Notes and News

Men are More Vulnerable to Coronavirus than Women

A first study on immune response to the coronavirus by sex as reported in Nature on August 26 concludes that older men are up to twice more vulnerable to coronavirus than women of the same age. The study led by Akiko Iwasaki at Yale University reasons: 'Men produce a weaker immune response to the virus than do women.' This suggests that men over age 60, may be dependent more on vaccines to protect themselves against this infection.

Dr. Iwasaki's team analyzed immune responses in 17 men and 22 women who were admitted to the hospital soon after they were infected with the coronavirus. The researchers collected blood, nasopharyngeal swabs, saliva, urine and stool from the patients every three to seven days.

The analysis excluded patients on ventilator and those taking drugs that affect the immune system "to make sure that we're measuring natural immune response to the virus," Dr. Iwasaki said.

Over all, the study showed that women's bodies produced more so-called T cells, which can kill virus-infected cells and stop the infection from spreading. Men showed much slower activation of T cells, and that lag was linked to how sick the men became. The older the men, the weaker their T cell responses.

"When they age, they lose their ability to stimulate T cells," Dr. Iwasaki said. "If you look at the ones that really failed to make T cells, they were the ones who did worse with disease." But "women who are older — even very old, like 90 years old — these women are still making pretty good, decent immune response," she added.

Women are gifted with faster and stronger immune responses by nature, perhaps because their bodies are equipped to fight pathogens to protect unborn or newborn children from infections. But an immune system in a constant state of high alert can be harmful. Most autoimmune diseases in which immune system mistakenly attacks healthy cells, are much more prevalent in women than in men. However, the study does not offer any scientific reason for this difference in immune response.

Compared with health care workers and healthy controls, patients had elevated blood levels of cytokines, proteins that activate the immune system to action. Some types of cytokines, called interleukin-8 and interleukin-18, were elevated in all men but only in some women.

Women who had high levels of other cytokines became more seriously ill, the researchers found. Those women might do better if given drugs that blunt these proteins, Dr. Iwasaki said.

The study has its limitations because the sample studied was small and the patients were older than 60 on an average, making it difficult to assess how the immune system changes with age. Yet she concluded that "The more robust T cell responses in older women could be an important clue to protection and must be explored further."

Dr. Marcus Altfeld, an immunologist at the Heinrich Pette Institute and at the University Medical Center Hamburg-Eppendorf in Germany and other experts opined that the findings may play a significant role to understand the need for companies pursuing coronavirus vaccines to analyse their data by sex and may influence decisions about the dose.

"You could imagine scenarios where a single shot of a vaccine might be sufficient in young individuals or may be young women, while older men might need to have three shots of vaccine," Dr. Altfeld said. ❐

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On 100th year of discovery of Urea Stibamine by Sir U. N. Brahmachari

Noted structural biologist Prof. Siddhartha Roy, Former Director, CSIR-IICB and Bose Institute mentioned in an interview: 'First real drug against an infectious disease

(infectious diseases were the scourge worldwide in early part of 20th century) was Paul Ehrlich's Salvarsan. The second infectious disease drug actually originated in India, which is U. N. Brahmachari's Urea Stibamine (US) against Kala-azar. It saved almost as many lives as Penicillin or other drugs. Discovery of five drugs got Nobel Prize but not U. N. Brahmachari's US. He was an unsung hero'.

Visceral Leishmaniasis (VL) or Kala-azar is a dreadful and potentially-fatal human disease caused by the protozoan parasite *Leishmania donovani* and infected female sandfly *Phlebotomas* sp (2-3 mm size) is the carrier of *L. donovani*, facilitating transmission of VL *via* its bites. Since 1870s, VL epidemic was rampant in towns and villages in eastern India in Assam, Bihar, undivided Bengal, eastern Uttar Pradesh and Madras, victims exhibited enlargement of spleen and liver, irregular spells of fever, anaemia and black pigmentation. Aim of its treatment is killing of *L. donovani*. With regards to VL therapy, discovery of US (or Brahmacharoid stiburea) was a landmark achievement and contribution of Sir Upendra Nath Brahmachari, a great benefit of humankind. Discovery, first-time synthesis, nomenclature and description of this wonderful clinically-useful drug were made by Sir Brahmachari in 1920 at the then Campbell Medical School (now Sir Nilratan Sirkar Medical College and Hospital, Kolkata) while workingas teacher in Medicine and physician, since 1905. He gave it to the world in 1922, which gained wide acceptance as a treatment for human VL. Side effect of his formulation led to emergence of Dermal Leishmanoid in certain cured VL patients in post-VL situation; which was unknown to science at that time. This disease was identified by Sir Brahmachari. It could be arrested when US in combination with Neo-Stibosan (amine salt of para aminophenylstibinic acid), plant alkaloid berberine (Rasaut: crude form of Berbenne available in market) were used.

