Blunt pointers

The BJP did well in the by-elections, but the Congress arrested its slide in Karnataka

By-elections are no more than pointers to the popular mood. They are not firm trend-setters for a general election. When the winners of polls in 10 Assembly constituencies in eight territories are representatives of four different parties, there is no one big lesson to be drawn from the results. Even so, these will inevitably be interpreted as indicators of the public mood, especially when four of the States, which held by-elections, are due for Assembly elections by the end of 2018. The Bharatiya Janata Party, which is sitting pretty after sweeping the elections in Uttar Pradesh and Uttarakhand earlier this year, did well to best the Aam Aadmi Party in Delhi, and win a seat each in Rajasthan, Himachal Pradesh, Madhya Pradesh and Assam. The victory in Delhi should be especially satisfying for the BJP as AAP leader, and Chief Minister, Arvind Kejriwal attempted to cast himself in a larger-than-life image, pitting himself directly against Prime Minister Narendra Modi in his campaigns and public statements. That the AAP candidate lost his deposit is a shocker: the party had won 67 of Delhi's 70 seats in the 2015 Assembly election. As the AAP seeks to extend its reach and increase its clout, it seems to be losing out on its home turf. More than the victory in Assam, or even in Rajasthan and Himachal Pradesh, what will be more gratifying for the BJP is the second place finish in West Bengal. Its candidate was ahead of both the Left Front and Congress candidates in Kanthi Dakshin in West Bengal, an indication that the party could grow in opposition to the ruling Trinamool Congress in the years ahead. That must be truly worrying for the Communist Party of India (Marxist), which had held power in the State for a record 34 consecutive years until 2011. As the 2014 Lok Sabha election showed, the BJP is no longer a party of the Hindi belt alone, and is now national in character.

If the BJP has cause to celebrate its position at the top of the heap, the Congress can draw some comfort in having arrested its slide in Karnataka. The party won both seats in the State, beating back the challenge from the BJP, which was on the comeback trail after the return of former Chief Minister B.S. Yeddyurappa to its fold. Chief Minister Siddaramaiah, who was under pressure from sections within his own party, should get some additional breathing space till the Assembly election next year. By retaining one seat in Madhya Pradesh, the Congress has shown it cannot be written off despite having lost three successive elections to the BJP. Indeed, if there is one lesson for all parties in this round of by-elections, it is that there is still everything to fight for in the Assembly elections, whether they are to be held next year or later.

Cool minds

De-escalation, not deal-making, is needed to reduce tensions in the Korean peninsula

With tensions in the Korean peninsula continuing to escalate, Beijing took the rather extreme step on Friday of warning that something needs to be done to wind down the U.S.-North Korea confrontation, saying the "the storm is about to break". The heightened rhetoric of recent days follows Washington's display of naval power with the despatch of a U.S. aircraft carrier strike group to the waters off the Korean coast. Though U.S. officials described the move as merely cautionary, President Donald Trump, who has made North Korea a key foreign policy concern of his administration, used the word "armada" somewhat ominously. For their part, the North Koreans have threatened nuclear retaliation in the event of any attack. In late March, the U.S. had commenced installation of the so-called Terminal High Altitude Area Defence (THAAD) anti-missile system in South Korea in response to missile tests by the North. The agreement, in the works since last year, has already increased regional tensions, entangling China as well. Washington and Seoul have emphasised that intercepting the North's advanced development of inter-continental ballistic missiles was the real objective behind the new system. But apprehensive that its own nuclear infrastructure would be inevitably exposed to snooping by the THAAD radar, Beijing has sought to counter Seoul with trade and tourism boycotts.

Mr. Trump's threat of unilateral action against Pyongyang in the event that China fails to rein in North Korea may partly echo the mood in Washington after the recent missile strikes in Syria. If the Chinese government views Pyongyang's growing nuclear capability with concern, as it professes to, then it must do much to use its leverage effectively. Merely stressing the need for a peaceful resolution to the conflict is not enough. Japan, Washington's important regional ally, would view with no less consternation any potential threat to stability in its neighbourhood. American air strikes in Syria last week have raised very valid concerns about their legitimacy under international law. But they also indicate that the Trump administration may be shifting politically from a populist-driven isolationism to more conventional interventionism. His latest observations on China point to a shift from open confrontation to a possible constructive engagement. Notable here, for instance, is a willingness to eschew the previous rhetoric on China as a currency manipulator. Against this emerging backdrop, a return to a reasoned and nuanced approach on North Korea would be a most positive development in these volatile times. That would, however, require a spectacular roll-back by Pyongyang of its current nuclear capability, which includes long-range missiles that can reach targets in the Pacific. As well as sustained cooperation between China and the U.S., it is time for cooler minds to weigh in – there is nothing to be gained by aggressively staring down adversaries.

