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Indian Medical Parliamentarians' Forum
Newsletter

Vol. 7, No. 3 **Winter Session Issue** **November-December 2021**

On behalf of the IMPF, we are pleased to present the Winter Session, 2021 issue of the IMPF Newsletter.

IMPF calls for stringent implementation of public health and social protection measures as COVID-19 cases increased across the country. A third wave of the pandemic is imminent sooner than later. Although every COVID-19 case is not an Omicron infection, Omicron variant should not be dismissed as 'mild'. As WHO has repeatedly stated, Omicron is highly infectious variant. Other variants, including Delta, Deltacron (reportedly) are also circulating globally, which, as we know cause severe infections and deaths.

It is important to protect ourself and others around by taking appropriate COVID protocols and precautions. Wearing well-fitting masks and avoiding big gatherings, along with taking other measures remain critical.

EMERGENCY

Coronavirus disease (COVID-19) Pandemic

India is taking all necessary steps to ensure that we are prepared well to face the challenge and threat posed by the pandemic. Scaling up vaccination coverage is another key preventive measure for COVID-19. India has crossed admirable milestones in its vaccination drive. Besides the roll-out of the teen vaccination, India has begun the vaccination of frontline workers and vulnerable elderly people with precautionary and booster doses as well.

Each case of COVID-19 positive is a cause of concern. IMPF is committed to bringing the most pressing public health issues before the policy makers and leaders, thereby addressing the concerns and improving the health sector.

We express our gratitude to all contributors who have made this newsletter very relevant and informative for parliamentarians across parties.

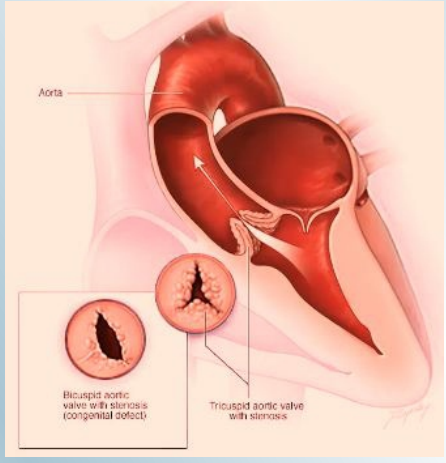
Dr. Rajdeep Roy &
Dr. DNV Senthilkumar. S.
Joint-Convenors

Dr. Kirit Premjibhai Solanki
Chairperson

At a glance:

Medical Advancements in Cardiovascular Diseases in India: Where Do We Go from Here?

A large population in India suffers from heart valvular diseases, making it a critical disease affecting citizens. Timely interventions to improve quality of medical care and increased focus on prevention are some of the reasons why people live longer. While degenerative heart valve diseases mostly affect older people, developing countries such as ours witness the prevalence of rheumatic heart valve disease mainly affecting the younger population.



There were some key developments that have pushed the boundaries of medical technologies to deliver better and safer patient outcomes over the course of the past six decades. Pioneering work in the field of heart valve replacement started in the early 1950s with the first major revolution in 1960s.Mechanical valves were introduced to replace the natural valves in the human heart and treat valvular heart disease. However, one of the inherent limitations to this technology included requiring patients to be on life-long blood thinners.

A better solution was proposed in 1970s with the development of biological tissue valves using either porcine (pig) or bovine (ox) pericardium, which allowed for patients to lead a better quality of life. On the flip side, tissue valves presented the limitation of degeneration which would require repeat surgery. While some of the earliest tissue valves boasted of 18+ years of longevity in patients over the age of 60,the newer tissue valves exhibit the evidence of upto 30 years longevity among patients more than 60 years. With the exception of a population subset that absolutely needed to lead an active lifestyle (e.g., women of childbearing age, sportspeople, etc.), most patients under the age of 60 were still provided mechanical valves as a preferred option, since the rate of degeneration of tissue valves was faster in these patients.

Over time, multiple companies have worked to improve tissue treatment technologies. Advancements have been seen in anti-calcification treatments, with some latest developments also permitting dry storage of tissue valves inevitably improving the life of the valve and reducing the need for repeat surgeries.

Besides improvements in tissue durability, heart valve replacements have also benefited from advances in surgical approaches. Increased adoption of minimal invasive cardiac surgery across India is also indicative of how increasingly, patients are benefiting from faster recovery and reduced post-operative risks.