In 1919, Sir Brahmachari prepared p-stibanilic acid and its various salts. Over the next year, he pursued towards perfecting his formulae which led to production of US, the most effective and safe drug. Replacing aminophenylstibinate salt of sodium, Sir Brahmachari synthesized the urea salt of p-stibanilic acid in 1920 and named it US. In other words, it is Para-aminophenylstibinic acid in combination with urea. Precisely it composed of diammonium salt of 1,3bis-(4-stibonophenyl)urea VIII - together with urea, stibacetin and a pentavalent organo-antimonial compound of undetermined structure. US was obtained by addition of urea to warm suspension of stibanilic acid, freshly prepared by hydrolysis of stibacetin. US is brown amorphous powder, its solution is not easily decomposed by boiling for few minutes. Report on first series of successful cases of treatment of VL with US was published in October 1922 in Indian Journal of Medical Research. Intravenous injection of US every 24 hours (total 1.5gm) and 6-8 day course was the protocol followed for VL treatment, which cured the disease within three weeks.

Following timely introduction of US in early 1922, its reputation quickly spread all over Assam, Bengal, Bihar and Orissa and to more distant places in India like Madras, Sanawar, Simla Hills and others. It effectively countered VL epidemic in British India. After introduction of US, death rate due to the disease fell dramatically in vast track of Gangetic plains and Brahmaputra valley, the epicenter of VL or Kala-azar at that time. With use of US, prevalence of VL decreased from 95% to merely 7%. In Presidential Address at Annual Anniversary Meeting of the Asiatic Society of Bengal in 1929, Sir Brahmachari mentioned: '…… *Today Urea Stibamine stands preeminent in the treatment of Kala-azar in India and as a powerful prophylactic against the disease*'.Year 2020 happens to be one-hundredth anniversary of discovery of US by Sir Brahmachari.

Sir U. N. Brahmachari was a nominee as Indian candidate for Nobel Prize in Medicine both in years 1929 and 1942. He got one and five nominations for the years 1929 and 1942 respectively (Courtesy: Dr Rajinder Singh, Research Group - Physics Didactic and History of Science, Physics Institute, University of Oldenburg and Dr Syamal Roy, Dean, National Institute of Pharmaceutical Education & Research, Kolkata). Sir Brahmachari's life was a real struggle for the promotion of medical science in the service of mankind (Courtesy: Dr Syamal Roy). He died in 1946 at 72 years of age. Many learned persons feel that Sir U. N. Brahmachari and Dr S. N. De (discoverer of cholera enterotoxin), significant contributors in advancement of medicine and medical science, have not received the attention and recognition that they deserved. ❐

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Food Processing Conclave - Leveraging Opportunities

In order to provide linkage and synergy between network of stakeholders involved in food supply chain and industries so to have safe, healthy and nutritious food, the 5th Food Processing Conclave - Leveraging

Opportunities was organized by Confederation of Indian Industry (Eastern Region) at ITC Royal Bengal, Kolkata on March 13, 2020. In the Inaugural Session, Sri A. K. Banerjee, Co-Chairman, CII-ER Agriculture & Food Processing Subcommittee and Vice-Chairman-cum-Managing Director, IFB Agro Industries Ltd spoke about importance of food processing industry in Indian economy; entrepreneurs can invest in WB in fish and shrimp processing and aquaculture; increase in shrimp production and expansion of allied industry in WB; growth of organic food market and organic shrimp; establishment of cloud kitchen, importance of adoption of modern technology TQM, food safety, quality assurance, hygiene maintenance; highlighted case of shrimp consignments from India rejected abroad due to high quality norms and presence of traces of *Salmonella* sp and antibiotics. He discussed about 'frozen prawn - better than fresh', value addition and frozen food sector; proper technology can reduce wastage, increase yield and efficiency; export of cooked product; value-added (VA) Indian aqua-product comparable to that of Indonesia and Vietnamese standards.

