News and Views

Phage Therapy for Cystic Fibrosis

An trial supported by National Institute of Health's National Institute of Allergy and Infectious Diseases to investigate the safety and efficacy of an experimental phage therapy "WRAIR-PAM-CF1" against chronic *Pseudomonas aeruginosa* infection in the airways of adults with cystic fibrosis (CF) has started in the United States. The phase 1b multicenter trial conducted by the Antibacterial Resistance Leadership Group (ARLG) will recruit up to 72 patients with CF from across the country.

According to an NIH press release, the components of WRAIR-PAM-CF1 include "a cocktail of four bacteriophage species that naturally infect *P. aeruginosa* and take over its cellular processes, killing the bacterium in the process. The phages in the cocktail are highly specific and do not attack human cells". The press release further states that these phages do not carry harmful genes such as those pertaining to antibiotic resistance, which could inadvertently be transferred to the bacteria they infect.

Three doses of the anti-pseudomonal phage therapy would be tested. One of the three doses would be administered to each participant as a single IV infusion. To begin with, in stage 1 of the trial, the three doses would be tested on two participants for each dose followed by close monitoring of the volunteers for 4 days. A preliminary analysis will be carried out to determine the dose. Up to 50 participants would be enrolled for stage 2 of the trial if there are no significant severe safety concerns in stage 1. The study subjects would then be randomized to receive either the selected dose of the experimental therapy or a placebo. They would be regularly screened on follow-up visits.

Will phage therapy circumvent the escalating crisis of antibiotic resistance? Only time will tell.

(*Source: NIH Press Release, October 4, 2022. Available at: https://www.nih.gov/news-events/news-releases/nih-supported-clinical-trial-phage-therapy-cystic-fibrosis-begins*)

A Vaccine to Protect Newborns from Whooping Cough

A vaccine to protect newborns from pertussis (whooping cough), has been approved by the US Food and Drug Administration (FDA).

The Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed (Tdap) is the first vaccine, which can now be given to pregnant mothers during the third trimester of pregnancy to prevent whooping cough in infants younger than 2 months of age. Administration of the vaccine during pregnancy enhances antibody levels in the mother, which are transferred to her baby. The vaccine has shown 78% efficacy in preventing whooping cough in infants less than 2 months of age.

"Infants younger than 2 months of age are too young to be protected by the childhood pertussis vaccine series", said Peter Marks, MD, PhD, Director of the FDA's Center for Biologics Evaluation and Research.

The vaccine is administered in a single dose of 0.5 mL.

The most commonly reported adverse effects in clinical trials have been local pain and redness at the site of injection. Headache, fatigue and gastrointestinal symptoms have also been reported. No vaccine-related maternal or fetal/newborn side effects have been observed with the vaccine, as per the FDA.

(*Source: US FDA News Release, October 7, 2022*)

Decline in the Levels of Amyloid Beta Protein Leads to Alzheimer's Disease

In a study published in the *Journal of Alzheimer's Disease*, researchers revealed that Alzheimer's disease is caused by a decline in levels of a protein called amyloid-beta. In the study, they hypothesized that plaques are simply a consequence of the decreased levels of soluble amyloid-beta in the brain. These levels decrease because the normal protein, under situations of biological, metabolic or infectious stress, transforms into abnormal amyloid plaques.

In the study, the researchers analyzed the levels of amyloid-beta in a subset of patients with mutations that indicate overexpression of amyloid plaques in the brain, which is thought to increase the risk of the likelihood of developing Alzheimer's disease.

The researchers found that with a baseline level of soluble amyloid-beta in the brain above 270 pg/mL, people can remain cognitively normal regardless of the number of amyloid plaques in their brains. In comparison to the control, they found a similar pattern

in patients who were thought to have the highest risk of Alzheimer's disease.

The findings of the study also revealed that individuals already accumulating plaques in their brains who can generate high levels of soluble amyloid-beta have a lower risk of evolving into dementia.

