INDIAN COUNCIL OF MEDICAL RESEARCH
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VIROdesk
Newsletter

Volume 1, Issue 2
July-September 2021

DIRECTOR'S MESSAGE

We are already halfway through 2021, and events are moving along at such a rapid pace that we hardly have time to stop and think! However, unless we take time out to ponder and plan we will be unable to work effectively and utilize our resources optimally. We are pleased to bring you the second issue of the NIV-Newsletter which features mainly on the World Hepatitis Day. World Hepatitis Day is observed each year on 28th July to raise awareness on viral hepatitis. This is, to commemorate the birthday of Dr. Baruch Blumberg (1925–2011) who discovered the hepatitis B virus and developed the first hepatitis B vaccine. This year's theme is "**Hepatitis Can't Wait**". With a person dying every 30 seconds from a hepatitis related illness even in the current COVID-19 crisis – we can't wait to act on viral hepatitis. In 2014, The World Health Organization (WHO) established the Global Hepatitis Programme which helped in making the first direct-acting antivirals for the treatment of Hepatitis C virus. WHO set out to produce treatment guidelines for managing hepatitis and started to work directly with countries (more than 80 till today) and multiple stakeholders to develop their national programmes. ICMR-NIV has made significant contributions in the understanding of viral hepatitis and also in developing molecular diagnostics with high sensitivity and specificity. Efforts towards the development of a reliable Hepatitis E vaccine candidate are also ongoing at the institute. There have been some milestone research contributions from the scientists of the ICMR-NIV hepatitis group.

We have some interesting sections, which include a walk-the-talk with Dr. Vidya Arankalle about her research journey in ICMR-NIV, development of an RT-LAMP based diagnostic assay for SARS-CoV-2 infection, various activities related to COVID-19 and Polio from our Mumbai unit, our recent publications on SARS-CoV-2 variants, the obituary of Dr. B. Lalitha Rao, and the Students' Corner. I hope you enjoy this issue of the newsletter and would welcome any feedback, articles or letters from you. Wishing you and your families, safe days ahead!

Happy Reading!

Priya Abraham

Jai Hind!

Viral hepatitis-Challenges faced by a hugely diversified country

Dr. Avinash Deoshatwar, Dr. Shilpa Tomar

In terms of deaths and disability-adjusted life years [DALYs], viral hepatitis causes more burden on humanity than many other infections like HIV, tuberculosis, or malaria. Moreover, unlike many other infectious diseases, the burden of viral hepatitis has increased globally from 1990 to 2013 (*Stanaway et al., 2016*) and probably beyond as well. The Sustainable Development Goals (SDG) mentioned a target to 'End the epidemics of HIV, tuberculosis and malaria' by 2030, but only to 'combat viral hepatitis' (*Wiktor et al., 2016*). The very fact, that the hepatitis fraternity had to make conscious efforts of advocacy to persuade the WHO to declare the goal of 'Elimination of viral hepatitis by 2030', shows that viral hepatitis as a public health issue is not given due attention. In India, efficient surveillance systems to assess the burden of viral hepatitis are lacking. Water-borne (Hepatitis A and E viruses) and blood-borne (Hepatitis B, C and D) hepatitis viruses remain major public health concerns in India; however, accurate estimates about their disease burden are lacking. For HEV, burden estimates are available in the form of seroprevalence; 27.15% [95% CI – 19.3 to 35.7] (*Li et al., 2020*).

India falls in the 'intermediate endemicity' category for HBV and has an estimated 40 million chronically infected people, which constitute approximately 11% of the estimated global burden. For HCV infection, the estimated prevalence in India is about 0.5–1.5% *(Dhiman et al., 2016)* though regional variations have been reported. The WHO documents on 'Elimination of viral hepatitis' are restricted to the blood-borne hepatitis viruses leaving the elimination of water-borne hepatitis viruses to the individual countries.

ICMR-NIV has made seminal contributions to the understanding of viral hepatitis in India. Outbreaks of blood-borne hepatitis viruses [hepatitis B outbreak in Modasa, Gujarat 2012 and hepatitis C outbreak in Jammu & Kashmir 2013], which are very rare phenomena, were successfully investigated; the causative agents were identified and control measures were suggested. Additionally, ICMR-NIV has been providing technical guidance to the network of Viral Research and Diagnostic Laboratories on viral hepatitis which has generated valuable information on the disease in various parts of the country.

Milestones in Viral Hepatitis Research in ICMR-NIV, Pune

Dr. Anuradha Tripathy, Dr. Kavita Lole

Genomic characterization of viruses, molecular epidemiology and evolution

- Identification of hepatitis E virus (HEV), as the cause of the majority of waterborne NANB epidemics, starting from the historic 1955 epidemic in New Delhi
- Identification of a new subgenotype of HCV, 3i accepted by International Committee on Taxonomy of Viruses (2008).
- Identification of prevalence of HEV genotype-1 in humans and genotype-4 in pigs in India
- First full genome sequencing of HEV genotype 1 (human) and genotype 4 (swine) viruses from India (2002)
- Documentation of the new 9th HBV genotype “I” in India (2014)
- Characterization of simian HAV (genotype V), recovered from a captive rhesus monkey
- Reported the predominance of genotype IIIA of HAV in India since 1981
- Detection of a newly discovered KIs virus in India (2017)

Epidemiology, virus transmission and animal studies

- Determination of prevalence of HAV, HEV, HBV and HCV by age-stratified serosurveys in both urban and rural populations
- Periodic serosurveys by NIV revealed epidemiological dynamics of HAV and aided prediction of HAV epidemics in India
- By serosurveys in at-risk populations generated knowledge for decision making on vaccination policies
- Reported Hepatitis G virus (HGV) and Transfusion transmitted virus (TTV) to be of no significance in causing liver diseases
- Detection of anti-HEV antibodies in various animal sera suggested possible zoonotic transmission of the virus
- Possibility of transfusion-associated hepatitis E, presence of virus seen in blood units from donors
- Experimental HEV infection in rhesus monkeys to study the natural course of the disease and its possible utility in vaccine studies
- Demonstrated the beneficial effect of immune serum globulins (ISG) to pregnant women from hepatitis E

infection that suggested testing of high-titred ISG for protecting pregnant women during epidemics of hepatitis E

- Reported persistence of anti-HEV antibodies for 30 years post HEV infection in hepatitis E recovered individuals
- Screening of blood donors for HEV prevalence & occult HBV infection demonstrated the need to consider cost-effective evaluation for pooled HEV RNA testing in blood banks in HEV endemic regions & also pooled HBV DNA screening

Development of diagnostic tests

Serological

- Development of ELISA for detection of anti-HBs antibody, as well as for IgM and IgG antibodies against HAV and HEV