Cross signals across the Himalayas

India must realise that China is no longer willing to remain a status quo power

M.K. NARAYANAN

The 14th Dalai Lama, Tenzin Gyatso, was in Arunachal Pradesh recently, which has greatly ruffled China's feathers. Any reference to Arunachal Pradesh ('Southern Tibet' as China prefers to call it), in context or out of context, has the effect of raising temperatures in Beijing. The prolonged stay of His Holiness in the Tawang Monastery was, hence, the straw that broke the camel's back.

The mild-mannered Dalai Lama spoke with unusual candour during his visit to Arunachal Pradesh, seeming to be at times even obliquely critical of China, something he had previously avoided. All these years, he had displayed remarkable restraint, despite constant Chinese provocations. On this occasion, his statements should, therefore, have come as a surprise to China.

Choice of words

Nothing that the Dalai Lama said during his visit can even be remotely viewed as accusatory of China, but the words he employed – "I've long forgiven China's Communist Government for occupying Tibet"; we support a 'One China policy', "all we want is the right to preserve our culture, language and identity"; "the 1.4 billion Chinese people have every right to know the reality (of Tibet)", "once they know the reality they will be able to judge", "until now there has been only one-sided, wrong information" – had the effect of a whiplash and was bound to irk China. What should have provoked the Chinese even more is that at one point, reacting to Chinese objections to his Arunachal Pradesh visit, the Dalai Lama said, "I am the messenger of ancient Indian thoughts and values. I thank the Government of India for the support."

So far, China's reactions have been on predictable lines, though perhaps more incendiary than in the past. Beijing has issued a series of warnings, viz., that the Dalai Lama's visit to Arunachal Pradesh would cause "deep damage" to Sino-Indian ties, that New Delhi would need to make 'a choice' in its dealings with the Tibetan spiritual leader, that India had breached its commitment on the Tibet issue, taking particular umbrage at the Arunachal Pradesh Chief Minister's statement that the State did not share its borders with China but with Tibet and asking India to stick to its 'political pledges' and not hurt China-India relations.

Official démarches were couched in still more intemperate language. Some were in the nature of a threat, that the visit would escalate disputes in the border area, fuel tensions between the two countries, impinge on China's major concerns and core interests, territory and sovereignty, and thus damage India-China relations. Chinese official media and the Chinese Communist Party, in turn, stepped up pressure on the Chinese government to take action against India. The *China Daily* observed that "if New Delhi chooses to play dirty... Beijing should not hesitate to answer blows with blows". Chinese official spokespersons have rounded off this kind of diatribe by affirming that issues concerning Tibet have a bearing on China's "core interests".

China's verbal outbursts on this occasion do not conform to type, even where they relate to the Dalai Lama. For China, a visit by the Dalai Lama to Arunachal Pradesh, including a sojourn in the Tawang Monastery, one of the holiest of Tibetan Buddhism, is no ordinary matter. As it is, China has certain deep-seated concerns about increasing political instability in areas such as Tibet, apart from the happenings in Xinjiang as well as other security problems. The Dalai Lama's visit to Tawang at this time could, hence, look like a provocation.

GETTY IMAGES/ISTOCKPHOTO

Very recently, China had floated the idea of an Integrated National Security Concept, reflecting the extent of its prevailing insecurities. This has introduced certain 'red-lines', that China would never compromise its legitimate rights and interests, or sacrifice its "core national interests". On more than one occasion during the current exchanges, Chinese Foreign Ministry spokespersons had referred to issues concerning Tibet (and Southern Tibet) as having a direct bearing on China's "core interests".

