FEBRUARY 2023

THE GREY MATTER

VOLUME 16

QUARTERLY NEWSLETTER FOR MEDICAL STUDENTS

THE UNCOMMON UNVEILED

An account of Rare Diseases

Share your Colours!

Life is a game of chance. Over the course of evolution, our bodies have always tried different combinations of characteristics to fulfill our primary goal as a species - to adapt and endure. Minute details such as the lengths of our extremities, the size of our cells, our enzyme profile have all been determined through a rigorous process of gene selection and mutations. This wide array of varying features continues to exist in our genetic material and sometimes they are expressed unexpectedly.

Every unique character one holds within themselves inevitably becomes the defining factor of how they stand out as a person.

Approximately 4% of the total world population is affected by a rare disease at any given time. These noticeably uncommon beings lead an orphic life and through the lenses of our new edition, we attempt to give you a bird's eye view of their metanoia. As they strive to push through their limitations and persevere against all odds, their stories often remain unsung.

What does it mean to be different, when what sets someone apart is chemically rooted deep into their DNA? Here's your chance to find out, right here in Volume 16 of The Grey Matter :
The Uncommon Unveiled.

- Gauri Hirekerur and Neel Waghu, Co-editors

Happy Reading!

CONTENTS

IN THIS ISSUE

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THE PRICELESS TREATMENT: ORPHAN DRUGS

by Jainil Devani, III/II M.B.B.S., GMERS Gotri Hospital, Vadodara

When we speak of rare diseases, we must understand that drugs that treat them are naturally also a rarity. 'Orphan Drugs' is the epithet given to medicines which are used to treat 'Orphan Diseases', or those that affect very few people. Such drugs are hard to come by since pharmaceutical companies producing them rarely get the financial profit they need from funding them.

To contextualise the dilemma surrounding orphan drugs, we must first understand how drugs and research are funded. The main funding these days comes from pharmaceutical megacorporations, which are in it mainly for the profit. Thus, money gets fuelled into innovations that bring in a hefty turnover. When the disease is a rare occurrence with a few patients on a national or global scale, these corporations are all the more reluctant to inject funds into research for the same.

This creates yet another barrier for patients with relatively rare disorders. Their treatment or control with drugs becomes harder to achieve simply due to inavailability. To alleviate this situation to a certain extent, governments of the USA and European Union have come up with several measures in place to ensure that pharmaceutical giants receive certain incentives to fund the research and development of orphan drugs.

The Orphan Drug Act (ODA) which was passed by the USA in 1983 encompasses drugs, vaccines and other diagnostics that are meant for rare diseases which entail disorders affecting less than 2,00,000 American citizens. Drug companies receive hefty tax breaks and extended exclusivity licenses over such drugs. A similar act within the European Union also extends its Orphan medical treatment coverage to some tropical diseases commonly found in developing nations. It grants an exclusivity license of up to ten years.

These schemes have aided several breakthroughs, including drugs for Wilson's disease and Cystic fibrosis. Penicillamine, which was initially developed to treat Wilson's disease was later found useful for common ailments like arthritis. Another notable example includes Statins. These drugs, which are now in regular use were originally formulated to treat a rare disease, Familial Hypercholesterolemia. Now statins are commonly used to lower cholesterol levels in a myriad of patients.

However, such policies have often been abused by corrupt pharmaceutical megacorporations. A drug may be used to treat several conditions. Companies may register it as an orphan drug, but then market it for common disorders. While governments have tried to put mechanisms in place for such fallacies, it is imperative to maintain schemes for Orphan Drugs.

The main reason for it is that the profit-to-reward ratio for companies is still complicated. The research and funding on orphan drugs takes the same amount of money and energy as drugs for common diseases do, but the consumers that companies find for orphan drugs are far, far less. Because of this disparity, the additional cost gets passed down to the patient, resulting in skyrocketing drug prices. This impacts insurance companies as well. Hence, it becomes essential to have policies in place to tackle this. Tax breaks of up to 50% are included in such schemes to benefit patients and incentivise companies.

The situation in India is vastly different, and even more complex. For a country like ours, where the public health landscape is still reeling with common diseases and providing effective, affordable care in remote areas to a diverse population, rare diseases become even more difficult to diagnose and treat. Here, orphan drugs and their costs require creative solutions.

India has long since lacked a government policy for rare diseases and orphan drugs. This was rectified by the Ministry of Health and Family Welfare by launching 'National Policy for Rare Diseases, 2021'. This policy outlines how to tackle rare diseases and the scarcity of orphan drugs in our country. It recognises the lack of funding for rare disorders and their drug treatment, and how it fits into the complex tapestry of Indian Healthcare. It also gives a comprehensive list of rare diseases, classification of orphan drugs and related diseases, and arrangements for the same. It highlights how some rare diseases can be prevented by neonatal screening and other means of primordial prevention.