Molecular

- Diagnostic PCR assays for all hepatitis viruses (HAV, HBV, HCV, HEV, HGV & TTV)
- Genotyping and phylogenetic analyses based on partial and full genome sequences of hepatitis viruses
- Standardization of TaqMan assays for the detection and quantitation of HAV, HBV, HCV, HEV for diagnosis/research purposes
- Development of a method for hepatitis E virus concentration from water samples and detection by RT-PCR

Development of candidate vaccines

- Hepatitis E: successful pre-clinical studies in rhesus monkeys
- Immunogenicity studies in mice and pre-clinical study in rhesus monkeys done for combination vaccine (HBV+HEV)
- Recombinant proteins based HCV candidate vaccines tested in mice

Molecular virology

- Determined the role of HEV ORF1 encoded non-structural proteins replicase, helicase, protease and macrodomain in HEV replication
- Development of infectious clones of HEV, HBV and HCV and their utilization in studying molecular events during in vitro virus replication, host-virus interactions and antiviral testing
- Development of HAV VLPs and utility in diagnostic ELISA
- Determined cellular innate antiviral responses during HEV infection
- Involvement of miRNA 122 in HEV replication
- Induction of cellular autophagy by HEV for efficient replication

Biomarker Studies

- Documentation of pivotal protective role of chemokines CCL4 and Natural Killer T cells in acute self-limiting Hepatitis B infections
- Demonstrated pro-inflammatory IL-1α & soluble IL-2Rα as markers of inflammation in hepatitis E
- Established the protective role of T regulatory cells (Tregs) in self-limiting hepatitis E virus infection
- Demonstrated the putative role of TGF-β1 as a possible supplement for boosting Treg cell response and subsequent protection from the fatal outcome in patients with fulminant hepatitis E
- Identified the importance of epitopes presented by HLA-DRB1* 11 towards induction of protective immune response in hepatitis E and hepatitis C infections

An interview with Dr. Vidya A. Arankalle

(Former Group Leader, Hepatitis Group, ICMR-NIV, Pune)

1. What inspired you to pursue research, and virology? Please share some of your early-career influences.

After obtaining my scholarship, I joined Virology Department of Haffkine Institute for my Ph.D. under the tutelage of Dr. Gaitonde, the then Director, Haffkine Institute. He was a pharmacologist and my topic was in Virology (rabies). Thus, application of knowledge to a different field with absolute analytical mind and clarity was my first lesson. He was a busy person and hence students had to take responsibility in planning the experiments and interpretation of results.

2. How were your initial years and the work environment in NIV? Could you summarize some of the focus areas in your research career, and the major achievements?

When I joined NIV in September 1981, the major focus of research was arboviruses. New viruses causing Influenza and hepatitis were recent additions. Hepatitis was a group of young enthusiasts, ready to work all the time. We had space constraints but not funds. Through proper planning and execution and with support from then directors, we were able to put in all the efforts to achieve our goals.

During my entire career at NIV, we explored several areas of enterically transmitted non-A, non-B viral hepatitis (ET-NANBH, termed

hepatitis E later), mainly because of our involvement in epidemic investigations. Initial years were devoted to the identification of virus in faecal samples. We stood outside toilets with liquid nitrogen tank so that we don't miss the chance of getting the virus. We worked on all aspects of hepatitis E - first visualization of the virus in the country, development of diagnostic tests, understanding transmission and pathogenesis with special reference to pregnancy, characterization of viral genomes, genomic variations, identification of swine HEV in India, transmission and challenge experiments in rhesus monkeys and development of an effective vaccine with preclinical studies in rhesus monkeys. We also pursued another non-A, non-B virus (Hepatitis C Virus, HCV) and identified novel Hepatitis B virus (HBV) and HCV genotypes.

With the emergence / re-emergence of viruses such as Chandipura, Chikungunya, Nipah, H5N1, swine H1N1 we contributed in various spheres.

3. How do hepatotropic viruses impact the functioning of this vital organ? What are the current challenges in studying viral infections of the liver?

To add to the complexity of liver, the five major human hepatitis viruses belonging to different viral families (Hepatitis A, E and C viruses are RNA viruses, HBV is a unique DNA virus while Hepatitis D virus is a defective RNA virus) have different disease presentations and biology. Emergence of mutants and development of drug resistance are additional challenges for the treatment of chronic hepatitis.

The lack of suitable cell culture systems, small laboratory animal models, requirement of non-human primates and growing restriction on the use of such animals have always been a limitation. Understanding the pathogenesis in relation to variable factors remains a major challenge. However, with formulation of studies following brainstorming sessions involving experts from different fields, proper planning with minute details, resource availability and timely execution they can be addressed.

4. How do you see the recent advances in the diagnosis, treatment and control of Hepatitis B and C infections in India? Has there been any underutilized platform or technology in studying viral infections of the liver?

Recent advances in the diagnosis and treatment of hepatitis B and C are worth applauding. Hepatitis B vaccination and advances in the treatment of both the diseases have certainly helped in controlling the infections and improving quality of life of infected people.

However, such benefits are remote from the large rural population including many Indian tribes and the implementation of effective measures should be strengthened to protect them. The application of various OMICS to the research in viral hepatitis is far from desirable.

5. How do you see the impact of COVID-19 on viral hepatitis in India? Do you see any parallels between the disease biology of COVID-19 and viral hepatitis?

COVID-19 has impacted all the diseases including viral hepatitis. Due to the scare of infection with SARS-CoV-2 and imposed restrictions, unless in emergency, people preferred to stay home than visit a doctor. Self-recovering hepatitis A and E infections remained unnoticed. Though scanty reports are available globally, chronic viral hepatitis/carrier state as a comorbidity for severe COVID-19 needs to be evaluated in India.

6. How would you place the role of good mentorship in science and research?

Good mentorship plays an important role in the initial development of a researcher. Once the right qualities are imbibed, one would expect fair and quality research. Based on the experiences encountered, every researcher will develop her/his own qualities. At later timepoints, healthy and open discussions with seniors would be helpful.

7. What would be your message to the future generations of researchers and students in virology?

Virology is an exciting field with ever-growing challenges. Whichever area of biomedical research you may be interested in, virology will provide you the ideal platform to explore. Come and Contribute! Your participation is most valuable.

Dr. Vidya A. Arankalle is currently associated with the Interactive Research School For Health Affairs, Pune.

