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2021 | Vol.4 | Issue No.34 - 36

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NEWS BULLETIN

23 Aug-6 Sep 2021 | Vol.4 | #34-36

A weekly publication from NIRT Library

The Indian EXPRESS

Covid can make one more susceptible to developing active tuberculosis: Health Ministry

The ministry said notification of tuberculosis cases had decreased by about 25 per cent in 2020 due to Covid-related restrictions and special efforts are being made to mitigate this impact through intensified case findings.

By: **PTI** | New Delhi | July 17, 2021 9:36:48 pm

The ministry said SARS-CoV-2 infection can make an individual more susceptible to developing active TB disease, as it is an "opportunistic infection like black fungus".

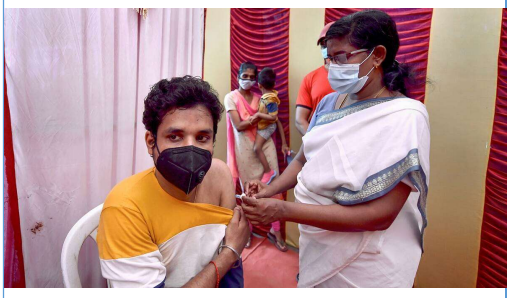
Covid-19 can make a person more susceptible to developing active tuberculosis as it is an "opportunistic" infection like black fungus but currently there is not enough evidence to

The Indian EXPRESS

Want to get vaccinated in Chennai? Here's the list of centres that function 24×7

To further enhance vaccination coverage, the civic body has started camps in 15 zones that would function round the clock. The officials said ample healthcare personnel have been deployed and vaccine doses supplied to these camps.

Written by Janardhan Koushik | Chennai | September 6, 2021 2:34:26 pm



Earlier, the state health department had opened such 24x7 centres in 55 medical college hospitals across Tamil Nadu. The first of these centres was opened at the DMS complex in Chennai. (PTI photo)

The Greater Chennai Corporation Saturday opened 24×7 vaccination centres in all the 15 zones of the city. Minister for Municipal Administration and Water Supply KN Nehru inaugurated the camp at Urban Community Health Centre in Adyar.....

Continued in page no.4

suggest TB cases have risen due to the viral disease, the Union Health Ministry said on Saturday.

The ministry said notification of tuberculosis cases had decreased by about 25 per cent in 2020 due to Covid-related restrictions and special efforts are being made to mitigate this impact through intensified case findings.

In a statement, the Health Ministry said there have been some news reports alleging that a sudden rise in TB cases have been noticed among patients infected with Covid-19 recently, leaving doctors, who have been receiving around a dozen similar cases every day, worried.
"It is clarified that tuberculosis screening for all Covid-19 patients and Covid-19 screening for all diagnosed TB patients has been recommended by Ministry of Health and Family Welfare," it said.
The ministry said SARS-CoV-2 infection can make an individual more susceptible to developing active TB disease, as it is an "opportunistic infection like black fungus".
There is not enough evidence currently to suggest that there has been an increase in TB cases due to Covid-19 or due to increased case finding efforts, it said, adding states and Union Territories have been asked for convergence in efforts for better surveillance and finding of TB and Covid-19 cases as early as August 2020.
Also, the health ministry has issued multiple advisories and guidance reiterating the need for bi-directional screening of TB-Covid and TB-ILI/SARI.
"Due to the impact of Covid-related restrictions, case notifications for TB had decreased by about 25 per cent in 2020 but special efforts are being made to mitigate this impact through intensified case finding in OPD settings as well as through active case finding campaigns in the community by all states."
The dual morbidity of tuberculosis and Covid-19 can be further highlighted through the fact that both diseases are known to be infectious and primarily attack the lungs, presenting similar symptoms of cough, fever and difficulty in breathing. But TB has a longer incubation period and a slower onset of disease, the health ministry said.
"Furthermore, TB bacilli can be present in humans in a dormant state and has the potential to start multiplying when the individual's immunity is compromised for any reason.

The Indian EXPRESS

Covid-19 testing for airport arrivals: how rules vary between states

Several state and city administrations had imposed the requirement for passengers to have their RT-PCR tests conducted before travelling to prevent anyone infected with coronavirus from travelling into their jurisdictions.

Written by **Pranav Mukul** , Edited by Explained Desk | New Delhi | Updated: September 7, 2021 9:28:14 am

Travellers wearing face masks, shields and gloves on a flight during the pandemic (File photo)

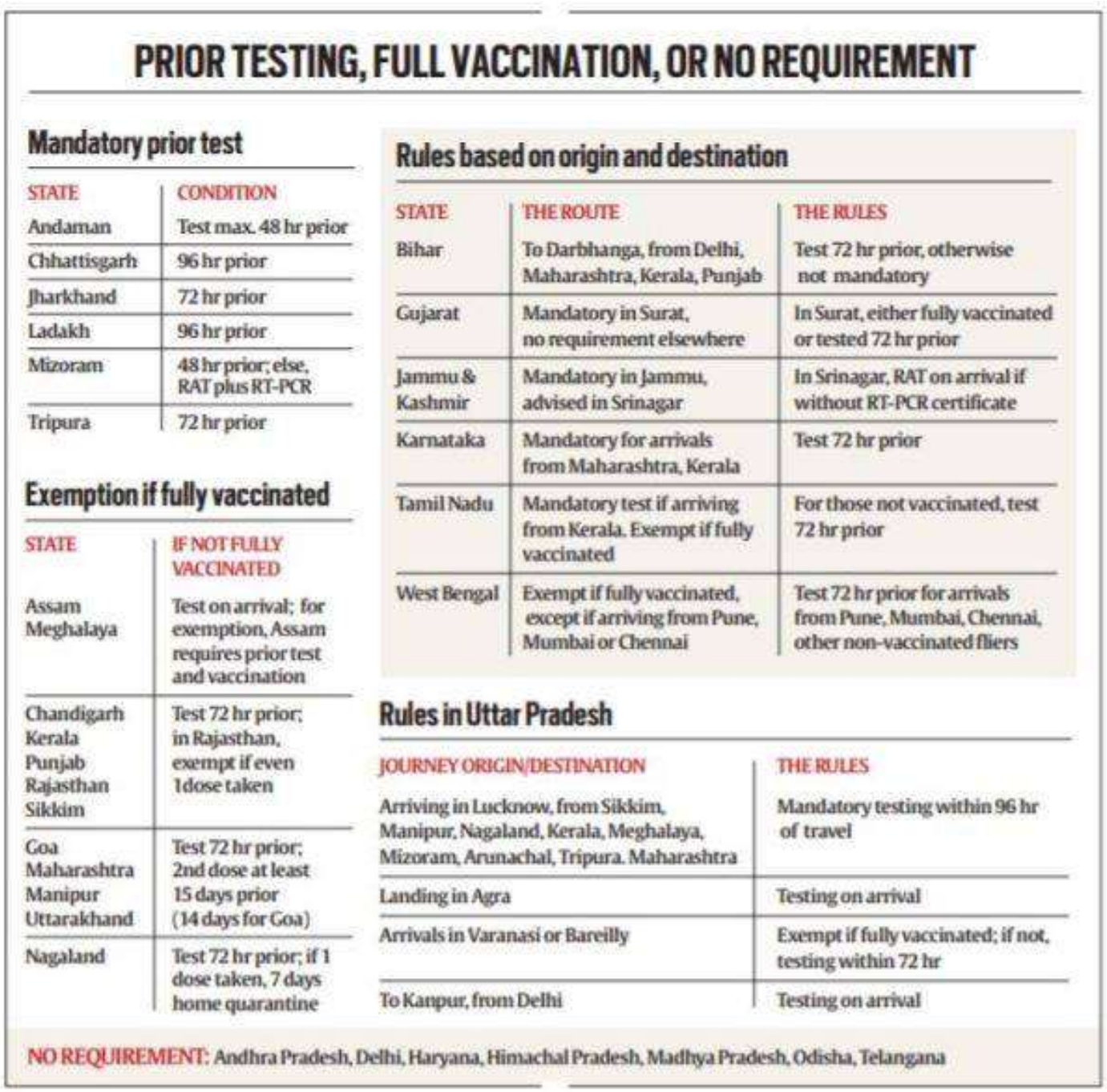
As more and more people get vaccinated across the country, an increasing number of states are now offering exemption from RT-PCR testing requirements to vaccinated passengers traveling into their jurisdictions. In addition

to Covid-19 testing requirements, a number of states are also doing away with quarantine rules for those who are fully or partially vaccinated against Covid-19.

