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THE GREY MATTER

QUARTERLY NEWSLETTER FOR MEDICAL STUDENTS

BASED IN M.I.M.E.R. MEDICAL COLLEGE

DNA

To Edit or Inherit

DNA : A four letter word

Humans have evolved far beyond the instinctive survival thinking that our genes originally drove us towards. At this stage of existence, we recognise ourselves based on the society around us. We relate ourselves to the exchange of material, information and ideas taking place in this very society. The existence of this newsletter gives us the tag of editors before our names.
Yet, we are reminded of the fundamental force that has been driving the life form on this planet when we take a glance at our photo album to find similarities between one's grandma, mom and oneself. This fascination of inheritance is limited to the facade of looking alike, beyond appearances it has the potential of causing peril.

In today's world where almost every disease we read about comes with a genetic facet, the question about inheritance being a boon or a bane arises. We have reached a point where we have found the genetic aspect of most commonly occurring diseases, and are headed towards a world where every treatment will have a genetic basis to it. Essentially, the disease as well as the treatment will be an application of your own DNA. We have spent decades searching for treatments of multiple diseases and all this while we have been inheriting them.

We are nothing but different combinations of letters from A to C along with the Gs and Ts. Every permutation has the capacity to decide the fate of an individual in its own distinct way. So, with this edition we chose to explore the field of the commodity that is simultaneously our one commonality and yet it is what makes each and everyone one of us different, the human genetics. In this edition *'DNA: To edit or inherit'* we are highlighting the scope of genetics in research and application for better understanding of existing diseases as well as development of newer and finer techniques. By curating pieces on recent inventions and ongoing projects in the field of genetics, we hope to offer a glimpse of what the future of medicine holds for us.

Keep reading, keep inheriting.
- Khushboo Doshi & Unnati Shukla, co-editors

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A CHILD'S PLAY

By Aditya Gore & Ishan Gokhale
II/I M.B.B.S. , M.I.M.E.R. Medical College, Pune

When was the last time you were irritated to the core by your younger sibling and questioned the purpose of his/her existence in this world? Before fixating on your answer, can you consider the remote possibility of him/her being your guardian angel? The possibility that the sole objective of his/her origin was to save you; to be your 'saviour sibling.'

One such pair of Saviour Siblings resided in Denver. In 1994, Lisa and Jack Nash gave birth to Molly, a patient of Fanconi's anaemia which is a rare but serious autosomal recessive disorder. Clinically, the patient presents with short stature, strabismus, low set ears with a chance of deafness and aplastic anaemia. Life expectancy in such cases is short. The only treatment available was performing a bone marrow transplantation with the prerequisite of perfect Human Leukocyte Antigen (HLA) match. Since Molly had no direct siblings, a perfect HLA match was out of scope. The time required to find a perfect donor was overwhelming. At the same time, the chances of success were merely 65%. It was at this hour that the Nashs were introduced to the life changing idea that involved conception of a second child through IVF with a closely monitored genetic makeup. This was done through Pre-Implantation Genetic Diagnosis (PGD) and HLA matching. Finally, in 2001, the Nashs gave birth to their son, Adam. Adam's bone marrow was used to transplant and cure Molly's anaemia. 20 years after this revolutionary feat, both Molly and her Saviour Sibling are now perfectly healthy adults.

What exactly is a Saviour Sibling?

It is a child that is conceived through selective IVF as a potential source of donor organs or cells for an existing brother or sister with a life threatening medical condition. The only requirement that needs to be met in this procedure is the perfect HLA match. A Haematopoietic Stem Cell Transplantation (HSCT) with a perfect HLA match is the only permanent cure for a lot of fatal diseases.

IVF and PGD techniques are employed to create multiple embryos which are then screened for an HLA match and any genetic disorders. The embryo which is best suited and has a perfectly matched HLA is then implanted into the mother's womb. On birth of the saviour sibling, the umbilical cord blood is used for HSCT. A variant method of this technique involves the use of bone marrow of the saviour sibling at a suitable age of growth.

India saw its first saviour sibling pair in 2020. Abhijeet Solanki was born in Ahmedabad, Gujarat with beta thalassemia major, a defect in the 11th chromosome.

(Molly & Adam Nash)

The defect results in a malformed haemoglobin beta chain. Abhijeet had to undergo complete blood transfusions every 25 days. He was also being treated with chelation therapy since iron overload is a potential threat in repeated blood transfusions. All this would eventually take a toll on his health. By the age of 6 years, he had already undergone 80 transfusions; the clock was ticking! Further, after 3 cycles of IVF and 18 possible zygotes created, the doctors found a perfect HLA match for Abhijeet; and Kavya Solanki was born on October 18, 2018. For a safe transplant, the doctors waited till Kavya was 10 kgs. The transplantation took place in March 2020. Since then Abhijeet has not required any more transfusions, and the sibling pair is in good health.

If you had a sick child, how far would you go to save them? This is the question that drives the progress of this modern technique. Moreover, it comes with its own host of ethical dilemmas as the zygote that is most fit is deliberately selected, denying nature its ability of chance. This technique is being negotiated and debated on various avenues.

The saviour sibling is not 'wanted' but 'needed' thus leading to commodification of human life which becomes an ethical concern. The argument that is most frequently brought forward is whether the child is solely created to advance a further end or did the parents really want another child? The saviour sibling would not be an instrument but in fact instrumental to his/her elder sibling. The selection of embryo is against nature and will eventually be a slippery slope leading to the introduction of designer babies, a fate least welcome in our mortal world. Although setting proper laws that define when such PGD techniques are allowed will solve this argument, these laws are still unclear with many loopholes yet to overcome.

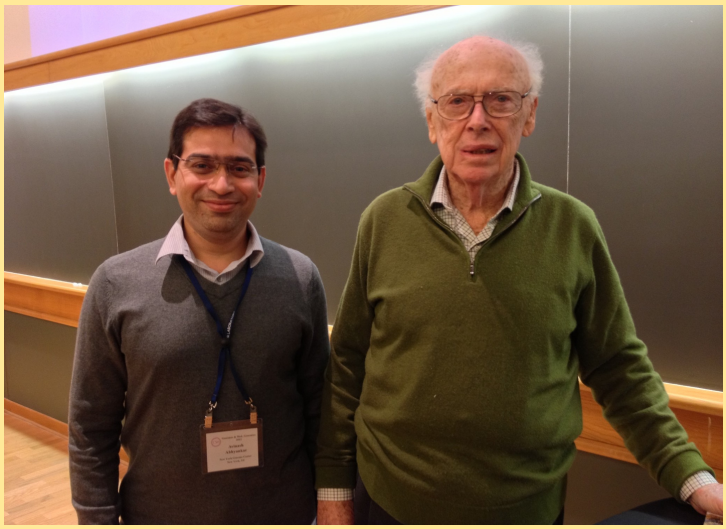
The stand of the saviour sibling is still vague. Till date no adverse effects have been observed during the short duration that these techniques have existed. As for the psychological impact, there is a good chance that the knowledge of the circumstances of his/her birth would scar the saviour sibling. But the odds of him/her being content with the fact that they played a role in curing their sibling are significant. Thus, any and every ethical consideration falls apart until proper law enforcement and parental guidance are figured out. Until these problems are resolved, the question persists - ARE WE PLAYING GOD ?