Scientific Desk

Neutralization of Beta and Delta variant with sera of COVID-19 recovered cases and vaccinees of inactivated COVID-19 vaccine BBV152/Covaxin

Yadav PD, Sapkal GN, Ella R, Sahay RR, Nyayanit DA, Patil DY, Deshpande G, Shete AM, Gupta N, Mohan VK and Abraham P. Neutralization of Beta and Delta variant with sera of COVID-19 recovered cases and vaccinees of inactivated COVID-19 vaccine BBV152/Covaxin. **Journal of Travel Medicine** 2021 Jul 6 : taab104. Published online 2021 Jul 6. doi: 10.1093/jtm/taab104

(**Summary:** SARS-CoV-2 variants are emerging at a faster rate and causing serious public health threats because of its association with higher transmissibility and potential immune escape properties. In the present study, authors have tried to understand the neutralization properties of the sera of Covaxin vaccinees and COVID-19 recovered individuals against the variants of concern such as Beta and Delta by live virus neutralization assay, and compared with the prototype B.1 (D614G). For this, serum samples of 20 COVID-19 recovered cases post 5–20 weeks of infection and 17 vaccinees 28 days after two doses of Covaxin were used. The geometric mean titre for the vaccinees sera against B.1, Beta and Delta variants were found to be 187.5, 61.57 and 68.97, respectively and for the sera of the recovered individuals as 97.8, 29.6 and 21.2, respectively. The sera of vaccinees and recovered cases showed a significant reduction in the neutralization titre for Beta and Delta variants in comparison to B.1. The study demonstrated the neutralization potential of Covaxin against Beta and Delta variants despite a reduction in the neutralization titers.)

SARS-CoV-2 Spike Mutations, L452R, T478K, E484Q and P681R, in the Second Wave of COVID-19 in Maharashtra, India

Cherian S, Potdar V, Jadhav S, Yadav PD, Gupta N, Das M, et al. SARS-CoV-2 Spike Mutations, L452R, T478K, E484Q and P681R, in the Second Wave of COVID-19 in Maharashtra, India. **Microorganisms** 2021;9(7)1542.

(**Summary:** The study reports the identification of three new SARS-CoV-2 variant lineages from India and stresses the importance of genomic epidemiology and genome sequencing tools for continuous monitoring of emerging variants. An upsurge in SARS-CoV-2 cases was observed in the Maharashtra state since January 2021. Whole genome sequencing analysis for spike protein mutations was performed for 2204 whole genomes obtained from nasopharyngeal swabs collected from COVID-19 patients during the period. The analysis revealed three newly identified lineages B.1.617.1, B.1.617.2 and B.1.617.3. Aminoacid substitutions L452R, T478K, E484Q, D614G and P681R were identified in the spike protein of the new lineages. The structural analysis of L452R, T478K and E484Q receptor binding domain (RBD) mutations revealed that these may possibly result in increased acetylcholinesterase-2 (ACE2) binding and P681R in the furin cleavage site could increase the rate of S1-S2 cleavage, resulting in better transmissibility. The two RBD mutations, L452R and E484Q, indicated decreased binding to REGN10933/P2B-2F6 monoclonal antibodies and may affect their neutralization potential. Lineage B.1.617.2 has been designated as a variant of concern, Delta and B.1.617.1 as a variant of interest, Kappa by the World Health Organisation and they are being widely reported in the rest of the country, as well as, globally.)

News From The Field: ICMR-NIV, Mumbai Unit

COVID-19 News

SARS-CoV-2 infection and risk of variant generation in patients with Primary Immunodeficiency Disorders

Primary Immunodeficiency Disorders (PIDs) are a group of inherited disorders. Patients with PIDs are at an increased risk of developing severe COVID-19. ICMR-NIV, Mumbai Unit (Dr. Madhu Mohanty and team) in collaboration with ICMR-NIIH and Bai Jerbai Wadia Hospital for Children, Mumbai, detected prolonged fecal shedding (> 100 days) of SARS-CoV-2 in asymptomatic children with PIDs (first report). This raises the possibility of feco-oral transmission and generation of intra-host SARS-CoV-2 variants. Since diarrhoea is a frequent symptom in patients with PIDs, further investigations in these patients are needed.

Towards Global Polio Eradication

Risk of immunodeficiency related Vaccine Derived Polio Viruses in Polio Endgame Strategy

Patients with PIDs vaccinated with Oral Polio Vaccine may shed Vaccine Derived Polio Viruses (iVDPVs) due to prolonged intestinal replication of the virus. In the absence of routine screening of these patients for poliovirus infection and excretion, India faces the risk of re-establishment of poliovirus transmission. team has established an iVDPV surveillance program and research studies on excreted polioviruses from PID patients of India, in collaboration with WHO, ICMR-NIIH and six reputed medical institutes across the country to address the issue. The study has investigated several PID patients and identified a PID patient from Mumbai site diagnosed with Hyper IgM syndrome for iVDPV type 1, the first iVDPV case in India. The study aims to expand to other PID diagnostic facilities/hospitals across India, align the study to the global guidelines of iVDPV surveillance (WHO) and gain insights for its implementation in the national program.

ICMR-WHO iVDPV study site investigators across India

Visit of WHO team to ICMR-NIV, Mumbai Unit for iVDPV study

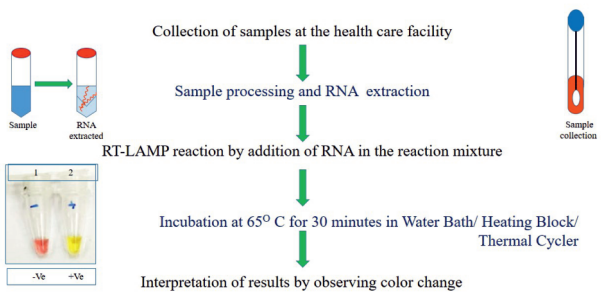
(With inputs from Dr. SD Pawar, Dr. Madhu C. Mohanty, and Dr. Deepa Sharma, ICMR-NIV, Mumbai Unit)

Featured Technology

RT-LAMP technology for sensitive, cost-effective and rapid diagnosis of SARS-CoV-2

The scientists of ICMR-NIV, Mumbai unit developed a novel colorimetric isothermal amplification assay to detect SARS-CoV-2 in clinical samples. It is an easy, low-cost, rapid diagnostic technology. The schematic workflow of the assay is given below. The colorimetric visual endpoint RT-LAMP technology has been tested on clinical samples and the results are equivalent to the real-time PCR with a diagnostic sensitivity of 98.46% and specificity of 100%. This technology is patented by the IPR Cell, ICMR-Headquarters, New Delhi. The main advantages of this assay are its rapidity (completion within 30 minutes), visual interpretation of results, and non-requirement of sophisticated equipment. The test has been designed into a portable kit to enable point-of-care testing at locations such as airports, railway and bus stations, emergency departments, physician clinics, and other low-resource settings, such as in villages. The 1st Batch of the RT-LAMP kit has been validated by the National Institute of Biologicals, Noida with 100% sensitivity and 100% specificity. The technology transfer of this assay has been initiated to two companies. The RT-LAMP kit would soon be available in the Indian market for ramping up the national testing capacity. The scientists of ICMR-NIV, Mumbai unit acknowledge the guidance of Dr. Balram Bhargava, Director General, ICMR, Prof. (Dr.) Priya Abraham, Director, ICMR-NIV, and Dr. Jagadish Deshpande (ICMR Chair for Disease Elimination).