The advent of transcatheter valve replacement as an alternate to surgical intervention in severe aortic stenosis patients is the most recent revolution. Transcatheter aortic valve implantation, or TAVI/TAVR for short, does not require open-heart surgery. Instead, a small incision in the groin area is used to insert a tube (catheter) into the artery and then to the heart, or directly into the left ventricle. The replacement valve is passed through the catheter to the heart, then expanded within the faulty valve. TAVI/TAVR reduces risk factors such as the post-operative complications, length of hospital stays, re-hospitalisation and recovery period, thereby improving quality of life.

Various trials over last few years have proved instrumental in changing ESC and ACC guidelines and making TAVI as a preferred treatment method for native calcific aortic stenos is at any or all levels of surgical risk, for open heart surgery in elderly patients. TAVI/TAVR is also the preferred means of treatment for symptomatic heart disease due to a failing aortic bioprosthetic valve or a failing mitral surgical bioprosthetic valve (with Balloon Expandable Transcatheter Heart Valve) which are judged by a heart team to be at high or greater risk for open surgical therapy.

- Dr. Kirit Premjibhai Solanki,
Member of Parliament

Need for Compulsory License for TB Drugs in India

In 2020, India had notified 18,05,670 cases of Tuberculosis (TB), which accounts for 26 per cent of total global TB burden. The fight against ending TB by ensuring timely access to essential drugs is a continued concern. Yet, India is not utilising the available tools including the use of TRIPS flexibilities such as the Compulsory License (CL) to ensure increased access to TB drugs.

Multi drug-resistant TB (DR-TB) and extreme drug resistant TB (XDR-TB) are severe forms of TB where the patient is resistant to more than two drugs, limiting the treatment options available to them. The treatment for MDR-TB and XDR-TB, comprising injectables and drugs with severe side-effects, has traditionally been very painful. The World Health Organisation (WHO) recommends an all-oral treatment regimen for DR-TB, a recommendation also adopted by the National Tuberculosis Elimination Programme (NTEP) in India. The drug called Bedaquiline forms the backbone of the all-oral regimen recommended for MDR-TB. Further, a combination of Bedaquiline with another drug called Delamanid is considered a salvage regimen for those affected by XDR-TB. Delamanid is also important as it acts as a preferred replacement of injectable agent for children affected by MDR-TB or XDR-TB.

India reported 49,679 persons affected by MDR-TB, just in 2020. As per recommendation, all these notified persons should have been initiated on a Bedaquiline-containing regimen. However, the India TB Report 2021 indicated that only 8434 persons were put on an all-oral regimen. In the same year, of the total reported 1232 XDR-TB cases, only 349 were put on Delamanid-containing regimen in the country.

Bedaquiline and Delamanid are protected by patents held by Janssen Pharmaceutica N.V. and Otsuka Pharmaceuticals Co., respectively, in India. The procurement of Bedaquiline and Delamanid for NTEP, mostly small in quantity, has been predominantly through donations from the patentee. The NTEP has also been procuring these drugs through the Global Fund.

While Bedaquiline is priced at about INR 26,600 for a six-month course per patient, Delamanid is priced at about 91,414 for the same duration. Pertinently these drugs are available only through the NTEP and cannot be purchased in the private market. However, the procurement appears to be affected with lack of response to call for tenders made by the government. It doesn't help that third parties

cannot submit tenders, due to the risk of patent infringement. Reportedly, requests by third parties to Janssen Pharmaceutica N.V. for manufacturing license for Bedaquiline were not been accepted by Janssen. Similarly, Otsuka has granted a license to Mylan in India, whose terms of engagement and the capacity to cater to the demand for Delamanid is unclear. It is not even clear whether the NTEP has been able to procure Delamanid for 2021.

A TB survivor and Jan Swasthya Abhiyan (JSA) Mumbai filed a petition in early 2021, before the High Court of Bombay seekinga direction to the central government to issue CL on these drugs. The Court directed the Department of Promotion of Industry and Internal Trade (DPIIT) to consider the representations of the petitioners regarding issuance of the CL. However, the DPIIT rejected the request. It stated that the Ministry of Health and Family Welfare (MoHFW) indicated that there is no TB related emergency. The representation was not even referred to the Committee set up under the MoHFW for issuing CL for drugs in the country.

There is a serious situation of stock-outs and unavailability of Delamanid. While India is leading the fight at the WTO Council demanding a temporary waiver of intellectual property rights (IPRs) on COVID-19 technologies, it is refusing to use the TRIPS flexibilities like the CL to protect access to medicines and end TB in the country.