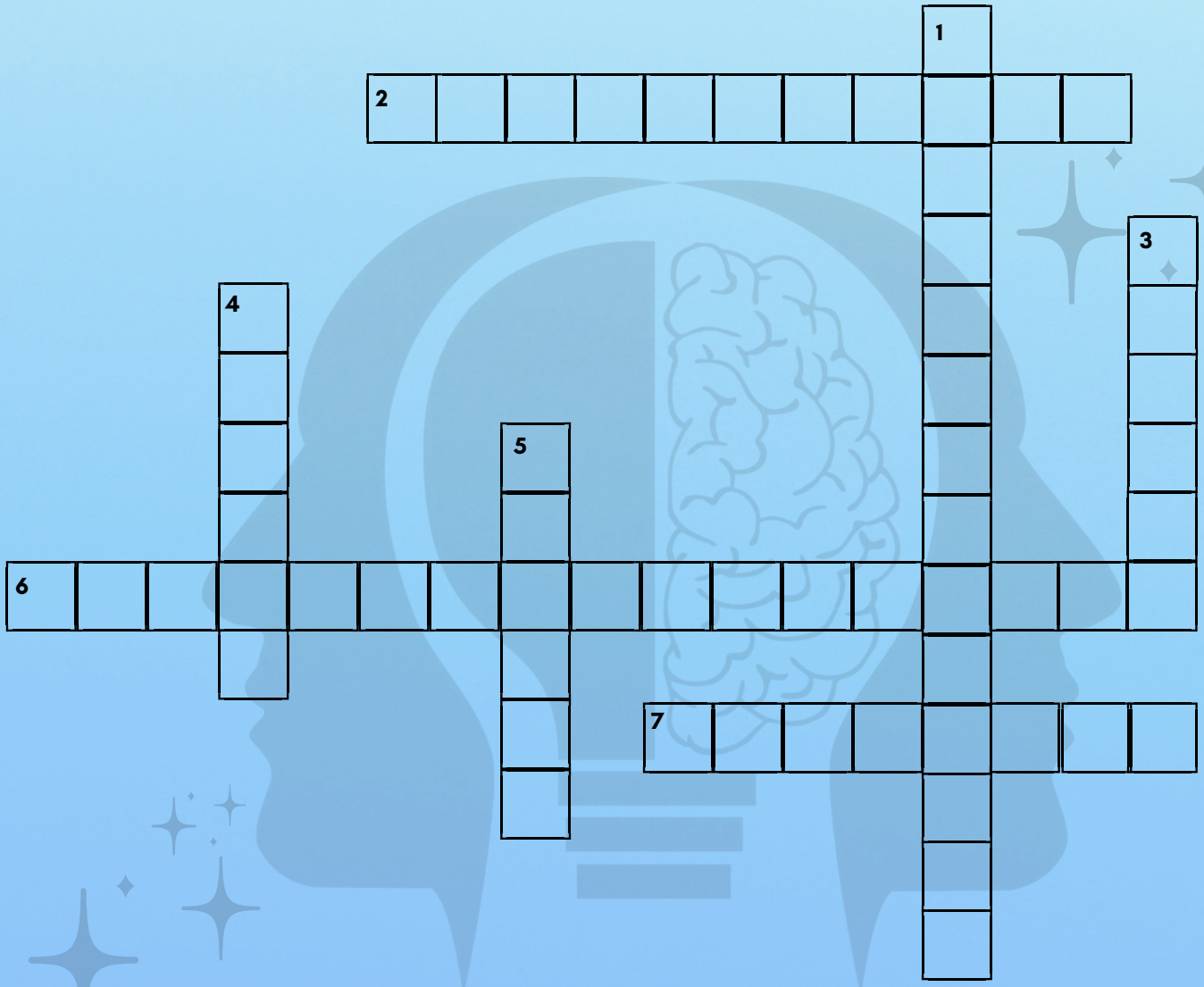
For a developing country like ours, the same focus and interventions for orphan disease treatment cannot be adopted like those in developed nations. The National policy gives a broad overview of how other countries have faired in this aspect and details the Indian perspective. It would be wrong to shift the focus to rare diseases presently when India still requires hefty research funding in other major areas. At the same time, all patients should be supported and cared for equally. The policy encourages creative alternatives such as special dietary formulae and other methodologies.

The picture of orphan drugs and rare diseases in India is unconventional, unique from developed nations and comes with its own set of challenges. However, the act of recognition and policy development by the Indian government for the same is an endeavour in the right direction.

CORTEX

Crossword

by Nupur Chaturvedi and Saneeka Vaidya, Internship, M.I.M.E.R. Medical College, Pune



Across

2. Blue sclera + otosclerosis + osteogenesis imperfecta
6. Ashleaf macules
7. Happy Puppet syndrome

Down

1. Genetic disorder with Gp-Ib/Ia mutation in platelets
3. Diverticulosis of colon + cholelithiasis + Hiatal hernia
4. Aortic stenosis + angiodysplasia of colon + von Willebrand disease
5. _____Fibrosis : Chloride channel defect causing bronchiectasis

Answers
1. Bernard Soulier 2. Van der hoeve
3. Saint's 4. Heyde's 5. Cystic
6. Tuberous sclerosis 7. Angelman

The 'Ode' of Ranvier

GUEST INTERVIEW

Dr. Chandrashekhar Meshram, M.B.B.S., M.D., D.M., Neurologist, President of Tropical and Geographical Neurology Specialty Group of WFN, trustee of World Federation of Neurology.

In conversation with Gauri Hirekerur, III/I M.B.B.S. and Aaditya Kiratkar, II M.B.B.S., M.I.M.E.R. Medical College, Pune

Dr. Chandrashekhar Meshram

Dr. Chandrashekhar Meshram is a renowned Neurologist who completed his M.B.B.S. from GMC Nagpur and later his M.D. and D.M. from PGIMER, Chandigarh. Dr. Meshram is the trustee of World Federation of Neurology, the first Indian member to do so since 1957. He served as the Secretary and President of the Indian Academy of Neurology. He is currently serving as the President of Tropical and Geographical Neurology Specialty Group of WFN since 2017 after being re-elected for a second term. He has represented India seven times as a national delegate for the council of delegates meeting of WFN in several countries.

Q) How do you go about the investigation of Multiple Sclerosis since there are no confirmatory signs and symptoms nor any laboratory tests?

There is no fixed number in terms of prevalence of Multiple Sclerosis; the numbers vary from community to community, age, gender and other factors. You have to be observant of the classical symptoms like unilateral visual loss, diplopia, optic neuritis, trigeminal neuralgia, nystagmus, cerebellar ataxia, asymmetric limb weakness. So you initially suspect, examine the signs and to support your probable diagnosis you run an MRI with contrast study. That is the best way to diagnose Multiple Sclerosis. An important characteristic found on a MRI is new lesions along with older ones distributed over regions like subcortical lesions or lesions in the spinal cord. To support your diagnosis, you test the CSF of the patient for oligoclonal bands. 90% patients show presence of oligoclonal bands which confirms your diagnosis. Presence of oligoclonal bands does not simply indicate MS because it could also be a case of neuromyelitis optica. All in all you need to build up on your assumption backed by a MRI to claim that the patient has Multiple Sclerosis. McDonald's criteria can also be used to confirm the diagnosis of Multiple Sclerosis.

Q) Other than drug therapy, what other treatment options in context with palliative care are available for Multiple Sclerosis?

There is a three pronged approach to the treatment of MS. If it is an acute episode you treat it with methylprednisolone IV preparations. There is a disease modification therapy to prevent the disease from advancing. A symptom based therapy where you approach the disease by treating associated pain, bladder or bowel symptoms is also in use. Another aspect is physiotherapy and rehabilitation like gait training, yoga etc.