QnA ON DNA

GUEST INTERVIEW

Dr. Avinash Abhyankar, MD, PhD

In conversation with Unnati Shukla & Khushboo Doshi ,
II/I M.B.B.S., M.I.M.E.R. Medical College, Pune



Dr. Avinash Abhyankar with Dr. James Watson

Dr. Avinash has formal training in medicine, human genetics and computational biology. After completing M.B.B.S. and M.D. in India, he earned MS in Bioinformatics and PhD in Human Genetics in Sweden. His post-doctoral research at the Rockefeller University, New York focused on using next-generation sequencing technology to unravel genetic defects underlying susceptibilities to infectious diseases. During his career he has made major contributions to the understanding of genetics of complex disorders like type 2 diabetes to rare monogenic forms of severe pediatric disorders. Dr. Avinash is also a New York State Certified Molecular Geneticist with extensive experience in clinical genomics.

Q. What about the field of genetics piqued your interest?

When I was studying for my M.B.B.S. and M.D., genetics wasn't formally taught to us. We were just introduced to the subject and that was about it. However, after my internship I started reading more about genetic disorders, and the more I read about them, I realised there is so much left to discover in this field. The methods used for genetic diagnosis fascinated me. Since I was so intrigued by the field I decided to obtain some formal education in it, so that I could figure out whether it was something I liked or not and this is where it got me.

Q. Bioinformatics is not a common choice of field after having done your post graduation in infectious diseases, so can you tell us what inspired you to choose that?

As I read about methods like RT-PCR and restriction enzymes, I got interested in learning how these methods are actually performed. One thing that really made me curious was how people amplify a small fragment of DNA.

As you can imagine, our body has trillions of cells and each of those cells contain DNA and you could target a specific segment of DNA to amplify it; that very idea was captivating for me that time. As I read papers on these topics, I recognised that to get the most out of these assays, some or the other kind of computational method is required to accommodate the vast data collected. I wanted to give learning these computational methods a shot so I took up a course to learn C language. It was difficult at first but as I learnt the basic concepts it started to get interesting. When you have the ability to write computational algorithms it gives you the power to do a lot of things. As I got the hang of it I made up my mind to take up bioinformatics. During that time, it was still a budding field and Sweden was one of the countries at the forefront of it. Hence, I applied for the course, got in and through my learnings I realised that this is something I would like to do for the rest of my life.

Q. Could you tell us a little bit about your journey to the New York Genome Centre?

After I completed my M.Sc. in bioinformatics from Sweden I enrolled for a PhD, during which I worked on the energy metabolism of type II diabetes. This involved a lot of work with molecular biology and genetics. I applied for a post doctorate at various labs after my PhD. One particular lab that intrigued me was the Human Genetics lab at Rockefeller University, New York so I took up a position there. Through the course of my postdoctoral I was involved in understanding the genetic basis of susceptibilities to infectious diseases using next generation sequencing.
At the same time, this era of the next generation sequencing was beginning, techniques were getting better, error rates were going down. Even so, not everyone had access to these assays. That's when The New York Genome Center was reconceptualised with the basic idea of providing research facilities to people across various research labs. Setting up these facilities was an expensive job, hence the idea was to make them easily available. Initially it was confined to the founding members who were various universities in New York, mainly Cornell, Columbia and Rockefeller University. Later, we expanded to the entire country and now we're planning to offer services across the world. Initially, I joined as a bioinformatics scientist and did a lot of research work involving the molecular basis of various diseases. I published a number of papers during these years. A couple of years later, I got the opportunity to set up a clinical laboratory with the aim to design next generation sequencing assays to diagnose paediatric disorders and cancers.

Currently, we offer whole genome assays for constitutional disorders. We also sequence DNA and RNA for cancer. The idea behind this is to identify somatic mutations of a particular type of cancer and based on the molecular profile of that case, we provide recommendations for treatment of that patient.

Q. Our theme for this edition is Genetics. Given your expertise, we would love to hear your views on how we have progressed in using genetic treatments for various diseases.

Let me give you a little bit of a background about precision medicine. In January 2015, the then President of the United States, Barack Obama announced the precision medicine initiative which would get us closer to not only curing diseases like cancer, but also achieving the dream of personalised medicine. The reason this was possible was the advancement of technologies in genomics. This has made it possible to design prevention and treatment strategies based on an individual's data. If you look back into history, the concept of personalized medicine is not really new. For example, in 500 BC itself some people experienced an adverse reaction after eating fava beans while some did not. Eventually it was discovered as G6PD deficiency. Once we got the molecular structure of DNA from Watson and Crick, it led to the birth of molecular biology and modern genetics. A lot of hard work went into the Human Genome Project in an effort to get a map of the human genome. Now we have the ability to sequence millions of genomes everyday and this has made a huge difference to how genetic diagnosis is made. Finally, we're using it on a regular basis, for instance, neonatal screening has started involving whole genome assays at birth, which can later be updated throughout one's lifetime. This is the way forward. I would not be surprised if in the coming years a sequencing test at birth will be as usual as getting the BCG vaccine. There are so many genetic diseases that are preventable or at least proper genetic counselling can be provided to prevent economic burden and mental stress faced due to different genetic disorders.

Q. Has the advancement in genetic technology made treatment more available for the common people or has it become unaffordable?

It depends on where you live. In the USA, the insurance companies usually reimburse for these tests so it's not completely unaffordable. But that is not the problem, when you reach a diagnosis based on a genetic assay you need to have some information about the local population. Most of the research that has been done until now has involved Caucasian people. The landscape of genetic mutations known to us is confined to a specific population. To be able to apply the same principles to different populations and genetic architectures we need to do more than just running the same standardised assay. To do so in India is really expensive. The reagents and materials required are expensive. It is different from almost all other diagnostic methods which are in fact cheaper in India than anywhere else.
Hence, there aren't a lot of labs that perform these assays and those that do, charge exorbitant prices. The technology has gotten cheaper but when it is offered to people it is not cheap and that needs to change. Efforts need to be made to not only make them more affordable but also more accessible. Currently, only a handful of physicians order these tests the reason being that genetics has not been a part of their curriculum. Understanding the results of these genetic tests also requires proper training.

Q. In the current scenario, how has the ongoing pandemic changed your perspective of the healthcare sector and its research aspect?

There is absolutely no doubt that this period has been difficult for everybody. The hardships of the pandemic have not spared the healthcare workers neither the general population. There have been numerous instances where people have had to struggle to make their ends meet. On the brighter side, we as a population have realised the scope of productivity in working from home even when it comes to research. In my perspective, the commute duration is a complete waste of time and avoiding that everyday has enabled better productivity in general.
When it comes to the research, collaboration has proven to be an industry changing idea. For instance, usually preparation of a vaccine requires years of work but it was due to extensive collaboration between scientists and labs that has resulted in formulation of Covid-19 vaccine in less than a year. I, myself am involved in a project which is a collaborative effort to study the disease pattern of individuals who are a part of the low risk population, yet contracted severe form of Covid-19. For this specific research we have a consortium of over 50 labs and clinics over the world. So clinics across the globe would identify such cases and send in their samples, then multiple laboratories that are experts in different fields would process the sample. The assays would give us an idea of the mutated vector in different patients and based on this outcome other labs would perform experiments on the sample culture. I strongly believe that these joint efforts are a great discovery and need to be continued beyond the pandemic in order to make greater progress in shorter durations.