But despite the economy having opened up progressively, the rules that have been put in place across states present a mishmash of discordant stipulations that could end up confusing air travellers.

Why is RT-PCR testing important for travellers?

Several state and city administrations had imposed the requirement for passengers to have their RT-PCR tests conducted 48 hours before travelling – or sooner – to prevent anyone infected with coronavirus from travelling into their jurisdictions. With the inoculation drive gaining momentum, several states have done away with this requirement.



PRIOR TESTING, FULL VACCINATION, OR NO REQUIREMENT

Mandatory prior test

STATE	CONDITION
Andaman	Test max. 48 hr prior
Chhattisgarh	96 hr prior
Jharkhand	72 hr prior
Ladakh	96 hr prior
Mizoram	48 hr prior; else, RAT plus RT-PCR
Tripura	72 hr prior

Exemption if fully vaccinated

STATE	IF NOT FULLY VACCINATED
Assam Meghalaya	Test on arrival; for exemption, Assam requires prior test and vaccination
Chandigarh Kerala Punjab Rajasthan Sikkim	Test 72 hr prior; in Rajasthan, exempt if even 1dose taken
Goa Maharashtra Manipur Uttarakhand	Test 72 hr prior; 2nd dose at least 15 days prior (14 days for Goa)
Nagaland	Test 72 hr prior; if 1 dose taken, 7 days home quarantine

Rules based on origin and destination

STATE	THE ROUTE	THE RULES
Bihar	To Darbhanga, from Delhi, Maharashtra, Kerala, Punjab	Test 72 hr prior, otherwise not mandatory
Gujarat	Mandatory in Surat, no requirement elsewhere	In Surat, either fully vaccinated or tested 72 hr prior
Jammu & Kashmir	Mandatory in Jammu, advised in Srinagar	In Srinagar, RAT on arrival if without RT-PCR certificate
Karnataka	Mandatory for arrivals from Maharashtra, Kerala	Test 72 hr prior
Tamil Nadu	Mandatory test if arriving from Kerala. Exempt if fully vaccinated	For those not vaccinated, test 72 hr prior
West Bengal	Exempt if fully vaccinated, except if arriving from Pune, Mumbai or Chennai	Test 72 hr prior for arrivals from Pune, Mumbai, Chennai, other non-vaccinated fliers

Rules in Uttar Pradesh

JOURNEY ORIGIN/DESTINATION	THE RULES
Arriving in Lucknow, from Sikkim, Manipur, Nagaland, Kerala, Meghalaya, Mizoram, Arunachal, Tripura. Maharashtra	Mandatory testing within 96 hr of travel
Landing in Agra	Testing on arrival
Arrivals in Varanasi or Bareilly	Exempt if fully vaccinated; if not, testing within 72 hr
To Kanpur, from Delhi	Testing on arrival

NO REQUIREMENT: Andhra Pradesh, Delhi, Haryana, Himachal Pradesh, Madhya Pradesh, Odisha, Telangana

How are states updating their travel guidelines?
While some states have completely done away with any testing requirement, some are exempting passengers who have been vaccinated from getting tested before travelling. However, there are still a number of states and cities that are compulsorily seeking RT-PCR test certificates — in some cases even when the passengers are fully-vaccinated.

Is there a set of central guidelines for vaccinated travellers?
While the Union government has advised states that those who are fully vaccinated do not need RT-PCR test certificates to travel, some states have continued to insist for pre-arrival or on-arrival testing.

Continued from page no.1

Want to get vaccinated in Chennai? Here's the list of centres that function 24×7

……The initiative comes after the state health department had opened such 24×7 centres in 55 medical college hospitals across Tamil Nadu. The first of these centres was opened at the DMS complex in Chennai.

The corporation, which had 45 camps initially (with three camps per zone), later extended the number up to 200. This meant that each ward had one camp that would function from 8 am to 4.30 pm.

To further enhance vaccination coverage, the civic body has started camps in 15 zones that would function round the clock. The officials said ample healthcare personnel have been deployed and vaccine doses supplied to these camps.

As per the release, special camps have been organised by the corporation for differently-abled citizens, people from lower-income groups, pregnant and lactating mothers, and those with other co-morbid conditions. The corporation had recently launched a drive to administer vaccines at home for those who are more than 80 years old.

Also, special camps for all government/private school teaching and non-teaching staff as well as students are also being conducted across the city.

Here is the list of vaccination centres that will function 24×7 in Chennai:

Zone 1 (Tiruvottiyur): Ward 11 (Tiruvottiyur Urban Community Health Centre)

Zone 2 (Manali): Ward 21 (Manali Urban Community Health Centre)

Zone 3 (Madhavaram): Ward 23 (Puzhal Urban Community Health Centre)

Zone 4 (Tondiarpet) Ward 47 (RK Nagar Urban Community Health Centre)

Zone 5 (Royapuram) Ward 58 (Perumalpet Emergency Maternity Hospital)

Zone 6 (Tiru Vi Ka Nagar) Ward 73 (Pulianthope Urban Community Health Centre)

Zone 7 (Ambattur) Ward 87 (Padi Urban Community Health Centre)

Zone 8 (Anna Nagar) Ward 97 (Ayanavaram Urban Community Health Centre)

Zone 9 (Teynampet) Ward 119 (Mirsahibpet Urban Community Health Centre)

Zone 10 (Kodambakkam) Ward 134 (Vadapalani Urban Community Health Centre)

Zone 11 (Valasaravakkam) Ward 151 (Porur Urban Community Health Centre)

Zone 12 (Alandur) Ward 160 (Alandur Urban Community Health Centre)

Zone 13 (Adyar) Ward 175 (Adyar Urban Community Health Centre)

Zone 14 (Perungudi) Ward 184 (Perungudi Urban Community Health Centre)

Zone 15 (Shollinganallur) Ward 195 (Kannagi Nagar Urban Community Health Centre)

THE TIMES OF INDIA

39 medicines added to list of essentials, prices to come down

TNN | Sep 4, 2021, 02.24 AM IST

NEW DELHI: In a move that may bring down prices of some widely used essential drugs, the government has revised the National List of Essential Medicines, adding 39 new ones under the list for proposed price cap, a source said. Those that have been added to the list include drugs to fight cancer, diabetes, tuberculosis and HIV apart from some antivirals.

The government has also deleted 16 drugs from the existing list and the final NLEM 2021 now contains 399 essential medicines, up from 376 drugs that are currently under direct price control.

The revised list, prepared by an expert committee under the Indian Council of Medical Research, was submitted to health minister Mansukh Mandaviya on Thursday. Once the list is notified by the health ministry, it will be evaluated by the Standing Committee on Affordable Medicines and Health Products (SCAMHP) to assess which of the medicines require price capping

The final price capping will be done by the National Pharmaceutical Pricing Authority based on the recommendations of the SCAMHP, headed by Niti Aayog member-health Dr V K Paul Those that have been added to the list include drugs to fight
cancer, diabetes, tuberculosis and HIV apart from some antivirals.

