Lowest national Covid cases

Lowest national Covid cases since June (The Tribune: 20210111)


Tally reaches 1,04,66,595; death toll mounts to 1,51,160

Lowest national Covid cases since June

India's COVID-19 caseload rises to 1,04,66,595 with 16,311 fresh infections

With 16,311 new coronavirus cases being reported in a span of 24 hours, the lowest in around six-and-half months, India’s COVID-19 tally rose to 1,04,66,595, while the recoveries have surged to 1,00,92,909, according to the Union Health Ministry’s data updated on Monday.

The death toll reached 1,51,160 with 161 more fatalities, the lowest in the last seven-and-half-months, the data updated at 8 am showed.

The number of people who have recuperated from the disease surged to 1,00,92,909, pushing the national COVID-19 recovery rate to 96.43 per cent, while the case fatality rate was recorded at 1.44 per cent.

The COVID-19 active caseload remained below three lakh. There are 2,22,526 active coronavirus infections in the country which comprise 2.13 per cent of the total caseload, the data stated.

India’s COVID-19 tally had crossed the 20 lakh-mark on August 7, 30 lakh on August 23, 40 lakh on September 5 and 50 lakh on September 16. It went past 60 lakh on September 28, 70 lakh on October 11, crossed 80 lakh on October 29, 90 lakh on November 20 and surpassed the one-crore mark on December 19.

According to the ICMR, 18,17,55,831 samples have been tested so far with 6,59,209 samples being tested on Sunday.
A total of 1,51,160 deaths have been reported so far in the country, including 50,061 from Maharashtra followed by 12,222 from Tamil Nadu, 12,140 from Karnataka, 10,678 from Delhi, 9,941 from West Bengal, 8,495 from Uttar Pradesh, 7,129 from Andhra Pradesh and 5,445 from Punjab.

The health ministry stressed that more than 70 per cent of the deaths occurred due to comorbidities.

"Our figures are being reconciled with the Indian Council of Medical Research," the ministry said on its website, adding that state-wise distribution of figures is subject to further verification and reconciliation. PTI

**COVID-19 ICU patients**

**COVID-19 ICU patients at risk of acute brain dysfunction, says study (The Tribune: 20210111)**


According to the scientists, the choice of sedative medications and curbs on family visitation played a role in increasing acute brain dysfunction for these patients.

**COVID-19 ICU patients at risk of acute brain dysfunction, says study**

COVID-19 patients admitted to intensive care in the early months of the pandemic experienced a higher burden of delirium and coma than is typically found in those hospitalised with acute respiratory failure, according to the largest study of its kind to date.

The research, published in The Lancet Respiratory Medicine journal, tracked the incidence of delirium and coma in over 2,000 COVID-19 patients admitted before April 28, 2020, to 69 adult intensive care units across 14 countries.

According to the scientists, led by those at Vanderbilt University Medical Centre in the US, the choice of sedative medications and curbs on family visitation played a role in increasing acute brain dysfunction for these patients.

They said ICU delirium was associated with higher medical costs and greater risk of death and long-term ICU-related dementia.

Nearly 82 per cent of the patients in the study were comatose for a median of 10 days, and 55 per cent were delirious for a median of three days.
The scientists noted that acute brain dysfunction lasted for an average of 12 days.

“This is double what is seen in non-COVID ICU patients,” said study co-author Brenda Pun from VUMC.

The scientists believe COVID-19 could predispose patients to a higher burden of acute brain dysfunction.

However, they also noted that patient care factors, some of which are related to pressures posed on health care by the pandemic, also appear to have played a significant role.

With respect to COVID-19, the scientists believe there has been widespread abandonment of newer clinical protocols that are proven to help ward off the acute brain dysfunction that usually affects many critically ill patients.

“It is clear in our findings that many ICUs reverted to sedation practices that are not in line with best practice guidelines and we’re left to speculate on the causes,” Pun said.

“Early reports of COVID-19 suggested that the lung dysfunction seen required unique management techniques including deep sedation. In the process, key preventive measures against acute brain dysfunction went somewhat by the boards,” she added.