Q. Given that you have studied in India, Sweden and are currently in the States, what are the major differences in the healthcare systems of these countries that stand out to you?

There are positives and negatives in every system, but in my opinion, Sweden stands out. The healthcare system there was optimum and the public did not have to spend a single Krona for any treatment whatsoever.

In the USA everything is business, the ones running these businesses do not care about the impact of cost and difficulties of people seeking help. This is the price they pay for making sure that the facilities provided are up to date.

They put immense efforts in making every possible technology available for treatment. There is also an intense sense of responsibility when it comes to patient privacy. Doctors over here will never openly discuss a case or post about their OT, which is really professional of them.
When it comes to India, lately there have been increased cases of unjustified admission in order to extract money from the patient, which is obviously unfair. Talking about the quality of doctors, the amount of patient exposure during our M.B.B.S. ensures Indian students a lot of confidence and accuracy without depending on assistance from tests and imaging when it comes to their practice. This is appreciated worldwide. I am personally glad to have done my M.B.B.S. from India.
In the western countries you may find each appointment an extensive one. The doctors need to be thorough on the knowledge about the patient and hence give them a lot of time. This increases patient satisfaction and reduces the scope of errors. Perhaps such form of practice is not practical in India given the vast population, working towards patient satisfaction can be a development for the Indian healthcare system.

Q. With your hectic schedule, how do you manage to keep the stress away ?

Stress is a very subjective concept. Different people find a given set of tasks stressful upto different levels. But you have to realise the scope of your work beforehand to be able to prepare yourself for leisure as well as hectic days. I always try to prepare myself based on the intensity of the day that follows and be it any case, my aim is to reach thorough results despite the clock running out of hours. Basically, if you are mentally prepared to put in efforts and realise your ultimate goal, stress wouldn't be bothersome at all. The one thing I would like to press upon is that you should not promise more than you can deliver. Even if this means keeping expectations very low.
Outside of work, I love watching TV. Be it Hindi or Marathi serials even the ones that make no sense, I will sit down and watch them. It helps me cut off from the world after a full day of work.

Q. Can you comment on the Indian education system?

The Indian education system is geared towards high grades, little attention is paid to concepts and the process of learning. This is quite contrasting to what I see in the States right now, the flexibility of the system here lets students' interest persist and progress with the things that they choose to learn. Hence I think there is a scope for improvement.
We are aware about the exceptional quality of doctors India gives every year.

The kind of patient interaction Indian medical education system provides to the students is commendable. Speaking from my expertise, the only thing it lacks is training in the genetic aspect of everything. Teaching it as a small part of other subjects is not going to be enough in the future where the basis of most diagnosis and treatments is going to be genetics. Formal training is required to learn these fine techniques and their outcomes well enough to be inculcated in your routine practice.

Q. Is there any advice that you would like to give to current Medical students?

Coming from my own experience, I found the subjects we study during M.B.B.S. interesting but I never loved any of them. The sole reason why I came across genetics was my will to explore. You need to have a curious mind to read up about the associated concepts of the things mentioned in your textbooks. You cannot think what you don't know, so with every concept you study, you should try to dig a little deeper beyond your lectures. By reading research papers, which you may not understand completely, you are familiarising yourself to new terms and improving your thinking power, which will help you in the long run.
I myself was managing to just get through medical school like most students. But now I realise that my performance wasn't excellent because my interest was laid in something beyond our subjects. So the key is, finding your calling by keeping a curious and an open mind.

Mental Health and Behavioral Genetics

By Apurva B. Gokhe
II/I M.B.B.S., H.B.T. Medical College, Mumbai

As medical science advances, the classical concept of mental health appears a bit too basic. It was almost like a recipe, a cup of symptoms, a little sprinkle of illness route and a dash of family history coming together and yielding the diagnosis, if any. Atypical concentrations of neurotransmitters would make it even simpler to give the pathogenesis.

Science has been digging deeper and realizing that mental health has some relation with the "genes". Not just a lone gene, but the intricacy of the genetic composition combined with non-genetic factors which produces the state of mental health. Before we jump into the complex genetic blame game, it is necessary to talk about the complexity of the brain itself. Weighing just a few pounds, it's the most complex organ in the entire ocean of bioscience. Its development consists of complicated gene-gene and gene-environment interactions. About 100 billion neurons, each one synapsing with either neighboring or distant neurons giving rise to 100 trillion such connections, tons of neurotransmitters acting between these connections, each one having a specific role to play. And even this amazing complexity is not static; its structural architecture keeps on changing. If a thing is meant to be so complex, the chances of potential risk factors arising during the process increases. But what can help is keeping a watch on the expression of risk genes during brain development and their functional manifestations. Moreover, this knowledge should also help us direct the search for modifiable environmental risk factors that convert risk into illness.

Mental health, defined by the World Health Organization, is 'a state of well-being in which the individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community.' Now the question arises, does mental health have anything to do with genes? Of course, it does. The hereditary nature of behaviors and thought processes has been mentioned before. Why didn't we know about this if it's that well known? Firstly, the Human Genome Project wasn't complete until 2003. Secondly, this particular aspect of health is polygenic, which means that a number of genetic effects add and subtract each other to give you the final effect.

The proteins synthesized by these genes and their functional accuracy plays a very big role in all the neurological processes taking place in our brain. Not only do the gene protein products take part in establishing the synaptic structure of the brain, but the activity of synapses which partly results from experience, play a big role.

Nevertheless, genes are the essence of brain map development and execution. Variations in the DNA sequence of genes may lead to the expression of an altered protein with loss of function or with a gain of a function that might be beneficial, neutral or not really favourable to brain cells. Variations in either protein coding regions or regulatory regions of DNA might also result in a complete failure to express a protein. Genetic sequences that affect behaviour, including the risk of mental illness, must affect neurons in such a way as to change the architecture, function or adaptability of neural circuits in the brain.

How much of mental health is genetic? If we look at the research studies, anxiety disorders, PTSD (post-traumatic stress disorder), OCD (obsessive-compulsive disorder), and major depressive disorder are about 20-45% inherited; alcohol dependence and anorexia nervosa are 50-60% inherited; whereas bipolar disorder, autism spectrum disorders, schizophrenia and ADHD (attention deficit hyperactivity disorder) are upwards of 75% inherited.

Everything said and done, there is still a huge scope in the development of neurogenetics. It is the complexity of the two intricate systems that makes it so difficult. In the immediate future, it is necessary to get a hold of genetic resources from well-defined pedigree charts along with reference human genomic information, readily available to all investigators, while building the technological platform for performing a perfect study. This study along with the knowledge of environmental modifying risk factors would help a lot to discover the roots of mental well-being. The field of behavioural genetics still has a lot to give to this world and we can surely see it bringing great advantage to the human race.

TAAZA KHABAR

by Richa Sinha, II/I M.B.B.S.,
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Blooming Skin

While the title might trick you into thinking that I am going to be talking about the multitude of ways that could give you flawless, blemish and acne-free skin, this piece is actually here to tell you about how we can now use this term "Blooming skin" quite literally.