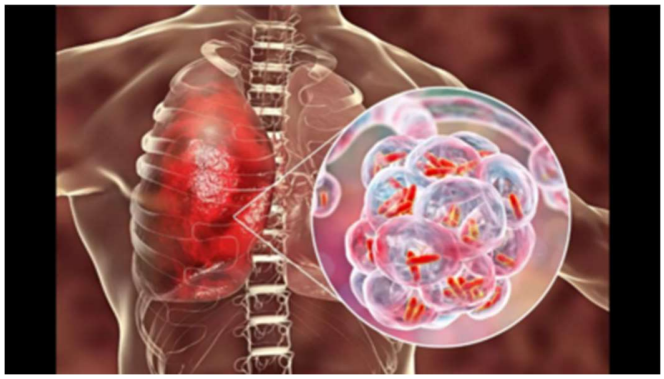
Those that have been added to the list include drugs to fight cancer, diabetes, tuberculosis and HIV apart from some antivirals.

THE TIMES OF INDIA

157 recovered from Covid affected by tuberculosis in Karnataka

TNN | Sep 3, 2021, 05.51 AM IST

BENGALURU: About 157 persons, who had recovered from Covid-19, were found to be suffering from active tuberculosis in Karnataka. That's out of the 7 lakh persons, including Covid-



India has set a 2025 targetto be free from TB (Representative Image)

recovered and their household contacts, who were screened on August 31 for TB. The health and family welfare department has been conducting a campaign to detect TB cases from August 16 among Covid-recovered individuals, who had tested positive between January and June 2021. On Thursday, state officials participated in a video conference with the union health ministry to review the progress in the fight against TB. India has set a 2025 targetto be free from TB. The union ministry has directed that all cases of severe acute respiratory infections and influenza-like illnesses must be evaluated for Covid-19.

THE TIMES OF INDIA

HIV+ man with spinal TB is operated upon, process streamed live

PTI | Aug 31, 2021, 04.19 AM IST

New Delhi: A 22-year-old HIV-positive man with spinal tuberculosis got a new lease of life after undergoing a four-hour surgery, which was streamed live as part of an international event hosted online, the organisers said on Monday. As the number of cases of spine-related issues has gone up during the ongoing Covid-19 pandemic, the Association of Spine Surgeons of India (ASSI) held a three-day programme, which included instructional courses on spine and live spine surgeries. The event was held from August 27-29. On the third day of the event, surgeons performed the four-hour live surgery, giving the patient a new lease of life, a spokesperson of the ASSI said.

He had visited the Indian Spinal Injuries Centre, where his MRI was performed after sedating him with anaesthesia and he was diagnosed with lumbosacral tuberculosis, a destructive form of tuberculosis that is more common in children and young adults, the event organisers said. The surgery was performed by a team of spine surgeons using modern technology. pti

THE TIMES OF INDIA

Tuberculosis care a financial strain on households

TNN | Aug 29, 2021, 04.57 AM IST

KOCHI: Under the national TB programme, diagnosis and treatment facilities are provided free of cost to all TB patients. However, the reality is that almost 50% TB patients are going through 'catastrophic' health expenditure due to which a patient's household is forced to cuts its basic expenses, shows a new study - "Rising healthcare expenditure on tuberculosis: Can India achieve the end TB goal?" Handling of TB cases is also crucial during the pandemic as there are concerns that Covid is flaring up TB cases in the country. India has the highest number of TB cases (27% of the global share) in the world. Currently, there are about 24,500-plus TB patients seeking treatment in the state, with two-thirds of the cases reported among the economically productive

age group (14–59 years). To examine the out-of-pocket expenditure (OOPE), healthcare burden, catastrophic health expenditure, hardship financing and impoverishment effects of TB treatment in India, the authors studied data from three rounds of national statistical surveys — 2004-05, 2013-14 and 2017-18. The present analysis helps understand the financial burden TB treatment causes on households for the past 15 years. It provides evidence to policymakers for more effective channelling of resources in order to achieve a TBfree India by 2025.

The analysis shows that OOPE, healthcare burden, hardship financing and catastrophic health expenditure are considerably higher for those utilising private hospital services and among poor, rural households. Overall, 49% of hospitalised patients and 52% of OPD patients with TB in 2018 were exposed to catastrophic healthcare expenditure. Incidentally, males were affected by TB more than females and this also has an impact on family's earning. In 2004, the ratio of men and women seeking outpatient TB care was almost the same, whereas in 2014 and 2018, it was 80% to 20%. In the case of hospitalisation, the number of male patients is higher than females. "End TB strategy milestones for 2025 and 2035 has an objective that no affected families face catastrophic costs due to TB. Based on our analysis using various rounds of NSSO, this is far from achieving a reality in India," said Denny John, adjunct assistant professor, Amrita Institute of Medical Sciences & Research Centre, and co-author of the study

THE TIMES OF INDIA

Govt hospital gets machine to detect tumour in lungs

TNN | Aug 27, 2021, 04.49 AM IST

Printed from Udaipur: In order to diagnose tumour in lungs and windpipe blockages an endobronchial ultrasound machine was installed in the Government Tuberculosis Hospital of Udaipur. This is the first machine installed in a government hospital. The cost of the machine is Rs 2.5 crore. In private laboratories, the investigations done by this machine are very expensive and may go up to Rs 35,000. With the help of this machine, the investigations will be done for as low as Rs 3,000. The senior citizens and BPL families can get their tests done free of cost. In yet another development, the Government has installed a TB disease testing TrueNat machine costing about Rs 15 lakh in Kotra and Jhadol region of the district. The machine will detect TB disease within a few hours. Earlier, patients from Kotra and other areas had to go to the district headquarters due to non-availability of this facility in local hospitals. Truenat machine is based on advanced technology, along with common TB, immunological conditions like MDR TB will also be tested and identification and treatment of TB patients will also be faster due to the availability of local level testing. With this machine TB bacteria can be detected with 100% reliability and a test report is also received within an hour.

EBUS bronchoscopy is a procedure used to diagnose different types of lung disorders, including inflammation, infections or cancer. Performed by a pulmonologist, EBUS bronchoscopy uses a flexible tube that goes through your mouth and into your windpipe and lungs.

THE TIMES OF INDIA

Patients who recovered from Covid susceptible to TB, finds survey

Aug 19, 2021, 04.00 AM IST

Printed from Mysuru: Patients who have won the battle against Covid-19 but struggling with cough lasting more than two weeks, fatigue, fever and suffered weight loss, are being advised to get themselves tested for tuberculosis (TB). A survey and subsequent analysis of the condition of those who recovered from Covid-19 indicated that their immune system had suffered considerable damage, not to mention the weakened state of their lungs, increasing the chances of their contracting TB. Tuberculosis spreads through air, and from droplets expelled by an infected patient. The sooner it is detected, the better the chances of recovering from the disease. In Mysuru, nearly 82% of the 4,232 patients in Mysuru who contracted TB recovered from the disease, while 79% of the 3,194 people who were diagnosed with TB were cured in 2020. As on Wednesday, the district has recorded 2,140 cases of tuberculosis in 2021. The district health department, meanwhile, compiled a list of more than one lakh patients who have recovered from Covid-19, sputum samples from whom are being collected and tested for TB in the course of a 15-day campaign. In Mysuru, as many as 88 samples were collected on the first day of the campaign Mysuru district TB control officer Dr Mohammed Shiraz said, "We are hoping to subject all 1.14 lakh patients who have recovered from Covid-19 across Mysuru district to a TB test. Those who contracted Covid-19 between January and June 2021 will be tested during this campaign. If any of them exhibits symptoms of TB, we will collect their sputum sample at their doorstep. We appeal to the public to cooperate with the health department personnel.

THE TIMES OF INDIA

Man kicks out pregnant wife from home over TB infection

TNN | Aug 20, 2021, 04.08 AM IST

Surat: A diamond artisan and four of his family members were booked for allegedly harassing and pushing his 19-year-old pregnant wife out of home after she was found infected with tuberculosis. According to a complaint lodged with Godadara police station on Wednesday, the woman, daughter of a migrant labourer alleged that the accused even threatened to kill her when she went back to collect her clothes after they had kicked her out sans her belongings. Police booked husband Samadhan Sonavane, his mother Sunanda, father Shivaji, sister Aasha Kapad and Usha More under various sections of Indian Penal Code for subjecting a woman to cruelty, causing hurt, intentional insult, criminal intimidation and others.