Analysing patient characteristics from electronic health records, and care practices and findings from clinical assessments, the scientists found that about 90 per cent of patients tracked in the study were invasively mechanical ventilated at some point during hospitalisation, and 67 per cent on the day of ICU admission.

Patients receiving benzodiazepine sedative infusions were at 59 per cent higher risk of developing delirium, they added.

In comparison, the patients who received family visitation were at 30 per cent lower risk of delirium, the study noted.

“There’s no reason to think that, since the close of our study, the situation for these patients has changed,” said study senior author, Pratik Pandharipande.

“These prolonged periods of acute brain dysfunction are largely avoidable. ICU teams need above all to return to lighter levels of sedation for these patients, frequent awakening and breathing trials, mobilisation and safe in-person or virtual visitation,” Pandharipande added.

PT

**Anxiety, depression**

**Religious people cope well with anxiety, depression: Study (The Tribune: 20210111)**
Religious people look for positive ways of thinking about hardship, a practice known to psychologists as "cognitive reappraisal."

Religious people cope well with anxiety, depression: Study

Religious people look for positive ways of thinking about hardship, a practice known to psychologists as "cognitive reappraisal."

A new study has revealed that religious people are making use of some of the same tools that psychologists have systematically identified as effective in increasing well-being and protecting against distress, anxiety and depression.

Religious people look for positive ways of thinking about hardship, a practice known to psychologists as "cognitive reappraisal." They also tend to have confidence in their ability to cope with difficulty, a trait called "coping self-efficacy." Both have been shown to reduce symptoms of anxiety and depression, said the team from the University of Illinois Urbana-Champaign in the US.

"This suggests that science and religion are on the same page when it comes to coping with hardship," said Florin Dolcos, a professor of psychology at the University of Illinois Urbana-Champaign.

The research was prompted in part by earlier studies demonstrating that people who are religious tend to use a coping strategy that closely resembles cognitive reappraisal.

For example, when somebody dies, a religious person may say, 'OK, now they are with God,' while someone who isn't religious may say, 'Well, at least they are not suffering anymore.

In both cases, the individual finds comfort in framing the situation in a more positive light, said Dolcos in a paper published in the Journal of Religion and Health.

To reach this conclusion, the researchers recruited 203 participants with no clinical diagnoses of depression or anxiety.

Fifty-seven of the study subjects also answered questions about their level of religiosity or spirituality.

The researchers asked participants to select from a series of options describing their attitudes and practices.

The researchers also evaluated participants' confidence in their ability to cope and asked them questions designed to measure their symptoms of depression and anxiety.
"If we are just looking at the relationship between religious coping and lower anxiety, we don't know exactly which strategy is facilitating this positive outcome," said study co-author Sanda Dolco.

"The mediation analysis helps us determine whether religious people are using reappraisal as an effective way of lessening their distress." The study should be of interest to clinical psychologists working with religious clients.

"I hope this is an example of where religion and science can work together to maintain and increase well-being," Florin said.

**Bird flu virus**

**Bird flu virus is heat-labile, gets killed at 'cooking temperature'** *(The Tribune: 20210111)*

These viruses occur naturally among wild aquatic birds worldwide.

Bird flu virus is heat-labile, gets killed at 'cooking temperature'

One should avoid going to open markets that sell poultry as they are the focal point of the spread. PTI photo.

Contrary to what some people think that the bird flu virus, also known as Avian influenza, is spread to humans via consumption of cooked poultry products, health experts on Sunday stressed that it usually does not infect people as the virus is heat-labile (degraded and killed when subjected to heat).

Avian influenza refers to the disease caused by infection with avian (bird) influenza (flu) Type A viruses. These viruses occur naturally among wild aquatic birds worldwide and can infect domestic poultry and other bird and animal species.

According to the World Health organisation (WHO), cooking of poultry (e.g. chicken, ducks and geese) at or above 70 degree Celsius so that absolutely no meat remains raw and red, is a safe measure to kill the virus in areas with outbreaks in poultry.

Richa Sareen, consultant (pulmonology) at Fortis Vasant Kunj in New Delhi, said the virus is heat-labile and it gets killed with cooking temperatures.