Sri A. Kumar, General Manager, NABARD spoke about improving income level of farmers and farm productivity; 300nos Farmer-Producer Organizations (FPOs) promoted in WB and 2500nos in entire country; linking farmers with market and industry; NABARD initiated training and capacity building for FPOs; adoption of latest management practices. He raised an issue that members of FPOs have limited capital and aren't able to get bank support; 'No farmer must be left out of FPOs' as strategy taken by NABARD; extending capital support to FPOs and banks must come forward to finance them. Sri Kumar opined that research organizations and Government must extend support and join hands, which will benefit the society, farmers and economy. Sri P. Majumdar, Advisor to Hon'ble Chief Minister of WB on agriculture and allied sector uphold the resource and income of small and marginal farmers cultivating in smaller patches of plots; development strategy to be both market- and technology-driven; emphasized on mitigating two uncertainties that agriculture is vulnerable to *i.e.*, market and monsoon; improving production of crops under demand and meeting consumer preference.

In the Session 'Managing food value chain responsively', Sri S. Kar, Programme Lead, Badabon Farmer Producer Company Ltd spoke about three issues namely traceability and knowing history of one's food, climate change and epidemics (falling production of staple cereals) and risk of air-borne pathogens. Sri P. R. Dasgupta, Advisor to Syngenta Foundation of Sustainable Agriculture spoke on 'Key issues concerning vegetable value chain in eastern India from primary producers to consumers'. He discussed about production of vegetables in WB, productivity and value creation; WB created highest value from agricultural and horticultural crops; middlemen are constraint for small farmers with small holdings; 186nos Krishakbazars established in WB under RKVY Scheme; producer's share in consumer's price for selected vegetables in WB; 'Operation Green' to promote FPOs for processing and management for development of tomato, onion and potato value chain; farmers' share *i.e.*, profitability is low and are earning lesser share of value chain; vegetable growers' share to each rupee a consumer spends varies between 26-60% in WB but is higher in Punjab and Tamil Nadu. Dr I. Chakraborty from Bidhan Chandra KrishiViswavidyalaya spoke on 'Post-harvest handling and value addition of fruits and vegetables'. She discussed about pre-harvest factors affecting quality of produce (harvesting at correct stage of maturity, selection of proper planting material); factors affecting their quality and storage life; grading process of fruits and vegetables in packhouses, precooling and packaging; possibility of installing zero energy cold chambers in farms and cabinet air dryer in Primary Agricultural Cooperative Societies at Block level; drying mango slices in cabinet dryer; explained features of fermented vegetable pickle, fruit juice concentrate, healthy extruded puff snacks without sugar, lentil mangobar and vacuum-dried snacks.

Sri M. Singh, Sr. Associate Director at Kellogg India Pvt Ltd mentioned that only 10% of total food produced is processed into VA products in India but it is 65% in USA; explained poor supply chain linkages and infrastructure bottlenecks as challenges in food processing industry; growth in food exports and change in consumer taste & preferences as key drivers; increase in consumer demand for plant-based food (burger); explained natural and Ayurvedic, innovative confluence, Go Gourmet, pack-size portion, health and wellness foods, protein-mix and dairy yoghurts, urbanization and time pressure, strong regional preferences, online food & grocery retails and start-up foods as ten trends observed in India; making food products accessible and affordable to masses. Sri R. K. Mondal, Regional Head, Agricultural and Processed Food Products Export Development Authority; Dr A. Sarkar, CEO, Happymate Foods Ltd and Sri D. P. Guha, Consultant, Food Safety and Standards Authority of India also spoke in this Session.

In the Session on Fisheries, Sri N. Roy from Agri-Business unit of SBI spoke about fishery schemes. Dr S. B. Bhattacharyya from Marine Division of IFB Group

discussed about pisciculture as a viable option for low-cost treatment of domestic wastewater and producing fish from same system. He described features of East Kolkata wetland model as freshwater sewage-fed bhery (SFB) or fish ponds, North 24 Parganas model as large brackishwater SFB, principles and practices of modern fish farming technologies *viz.*, Recirculatory Aquaculture System, Biofloc model and Integrated Multi-Trophic Aquaculture. ❐

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International Webinar on COVID-19 – The Current Scenario

As a part of Frontiers in Biological Sciences (Chapter-IV) 2020, an International Webinar entitled 'COVID-19 – The Current Scenario' was organized by Department of Microbiology, St. Xavier's College (Autonomous), Kolkata in collaboration with IQA Cell of this college on 2nd and 4th July, 2020. Rev. Dr D. Savio, S. J., Principal, St. Xavier's College in his introductory note mentioned that this webinar will expand our knowledge on description of the virus SARS-CoV-2 and will make us more equipped to fight the pandemic COVID-19. He spoke about clinical and psychological aspects of this pandemic, the psychological toll it is taking on us and standing in solidarity to curb this invisible enemy.