In her complainant, the woman said that she had an arranged mariage with Sonavane in Kholsar village of Jalgaon in Maharashtra on December 15, 2020. After marriage, she came to Godadara where she lived with lived with her husband and inlaws. However, five months into the marriage, her in-laws started harassing her over petty issues and started demanding for gold jewellery.

Meanwhile, in July the woman developed a tumor in her neck and her husband took her to the doctor. Tests confirmed that she was infected with TB and doctors suggested surgery. However, she went to her parental home after consulting a

doctor who told her that TB can be treated with medicine for a few months.

Upon her return on July 3, the in-laws started accusing her father of getting her married to Sonavane surreptiously without informing them about the disease. Despite knowing that she was five months pregnant, the family continued their torture and after sometime, she called her mother and left the home on July 7. She returned to collect her belongings on July 11, but the family members refused to allow her to enter the house. Sonavane even slapped her and threatened to kill her if she came again, the woman alleged. Registering an offence, the police started an investigation into the allegations.

The Indian EXPRESS ie தமிழ்

டெல்டா வகையுடன் கோவிட் - 19 தடுப்பூசிகள் எவ்வாறு செயல்படுகின்றன?

How vaccines fare with delta variant coronavirus Tamil News

டெல்டா மாறுபாட்டிற்கு எதிரான தடுப்பூசி செயல்திறனைக் குறைத்தது கண்டறியப்பட்டது.

How vaccines fare with delta variant coronavirus Tamil News : SARS-CoV2 வைரஸின் டெல்டா மாறுபாட்டின் விரைவான பரவலுக்கான சாத்தியமான விளக்கத்தில், நேச்சர் இதழில் வெளியிடப்பட்ட ஒரு ஆய்வில் இந்த குறிப்பிட்ட மாறுபாடு, தொற்று ஏற்படுவதற்கான அதிக திறனைக் கொண்டிருப்பதையும், முந்தைய நோய்த்தொற்றுகள் மூலம் பெறப்பட்ட நோயெதிர்ப்பு ரெஸ்பான்ஸை தவிர்ப்பதையும் கண்டறிந்துள்ளது.

மகாராஷ்டிராவில் முதன்முதலில் கண்டுபிடிக்கப்பட்ட டெல்டா மாறுபாடு அல்லது பி.1617.2 பரம்பரை, இந்தியாவில் மட்டுமல்ல, பல நாடுகளிலும் ஆதிக்கம் செலுத்துகிறது. உலக சுகாதார அமைப்பின் படி, டெல்டா மாறுபாடு தற்போது குறைந்தது 170 நாடுகளில் உள்ளது.

பல இந்திய நிறுவனங்கள் உட்பட சர்வதேச ஆராய்ச்சியாளர்கள் குழு நடத்திய இயற்கை ஆய்வு, மே இறுதி வரை இந்தியாவில் இருந்து சேகரிக்கப்பட்ட தரவை அடிப்படையாகக் கொண்டது. முன்கூட்டியே மதிப்பாய்வு செய்வதற்கு முன், ஜூன் மாதத்தில் முன்-அச்சு பதிப்பு கிடைக்கப்பெற்றபோது அதன் முடிவுகள் முதலில் தெரிவிக்கப்பட்டது.

முக்கிய கண்டுபிடிப்புகள் என்ன?

மீட்கப்பட்ட நபர்களிடமிருந்து, சீரம் நடுநிலைப்படுத்தும் ஆன்டிபாடிகளுக்கு டெல்டா மாறுபாடு 6 மடங்கு குறைவான உணர்திறன் கொண்டதாகவும், வைரஸின் அசல் வுஹான் ஸ்ட்ரெயினுடன் ஒப்பிடும்போது தூண்டப்பட்ட ஆன்டிபாடிகளுக்கு தடுப்பூசி 8 மடங்கு குறைவான உணர்திறன் கொண்டதாகவும் ஆய்வில் கண்டறியப்பட்டுள்ளது.

அசல் வைரஸுடன் ஒப்பிடுகையில் டெல்டா மாறுபாடு, தடுப்பூசி போடப்பட்ட மக்களிடையே 8 மடங்கு முன்னேற்ற நோய்த்தொற்றுகளை ஏற்படுத்துகிறது. மேலும், முந்தைய நோய்த்தொற்றுகளிலிருந்து மீண்டவர்களை மீண்டும் 6 மடங்கு பாதிக்கிறது. ஆய்வுக்குப் பரிசீலிக்கப்படும் தடுப்பூசிகள் அஸ்ட்ராஜெனெகா மற்றும் ஆக்ஸ்போர்டு பல்கலைக்கழகம் மற்றும் ஃபைசர் மற்றும் பயோஎன்டெக் ஆகியன உருவாக்கியவை.

கூடுதலாக, டெல்டா மாறுபாட்டில் அதிக "பிரதி மற்றும் ஸ்பைக் mediated நுழைவு" உள்ளது என்று ஆய்வு தெரிவித்தது. அதாவது, B.1.617.1 பரம்பரையுடன் ஒப்பிடுகையில், மனித உடலுக்குள் தொற்று மற்றும் பெருக்கத்திற்கான அதிக திறன் கொண்டது.

இந்த ஆய்வு, மூன்று தில்லி மருத்துவமனைகளில் முழுமையாகத் தடுப்பூசி போடப்பட்ட சுகாதாரப் பணியாளர்களிடையே 130 நோய்த்தொற்றுகளைப் பார்த்தது. மேலும், டெல்டா மாறுபாட்டிற்கு எதிரான தடுப்பூசி செயல்திறனைக் குறைத்தது கண்டறியப்பட்டது.

"டெல்டா மாறுபாடு வேகமாகப் பரவுவதையும் முந்தைய நோய்த்தொற்றுகள் அல்லது தடுப்பூசிகளிலிருந்து பாதுகாப்பைக் குறைப்பதையும் ஆய்வின் முடிவுகள் காட்டுகின்றன" என்று டெல்லியைச் சேர்ந்த சிஎஸ்ஐஆர்-இன்ஸ்டிடியூட் ஆப் ஜெனோமிக்ஸ் மற்றும் ஒருங்கிணைந்த உயிரியலின் இயக்குநரும், ஆய்வின் இணை ஆசிரியருமான அனுராக் அகர்வால் கூறினார். .

"இருப்பினும், இதில் நல்ல செய்தி என்னவென்றால், தடுப்பூசி நோயின் தீவிரத்தைக் குறைக்க வழிவகுக்கிறது" என்று அவர் கூறினார்.

டெல்டாவுக்கு எதிரான தடுப்பூசிகளின் செயல்திறன் குறித்து வேறு என்ன ஆதாரம் உள்ளது?

சமீபத்தில், உலக சுகாதார நிறுவனம், அமெரிக்காவில் இரண்டு, இங்கிலாந்தில் ஒன்று, மற்றொன்று கத்தார் என நான்கு ஆய்வுகளை மேற்கோள் காட்டியது. இவை டெல்டா வகைக்கு எதிரான தடுப்பூசிகளின் செயல்திறனைக் குறைப்பதற்கான ஒத்த ஆதாரங்களை வழங்கியுள்ளன.

உதாரணமாக, இங்கிலாந்தின் ஆய்வு, ஆல்ஃபா வேரியன்ட் ஆதிக்கத்தில் ஒப்பிடுகையில், டெல்டா மாறுபாடு நாட்டில் மிகவும் ஆதிக்கம் செலுத்திய காலத்தில், அஸ்ட்ராஜெனெகா தடுப்பூசியின் செயல்திறனைக் குறைத்தது.

தடுப்பூசிகள் எவ்வளவு முக்கியம்?