Current China-India exchanges, hence, need to be examined from the purview of both international relations as well as the domestic situation prevailing in China. It must not be overlooked that the that Sino-Indian conflict of 1962 occurred soon after China's disastrous Great Leap Forward, in which a large number of Chinese perished, and the Dalai Lama fleeing Tibet and taking sanctuary in India. In 1962, Beijing had masked its intentions skilfully, while India, in the absence of any major overt action by China, was lulled into a false sense of complacency.

We need to ensure that there is no repetition of lack of vigil on our part. In 1959-60, the Dalai Lama had not quite attained the same international stature that he currently enjoys as the most revered symbol of Tibetan Buddhism. Yet, China was even then willing to risk a conflict with India, then the undisputed leader of the Non-Aligned Movement, angered by the grant of asylum to the Dalai Lama. The stakes for China are, if anything, greater today, as it seeks to emerge as a global leader. China would like to ensure that its 'rear' remains quiescent, rather than troubled, so as to devote its energies to attain its goals.

The Tawang factor

Indian commentators keep referring from time to time to the fact that China had shifted its stand on Tawang. This may be true, but there is little doubt about the centrality of Tawang (the birth place of the sixth Dalai Lama) in China's scheme of things for this region. During several rounds of discussions on the Sino-Indian border, my counterpart as the Chinese Special Representative for boundary talks, Dai Bingguo, made it amply clear to me that Tawang was non-negotiable. In 2005, China signed an Agreement on the Political Parameters and Guiding Principles for the Settlement of the India-China Boundary Question (Dai Bingguo and I were the signatories) which stipulated that areas with settled populations would not be affected in any exchange. Even before the ink was dry, China began to dissimulate as far as Tawang was concerned, even though Tawang is the most 'Indianised' place in the entire Northeast. All this leaves little scope for compromise with regard to areas like Tawang.

Understanding the way the Chinese mind works is important. It tends to be eclectic, contextual and relational, leaning towards systemic content and history. Chinese thinking tends to be convoluted and its methodology obtuse. Chinese assertiveness is often rooted in strategic insecurity and a perceived sensitivity to domestic tensions. China constantly flaunts its 'exceptionalism' and its 'uniqueness'. Chinese exceptionalism tends today to be largely historical and revivalist. A combination of Mao's utopianism and Deng Xiaoping's realism has left China in a kind of philosophical vacuum. It has led to an excess of nationalism and nationalistic fervour, making China's objectives clear-cut.

China's policymakers are cautious by temperament but are known to take risks. They are skilled at morphing the gains favoured by each past civilisation and adjusting these to modern conditions. They prefer attrition to forceful intervention, a protracted campaign to gain a relative advantage.

Currently, China has jettisoned the Guiding Principles laid down by Deng Xiaoping, "coolly observe..., hide your capacities, bide your time". Buoyed by its military muscle, and with a defence budget of $151.5 billion (2017) which is much larger than that of all other nations with the exception of the U.S., China is no longer willing to remain a status quo power, or play by existing rules governing the international order. India must realise this, and avoid being caught unawares.

The OBOR outlier

As it is, China is constantly seeking ways to isolate India. It is engaged in building advantageous power relations, acquiring bases and strengthening ties with countries across Asia, Africa and beyond. China's latest One Belt, One Road (OBOR) initiative signifies its new outreach, extending from the eastern extremity of Asia to Europe – the China-Pakistan Economic Corridor represents its most significant strategic aspect – and has the backing of most countries in the region. India is an outlier in this respect, and perhaps the only major Asian nation that has not yet endorsed the concept. If as China anticipates that OBOR has the potential to alter the status quo across the region with most nations accepting a long-term commitment to China, India could find itself friendless in Asia and beyond.

M.K. Narayanan is a former National Security Adviser and a former Governor of West Bengal

Doctors under siege

Workplace violence against health-care workers can only be checked in the backdrop of improved infrastructure

GEORGE THOMAS & J. AMALORPAVANATHAN

There have been numerous media reports of instances of violence against doctors and health-care institutions across India. In most cases, the proximate cause is the death of a patient. All reports suggest that most of these patients could not have been saved with the infrastructure available in the institution, yet their deaths have been seen as a case of neglect by medical personnel. Doctors have responded to these attacks with anger and anguish, by striking work, demanding more security and even taking to social media with messages about how the profession is seen as an easy target.

