Innovations for Human Health and Diseases

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Health innovation refers to the deliberate instigation and application of ideas, processes or procedures, new to the relevant unit of acquisition, designed to significantly benefit the mankind. It is increasingly important to collect data about patients and the quality of patient care. This information can help discover variation in treatment approaches, and hence help improve quality by expanding on to the existing strategies and expect better care with declining costs and rising performances. The successful exploitation of new ideas is crucial to bring new and improved healthcare services. The imperative to think and do things differently is very relevant for the technology to advance as there will always be new and exciting solutions. Gaps in existing knowledge can be viewed as opportunities for improving ideas, practices and technology. Improvement in both diagnosis and treatment of diseases is crucial for health management. Although, there have been tremendous breakthroughs in the field of "Health and Diseases" in last few years and one should not be oblivious to some of the important technological advancements listed in the text.

About a year back, generation of "Xenogeneic chimeras", by blastocyst complementation was reported first time. In this technique, Pluripotent stem cells were generated from the patient requiring transplantation and injected into a large animal blastocyst (eg. pig), leading to the creation of organ(s), therefore serving as an unlimited source of human organs and that too without eliciting immune responses thereby reducing the risk of transplant rejection. Making life easier, 3-D printers have been developed that can bioprint human organs. Both of these novelty approaches are still farfetched in terms of clinical practice but have the potential to supersede the existing technology of organ transplantation.

More recently, new ways of treating brain cancers have been discerned. An oncolytic virus called Mammalian orthoreovirus type 3, has been found as the first virus to penetrate blood brain barrier and has the ability to kill cancerous cells by eliciting host's immune response and influx of immune cells can fight tumor cells without affecting normal cells. Since this virus is not known to cause any symptomatic infections in humans, therefore combination of this oncolytic virus therapy along with chemotherapy and radiotherapy is a possible solution to treat highly metastasized brain cancers. Therapy using a live therapeutic virus is an innovative approach to treat cancers.

Researchers all over the globe are trying best to improvise the available ways of treating diseases. The diseases for which treatments are available, more effective drugs and therapies are devised to improve health in better ways. But for some diseases finding a possible cure is itself a challenge and Alzheimer's is one of those diseases. Affecting some 6 million people, Alzheimer's is the most common neurological condition. The disease is the only one in the top five causes of death that has no effective cure. Between 1998 and 2011, 101 drugs aimed at treating the disease failed, currently estimating 73 Alzheimer's drugs are in development. Finding a cure for Alzheimer's has been a challenge lately but recent findings about the pathophysiology of the disease can bring insights into possible ways to treat it. Recently it has been figured out that the Alzheimer's protein spread like infection from neuron to neuron supporting the "transneuronal spread" hypothesis for Alzheimer's disease. The diseased brain is characterized microscopically by the combined presence of two classes of abnormal

structures, extracellular amyloid plaques formed by amyloid-β (Aβ) peptides and intraneuronal neurofibrillary tangles. These tangles are twisted fibers of a protein called tau. These Tau deposits are found inside neurons, where they are thought to inhibit or kill neurons and the junctions between them. Researchers have found the largest concentrations of the damaging tau protein in brain regions which are heavily wired to others and thus spread intracellularly just like infections. Delivering drugs specifically at these densely wired regions of brain that can block the intracellular spread of this protein could be an innovative way to treat it's infection like pathology. Two pre-requisites to begin with such an approach are the availability of high affinity binders that can bind the intracellular protein thus preventing its spread and a delivery agent that can deliver these binders across the blood brain barrier (BBB) or in the highly circuited regions of brain. Since the diseased tau protein differs from the normal tau protein in conformation, therefore conformation specific monoclonal antibodies can be generated which can bind only the abnormal tau protein in a highly specific manner, so that the levels of normal tau protein left unaltered in cells. Therefore purified abnormal tau protein, can be used to generate high affinity binders by phage display techniques. Phage display technique will aid in selecting conformation specific, non-cross reactive and high affinity binders that can bind altered tau protein not the normal tau protein. Moreover full length antibodies need not to be generated in this case because these antibodies cannot penetrate cells, therefore "nanobodies" *that is* Single- domain antibodies can be generated and a cell penetrable binder can be selected using *in vitro* penetration assays. After the selection of such binders, their delivery mode has to be decided. Using nanotechnology to deliver these across BBB could be one approach but again drug delivery using nanoparticles has not shown promising results in other cases. Therefore this approach can make use of a recently developed miniaturized device called "MiND(S)" by MIT researchers to deliver drugs directly to brain. They have developed an ultra thin needle that can deliver very low doses of drugs in very specific brain circuits without affecting other regions of brain. This can even eliminate the need of oral or intravenous routes of drug administration that often decreases the bioavailability of drugs.

The novelty of this approach lies in the fact that once the disease is diagnosed, abnormal tau specific nanobodies can be delivered using "MiNDS" in highly connected regions of brain thus inhibiting the spread of this protein from one neuron to another reducing the severity of disease. This way very low doses of nanobodies are required thereby reducing the number of doses as well the cost per dose for a complete and successful treatment of Alzheimer's.

Adding to this, innovative approaches for treating diseases like obesity have come up where drugs are shown to reduce obesity without hampering the appetite. Many more such approaches are required for a better and healthy future; approaches that are just a thought away.

Innovations for human health and diseases

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'He who has health has hope; and he who has hope has everything."

The definition of health has evolved over time. In keeping with the biomedical perspective, early definitions of health focused on the theme of the body's ability to function; health was seen as a state of normal function that could be disrupted from time to time by disease.

In the early days of mankind, health per se, was never seen as a problem, this was because diseases barely affected humans, as much as they do today and even if they did, natural remedies were the first choice. The impact was less severe.