"At this time, people should eat fully cooked chicken and eggs and not raw or partially cooked ones. One should avoid going to open markets that sell poultry as they are the focal point of the spread," Sareen told IANS.

"People who handle poultry should take special precautions. They should wear PPE, gloves and masks while handling birds and should practice frequent hand washing," she added.
Although the virus causing bird flu usually does not infect people, rare cases of human infection with these viruses have been reported, especially in individuals working with infected domestic birds.

"The possible cause of infections in humans is when they come in contact with birds with the viruses and enough viruses get into a person's eyes, nose or mouth, or is inhaled through the excretions of birds," said Kunal Kothari, Senior Physician, Internal Medicine, SMS Medical College in Jaipur.

"The spread of Bird Flu from one individual, who is sick to another has been very rare and data is limited, inefficient and not sustained but as a precaution, we should all be watchful of public health advisory," Kothari added.

Bird Flu is a communicable virus among the avian population and human to human spread is not too prominent with the current strain.

However, viruses are prone to mutation, so if this virus undergoes mutation in future, it has the potential to spread from human to human and cause a pandemic.

Bird flu mostly infects the respiratory system of humans. Common symptoms are fever, runny nose, sore throat, cough, muscle aches, etc.

"If severe, it can cause ARDS, multi-organ involvement and even death. The sporadic data on bird flu from the past shows very high mortality, to the tune of 60 per cent. Thus, it becomes important to take precautions now," Sareen mentioned.

Nevertheless, maintaining distance from birds in the environment is important as the spread of the avian virus is through the saliva, faecal matter of an infected bird.

"The avian virus is airborne. Notify the community health department on seeing sick or dead birds and try not to come in direct contact with these birds without proper masks, gloves and disinfectants," Kothari noted.

**OVID-19 vaccine race**

**OVID-19 vaccine race: Where they stand currently (The Tribune: 20210111)**


10 vaccine candidates have been either approved by several countries or are under limited emergency use

COVID-19 vaccine race: Where they stand currently
Vials of the Pfizer-BioNTech COVID-19 vaccine are seen at a coronavirus disease vaccination center inside a gymnasium in Taverny near Paris, on January 9, 2021. Reuters

Almost a year into the COVID-19 pandemic, about 200 vaccine candidates are in the works and 10 have been either approved by several countries or are under limited emergency use.

As India prepares to launch its vaccine drive on January 16, here is a look at the options:

Developed by Bharat Biotech in collaboration with the Indian Council of Medical Research and the National Institute of Virology, the indigenous vaccine was granted emergency use authorisation in ‘clinical trial mode’ by the Indian government this week.

It is an “inactivated” vaccine developed by chemically treating novel coronavirus samples to make them incapable of reproduction. This process leaves the viral proteins, including the spike protein of the coronavirus which it uses to enter the human cells, intact.

Given as two doses, three weeks apart, the viral proteins in the vaccine activate the immune system and prepare people for future infections with the actual infectious virus. According to Bharat Biotech, the therapeutic can be stored at room temperature for at least a week.

A study on the Phase ½ trial published in the preprint server medRxiv in December showed the therapeutic doesn’t cause any serious side effects. However, there has been no further data released in the public domain which could demonstrate that the vaccine is safe and effective.

“ICMR-Bharat Biotech vaccine is a killed whole-virus vaccine and there are absolutely no data available so far on its protective efficacy. I am critical of its getting approval by the authorities,” immunologist Vineeta Bal, affiliated with the National Institute of Immunology in New Delhi, told PTI.

Co-developed by the University of Oxford and British-Swedish company AstraZeneca and known as Covishield in India, the vaccine was the first on which a scientific study was published based on Phase 3 clinical trials.

It has so far been given emergency use authorisation in the UK, Argentina, Mexico and India.

Scientists have engineered a version of adenoviruses that infect chimpanzees to carry the gene responsible for the spike protein of the novel coronavirus.

It requires two doses, provided four weeks apart, to produce the desired effects.

Manufactured by the Serum Institute of India, Covishield will be sold at Rs 1,000 per dose in the private market but cost the Indian government only Rs 200, said SII CEO Adar Poonawalla.