Growing violence

Violence against doctors is not new. The World Health Organisation published guidelines on handling workplace violence in 2002. However, the incidence and intensity of violence against medical professionals in India is on the rise.

It is important to reflect on how the medical profession – always held in respect in our society – has come to such a sorry pass where health-care workers need protection from the very people they are meant to take care of. It appears that these attacks are symptomatic of a larger malaise, manifested in a general increase in violence as a method of demonstrating power, loss of faith in institutions, anger against perceived marginalisation, and lack of understanding of science and society. The state has failed to stand firm on the rule of law. Civil society has been complicit. Each group in our fractured society becomes vocal only when its interests are affected. Thus doctors, pillars of the establishment, have failed to ensure the security of the established society by standing up against violence as a method of settling differences.

The present health-care system in India has inequity built in. Patients can see it. The demand by medical professionals for better pay is seen as selfish. It has to be coupled with demands for patient care such as better access, better facilities, and more personnel so that individual attention can be given. At present, most doctors are not advocates for patients. They play along with governments unwilling to spend on health care and accept the prevalent view that providing public sector health care is a favour and not a right. Doctors are seen as a part of the power structure. When they are attacked, public support and empathy is lacking.

REUTERS

A divide

Also, tremendous technological advances in medicine are not available to the majority in India. Increasing privatisation, corporatisation and commercialisation of medical care have ensured that many procedures cannot be accessed by the general public. Examples of the privileged having access to extremely expensive care in the private sector, though many of these interventions are usually futile, propagates the idea that modern medicine can salvage even the most critically ill provided enough money is spent.

There is also a failure to establish and propagate a good understanding of modern science in India. Such understanding would encompass the knowledge that although medicine in the modern world has greatly improved the chances of survival in many serious conditions, there are also many situations in which no intervention will succeed. Otherwise, there remains a suspicion that all was not done to save the patient and that much more would have been done had the patient paid more for an expensive hospital and doctor. The frustration against their own position in society is vented by attacking the doctor and the facility.

A way out

What can be done? An immediate step is to ensure exemplary action against violence as a means of settling issues. More long-term measures require vastly improved health infrastructure, fewer patients per doctor in line with international norms so that care can not only be given but seen to be given.

Doctors should participate in spreading understanding of science and society. At present, the public often does not understand the deeper structural problems underlying the apparent failures of the doctors. Medical practitioners should help highlight these.

Peoples' committees in hospitals will be a welcome step. There must be a constant audit of the working hours of medical personnel and the fatigued doctor should not be left in the front line to deal with an emotionally charged public. Social workers in crucial departments such as accident and emergency wards to handle anxious crowds will certainly reduce the stress of already overburdened postgraduates and house surgeons.

Civil society and the medical community must together to demand better health care for our population. We cannot falter now.

George Thomas is an orthopaedic surgeon at St. Isabel's Hospital, Chennai and J. Amalorpavanathan is former Director, Department of Vascular Surgery, Madras Medical College, Chennai

LETTERS TO THE EDITOR

Letters emailed to letters@thehindu.co.in must carry the full postal address and the full name or the name with initials.

The decline of AAP

Caught between the corrupt Congress regime and the purported communal intentions of the BJP, the formation of the Aam Aadmi Party provided the hapless common man a glimmer of hope. It was looked upon as a party with a difference and which upheld ethical values in public life, boosted by the presence of professionals who were joining politics after sacrificing their highly paid jobs.
But power seems to have got the better of the AAP, which had promised good governance and values. Dogged by one controversy or the other, it has taken the easier way out by hitting out at those who criticise it in order to cover up its misdeeds. You can't fulfil the aspirations of people by merely indulging in rhetoric. Its bizarre reaction when dengue threatened Delhi is an example. Given this trend, it is no surprise that people are losing faith in the party. ("BJP extends winning streak in byelections", April 14).

V. SUBRAMANIAN,
Chennai

Rise of vigilantism

The death of a man at the hands of "cow vigilantes" in Rajasthan's Alwar district is not an isolated event (Editorial - "Barbarism unlimited", April 7). It is the result of continuous hate propaganda that is being propagated across the country. It is also an attempt to isolate a particular community in order to serve the vested interests of a few. There is an attempt to turn people into a mindless and faceless mob. What is the meaning of all the talk about development and economic growth when we cannot ensure the security and safety of a citizen? We must rein in the temptation to label all these as sporadic incidents. Today it is about Muslims. Tomorrow it could be about Dalits, Christians or for that matter, anyone with a different point of view. There is an attempt to inject this poisonous venom of hatred in all of us. It is not a fight for any community but about the fight to save the idea of India.