A collaborative effort by IIT-Kanpur, led by Prof. Sri Sivakumar and Tata Consultancy Services' Tata Research Development and Design Centre (TRDDC), led by their principal scientist Dr. Beena Rai has culminated a technology to use Bougainvillea to grow human skin cells. The nano-roughness of Bougainvillea flower makes it eligible for cell attachment and proliferation. The intimate vein structure resembles those of the human skin cells, indicating this species of flowers to be the most ideal out of the 80 species that were evaluated.

A biocompatible scaffold was created by removing all plant cells and coating it over with mammalian skin cells using tissue engineering that led to the development of a 3D tissue. The ultimate validation for these scientists came in the form of biomarkers, collagen III and collagen IV that were found in these skin cells while they grew over the template. What were beautiful Bougainvillea flowers adorning the gardens of IIT-Kanpur, were now cultured into human skin cells in 3 days.
This effort now opens the door for drug and cosmetic testing while putting an end to the horrors of animal cruelty.

Lights, Camera, Prescription.

Do you love watching medicine related movies?
Here's a list of movie recommendations compiled by us!

1. Concussion :
This movie takes us on a journey of discovering 'Chronic Traumatic Encephalopathy', a brain disorder that the National Football League didn't want you to know about. A forensic pathologist, potrayed by Will Smith is up and against the authorities of the NFL. His journey was a rather rocky one, depicting the realities of early 2000s' America. For all the sports fanatics out there, this gripping 2015 sports drama is a must watch to find out how the NFL was beaten.

2. Girl, interrupted :
This movie is an unsettling account of a young female's journey through mental illness. Susanna Kaysen played by Winona Ryder, the protagonist ventures through this psychological drama with her peers from the wards. Her journey of finding and understanding herself is a must watch for a graphic understanding of what follows a mental illness.

3. Gattaca :
The movie revolves around the concept of eugenics, the superiority of genetically cultured humans and the struggle of a man as he defies the rules of society and science to illegally get a shot at fulfilling his dream.

4. Human nature :
Have you ever wondered about a perfect world devoid of cruel genetic disorders? If so, welcome to the club. Watch a couple of genetists contemplate over a termination for sickle cell anemia with CRISPR. Will similar steps shape a better future or compel us to worry about evolution and diversity?

5. Outbreak :
This movie based on the outbreak of a dangerous virus that threatens to end civilisation is a must watch. The thriller will keep you on the edge of your seat as you watch the protagonists fight to contain the virus and find a cure. Considering the relatable world like theirs that we live in right now, this movie is definitely worth a shot.

Non Teaching Staff Interview

Nilesh Marathe,
Surgery OPD attendant
In conversation with Neel Waghu, I M.B.B.S., M.I.M.E.R. Medical College, Pune.

Q. Could you tell us something about yourself and your role in the surgery ward?

My name is Nilesh Marathe. I work as an attendant in the surgery OPD in Dr. Bhausaheb Sardesai Talegaon Rural Hospital. My day starts at around 8 am. All the benches, chairs and tables need to be cleaned and sanitized for use. Managing patients is an entirely different job in itself. Often there is crowding and they need to be managed until the doctor arrives. Throughout the day I run different errands. The minor OT also has to be taken care of.

Q. How was the Surgery Department keeping up with the pandemic?

Strict social distancing norms were followed. During the pandemic, proper sanitation was the biggest challenge. Patients were always on the edge as the patient-doctor interaction had greatly reduced. So systematically handling all of that helped.

Q. What do you like about this job and more specifically the surgery OPD?

The students of course! Over the course of time, I've started understanding the basic workings of the surgery OPD. Many new students, right from UG to PG wander around the halls with confused faces and it's an absolute delight to help them. Many doctors come and go but it's these interactions with young faces which make me smile at the end of the day.

Q. Would you like to give a message to all the aspiring doctors out there?

Observe doctors day in and day out, I think that the field may be complicated but being a 'good' doctor has a relatively simple mantra. My advice would be- " Khub padhai karo; Khub mehnat karo; Ache doctors bankar bas aage badhte raho".

MY SISTER'S KEEPER

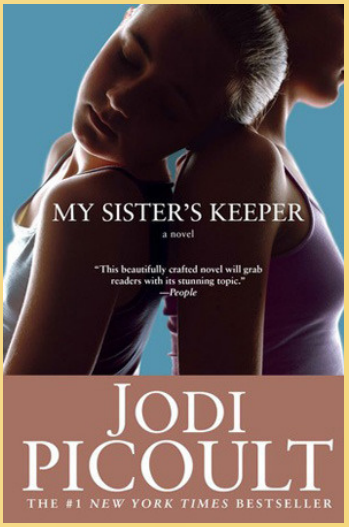
-BY JODI PICOULT

Book Review by Radhika Shah, II/I M.B.B.S., B.J. Medical College, Pune

My Sister's Keeper, a novel by author Jodi Picoult, won international acclaim for its exploration of the medical, legal, and ethical concerns related to a long term illness and the role of a saviour sibling.

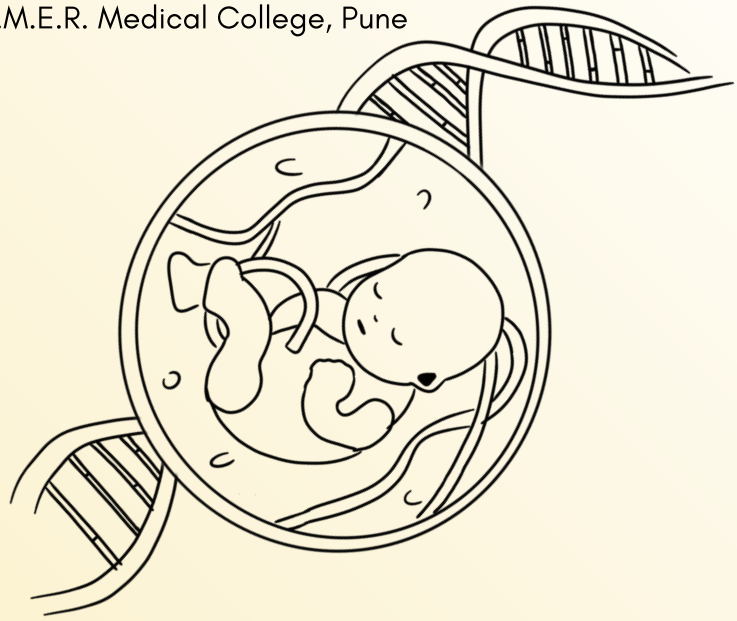
The book follows Anna Fitzgerald, born as a perfect genetic match for her elder sister Kate, her relationship with her family, the conflict she faces growing up as a saviour sibling, and her struggle for autonomy.
Though initially, she was conceived to provide umbilical cord stem cells to her sister, who is suffering from polymyelocytic leukaemia, Anna has grown up seeing too much of the inside of hospitals. The stem cell treatment works but eventually Kate relapses and Anna is called upon once again. Over the course of her thirteen years, she has donated blood, bone marrow, leukocytes and undergone multiple surgical procedures and hospital visits, unnecessary for her own health but to provide treatment for her sister.
Usually, Anna willingly donates whatever it is that Kate requires, but when she turns thirteen and is told Kate requires a kidney as she has gone into kidney failure, Anna refuses. It is a major surgery they would both be required to undergo, and there is no guarantee of it working, as the stress from the operation might kill Kate anyway, and the loss of the kidney would affect Anna's quality of life.
Their mother, anxious to save Kate, advocates for the surgery vehemently, causing a rift in the family. Anna comes to a decision to petition for medical emancipation, so that she may be allowed to make her own decisions regarding her medical treatment and the donations asked of her.