“Oxford-AstraZeneca-Serum Institute vaccine has shown protective efficacy in global trials to the tune of 60-70 per cent. While clear data from bridging trials in India are not available, the vaccine is certainly proven safe,” Bal said.
Vaccines

Vaccines to arrive in Capital by Thursday Hindustan Times: 20210111)

Modi to meet CMs virtually today to take stock of preparedness across the country

https://epaper.hindustantimes.com/Home/ArticleView

A health worker and a volunteer participate in a vaccination dry run at a hospital in New Delhi on Friday. AJAY AGGARWAL /HT

Delhi health minister Satyendar Jain said on Sunday the government has finalised 89 sites for the vaccination drive against the coronavirus, with stocks of the jabs expected to arrive in the Capital between January 12 and January 14, a remark that came a day ahead of Prime Minister Narendra Modi’s interaction with chief ministers to take stock of the immunisation exercise that begins on January 16.

India’s vaccination drive, the world’s largest such exercise against the coronavirus disease (Covid-19), will kick off on January 16 with priority to about 30 million health care and frontline workers, the government has said. India plans to vaccinate 270 million others in six to eight months.

“Each centre will be managed by 8-10 staff. Cold storage facilities are ready and security arrangements are in place. The vaccines should arrive in the city between January 12 and 14,” Jain said.

The Prime Minister, meanwhile, will interact with CMs to review the arrangements for the drive. This will be Modi’s first interaction with chief ministers since the Drug Controller General of India on January 3 offered emergency use approval to a pair of Covid-19 vaccines – Pune-based Serum Institute of India’s Covishield, developed by Oxford University and AstraZeneca, and Hyderabad-based Bharat Biotech International’s indigenous candidate Covaxin, which is still in Phase 3 trials.

Three dry runs have so far been conducted across the country for the vaccination campaign. The vaccine roll-out will initially target 10 million health care workers and 20 million other front line workers, and will later cover high-risk population such as senior citizens and those with comorbidities numbering about 270 million.
Covid-19, which originated in the central Chinese city of Wuhan in December 2019 and spread rapidly throughout the world, has claimed 151,215 lives in India and affected 10,467,429, making it the country worst hit by the viral disease after the United States.

On the eve of the meeting with the Prime Minister, the Delhi health minister said that the city-state’s administration had shortlisted 89 vaccination centres. Forty will be in public hospitals and 49 in private hospitals, he said.

In the first phase, the vaccine will be administered to health care workers. While the Delhi government had estimated their number at 300,000, around 225,000 of them have registered to receive the vaccine, said a senior government official. Health care workers will be followed by an estimated 600,000 front line workers – employees across government departments, agencies and civic bodies – engaged in Covid-19 management.

Next in line would be people aged above 50 years and individuals with comorbidities such as hypertension and diabetes.

Their number has been currently pegged at 4.2 million but it is bound to increase as the Delhi government is still updating its database for these groups and creating mechanisms for self-registration to ensure nobody misses the shot, said a government official who requested anonymity. HT had reported on January 5 that the government is working on a plan to grade the last group on the basis of age, number of comorbidities and the type of comorbidities.

Delhi’s main vaccine storage centre has been set up at the Rajiv Gandhi Super-Speciality Hospital. There is another centre in Civil Lines as a back-up. The government has also drafted a plan to set up a third centre for bulk storage at the directorate of health services in Karkardooma. Other than that, there are 609 cold chain points and a plan for 1,000 vaccine administration centres for later stages.

Jain said at a media briefing earlier on Sunday: “We have urged the central government to make Covid-19 vaccines free for all residents of India. I highlighted the issue in a recent meeting with the Union health minister and yesterday chief minister Arvind Kejriwal also appealed to the central government.”

On Saturday, Kejriwal posted a tweet urging the central government to consider making Covid-19 vaccines free for all Indians.

On the day of the first vaccine dry run on January 2, Jain had said that the Covid-19 vaccine would be free for all residents of Delhi. Union health minister Harsh Vardhan assured free vaccines for health care and frontline workers in the first phase.

Asked if the Delhi government would administer the vaccine free to all the residents of the city, Jain said: “We have requested the Union health minister. He has said that he will consider the proposal. We should wait.”