Work flow of RT-LAMP for detection of SARS-CoV-2



Prof. Dr. Balram Bhargava (Hon. Secretary, DHR and Director General, ICMR), Dr. Samiran Panda (Scientist G, Head, ECD Division, ICMR), Dr. Nivedita Gupta (Scientist F, Head, Virology Unit, ICMR), at the launch of the RT-LAMP Kit for diagnosis of SARS-CoV-2 infection, with the team

[With inputs from Dr. S.S. Nandi and Team (Dr. Upendra P. Lambe, Post-Doctoral Fellow, Ms. Sonali A. Sawant, Technical Assistant & Ms. Trupti Gohil, Jr. Research Fellow), ICMR-NIV, Mumbai]

Obituary

Dr. B Lalitha Rao
(1944-2021)

The ICMR-NIV family is deeply saddened to learn about the untimely demise of Dr. B Lalitha Rao on 21st June 2021. Born in 1944 in Karnataka, she completed her M.B.B.S. degree and joined the ICMR-NIV in 1970 as a Research Officer. She earned her M.D. (Microbiology) degree from the Savitribai Phule Pune University, Pune. Throughout her journey, she played a pivotal role in establishing the discipline of influenza at ICMR-NIV and retired after 34 years of service as Deputy Director, Senior Grade, in September 2004.

Foresighting the significance of studies on influenza, a separate department of Influenza was initiated in 1976 under the leadership of Dr. Rao. This was later recognized by the World Health Organization (WHO) as the 'National Influenza Center' (NIC). As a part of influenza surveillance, several outbreaks of influenza were investigated and more than 500 strains covering several antigenic variants of A(H1N1), A(H3N2), and type B were isolated. This information on the prevalence of influenza virus strains was useful for updating the influenza virus vaccines for the Northern hemisphere. Periodical serological surveys were also conducted in Pune to determine the immune status against the epidemic and pandemic strains of influenza.

Dr. Rao's keen interest and vision also steered her to conduct studies on human Respiratory Syncytial Virus, adenoviruses, and other newly discovered respiratory viruses. She also forayed into studying respiratory viruses from pediatric patients with acute respiratory disease and infectious diseases at the human-animal interface (birds and animals, swine and equine influenza). Her studies on influenza became the basis for multi-centric studies on influenza in India and the establishment of the influenza network in 2004. This network played an instrumental role in the mitigation of the influenza pandemic caused by the 2009 H1N1 virus. Her wide and in-depth knowledge in the field of virology and her logical way of thinking, encouragement, and personal guidance was of great value to her students.

Dr. Rao, a very kind-hearted and considerate person, possessed an unparalleled combination of brilliance, scientific intuition, and creativity. Her strong sense of sensitivity towards nature reflects in the poem 'NIV Tree', which she wrote on a tree that had collapsed at the NIV, Ambedkar Road campus. She also took the initiative to plant another tree at the same place. Among her several noteworthy creations are her poem, 'The Viruses Speak' which depicts the properties and pathologies of several viruses amusingly, appealing to children, adults, biologists, and laymen alike! She has authored several poetry books and recitations of her poems as audio cassettes. Dr. Rao was also was a talented singer. She is survived by a son, daughter, and grandchildren. She will be sorely missed and fondly remembered for her contributions in the field of influenza research in India.

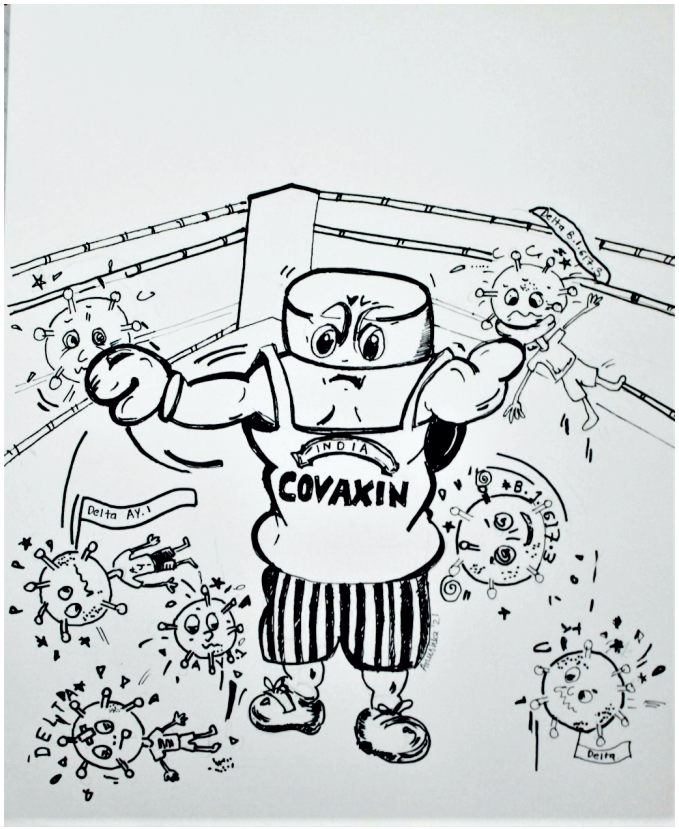
Dr. Shailesh D. Pawar
Scientist-E & Officer-In-Charge
ICMR-NIV, Mumbai Unit

"The Viruses Speak"

(A poem by Dr. B. Lalitha Rao)

We are innocent but make you nosy
(Rhinoviruses – Common cold)
We are beautiful but make you ugly
(Chickenpox viruses – Chickenpox)
We are artists but make you funny
(Mumps viruses – Mumps)
We are affectionate but make you cry
(Crying child appearance – Measles)
We are quiet but make you angry
(Acute haemorrhagic conjunctivitis – Red eyes)
We are radiant but make you cold
(Corona viruses – Common Cold)
We are pale but make you colourful
(Hepatitis viruses – Jaundice)
We are sane but make you mad
(Rabies viruses – Rabies)
We are lazy but keep you busy
(Rotaviruses – Diarrhoea)
We are perfect but make you defective
(Rubella viruses – Congenital defects)
We are mysterious and make you curious
(Influenza viruses – Epidemics & Pandemics)
We are active but make you lame
(Polioviruses – Paralysis)
We are wingless but reach you flying
(Arboviurses transmitted by mosquitoes – Encephalitis)
We are victims and you are victors
(Smallpox viruses – Eradicated from the world)
We are powerful but make you defenceless
(Human immunodeficiency viruses -AIDS)

Indian Grey Hornbill (Ocyceros birostris), a rare visitor to ICMR-NIV, Pashan campus.
[Photo by Ms. Malvika Salve, MSc Virology Alumna]



(Contributed by Ms. Anushka Kalaskar, First Year MSc Virology Student)

The story of the 'Human Placental Virus'

There was a virus, happy and thriving inside its host.
It had DNA, its genome, and a pretty good life to boast!
Now in order to reproduce and to complete the cycle of life,
It made a protein Syncytin inside the host, rife.