But in the post industrialization era, where globalization is not a choice but a compulsion not only has the polluted air, water and soil impacted the human race, but all species at large have been affected and hence improvement in the 'health status' is what is of primary importance. Somehow the damage caused to us, by us, has escalated so much that the earlier methods of prevention, diagnosis and therapy have not been able to cope up with the need of the current times and here comes the need to introduce innovative approaches to solve the clichéd problems!

From the Economist to Wikipedia to Websters to Barack Obama, around the globe, we seek tangible answers for an intangible question: 'What is innovation?'

'Technically, "innovation" is defined merely as "introducing something new";' there are no qualifiers of how ground breaking or world-shattering that something needs to be- only that it needs to be better than what was there before!

Any creative idea, getting implemented or realized successfully, is innovation.

It includes venturing away from familiar ground into unchartered territory; to see beyond what the eyes can see and comprehending challenges beyond the human brain.

Hence, combining health and innovation is the need of the hour for a country with a population of 1.3 billion; also where the potential to plan and execute such ideas is immense.

25 years ago mobile phones and the internet were in their infancy. Their expansion might have been a predictable technological development but the human response was perhaps unforeseeable. The way these technologies have made the world smaller and faster, and their effects on the people living in it, could not have been predicted.

We can speculate on the problems posed by antibiotic resistance, climate change, and the resultant changes in patterns of infectious disease, but the course these events will take is largely influenced by the human reaction to these situations, of which we are all a part. So humans are not only the problem, but also, very much a part of the solution.

These three dimensions, humans, innovation and health are the three angles of an equilateral triangle, which need to be explored hand-in-hand.

In the post-genomic era, the opportunity to combine and integrate interesting concepts has allowed the birth of Foodomics, 'a discipline that studies the Food and Nutrition domains through the application of advanced 'omics' technologies to improve consumer's well-being and health'.

Since then, this discipline has rapidly evolved and researchers are now facing the daunting task to meet the consumers' needs in terms of food sustainability, quality and safety.

Most importantly, today, it is imperative to provide solid evidence of the mechanisms through which food can promote human health and well-being.

Food and nutrition is the primary area involving innovative technologies to promote health and wellbeing of an individual as well as the community at large.

The intestine harbors numerous microbes is a concept known to mankind since the twentieth century but recent explorations of the human gut micro biota suggest that, perturbations of microbial communities may increase predisposition to different disease phenotypes. Dietary nutrients are converted into metabolites by these microbes, which in turn serve as biologically active molecules, affecting the regulatory functions in the host.

Probiotics may restore the composition of the gut micro biome and introduce beneficial functions to gut microbial communities, resulting in amelioration of gut inflammation and other intestinal or systemic disease phenotypes. These constitute the new buzz word in human dietary portfolio and are currently the major focus of attention across the world including India and other developing countries due to their enormous health potentials.

Our understanding of the functionality of human gut microbiota and increasing use of probiotic organisms, specifically lactobacilli and bifidobacteria as functional microbial dietary ingredients for promoting human health have made considerable impact on the consumers and the application of probiotics offers an innovative approach for development of novel probiotic formulations for the management of specific diseases particularly chronic inflammatory gastrointestinal disorders and other similar medical conditions.

Until a few years ago it was hard to believe that the gut microflora could be a solution to some of our most common health problems!

Hence, probiotics offer a classic example of how a simple exploration can give rise to miraculous results. A simple idea but an effective one!

In 2016, one of the leading newspapers had the following headline: "India is the diabetes capital of the word!" Alarming since more than 50 million of the population was affected. Then came in a new technique 'Solid wax printing', using microfluidic paper to quantify the blood glucose levels at a cost much lower and sensitivity comparable to what was already existing in the market. Such novel approaches are hence required by any nation to sustain its health.

Apart from maintaining the health status, early and accurate diagnosis of diseases is what is absolutely essential to provide the impetus for a flourishing human race.

Infectious diseases majorly affect the developing countries and India is no exception. Emerging and re-emerging infectious diseases are just the most vivid evidence that all infectious diseases are constantly evolving in the interplay between pathogens, their hosts and other environmental factors influencing both of these.

Hence, not only is their prevention important but early diagnosis is what is required to combat these.

Virochip a single step diagnostic chip based assay to detect a wide flora of viruses and is a new approach to enable early diagnosis. Nucleic acids hybridize to their complementary counterparts is what we have known since the beginning of the Molecular Biology era but this assay is just the perfect application of such an important concept. More than twenty two thousand spots of single stranded DNA spots can be impregnated on the chip and all viruses with sequenced genomes can be represented and analyzed using 'mega softwares'.

Apart from the detection of viruses, another microbial detection system, set up to identify pathogenic bacteria based on substrate utilization and cellular metabolism, called as Biology has been invented. A selected carbon source is impregnated on a micro plate and produces a characteristic "Metabolic fingerprint" based on carbon source utilization and this technique can be used for the diagnosis of more than twenty thousand bacterial strains.

Infectious diseases are not the only problem faced by our country. An innovative approach to maintaining the health status of a population susceptible to neurodegenerative diseases like Parkinson is the Parkinson's voice initiative undertaken by Dr. Max Little, where in voice processing tools analyze the sound recordings and compare them to a database of recordings of Parkinson's patients and non-Parkinson's patients that serve as a control. The algorithm developed by this research team is able to detect specific variations in sound vibrations linked to vocal tremors, breathlessness, and weakness. By detecting such voice changes that are indicative of neurological degeneration, the algorithm is able to generate accurate diagnoses and predict disease progression based on the presence and severity of such degenerative symptoms.

This is an amazing approach to diagnosis especially since Parkinson's disease is the second most common neurodegenerative disease, affecting 6.2 million people globally and also effective treatment and early diagnosis for Parkinson's disease are hindered by a lack of quantifiable biomarkers and objective measures of disease progression.

Apart from neurodegenerative diseases, cancer is a disease which has impacted the world globally. It is among the leading causes of death worldwide. In 2012, there were 14 million new cases and 8.2 million cancer-related deaths worldwide. The number of new cancer cases has been approximated to rise to 22 million within the next two decades.