As the family struggles with the fallout between their members and the aftermath of Anna's decision, the readers are taken through the ethical and moral pitfalls of what it means to have control over your own self, the relationships between the siblings, and the delicate balance between legality and morality that comes with saviour siblings.



THE QUEST FOR THE PERFECT BABY

By Dhruva Nair, II/I M.B.B.S., M.I.M.E.R. Medical College, Pune



With the advent of newer technology and advancements in the field of biology in the 20th century, scientific research was no longer the duopoly of Physics and Chemistry. Moreover, biological research was no more the livelihood for the family dunce. When Watson and Crick published the 'Molecular Structure of DNA' in 1953, it was akin to the Manhattan Project, but in Biology. It was the progenitor of modern molecular biology.

This begged the question, can the human germ cell genome be modified and edited in such a way that a change acquired is heritable, thus eliminating the risk of infants being predisposed to inheritable diseases? Could this be coupled with adding favourable traits as well?

A designer baby is the one whose genetic makeup has been altered to provide the desired genome.
There are 3 kinds of genetic technology, all based on post fertilisation manipulation of fertilised eggs, before IVF. They are-

1. Pre-implantation genetic diagnosis, which consists of choosing between viable eggs for one that best satisfies the parents' needs, be it as a screening to prevent diseases or even to predetermine gender.
2. Transcription Activator Like Effector Nucleases (TALENs), which are enzymes that remove extremely specific bits of the DNA strands, and are then replaced by desirable strands.
3. CRISPR, a process discovered in certain bacterial sequences which were found to have snippets of invasive viral DNA incorporated into the bacterial cell, to allow them to recognise similar threat in the future.

But can these be used in actual practice? Only PIGD is being used currently, as it is a screening process and doesn't involve any actual genetic modifications. For the practical use of TALENs and CRISPR, there's still a long way to go before they are safe for human use. However, there exist options where eggs can be screened for gender, appearance, intelligence and disease, the most common being screening for inheritable diseases. Perhaps the screening for all other parameters is highly frowned upon and illegal in many nations.
Another is the development of 3 person baby technology, where a surrogate provides the mitochondrial DNA, thus eliminating the risk of diseases such as muscular dystrophy, heart or liver conditions.
The future holds virtually endless possibilities for designer babies as scientists gradually make advancements in the fields of CRISPR and TALENs.

It may be theoretically possible to modify every bit of the genome for desirable traits, be it eye color, disease resistance, increased brainpower, longer lifespans, or dare I say, new human abilities, so much so that creating Real Life X-Men may no longer be a pipe dream.

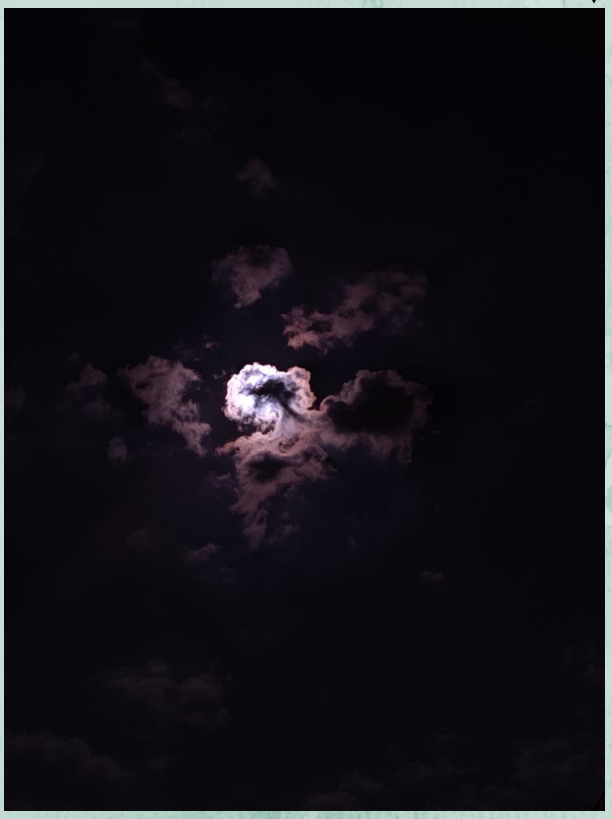
But how will these changes affect society? There is a wide range of clear benefits, but as all coins, there's always a downside. As there will be an increasing number of terminated embryos, considered by many to be living beings and there would be a loss of individuality. Since some genes have more than one effect, unscrutinised editing may have wildly veering consequences and may cause development of newer diseases. The main ethical dilemma is who determines which genes are good or bad? This process is also, for the next considerable time period, a very costly procedure, further marginalising the lesser privileged sections of society.

However, for safety, ethical and social reasons, this was determined by the scientific community to a be red line that should not be crossed. But in 2018, a Chinese scientist, He Jiankui, made the maiden use of gene editing to combat HIV related infertility cases using IVF services and CRISPR technology. Although the twins born were reported to be healthy, this act received widespread criticism due to breach of ethics and order.

In a nutshell, this technology may perform unimaginable wonders, or as we've seen in sci-fi films, lead to unspeakable horrors. The human mind has to function in the tiny grey zone that is governed by both science and ethics and until all these innumerable issues are adequately met, real life super babies seem to be a very distant and polarising idea. But then again, the grass is always greener on the other side.

Shutterbug

Pune



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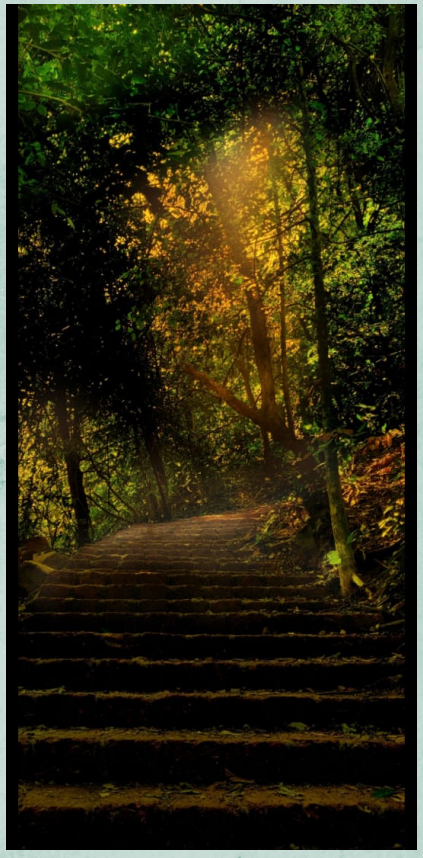

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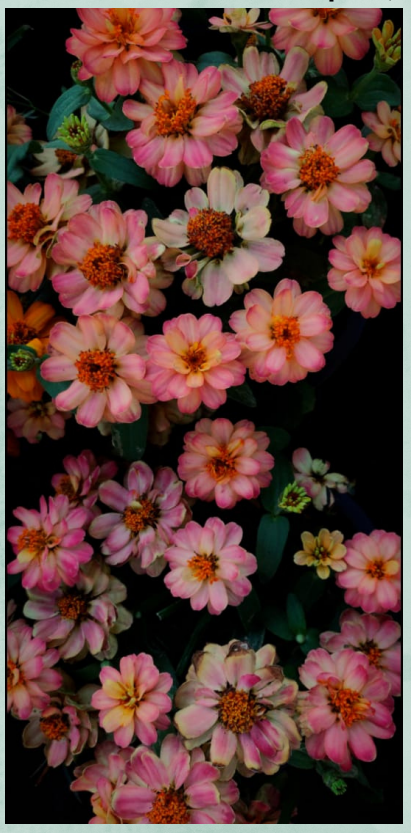

