13TH GABRIEL NETWORK MEETING

NOVEMBER 27-29, 2024
LES PENSIÈRES CENTER FOR GLOBAL HEALTH
VEYRIER-DU-LAC, FRANCE

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Special Report

From November 27 to 29, 2024, over 100 delegates representing researchers, physicians, specialists in laboratory diagnostics, academics, and scientists from both the public and private sectors in 22 countries gathered at Les Pensières Center for Global Health for the 13th international meeting of the GABRIEL network. This document highlights key aspects of the symposium, summarizing speeches and core discussion points.

The GABRIEL international meetings have become a platform for members to exchange experiences, explore new opportunities for collaboration, assess advancements in quality evaluation, and delve into the latest scientific developments in infectious diseases. This year's program specifically addressed the epidemiology and surveillance

of factors contributing to the emergence of infectious diseases. In addition, sessions were devoted to the global burden of tuberculosis, antimicrobial resistance, acute respiratory infections, and meningitis. This program offered researchers a valuable opportunity to identify diagnostic challenges and gaps, while fostering knowledge exchange to enhance surveillance strategies and improve clinical management.

As in previous years, the program featured the "GABRIEL Young Scientist Award" that supports promising young researchers from low- and lower-middle-income countries. This initiative enables them to present their work at international scientific symposia, thus helping them enhance their career development. Two winners were selected for this year's best presentations.

SYMPOSIUM DAY – NOVEMBER 27, 2024

Welcome Address

Mr. Alain Mérieux, President of the Mérieux Foundation, delivered the welcome address to the audience, sharing the following reflections:

"The world has become increasingly complex and unpredictable. Urbanization is accelerating, forests are undergoing profound changes, and the climate is shifting dramatically—yet the persistent threats of viral and bacterial pathogens remain. We must stay vigilant in the face of these challenges, and maintain a long-term perspective, because biology recognizes no borders. Our only option is to confront these adversities with resolve. As part of our efforts, we continue to collaborate closely with the Pasteur Institute, united by a shared vision. This partnership is exemplified through joint initiatives in countries such as Cameroon and Senegal."

The President expressed his optimism for the future of GABRIEL, even as he acknowledges the challenging environmental conditions and persistent geo-political turbulences the network faces in various parts of the world.

Dr Florence Komurian-Pradel, Head of the GABRIEL network, introduced the GABRIEL network, which is dedicated to enhancing the research capacity of developing countries in detecting, analyzing, characterizing, and monitoring infectious disease pathogens. The network also aims to promote the sharing of expertise, tools, and knowledge vital for advanced applied scientific research on infectious

diseases, antimicrobial resistance, and emerging pathogens. Recent advancements have been achieved through the collaborative efforts of GABRIEL's international working groups, which focus on respiratory illnesses and hepatitis.

Session I – Methods to predict and detect the emergence of pathogens and outbreaks

Chaired by Dr. Ana Tereza Ribeiro de Vasconcelos, Brazil, and Dr. Daniel Mukadi, Democratic Republic of Congo

Community based surveillance of infectious diseases

Dr. Jose Guerra from the Sigia Consultancy, Portugal, opened his presentation with the WHO definition of public health surveillance "the systematic ongoing collection, collation and analysis of data for public health purposes and the timely dissemination of public health information for assessment and public health response as necessary". Public health surveillance is mostly used for long-term health planning and monitoring but also plays a vital role in the early detection and response of outbreaks to minimize their impact on the population. To this aim, it relies on two main processes: indicator-based surveillance mainly from healthcare facilities, and event-based surveillance from multiple sources, including community members.

While the term community-based surveillance is still used with different meanings and for different purposes, its definition was clarified in 2018 by a WHO working group as "the systematic detection and reporting of events of public health significance within a community-by-community members". There is still no consensus on how to conduct community-based surveillance, but for early detection of outbreaks, its scope is usually put on unexpected events and suspect cases of a few outbreaks' prone diseases. Community health volunteers or workers are then tasked to collect and report information to supervisors in charge of discarding irrelevant information and escalate it for verification, risk assessment and response.

Community-based surveillance can allow the capture of information before cases occur in the healthcare system, which is of special interest to remote areas and marginalized groups. Yet, it also faces several challenges, such as high costs due to the need for complex infrastructure, the risk of overburdening volunteers, or the difficulty of providing observable benefits to the community. Guidance and training materials have been published on the topic and are available to support implementation. As research is still required to assess its real value for early detection and response and the best modalities to be used, it is crucial for implementers of community-based surveillance systems to ensure feasibility and sustainability from the design phase.

Wastewater-based infectious disease surveillance

Dr. Albert Bosch from the University of Barcelona, Spain, spoke about the diverse range of infectious viruses present in human wastewater that can cause diseases such as dengue fever, influenza, SARS-CoV-2, poliomyelitis, Ebola, and chikungunya. These viruses, characterized by their ability to rapidly mutate and recombine, present significant challenges for vaccine and anti-viral drug developments.