புனேயில் உள்ள இந்திய அறிவியல் கல்வி மற்றும் ஆராய்ச்சி நிறுவனத்தின் (ஐஐஎஸ்இஆர்) நோயெதிர்ப்பு நிபுணர் வினீதா பால், தடுப்பூசிகள் பயனற்றவை என்று மக்கள் நம்புவதற்கு இந்த ஆய்வு வழிவகுக்கக்கூடாது என்று சுட்டிக்காட்டினார். இந்த நேச்சர் ஆய்வு ஒரு ஆய்வக சூழலில், விட்ரோ மாதிரிகளில் மேற்கொள்ளப்பட்டது என்று அவர் சுட்டிக்காட்டினார்.

"விட்ரோ ஆய்வுகளில் இருந்து வெளிவரும் அனைத்து தரவுகளும் உடலுக்குள் உண்மையில் என்ன நடக்கிறது என்பதற்கு பதிலாக surrogate மதிப்பீடுகள் ஆகும். இதிலிருந்த வரம்பு என்னவென்றால், நடுநிலைப்படுத்தும் ஆன்டிபாடிகள் (ஆய்வில் சோதிக்கப்பட்டவை) முழு ரெஸ்பான்ஸை அளிக்காது. ஆன்டிபாடிகள் மற்றும் டி-செல் பதில்களை நடுநிலையாக்குவதன் மூலம் நோயெதிர்ப்பு பாதுகாப்பு வழங்கப்படுகிறது. தடுப்பூசி போடப்பட்ட அல்லது முன்னர் பாதிக்கப்பட்ட நபர்களில், ஆன்டிபாடிகள் மற்றும் டி-செல்கள் இரண்டும் பாதுகாப்பிற்குப் பங்களிக்கின்றன. இந்த ஆய்வு டி-செல்கள் பற்றிய தரவைக் காட்டாது. இதனால் நோயெதிர்ப்பு ரெஸ்பான்ஸின் முக்கிய கூறு கருத்தில் கொள்ளப்படாமல் போகிறது" என்று அவர் கூறினார்.

இருப்பினும், இந்த ஆய்வின் முடிவுகள் ஆச்சரியமாக இல்லை என்று பால் கூறினார்.

"தற்போது, பெரும்பாலான தொற்றுகள் டெல்டா மாறுபாட்டால் ஏற்படுகின்றன. மேலும், இது மீண்டும் தொற்று நிகழ்வுகளில் அல்லது தடுப்பூசிக்கு பிந்தைய நேரங்களில் காணப்படும் பொதுவான வைரஸ் என்பதில் ஆச்சரியமில்லை" என்று அவர் கூறினார்.

"எந்த தடுப்பூசியும் 100% பாதுகாப்பை வழங்காது. Breakthrough தொற்று அசாதாரணமானது அல்லது கேள்விப்படாதது அல்ல. இருப்பினும், தடுப்பூசி போடப்படாத அல்லது தொற்று இல்லாத குழுக்களுடன் ஒப்பிடும்போது, கடுமையான நோய் மற்றும் மருத்துவமனையில் சேர்க்கப்படுவது தடுப்பூசி போடப்பட்ட குழுக்களைக் காட்டிலும் கணிசமாகக் குறைவாக இருக்கும்" என்று அவர் கூறினார்.

புனேவில் உள்ள தேசிய ரசாயன ஆய்வகத்தின் விஞ்ஞானி அனு ரகுநாதன் கூறுகையில், டெல்டா

வகையைத் தடுக்க அதிக அளவு ஆன்டிபாடிகள் தேவைப்படும் என்று ஆய்வு கூறுகிறது.

"தடுப்பூசிகள் இன்னும் பயனுள்ளதாக இருக்கும். டெல்டா மாறுபாடு ஆன்டிபாடிகளை நடுநிலையாக்குவதற்கு குறைவான உணர்திறன் கொண்டது. டெல்டா மாறுபாட்டைத் தடுக்க முதல் அலையின் போது அசல் வைரஸுக்கு எதிரான அதே வகையான நோயெதிர்ப்பு மறுமொழியை வெளிப்படுத்த ஐந்து முதல் எட்டு மடங்கு அதிக ஆன்டிபாடிகள் தேவைப்படும் என்று அர்த்தம்" என மேலும் அவர் கூறினார்.

புதிய வகைகளைக் கையாள்வதில் முன்னோக்கிச் செல்லும் வழி என்ன?

அசல் வுஹான் வைரஸ், அடுத்தடுத்து மிகவும் ஆபத்தான ஆல்பா, பீட்டா, கப்பா மற்றும் டெல்டா வகைகளாக உருமாறியது. வைரஸ் புதிய வடிவங்களுக்கு மாறிக்கொண்டே இருக்கும். ஆனால், அனைத்து பிறழ்வுகளும் மிகவும் தீங்கு விளைவிக்கும் என்று அர்த்தமல்ல.

தடுப்பூசி அல்லது கோவிட்-பொருத்தமான ரெஸ்பான்ஸை கடைப்பிடிப்பது போன்ற நடவடிக்கைகள் மூலம் நோய்த்தொற்றுகள் பரவுவதைக் குறைப்பதே புதிய வகைகளின் தோற்றத்தைக் குறைப்பதற்கான ஒரே சிறந்த வழி என்று நிபுணர்கள் கூறுகின்றனர்.

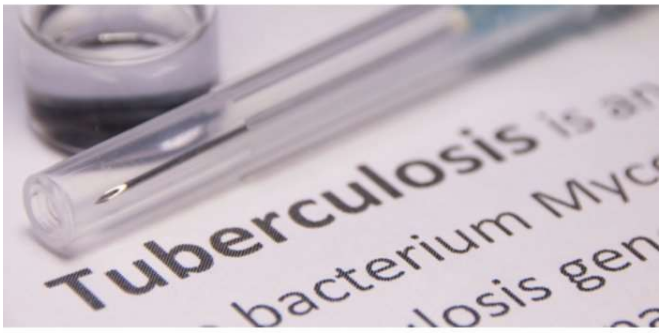
"இந்த ஆய்வைப் போலவே, புதிய மாறுபாடுகளுக்கு எதிரான ஆன்டிபாடி ரெஸ்பான்ஸின் செயல்திறனைத் தொடர்ந்து கண்காணிப்பது மற்றும் பூஸ்டர் தடுப்பூசி அளவுகள் தேவையா அல்லது தடுப்பூசிகள் புதுப்பிக்கப்பட வேண்டுமா என்பதை மதிப்பிடுவதற்கு ஒரு முக்கியமான தேவை உள்ளது. அதே நேரத்தில், புதிய வகைகளின் மரபணு கண்காணிப்பு தொடர வேண்டும்" என்று ரகுநாதன் கூறினார்.

"இது நம் தடுப்பூசிகளை மேம்படுத்தவும், புதிய, மிகவும் பயனுள்ள மருந்துகளை உருவாக்கவும் உதவும். தற்போதைய சூழலில், தடுப்பூசிகளின் கூடுதல் பூஸ்டர் ஷாட்கள் தேவைப்படலாம். கூடுதலாக, புதிய மற்றும் மிகவும் பயனுள்ள தடுப்பூசிகள் சந்தைக்கு வரும்போது, அவை அனைவருக்கும் விரைவான வேகத்தில் கிடைக்கச் செய்வதை உறுதி செய்ய வேண்டும்" என்று அவர் கூறினார்.

DH DECCAN HERALD

Tuberculosis diagnosed in 104 recovered Covid patients, 51 of their contacts

Covid-19 and TB are respiratory diseases that manifest themselves with similar symptoms of cough, fever and difficulty in breathing



Suraksha P, DHNS, Bengaluru, AUG 30 2021, 22:57 IST
UPDATED: AUG 31 2021, 00:40 IST

Karnataka, during its campaign for finding Tuberculosis (TB) cases (August 16-31) among recovered Covid individuals (who recovered between January 1 and June 31) and their household contacts has identified 155 TB cases till August 29. TB was diagnos... n 104 recovered Covid patients and 51 of their household contacts. The health department may continue the drive after August 31 to cover the rest of the Covid-recovered individuals, but the coverage was a mere 31% till August 29. During this period peripheral health workers visited the houses of recovered Covid individuals and asked for TB-specific symptoms. If found symptomatic, sputum samples were collected. The samples were tested in TB PCR labs (Truenat) in all districts of Karnataka.

