

News from here and there

Innovative efforts in organizing epilepsy care during the Covid-19 pandemic

The devastating effect of the Covid-19 pandemic is being felt globally. In addition to the direct health effects of Covid-19, other administrative measures such as lockdown and restricted mobility have seriously affected care of patients with other diseases. The pioneering efforts of Dr Bhuma Vengamma in organizing community-level care of epilepsy by conducting a monthly 'free epilepsy camp' that has been going on uninterrupted since February 1999 incurring a cumulative expenditure of over ₹2.25 crore has been reported in the *Journal* a decade ago (Epilepsy care at community level: A ray of hope. *Natl Med J India* 2011;24:381). In order to get over the Covid-19-related logistic problems that had hampered patients' travel, physically attending the camp and collecting the monthly prescription of free anti-epileptic drugs, Dr Bhuma Vengamma (presently Director-cum Vice-Chancellor and Professor [Senior Grade], Department of Neurology, Sri Venkateswara Institute of Medical Sciences [SVIMS], Tirupati and also president, Indian Epilepsy Association [IEA]) designed an innovative approach to organize epilepsy care at the community level to overcome Covid-19-related restrictions. In this marathon effort, Dr Vengamma held discussions with the IEA, Tirupati branch and the Collectors of Chittoor, Kadapa and Nellore districts of Andhra Pradesh (from where the patients came), to utilize the services of health infrastructure through the District Medical and Health Officers (DM&HOs). A 24x7 mobile telephone helpline was set up and handled by a dedicated team constituted by the faculty of neurology and residents pursuing DM (Neurology), nursing college faculty, nursing students and members of IEA, Tirupati chapter. All patients (more than 700 in number) were contacted telephonically regarding their health status. Patient-wise medication boxes that contained the monthly medications were prepared and were packed based on location. The address of the patients and their availability was rechecked and confirmed telephonically. The consignment of patient-wise

boxes was transported to the primary health centre (PHC) that was nearest to the patients' home. The existing district health infrastructure, including PHC medical officers, accredited social health activist (ASHA) workers and health volunteers, was used for delivery of the patient-wise monthly treatment box to the doorstep of the patient (Fig. 1) so that anti-epileptic treatment would continue uninterrupted. The successful receipt of the monthly treatment box was verified over a phone call. Thus, all patients received uninterrupted epilepsy treatment throughout the first-wave (in 2020) and continued to receive treatment during the second-wave (in 2021) of Covid-19 and its aftermath.

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Complete sequence of the human genome

In a 27 May 2021 preprint titled 'The complete sequence of a human genome' (Nurk *et al.* Preprint at bioRxiv <https://doi.org/10.1101/2021.05.26.445798>), researchers from the Telomere-to-Telomere (T2T) Consortium have reported sequencing of the remaining 8% from the 2013 genome sequence. Till date, the 2013 genome sequence was used as the reference (GRCh38.p13).

The International Human Genome Sequencing Consortium and the biotechnology company, Celera Genomics, had first published the initial draft of the human genome in 2001. This sequence was not complete, since around 15% was missing. Due to the prevailing technological limitations, researchers were not able to identify how particular stretches of DNA fitted with each other. This was so particularly for those stretches with many repeating base pairs.

Much of the puzzle was deciphered over the past two decades and the euchromatic fraction of the genome was effectually analysed. However, the 2013 human genome still lacked 8% of the full sequence. These included the heterochromatin and most of the other complex regions whose sequencing was either flawed or unfinished.

The T2T Consortium has now accomplished the most accurate 3.055 billion base pair (bp) sequence of a human genome. This has been dubbed the T2T-CHM13. It introduces almost 200 million bp of original sequence with 2226 paralogous gene copies. Of these 115 are believed to be important for protein coding. The T2T-CHM13 reference includes all 22 autosomes and chromosome X. All centromeric satellite arrays and the short arms of the five acrocentric chromosomes (Chr13, Chr14, Chr15, Chr21, and Chr22) are included.