GAURAV VATS,
Patna

■ The activities of self-proclaimed cow vigilantes are disturbing the social order. The majority of the people involved in the trade related to cattle are Dalits and Muslims. Vigilantes are using the pretext of protecting cows to attack Dalits and Muslims and their actions are hurting livelihoods and the economy. These acts are growing so fast that it is becoming difficult to control their actions. It is time their activities are curbed before it leads to complete chaos.

KAMIL S.V.,
Andrott, Lakshadweep

The tree we love to hate

At last, the axe seems to have fallen on the *seemai karuvelam* (*Prosopis juliflora*), the firewood tree that is the woodcutter's favourite in Tamil Nadu, now orphaned by a High Court diktat and whose demise is being hastened by some politicians in Tamil Nadu who are spearheading a campaign for its eradication ("HC judges release book on ills of *seemai karuvelam*", April 14). It is said in our scriptures that no plant life, including weeds, is bestowed on our planet by nature without a purpose. If nothing, the species provides shade to living creatures. While passing through villages in Andhra Pradesh, I have seen poor mothers making cradles and swings for their children by tying their old saris on the branches of this tree. The sight of rural children playing a variety of rustic games under the canopy of these trees is a sight to watch. The tree demonstrates how to brave and survive the hot sun of tropical India. There are large tracts and forests of these trees providing cover to an otherwise parched land. While we are always good at hasty deforestation, we need to scientifically assess what the botanical worth of this species to the Indian subcontinent is and whether we are on the right side of nature when we start loving to hate it.

PUSHPA DORAI,
Nurani, Kerala

Discrediting judiciary

The manner in which Calcutta High Court judge, C.S. Karnan, has passed an order directing seven judges of the Supreme Court, including the Chief Justice of India, to appear before him on April 28 at his residence in Kolkata is baffling ("Karnan directs SC judges to appear before him", April 14). How can a learned and respected judge function in such a manner? Will it not encourage 'lawlessness'? The President of India should intervene immediately to remove him to save the prestige of the judiciary.

G. CHITTIBABU,
Madurai

MORE LETTERS ONLINE:
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CORRECTIONS & CLARIFICATIONS:

The name of the U.K. aircraft carrier is Prince of *Wales* and not Prince of *Whales* as mentioned in the penultimate paragraph of a report, "Rolls-Royce, DRDO to tie up" (April 14, 2017).

It is the policy of The Hindu to correct significant errors as soon as possible. Please specify the edition (place of publication), date and page. The Readers' Editor's office can be contacted by Telephone: +91-44-28418297/28576300 (11 a.m. to 5 p.m., Monday to Friday); Fax: +91-44-28552963; E-mail:readerseditor@thehindu.co.in; Mail: Readers' Editor, The Hindu, Kasturi Buildings, 859 & 860 Anna Salai, Chennai 600 002, India.
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The interpretation of a malady

The poignant story of an Agra family, where six children have the Nalband mutation. **Jacob Koshy** reports on how a group of scientists linked it to a rare and crippling neurological disease

Deviant gene: "For more than 15 years, Nazir and Tabassum have watched six of their eight children debilitated by a malevolent neurological disease called megalencephalic leukoencephalopathy, which destroys neurons and wastes away muscles." The family at their home in Agra. (Below) Researchers at the Institute of Genomics and Integrative Biology lab in New Delhi where DNA samples are prepared for analysis. ▪ SANDEEP SAXENA

It's been two years since Mohammad Nazir, 44, petitioned the government that six of his children be euthanised. Nazir and his wife Tabassum's desperate plea to terminate the lives of their children was preceded by 15 agonising years of watching six of their eight children debilitated by a malevolent disease that destroys their neurons and steadily wastes away their muscles.

Suleim, 19, a once-frisky four-year-old, has legs that have shrivelled to the size of bamboo reeds and are locked into each other at the ankles. Head bloated at the temples and browning teeth, the muscles that control his jaw and throat are flaccid too, making speech impossible. "He understands everything," says Tabassum, 36. "Look Suleim, who's come to see...," she trails off, interrupted by a wail. That's Shoeb, his 16-year-old brother. He's lying on a bed in the courtyard and shares his brother's shrivelled legs though they aren't yet locked in.