Dr Suneela Garg, a professor at the Maulana Azad Medical College in Delhi and an adviser to the Indian Council of Medical Research (ICMR), said: “Now that the city has witnessed
successful dry runs, the next few days should be spent on revisiting the exercise, especially areas such as crowd management and monitoring of patients after vaccination. Delhi is prepared for the vaccination drive.”

A Pune-based executive with a logistics firm that has been hired to transport the vaccine vials said, meanwhile, that it had deployed a fleet of 300 refrigerated trucks at various locations in the country to transport the vaccine. The transport of the vaccine manufactured by the Serum Institute of India will be initially by air and then through road, for which the Pune Police have arranged for two-tier security.

Executives from Koolex Integrated Cold Chain Solutions held a meeting with Pune Police chief Amitabh Gupta on Saturday, according to a report in HT’s Sunday edition.

“We have a fleet of 300 refrigerated trucks which was upgraded from 200 in the last six months. All are indigenous trucks with refrigeration infrastructure installed locally as well. We carry extra fuel for the road as well. Even we are not sure about the routes and destinations yet but we have 30 branches of our own and our nodal point will be at the cold storage in Bhiwandi, Thane. Our vehicles, however, are on standby,” said Rahul Agarwal, founder of Koolex Integrated Cold Chain Solutions. A logistics official will be appointed by the Serum Institute of India who will assign the number of vials to be carried by each commercial airline. The Indian Air Force will also be in the mix for the transport of the vaccine in remote areas, according to an earlier report published by HT.

The Serum Institute of India, which had stockpiled 50 million doses by the first week of January, said that the vials need to be maintained at a temperature between 2 and 8 degrees Celsius. The refrigerated trucks are equipped to maintain the required temperature and live-track the location as well, according to Agarwal.

The federal ministry of health and family welfare announced on Saturday that the nationwide vaccination drive will commence on January 16.

Prime Minister Modi chaired a meeting on Saturday to review the status of the pandemic in the country along with the preparedness of the states and Union territories to begin the vaccination drive. The meeting was attended by the cabinet secretary, principal secretary to the PM, health secretary, and other senior officials.

Modi reiterated that India has a global role in the vaccination drive against Covid-19. “Being the pharmacy of the world, India has supplied important medicines to all those in need in the world in the past and is also doing so now. The world is not only waiting for Indian vaccines but is also watching how India runs the world’s biggest vaccination programme,” he said at the Pravasi Bharatiya Divas on Saturday.
As India starts on vaccination, the government must bolster public trust in the process

India now has a firm date to roll out the biggest vaccination programme in its history. Prime Minister Narendra Modi has said that from January 16, after the Makar Sankranti and Pongal festivities, doctors, nurses and sanitation workers, who are part of the priority group, would begin getting the vaccine. India has approved two vaccines in emergency-use mode — Covishield by the Serum Institute of India, Pune, and Covaxin by Bharat Biotech Ltd. While it still is unclear who gets which vaccine, there are more doses of Covishield available at present than Covaxin, almost five to one, and it could take a few months before the 30 million prioritised get one of their doses. Others, those in the 50-plus age group and those with comorbidities, will have to wait much longer, especially in a situation where vaccines such as those by Pfizer and Moderna are not made available for import by the private sector.

However, the vaccination begins under a cloud. Covaxin belongs to a league of vaccines that has been approved without establishing its efficacy, namely, the extent to which vaccination protects from COVID-19. There have been differences among scientists such as on the best testing strategy, treatment, extent of infection, but none more divisive than on the approval of Covaxin. Several experts have made the case that the declining rate of infections and low relative mortality meant that India was not in as dire a state of emergency that required it to approve an untested vaccine when more clarity would likely have come by March. Covaxin is best kept as a backup in the event of a sudden surge of cases till its efficacy data are available and acceptable. Also, reports have emerged of trials in Bhopal where volunteers were seemingly under the impression that they were getting a protective shot when some were likely getting a placebo. They also complain of no medical follow-up when some developed symptoms such as fever, body pain and loss of appetite. The vaccine may eventually prove protective and the adverse symptoms reported, seen as part of the variety of the human body’s response — there are 28,500 volunteers after all. However, a vaccine that evokes distrust is self-defeating. With childhood immunisation, India has proven that it has the infrastructural backbone to inoculate millions. The dry runs to test the Co-WIN management software have reportedly given authorities valuable feedback on perfecting the prospective rollout. However, this could be undone if people do not turn up, and worse, if vaccine hesitancy rises. The pandemic gave India an opportunity to examine its dispensation of health care. Along with improving access, the government must seriously examine the conduct of vaccine trials and work hard to bolster public trust in it, and monitor the vaccination process for adverse reactions.
Newborn deaths