The researchers used a cell line that was derived from a complete hydatidiform mole (CHM), rather than using DNA from a living person. The hydatidiform mole cell line consists of two X chromosomes, both of which are derived from the father (sperm). CHM genomes are homozygous for a single set of alleles. This removes the confusing effect of heterozygous variation. CHM 13 was selected for its established 46, XX karyotype when compared to other CHMs.

Multiple sequencing technologies were used for sequencing



FIG 1. Preparing patient-wise monthly anti-epileptic treatment boxes, transporting them with the help of the district health infrastructure and ensuring delivery of the medicines at the patients' doorstep

the T2T genome. These include the 30× PacBio circular consensus sequencing, the 100× Illumina PCR-Free sequencing, the 120× Oxford Nanopore ultra-long read sequencing, the 70× Illumina/Arma Genomics Hi-C, Strand-seq and BioNano optical maps.

Traditionally, conventional sequencing methods read only a few hundred bp of DNA at a time. Researchers then need to reconstruct these stretches like the pieces of a puzzle. With the new technology, the puzzle pieces can be put together easily, since there are more overlapping sequences.

The T2T-CHM13 genome has no gaps, but it is estimated that around 0.3% of the genome may contain errors wherein quality checks are problematic. Since the CHM mole lacked the Y chromosome, researchers still need to sequence one.

The T2T Consortium has associated with the Human Pangenome Reference Consortium to sequence over 300 human genomes globally over the next 3 years. The T2T-CHM13 genome will be used as a reference. Such a collection of first-rate, complete reference haplotypes will help us understand the multiplicity of human genetic variation.

Dr Ashwin Dalal (Head, Diagnostics Division, Centre for DNA Fingerprinting and Diagnostics, Hyderabad, [Ministry of Science and Technology, Government of India]) told this correspondent, 'I fully agree there is a need for multiple reference genomes from each ethnicity so that proper analysis of genome sequencing can be achieved. This consortium has achieved what was thought impossible at a point of time due to the repetitive nature of the DNA especially in heterochromatin and short arms of acrocentric chromosomes. Sequencing of multiple T2T genomes will broaden the horizons of application of genomics to healthcare and other fields.'

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Kirigami, a 7th century Japanese paper-cutting art acts as a template for development of new drug delivery stent for the gastrointestinal tract

Kirigami, the Japanese art form associated with paper cutting, folding and handmade pop-up cards has its roots in the Japanese words 'kiru': to cut, and 'gami': paper and its origin in 'jian zhi', the original Chinese papercutting art that appeared in 4th and 5th century AD, two centuries after the invention of paper in China.

Engineers at Massachusetts Institute of Technology, Boston, Massachusetts, USA (MIT) have drawn inspiration from this 7th century Japanese art of kirigami to design and develop three-dimensional stents that can act as drug-delivery systems to hollow tubular organs such as the gastrointestinal and respiratory tracts, hepatobiliary and pancreatic ductal pathways and blood vessels. The stents have an inner core made of silicone-based rubber and an outer plastic coating etched with needles that pop up when the tube is stretched. Drug-containing microparticles fixed onto these needle points are deployed as the stent is stretched into position and act as extended drug delivery systems over time, even after the stent has been removed. The stents are designed to have flexible shapes (flat- and three-dimensional) and the kirigami needles attached are devised to have personalized sizes and shapes to ensure penetration across tissues of varying thickness. By

adjusting the architecture, as well as the thickness of the plastic sheet, researchers can control how deep the needles penetrate into the tissue.

The shape of the kirigami-inspired stents was engineered to mimic scales seen on invertebrates such as snakes and sharks. The needles deployed when the stent was in position were tested in *in vitro* and *in vivo* experiments on porcine oesophageal submucosa, using micro-computerized tomography to ensure the wall of the oesophagus was not perforated by the needles. Subsequent histopathological evaluation was used to confirm restriction of the needles to above the muscularis propria.

Currently, the stent is being studied as a treatment modality for inflammatory bowel disease and eosinophilic oesophagitis. Initial trials have used sustained release budesonide for about one week. The use of stents to open obstructed lumens has previously been used with varying degrees of success in the gastrointestinal, respiratory, vascular and intracranial pathways. However, those stents were unable to release medications in a time-dependent manner. Kirigami-inspired stents, by virtue of their architectural design, can act as scaffolds as well as drug delivery devices, across a predetermined interval of time.