(*Source: https://theprint.in/health/research-reveals-that-alzheimers-disease-is-caused-by-decline-in-levels-of-amyloid-beta/1155245/*)

More Than 60 New Genetic Regions that may Cause Stoke has been Identified

The study published in the *Nature Journal* revealed 61 new genetic regions associated with stroke that are potential drug targets to prevent or treat the second leading cause of death worldwide. In the study, data from 2.5 million people from five different ancestries, more than 2,00,000 of whom had a stroke, was analyzed by the members of the GIGASTROKE consortium.

The consortium included Professor Dr Kameshwar Prasad, Former Head of the Department of Neurology at the All India Institute of Medical Sciences (AIIMS), Delhi, who stated that the population studied in the research has a fairly global representation, including South Asia, which includes India and Pakistan, Africa, East Asia, Europe and Latin America. He further added that the combined results from different ancestries and regions made things clearer at a micro level.

The study included 1,10,182 patients who had a stroke and 1,503,898 participants as control individuals. Based on the participant data, the team identified association signals for stroke and its subtypes at 89 (61 new) independent gene loci. During a follow-up including 89,084 additional cases of stroke and 1,013,843 control individuals, it was seen that 87% of the primary stroke risk regions and 60% of the secondary stroke risk regions were replicated.

The findings of the study highlighted the F11, KLKB1, PROC, GP1BA, LAMC2 and VCAM1 regions as possible targets, with drugs already under investigation for stroke in the F11 and PROC regions. They also found that the frequency of a genetic region called COBL was higher in people suffering from neurological disorders in India and Pakistan, while no such frequency of this region was identified in patients from other ancestries.

(*Source: https://www.tribuneindia.com/news/health/over-60-new-genetic-regions-behind-stroke-identified-may-lead-to-new-therapies-438097*)

High Levels of Stress were Flagged in the Age Group of 31 to 40 Years in a Survey

Healthians, a diagnostics company, surveyed over 250 Indian cities. The survey revealed that 6 in every 10 Indians had abnormal levels of bad cholesterol, with the highest prevalence among the 31- to 40-year age group. The survey conducted by the firm anonymized the data collected from 2.66 million people in the age group of 20 years and older and revealed that 63% had high low-density lipoprotein (LDL) cholesterol levels in their blood.

Mr Deepak Sahni, Founder and CEO of Healthians, stated that in the 31- to 40-year group, 69% of the patients tested had abnormal levels of LDL. He added that this could be an indication of high-stress levels in that age group.

This, according to doctors, is the cause of the recent increase in cardiac arrests. She added that, as per the survey, 3 in every 10 Indians have abnormal levels of total cholesterol in their bloodstream, with the highest prevalence amongst the 31 to 40 age group.

The survey results also showed that 36% of Indians in the 40 to 60 age range have abnormal levels of total cholesterol. Interestingly, those who are older had lower levels of total cholesterol. The corresponding percentage was 30% in the 60 to 70 age group, while it was 24% in the 70 to 80 age group.

When the data were analyzed based on the gender criteria, it was found that males had a higher prevalence of abnormal levels of LDL, triglycerides and total cholesterol. About 64% of the males tested had abnormal LDL, 47% had abnormal triglycerides and 32% had abnormal total cholesterol compared to 63%, 30% and 29% in females, respectively. However, more females had abnormal high-density lipoprotein (HDL) levels compared to males.

(*Source: https://www.thehindu.com/sci-tech/health/diagnostics-firm-healthians-flags-high-stress-level-in-31-40-age-group/article65967463.ece*)

Blueprint for Research Released by WHO on Dementia, Dubbed as the 7th Leading Cause of Death

Recently, the World Health Organization (WHO) announced the development of a blueprint for dementia research, a first-of-its-kind initiative for non-communicable diseases. In a statement, the WHO noted that the blueprint has been designed to guide policymakers, funders and the research community on

dementia research. The blueprint will make decision-making and research more efficient, equitable and impactful.