Once propped up, Asim, 14, too can continue sitting against the wall. "He's the sharpest of all and can recite poetry and verses from the Koran," says Tabassum, with one eye out for Kasif, 11, who appears the most reticent and the only one of the boys with dark eyes unlike his siblings whose eyes are a light brown. The quivering limbs and the seizures – early signals of the onset of megalencephalic leukoencephalopathy, aka the neurological disease – have set in but so far he can stretch his limbs out and ease the weight of his body on his palms.

Because none of them can stand and there's no nurse, it's Tabassum who must attend to everything from taking them to the toilet, feeding and washing them (full-fledged baths are rare). When Nazir comes home for lunch, he helps them with physiotherapy. "Most days it's me alone... they are heavy. It's hard for me to lift them," says Tabassum, who says she's never left her house for a social function in more than a decade. Nazir was a daily-wage labourer until three years ago and now manages a sweet shop in Agra's central bazaar.

When he'd written that petition in the summer of 2015 it was, he says, because he had neither hope nor money anymore to spend on doctor visits, physiotherapy, acupuncturists and religious offerings. The petition worked, to the extent that local newspapers carried accounts of the family's predicament.

Earlier visits to hospitals in Agra and one to the All India Institute of Medical Sciences (AIIMS), Delhi, confirmed that the children suffered from a "rare disease", and treatment largely consisted of muscle relaxants and for controlling the seizures. "We couldn't understand our fate. Neither my wife's siblings nor mine had ever seen anything like this in our families," says Nazir. To Tabassum, the reason was simple. "My womb is cursed," she laments. But 200 km away, in Delhi, a group of geneticists read about the Nazir family online and realised that they were peering into a medical jigsaw puzzle.

Decoding the mysterious malady

Unravelling the mysteries of the DNA is the nucleus of research at the CSIR- Institute of Genomics and Integrative Biology (CSIR-IGIB). Nearly a decade ago, resident scientists Sridhar Sivasubbu, 44, and Vinod Scaria, 36, were part of a team that first sequenced the entire genome of an Indian. Six years after a consortium of European and American scientists had first cracked the blueprint of the human genome in 2003, the Indian genome sequencing project had isolated the DNA of a 52-year-old Jharkhand man and mapped the same. While the human genome provides the ultimate reference point of the location and sequence of genes that define humans, the promise of indigenous exercises – bragging rights apart – is to have a reference base of how genes in Indian communities vary from, say, African, West Asian or Caucasian genes and then study the extent of these variations in these genes to understand diseases.

A sequenced genome is like the innards of your computer made transparent. Every cell in the human body consists of strands of nucleic acid called DNA (deoxyribonucleic acid), which are chains of four kinds of molecular bricks or nucleotide bases. These bases form exclusive pairs with each other and their order determines how proteins are made. The creation and execution of every physiological process is determined by proteins functioning stably. The genome, as the bases, DNA and other hereditary molecules are collectively referred to, consists of around 3.1 billion base pairs and 20,000-odd protein-coding genes. Some changes in the base pair sequence, otherwise called mutations, could mean vital proteins are absent or formed in ways that are harmful to health.

> **In our conservative estimate, if you can prevent an infant with a rare genetic disorder from being born [through prenatal screening], that's ₹50-80 lakh saved over a lifetime.**
>
> SRIDHAR SIVASUBBU
> Resident scientist at the CSIR- Institute of Genomics and Integrative Biology

Over the years, several projects across the world have sequenced scores of genomes, and geneticists know the sequence of bases that make up a typical Caucasian, Indian or Chinese genome as well as the stretches of genes that make up skin colour, the size of your head, how many fingers you will have and whether you will be lactose-intolerant.

Genes are unevenly distributed in 46 clusters in the cell called chromosomes. We inherit half our chromosomes from each parent. When a sperm fertilises an egg, 22 of 23 chromosome pairs carry one copy of gene each and chance determines which of them is passed on.