SARS-CoV-2 variants with specific mutations have been investigated using duplex quantitative real time RTqPCR assays which serve as a complementary method for rapid variant tracking and surveillance in wastewater-based epidemiology.

Poliovirus type 1 is responsible nowadays for most cases of wild-type polio, which is concentrated in two countries: Afghanistan and, particularly, Pakistan. However, viral mutations have led to the emergence of pathogenic vaccine-derived polioviruses from attenuated viruses present in the oral Sabin vaccine. The mutated poliovirus variant cVPDV2 derived from a vaccine strain was detected in Barcelona wastewater in September 2024. A phylogenetic analysis revealed that this variant closely aligns with strains circulating in Algeria, Mali, and Guinea.

Besides poliovirus, other enteroviruses may also cause acute flaccid paralysis, among them enteroviruses A71 or D68. An enterovirus A71 outbreak that occurred in Catalonia, Spain, in 2016, causing acute flaccid paralysis and rhombencephalitis. In 2023 and 2024, cases of paralysis related with enterovirus D68 were also reported in the United States.

Wastewater-based surveillance of viruses enables to elucidate the circulation of virus infections, not only symptomatic but also asymptomatic, thus providing more light into the epidemiology of viral syndromes.

Modelling emerging infectious diseases

Dr. Janne Estill from the University of Geneva discussed the use of mathematical models that assess the risks associated with infectious disease transmission. While no model can be fully accurate, these tools help conceptualize real-world phenomena and make predictions, offering valuable insights for public health policy and decision-making.

Mathematical models integrate data from various sources to generate estimates and plausible scenarios that simulate transmission dynamics. These dynamics are influenced by environmental, social, demographic, and economic determinants. However, no single model can account for every variable.

Mathematical models are widely used to describe the mechanism of evolving epidemics. When combined with certain sampling methods, these models can analyze

public health surveillance data, evaluate the effectiveness of interventions (e.g., social distancing and quarantine), and forecast disease progression.

For example, during the early stages of the SARS-CoV-2 pandemic in 2020, a model focusing on the age distribution of vulnerable populations was used to project the epidemic's trajectory. It showed that while children were not primary drivers of the epidemic, they played a significant role in transmission dynamics. Predictive scenarios suggested that lifting all restrictions would cause a rapid rebound of cases within weeks. However, the model's most severe outcomes were considered unlikely. The model emphasized that a comprehensive prevention strategy targeting all population groups is essential until a vaccine becomes available.

As another example, HIV transmission in southern Malawi was examined, using a flexible individual-based model incorporating spatial and individual-level factors. Calibrated to Malawi's epidemic, it successfully explained the variability in HIV prevalence within the country.

Artificial intelligence-based tools to detect healthcare-associated infections and emerging pathogens.

Dr. Anna Odone from the University of Pavia, Italy, stated that AI-based tools can significantly improve the prevention, detection, and monitoring of healthcare-associated infections. These tools can also be used to identify at-risk patients, as well as develop personalized healthcare plans and analyze patterns of bacterial resistance.

Studies have demonstrated that AI-based models perform as well or better than non-AI based models. Their performance metrics favor specificity and negative predictive value, over sensitivity and other performance measures. This points to the potential of AI models to effectively distinguish non-infected from infected individuals.

While structured data, such as electronic health records, continues to predominate, there is growing utilization of unstructured data (e.g., free-text clinical notes and wound images). The integration of combined data sources reflects AI's advancing ability to process increasingly complex datasets. Additionally, there has been a significant growth in the use of natural language processing techniques.

Other evidence suggests that AI-based models perform as well or better than traditional methods (in terms of clinical scores, standard or automated surveillance, logistic regression). However, challenges persist in performance evaluations, with many studies lacking comparators and few prospective assessments. In addition, AI's organizational impact and its implementation in clinical practice has yet to be fully evaluated.

A case study evaluating the use of an AI-driven multivariable predictive algorithm to screen surgical site infections in hospital patients found that the AI model reduced

manual record screening time by 88%. In general, detection models outperform in key metrics, such as accuracy, specificity, and negative predictive value. The successful integration of AI in healthcare prevention requires transparent data governance, high-quality studies, and a multidisciplinary collaboration between IT experts and clinical professionals.