Covid-19 and TB are respiratory diseases that manifest themselves with similar symptoms of cough, fever and difficulty in breathing. Studies suggest that the presence or history of TB increases the risk of SARS-CoV-2 infection and TB co-infection in increases the risk of severe Covid-19 disease. TB/SARS CoV-2 co-infection is associated with rapid and severe symptom development and disease progression, with poor outcomes for both diseases. Both diseases require early detection and treatment to improve patient outcomes and reduce transmission among contacts and within communities.

The Indian EXPRESS

To light up an otherwise dark year, US nurse creates chandelier using empty Covid vaccine vials

Netizens were left mesmerised by the beautiful piece created by Laura Weiss which she called the 'Light of Appreciation'

By: **Trends Desk** | New Delhi |
Updated: September 7, 2021 10:01:14 am

Laura Weiss is a nurse working with Boulder County Public Health

A nurse from Colorado in the United States has left netizens impressed after she created a chandelier using empty Covid vaccine vials.

Laura Weiss, a nurse working with Boulder County Public Health, used empty Covid vaccine vials to show her appreciation for the efforts of healthcare workers and volunteers who helped in vaccinating the residents of Boulder County.

Thanking Weiss for sharing her artwork with the community, the Boulder County Public Health wrote on its official Facebook page, "One of our talented Public Health Nurses, Laura Weiss, created this gorgeous piece of art using empty COVID vaccine vials."

The post had a comment from Weiss in which she referred to her creation as the 'Light of Appreciation' and said, "As a Boulder County Public Health nurse, I was witness to the inexhaustible efforts of healthcare workers and volunteers who assisted in vaccinating Boulder County residents. I was inspired to repurpose hundreds of Moderna vaccine vials and create this 'Light of Appreciation.'"

"It is meant to honour and show appreciation for all those who have helped keep people alive, either by getting the vaccine to protect themselves and others, caring for those suffering from COVID or by assisting in the vaccination effort. We are all connected in this effort. After so much loss, uncertainty, and anxiety, may the light bring hope for a brighter future."

Talking to CNN, Weiss said she was a retired nurse and had been asked by Boulder County Public Health to assist in vaccination. "I had noticed all these hundreds and hundreds of empty vaccine vials that were otherwise going to be wasted, and I thought they were just really beautiful and wanted to do something significant and meaningful with them."

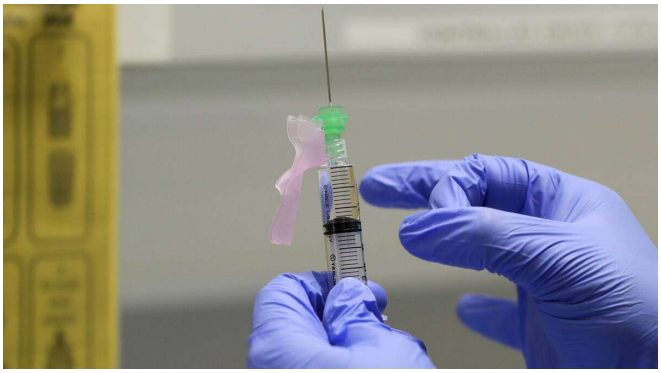
Weiss added that she wanted to do something with light since she felt that it had been a dark and challenging year for many. Netizens appreciated her creativity and were left mesmerised by its beauty.

The Indian EXPRESS

DCGI approves Hetero's Tocilizumab for emergency use against Covid-19

Tocilizumab, which is a biosimilar version of Roche's Actemra/RoActemra, would be available in the market by September end.

By: **Express Web Desk** | New Delhi |
September 6, 2021 3:55:36 pm



Hetero's associate company Hetero Healthcare will market its biosimilar version of Tocilizumab under the brand name Tocira.

The Drugs Controller General of India (DCGI) has approved emergency use of drug firm Hetero's Tocilizumab for treatment of hospitalised adults suffering from Covid-19, said Hetero in a statement.

Hetero's statement added that medical practitioners would be able to use the drug for treating Covid-19 in adults who receive systemic corticosteroids, and even those who require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation.

B Partha Saradhi Reddy, Hetero Group Chairman said, "This approval is extremely crucial for supply security in India considering a global shortage of Tocilizumab. We will be working closely with the government to ensure equitable distribution."

The drug firm's Tocilizumab, which is a biosimilar version of Roche's Actemra/RoActemra, would be available in the market by September end.

Hetero's associate company Hetero Healthcare will market its biosimilar version of Tocilizumab under the brand name Tocira, PTI reported. The drug would be manufactured by Hetero Biopharma, Hetero's biologics arm, at its facility at Jadcherla in Hyderabad.

The Indian EXPRESS

Allow Covishield second dose scheduling after 4 weeks for paid jabs: Kerala HC to Centre

A writ petition contended that Kitex purchased Covishield doses for its workers. However, they could not be administered as the Centre insisted on the interval of 12-16 weeks and registration for the same on the Co-Win portal.

Written by **Vishnu Varma** | Kochi |
Updated: September 6, 2021 10:45:20 pm

The Kerala High Court on Monday directed the Centre to make changes on the Co-Win

The court however said that it has not considered the same question in the light of the free vaccine distributed by the government. (File photo)

vaccination portal to enable scheduling of the second dose of Covishield vaccine after four weeks of the first dose for those who are willing to pay for it.

The single bench of Justice PB Suresh Kumar examined whether a person covered by the national vaccination programme is entitled to choose between early protection and better protection from Covid-19 infection in the matter of accepting paid vaccines.

"If the government can permit persons who are intending to travel abroad to exercise a choice between early protection and better protection from Covid-19 infection, there is absolutely no reason why the same privilege shall not be extended to others who want early protection in connection with their employment, education etc," the court order read.

"Further, the stand taken by the Central government that the court shall not grant the relief sought for by the petitioners, for they have not approached the Central government, cannot be accepted, for as indicated, the very premise on which the present writ petition is instituted is that the decision of the government in providing relaxation in the protocol regarding administration of second dose of vaccine to certain classes of persons alone amounts to discrimination and the directions sought are directions to extend to the petitioners also the same relief."

The court, however, said that it has not considered the same question in the light of the free vaccine distributed by the government.

The court was hearing a writ petition filed by Kitex Garments Ltd and Kitex Childrenswear Ltd, two garment firms based in Ernakulam, Kerala. The petitioners contended that they had purchased Covishield vaccine doses for their over 10,000 workers and their families. However, they were unable to administer the second dose to the beneficiaries as the Centre insisted on the interval of 12-16 weeks and registration for the same on the Co-Win portal.

Healio

Glycemic changes common in patients with tuberculosis but no diabetes

August 30, 2021 | 1 min read

Glycemic changes may play an important role in response to treatment among patients with tuberculosis who do not have diabetes, according to data published in the *American Journal of Respiratory Critical Care Medicine*.

"Several studies have found that patients with newly-diagnosed tuberculosis often have abnormal and inconsistent glycemic measurements when tuberculosis is diagnosed, during tuberculosis treatment and after treatment," **Qiao Liu, MD,** with the department of chronic communicable disease at the CDC of

Jiangsu Province and the department of epidemiology at the School of Public Health at Nanjing Medical University, China, and colleagues wrote. "Distinct glycemic trajectories after tuberculosis diagnosis are not well characterized and whether patients with stress hyperglycemia have poor treatment outcomes is not known."

Researchers identified 500 patients (median age, 42 years; 65.2% men) with newly-diagnosed, drug-susceptible tuberculosis who had at least three fasting plasma glucose tests at the time of diagnosis and during the third and sixth months of treatment. At 2 and 4 months post-treatment, all patients underwent an additional fasting plasma glucose test.

In the cohort, 405 patients had five fasting plasma glucose tests from tuberculosis diagnosis to post-treatment and 95 participants had three tests.