Syncytin helped the virus, very well you see,
It fused with the host's membrane so together they'd be!
Multiplying away to glory, viruses- ever so sleazy
Syncytin was rockin' making their 'life' easy!

Along came evolution, waving its magic wand
The virus and the host cell? Immortal became their bond!!
The virus lost its identity now, its genome was one
With the primate host's DNA, they integrated for fun!

When the host bore young ones, placenta was made
Through the one cell thick placenta, nutrients came to its aid!
This happened long long ago, before the world as we know it,
We owe our birth to a virus, seems absurd but have to admit!

Written by:
Deeksha Tare
ICMR-Senior Research Fellow
[Polio Virus Group (former Avian influenza)]
ICMR-NIV, Pune

Major Events at ICMR-NIV

An MoU for establishing ICMR-NIV, Punjab was signed by the Department for Medical Education and Research (DMER), Govt. of Punjab and ICMR-NIV, Pune, on 26th July, 2021 at Punjab Bhawan.

Seen in the photo (from left to right) are Dr. R. Lakshminarayanan [Deputy Director General (Admn.), ICMR], Dr. Sujata Sharma (Director, DMER), Prof. Dr. Priya Abraham (Director, ICMR-NIV), Shri. Om Prakash Soni (Minister for Medical Education and Research] and Mr. Alok Shekhar (Principal Secretary, Medical Education & Research).

Members of the Central and State Government teams visited ICMR-NIV on 6th August, 2021, after the confirmation of the first Zika case in Pune.

The 74th Independence Day of India was celebrated with full patriotic fervor in the institute on 15th August, 2021. Prof. Dr. Priya Abraham, Director, presided over the function.

Outbreak Response

Zika virus outbreak in Thiruvananthapuram, Kerala

- Confirmed the etiological agent of the outbreak of an febrile rash syndrome among health care workers in Thiruvananthapuram, Kerala as Zika virus (ZIKV)
- Capacity building of the state for the ZIKV surveillance by conducting online training of 4 Virus Research and Diagnostic Laboratories in Kerala and provided diagnostic reagents
- Phylogenetic analysis showed it to be similar to the ZIKV strain which caused the 2018 outbreak in Rajasthan

Nipah virus disease in Kozhikode, Kerala

- Confirmed the index case of Nipah virus infection in Kozhikode district, Kerala on 5th September, 2021
- Established an on-site Nipah diagnostic facility [with Point of Care assay and Real time RT-PCR] at Government Medical College, Kozhikode, on 6th September, 2021
- Conducted bat survey in the area to track the source of Nipah virus infection and detected the presence of antibodies against Nipah virus in bats
- Capacity building for the state for Nipah diagnosis by intensive training of VRDL staff on biosafety and laboratory diagnosis

Superannuating Staff

Mrs A S Palshikar
Admin. Officer
(1986-2021)

Mr A V Kondaiah
Lab Asst.
(1979-2021)

Mr K N Lekhraj
Lab Asst.
(1979-2021)

Mr P D Khude
Sr. Tech. (3)
(1990-2021)

Mr S R Saware
Lab Asst.
(1989-2021)

Mrs T P Subbayya
Lab Asst.
(1990-2021)

Awards & Honors

Prof. Dr. Priya Abraham, Director, ICMR-NIV, Pune, gave the Dr. Ajita Mehta Oration at the XVII Annual Hospital Infection Control Society - India (HISICON 2021) on 29th July 2021.

Dr. Pragya D. Yadav, Scientist E & Group Leader, Maximum Containment Facility, received the Dr. K.M. Bhansali Oration Award in the 69th Annual Conference of the Indian Association of Occupational Health, Mumbai Branch, on 12th July, 2021.

Dr. Daya D. Pavitrakar, Technical Officer-B, Encephalitis Group, won the Best Poster Award for the work titled "In-silico approach for designing multi-epitope based vaccine candidate against Chandipura virus" presented in the online conference 'Recent Trends in Biomedical Sciences (RTBS-2020)' organized by Lovely Professional University, Phagwara, Punjab, during 2nd - 3rd July, 2021.

Mrs. Sadhana S. Kode was awarded a Ph.D. degree in Microbiology for her thesis titled 'Susceptibility of avian influenza viruses isolated from India to antiviral drugs' completed under the guidance of Dr. Shailesh D. Pawar (Scientist E, ICMR-NIV, Pune) in March 2021.

[**Thesis summary:** Avian influenza outbreaks are a prevalent threat in India since 2006, and influenza A(H5N1) and A(H9N2) viruses are major etiologic agents among many. This thesis examined the prevalence of mutations in the neuraminidase (NA) and matrix (M) genes of highly pathogenic and low-pathogenic avian influenza virus isolates from India, associated with susceptibility to antiviral agents. The work revealed the presence of several mutations in these isolates, including a few novel molecular markers associated with potential cross-resistance to NA inhibitors. The study also evidenced a gradual increase in amantadine resistance markers among H9N2 viruses. The work indicated an urgent need for antiviral surveillance in the avian influenza viruses circulating in India.]

NIV in news

Covaxin effective against Delta Plus, says ICMR study

PNS ■ NEW DELHI

Bharat Biotech's Covaxin, India's first indigenous vaccine to fight Covid-19, is effective against the Delta Plus (AY.1) variant of SARS-CoV2 virus, a new study by the Indian Council of Medical Research (ICMR) has said. Despite a slight reduction in neutralisation of antibody titres, Covaxin is effective against Delta, AY.1 (Delta Plus) and B.1.617.3 variants, the study added.

Covaxin has been developed by the Hyderabad-based pharma major, in collaboration with ICMR. As per the website, when the vaccination was launched on January 16, just a little over 5 crore doses of Covaxin have been administered in the overall 45 crore immunisation so far. Majority has been contributed by Serum Institute of India, a Pune based vaccine manufacturer which is making Covi-shield.

So far 70 cases of the Delta Plus variant have been found by INSACOG, a group of 28 laboratories involved in genome sequencing. Delta Plus is a mutated form of the Delta variant, first discovered in India. It is characterised by increased transmissibility.