Dr R. Chakraborty, Professor of Microbial Genetics and Genomics, Department of Biotechnology, University of North Bengal spoke on 'Insidious SARS-CoV-2: molecular peculiarities and genomic plasticity'. He described the virus SARS-CoV-2, having its origin as enzootic bat viruses, spoke about influenza outbreak in 1918 pictorially; first use of word 'quarantine' by novelist Sarat Chandra Chattopadhyay; death toll due to COVID-19 worldwide, total active Coronavirus cases reported in India and West Bengal till 1/7/2020; 1.8 and 2.0-2.5 as Mean Reproductive Number for 1918 flu pandemic and COVID-19 pandemic respectively; first concrete evidence of human-to-human transmission of the virus; its high degree of mutation; interaction between human cell surface receptor ACE-2, furin and unique spike protein of virus, features of Coronavirus entry point; structural details of interface between receptor binding domain (RBD) of virus and ACE-2; switching of this RBD (spike protein) between standing up and lying down positions for receptor binding (infectious state) and immune evasion respectively; receptor recognition mechanism regulates infectivity of the virus and its understanding may be key to tackle COVID-19. Dr Chakraborty also discussed about SARS-CoV-2 genome, its 16 non-structural proteins; magnanimity of COVID-19 and cunningness of virus (human immune system cannot catch hold of it); case fatality rate (CFR) of major viruses; architecture of virus transcriptome; mysteries of its spike as target of vaccine designing; transversion mutations in the spike of SARS-CoV-2; finding out drugs that can inhibit RdR Penzyme function of this virus.

Dr (Ms) A. Banerjee, academic mentor and consultant psychologist, Kolkata spoke on 'Impact of Coronavirus and lockdown on psycho-social atmosphere: strategies to combat the detrimental effect'. She stated that our physical as well as psychological well-being is damaged in these few months arising out of fear (of getting infected) and anxiety. In this seemingly pandemic situation she emphasized that we need to apply problem-focused strategy and emotion-based strategy (less important) while confronting anxieties and fighting stressors; spoke about increasing frustration tolerance level, importance of practicing resilience; not to think about something fatal and drastic at very beginning with minor health discomfort; consequences of disturbed sleep; ways to deal with stress, contain and combat emotional stressors as stress can impact our sleep cycle and effect our immunity detrimentally.

Dr (Ms) S. Mundhra, immunologist and infectious disease specialist at USA spoke on 'The science of COVID-19: an overview'. She lucidly discussed about SARS-CoV-2 spike glycoprotein, factors responsible for infectivity of this respiratory virus and entry into human cell (mainly lung alveolar epithelial cells); R0 as a measure of virus transmissibility and its contagiousness; Coronavirus replication cycle; 'superspreaders' as carriers of large quantity of SARS-CoV-2 and people with low amounts of virus; CFR value 3.4 for Coronavirus and same for Ebola, smallpox, birdflu are higher; compared epidemiological perspectives of respiratory viral infections and 'Flattening the curve' between USA and India graphically. She explained in detail how SARS-CoV-2 infects and spreads after entering mucous membranes and cause of Acute Respiratory Disease Syndrome by which Coronavirus attacks; successive steps of COVID-19 diagnostic testing by RT-PCR and serological assays; symptoms of COVID-19 (if at all manifested),variability in patient journeys of SARS-CoV-2 infection exhibiting nil, mild, severe and critical symptoms and how far are they contagious;

bidirectional relationship between sleep and immunity against SARS-CoV-2 infection.

Dr Mundhra further discussed about developing 'herd immunity' as management goal of COVID-19; several repurposed approved drugs with potential broad-spectrum anti-viral activity; drugs targeting Cytokine Storm and viral replication; clinical phase vaccine candidates for COVID-19; improvement of our immune functioning and anti-oxidant status *via* regular yoga practice. According to her, meditation helps regulate stress response and maintains a healthy gut microbiota that function as barrier; good hygiene and effective public health interventions will decrease R0 of virus; social distancing helps in 'Flattening the curve' and remodifying R0; explained possible effects due to measures taken and not taken to slow the spread of SARS-CoV-2 infection.

Dr (Ms) C. Datta, Quality Assurance Manager, Clinical Bio-manufacturing facility at University of Oxford, UK spoke on 'Aspects of quality assurance in vaccine manufacturing'. She discussed about origin of vaccines; Quality Assurance Vaccine production; core processes used to monitor and maintain quality management system; rules of good management practices; current COVID-19 vaccine projects now under clinical trials worldwide; showed Videographic journey on 'How the battle is being fought against COVID-19'. Dr Datta is working in the team conducting Ph-II and Ph-III of human trials of the vaccine namely ChAdOx1 nCov-19. ❐

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