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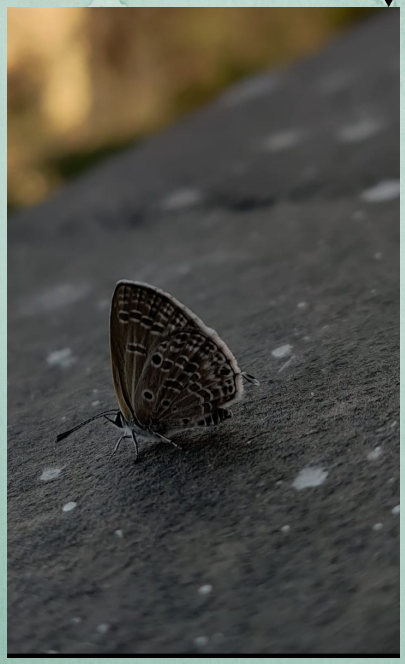

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DIALOGUE

DR. ABHIJEET BOTRE, DEPT. OF PAEDIATRICS, M.I.M.E.R. MEDICAL COLLEGE, PUNE

In conversation with Revati Pathak, Intern, MAEER's Physiotherapy College, Pune and Gauri Hirekerur, I M.B.B.S., M.I.M.E.R. Medical College, Pune

Dr. Botre is a consulting paediatric neurologist and a valued part of the M.I.M.E.R. family He has done his M.B.B.S. from Government Medical College, Miraj. He completed his DNB (Pediatrics) from Maulana Azad Medical College, Delhi and DCHS from Seth GS medical college and KEM hospital, Mumbai. He also did his fellowship in pediatric neurology at Hinduja Hospital, Mumbai and a fellowship in pediatric epilepsy at Cleveland Clinic, Ohio, USA. He practices at KEM Hospital (Pune), Columbia Asia Hospital (Pune) and has a Pediatric Epilepsy clinic in Pune. He is an epilepsy surgeon at Sahyadri Hospitals, Pune.

Q. What drew you to the field of neurology and paediatrics? Was it any experience that you'd like to share with us?

While I was pursuing MBBS, the subject that fascinated me the most was Medicine. The diagnostic process is like a jigsaw puzzle where we gather the pieces in the form of history, evaluation & investigations and place them together to complete the puzzle. I was intrigued by this process, which is why I decided to make a career out of it. Further, being the eldest among my cousins, I have always been fond of children. Having witnessed them growing up, right from their birth instilled a sense of responsibility in me, which I was able to implement in my work as well.

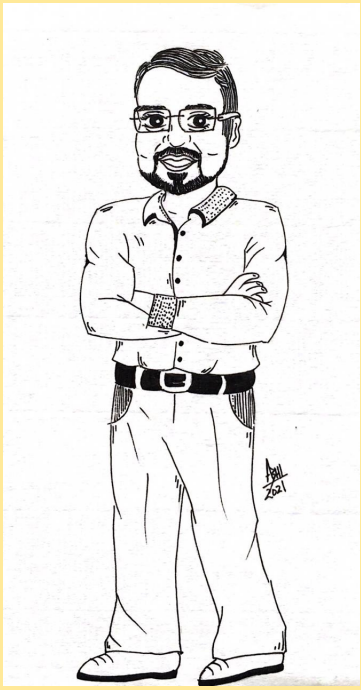
Q. How different is the field now as compared to when you started off?

The last 10 years have seen tremendous growth and innovation in artificial intelligence, technological advancement, exchange of knowledge with developed countries and newer, more advanced treatment modalities. The accessibility and availability of information has become so much better with the introduction of online academic as well as research material. Additionally, the drastic improvement in diagnostic tools, as well as their increased availability has made them more feasible and accessible to the physician even at the most basic levels of healthcare such as a primary health centre.

Q. How has the approach to motor, speech, learning disorders and their treatment options progressed till date? Have you observed a change in parents' compliance regarding the same?

Over the years, I have seen an increased awareness among parents and guardians about what is and isn't considered normal or ideal in terms of health, growth and development in a child.

They are becoming more proactive and participating in their child's recovery and treatment process. Additionally, the approach towards the diagnosis has become more detailed, well-rounded and definitive, with better tools to aid in finding the root cause of the presenting condition. The prognosis of many conditions has improved greatly, thanks to the evolution of treatment options. Additionally, the government has also extended a helping hand through various policies and plans created specifically for children living/ born with disabilities.



Q. How do you counsel or advise parents whose children have been diagnosed with Down's or genetic conditions?

The first step is acceptance by the parents. Once they have accepted and adjusted to the reality of the situation, we can educate them about the condition/ diagnosis. With my patients, I prefer to give them time and resources that they can refer for more information, ask them to attend support groups to meet and communicate with other parents who are in the same situation as them, which might help them in coping with it. The diagnosis should not be dropped onto the parents out of the blue, but should be graded. The treatment strategies and possibilities should be carefully explained. They need to be educated about the available resources, hospitalisation, referred to appropriate rehabilitation specialists, and informed the economic aspect of it. Prenatal and genetic diagnosis can help them in planning for a future child, avoid possible recurrence of the condition and family discord regarding the pregnancy.

Q. In what ways does the diagnostic process differ when treating a child as compared to an adult patient?

In my opinion, the lack of verbal communication is what sets the pediatric patients apart. In place of that, there are other things like the baby's cry, behavioral aspects and other observatory findings that help determine the underlying cause behind their presenting symptoms.

To aid with that, it is important for the physician to ask the right questions and obtain the essential pieces of information from the mother (or any other appropriate guardian). The pediatrician, therefore, needs to have a very specific and definitive approach to obtain the correct diagnosis.

Q. How has the practice of pediatric neurology benefited from the advancements in genetic sciences and research?

When I started my career, genetic tests seemed far-fetched and non-economical. A single gene testing used to cost thousands, or even lakhs. There were some tests which required the samples to be sent to Germany for testing. However, we have come a long way in this field now. The tests are now more economical, require lesser time to process (turnaround time- 6 weeks) and can be done locally. In my opinion, it is important because now we can have clues towards diagnosis as well as prognosis of the baby and furthermore, for prenatal genetic testing & counselling for any rare genetic disease which the baby may have. This also simplifies the choice of treatment, depending on the course of the disease. But sometimes karyotype tests, CMA, whole genome sequencing etc. are under-utilised because of lack of knowledge and awareness.

Q. We would love to hear about your experience with the epilepsy clinic, the advancement in technology and its treatment modalities.

I have worked exclusively with epilepsy patients for almost 8 years, for 5 of which I have worked in the epilepsy clinic. Epilepsy is associated with many diseases in paediatric neurology and I've seen quite a wide spectrum of causes, from hypocalcemic seizures to terrible genetic encephalopathy. Fortunately, growing awareness as well as technological evolution has made the diagnostic process smoother, aiding in finding the root cause and ultimately, its management. With the advent of around 20 anticonvulsants, ketogenic diets, corrective epilepsy surgeries, vagal nerve stimulation, among many other modalities, epilepsy has become easier to manage.