Supportive therapy like psychological support and family counselling is sometimes a prerequisite.

Q) Is there a unique patient or a rare disorder apart from Multiple Sclerosis where you've been intrigued either by their symptoms, your own clinical findings or the response of the patient towards the treatment? How do you counsel patients in such cases?

There was a patient who had been diagnosed with Multiple Sclerosis by another doctor due to his manifestation of visual loss. By looking at their MRI I initially arrived at the conclusion that this may not be MS. With contrast studies I diagnosed it as IgG4 disease, a type of pachymeningitis where I could see that the meninges were thickened around the orbit which is why it was presenting as Multiple Sclerosis. There was another patient with chronic backache whose MRI didn't reveal what had exactly happened. Upon further investigation it turned out to be Sarcoidosis.

Some patients upon diagnosis refer to the Internet, don't understand it completely, jump to conclusions and get scared. When a person gets diagnosed with a rare disease, you counsel them in a comforting manner, inform them about what to expect, the management, risks, complications because multiple sclerosis occurs in multiple episodes. In an attempt to make the public aware, we do conduct sessions on patient care for the general public and healthcare workers.

Q) Do you think that these disorders which we term as rare now will be more prevalent or subside over time?

Speaking with reference to Multiple Sclerosis, it is an autoimmune disease. A decade ago patients of MS were a rare occurrence, just like a blood moon. Autoimmune diseases are invariably linked to the lifestyle a person leads; their diet, sleep pattern, stress, obesity and other similar factors. Hence, considering today's way of living, these non-communicable diseases are rising. What with increased life expectancy, they will be more prevalent because newer and improved machinery has led to us diagnosing more cases. Moreover, trends in disease patterns are dynamic. A couple of decades ago Neuromyelitis Optica and Multiple Sclerosis were considered to be on the same spectrum. Now with advancement in medical sciences we have learnt that these are quite different and need to be tackled separately in their own rights.

Q) What are the obstacles that patients diagnosed with such rare disorders face?

Patient awareness is paramount to diagnosis and timely treatment of any disease. Curable diseases like epilepsy are left undiagnosed due to minimal awareness. Awareness will lead the concerned patient to avail help from a certified doctor in due time. The public often ignores the obvious solutions especially with regard to diseases they know little about and then consults someone inexperienced or underqualified who gives them a dose of 'placebo'. As they see an initial improvement, they are led to believe there's progress but in reality, the disease is left untreated which may lead to more complications.

The World Health Organisation along with the World Federation of Neurology have initiated a plan termed 'Intersectoral Global Action Plan Against Neurological Disorders' where we make the populace aware about what the government and people can achieve together. Secondly, economic conditions do come into play here. Some of the newer drugs employed in the treatment of Multiple Sclerosis are very costly with the final bill produced in lakhs. And although there are alternatives now that weren't present before- which the common man can afford-the economically backward who have never seen the occurrence of such disease do have doubts; and looking upon the cost of the procedures and treatment they start to backtrack. For such cases we do try our best to waive off their fees wherever possible but the people are still understandably hesitant which brings us back to the point of awareness. There's a lack of infrastructure for diagnosing rare diseases in our country which again is a major factor in them being left untreated. For rare diseases like Multiple Sclerosis it is very difficult to make a clinical diagnosis and is often unhelpful.

Q) Can you tell us about the measures/policies undertaken by the government, which enable the patients to receive top notch healthcare with no obstruction or about the absence of such policies?

It is safe to say that there are no policies that tackle 'rare diseases' at the moment. There is a list of "Priority Diseases" but unfortunately it has remained unchanged for decades. Diseases included in that list have a priority order based on prevalence and since the prevalence of diseases like Multiple Sclerosis and other rare neurological diseases is already low, they are currently not on the government's radar. Through various programmes via the World Federation of Neurology and the World Health Organisation we're trying to make the government aware about special cases and the special requirements that medical professionals need to tackle them. I had also personally written to a Member of Parliament about the cost of treatment for diseases like Multiple Sclerosis and other less prevalent neurological disorders, and after raising the issue in Maharashtra Assembly, it has contributed in lowering the prices of drugs administered for these diseases. The impact you create via awareness can go a long way to wake up the government and mobilise it to take necessary action.

Q) How promising does the research department seem with respect to new technologies and advancements in your field?

Let us consider the disease MS here as an example. The earlier technology wasn't advanced enough for accurate screening of the actual number of cases. Now with new developments, we are aware of the increased incidence not only in the number of patients but also the varied manifestations. For instance, when previously the prevalence was around 50 patients per 100,000 in the USA, it has now reached a new high of 300 per 100,000. 7-Tesla MRI which shows us an in-depth picture of the brain like a microscope is now available to us albeit only in a few countries, which wasn't the case before. A plethora of new methods to diagnose MS, better laboratories, better techniques, biomarkers and genetic studies are now at our disposal which have helped us in knowing the disease better and finding out ways to treat it more efficiently.

Q) What do you think is the biggest challenge that young medical professionals face when they come across rare diseases and how should they go about them?

I think with constant new findings and developments in the field, being up to date with all the information about any particular condition, diagnostic equipments, pharmacological advances, etc is really challenging. As a medical professional you need to constantly keep updating your knowledge. So being observant and curious are key qualities. Medical knowledge is obtained by attending actual patients, so you need to seize every chance you get and study the rare cases at your institutes.

This is where the clinical postings in your MBBS years come in handy. Presenting of cases goes a long way in improving your clinical judgement. To know how to present such cases, you need to go through existing literature, try to find unique features and take active efforts to publish it. Lastly, despite the growing competition in our field, I think a healthy collaboration with your colleagues, discussions regarding interesting cases and exchange of knowledge will help you understand the disease better.

Lights, Camera, Prescription

by Unnati Shukla, III/II M.B.B.S., M.I.M.E.R. Medical College, Pune

- **The Elephant Man (1980)**

John Merrick is born with a congenital disorder called Proteus Syndrome and wields his genetic impairment to earn a living in a circus freak show as the "Elephant Man." When London surgeon Frederick Treves discovers this performer with severe skeletal and soft-tissue deformities, he assumes that he must be intellectually disabled as well. As the two men spend more time together, Merrick reveals the intelligence, gentle nature and profound sense of dignity that lie beneath his shocking appearance, and he and Treves develop an unconventional friendship.