Early diagnosis is the key to survival. A biosensor chip designed by Sanjiv Gambhir is a possible solution to our problem. The chip utilizes a magnetic detection nanotechnology and can be used to detect cancer associated protein biomarkers. Although this technique requires well controlled reaction conditions and has a small, linear dynamic range but could serve as a stepping stone for future advances in the field of early cancer diagnosis.

These enticing new techniques are paving a way for developing a healthcare approach which is at par with the current demands of the health sector and are both effective in detection as well as economical.

Apart from maintaining a healthy self and early diagnosis, prevention and treatment also play a major role in maintaining the health status of a population. Newer approaches include introduction of subunit and recombinant vaccines, both with a prophylactic and an anaphylactic response.

Something as simple as the face mask used to protect against air pollution is an innovative approach to maintain health!

Therefore, newer advances are coming up, health and disease control is on the fore front. Newer technologies are coming up but the road to success is a long one!

As Steve Jobs said, “Innovation is what distinguishes a leader from a follower”, the current trends in innovation need to continue and newer ideas need to come up to achieve a utopian society sans disease, where ‘healthy’ is not just an abstract idea but a stark reality.

One doesn’t need magic to change the world, we carry all the power we need inside ourselves already: we have the power to imagine better. – JK Rowling

Milestones in Improving Human Health and Preventing Diseases

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Since time immemorial man has been putting considerable effort in improving human health and lifespan. This preoccupation and a sense of general curiosity triggered many a seminal theories and discoveries by scientists like Robert Hooke, Charles Darwin, Louis Pasteur and others. These biological advancements were complimented by some truly great leaps in the field of technology such as the invention of microscope, identification of X-rays, development of anaesthesia, etc. which provided a fertile ground for the betterment of human health. Moreover, a greater emphasis of the society as well as the authorities on the importance of proper hygiene, nutrition and clean environment also contributed immensely in enhancing the wellbeing of human health and curbing diseases.

The Beginning – *Epidemiology and environment*

Darwin's theory of evolution and Mendel's theory of inheritance provided path changing concepts which profoundly influenced the realm of biology. A significant factor in improving human health was the realization of the fact that environment also has crucial role in generating diseases. Primitive man used to hunt and gather food so the disposal of waste was not a problem. But gradually with the commencement of agricultural revolution and the establishment of human settlements the improper disposal of waste became a source of pathogenic vectors and diseases. Despite early attempts to link imbalance in environment, diet and hygiene to be causal factors for diseases there were no appropriate sanitary practices. A major turning point in this direction was the Bubonic plague epidemic of 1300s caused by the bacterium *Yersineapestis.* The plague was believed to have its origins in Asia and spread its tentacles to Europe by the late 1700s. For a long time the plague was popularly believed to have been caused by *miasmas,* which are vapors emanating from swamps and cesspools. A primary reason for such belief was the lack of structured and systematic thinking about the genesis and the determinants of diseases. Such thinking developed over the course of centuries and enabled people to find ways and means for preventing and treating ailments. With contributions such as the invention of compound microscope by Anton van Leeuwenhouk (1670s) to study insects and plants at the microscopic level and Robert Hooke's discovery of cell, science gained a major headway in understanding human physiology through basic and clinical research along with the associated patho-physiology.

In the 1740s, John Pringle, a Scottish physician to the British forces during the War of the Austrian Succession (1740–48),proposed proper sanitation and hygiene as remedial measures in preventing typhus or 'jail fever' among soldiers and jail prisoners.

Another defining moment in history of human health was the rise of cholera infection in the 1800s throughout Europe and America. John Snow, a London based physician, studied cholera for decades in a systematic manner and in his paper published in 1849 he stated that the disease is caused by the ingestion of contaminated water. Owing to his contributions in scientific epidemiological thinking, he is rightly titled the 'father of epidemiology'. But it was Edwin Cadwick's concept of sanitation which ultimately resulted in the enactment of the Health Act of 1848that empowered local authorities to take care of environmental garbage.

The idea of sterilization was introduced among the masses by a French biologist Louis Pasteur in 1853. He successfully demonstrated that microbes in the milk could be killed by heating milkat 130 degree Fahrenheit. This sterilization process was named after him and is called pasteurization. In 1908, the use of Chlorine for removing impurities from drinking water was also a milestone towards improving the quality of life through providing safe drinking water.

James Lind, a Scottish naval surgeon performed in what is believed to be the world's first controlled clinical trial on 12 sailors with scurvy. He divided the soldiers into pairs and administered sea water, various other concoctions, and lemons and oranges to them. He found those that received the citrus fruits were cured of scurvy but others were not, thereby proving his hypothesis. Unfortunately, it was only 50 years later that the use of lime juices came into practice for treating sea sailors.

It is because of the epidemiological approach towards diseases that we have acquired a wholly new understanding of our environment and its role in causing diseases. This approach has also made us aware of concepts like 'risk factors' responsible for the early onset of a disease. For example, lack of exercise, obesity and high blood pressure can lead to heart related disorders while smoking can cause tuberculosis and tobacco chewing can cause oral cancer. These ideas, concepts and innovations provided important underpinnings for public health.

Vaccines and Drugs– *Big guns in small packages*

One of the most revolutionary innovations in the field of science was the development of vaccines. Though Louis Pasteur was believed to be a pioneer in engineering the use of weakened microbes as vaccines, this chapter actually began much earlier with Edward Jenner.In1796, Edward Jenner discovered that milkmaids who had been previously infected with cowpox became resistant to smallpox. Later on with medical and technological advancements small pox was completely eradicated by 1977.