Researchers observed the following distinct glycemic trajectories from time of tuberculosis diagnosis to post-treatment:

- consistently normal glycemic testing results (43%);
- transient hyperglycemia (24%);
- erratic glycemic instability (12%);
- diabetes (16%); and
- consistent hyperglycemia without diabetes (6%)

Patients with transient hyperglycemia were more likely to experience treatment failure (adjusted OR = 4.20; 95% CI, 1.57-11.25; *P* = .004) or erratic glycemic instability (adjusted OR = 5.98; 95% CI, 2.00-17.87; *P* = .001) compared with those with a consistently normal glycemic trajectory. Patients with diabetes also had an increased risk for treatment failure (adjusted OR = 6.56; 95% CI, 2.22-19.35; *P* = .001); this risk was modified by glycemic control and metformin.

"Glycemic changes, regardless of diabetes status, may be an important marker for the patient response to tuberculosis treatment," the researchers wrote. "Understanding potential mechanisms for these changes may be useful for providing risk-stratified approaches to antituberculosis treatment."

SO:
https://www.healio.com/news/pulmonology/20210827/glycemic-changes-common-in-patients-with-tuberculosis-but-no-diabetes

Substantial public investments in GeneXpert underscore need for affordable pricing

PLOS ONE publishes TAG's comprehensive analysis of public investments in the development of rapid technology for diagnosing infectious diseases.

August 31, 2021 – Treatment Action Group (TAG)'s comprehensive analysis found that the public invested at least $252 million USD in the research and development (R&D) of GeneXpert. GeneXpert cartridges and instruments are used to diagnose tuberculosis (TB), HIV, viral hepatitis, sexually transmitted infections, COVID-19, and other infections. This substantial public

investment stands in stark contrast to the lack of affordable pricing and favorable service and

maintenance terms from the diagnostics company Cepheid. The finding is detailed in the new *PLOS ONE* study, "**Public Investments in the Development of GeneXpert Molecular Diagnostic Technology**."

"This analysis is, to our knowledge, the only published study to quantify, in detail, public sector investments in the development of a diagnostic technology," said Dr. Dzintars Gotham, the principal researcher and author of the study. "Where there are substantial public investments in developing a health technology, it is important to examine whether the public sector has received adequate returns for its investments."

The $252 million figure accounts for early development at U.S. government labs, research funded by the U.S. National Institutes of Health, U.S. government grants, R&D tax credits, and funding from non-profit and philanthropic sources, but given the limited data available in the public domain, this figure should be considered a conservative estimate.

"Earlier analysis by Médecins Sans Frontières (MSF) showed that it costs Cepheid less than $5 to produce one test while Cepheid is charging low- and middle-income countries a mark-up of at least 100% for TB tests and 300% for COVID-19 tests," said Stijn Deborggraeve, Diagnostics Advisor for Infectious Diseases at MSF Access Campaign and co-author of the new PLOS ONE study. "Cepheid's profiteering during the COVID-19 pandemic is unacceptable, especially considering the massive amount of public funds that Cepheid received to develop the GeneXpert technology and roll out the system in low- and middle-income countries."

"This study brings to light the extensive public funding that subsidized Cepheid's R&D costs and further supports global demands for the company to make GeneXpert tests available at fair and equitable prices that reflect the cost of production plus a reasonable profit markup, with volume-based price reductions," said David Branigan, TB Project Officer at Treatment Action Group and co-author of the PLOS ONE study.

This analysis highlights the importance of ensuring that public funding for health product development comes with conditions that promote transparency and equitable access. It complements the results of an earlier study, which found that public investments in the development of the life-saving TB drug bedaquiline far exceeded those of Johnson & Johnson, the proprietor of the drug; meanwhile the price of bedaquiline remains a barrier to scaling up treatment coverage.

About GeneXpert

GeneXpert tests are rapid, accurate, and automated diagnostic tests, making them ideal for use in decentralized settings without extensive laboratory infrastructure. GeneXpert instruments are priced at $17,000 per four-module unit, service and maintenance plans cost approximately $2,000 to $3,000 annually, and individual test cartridges are currently priced from $9.98 (TB) to $19.80 (COVID-19) per test.

An independent cost-of-goods-sold analysis commissioned by MSF Access

Campaign found that it costs Cepheid from $2.95 to $4.64 to produce each test cartridge at annual volumes of 10 million, which was exceeded in 2017 for TB tests alone. The civil society Time for $5 Coalition has demanded Cepheid reduce the price of GeneXpert tests to $5, inclusive of service and maintenance, across diseases.

About Treatment Action Group

Treatment Action Group (TAG) is an independent, activist, and community-based research and policy think tank committed to racial, gender, and LGBTQ+ equity; social justice; and liberation, fighting to end HIV, tuberculosis (TB), and hepatitis C virus (HCV). TAG catalyzes open collective action by affected communities, scientists, and policymakers to ensure that all people living with or impacted by HIV, TB, or HCV — especially communities of color and other marginalized communities experiencing inequities — receive life-saving prevention, diagnosis, treatment, care, and information. We are science-based activists working to expand and accelerate vital research and effective community engagement with research and policy institutions for an end to the HIV, TB, and HCV pandemics.

About MSF Access Campaign

The Access Campaign is part of Médecins Sans Frontières (MSF), an international, independent, medical humanitarian organisation. Our work is rooted in MSF's medical operations and supports people in our projects and beyond. We bring down barriers that keep people from getting the treatment they need to stay alive and healthy. We advocate for effective drugs, tests and vaccines that are: available, affordable, suited to the people we care for, and adapted to the places where they live.
So:
https://www.tbonline.info/posts/2021/9/10/substantial-public-investments-genexpert-underscor/

UCSF School of Pharmacy

Data-driven drug dosing speeds tuberculosis treatment to four months

UCSF research leads to breakthrough in treating the global pandemic

By Levi Gadye / Mon Aug 30, 2021

It's a disease of the lungs. It spreads through the air. It can kill millions in a year. And it's the cause of an ongoing pandemic.

The disease isn't COVID-19. It is tuberculosis (TB). Each year, nearly ten million people are diagnosed with TB and over a million die. Prior to COVID, TB was the deadliest infectious disease on the planet. Yet the gold standard for treatment is a prolonged, daily regimen of multiple antibiotics, taken for a minimum of six months, that hasn't changed in decades—a regimen that places a huge burden on patients already struggling to make ends meet.

A clinical trial of new treatment regimens, led in part by researchers at UCSF, recently demonstrated that a more potent combination of antibiotics could shorten the duration of treatment for TB, giving patients back two months of their lives and improving their chances of taking every dose. The results from the trial were published on May 6 in the New England Journal of Medicine.

"The existing treatment for TB is six months long, it's hard, and there are a lot of issues with it," said UCSF School of Pharmacy faculty member Rada Savic, PhD, whose work on TB drug pharmacology served as the basis for the trial.

"The entire drug development process has focused for 40 years to try to shorten it, many trials have failed, and this is the first success."

Findings from the trial were so robust that the World Health Organization (WHO) endorsed the regimen this summer, enabling health care providers and TB programs around the world to use it.

"This landmark trial was the largest randomized, registration-quality trial of new regimens for pulmonary TB to date," said Payam Nahid, MD, MPH, who served as the clinical trial protocol co-chair and serves as director of the UCSF Center for Tuberculosis. "Rada's thorough data analyses gave the team insight into how to optimize the dosages and duration of the regimen, and it worked. It's a model for others to follow in infectious disease."

Advances in TB treatment stalled in the 1980s

A sanatorium in Vianden, Luxembourg. Prior to the advent of antibiotic treatments, sanatoriums were used to quarantine patients with TB.

TB is one of the oldest infectious diseases known to afflict humans, with tests of human remains from 9,000 years ago turning up TB positive.

But well into the 20th century, the medical field could do little for TB patients. In some countries, these patients were encouraged or even forced to quarantine in sanatoriums—facilities isolated from the population—that did nothing to treat the disease.