- **Lorenzo's Oil (1992)**

Five-year-old Lorenzo is diagnosed with ALD (adrenoleukodystrophy), an extremely rare and incurable degenerative brain disorder. A disease so rare that nobody is working on a cure, hence his parents decide to immerse themselves in research and tackle the problem themselves. Frustrated at the failings of doctors and medicine in this area, the Odones begin to educate themselves in the hope of discovering something which can halt the progress of the disease. This is the story of Augusto and Michaela Odone and their persistence that leads to the cure that saves their boy and re-writes medical history.

- **The Mighty (1998)**

The Mighty is a tale of two social outcasts. Kevin is a bright 13-year-old with Morquio syndrome, a progressive disease which causes his bones to stop growing even though his organs continue to expand, until finally, in the movie's words, "his heart will get too big for his body", and Max, a child with dyslexia, mocked for his vast size. The two form an unlikely friendship when Kevin becomes Max's reading tutor.

- **Paa (2009)**

Auro is an intelligent, witty 13-year-old boy with an extremely rare genetic defect, a Progeria-like syndrome. Mentally he is 13, a typical young boy, but physically he looks five times older. His father, a young politician, tries to help his son cope with his condition which causes the young boy to age beyond his years.

- **Hichki (2018)**

Naina Mathur is an aspiring teacher who suffers from Tourette Syndrome. After several interviews and numerous rejections, she lands her dream job as a full-time teacher in one of the most elite schools in the city. However, she soon realises that the class she has been assigned comprises of defiant and impish students who can't seem to keep out of trouble. Despite a few initial hiccups, she manages to make the troublemaking students realize their full potential.

Comic by Anuja Argade III/I M.B.B.S., M.I.M.E.R. Medical College, Pune

Stigma related to rare diseases

by Zoya Mhaisale, III/I M.B.B.S., M.I.M.E.R. Medical College, Pune

'Compassion with Christ ... is faith so strong and so deeply incarnate that it leads to the individual embodiment of the contemplated pain."- Ivan Illich.

The word stigma finds its origin in the Greek word - stigmata. The stigmata are bodily wounds and scars which appear in locations corresponding to the crucifixion wounds of Jesus Christ: the hands, wrists and feet. It is believed that stigmata result from exceptional poignancy of religious faith and the desire to associate oneself with the suffering Messiah. The true attribute of being stigmatised is associated with suffering.

Societal stigma against people with gross medical conditions has been prevalent since ancient times. People were disgusted at the mere site of lepers. They were made to beg and suffer. Dwarves were paraded around in cages as circus animals. Is this the price of being different? Or the wrath of an ignorant society?

Similarities to each other are what bind us together. Ever wondered why all of us start staring at each other as soon as we see a foreigner at a restaurant? The minute we see something out of the ordinary, our guard is up.

People who suffer from rare diseases which affect their appearance are under constant scrutiny. They have to face two battles – one against the disease itself and the other living in a world where few people understand what you're up against. They have to struggle with minimal resources, marring their social, mental, physical and emotional health. This puts an unbearable amount of stress on their mental well being.

Stigmatization heavily criticizes alterations in certain preconceived notions. To this day, profound stigma exists around diseases which are well known and well researched into. Rare diseases are no exception to this. A rare disease manifests itself not only in the psychological front but also in the social front. Stigmatization affects the 'social front' leading to isolation.

An Alpha-1 antitrypsin deficiency patient which has been misdiagnosed, or has had a delayed diagnosis is highly susceptible to impaired lung and liver diseases progressing to deteriorating systemic ailments. Timely detection of the disease could easily curb the ill effects and agitation of the disease can be avoided by taking precautions.

The core of the problems encountered while dealing with these conditions lies in the lack of information, sensitization and awareness, not only amongst the general public but also the medical professionals. In a country riddled with superstition, it is imperative to educate people about these conditions and assure them that it is not black magic done on a voodoo doll.

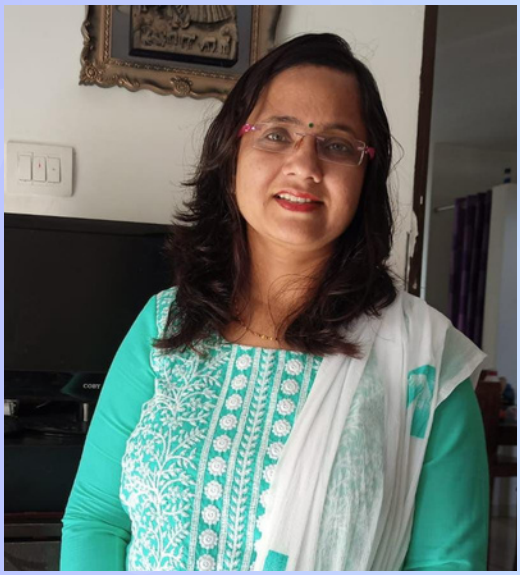
Rigorous research and development must be the main stay for uprooting this stigmatization. Attention to mental health disorders as a result of a rare disease should be addressed with as much care and sensitivity as for any other disease. A communion would definitely induce a feeling of inclusion for patients who are being worn down by societal scrutiny.

Patients and medical professionals must be duly informed of the national rare disease policies and the legal justice benefitted from it.

High pricing and low availability of orphan drugs might be a curtailing factor in patient care. The shame, guilt and embarrassment encompassing the thought of being 'different' must be eradicated. Rare is unique! It is a whole new spectrum that propagates 'inclusion and support' in waves ranging through all frequencies.

Diagnosis, please!

Mrs. Manisha Sharad Avhad, Lab technician at Dr. BSTRH, Talegaon in conversation with Neel Waghu, III/I M.B.B.S., M.I.M.E.R. Medical College, Pune



Mrs. Manisha Sharad Avhad

Mrs. Manisha Sharad Avhad is a lab technician working day in and day out at Dr. BSTRH, Talegaon. Her work entails bridging the gap between the patients and the doctors to ensure a swift and accurate diagnosis. In the following interview Mrs. Avhad provides us a fresh perspective regarding the advancing laboratory care and its influence on health care.

Q) Pathology as a clinical branch has to deal with a number of responsibilities. Which ones does your department undertake?

Right here we have specimen collection for the Biochemistry and Pathology department. This includes thyroid tests, LFT, CBC, ESR, urine routine and so on. We have started using machines for some of these tests.