Q. What would your advice to the generation of budding doctors be, especially for somebody aspiring to enter the field of pediatrics?

Multiple things should be taken into account, one of them being a holistic approach towards the patient. Whenever you treat a patient, remember to always show empathy and compassion towards them. Make sure the parents know that you are a team. Try to keep hesitation at the door and keep in mind to be appropriate, efficient and cooperative. I was lucky to find very supportive mentors in my professors and senior doctors, so I believe that mentors play a fundamental role in your career. Along with proper knowledge, the way you counsel a particular patient is a very important part of successful practice. Lastly, I would like to advise you to never abandon the learning process and always be updated with new research.

The best kind of Salary

For a doctor, the most valuable payback for their work is patients' appreciation and their kind words of gratitude. Here's one such incident, Dr. D.P. Kotnis shared with us.

We come across many cases that stay with us but this particular one has a special place in my memory. It was like any other day in the ENT OPD when a 2 year old girl was brought in with a sapota (a chiku bean) stuck in her larynx. She had stridor and cyanosis by the time I started examining her. They were from a really poor family who had taken an ST bus from a village far away as this happened to be the closest government hospital for them. I took a call and decided to pull it out using a laryngoscope, as time was of the essence. And just like that, the girl was saved without having to take her to the OT or having to anaesthetize her. Her parents were eternally grateful. The ultimate satisfaction came by not only saving the little girl, but also treating her parents' helplessness.

Compiled by Richa Sinha,
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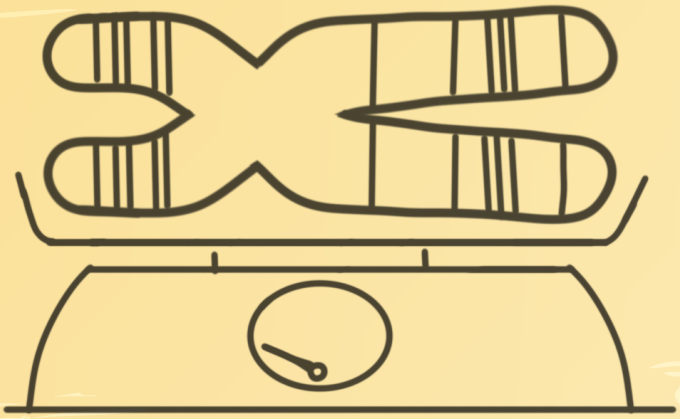
If you have any such good appreciation notes or messages from your patients, please write to us about them at **thegreymatter.mimer@gmail.com**

Do these genes make you look fat?

By Shriya Shah
II/III M.B.B.S. , Dr.Vaishampayan Memorial Government Medical College, Solapur



Studies show that over the last few years the “weight loss” industry seems to have raked in over 150 billion USD annually. These figures were seen rising especially during the ongoing pandemic because people had a lot of free time at hand and a perpetual need for Endorphins that exercise seemed to fulfil. Ironically, Worldwide Obesity rates were also seen increasing tremendously and that matters because obesity now kills more people than malnutrition does!

So, what is going on? Why are self-control and diet unable to curb the spread of this global obesity epidemic? The answer lies within us: Genes!

Genetic basis of obesity was noticed when two Pakistani siblings first reported in Cambridge university in 1997 with “excessive weight gain”. The elder one, 8 year old weighed 86kg, as much as a tall grown man and the younger 2 year old boy, tipped the scales at 29kg. Both the children failed to be satiated no matter how much they eat. Some quick tests pointed the scientists towards the problem: both children lacked leptin, a hormone that regulates appetite. The scientists found that the brothers had a mutation in the gene responsible for leptin production — called 'ob' for obese.

According to the 'thrifty gene' hypothesis, our ancestors evolved genes for efficient food collection and fat deposition in order to survive periods of famine and now that food is continuously available, these genes are proving to be disadvantageous because they are preparing our bodies for a famine that never comes, thus creating an “obesogenic” environment. The obesity epidemic can be considered as a collective response to this environment.

Clear Inheritance patterns for obesity among families are yet to be established but there are a few variants of genetic inheritance of obesity like Monogenic Obesity, Syndromal Obesity and Multifactorial Obesity.

Rarely, obesity occurs in families due to the inheritance of mutations of a single gene. The genes responsible are most often the basis for signals and responses that guide food intake and energy expenditure. They may also be associated with certain biochemical and metabolic processes that regulate adiposity. When it comes to syndromal obesity,

it is associated with phenotypes that include intellectual disabilities, abnormal facies or organ-system specific abnormalities. But obesity most commonly results from complex interactions among multiple genes that influence certain obesogenic behaviours or alter some metabolic processes or both.

These genetic alterations most commonly occur in genes that code for substances that regulate the balance between orexigenic and anorexigenic hypothalamic pathways, more specifically affecting the melanocortin-leptin metabolism. Epigentics, environment and dietary factors or gut microbiota can influence the programming of parental genes. Adiposity associated with complex genetic influences can be diagnosed with a history suggestive of hyperphagia (overeating), endocrinological co-morbidities and a detailed pedigree including the history of consanguinity. Also routine family history collection helps to identify people at high risk for obesity-related diseases.

Obesity is a family heirloom no one asked for and self-control alone is rarely enough to overcome the powerful effects of genes. Although for most genetic causes of obesity, management of nutrition with long term restriction of calorie intake and physical activity remains the first line of therapy, certain medications used as replacement therapies in deficiencies are also under trials. Bariatric Surgery is increasingly being used as an effective treatment for severe obesity with or without concomitant co-morbidities in adolescents and adults.

Researchers working to untangle how genetics, epigenetics and the environment work together to drive obesity away have set a giant task for themselves. But it's one they must accomplish if they hope to turn the tide over this global obesity epidemic.

Pigment

RadhaKrishna

Madhuraa Patil
II/I M.B.B.S., M.I.M.E.R. Medical College, Pune

Flamingo

Dnyanada Lolage
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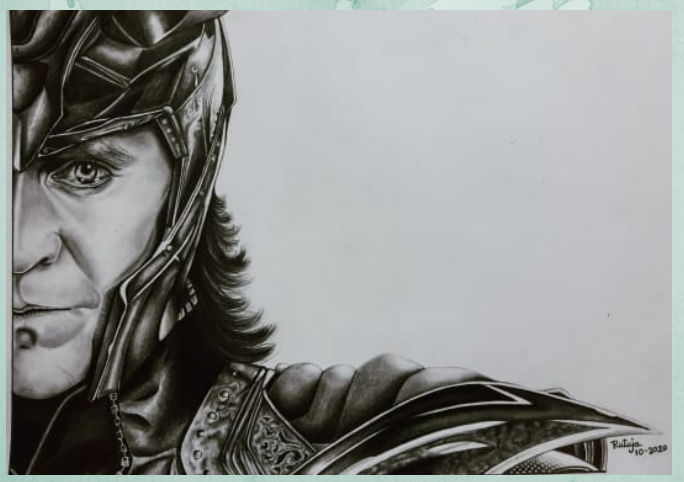

Kneel before me

Rutuja Waghmode
I M.B.B.S., M.I.M.E.R. Medical College, Pune

Vex Ed : A step towards a sex-positive society

By Neha Mahindrakar, III M.B.B.S., SSIMS and RC, Karnataka.