Dementia is one of the greatest health challenges of our generation, dubbed as the 7th leading cause of death globally. However, dementia research accounts for <1.5% of total health research output. According to WHO, strategies are needed for better understanding, preventing and treating the underlying diseases that cause dementia and, at the same time, providing care and support for people with dementia. Moreover, dementia research needs to be conducted within an enabling environment where collaborations are fostered and equitable and sustained investment is realized.

The blueprint for dementia research is built on lessons learned from WHO efforts to prioritize research and coordinate research activities for infectious diseases, such as considering the entire dementia research spectrum, incorporating diagnostics and therapeutics, as well as emerging scientific and technological advances such as artificial intelligence, multi-omics and biomarkers, and also encompassing epidemiology, health economics, care and carer research, risk reduction, and brain health across the life course. The blueprint also provides insight into different drivers of research, such as sustainable funding, diversity and equity, and the involvement of people with lived experience of dementia throughout the research development process.

(*Source: https://health.economictimes.indiatimes.com/news/industry/dementia-who-gives-blueprint-for-research-on-7th-leading-cause-of-death/94656644*)

Smartphone-linked Artificial Pancreases Developed by IISc to Monitor Blood Sugar Level

A research team from IISc, Bengaluru, in collaboration with doctors from MS Ramaiah Medical College, has developed an artificial pancreas system. This can monitor and control blood sugar levels in real-time to help people with type 1 diabetes who need to take insulin regularly to avoid low blood sugar (hypoglycemia) or high blood sugar (hyperglycemia).

The Artificial Pancreas (AP) setup developed by Dr Radha Kant Padhi, Professor in the Department of Aerospace Engineering and Robert Bosch Centre for Cyber-Physical Systems, mimics the body's closed loop system that regulates insulin production. The setup has three parts, namely a sensor, an insulin pump and an Android app.

The sensor is a small coin-like device with a tiny needle-like extension that is stuck to the skin like a patch or band-aid that will monitor the glucose concentration in the subcutaneous tissue continuously. The sensor is connected to an insulin pump that will infuse insulin under the skin. The pump is a small rectangular device that can be carried around in a pocket. Both the sensor and the pump are connected to the android app. The app analyses the data sent by the sensor and determines how much insulin should be pumped into the body through the insulin pump. The key component of the app is the Model Predictive Control (MPC). This predicts how much insulin is required based on the sensor's data and sends the signal to the insulin pump. This predictive nature makes MPC a good algorithm for the AP system since blood glucose levels of type 1 patients need to be continuously regulated.

(*Source: https://health.economictimes.indiatimes.com/news/medical-devices/bengaluru-iisc-develops-smartphone-linked-artificial-pancreas-to-monitor-blood-sugar-levels/94673859*)

In India, Vedanta's Medical Arm Ties Up with Anuva for Cancer Research

Recently, Vedanta's BALCO Medical Centre (BMC), one of India's leading cancer hospitals, announced a strategic collaboration with Anuva, a genomics biotech company, to build a Cancer Genomics Biobank for cancer research in India. The companies aim to use this cancer bio/data bank to identify and develop precision medicine for cancer treatment in India.

Dr Jyoti Agarwal, Chairperson of BALCO Medical Centre, stated that the collaboration with Anuva will bring together the best of knowledge, technology and research to serve the people of India better through precision medicine and targeted treatment.

She continued by saying that this cancer-specific bio/data library will speed up research initiatives by fusing biological characteristics with known risk factors to identify the key genes that drive cancer progression. The resulting knowledge will improve the understanding of how genetic variants influence cancer, thereby increasing the effectiveness of diagnosis and treatment.

(*Source: https://www.tribuneindia.com/news/health/vedantas-medical-arm-ties-up-with-anuva-for-cancer-research-in-india-438735*)

Risk of Dementia is Increased by 2.5 Times Due to Schizophrenia

A new systematic review and meta-analysis published in *Psychological Medicine* reveal that psychotic disorders have a strong link with dementia in comparison to other mental health disorders, such as depression or

anxiety. The study showed that people with psychotic illnesses such as schizophrenia are 2.5 times more likely to develop dementia than those who do not have a psychotic disorder.