Q) How has the use of automated devices affected this field?

We hardly do any tests manually. These include ESR, urine testing and electrolyte testing. Although machines look very impressive superficially, it can get very tedious to supervise their use. We use barcodes now. But patients keep on putting up the wrong barcodes or get them mixed up. This creates a lot of confusion and is not only time consuming but also decreases the viability of the sample. With all this new technology popping up, learning to efficiently use them is often overlooked.

Q) How was the extreme surplus of specimens managed during the COVID-19 pandemic?

Now that was a tough time! Right from the irritating masks to the ever increasing number of samples, the workload kept on piling up. Tests like CRP had to be run constantly and everyone was on deck at the lab. But it was fulfilling knowing that we played our part in controlling this dangerous pandemic.

Q) What protocol do you follow for diagnosis in emergency situations?

Emergencies are part and parcel of a technicians job. Tests like ABG, CK-MB have to be run as as soon as possible. Sometimes the sample gets clotted and it has to be collected again. We are continuously in contact with the hospital to keep a track of all the samples that arrive and the urgent ones are prioritised.

Q) What was your motivation behind choosing this profession?

I was always intrigued about the paramedics who diligently work behind the scenes. They are essentially the backbone of the healthcare system. Our tests and reports help the doctors to reach a diagnosis and eventually heal the patients. With the vast array of illnesses and diagnostic procedures, everyday becomes a new learning opportunity.

Q) Do you have a message for our readers?

Well, first of all, when the lectures of the new students start it's a pleasure seeing them all confused and excited when they first visit the CCL. Over the years I see them evolve into competent clinicians. It is fulfilling knowing that the future of healthcare is in responsible hands. I'll conclude by saying - "Stress toh jarur hai but MBBS worth it hai!"

TAAZA KHABAR

by Anushka Gupta, II M.B.B.S., M.I.M.E.R. Medical College, Pune

In a world chasing after new innovations and technologies in hopes of finding a cure, aid comes from an unlikely source. Sildenafil, popularly known by its brand name Viagra, is renowned for curing erectile dysfunction. According to researchers, this magic pill might be the cure for a rare lung disease with a poor prognosis.

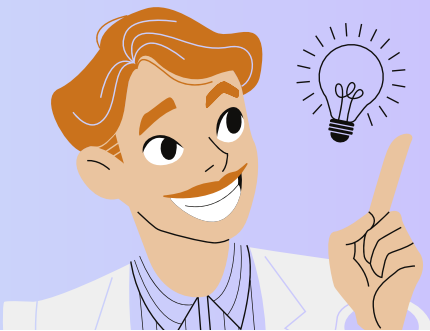
Pulmonary Arterial Hypertension (PAH) affects the delicate arteries in the lungs and the heart. Over time the lumen of these arteries gets permanently narrowed due to vasoconstriction, causing reduced blood flow and increased blood pressure in the lungs. Patients present with one or more symptoms of chest pain, shortness of breath, dizziness, cyanosis, etc. Untreated, it may progress to heart failure which is fatal.

How does Viagra fit into the picture here? Let us focus on how it gets the job done. Sildenafil inhibits an enzyme called phosphodiesterase V through a series of complex reactions bringing about vasodilation. Vasodilation leads to increased blood flow, meaning an erection if we're talking about the penis. Apply this mechanism to the lungs, and you get a wider arterial lumen which reduces blood pressure for better breathing.

Researchers in several clinical trials observed that it not only reduced the rate of disease progression by 12.7% but also improved exercise capacity (measured using the six-minute walk test) by 50 metres.

The use of Sildenafil in treating PAH is already well-established as 'effective and approved for use' in Canada under the brand name Revatio. The drug has also proved beneficial in treating other lung diseases like Idiopathic Pulmonary Fibrosis and Chronic Obstructive Pulmonary Disease.

For a disease with no clear aetiology, a limited patient pool and zero established cures, this discovery is like a breath of fresh air to the afflicted. It opens doors for researchers to develop a better understanding of its cause and course. Proving to be quite the wonder drug, Viagra will ultimately assist in synthesizing an improved treatment.



the Mind-y project

by Soba Inamdar, III/I M.B.B.S., M.I.M.E.R. Medical College, Pune

"It's not what you are that holds you back, it's what you think you are not. "

~ Denis Waitley.

"If we were to make a depiction of ourselves from the eyes of an acquaintance, be it family or friends, what would it look like?

An enthusiast, a loving, jolly ray of sunshine or a rude, self-centred narcissist?

Or maybe none of that, because we unknowingly spend so much of our time worrying about how we are perceived by others that we neglect our own opinion.

Here we are, within this tiny infinitesimal moment of time, so tied up with everything we are and everything we do. We think this sliver of something means everything because to us, it does. But to everything, we mean nothing. And that's not to demean the greater ideology of us as individuals having meaning and purpose in our lives. Because we do matter and so do our actions, but not enough to make ones overthinking keep them up all night. It is to highlight the truth that the multiple million people who walk the earth right alongside us, don't really spend much or any of their precious seconds giving a second thought about you. We never allow ourselves to be appreciated or loved when we stand in front of a mirror. Years of self deprecation have made us recite flaws that don't exist. Maybe it is social media to blame or some bullies at school or the wonderful society we live in, but none of us deserve to be shamed by self, or live in the fear of being a horrible main character in a movie. As Buddha's saying goes, "Nothing can harm you as much as your own thoughts unguarded." We shouldn't let the possibility of what could go wrong keep us from going that extra mile, but let the excitement of everything that could go right propel us like a gust of strong wind.

And the next time we think we did something embarrassing in public, maybe we should look around to realize that no one had their heads out of their devices to even notice. We are the only main characters in our movies playing in our heads and the only real audience is ourselves, so go out there and don't let the fear of judgment stop you from being your unique self! "

‘The apple doesn't fall far from the tree’

Consanguinity and Complex Diseases

by Madhav Bansal, III/II M.B.B.S., Institute of Medical Sciences, Bhubaneswar

There are numerous ethnic and religious communities around the world that have various types of marriages. Marriage between second cousins or closer relatives is termed consanguinity.

The number of genetically contributing grandparents is lower in consanguineous marriages than in unrelated marriages. Recessive genes may become more common in an inbred population compared to an outbred population due to limited natural selection. A shocking fact is that as many as half of the marriages in some South Asian, Middle Eastern, and North African countries are consanguineous!

