grateful to my professors and the lab staff for taking so much care, correcting my mistakes and teaching me so many new things. Wherever I'll reach academically, I would always be thankful to the department for helping me build my academic foundation.

Pallavi Dutta (Batch of 2018-21), MSc Biotechnology, Jawaharlal Nehru University

The three years that I have spent in Department of Biochemistry, Shivaji College have been the best years of my life. This place has not only been an excellent place for learning, but also a place where are looked after and taken care of, giving us opportunities to grow and blossom. This place has helped me develop scientific aptitude and critical thinking, helping me look at life around me in a different way. Department of Biochemistry has helped me not only as a student but also as an individual, a person who has to survive the real world. This place has taught me real life values for which I will forever be grateful. I will forever be thankful to all the teachers and staff members for helping and guiding me through the three years that I spent here, helping me grow as a student and an individual.

Vinayak Joshi (Batch of 2018-21), M. Sc. Biochemistry, University of Delhi, South Campus

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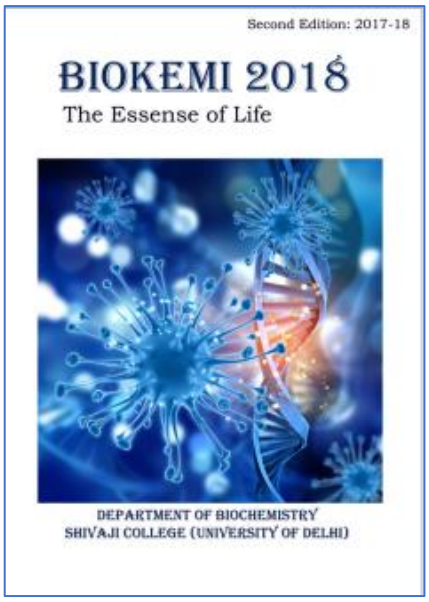

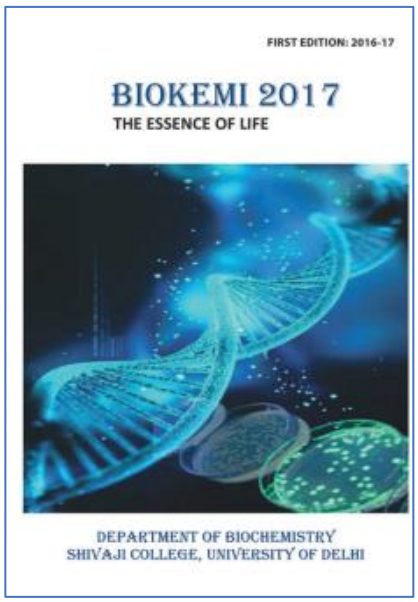

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