While most diseases are caused by several genes going awry, some are the result of a single, aberrant one. When AIIMS professor and paediatric neurologist Sheffali Gulati, who specialises in the neurological disorders affecting children, saw Nazir's children, the symptoms appeared to fit a pattern of a rare class of genetic disorders called leukodystrophies. While there are several forms, leukodystrophies are marked by the brain gradually losing white matter. White matter helps the brain's cerebral cortex – the grey matter – communicate with one another and the rest of the body.

Zeroing in on Nalband mutation

The Nalband community, all Muslim, to which Nazir belongs, is about 5,000 strong, and spread across Uttar Pradesh, Haryana, Rajasthan and Pakistan. The name literally translates to 'makers of horse shoes' though today, a wide range of professions characterise the members of the community. One of Nazir's siblings is a local politician, another relative who lives nearby is an Unani doctor. Their father was a carpenter. Despite the internal social stratifications, the family is fairly endogamous. Nazir and Tabassum are first cousins and their siblings are married to each other too.

Shamsudheen K.V., 29, who works with Scaria and Sivasubbu at CSIR-IGIB, is the institute's point man for GUaRDIAN (Genomics for Understanding Rare Diseases India Alliance Network), which has about 100 clinicians spread across 30 centres across the country. In 2015, while still wrapping up his doctoral dissertation, Shamsudheen chanced upon Nazir's story online and got in touch with him through the newspaper that wrote about him. Around the same time, Human Welfare Foundation (HWF), a Delhi-based charity, also offered to aid Nazir. "We were appalled," says Muhammad Arif, a deputy director at HWF, "a man who's suffering to the extent of wanting his children dead and we were unable to do anything about it." Shamsudheen and Arif met and agreed to collaborate in rehabilitating the family and then arranging for the logistics and medical expenses at AIIMS.

That also marked Shamsudheen's two-year tryst with Agra where he would tag along with HWF workers and knock on several doors, give crash courses in genetics and cajole the residents of Nazir's neighbourhood for blood samples, from where DNA and the tapestry of genetic relatedness in the community could be fleshed out.

While DNA resides in slimy cells and must be extracted by concoctions of chemicals, isolating genes is largely about harnessing powerful computers and writing efficient algorithms to find out the common stretches of base pairs that are present in all who carry the disease but are absent in those free of it. The winnowing process, that can extend over weeks, is a laborious trial-and-error exercise.

Eventually, the CSIR-IGIB team found it. Tucked away on the MLC-1 gene on chromosome 21, the researchers informally call it the "Agra" or "Nalband" mutation. Usually when potential genes – that may be out of step from their normal variants by a single letter or an extra letter – are narrowed down, researchers must test out these combinations of base pairs either in lab-cultivated cells (to see if they indeed trigger awry cell growth) or in animal models such as zebrafish.

In the case of Nazir's family, there were multiple reasons why the 'Nalband mutation' was responsible for the disease. One, the gene, MLC-1, where the mutation was discovered, has previously been known to play a role in neurodegenerative disease. Second, all sick children in Nazir's, and three others in his extended family, had exactly the same mutation. "The odds of it not being responsible were infinitely small," says Shamsudheen. The results are in the process of being published in a journal.

Genes and the endogamy trap

Finding mutations isn't as important to the CSIR-IGIB as using this to tackle rare diseases. A July 2016 *Current Science* editorial notes that though precise statistics of rare disease were absent in India, extrapolating U.K. estimates of 1 in 20 implied that there were 60 million Indians afflicted with such conditions. Sitting in the CSIR-IGIB lab, Sivasubbu says, "In our conservative estimate, if you can prevent an infant with a rare genetic disorder from being born [through prenatal screening], that's ₹50-80 lakh saved over a lifetime." A prenatal screening is useful because a child with two mutated copies of the gene will certainly manifest the disease, according to Scaria. With at least 25,000 endogamous communities estimated, the team has so far worked on 500 families and hopes to find at least 1,000 within the next year.

Disease, as the GUaRDIAN's quest over the years has revealed, shows that economic liberalisation, migration and digitisation have only glacially changed the practices of several thousands of communities that strictly practise endogamy. On the other hand, it also shows how several Indian communities – antipodes in religion and cuisine – are frequently closely connected to Turks, Iranians, Saudi Arabians and Egyptians in the mutations that they inherit and bequeath. According to Scaria, a report from Iran seemed to suggest that the "Agra mutation" may have been reported in a child in that country. Were you to ask Tabassum or Nazir if they've encountered anyone in their extended family expressing the same symptoms as their children, they emphatically deny it.