Prevention is preferable to cure.
– Hippocrates

In 1885, Louis Pasteur developed vaccine against rabies and thus aided in preventing this scourge. Such success stories paved the way for the development of vaccines for other diseases like cholera, tuberculosis, diphtheria, tetanus, and pertussis, etc. Vaccines also found application in preventing viral infections for example, oral vaccine for polio and the vaccines for measles, mumps, rubella, etc. Out of these, the polio vaccine has become a household name thanks to robust campaign and aggressive marketing. In the beginning, vaccines were primarily made by way of attenuating or inactivating pathogens. Now a days recombinant approaches have added another dimension to this area. The recombinant proteins or DNA vaccines for immunizing against HIV, Hepatitis B, malaria, etc., peptide vaccines, live viral/bacterial vector based vaccines are a few examples of it.

While vaccines have been a means of prevention, treatment strategies have found the form of anti-bacterials, anti-virals and drugs. The field of antibacterial witnessed a tremendous boost after the seminal discovery of *Penicillin notatum* by Alexander Flemming in 1928. The fungus was observed to be capable of killing bacteria and later on the active component was found to be penicillin which is now a widely used anti-bacterial agent. Subsequently a number of antimicrobial agents which are effective against bacteria, fungi, viruses, protozoa, and helminthes were also discovered. Similarly, the use of drug therapy for treating human diseases was another breakthrough in the field of pharmacology. The use of aspirin from 1899

extensively promoted by Bayer Company of Germany was a revolutionary, safe and effective drug which was found to be non-addictive. Some of the effective drugs that developed thereafter include antacids, anti-spasmodics for digestive tract, diuretics and beta-blockers, for heart disease control, NSAIDS and anaesthetics for relieving pain, etc.

Technological Milestones– *Breakthroughs in surgery and therapy*

A major technological breakthrough was the advent of surgical interventions in treating injuries and trauma. Cardiac, brain, retinal surgery and hip replacement surgery have made possible the effective treatment of diseases associated with these organs. Furthermore, surgical removal of tumors is another possibility. The discovery of X-rays by William Roentgen in 1895, the invention of electrocardiograph by a Dutch physician, Willem Einthoven, in 1903 and the advent of laparoscopic, or minimally-invasive surgery which uses a thin tube with a tiny camera and light at the end that sends images to a video monitor in the operating room to guide doctors during surgery were some of the technological innovations that helped in the evolution of surgery. The invention of artificial pacemakers and innovations in instrumentation as well as imaging tools such as NMR, isotope scanning, MRI, computer tomography, positron imaging tomography, and improved ultrasonography as non-invasive diagnostic methods further revolutionized this field. In 2000, the Intuitive Surgical, Inc. developed *The da Vinci® Surgical System* which gives a 3D HD view inside the body of a patient. This transcendental technology uses robotics to translate the surgeon's hand movements into smaller and precise movements of tiny instruments placed inside the patient. This system since its development has found application in cardiac, colorectal, general, gynecologic, head & neck, thoracic and urologic surgeries.

Earlier the process of surgery was quite painful for the patients. The identification of the first aneasthetic agent, Ether, by William T G Morton in 1846 made the procedure remarkably less painful.Thereafter, Chloroform was given as an anaesthetic by the physician James Snow in 1853 to Queen Victoria when she gave birth to a child. Nowadays a wide variety of anaesthetics like barbiturates, Amobarbital (trade name: Amytal), Methohexital (trade name: Brevital),ketamine, propofol to name a feware used in surgery. Another pioneering work in this direction was the introduction of antisepsis, which was basically the use of sterilized surgical equipments. Initially, Joseph Lister sprayed carbolic acid for sterilizing his equipments which reduced the incidents of gangrene in patients that underwent surgery. From then on several antiseptic agents were identified which found their way in common practice.

A complex tie up between surgery and immunology which gained tremendous applicability was the procedure of transplantation. The first transplantation was performed for kidney in 1954 by Joeseph E. Murray followed shortly by that of liver in 1967 by Thomas E. Starziand heart in 1968 by Christiaan Barnard. Presently, this technology is also used for bone marrow transplantation. Organ transplants have their own complications such as graft *vs* host response which may lead to organ rejection. To overcome this limitation, stem cells from embryos or adult and fetal tissues were brought into the picture for generating cells of the diseased organ. But this technology too required a compatible donor and suffered the drawback of rejection by the host's immune response. As a solution to this problem, came a better advancement known as *somatic cell nuclear transfer*. In this technique, the nuclei of a healthy donor would be transferred in the egg of the recipient following which the newly developed embryo would be used for regenerative therapy by supplying embryonic stem cells. It remains to be seen if this technological innovation overcomes the technical problems and ethical concerns standing in its way before emerging as a clinical tool.

The 'omics' era–*Ashift in paradigm*

The discovery of DNA in 1951 by James Watson and Francis Crick piqued the interest of many scientists in unraveling the chemical code and its function. Recently the Human Genome Project initiated by Craig Ventorhas enabled the studying of our entire genetic blueprint with not only screening but also comparative approaches. This boom in genomics together with innovations in high throughput technology has heralded a new era of personalized medicine. Personalized medicine by definition is 'a medical model using molecular profiling technologies for tailoring the right therapeutic strategy for the right person at the right time, and determine the predisposition to disease at the population level and to deliver timely and stratified prevention.' However, the concept of personalized medicine will require a long journey from bench to bedside for a multitude of reasons like cost effectiveness, trained manpower, etc.

Other 'omics' which are being considered to be incorporated into genomics are proteomics, the study of entire proteome of the cell along with metabolomics which studies the entire set of metabolites such as lipids, carbohydrates and other small molecules. An approach based on mutli-omics is considered to include genome analysis determining the genetic variations which cause diseases followed by phenotypic analysis by way of understanding the pathways and interactions in cell that are affected or give rise to the said diseases and lastly analyzing environmental factors which perturb the genetic and phenotypic factors. A tantalizing potential and a bigger challenge will be the discovery, evaluation and validation of bio-markers and bio-signatures using these approaches for the common diseases.