Chapter 8 in the CBSE science textbook for 10th grade is called 'How Do Organisms Reproduce'. I still remember it being the shortest lesson taught to us. There is no better example which demonstrates the taboo that revolves around sex and sexuality in our country.

With a population of 136.6 crore, more than half of whom are sexually active, the lack of awareness around sex and related issues is truly daunting. Studies show that majority of parents in our country do not provide sex education to their children. We can all relate to the awkward silence in the living room whenever a condom advertisement plays on the TV. Apart from this, the non-existent curriculum on sex ed in most cases and teachers unwilling to take up the topic despite the curriculum being present in others, forces most adolescents to turn to the internet, magazines or pornography to gather information about sex and sexuality. This is harmful in many ways, causing misinformation, unrealistic body image, normalisation of objectification, violence, abuse and unsafe sexual practises to name a few.

Vex Ed, co-founded by Vartika Mishra and Mallika Bawa, two 20 year olds, aims to modify these statistics and create awareness around sex and the wide range of topics associated with it. The team has over 15 members now, working through content creation and extensive social media outreach. Vex Ed also has a group of advisors, who with their experience and expertise, help guide us through every step of the process. The content on social media, including an online blog and an Instagram page, is curated so as to spread awareness amongst the followers about a vast array of topics, some of which include - Sex positivity, Bisexuality, Prostrate cancer, Endometriosis and Period sex. These posts are worded simply and help in easy understanding of lesser known topics. The page also puts out a 'question answer' session every Sunday, known as 'Sex Ed Sundays' which allows followers to ask questions or clear any doubts that they may have. Every day of the week is made interactive and fun by introducing Myth busting Mondays, Tally Tuesdays, Wellness Wednesdays, Thankful Thursdays, Fluid Fridays and Shout out Saturdays.

The ultimate goal of Vex Ed is early intervention and providing the right kind of information at the right time. This can be achieved by providing comprehensive sex Ed to students by visiting schools across the country.

Comprehensive sexuality education covers a broad range of topics related to:

- Human Development (including reproduction, puberty, sexual orientation, and gender identity)
- Relationships (including families, friendships, romantic relationships and dating)
- Personal Skills (including communication, negotiation, and decision-making)
- Sexual Behavior (including abstinence and sexuality throughout life)
- Sexual Health (including sexually transmitted diseases, contraception, and pregnancy)
- Society and Culture (including gender roles, diversity, and sexuality in the media)

One of the driving forces behind the resistance to sex education is the orthodox belief that sex education might 'corrupt' the younger generation. This is as far from the truth as it can be. Studies have shown that sex education among youth reduces the rate of teenage pregnancies, sexually transmitted diseases and sexual abuse. Countries like The Netherlands have a successful sex ed curriculum where children as young as 4 years olds are taught about sex and sexuality through contextually relevant and age-appropriate content. As a result, Netherlands has one of the lowest rates of teen pregnancies and sexually transmitted diseases and is also one of the most gender-equal countries.

It's time for India to follow this path and take a liberal approach to sex and sexuality. As a starting point, we need to take discussions on sex education more seriously and focus on creating a robust sex ed curriculum that works for the Indian culture. The curriculum should include children, teachers and parents as well. The primary focus should be providing young adults with the necessary information about all the relevant topics which will help them make informed decisions- and that is exactly what Vex Ed intends to achieve. Our biggest hope for Vex Ed is to be able to empower the youth to make better decisions and develop into well-functioning adults of the society. In the long run, we envision a reduction in sexual crime rates through impacting awareness amongst today's youth and tomorrow's society.

Satisfaction for us comes from the fact that we are doing our part in creating a society where - all individuals irrespective of their sexuality are valued and respected, sex is a consensual and safe experience for all, people are informed and educated about STDs, individuals have the right to make decisions about their own bodies, and people understand the true meaning of feminism. It's a long way to go but Vex Ed is a step forward.

GENDICINE

By Zoya Mhaisale
I M.B.B.S., M.I.M.E.R. Medical College, Pune

The idea for Gendicine —a type of DNA-based medicine that inserts a healthy gene into cells to replace a mutated, disease-causing variant—was first published in 1972. After decades of disputed results, treatment failures and some deaths in experimental trials, the first gene therapy drug for a type of skin cancer was approved in China in 2003. The rest of the world was not easily convinced with the benefits, however it was not until 2017 that the U.S. approved one of these medicines. Since then the pace of approvals has accelerated quickly. At least nine gene therapies have been approved for certain kinds of cancer, some viral infections and a few inherited disorders. A related drug type interferes with faulty genes by using stretches of DNA or RNA to hinder their workings. After nearly half a century, the concept of genetic medicine has become a reality.

In human DNA, certain genes are responsible for preventing cells from becoming cancerous. The p53 gene is one of the most important of these tumor-suppressor genes. Healthy cells can become cancerous when carcinogens damage their DNA and cause them to start dividing and reproducing uncontrollably. The p53 gene prevents this by activating proteins that arrest cell division and repair corrupted DNA. In cases where the DNA damage is irreparable, the p53 gene initiates a process called apoptosis that destroys the cancer cell before it reproduces itself. The p53 gene can also limit blood flow to tumors, which prevents growth and alerts nearby immune cells to attack cancer cells. When the p53 gene itself is corrupted, however, cells lose a natural safeguard against becoming cancerous. Doctors have observed that more than half of human cancer cases involve mutated p53 genes. Improperly functioning p53 genes allow cancer to spread faster and become more resistant to treatment.

If doctors find an effective way to repair or replace mutated p53 genes in cancer cells, it could lead to a radical improvement in the treatment of many types of cancer. Many researchers believe the emerging science of Gendicine holds the key. The great challenge of gene therapy is to find a reliable way to deliver the tumor-suppressor gene to the cells that need it. Researchers have tested a few different DNA-delivery vehicles, or vectors, on several types of cancer, but so far, none of these gene-therapy techniques have been approved by the FDA for cancer treatment.

Many researchers have tried using genetically engineered viruses to deliver p53 genes to cancer cells. Researchers first remove the dangerous viral DNA from the viruses to ensure they cannot cause an infection in the patient.

Then the researchers inject the altered viruses directly into the tumors. This approach has proven safe, with very mild side effects, but it is currently inefficient for transmitting genes to cancer cells. The harmless viruses may not reach all the cancer cells in the tumor, or the body's immune system may hunt them down before they can deliver the p53 genes. A Gendicine treatment based on restoring p53 could be safely combined with traditional cancer treatments such as surgery, chemotherapy or radiation therapy to increase the overall effectiveness of the treatment plan. Gendicine is one of several new treatments that researchers are hoping will bring us closer to a cure for cancer. Another form of gene therapy in development for cancer includes suicide gene therapy.

Unlike traditional medicines or therapies, Gendicine is a potential one- time treatment aimed at targeting the underlying cause of a disease at the cellular level and may deliver transformational improvement in quality of life. This approach maybe significant for patients with genetic diseases, and has the potential to deliver breakthroughs that change patients' lives - today and in the future.

Comic by Atharva Rane,
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