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Delta and its sublineages reduce Covaxin antibodies: ICMR study

Despite this, the vaccine provides protection, it says

JACOB KOSHY
NEW DELHI

Antibodies produced in response to Covaxin were reduced when tested against the Delta variant and its sub-lineages but continued to be high enough to remain protective, according to a study by scientists at the Indian Council of Medical Research-National Institute of Virology.

The antibodies were collected from fully vaccinated individuals, some of whom had reported breakthrough

Virus shield: A beneficiary taking a jab during a vaccination drive in New Delhi on Monday. ANI FILE PHOTO

the neutralising antibodies were reduced by about 23% when tested against the Delta variant; 33% against AY.1 and nearly 47% against AY.3. These reductions were in against AY.1 and 72% against AY.3.

Role of memory cells

"This demonstrates the possible role of memory cells in immune boosting with post-infection or infection after immunisation. The comparative analysis of all the groups revealed that the B.1.617.3 (AY.3) variant seems to be less susceptible to neutralisation followed by Delta AY.1 and Delta variants compared to B.1," the authors, including several senior scientists from the ICMR, noted in their preprint publication, which is yet to be peer-reviewed.

Despite these reductions, nearly 60% reduction when faced with the Delta variant, 70% compared with AY.1 and about 72% with AY.3.

The highest average neutralising antibodies were in

बहुत बीमार कर सकता है कोरोना का ये नया रूप

यूके और ब्राजील से आए मुसाफिरों में मिला

■ टीएनएन, नई दिल्ली

नैशनल इंस्टीट्यूट ऑफ वायरोलॉजी, पुणे ने ब्रिटेन और ब्राजील से भारत आए लोगों के सैंपल की जीनोम सीक्वेंसिंग से नए कोविड वैरिएंट - B.1.1.28.2 का पता लगाया है।

Nipah found in bats in Maha for first time

Mumbai/Pune: The deadly Nipah virus has been found in two species of bats in Maharashtra for the first time by scientists from the Pune-based National Institute of Virology (NIV), report Malathy Iyer & Umesh Isalkar.

The Nipah-carrying bats were found in a cave in Mahabaleshwar in March 2020. Dr Pragya Yadav, the study's lead investigator, told **TOI** that none of the bat species in Maharashtra had previously shown exposure to Nipah. The virus fea[illegible]res in the top 10 priority list of [illegible]athogens identified by the [illegible]orld Health Organisation

ICMR-NIV unveils rabies lab for surveillance; hopes to meet 'zero death' target set for 2030

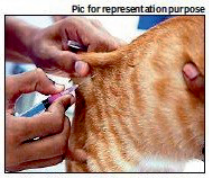
TIMES NEWS NETWORK

Pune: Indian Council of Medical Research-National Institute of Virology (ICMR-NIV) launched a dedicated rabies laboratory on Tuesday which was World Rabies Day.

The lab is expected to enhance rabies surveillance in the country. Balram Bhargava, secretary of the department of health research and director-general of ICMR dedicated the lab to the nation.

ICMR-NIV also organized a

Pic for representation purpose



Rabies kills an estimated 20,000 people in India annually

number of scientists, medical faculty, researchers, and students from all over India parti-

a major public health burden in India. The disease kills around 60,000 annually worldwide, with about 20,000 of these deaths in India alone.

Though rabies is 100% preventable with vaccination, the general awareness about the disease remains quite low, leading to deaths, experts attending the webinar said.

A global call for action, called 'Zero By 30' has been initiated by the World Health Organisation and other agencies, for eliminating dog-mediated

Several experts in the field of virology including Priya Abraham, director, ICMR-NIV, Nivedita Gupta (scientist F) and in-charge of virology unit of ICMR, state surveillance officer Pradip Awate, medical expert Reeta S Mani, additional professor of neurovirology, NIMHANS, Bengaluru and medical expert Anita Mahadevan, head, department of neuropathology, NIMHANS and medical expert Sudhir Patsute, medical superintendent of Naidu Infectious Diseases ho-

अगले महीने आ सकती है बच्चों के लिए कोविड वैक्सीन : डा. प्रिया

नई दिल्ली, एएनआइ

कोविड-19 की तीसरी लहर की आशंकाओं के बीच यह खबर राहत प्रदान करने वाली है कि अगले माह बच्चों के लिए कोविड वैक्सीन आ सकती है। भारतीय चिकित्सा अनुसंधान परिषद (आइसीएमआर) के प्रमुख संस्थानों में शुमार राष्ट्रीय विषाणु विज्ञान संस्थान (एनआइवी) पुणे की निदेशक डा. प्रिया अब्राहम ने कहा है कि बच्चों के लिए कोविड-19 वैक्सीन सितंबर या अक्टूबर तक उपलब्ध हो सकती है।

विज्ञान एवं प्रौद्योगिकी विषाण के एक ऑटोटी चैनल के साथ साक्षात्कार में डा. प्रिया ने कहा, '02-18 साल के बच्चों व किशोरों के लिए कोवैक्सीन के दूसरे व तीसरे चरण का परीक्षण जारी है। उम्मीद है कि उसके परिणाम जल्द आ जाएंगे। इसके बाद उन्हें निर्यामकों के समक्ष प्रस्तुत किया जाएगा। ऐसे में सितंबर या इसके तुरंत

दूसरे डोज की जरूर होगी सिफारिश

डा. प्रिया ने कहा, 'दुनियाभर में कोविड-19 की दूसरे डोज पर अध्ययन जारी है। कम से कम सात अलग-अलग वैक्सीन का दूसरे डोज के लिए परीक्षण किया जा रहा है। विश्व स्वास्थ्य संगठन (डब्ल्यूएचओ) ने अधिक देशों के टीकाकरण होने तक इस पर रोक लगा दी है, लेकिन भविष्य में दूसरे डोज की सिफारिश आना निश्चित है।

बाद बच्चों व किशोरों के लिए कोविड वैक्सीन आ सकती है।' एम्स के निदेशक डा. रणदीप गुलेरिया भी कह चुके हैं कि बच्चों के लिए भारत बायोटेक की वैक्सीन का परीक्षण अंतिम चरण में है और सितंबर तक उसके आंकड़े उपलब्ध हो सकते हैं।

डा. प्रिया ने बताया कि बच्चों के लिए जायडस कैडिला व

का भी परीक्षण जारी है। व
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वैरिएंट के खिलाफ भी प्रभावी

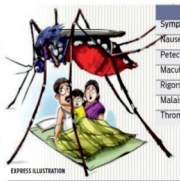
NIV Pune study finds severe dengue strain dominant in TS

The DENV-2 strain causes severe conditions like Thrombocytopenia, low platelet count or bleeding into the s

DONITA JOSE @Hyderabad

A retrospective study on Dengue serotypes conducted by National Institute of Virology, Pune, which was recently published in the International Journal of Infectious Diseases, has thrown light on Telangana's prevailing dengue strains. The State is affected predominantly by the DENV-2 strain which is known to cause severe conditions like Thrombocytopenia, low platelet count or bleeding into the skin more often than from other strains.