Felled by fire: On newborn deaths in Maharashtra hospital (The Hindu: 20210111)


To avert another Bhandara-like hospital inferno, govs must address underlying causes

The deadly fire that snuffed out the lives of 10 infants in the Bhandara District General Hospital in Maharashtra is a shocking reminder that safety norms in several medical facilities in India do not pass muster. The parents of the babies who perished in the sick new-born unit have been plunged into a lifetime of trauma. Some of the victims, a few just days old, had been brought to the hospital for better care from smaller health facilities; seven had a providential escape. There are reports of poorly trained staff failing to respond adequately. The terrible blaze joins the long list of such accidents recorded in government and private hospitals, underscoring a painful reality: safety protocols are yet to be institutionalised even in places where people legitimately expect a high degree of professionalism. Last year, there were devastating fires in COVID-19 facilities in Vijayawada and Ahmedabad, with several casualties, blamed on poor oversight by fire authorities or faulty electrical repairs. The Maharashtra government has ordered a probe into the Bhandara fire to be concluded in three days, and a fire audit of hospitals, but a perfunctory inquiry cannot effectively address the underlying causes. Hospital fires are a distinct entity, and research indicates that there are specific factors that trigger them off and aggravate their impact.

Intensive Care Units, neonatal ICUs and operating rooms are often the site of fires, implicating the presence of a high concentration of oxygen in a confined space. A review of Indian hospital fires published in the Journal of Clinical Anesthesia identified higher oxygen availability in intensive care facilities as the likely primary cause, with motors and electrical units in the room providing the ignition, and plastics fuelling it. It is worth considering, therefore, whether hospitals have been audited with such factors in mind, and to evaluate national building safety codes against international practice. Oxygen monitors for hospital rooms, to ensure that the ambient level is within safe norms — set at a maximum of 23.5% by the U.S. National Fire Protection Association — could help avert an accident. Locating electrical equipment for air-conditioners with sparking potential away from oxygen saturated areas may also reduce the risk. As the health sector expands, it is essential that all new infrastructure conforms to rigorous safety standards, a small premium to stop disasters such as the Bhandara carnage. If the
government sets the bar high enough, ensuring full adherence to safety in its buildings, regulatory authorities can compel commercial structures to fall in line. The Centre should also create a public platform for insights gained from inquiries into hospital fires to be shared. Hospitals should mandatorily hold regular safety and evacuation drills which are key to saving lives when disaster strikes.

**Blood cancer**

**Researchers find strategy to reduce treatment-related complication for blood cancer patients (New Kerala: 20210111)**


A study published in the New England Journal of Medicine by researchers of the Indiana University Melvin and Bren Simon Comprehensive Cancer Center sheds light on preventing a treatment-related complication of blood stem cell transplantation for blood cancer patients.

Sherif Farag, MD, PhD, found that using a drug approved for Type 2 diabetes reduces the risk of acute graft-versus-host disease (GVHD), one of the most serious complications to lifesaving blood stem cell transplantation in leukaemia.

GVHD occurs in more than 30 per cent of patients and can lead to severe side effects and potentially fatal results. Farag is the Lawrence H. Einhorn Professor of Oncology and professor of medicine at IU School of Medicine, a member of the IU Simon Comprehensive Cancer Center and program and medical director of the haematological malignancies and bone marrow and blood stem cell transplantation at IU Health.

In the IU clinical study, blood stem cell transplant patients received an oral drug called sitagliptin. Acute GVHD occurred in only two of 36 patients within 100 days of their transplant. The 5 per cent occurrence represents a drastic reduction of GVHD, which studies have found can affect 34 per cent to 51 per cent of patients in the first three months after transplant.