- Priyam Lizmary Cherian
Delhi based lawyer and a public health consultant

Hemodynamic Monitoring: Advancement in Healthcare

In high-risk patients, cardiac output (CO), which is the total output of oxygen-rich blood from the patient's heart, is an important indicator to estimate the amount of oxygen reaching the patient's organs and tissues. Hemodynamic monitoring helps detect hemodynamic changes, diagnose the underlying cause, and optimise oxygen delivery to the tissues of the patient. It helps optimise patient's hemodynamic status in perioperative patient management and critically ill patients in Intensive Care Units (ICUs). Furthermore, it helps evaluate the adequacy of therapeutic interventions such as appropriate volume administration or vasoactive medications.

Several markers and devices have been developed to aid the clinician assess volume status with the goal of optimising tissue oxygenation and organ perfusion. The first to be used was the Pulmonary Artery Catheter (PAC), introduced in the 1970s by Swan, Ganz and Forrester. It is still the gold standard in the clinical setting when compared to different methods of hemodynamic monitoring.

The last few decades have been characterised by a continuous evolution of hemodynamic monitoring techniques from intermittent to continuous and real-time measurements and from invasive towards a less invasive approach. Dynamic indices such as pulse pressure variation, stroke volume variation, and the real-time response of cardiac output to passive leg raising or to end-expiration occlusion, can be obtained and displayed. Even COVID treatment guidelines from WHO and MOHFW suggest monitoring of COVID -Sepsis patient using dynamic parameters.

Artificial intelligence, machine learning, big data, and predictive analytics are key words that infiltrate hemodynamic monitoring just as they do in any other technology-associated field of science. The October 2018 issue of the journal, 'Anesthesiology' was dedicated to this topic, summarising the first applications to the specialty

of hemodynamic monitoring. It states that *machine learning is used to analyse and model complex associations and relationship patterns between multiple variables that are otherwise occult to the human eye, are more simplistic vision interfaces such as patient data monitors or go beyond the limits of human understanding.*

Recent studies have shown strong associations between intraoperative hypotension like prolonged exposures below mean arterial pressure (MAP) thresholds of 65 mmHg increase risk of acute kidney injury (AKI) and myocardial injury. Hatib *et al.*, in the article published in same journal of Anesthesiology, describe the development of an algorithm to predict an upcoming hypotensive event (defined as a mean arterial pressure <65 mmHg). The algorithm subsequently developed—using several thousand data points—detects potential of hypotensive trending of a patient's MAP.

Multiple studies have shown that these technological developments:

- Achieve statistically significant reduction of hypotension when combined with a treatment protocol in noncardiac surgery vs. standard of care
- Demonstrate superior predictive abilities for hypotension than common hemodynamic parameters such as CO, stroke volume (SV), and changes in MAP.
- Have proven and reliable accuracy.

Hemodynamic monitoring is huge leap and has the potential to be a great supporting tool for clinicians to help manage critically ill patients.

- Dr. Rajdeep Roy
Member of Parliament

Comprehensive Response to COVID-19 Needs Meaningful Involvement of PLWNCDs

Universal Health Coverage (UHC) is pivoted on the principle of *"leaving no one behind"*. As the COVID-19 pandemic continues to ravage across the country, it has underscored the urgent need for an inclusive "people-centred" approach to healthcare, where the contours of healthcare delivery are shaped by the needs and priorities of the people, as key stakeholders and not merely as beneficiaries of the system.

Non-Communicable Diseases(NCDs), including cancers, cardiovascular diseases, chronic respiratory diseases, diabetes, mental health conditions and other chronic conditions, are the leading cause of death (63%annually) and disability (75% annually)in India. Apart from financial hardship and catastrophic expenditure (66% households based on outpatient and inpatient care), tackling NCDs also causes physical and mental stress to People Living with NCDs (PLWNCDs) living with one or more conditions and their care-providers.

Meaningful community participation is a best practice for achieving equitable healthcare. PLWNCDs have first-hand experience and expertise in navigating health systems (both

public and private), which can guide the process of strengthening the efficiency and outreach of services. They have had to bear the hardest brunt of the pandemic, given that their underlying conditions make them more vulnerable to severe COVID outcomes, and simultaneously continue to disrupt routine care and management of their conditions. As the healthcare system recalibrated to prioritise COVID mitigation, PLWNCDs have had to take ownership of self-care and management, reiterating their role as key stakeholders in effective NCD prevention and

management, not just as individuals and families, but as communities at-large.

While initiatives to recognise these voices in the country started from pre-pandemic days, these efforts garnered even more significance and momentum, as the nation continues to grapple with the pandemic. One such significant effort towards meaningful involvement of PLWNCDs was led by the Healthy India Alliance (HIA), also known as the India NCD Alliance, through its India Advocacy Agenda for People Living With NCDs, informed by several pan-India community conversations that highlight the needs, priorities and challenges of PLWNCDs.