In the study, the researchers analyzed the data from 11 studies from nine countries in four continents, which included almost 13 million participants in total. After analysis, they found that due to various psychotic illnesses, there was a greater risk of dementia in later parts of life, independent of the age at which someone first experienced their mental illness. Additionally, they discovered that individuals with a history of psychotic diseases are significantly more likely to receive a dementia diagnosis while they are still in their 60s than the general population. The findings of the study add to the list of modifiable risk factors for dementia. One such modifiable risk factor is post-traumatic stress disorder (PTSD), which can increase the likelihood of dementia along with other factors such as depression and anxiety. The author of the article stated that people with psychotic disorders are more likely to have other health conditions such as cardiovascular disease (CVD) or obesity, which can increase the risk of dementia. She added that they are also more likely to have a poor diet, smoke or use drugs, which may harm their health in ways that could increase their likelihood of developing dementia.

(*Source: https://www.hindustantimes.com/lifestyle/health/schizophrenia-might-enhance-dementia-risk-2-5-times-study-101665112009172.html*)

Risk of Obesity in Kids is Increased by the Intake of Ultra-Processed Food by Mothers

A recent study published in the *BMJ* revealed that a mother's use of ultra-processed foods was connected to an elevated risk of being overweight or obese in her kids, regardless of other lifestyle risk factors. According to the WHO, 39 million children were overweight or obese in 2020, leading to increased risks of heart disease, diabetes, cancer and early death.

The study suggested that mothers may benefit from limiting their intake of ultra-processed foods. The researchers also suggested that the dietary guidelines should be refined, including the removal of financial and social barriers to improve nutrition for women of childbearing age and to reduce childhood obesity. In the study, the researchers used data from the Nurses' Health Study II (NHS II) and the Growing Up Today Study (GUTS) I and II. The researchers also considered a range of other potentially influential factors, such as the mother's weight (body mass index [BMI]), physical activity, smoking, living status and partner's education, as well as children's ultra-processed food consumption, physical activity and sedentary time.

Based on the analysis, the study results showed that a mother's ultra-processed food consumption was associated with an increased risk of obesity or being overweight in her offspring. For example, a 26% higher risk was seen in the group with the highest maternal ultra-processed food consumption (12.1 servings/day) in comparison to the lowest consumption group (3.4 servings/day). It also found that prenatal ultra-processed food intake had no significant association with an increased risk of offspring being overweight or obese.

(*Source: https://theprint.in/features/study-mothers-intake-of-ultra-processed-food-associated-with-risk-of-obesity-in-kids/1156511/*)

New 3D Technique Developed to Treat Diabetic Foot Ulcers

Researchers at Queen's University Belfast have created a new cost-effective bandage therapy called a scaffold to treat diabetic foot ulcers, which provides better patient outcomes.

The scaffolds, which are created by 3D bioprinting, gradually release antibiotics over a 4-week period to cure the wound. The study was published in *The Journal of Drug Delivery and Translational Research*.

The scaffold structure, according to experts, is a unique carrier for cell and medication transport that improves wound healing. By using these scaffolds, which function like windows, surgeons can continuously monitor the healing process without having to remove them, as frequent interference for changing the dressing increases the risk of infection and slows down the healing process. "The 'frame' contains an antibiotic that kills the bacterial infection, and the 'glass', is made of collagen and sodium alginate, which might include a growth factor that promotes cell growth. The scaffold has two molecular levels, each of which is crucial to the healing of the wound."

This new development has been shown to enhance the quality of life among patients and decrease the cost of treatment and also the clinical burden in diabetic foot ulcer treatment.