Vaccines and antibiotics against TB first emerged around the turn of the century but struggled to gain widespread use. A critical advance was made in the late 1940s when the British Medical Research Council methodically tested two antibiotics in patients with TB without knowing which patients were receiving which drugs—the first-ever randomized clinical trial.

The trial showed that treating TB with two drugs at once was much more effective than with either drug alone. But the combination caused debilitating side effects and required a commitment of two years of daily pills. Miss a few doses, and the infection would come roaring back.

Over time, more-potent antibiotics were substituted into the drug cocktail, reducing the duration of treatment from 24 to 12 to 9 to 8 to 6 months, according to Nahid. But that progress stalled 40 years ago, saddling millions of patients with half a year on the drugs.

"We've heard from TB survivors how a reduction in duration would be a huge benefit to them, to get back to their lives, to get back to being comfortable around their family, their children, their friends," said Nahid.

Shortening the duration of the TB drug regimen also promised to free up some of the scarce resources used in the fight against the disease, which today is most prevalent in countries where health care is not always readily available. But clinical trials even in the late 2000s continued to come up short.

Following the data to the most effective dose

The successful clinical trial, known as Study 31/A5349, benefited from the lessons learned from recent, failed trials, combined with rigorous

pharmacological modeling and data integration from the Savic Lab.

Rada Savic, PhD, scrutinized data from prior, failed clinical trials of drug regimens for TB and used computational models to design a faster treatment for the disease.

Savic, a faculty member in the Department of Bioengineering and Therapeutic Sciences, a joint department of the Schools of Pharmacy and Medicine, is an expert in pharmacokinetics, or the study of how drugs move through the body. When it came to the six-month, four-drug regimen used to treat TB, experience had taught her to be skeptical that the drugs were being used to their greatest potential.

The six-month regimen had been designed in the 1970s around the lowest effective dose of its cornerstone antibiotic, rifampin, giving patients just enough medication to beat the disease. But TB is a disease in which the offending bacteria multiply out of control even in the presence of antibiotics, and many patients remain sick for years despite treatment.

Previous trials had attempted to replace rifampin with a more potent drug, rifapentine. Some of these trials with rifapentine made the dosing more intermittent—weekly, instead of daily—or upped the dosages in the final few months of the regimen. But none were as effective as the existing regimen with rifampin.

Savic wondered whether rifapentine could actually be given at higher doses, overwhelming the infection without hurting patients—a safe and more effective dose. Starting in 2012, Savic and her team reanalyzed the results from these failed clinical trials of rifapentine and made a pivotal discovery.

"When we rearranged the data, combining patients according to their raw doses of rifapentine, we started seeing beautiful dose responses to the drug," said Savic. "When we went further and looked into pharmacokinetics and plasma levels [in the bloodstream], we again saw that patients with the highest drug exposure have the best response and are most likely to recover."

Drugs are commonly dosed relative to the body weight of a patient—the smaller the patient, the thinking goes, the lower the dose. Yet in the field of pharmacokinetics, it's well known that this logic does not always hold up against the complexity of the human body, as borne out by Savic's work. The original analyses had missed this because they were analyzed according to patients' relative dosages of the drug—not their absolute dosages.

"I was not surprised by my findings," said Savic. "As a pharmacologist and pharmacist, I know there are better ways for finding the right dose, and our analysis was a textbook example of using the right approach to solve a dosing problem."

In addition to testing an optimized dose of rifapentine, the team also sought to test a substitution for another drug in the cocktail, replacing ethambutol with the stronger moxifloxacin to account for patients with more persistent cases of TB infection lodged deep in the lungs. Like the rifapentine substitution, the moxifloxacin substitution had a body of evidence, from animal models and computer simulations, to back it.

Savic next needed to prove that these proposed changes in TB treatment could actually provide an effective and expedient cure in the real world.

Getting the largest TB trial off the ground

In 2013, Savic joined forces with Nahid, who directs the UCSF Center for Tuberculosis and has led a wide variety of research and policy efforts to combat TB both for UCSF and the WHO, including clinical trials of new drug regimens.

Payam Nahid, MD, MPH, director of the UCSF Center for Tuberculosis, co-led the successful clinical trial of new drug regimens for tuberculosis.

Nahid had conducted early phases of clinical trials for TB over the years, but the strength of Savic's work lent new energy to get a large, phase 3 clinical trial for a new TB regimen off the ground. Phase 3 clinical trials represent the final bar that a treatment must clear in order to be approved. They involve hundreds to thousands of patients so there must be high confidence in the safety and effectiveness of a new therapy—a lot is on the line.

"The sophistication with pharmacometric, computational approaches, brought in by Rada's team in collaboration with others, allowed for a rich dialogue in the design of the trial and the selection of the regimens, and made it easier to get our international colleagues on board," said Nahid.

As investigators in the CDC-funded TB Trials Consortium (TBTC) and the NIH-funded AIDS Clinical Trials Group (ACTG), Nahid and Savic were able to engage with both groups' connections to TB experts and clinics around the world. The two worked collaboratively with a diverse international protocol team, convened by the TBTC and ACTG, to design and execute what they hoped would be a watershed trial.

"I've witnessed a lot of excellent pharmacokinetic work that doesn't move the needle for patients," said Savic. "My weapon was to keep showing the data to keep making the point, to build trust with the clinicians, to communicate our science in a way that people will accept and recognize the value."

In designing Study 31/A5349, the growing village of experts considered that any eventual new therapy would be destined for a diverse population of millions of people with TB.

"We sought to put in features to make the trial as close to the real world as possible, while retaining the essential components that are needed for FDA approval," said Nahid. "We allowed enrollment down to adolescence, 12 years and older, as well as patients living with advanced HIV, two populations that the most recent trials had overlooked."

In January 2016, the trial began to enroll participants with TB and the first patients began their months of treatment.

From computer model to WHO recommendation

Ultimately 2,516 patients were enrolled across 34 test sites on four continents and were randomly assigned one of three regimens:

1. A control, six-month regimen of rifampin, isoniazid, pyrazinamide, and ethambutol.
2. A four-month regimen of rifapentine, isoniazid, pyrazinamide, and ethambutol.

3. A four-month regimen of rifapentine, isoniazid, pyrazinamide, and moxifloxacin.

The trial followed each patient for 18 months to track whether they stayed TB-free for at least a year after the end of treatment.

The results bore out Savic's predictions: the four-month regimen with a high dose of rifapentine along with moxifloxacin was shown to be just as effective and safe as the existing six-month regimen.

A Study 31/A5349 clinical trial participant, left, attends a follow-up appointment at a Vietnam National TB Programme and UCSF-partnered district health center, Hanoi, Vietnam.

The results of the trial were so convincing that the World Health Organization convened a panel to review the data. In a rapid communication released in June, the WHO noted:

- The 4-month regimen, which is shorter, effective and all-oral, would be a preference for many patients and also national TB programmes, allowing faster cure and easing the burden on both patients and the healthcare system... Shortened treatment has the potential to improve adherence and reduce patient and health system costs.

It will take years for the new regimen to become routine in clinics across the globe. TB has long been a disease of poverty, one that divides society by class and offers little to no financial incentive for industry to invest in research and development. But with the nod from the WHO, change is finally here for millions with TB.

For Savic and Nahid, the work continues. They are now exploring how to further reduce the duration to two-month regimens.

"We want to take the same regimen, with the same drugs, and give it only for two months in easy-to-treat patients who can be identified with simple field tests," said Savic. "We have the evidence this will work, and we are working on a new round of clinical trials, rallying our collaborators again."

Nahid is optimistic that the professional connections forged during Study 31/A5349 and the data-driven approach to drug dosing and regimen optimization will inspire more bold clinical trials for diseases that, like TB, continue to plague humanity.

"It's been a shared common goal of so many of us to finally improve our therapies for TB," said Nahid. "It took over a decade, but we said, 'Let's all come together and roll up our sleeves,' even with limited funding, and we couldn't be prouder of the result."

So: https://pharmacy.ucsf.edu/news/2021/08/data-driven-drug-dosing-speeds-tuberculosis-treatment-four-months

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