> **My womb is cursed.**
>
> TABASSUM
> Mother of the children

"But that's not what the family tree says," says Scaria, pointing to a PowerPoint slide that shows the genetic relationships among 82 members of the community who live within half a kilometre of Nazir's family. "This is Nazir's uncle and it shows that there's a person here with the disease... and here and here... three more," says Shamsudheen, pointing to a flow chart with shaded circles that indicated members of the family with and without the disease and their relationships. "So far we've seen that 28% of the community are carriers of the disease gene."

Neither Dr. Gulati nor the researchers at CSIR-IGIB have a plausible explanation for why Nazir specifically is particularly unlucky. To Scaria, it only brings to fore the role of chance in genetics. That Nazir has had several children – all within two years of each other and not enough time to be aware of the disease's progression that begins only after they are toddlers – partially explains the odds.

However it is precisely for situations like this that genetic tests – still a fairly exotic proposition and accessible only to a fraction of Indians who can afford the necessary ₹10,000-20,000 for each such test – can be relevant to India.

The importance of genetic tests

The cost of finding a mutation – in the case of Nazir's family, the genes of two affected children were compared to unaffected siblings (here, the oldest son Khubeb, 21, who assists his father at the sweet shop) – including the man-hours and the logistics would be around ₹2,00,000, according to Sivasubbu, but once a specific mutation is known you can offer a diagnostic test that, even commercially, costs about ₹1,000. Such relatively inexpensive tests can be used to look for specific genes in an entire community and then expecting at-risk couples can be informed by genetic counsellors. "You further have the option of prenatal testing now, where the unborn child's genes can be tested," he says.

The researchers, as part of their investigation, have encountered clusters of villages in Maharashtra where hundreds of people – all bearing the same surname – have a disease that strikes men after 35 and makes them immobile. They've had people writing to them from communities in Gujarat, Andhra Pradesh where family members speak of diseases – such as flaking skin that peels off and makes wearing most clothes impossible or skins that resemble the scales of a fish – that have been plaguing them for generations. As part of their "odysseys", as Sivasubbu describes them, they've attended weddings, where the chances of meeting several extended members of a clan are highest and – away from the view of guests – collected blood samples to ferret potential mutations. In most cases, there are no cures and even the world over, pharma companies aren't incentivised to spend billions of research dollars on them because the patients are too few and the disease too challenging. In other cases, once a genetic mutation is identified, it gives doctors the confidence to recommend drugs and medicines that they would otherwise not.

> **We were appalled. A man who's suffering to the extent of wanting his children dead and we were unable to do anything about it.**
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> MUHAMMAD ARIF
> Deputy director, Human Welfare Foundation

After tracing an errant gene in another family, it emerged that administering a course of vitamin E dramatically improved patients' quality of life, Sivasubbu recounts. To further their project, the GUaRDIAN programme – that's funded by the Council of Scientific and Industrial Research – aims to have every medical college in every State with the capacity to conduct genetic screening. "In 2008, the dream of sequencing a genome was if we can we offer personalised genome testing and today, given that these technologies are affordable and a service and discovery arm is in place, it seems possible," says Sivasubbu.

Between hope and fate

Possibility is what Nazir sees today. After the 11-year-old Kasif, Mohammed has had twins – Teeba and Aban – who are eight years old and both have had seizures and the falls and loss of balance that mark the inception of the disease. Even so, they are able to go to school and seem to be much better than their older siblings were at the same age, according to their father. Because the genetic basis of their disease is apparent, they've been put on prophylactics to protect against the seizures and improve their muscle tone. "This will improve the quality of life but they too will eventually manifest the conditions," says Shamsudheen, who is a regular visitor to the family, "and so far there's no therapy or medicine even in early trials that offers a cure."

And then there's Ulfath, the youngest and a girl of 6. Like her eldest brother, Khubeb, she carries only a single copy of the gene and is therefore free of the disease. Khubeb is already betrothed to his cousin, in line with practices of his family. The bride-to-be, says Shamsudheen, is a carrier. To be sick or healthy, says Nazir, is "the will of Allah".