The use of kirigami to create 'buckling scaffolds' is already under investigation in the development of anti-skid soles for footwear. It is also being used to create dynamic meta-surfaces which are used as building blocks in the creation of robots, microelectronics and nanostructures.

Sahab Babae, an MIT research scientist was lead author of the paper while Giovanni Traverso (Assistant Professor of Mechanical Engineering at MIT, and a gastroenterologist at Brigham and Women's Hospital, Boston, USA) was senior author of the study. The study was published as a letter to the editor in *Nature Materials* in its June 2021 issue (Kirigami-inspired stents for sustained local delivery of therapeutics. *Nature Materials* 2021. DOI: 10.1038/s41563-021-01031-1, www.nature.com/articles/s41563-021-01031-1)

Noted former advertising professional and lateral thinker Abhijit Awasthi (co-founder, SIDEWAYS Consulting, Mumbai) emailed this correspondent: 'Similar to the concept of cross-pollination where the transfer of pollen from one flower to another leads to the creation of a new type of plant, thereby allowing for diversity in the species, connecting and combining concepts that on the surface may seem unrelated can give birth to an exciting mix of cross-genre ideas, resulting in a paradigm shift in thought patterns, and resulting in solutions that can be deemed truly innovative. Invention of The Slinky, one of the world's most successful toys by naval engineer Richard James, innovative research into trouser materials to develop Velcro by Swiss engineer Georges de Mestral, and the extrapolation of experience gained in an accident when a Canon engineer left a hot iron on his ink pen, leading to the concept of Inkjet printers, are all examples of such ingenuity.'

MAHARRA HUSSAIN, *United Arab Emirates*

Twist in medical education rule will hit those who have done an MSc, PhD

The National Medical Commission's (NMC) recent Teacher Eligibility and Qualification Guidelines have drastically reduced the number of MSc/PhD holders who can be hired as faculty for non-clinical subjects in medical colleges.

These changes are expected to affect not only the thousands of such degree holders serving as faculty in medical colleges, but also many more aspiring MSc/PhD students of anatomy, physiology, microbiology, biochemistry and pharmacology.

A severe scarcity of MBBS/MD faculty in the 1960s resulted in the appointment of MSc/PhD holders as faculty in medical colleges. Subsequent guidelines from the Medical Council of India (MCI), NMC's predecessor, permitted the appointment of MSc/PhD holders in the non-clinical specialties: anatomy, physiology, microbiology, biochemistry and pharmacology. The percentage of staff members was 50% for biochemistry and 30% for the others.

It is well-known that there is a paucity of faculty in the non-clinical specialties notwithstanding the fact that MD seats have been increased in these subjects. It is also clear that many MBBS graduates prefer higher studies in the clinical subjects.

The NMC has halved the permissible MSc/PhD faculty strength in anatomy, physiology and biochemistry, while

pharmacology and microbiology have been left completely bereft. The NMC subsequently clarified that this will apply to new medical colleges starting from 2021–22 onwards. The guidelines will also apply to the existing colleges that increase their number of MBBS seats. Additionally, all new appointments, whether in existing or new medical colleges, need to adhere to these norms.

It is all too likely that many MSc/PhD faculties on a tenure/contract basis will be affected. Their contracts may not be renewed, promotions will be denied, and many may become jobless. Also, the fate of over a thousand students studying the 3-year medical MSc courses in over 35 medical colleges across the country will be jeopardized.

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Conflicts of interest: The author has a medical MSc/PhD degree

The National Medical Journal of India invites contributions to the ‘**News from here and there**’ section. We are particularly interested in getting newswriters from the north and northeast regions of India as well as from other countries.

By news, we refer to anything that might have happened in your region which will impact on the practice of medicine or will be of interest to physicians in India. The emphasis of the news items in this column, which are usually of 200–450 words, is on factual reporting. Comments and personal opinions should be kept to a minimum, if at all. Interested correspondents should contact SANJAY A. PAI at sanjayapai@gmail.com or nmji@nmji.in