(*Source: https://m.dailyhunt.in/news/india/english/ani67917250816496966-epaper-anieng/new+3d+technique+developed+by+researchers+to+revolutionise+diabetes+treatment-newsid-n429702646?listname=topicsList&topic=health%20fitness&index=2&topicIndex=8&mode=pwa&action=click*)

Risk of Adverse Outcomes Increased by Long-term Antidepressant Use

Long-term antidepressant usage has been associated with an increased risk of adverse effects, including CVD, cerebrovascular disease (CV), coronary heart disease (CHD) and all-cause mortality, according to a study published in the *British Journal of Psychiatry Open*.

The study involved 2,22,121 participants whose information was connected to primary care records in 2018. They found that 10-year antidepressant usage was linked to an almost twofold increased risk of CVD and CVD mortality, a nearly twofold high risk of CHD, a greater chance of CV and an almost twofold increased risk of all-cause mortality.

At 5 years, selective serotonin reuptake inhibitors (SSRIs) were linked to a lower risk of developing diabetes. At 10 years, SSRIs were linked to a higher risk of CV, CVD and all-cause mortality, a lower risk of diabetes and hypertension, and a higher risk of CHD, CVD and all-cause mortality when compared to non-SSRIs.

Mirtazapine, venlafaxine, duloxetine and trazodone caused more adverse effects; however, SSRIs were also associated with an elevated risk.

The studies highlight the importance of proactive cardiovascular monitoring and prevention in patients with depression taking antidepressants, as both have been linked to greater risks.

(*Source: https://www.medscape.com/viewarticle/981951#vp_3*)

Dupilumab Reduces Eczema Symptoms among Infants and Young Children

A phase 3 clinical trial recently reported in *The Lancet* demonstrated that the monoclonal antibody drug dupilumab significantly reduced the symptoms of eczema in children between the ages of 6 months and 5 years old when administered in conjunction with a topical corticosteroid.

Dupilumab's safety and effectiveness were assessed in phase 3 clinical trial on 162 kids with uncontrolled moderate to severe atopic dermatitis between 6 months and 5 years. The study participants either received an injection of the drug and a topical corticosteroid of low potency every 4 weeks or only a topical corticosteroid in the placebo group.

According to researchers, more than half of the patients getting dupilumab showed 75% improvement in their Eczema Area and Severity Index (EASI)-75 after 16 weeks of treatment. The EASI-75 is a scale used by medical practitioners to assess the quantity and severity of inflammatory lesions on the body.

Additionally, after 16 weeks of treatment with dupilumab, researchers discovered that 28% of patients had clean or clear skin, and 48% had a decrease in itching. Some minor side effects, such as conjunctivitis/dry eye condition, were common, and overall the safety profile was very good, but more studies were necessary for dupilumab.

(*Source: https://www.medicalnewstoday.com/articles/new-drug-helped-reduce-eczema-in-75-in-infants-and-young-children#What-is-dupilumab?*)

Ascl1 Protein was Identified to Activate a Group of Genes Related to Cardiomyocytes and Help in Heart Muscle Repair

A recent study has discovered a quicker and more efficient method to rewire scar tissue cells (fibroblasts) into sound heart muscle cells.

Researchers at the University of North Carolina in Chapel Hill have developed a more effective technique for reprogramming scar tissue cells (fibroblasts) to transform them into healthy cardiac muscle cells. Their findings were reported in the journal *Cell Stem Cell* (cardiomyocytes). After a heart attack or as a result of a cardiac condition, fibroblasts create the fibrous, stiff tissue that results in heart failure. The researchers found that fibroblast-to-neuron conversion triggered a set of cardiomyocyte genes. This activation was caused by Ascl1, one of the master-programmer "transcription factor" proteins used to construct the neurons.

Ascl1 triggered the genes for cardiomyocytes; hence upon adding it to the three transcription factor combinations, they had been using to make cardiomyocytes to its effect. They were astounded to discover that Ascl1 had a 10-fold boost in reprogramming efficiency, or the proportion of successfully reprogrammed cells.