Graft-versus-host disease occurs when the donated blood stem cells (the graft) attack the transplant recipient's (the host) tissue."The rate looks very encouraging and it's achieved with a very simple and relatively inexpensive intervention of sitagliptin. This result is significant and offers a new approach and a new target for the inhibition of graft-versus-host disease. We achieved a much lower rate than we could have hoped," Farag said.

Sitagliptin targets an enzyme called dipeptidyl peptidase-4 (DPP-4), which is involved in a variety of processes in the body. It is used for Type 2 diabetes to improve insulin secretion and glucose control.

Hal Broxmeyer, PhD, a pioneer in the field of umbilical cord blood stem cell transplantation and distinguished professor at IU School of Medicine and a co-author with Farag, previously
found that DPP-4 regulates blood cell production and explored if taking sitagliptin would improve engraftment for cord blood transplants.

While there seemed to be some improvement in engraftment of cord blood transplants, one striking finding was the patients had a much lower rate of acute graft-versus-host disease than expected. Farag's lab took on that data and found targeting DPP-4 with sitagliptin inhibits the immune T cell activation that leads to GVHD.

Farag noted that repurposing sitagliptin offers a relatively inexpensive and accessible approach to preventing GVHD.

"These findings are very significant because there are a lot of other different drugs that are being tested, including ones that are very expensive or require administration intravenously for a prolonged time well beyond the time of recovery and transplant," Farag said. Patients in the study were ages 18 to 60 and had one of the following blood cancer or diseases acute myeloid leukaemia (AML), acute lymphoblastic leukaemia (ALL), chronic myeloid leukaemia, or myelodysplastic syndrome.

The patients in the study received sitagliptin orally one day before their transplant and the day of their transplant, plus 14 days after their transplant.

Patients in the study did not face any unexpected or unusual toxicities or higher relapse rates than what's expected post-transplant."This is a drug that is used to treat diabetes, and we're using it at a much higher dose. We asked if we are going to cause people to have low blood sugar or hypoglycemia--and we didn't find that," Farag said.

"As long as it's not combined with other drugs that lower the blood glucose in non-diabetic patients, it doesn't do that; we certainly confirm that in our findings," added Farag. Farag's findings now need to be confirmed with a larger, multi-centre randomized study. He also hopes to explore combination therapies with sitagliptin and if it could prevent chronic graft-versus-host disease.

Autoimmune diseases

New approach needed to study autoimmune diseases (New Kerala: 20210111)

A research team has recently determined that the Immune only focus of the current research must be updated to better understand autoimmune diseases such as type 1 diabetes and multiple sclerosis.

A team of researchers led by the Indiana Biosciences Research Institute Diabetes Center's Scientific Director Decio L. Eizirik, MD, Ph.D., has found that identifying new treatments for autoimmune diseases requires studying together the immune system AND target tissues. This study, "Gene expression signatures of target tissues in type 1 diabetes, lupus erythematosus, multiple sclerosis, and rheumatoid arthritis," is featured in the Jan. 6, 2021, edition of Science Advances.

"We must move away from the present "immune-centric-only" view of autoimmune diseases," explains Eizirik. "Indeed, trying to understand these diseases focusing on the immune system only, and forgetting the target tissues, maybe similar to attempting to fly a plane with only one wing."

Autoimmune diseases, which affect up to 5 percent of the population in different regions, suffer from a case of mistaken identity. The immune system is supposed to protect us from infectious diseases or tumors.

Yet, during autoimmune diseases, the immune system mistakenly attacks and destroys components of our body, which then causes, for example, type 1 diabetes (T1D), systemic lupus erythematosus (SLE), multiple sclerosis (MS), or rheumatoid arthritis (RA). These four autoimmune diseases share almost half of the same genetic risks, chronic local inflammation, and mechanisms leading to target tissue damage.

Despite these common features, autoimmune disorders are traditionally studied independently and with a focus on the immune system rather than on the target tissues. Knowing that there is increasing evidence that the target tissues of these diseases are not innocent bystanders of the immune system attack, but instead are active participants, Eizirik and his team hypothesized that key inflammation-induced mechanisms, potentially shared between T1D, SLE, MS, and RA, may drive similar molecular signatures at the target tissue level.