According to the study, roughly 34 per cent of the samples collected in 2018 from Telangana were affected with DENV-2 and another 10 per cent with multiple serotypes. Nationwide, nearly 4,963 samples were studied. The study found that the DENV-2 strain is predominant not only in Telangana but all of India and of the four strains is most likely to



EXPRESS ILLUSTRATION

SPECIFIC SYMPTOMS OF DENV-2	
Symptom	% prevalence
Nausea/vomiting	26.7%
Petechiae or spotting due to bleeding into skin	4.9%
Maculopapular rash or flat red rashes	6.2%
Rigors or shivering	6.2%
Malaise or feeling of discomfort	8.8%
Thrombocytopenia or low blood platelets	21.4%

STRAIN COMMON IN MANY STATES

DENV-2 is common in AP, Gujarat, Jharkhand, Odisha, Puducherry, Rajasthan, Tamil Nadu, Telangana and UP

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EXPRESS NEWS SE
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Locked homes, construction sites & cellars add to State's dengue peak

'New variant detected by NIV may cause severe symptoms'

Need Genomic Surveillance Of B.1.1.28.2: Study

SushmLDey@timesgroup.com

New Delhi: The National Institute of Virology, Pune, has detected a new Covid-19 variant — B.1.1.28.2 — through genome sequencing of samples from international travellers from the United Kingdom and Brazil to India.

The new variant is likely to cause severe symptoms. The findings of the pathogenicity evaluation show increased disease severity and point towards the need for screening of vaccine efficacy. The findings of the pre-print study has been published online on bioRxiv.

However, according to an incorrected manuscript of a separate study by NIV, Pune,

ed Syrian hamster model, the study said. The study pointed towards the necessity of genomic surveillance and characterisation of SARS-CoV-2 variants to understand their pathogenicity and immune escape potential for preparedness of counter measures.

Genome sequencing labs are looking at mutants which have significant potential of severely affecting disease transmission. Currently, 10 national labs under INSACOG (Indian SARS-CoV-2 Genome Sequencing Consortia) have sequenced around 30,000 samples. The government plans to ramp up genome sequencing and recently added 18 more labs to the consortium.

A health worker takes a swab sample of a fisherman in Chennai on Monday

J&K village first in India to be 100% jabbed

Wyan village of Bandipora district in Jammu & Kashmir has become the first village of the country to record 100% inoculation of all people over 18 years for Covid-19, reports **Saleem Pandit**. This national record is attributed to the "J&K Model", under which the administration reached out to the people, instead of the people flooding the vaccination centres. Residents over 18 years, 362 in all, have been vaccinated.

Fourth all-India sero survey to include 6+ kids

Aiming to assess the impact of the second wave of Covid-19 pandemic and plan measures for the future, the Indian Council of Medical Research (ICMR) is set to start the fourth nationwide sero-survey for Covid-19 in June with an expanded coverage of population above six years of age, reports **Sushmi Dey**. It will also cover healthcare workers in district hospitals.

The last serological survey, between December 17 and January 8, was conducted in population above 10 years of age. The findings showed 21.4% of the country's adult (18 years and above) suffered Covid by mid-December, whereas sero-prevalence among children aged 10-18 years was 25.3%. Among healthcare workers, sero-prevalence was 25.7%, with 26.6% in doctors and nurses. "The findings of the survey will help in ascertaining the current situation of Covid-19," ICMR director general Balram Bhargava said in a letter to states and UTs.

Antibody test after jab not recommended: ICMR-NIV

Umesh.Isalkar
@timesgroup.com

Pune: Experts from the Indian Council of Medical Research National Institute of Virology (ICMR-NIV) have said that they do not currently recommend antibody testing after Covid vaccination. The reason is antibody levels can vary according to a person's genetic makeup and even the type of test used.

And if a post-vaccination antibody test comes back as negative, it does not mean the vaccine has failed. The shots can stimulate memory cells and still confer some protection.

Experts also said people with antibodies can still contract Covid, even though it'll mostly be mild.

"Post-vaccination antibody testing is not recommended due to the variable sensitivity and specificity of the commercially available antibody assays (tests)," Priya Abraham, ICMR-NIV director, told **TOI**.

Also, the commercially available kits cannot differentiate between vaccine-induced antibodies and antibo-

PROTECTION DETAIL

File photo

ANTIBODY TESTS: MYTHS VS FACTS

MYTH | If my post-vaccine antibody is negative, the shot has failed

FACT | Vaccines also provide protection via memory cells

MYTH | I need to check my antibodies after vaccination

FACT | The ICMR-NIV does not recommend this practice. It's likely to cause confusion

MYTH | Covid antibodies

➤ SARS-CoV2 antibodies will certainly be present after vaccination, experts said

➤ There will be more antibodies and probably longer lasting ones, after the second shot

➤ Commercially

Asian strain of Zika virus found in Pune district: ICMR-NIV

Umesh.Isalkar@timesgroup.com

Pune: The Zika virus found in Pune belongs to the Asian strain or genotype.

Scientists at the city-based Indian Council of Medical Research-National Institute of Virology (ICMR-NIV) found it through complete genetic sequencing of the virus after isolating it from the blood sample of the Belsar woman (51), testing positive for the Zika virus during the routine outbreak investigation on July 30.

Zika virus (ZIKV) is classi-

THE CONCERN

If the Zika virus gets transmitted from a pregnant woman to her foetus, it can result in microcephaly and other congenital malformations in the infant, collectively referred to as congenital Zika syndrome

➤ The Zika virus infection by the American strain has shown the microcephaly (brain defect) when a mother gets infected during the first trimester, considered key for the development of the brain and nervous system cells in the growing foetus

➤ The Asian strain should also be considered as a risk for microcephaly unless proven otherwise, an NIV scientist had said in an earlier interview

also has the virus matching the Asian strain.

There are concerns that if the Zika virus gets transmitted from a pregnant woman to her foetus, it can result in microcephaly and other congenital malformations in the infant, collectively referred to as congenital Zika syndrome. The scientists have cautioned that the Asian strain may also cause microcephaly (smaller than normal head size), depending on the timing of Zika virus infection during pregnancy.

The state surveillance offi-

ICMR-NIV study: Covaxin protects against Delta, Beta variants

Sera collected from 20 recovered Covid patients, 17 vaccinated with two doses; study not yet peer-reviewed

ANURADHA MASCARENHAS
PUNE, JUNE 8

SCIENTISTS AT Indian Council of Medical Research- National Institute of Virology (NIV) have found that Covaxin offers protection from Delta (B.1.617.2) as well as Beta (B.1.351) variants of SARS-CoV-2, which causes Covid-19. The study, 'Neutralization against B.1.351 and B.1.617.2 with sera of Covid-19 recovered cases and vaccinees of BBV152', however, is yet to be peer-reviewed and was posted on bioRxiv preprint server on Monday.