(*Source: https://www.hindustantimes.com/lifestyle/health/researchers-identify-protein-partners-that-might-reprogram-scar-tissue-cells-repair-heart-muscle-101665153471213.html*)

Asthma Risk in Children could be Detected Using Childhood Asthma Risk Tool

A team of researchers associated with the CHILD Cohort Study (CHILD) have created an accessible revolutionary symptom-based screening tool to determine the risk of asthma in kids as early as 2 years old.

The efficacy of the tool known as the Childhood Asthma Risk Tool, or CHART was published in the

Journal of the American Medical Association (JAMA). In the study, CHART was used to analyze data from 2,354 children who participated in CHILD, a long-term study that began following about 3,500 Canadian children's physical, social and cognitive development from conception. CHART was able to predict which of these children will have a persistent wheeze by the age of 5, a crucial sign of asthma. The performance of CHART was compared to data from two more cohort studies to confirm the study's conclusions utilizing the CHILD data. This is the first study that, according to the experts, has created a noninvasive technique for the early diagnosis of asthma and persistent wheezing in a general population and that has now been validated in general and high-risk populations.

(*Source: https://www.tribuneindia.com/news/health/new-symptom-based-screening-technique-for-detecting-asthma-risk-in-children-439012*)

Omega-3 may Provide a Brain Boost for People in Midlife

According to a recent study published in *Neurology*, people who consume more omega-3 in their middle years are benefited more than those who consume less omega-3. The study included 2,183 men and women with an average age of 46. The researchers examined the fatty acid profile from the blood samples of each participant and also scanned their brains with magnetic resonance imaging (MRI) technology. Additionally, the individuals underwent neurological examination which evaluated the participants' executive function, thinking, processing speed and delayed episodic memory.

Twenty-five percent of the participants who had omega-3 fatty acids blood levels below 4% were put in the low group, while the rest participants having an omega-3 level of 5.2% were assigned to the higher group. The participants in the higher group had more grey matter and better reading and logical reasoning scores, while those in the lower group were more likely to smoke and have diabetes and were less likely to have a college degree. The study's findings suggest that there may be an association between consuming omega-3 in midlife and an improvement in brain function for adults.

(*Source: https://www.medicalnewstoday.com/articles/omega-3-may-boost-brain-health-for-people-in-midlife-study#Omega-3:Things-to-know*)

Alzheimer's Disease and Normal-Tension Glaucoma

Studies have speculated that glaucoma and Alzheimer's disease share common pathophysiology. Findings of a new retrospective study from Taiwan presented at the American Academy of Ophthalmology (AAO) 2022 Annual Meeting in Chicago has demonstrated an association between the two. According to the new study, over half of the individuals with normal tension glaucoma are likely to develop Alzheimer's disease compared to those who do not have glaucoma.[1,2]

A total of 15,317 patients with normotensive glaucoma diagnoses between January 2001 and December 2013 and age- and sex-matched 61,268 persons as controls were selected for the study from the Taiwan National Health Insurance Database. The patients were followed-up for 13 years (median).

The incidence of Alzheimer's disease in patients with normal-tension glaucoma was 6.7% compared to 4.2% in those who did not have normal-tension glaucoma with an adjusted hazard ratio of 1.52. Patients with normotensive glaucoma had higher prevalence of hyperlipidemia, hypertension, diabetes and coronary artery disease. The risk for Alzheimer's disease remained significant even after adjusting for these variables. Age, female sex and a history of stroke were significantly associated with the risk of Alzheimer's disease among patients with normal-tension glaucoma. No association was found between the various glaucoma medications and Alzheimer's disease.

Normal-tension glaucoma is a subtype of primary open-angle glaucoma, but with normal intraocular pressures. The disease can progress from loss of vision to bilateral blindness. It is often an incidental diagnosis. Clinicians should be aware of the association between Alzheimer's disease and normal-tension glaucoma. All patients of normal tension glaucoma, particularly those at risk, should therefore be screened for Alzheimer's disease.

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