An important consideration is also given to the role of microbes in improving human health. These microbes are present throughout the human bodyand are found to differ between a healthy and a diseased individual. This information has paved the way for microbiome analysis and has currently found its use in probiotics. Probiotics are live microorganisms including *Lactobacillus* and *Bifidobacterium* populations that are believed to provide health benefits especially of the digestive tract. Recent researches also link microbes with obesity. Prebiotics is another food component which is non-digestable and may be utilized for fermentation by the gut bacteria. Metagenomics is the analysis of the genome of those microorganisms which have been obtained from the environment and are difficult to culture. Metagenomics has provided a new layer of technology for studying the physiology and ecology of environmental microorganisms.

Future Challenges–*Things to do*

While we have listed the positive facets of the advancements in human health and diseases several dark elements emerge which pose new challenges in our way. The emergence of resistant strains is one among them. We may quote here the example of Penicillin resistant *Staphylococcus aureus,* the multi-drug resistant strains of Tb and anti-malarial resistant strains of parasite which are the manifestations of indiscriminate use of antibiotics and lack of combinatorial approach. Another challenge is the genesis of new life threatening diseases like the severe acute respiratory syndrome (SARS) epidemic of2002 which crippled thousands of people, the Ebola outbreak in West Africa of 2014 which is the largest and complex outbreak of the disease to date. Compounding to these problems is the non-availability of more suitable vaccines for diseases like tuberculosis, malaria, and HIV. Moreover, treatment strategies that exist for diseases, like cancer, only increase the survival of the patient to a certain extent but fail to completely cure the individual giving rise to the problem of relapse. Though

advancements in human health have increased our life span, our health has also succumbed to various life-style related disorders like obesity, diabetes, hypertension, etc.

The Road Ahead

While an effort has been made here to highlight some of the revolutionary and ground breaking breakthroughs in this area, it is quite possible that we may have missed out on many. One such area is the development of genetically modified crops. From the pioneering discovery in 1901 by J.C. Bose that plants are life forms our researches in plant kingdom have attained new heights. The GM crops can be engineered to not only provide more nutritional value but also to be resistant to pathogens. Another such area isoptogenetics, which refers to the combination of light and genetics to manipulate the activity of cells. This biological technology has given a whole new meaning to 'light therapy' by rapidly modifying depression and anxiety related behaviors in animal models. Then there is also the development of bionic eye and artificial heart. To be able to fully and properly utilize all our breakthroughs and advancements in the medical sciences, we mustaddress other related issues, like ethical aspects of various therapies, efficient and cost-effective health care delivery, robust public education of risk factors, increasing research programmes for important diseases, etc.

We have come a long way from our crude and humble beginnings and there should be no doubt that there is still a lot more to do. Due to the expanding horizons of our knowledge along with the ever increasing innovations in the field of science and technology, the prospect of improvement in human health and the fight against diseases looks brighter and these will now hopefully take place at a much faster pace and in an effective manner.

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INNOVATIONS FOR HUMAN HEALTH AND DISEASES

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The latest century has borne witness to tremendous prosperity in terms of science and technology. And not surprisingly, growth in science goes hand in hand with a thriving boom in the health sector. With the growing population and urbanization along with rise in lifestyle oriented diseases, there is a monumental burden on healthcare system to tackle the roadblocks as new medical and infrastructural changes are being essentially required. Health innovation mainly refers to novel introduction and application of ideas, processes, products or procedures, to significantly benefit societal needs. The three salient features of innovation encompass novelty, an application component and a projected benefit. When it comes to health innovations, the human race has perceived numerous spectacular novelties and the list is too hefty to squeeze together in a few sheets of paper. Nevertheless, taking into account the bigger picture, some discoveries stand out as bright constellations due to their grand impacts for the "greater good".

For instance, let us take ***antibiotics***. Antimicrobials are irrevocably one of the most efficacious forms of chemotherapy in the history of medicine and there is hardly any need for reiteration of the number of lives saved and the successful control of infectious diseases thanks to these wonder drugs. All of us are well acquainted with the serendipitous discovery of penicillin by Fleming in 1929, eventually leading to the mass production and distribution of the pioneer antibiotic. The phase between the 1950s and 1970s is regarded as the golden era in the discovery of novel antibiotics following the exemplary unearthing of the first three antimicrobials, Salvarsan, Prontosil, and penicillin. Albeit the wonderful applications of antibiotics, the years that followed, however, failed to encounter any new classes of antibiotics, and the related research has been full of scientific and, recently, economic hurdles. Microbes continue the fight to survive, and henceforth, the recent years have seen a decline in the discovery rate of novel antimicrobials, and the modification of existing antibiotics was the adopted mechanism to combat the emergence of drug resistance. A significant factor to consider is the indiscriminate use of antibiotics by humans. Although a lion's portion of infections has been brought under control attributable to the antibiotics, this equilibrium is fragile. The antibiotics market is faced with a set of limitations, including the fact that it is somewhat financially unattractive to developers. Therefore, there is a dire need to revolutionize the firms for more investments in the discovery and development of marketable novel antibacterial drugs. Among the directions that may yield new strategies are inclusive of species-specific antibiotics, exploitation of biofilms, and different "-omics" approaches. Chemical, biotechnological and combinatorial tactics are now being used to find new leads for novel chemotherapeutical agents and antibiotics. More precise targeting of pathogens and strictly prescribed use of antimicrobials alongside intricate investigation of the microbiome for potential mechanisms of antibiotic resistance can undoubtedly help to design the early warning and preventive measures to sustain the efficacy of chemotherapy.