The study evaluated the neutralisation potential of sera collected from 20 Covid-recovered cases and 17 people vaccinated with two doses of Covaxin against Beta and Delta variants and compared it with the prototype D614G variant.

Scientists decided it was imperative to assess the efficacy of available vaccines against these variants.

Researchers evaluated the neutralisation potential of people vaccinated with Covaxin and found that it offers protection against these two variants.

Dr Pragya Yadav, scientist 'E' and group leader, maximum containment facility, ICMR-NIV, said they had observed a reduction in neutralisation titre values in people vaccinated with Covaxin against Beta and Delta variants, but the reduction was lower than in people who had been naturally infected. Hence, the vaccine does offer protection against these variants, researchers said.

Neutralising antibody titres in the blood closely correlate with the protection provided by effective vaccination. The study checked on the neutralisation potential in people vaccinated with Covaxin and found a three and 2.7 fold reduction in neutralisation titres against the Beta (B.1.351) and Delta (B.1.617.2) variants, respectively. In comparison, the reduction in neutralisation titres with sera from people who had recovered from Covid-19 were 3.3 and 4.6 fold against these variants.

"There was a reduction in the neutralisation titre values in people administered Covaxin, against Beta and Delta variants, but this reduction was lower than in those who were naturally infected," Dr Yadav said.

Earlier, NIV scientists studied the neutralisation potential of Covaxin with the B.1, B.1.1.7, B.1.1.28.2 and B.1.617.1 and found it to be effective against these variants.

खुलासा

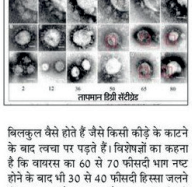
एनआईवी-आईसीएमआर के वैज्ञानिकों ने किया कोरोना वायरस पर गरमी के असर का पहला अध्ययन

50 डिग्री से ऊपर जलता है वायरस, 80 पर भी पूरा नष्ट नहीं

परीक्षित निर्भय

नई दिल्ली। कोरोना का वायरस 50 डिग्री तक बिना किसी प्रभाव के अपना काम करता रहता है। 50 से ऊपर तापमान जाने पर यह जलना शुरू होता है और 80 डिग्री के बाद भी यह पूरी तरह नष्ट नहीं होता। 80 डिग्री की तपिश झेलने के बाद भी इसका कुछ हिस्सा सक्रिय रहता है। कोरोना वायरस पर गरमी और बढ़ते तापमान पर पुणे स्थित नेशनल इंस्टीट्यूट ऑफ वॉयरोलॉजी और आईसीएमआर के वैज्ञानिकों ने पहला अध्ययन किया है।

अध्ययन के मुताबिक 50 डिग्री पर जलने के साथ ही इसकी बाहरी संरचना में मौजूद छतरीनुमा आकार के स्पाइक प्रोटीन नष्ट होने लगते हैं और भीतरी संरचना में जगह जगह चकत्ते के निशान रहते हैं। यह निशान



तापमान डिग्री सेंटीग्रेड

बिलकुल वैसे होते हैं जैसे किसी कीड़े के काटने के बाद त्वचा पर पड़ते हैं। विशेषज्ञों का कहना है कि वायरस का 60 से 70 फीसदी भाग नष्ट होने के बाद भी 30 से 40 फीसदी हिस्सा जलने से बच जाता है। अनुमान है कि इस हिस्से को भी नष्ट करने के लिए करीब 100 डिग्री तापमान की आवश्यकता पड़ सकती है।

2 से 80 डिग्री पर वायरस की जांच

वैज्ञानिकों ने कोरोना वायरस को 2 से 80 डिग्री तापमान पर रखते हुए अध्ययन किया गया। 50 डिग्री से कम तापमान पर वायरस के साइटोपैथिक प्रभाव में कोई बदलाव नहीं हुआ। वहीं 50 डिग्री या उससे अधिक तापमान जाने पर सबसे पहले बाहरी संरचना नष्ट होने लगी। तापमान बढ़ने के साथ ही वायरस की भीतरी संरचना को नुकसान होता गया। 80 डिग्री पर जब वायरस का अधिकांश हिस्सा जल चुका था लेकिन कुछ हिस्सा फिर भी बाकी था।

■ **25 से 35 डिग्री पर बढ़ता है वायरस**...अभी तक तापमान को लेकर वायरस की प्रतिक्रिया पर कोई अध्ययन नहीं हुआ है लेकिन यह देखने को जरूर मिला है कि 25 से 35 डिग्री तापमान पर वायरस अचानक बढ़ने लगता है और तेजी से नए मामले भी सामने आने लगते हैं। पिछले और इस साल मार्च में यही स्थिति देखने को मिली थी उस दौरान पहाड़ी क्षेत्रों में तापमान 20 डिग्री से कम था और वहां नए मामले भी नहीं थे।

इसलिए हर मौसम में एक जैसा वायरस

पिछले साल कोरोना को लेकर कयास लगाए जा रहे थे कि सर्दियों में शायद इसके प्रसार में तेजी आए क्योंकि यह भी इन्फ्लूएंजा के समान कार्य कर रहा है। इन्फ्लूएंजा वायरस को उसरित होने में सर्द मौसम काफी सहायक होता है। जबकि इससे पहले गर्मी और बरसात को लेकर भी कयास लगाए गए थे। नीति आयोग के सदस्य डॉ. वीके पॉल ने पहली लहर निकलने के बाद अक्टूबर माह से ही सर्दियों का हवाला देते हुए बयान दिए थे लेकिन अब वैज्ञानिक तौर पर यह साबित हो चुका है कि सर्दी, गर्मी और बरसात में कोरोना वायरस एक जैसा ही प्रभाव देगा क्योंकि 2 से 45 डिग्री तापमान पर वायरस में कोई बदलाव नहीं हुआ।

केवल कुछ ही इलाकों में रहता है 50 डिग्री तापमान

■ एनआईवी के वैज्ञानिकों के मुताबिक जब तापमान को लेकर देश के विभिन्न इलाकों को देखा गया तो पता चला कि अब तक 50 डिग्री या उससे ऊपर कुछ ही इलाकों में पारा पहुंचा है। ऐसे में इस तापमान में वायरस पर कोई असर नहीं पड़ता। चूंकि इन्सान इतना तापमान सहन नहीं कर सकते। इसलिए मौसम के साथ वायरस के नष्ट होने की परिकल्पना नहीं की जा सकती।

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