PLWNCDs in India and globally collectively informed the development of the NCD Alliance's Global Charter on Meaningful Involvement of People Living with NCDs. The Charter outlines fundamental principles and strategies to operationalise meaningful involvement in organisational practices. It is open for endorsement at the link: https://www.ourviewsourvoices.org/global-charter/endorse.

While COVID has exposed several vulnerabilities in healthcare and management, it has also reiterated the significance ofa united peoples' movement in dealing with unprecedented impediments when its mitigation disrupted routine services, including NCD care. Healthcare has diffused from medical facilities to homes and communities. PLWNCDs and citizens at-large have taken on the onus of care and management, playing a critical role in a hybrid, in-person and virtual healthcare system. Meaningful involvement of PLWNCDs warrants leadership and active involvement in all aspects of the NCD response including – governance, policy formulation and enforcement, design and delivery of programmes and services, community mobilisation, evidence generation and impact evaluation. The way forward in this regard is given below:

- Equity: investing more in health and ensuring investments are adequate to fulfil needs of the most vulnerable and affected populations
- Evidence-based decision making: Robust evidence generation is essential to feed into fulfilling gaps in current strategies and formulating new policies
- Capacity building for meaningful involvement: A people-led peer network should strengthen national and sub-national initiatives of PLWNCDs, securing them as decision-makers in shaping individual and community level health agendas
- Central role in government and civil society initiatives: The experience and expertise of PLWNCDs must inform multi-stakeholder and multi-sectoral initiatives to address NCDs and achieve UHC.

(On behalf of Healthy India Alliance: Ms Radhika Shrivastav, Dr Shikha Bhasin, Mrs Jyotsna Govil, Dr Nalini Vemuri, Ms Seema Bali, Ms Nupur Lalvani and Mr Rohan Arora).

Wrongly Granted Patents Prevent Access to COVID-19 Medicines in India

Patents granted to pharmaceutical drugs without properly complying with the patent law and guidelines are creating a huge access barrier in India. In 2020, the COVID-19 drug remdesivir was introduced in the country for emergency use for the treatment of SARS-COV2 infection. Shortage of this drug and its high price were causes of concern during the second wave of COVID-19 infection. One of the reasons for its shortage and high prices is the patent monopoly on the drug and the limited access provided by the voluntary license to generic companies. Remdesivir, a repurposed drug, was granted three patents in India. These patents were granted without following the public health safeguards incorporated in the Patents Act, 1970 and the guidelines for examination.

In 2005, while amending the patent law, the Parliament introduced certain public health safeguards in the Patents Act, 1970. These provisions, namely sections 3(d), 3(e) and 3(i) of the Patents Act, 1970— known as the anti-evergreening provisions— prevent the patenting of minor or marginal modifications of the existing

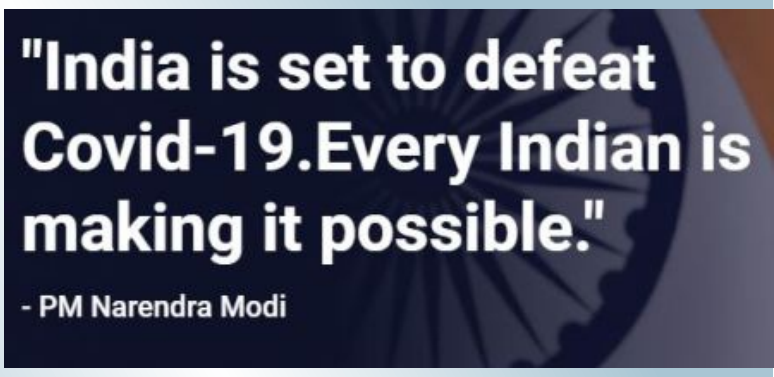
drugs in the country.

In April 2018, Feroz Ali *et al.*, published a report, titled "Pharmaceutical Patent Grants in India: How our safeguards against evergreening have failed and why the system must be reformed". The report highlighted that about 72 percent of the patents granted for pharmaceuticals are for minor or marginal improvements over already existing drugs. It emphasised that despite strict standards laid down in the Act, the actual practice is resulting in proliferation of pharmaceutical patents.

In addition to remdesivir, many cancer and cardiovascular drugs were granted multiple patents and are creating an access problem for patients. Further, pharmaceutical patents on minor improvements do not promote genuine inventions; instead, they perpetuate poor quality research and provide no social benefit to the society, as they contain no new or ingenious and monopolise what is already known or was obvious in the light of what was already known.