Speaking of chance discoveries, owing to the associated health benefits, ***probiotics*** are a popular area of focus amidst human dietary assortments across the world, including India. Russian scientist and Nobel Prize winner, Metchnikoff, discovered that *Lactobacillus bulgaricus* instigated longevity of a particular race, who happened to consume fermented yoghurt. The origin of the term "probiotic" is from the Greek language, which means "for life";

however the definition of probiotics has evolved over time and the currently accepted definition of probiotics designates it as "live microorganisms, which when administered in adequate amounts, confer a health benefit on the host." The number of microbial species that actually fit the criteria of this definition is impressive. The most valuable representatives include those belonging to the genera *Lactobacillus* and *Bifidobacterium*. The variety of food products containing probiotic strains is increasing every day, the popular sources being dairy-based and soy based products, nutrition bars, cereals and others. Intriguingly, a modest bowl of cereal is a reflection of historical significance, since John Harvey Kellogg, co-founder of our favorite cereal brand, was an early pioneer of probiotics. Amelioration in intestinal health, enhancement of the immune response, control of serum cholesterol, relief from chronic inflammatory gastrointestinal disorders, and reduction in risk factors of various diseases apart from introduction of a lot of food value from nutritional perspectives are some of the many beneficial effects of the probiotics reported in literature. Although the tradition of consuming probiotic microorganisms for health benefits is not exactly novel, recent years have seen an expansion in the scientific evidences that has aided in circumventing several physiological and technological weaknesses. Current and emerging technologies have helped in advancements in the science of probiotics in terms of efficacy, mode of action, interactions at molecular level, establishing the effective dosage and regulatory issues etc. Contemporary technological innovations have also come up with options to overcome probiotic stability and viability issues during processing and storage by enhancing their shelf life for instance. Microencapsulation technologies, on the other hand, have been developed to offer protection to the bacterial strain from damage induced by external environment. In addition, several other advancements offer different conveniences for consumer satisfaction. A major challenge associated with probiotics and their formulations is to establish the credibility of their health promoting functions for human consumption. Developments in the fields of genomics, transcriptomics, proteomics, metabolomics and emergence of new generation high throughput techniques have thoroughly helped for in-depth clarity in probiotic functionality and in deciphering its mode of action, while maintaining the safety norms. There is now sufficient substantiation and scientific clinical data to strongly support the immense potential of probiotics to promote better human health and to establish probiotic intervention as an effective strategy in controlling various types of diseases and allergic responses.

Infectious diseases represent a major health problem worldwide. An exceptional contribution of contemporary science in the field of boosting human health and immunity is ***vaccine***. In the 21st century, mankind has succeeded in eradicating several devastating diseases that used to destroy millions of lives earlier, thanks to the remarkable undertakings of Edward Jenner. The outcome of immunization is even considered as an insurmountable medical achievement of this century. Prevention of infant mortality from measles, polio, diphtheria, tetanus, pertussis and pneumonia has been the most cherished feat in terms of vaccine usage and the addition of candidate vaccines for AIDS, tuberculosis, malaria, ebola and dengue and infectious diseases like cervical cancer is further assertion for the growing improvements in vaccine development. Of late, there has been exponential transformation in vaccine development from a commercial, industrial-centric realm to a more disease-specific, "not-for-profit" product development. This is complemented by scientific rationale to better define the disease burden in developing countries and to identify and generate cost-effective ways for the affordable use of new vaccines. Exorbitant prices and lack of such information are more often the primary reason behind delay in uptake of new vaccines in poorer countries. A vivid example is the vaccine against meningitis A that was developed in less than 10 years for use in the low-income countries and has been approved by WHO based on its safety, effectiveness and quality. The societal impact of immunization is not simply with respect to improved public health but also in economic terms, including reduction in expenses related to health care. Despite the fact

that several promising vaccines are in the pipeline, only persistent thorough investment in basic research and clinical testing with awareness will fruitfully be able to translate them to marketable forms.

On a similar note, the tremendous progress in understanding the biology of cancer and the birth of global gene expression profiling and genome-wide analysis have laid the foundation for the design of single gene/protein or multi-gene "signature"-based endeavors for better therapeutic decision-making. Such sophisticated prognostic and predictive signature markers, termed as ***biomarkers***, can be utilized for the prompt diagnosis and precise screening of cancer patients. A promising candidate marker strongly correlates with the predisposition and disease progression in multiple cancers and analysis of its status can aid in early prediction of cancer, screening of cancer patients into high and low risk groups, deciding the course of treatment for best overall survival and better prognosis of patients. Few clinically applied cancer biomarkers comprise of the HER2 oncogene for breast cancer, mutation in BRAF for melanoma, the presence of fusion EML4-ALK in lung cancer, and serum PSA for monitoring disease progression of prostate cancer. The application of biomarkers has been a boon for many cancer patients, since late diagnosis is often the preeminent cause of cancer related mortality. Cancer biomarkers can help in recognition of distinct signature gene deregulation that can make one more prone to developing a particular cancer type. An earlier diagnosis is a valuable step to nip the disease right at its bud. Biomarkers can also help distinguish cancer patients into high risk and low risk categories, and thereby the prescribed therapeutic regimen would vary. The idea of patient-customized treatment is more of a reality due to the advent of biomarkers. Additionally, biomarkers are conspicuous markers to look out for to track the prognosis of a patient post-treatment, and can be useful to even determine recurrence, if any. However, there still exists an impressive gap between the initial discovery of a potent biomarker and its clinical translation from bench to clinical practice due to the confrontations in the process of cancer biomarker development. But with the novel maturity in the research related to biomarker discovery and its clinical validation, one can surely hope to see a growing number of biomarkers to come up in the next few years that can curb the rapid proliferation of this disease.