Consanguineous couples may pass on deleterious lethal genes to their offspring from their common ancestors, resulting in prenatal, neonatal, and child morbidity or mortality. Autosomal recessive disorders are twice as common in consanguineous lineages as in nonconsanguineous progenies. Consanguinity is a significant risk factor for many birth defects and metabolic errors. The most visible medical consequence of consanguinity is an increased birth preponderance of infants with inherited genetic abnormalities.

European history showcases that Roman Civil Law forbade a marriage if the couple was within four degrees of consanguinity. The church adopted such prohibitions as well. However, the rules did not apply throughout Europe, and consanguinity was common, especially in cultural and geographical outposts. The European nobility kept itself above the common law, and interrelated marriages were useful in consolidating class, territory, and power. Many other cultures have laws prohibiting relatives from marrying, and inbreeding has been and continues to be common in others. In some large populations of Asia and Africa, 20 to 50% of all marriages are consanguineous, and in certain areas of Pakistan, the majority of marriages are consanguineous.

Religion and culture, economic standing and aristocracy, geographic remoteness and small populations are all reasons for large-scale inbreeding.

The human genetics literature is replete with examples of rare genetic diseases in inbred populations that were geographically isolated (e.g., Finns and French Canadians) or culturally distinct (Ashkenazi Jews).

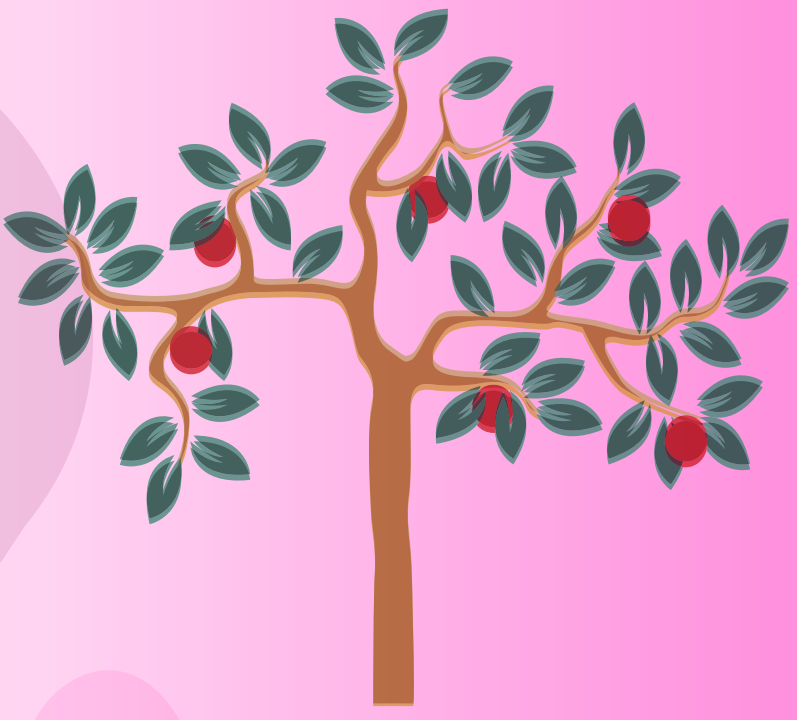
Surprisingly, despite the ancient rules against consanguinity aka kinship ties, scientific evidence on the harmful effects is relatively new. The first reports were published in the mid-1800s, around the time of Charles Darwin.

He was upset and demanded scientific evidence for a personal reason because he married his first cousin.

Disorders that only affect a miniscule portion of the population are known as rare diseases. If a disease affects fewer than 5 people per 10,000, or 0.05% of the population, it is considered rare according to the European Union. Similarly, the United States (US) classifies a disease as rare if there are less than 200,000 cases of it, which corresponds to a prevalence of 0.063% in a population of about 316 million people.

In the 27 member states of the European Union, it is estimated that about 6-8% of the roughly 500 million people live with such disorders, and a similar percentage (7.9-9.5%) has been reported for the US. As a result, ‘Rare Diseases’ present a significant threat to population health and call for etiological fieldwork.

From rare disorders to common diseases easily being seen in offsprings of a consanguineous couple it is definitely obvious that even genetic counseling, reproductive awareness have not penetrated through the religious and communal beliefs and ethos behind consanguinity and even in today’s age and time it doesn’t seem to get any better.