The case of Molnupiravir (MOL), an investigational COVID-19 drug, is further

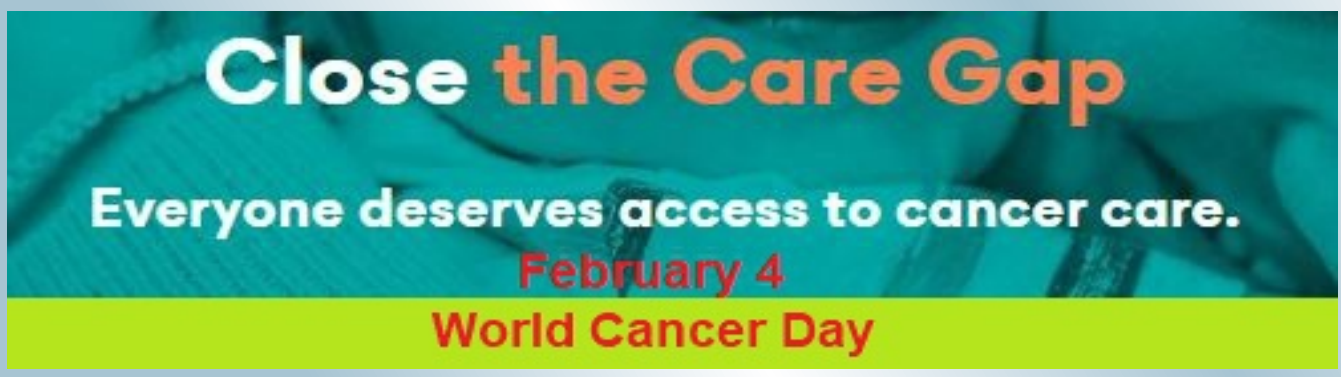
instructive of the problem of low-quality patent applications. MOL is a repurposed drug. Merck Sharpe & Dohme (MSD) has filed two patent applications on this drug in India, which are pending. Relying on these patent applications, MSD has been granting highly restrictive voluntary licenses to generic companies.



While several pre-grant oppositions are pending against the grant of patent to MOL, what is significant is the nature of the invention claimed in the patent applications. The active ingredient is known since 2004 for use against SARS coronaviruse. MOL is only a prodrug of the active ingredient, a well-known method of making the drug more available in human body. There is no genuine invention claimed in MOL. Given the emergency due to COVID-19, the patent applications should have been processed fast by the patent office, but did not happen. In the absence of monopoly on MOL and the restrictive voluntary licenses, the generic companies could have made this drug available at low cost.

Patent Offices play important role in promoting access to medicines by implementing the statutory provisions to secure access. They are expected to ensure the working of the TRIPS flexibilities – public health safeguards and public interest provisions incorporated in the Patents Act.

- Prathibha Siva
Third World Network



Dr. Mansukh Mandaviya, Hon. Union Minister, MoHFW visits Tamil Nadu Covid War Room facilities.

Box 1

The Pradhan Mantri Swasthya Suraksha Yojana (PMSSY) was announced in 2003 with the objectives of correcting regional imbalances in the availability of affordable/ reliable tertiary healthcare services and also to augment facilities for quality medical education in the country.

PMSSY has two components:-

(i) Setting up of AIIMS like Institutions

Each New AIIMS to add:

- State of the art Modular OTs and diagnostics facilities. 15-20 super specialty departments. 750 Beds. 100 UG (MBBS) seats. 60 B.Sc. (Nursing) seats. Focus on PG Education and Research.
- **Total 22 new AIIMS have been announced so far under this component.**
- 6 AIIMS are already functional.
- 16 more AIIMS are approved by the Cabinet.

(ii) Upgradation of Government Medical College (GMC)/ Institutions.

Each upgradation project would be adding:

- 8-10 Super Speciality Departments. Around 15 new PG seats. 150-250 beds.

75 Projects have been considered under this component under different phases .

Box 2

Schemes under Department of Health Research

Human Resource Development for Health Research (HRD).

- Establishment of a network of Laboratories for managing epidemics and Natural Calamities (VRDL)
- Grant-in-aid (GIA) Scheme for Inter-Sectoral Convergence & Coordination for Promotion and Guidance on Health Research
- Establishment of Multi-Disciplinary Research Units (MRU) in Government Medical colleges - Research Institutions

Details of the Schemes are available on: https://dhr.gov.in/schemes)

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