Another miraculous event in the history of medical science is the lifesaving practice of ***organ transplantation***. The initial attempts at organ transplantation were largely unsuccessful, firstly, because the organs used were of animal origin, secondly, since the surgical technique itself demanded refinement and thirdly, due to the immune response to the foreign substance. These limitations were thwarted eventually with the rapid development in science and technology, like the introduction of immunosuppressants for instance, and the first successful transplant was brought forth by Joseph Murray's team, who performed kidney transplant between identical twins. Kidney transplantation is by far the most frequently performed transplantation worldwide. The practice of organ transplantation has escalated over the past two decades and is often an indispensible tool for better quality of life or even survival in many cases. Transplantation of kidney, liver and heart are the most common organ transplantations carried out on a daily basis. Notwithstanding its life saving ability, the main concern of utmost severity is the hard truth of organ shortage- the sad fact remains that the number of patients requiring a healthy organ transplant is exponentially greater than the number of organ donors, despite the rise in the overall frequency of organ donation over the years. Another risk includes rejection of the transplanted organ by the recipient by launching a massive immune reaction against the foreign cells. In both the aspects, ***stem cell culture*** has proved to be quite beneficial and holds great promise for cell therapy, tissue regeneration apart from its therapeutic and biotechnological applications. Owing to their self-renewal capacity and the ability to differentiate into specialized cell types, depending on the source of isolation and physiological conditions provided, stem cells are now considered the ultimate treasure chest for medical

utility. Recent state-of-art approaches, such as three dimensional culture, allow expansion of stem cells for longer periods of time. The idea of creating synthetic organs from one's own cells can help combat the dual issues of organ shortage and rejection. In fact, in 2016, a team of scientists from Massachusetts General Hospital and Harvard Medical School has got a step closer in regenerating functional human heart tissue using adult skin cells, which will be a humongous step in the path to creating individualized organs for patients and thereby saving more lives in the years to come.

One of the greatest inventions in the field of science that deserves applause was the discovery of microscopes, but what was even greater was that this magnifying power channelled the ability to observe tiny microbes in water. In the mid-1800s, scientists were successful in linking the prevalent cholera epidemic to contaminated groundwater and ***water disinfection*** using chlorine proved extremely useful to control the growing disease. Chlorine, nonetheless, comes with its own delinquency, such as respiratory ailments. Over the years, several healthcare policies and regulatory boards and safety standards later, we now have the facility of the modern age Water Purification systems. In our modern practice, we hardly give a second thought while filling our glasses from our R.O.s but clean drinking water is now considered a basic human right and therein comes the significant importance of water purification machineries. Most third world countries see people succumbing to water borne sickness as they cannot procure clean, uncontaminated drinking water for consumption. The joint perseverance of countless organizations and government initiatives have made way for clean water for regular use in several parts of the world, which has helped in giving relief to numerous people. But clean drinking water is slowly becoming a rare commodity. India, for example, homes 17.5% of the global population with access to a mere 4% of the world's fresh water resources. Providing safe water to 1.2 billion inhabitants is an incredible challenge, with groundwater resources being exhaustibly extinguished and global climate change causing little rainfall. Nowadays, many rural areas, in southern India itself, boast of water ATMs, where the villagers have access to clean drinking water against a sum of money. Many people have taken up point-of-use techniques to treat their water, including UV technology, ultrafiltration, nanofiltration, reverse osmosis, ion exchange and other science novelties to rid water of its contaminants. A triumph of contemporary times has been the initiative to make seawater, the richest and vast source of water body on the planet, fit for human consumption. Starting with a handful, now we are proud to have about fifteen thousand desalination plants in 120 countries across the globe, and the trend, concentrated towards providing clean water, is expected to only increase with the expansion of science and technology.

Last but not the least, a special mention goes for the extremely fresh and virgin technology of ***nanoretina***. Nano retina is primarily focused on improving the quality of life of blind people by replacing their diseased retina with an artificial retina. Fostered by a group of researchers at UC San Diego, this high resolution retinal prosthesis is designed from wireless electronics and nanotechnology and a prototype of the device was shown to be effective in rat models *in vitro*. Such technology can give comfort to millions of people throughout the globe, who are prey to neurodegenerative diseases and loss of vision due to diabetes. But the clinical trials will be the litmus test and only time will tell of the success stories!

Inertia to any variation remains a ubiquitous barrier and health innovation is not an exception to that. Ancient healthcare policies and financial issues are the root hindrances to the adoption of health innovations. Future health innovations require the implementation of complex intervention strategies and post-marketing surveillance for the most productive outcome. The Indian healthcare industry, especially in the past few years, is delicately poised to come up with medical innovations over the next decade. *"One sometimes finds what one is not looking for"* were the famous words of Sir Alexander Fleming. With the ever growing

population and a finite source of resources, the stakes will be higher and higher to sustain that population. What sets human beings apart from other species is their desperate attempt at making them the fittest in the "survival of the fittest" contest by coming up with innovative solutions to even the most critical problems. Health innovations are the need of the hour for a better and longer life, and a tenacious effort in that direction can yield wondrous results for the human health.

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Innovations for Human Health and Disease

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An antidote to stagnation is Innovation…

-Robin Sharma

Since dawn of the history, a eukaryotic organism named *Homo sapien* had the courage to ponder upon the problems associated with ill suffering among them and exhibit a great courage to dream, think for new ideas and blend it with the creativity and values to shape it into new inventions and ultimately innovation, profiting human and society. Till the time mankind existence appeared on this planet, it is always accompanied by the factors affecting human health, eventually causing disease or tolling lives. In consideration of the development in areas of science and technology still approximately 105 people die every minute either due to ischaemic heart disease (leading cause of death), chronic obstructive pulmonary disease, lung cancer, diabetes, tuberculosis etc. Pointing towards our backlogs and enlightening the path for pursuing innovations that can increase the life expectancy as well as human wellness.