"This research is significant in reaching the JDRF's mission to cure, treat and prevent T1D," said Frank Martin, Ph.D., JDRF director of research. "Discovering the common pathways of tissue destruction across multiple autoimmune diseases will dramatically accelerate our path to a cure for T1D.

Drugs that are effective in one autoimmune disease could be equally beneficial for another and quickly repurposed to make a big impact on people living with that disease. Characterizing the similarities and differences between multiple autoimmune diseases has the potential to transform the way we treat and cure these diseases in the future."

To test this hypothesis, the research team obtained gene expression data from diseased tissue sampled from controls or individuals affected by T1D, SLE, MS, and RA. This indicated major common gene expression changes at the target tissues of the four autoimmune diseases
evaluated. One candidate gene in common between the four diseases is TYK2, a protein that regulates interferon signaling.

The team showed in its research that the use of TYK2 inhibitors - already in use for other autoimmune diseases - protects b-cells against immune-mediated damage. This finding reinforces the importance of studying the target tissue of autoimmune diseases, in dialogue with the immune system, to better understand the genetics and natural history of these devastating diseases and to identify novel therapies.

Critical enzymatic processes

Bone fracture risk increases due to decline of critical enzymatic processes
(New Kerala: 20210111)

According to the findings of new research the risk of a person's bones getting fractured increases due to loss of enzymatic processes within the body.

This new insight was recently published in eLife by an international team of scientists and engineers led by Deepak Vashishth, the director of the Center for Biotechnology and Interdisciplinary Studies (CBIS) at Rensselaer Polytechnic Institute.

Enzymatic processes are essential to any number of chemical reactions that occur within the body, including the production of the extracellular matrix within the bone that is critical for mechanical support. Phosphorylation -- one of those key enzymatic processes -- is the attachment of a phosphoryl to a protein and is critical for cellular regulation. This process plays a role in many diseases, but until now, researchers didn't know if it altered tissue integrity and organ function.

In this paper, researchers looked at a protein known as osteopontin, which plays a vital role in holding the matrix together. The researchers developed a process by which they could induce phosphorylation -- or its counterpart, dephosphorylation -- in bones from genetically modified mice, some that had osteopontin and others that did not.

By comparing results from the two groups, researchers found that fracture toughness, a measure of bone's mechanical strength, increased with osteopontin phosphorylation, and declined with dephosphorylation. More specifically, phosphorylation enhanced crosslinks and increased the attraction between the charged groups on osteopontin and bone mineral, making the bone stronger and its fracture more difficult.

"This is the first study that lays down that phosphorylation in bone matters, particularly how it assists bone in releasing energy, and that loss of this modification is bad for bone," Vashishth said.
The team also studied the effect of osteopontin phosphorylation levels in the rare bone diseases hypophosphatemia and hyperphosphatemia, which are associated with skeletal deformities. In both diseases, Vashishth said, osteopontin phosphorylation levels decreased, a finding that lays the groundwork for further exploration.

"Another promising discovery was that these levels do change with diseases in bone," Vashishth said. "Is phosphorylation directly affecting the fracture propensity of bones in these diseased conditions? And what therapeutic tools can we use to fix this? These are the questions that we want to investigate."

In the spirit of the New Polytechnic, the model that drives research and education at Rensselaer, this research was highly collaborative across multiple disciplines. Vashisht and his lab worked with researchers at McGill University in Canada, the University of Southampton in the United Kingdom, the University of Patras in Greece, Aarhus University in Denmark, and Vienna University of Technology in Austria. Each research team brought different expertise and a piece of this puzzle to the work.

The team's findings may also be applied to similar processes within other connective tissues and possible therapeutics to counteract abnormal osteopontin phosphorylation levels.

"This is not just specific to the bone, because phosphorylation is a more ubiquitous change in other tissues in the body," Vashishth said. "Osteopontin is not only in bone, it's in other tissues in our body, like our kidneys and several other places. This research can also shed light on other things that can happen throughout the body."

**Vaccination (Hindustan: 20210111)**

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