Shutterbug

Amritsar

Manjiri Kolhe
III/II M.B.B.S., M.I.M.E.R. Medical College, Pune

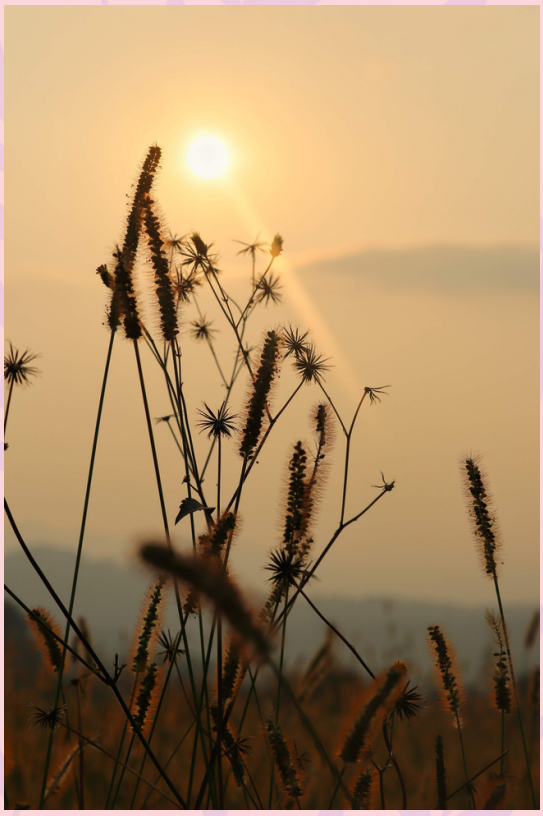
Manori Beach

Dr. Bansi Wade
JIIU'S IIMSR, Warudi

Khajjiar

Niraj Abhonkar
III/I M.B.B.S., M.I.M.E.R. Medical College, Pune

Bir Billing



Harshal Gajanan Bharad
Intern M.B.B.S., S.B.H.G.M.C, Dhule

Pigment

Wallflower

Samruddhi Waghmode

Intern M.B.B.S., S.B.H.G.M.C, Dhule

Pawfection

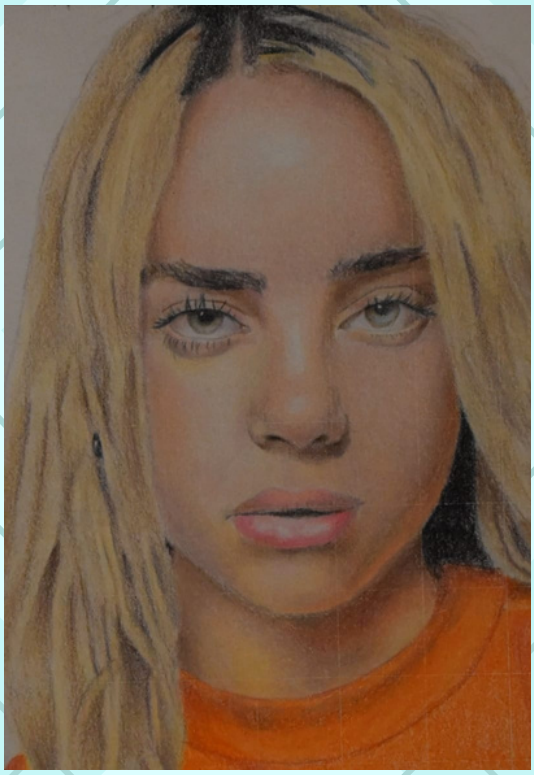
Sayee Kulkarni

III/I M.B.B.S., Smt. Kashibai Navale Medical College, Pune

The Soundtrack of your Life

Akshita Yadav

II M.B.B.S., DUPMC, Jalgaon



It's all inside you

Dhruv Sarode

III/I M.B.B.S., M.I.M.E.R. Medical College, Pune

DIALOGUE

Dr. Harsha Jaykar, Department of Pathology, M.I.M.E.R. Medical College, Pune

In conversation with Soba Inamdar, III/I M.B.B.S., M.I.M.E.R. Medical College, Pune

Dr. Harsha Jaykar is a professor of Pathology at MAEER's MIMER Medical College, Talegaon.
She completed her M.B.B.S. from Government Medical College, Nagpur and went on to pursue M.D. Pathology from LTMMC Sion, Mumbai.
She has obtained her post doctoral fellowship in Cytogenetics from Christian Medical College, Vellore, Tamil Nadu. In addition, she holds three national and three international publications to her name.

Dr. Harsha Jaykar

Q) Pathology is a vast subject to major in with branches exploring each clinical avenue. What was your inspiration behind picking this field?

Personally I think pathology is a very interesting subject because there is a step wise process as to how to do things and get answers to questions from information that we collect from specimens. What inspired me to major in Cytogenetics is that we directly get to observe a cell at the microscopic level, which gives us an insight into the in vivo status of that particular condition. So finding out more about the root of the cause is something that always intrigued me.

Q) Pathology is one of the only subjects at the cusp of teaching, research as well as working in cohesion with clinical sciences. What have been some newer milestones achieved by pathologists in their respective fields worldwide?

As pathologists, there are various achievements under our hats globally, starting development of automated methods in laboratory which has minimised manual errors. Secondly the introduction of newer techniques like karyotyping, FISH has been a proud success. In the last decade we also began 'next generation sequencing' which rapidly changed the scenario of genetic testing and immunophenotyping. This technique is used to confirm suspected hereditary disorders and is crucial for the diagnosis of genetic diseases like leukaemia before the onset of symptoms. The availability of a digital platform has allowed pathologists from all over the world to interact and report cases. This has been really helpful in collecting and analysing a global database. Similarly when it comes to educating young minds, online platforms made it easier for us to educate them during the pandemic when the colleges couldn't officially function offline.
Getting to share what we directly learn from a cell or a tissue to a class of medical aspirants is a great joy!

Q) Along the lines of our topic for this edition, what is your take on rare diseases and how could we spread more awareness about them?

There is no clear cut definition to which every country will agree. Because of variations in geography, climate and habitat, certain places display a prevalence of 1 in 5000 while some have a rare 1 in 1 lakh cases. This may also include diseases which may have high incidence but no proper cure. For such cases we have learnt that healthcare workers need to be trained to detect them earlier because the best shot at eradication is prevention since we lack an effective cure. Reporting such cases in journals is important so that your colleagues can get the information and the same can be shared over a large scale. This will also encourage more funding from the government to launch new projects for research. Facilitating the availability of better diagnosis and cures for these diseases is imperative.

Q) In recent times there has been a spike in the incidence selected rare diseases. What is your take on the same?

Previously, the patient load which was tested was inadequate and we also came across symptoms which did not match up to a particular prognosis. But now that more and more people get tested with newer technology like OMIM (Online Mendalian inheritance in Man), we are

Staying Alive

by Khushboo Doshi, III/II M.B.B.S., M.I.M.E.R. Medical College, Pune

learning the actual count of these lesser known diseases. This, I am hopeful will pave the way for effective management and a possible cure in the foreseeable future.

Q) How would you say pathology plays a role in monitoring and facilitating cure for certain rare diseases?

The recent addition of the gene editing tool makes it easy to not just detect a disease as early as in the womb but also guide the course of vaccine studies. It also aids to check if mutations in a population increase the risk of acquiring the disease more or acquire resistance instead. In 2020 a case of sickle cell disease was put through clinical trials and received gene editing tools. It became the first case to result in a cure. This is only the beginning of what gene editing can further do, alongside continuing with symptomatic and palliative care. Another example would be Gaucher's disease where we have symptomatic care working alongside gene therapy for the enzymopathies. While previously we were battling for a cure for these rare diseases, as we bring together novel discoveries like gene editing and continue our supportive treatment we are not far from having a stern answer there as well.

Q) How would you say pathology plays a role in global healthcare in case of a breakout?

If we begin with the CBC, different coagulation abnormalities, rising D-dimer counts etc., these tests assess the severity of the disease and highlight the importance of timely management. Even the post mortem specimens after autopsy for the study of tissues and getting to know the exact pathology of how the outbreak has affected different organs like the lungs or the brain are helpful in understanding how exactly the pathogen affects the body.