With a vision of improved life, much awaken innovations in science sector especially biology and medicine have been done or in its infancy. Recently a group headed by Dr. Doris Taylor (University of Minnesota), one of the world's leaders in heart organ repair and regeneration, have managed to grow heart on the muscle scaffold of rats by using stem cells. Her ambitions to grow fully functional organs for transplants have provided the wings to an idea of diminishing the death cases due to either heart or any other organ failure and even by accidents. Another, major contributing factor to pipeline came from extensive research in the field of probiotics. Realizing the enormous prospects and significance of probiotics in human health, even an international conference was conducted with theme title as "Probiotics for Human Health- New Innovations and Emerging Trends", wherein reputed speakers from India and abroad provided eminent proof that probiotics offers an innovative approach for being developed under category of functional foods for management of specific diseases particularly chronic inflammatory gastrointestinal disorders and other medical conditions. The major research in probiotics bids its stakeholders to even take into account the associated safety and efficacy issues which need to be answered before advancing further.

Development of effective vaccination regime to cope up with varied range of diseases can be viewed as one of the greatest innovations for human health and preventing disease. Vaccines have provided a means to prevent many infectious diseases that had been principal causes of mortality and morbidity, and their use has had a major impact on public health. Despite the obstacles, R&D sector is progressing very productively to improve the present generation of vaccines. Researchers at Imperial College London and Johns Hopkins University are making continuous effort to design vaccine to cure HIV by exposing HIV virus and thus stimulating adaptive immune response, orchestrated by immune cells. Such breakthroughs could drastically reduce the amount of resources devoted for treating and combating the disease and provides insight into fighting similarly complex diseases in the future.

Cellular "leapfrogging" or transmuting existing cells into a totally new form seems to cater innovation firm. Recently, researchers at the Stanford University School of Medicine developed a method of "leapfrogging" through which they have directly transformed laboratory

mice fully mature liver cells into functional neurons. Such advances could prove essential in generating essential cells for an ailing patient–or transmuting potentially dangerous or cancerous agents into benign cells.

Apart from manipulating the existing cells to new form, Dr. J. Craig Venter, co-mapper of human genome, took a step ahead by creating life in lab and developed totally new synthetic genome of a bacterium from painstaking process of stitching together all the chemicals composing DNA, having the potential to replicate inside a cell. His findings will be the first of a long line of lab-made creatures in synthetic biology. Such innovative creations open up the door for scientists to develop artificial versions of different viral and bacterial strains of disease, which can be experimentally exploited for development of better therapeutics, diagnostics or vaccines.

Not limiting to innovations in biology a colorful blend of interdisciplinary elements had put feathers in the hat of innovation for human health and ultimately treating disease. One of the feather came in recent years when robotics revolutionize surgery, wherein surgeons at Cleveland clinic performed surgery using tiny robotics hands to remove diseased organs through tiny openings in the human body, ultimately reducing operation time, enhancing accuracy and providing minimally-invasive surgery. Fortunately, doctors at Mayo Clinic in Scottsdale, Ariz and across globe pointed towards utilizing robotic for enhancing accuracy of surgery in cancer cases. Therefore, providing evidences that science and technology moves hand in hand with impacting on human health in a signatory way.

Bioengineering adds on to the cutting edge research being done to uplift and manage human health. Emerging technology including MelaFind optical scanner (MELA Sciences, Irvington, NY) using missile navigation system furnish additional information, a doctor can use in determining whether or not to order a biopsy. The goal is to reduce the number of patients left with unnecessary biopsy scars, with the added benefit of eliminating the cost of unnecessary procedures. The other one in the list is electronic aspirin for treating sphenopalatine ganglion (SPG), a technology under clinical investigation at Autonomic Technologies Inc (Redwood City, CA) where a patient-powdered tool is being utilized for blocking SPG signals at first sign of headache. An electronic implant of a nerve stimulating device will stimulate SPG nerve during severe headache and blocking the pain causing neurotransmitter. Alarming increase in number of Diabetic patients enhances the need for easy diagnostics. To overcome painful method of regular follow-up schemes, Echo Therapeutics (Philadelphia, PA) is working to develop a transdermal biosensor that reads blood analytes through skin without drawing blood for tracking patient's glucose levels. Similar to this kind, Google is also aiming to change the course of diabetes management by measuring blood glucose level from tears.

For amelioration of health and prevention of the diseases around world is ailing despite of astonishing advances made in health sector due to focus on commissioning for price and volume rather than quality and outcome, negligence of the desired government or funding agencies about betrothal of human health, regimen, delivery and cost effectiveness of the treatment and emergence of resistance among organisms against the currently used drugs. Such problems beg for the innovative solutions involving every aspect of healthcare—its delivery to consumers, its technology, and its business models. Indeed, a great deal of money has been spent on the search for solutions. Despite these associated problems, scientists, researchers and ultimately budding minds have the capability to think, innovate and finally modulate human health to enhance the quality and span of life.

Young minds should be motivated to dream as they have the capability to attain and fulfill them as mentioned by Dr. A.P.J Abdul Kalam, missile man of India, in his book entitled as "Ignited Minds". Scientific innovators along with specific direction to these motivated minds can do miracles in the upcoming times, benefiting human health and thus preventing diseases. For enhancing the effectiveness in human health, a perfect blend of interdisciplinary approach is required. Wherein, science and technology needs to go hand in hand.

Creativity, imagination and perfect approach to fulfill ignited ideas, lead to innovations that can enlighten whole humankind. Ideas such as developing ourselves based on neurological information as mentioned very beautifully by Ian Pearson in his book, You Tomorrow. To provide wings to this innovative idea, Google has hired Ray Kurzweil to create the ultimate artificial intelligence controlled brain. Recreational cyborgs, medical 3-D printing, real time diagnostics, digital pills, developing workable human organs for transplant and many more can be added to the far ending list.

"Innovation and best practices can be sown throughout any organization –but only when they fall on fertile grounds".

…. Marcus Buckingham

Similarly, a fruitful collaboration among researchers, companies and government have the ability to shape any innovative idea come true in reality, benefiting human health and ultimately preventing or eradication diseases.

And finally to conclude, I think there is a need to quote words by John S Herrington:

"There are no dreams too large, no innovation unimaginable and no frontiers beyond our reach".

Think innovative and live with a motive…