Q) Thank you for your insight ma'am, it has been a pleasure talking to you. What would you like to personally say to students and pathology aspirants reading this?

Pathology is a very wonderful subject especially for anyone who loves finding answers directly at the cellular level. I certainly love it because while studying any case I fancy myself a spy looking for clues in every tissue I observe. Just as you try to put the pieces of a puzzle together, connecting the dots of your findings with the clinical history of the patients gives you a sense of excitement when gathering results and answers to help the whole community.

This course of MBBS enables us to see the community in a different light. It is no more just a faction but an opportunity to improve lives every step of the way. The theme of applying our knowledge for the society along with rising rates of cardiac arrests together led us to stumble upon the opportunity of making a difference.

Basic Life Support is starting to gain traction, yet with the sight of an unconscious man, people tend to run away or wait for the ambulance to deal with the situation.

This gap between existing practices and the necessary change in attitude of people allowed us to come up with the idea of training and retraining the common man with BLS.

We started this project with the policemen of Pune. We tested their knowledge, skills and attitude followed by training them for CPR and life saving skills. Upon analysis, despite being trained, most individuals lacked basic knowledge and skills, but what surprised us was their willingness to step up if such situations present. Their sincerity to learn this life skill and apply it motivated our cause the most. We started this project with a small group of 10 policemen in a nearby police station, and continued it upto police headquarters. Our work was appreciated by the Centre for Police Research, Pune. Every interaction with policemen, showed us how our society can be self sustainable if given the correct resources.

In future, we hope to expand this project and train other professionals like teachers, coaches and bus conductors. The ultimate goal is to impart knowledge and build confidence in every member of the society to save a life.

Sturge-Weber Syndrome - A Nightmare in Pediatric Dentistry

by Dr. Sonali Waghmode B.D.S., M.D.S., Paediatric and Preventive Dentistry, Assistant Professor at K.I.M.S., Karad.

Hemorrhagic disorders are relatively rare genetic disorders characterized as the inability to form a blood clot that leads to abnormal spontaneous bleeding or profuse bleeding after the mildest provocatory event. Bleeding disorders are broadly categorized as deficiency of coagulation factors, platelet disorders, and vascular or fibrinolytic defects. Vascular defects are sparser in occurrence, usually associated with bleeding confined to skin or mucosa. Vascular defects are ordinarily marked by the presence of birthmarks.

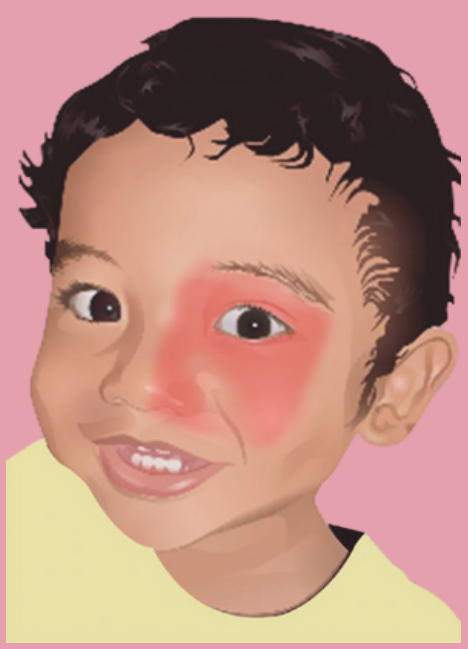
Sturge-Weber syndrome (SWS) is one of the vascular disorders, that has stupendous scope of clinical manifestations and life-threatening complications which makes it a critical and mandatory task to arrive at its accurate diagnosis. It is a congenital disorder, sporadic in origin and it is linked to syndromes of phakomatoses disorders (mother-spot diseases). Nearly a century ago (1860), Schirmer was the first one to describe SWS in alliance to angioma of face and buphthalmos. William Allen Sturge in 1879 highlighted dermatological and ophthalmic manifestations of SWS which were escorted by radiological alterations put forth by Weber. Anticipated occurrence of SWS is 1 per 50,000 live births. Sturge-Weber syndrome, also known as encephalofacial angiomatosis and encephalotrigeminal angiomatosis. It is among the neurocutaneous syndromes (NCS) characterized by a pathognomonic triad of facial cutaneous vascular nevus [nevus flammeus or port-wine stain (PWS)], neurological dysfunction, and ocular manifestations.

In 1992, Roach categorized SWS into three variants. Type I: Individual with a PWS on the face, leptomeningeal angioma, may have glaucoma. Type II: Individual with a facial PWS, absence of leptomeningeal angioma, and may have glaucoma. Type III: Individual with leptomeningeal angiomatosis, absence of facial PWS, and rarely, glaucoma. Intraorally, angiomatosis can outstretch to the buccal mucosa, palate, tongue, the floor of mouth, gingiva, and lips may show purplish-red discoloration. Gingival lesions vary from slight vascular enlargement to massive gingival growths. Oral vascular malformation accounts for approximately 40% of SWS patients. Routine dental and oral surgical procedures seem complicated due to the known risk of intra and postoperative hemorrhage. The considerable prevalence of oral manifestations of SWS makes it crucial to have comprehensive knowledge about this rare congenital disorder.

Management of SWS is based on the extent of involvement of tissues. The severe psychological trauma of SWS can affect a patient's personality development. Port-wine stain can be treated with dermabrasion, tattooing, and flash lamp pulse-dyed lasers. Different treatment techniques like sclerotherapy, cryotherapy, laser, and surgical excision have been carried out with varying degrees of success to vanquish intraoral lesions. It is a difficult task to perform dental procedures in a SWS patient owing to the risk of severe intra and postoperative bleeding. An important precaution to keep in mind is that a suitable armamentarium must be at stat available in case any complication emerges. A multidisciplinary approach is the core of the proper treatment of SWS patients.

Clinical significance - Port-wine stains should not be considered as just birthmarks and should be further investigated for its systemic involvement to arrive at a confirmatory diagnosis and treated accordingly with special precautions.

Take home message - Sturge-Weber syndrome often manifests as perioral and intraoral vascular lesions. Hence, comprehensive knowledge is crucial to provide an appropriate dental treatment without complications. Information regarding SWS's signs and symptoms as well as the knowledge of the best treatment to be performed will provide an overall health benefit to patients.



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