Session II – Factors contributing to the emergence of infectious diseases

Chaired by Dr. Sayera Banu, Bangladesh, and Dr. Ester Sabino, Brazil

Changes in biodiversity and their impact on the transmission of infectious diseases

Dr. Serge Morand from the CNRS, Thailand, emphasized the multiple factors driving the spread of epidemics and the rise in fungal diseases affecting animals and plants. Such factors include urban demographic transitions, the global dominance of domestic animal biomass, agricultural expansion, deforestation, declining biodiversity, and zoonotic disease transmission to humans. Outbreaks of vector-borne and zoonotic diseases have been linked to reduced forest cover and the massive increase in palm oil production. Additionally, declining biodiversity in Southeast Asia has been associated with a higher risk of rodent-borne diseases.

The One Health High Level Expert Panel was established in 2020 by FAO, OIE, UNEP, and WHO. Its mission is to provide strategic guidance and expert advice on implementing the One Health approach in the combat against emerging health threats at the human-animal-environment interface. By fostering communication and cooperation among these three sectors, it aims to develop sustainable solutions for improving health outcomes for people, animals, and ecosystems.

Different international initiatives were presented. PREACTS was founded as an initiative aimed at enhancing global preparedness and response to pandemics. PREZODE (PREventing ZOonotic Disease Emergence), too, is an international initiative launched in 2021 to proactively prevent the emergence of zoonoses through integrated and collaborative approaches. And finally, ASAMCO is an initiative focused on monitoring and managing contaminants in animals and the environment that may pose risks to human, animal, and ecosystem health.

These initiatives are aligned with the principles of the One Health approach, which recognizes the interconnectedness of human, animal, and environmental domains. The health of our ecosystems and the maintenance of biodiversity are vital to ensure resilience against our own health challenges.

Emerging infections in displaced populations

Dr. Souha Kanj from the American University of Beirut, underscored the consequences of ongoing worldwide armed conflicts. Beyond causing death and injury, these conflicts profoundly disrupt the lives and threaten the survival of civilian populations through forced migration, the spread of infectious diseases, and the deliberate use of famine as a weapon. Other contributing factors include the destruction of civilian infrastructure and healthcare facilities, limited medical laboratory capacity, drug shortages, disrupted supply chains, as well as overcrowded encampments and sexual violence. Displaced populations suffer from a wide spectrum of health issues that include vector- and water-borne diseases, traumatic wound infections, respiratory illnesses, sexually transmitted infections, and vaccine-preventable diseases.

The Syrian civil war has triggered a humanitarian crisis, leading to the resurgence of previously rare infectious diseases such as poliomyelitis, typhoid, and whooping cough. The mass displacement of refugees has resulted in overcrowded camps struggling to meet the healthcare needs of millions. Outbreaks of leishmaniasis have occurred in Lebanon, Turkey, and Iraq, while polio has re-emerged in Syria and Gaza, posing a potential international threat. In Yemen, dengue fever has become rampant, affecting displaced populations living in unsanitary conditions with limited access to medical care, exacerbated by flooding and inadequate mosquito control. Cholera-related deaths have been reported following the conflict in Sudan, and cases of antimicrobial-resistant tuberculosis have been rising in Ukraine.

National governments, humanitarian NGOs, international organizations, and local authorities are collaborating to combat the rampant spread of infectious diseases among displaced populations. Key measures include providing technical guidance for settlement planning, lifting restrictions on imported medicines, bolstering microbiological services with essential resources, improving clinical data collection in hospitals, and increasing support for healthcare workers. However, basic measures such as the upgrade of the sewage and water supply systems are undermined by ongoing military attacks and a blockade that has hindered the improvement of the health and sanitation systems.

Breakdown in public health measures

Dr. Marilda Siqueira from the Oswaldo Cruz Foundation, Brazil, spoke about the factors that have contributed to the breakdown in public health measures in Brazil. These factors include:

- vaccination hesitancy, or the reluctance or refusal of individuals to be vaccinated despite vaccine availability. This has resulted in the re-emergence of controlled or eradicated diseases, such as measles, polio, and diphtheria.
- the dissemination of fake news and misinformation causing confusion, fear, and distrust in health authorities. The low adherence to prevention protocols is an issue that was starkly evident during the COVID-19 pandemic.
- social inequity that raises barriers to equitable healthcare access and generates greater vulnerability of marginalized population groups. Disadvantaged communities often experience higher infection rates during seasonal influenza outbreaks, for example.
- insufficient healthcare infrastructure and the shortage of drugs, diagnostic tools, and essential supplies that undermine the capacity to track, monitor, and contain outbreaks. This is further compounded by delays in identifying infected individuals and implementing quarantine and treatment measures.

Measles is a prime example of a preventable disease that has re-emerged due to the interplay of the factors mentioned above. Recent measles outbreaks, even in developed countries, have been largely attributed to vaccine hesitancy and the global decline in vaccination rates. Anti-vaccine sentiments, fueled by misinformation such as the link between vaccines and autism, have weakened herd immunity.

With social inequalities exacerbating public health crises, it has become vital to address these disparities. This requires actions, such as strengthening global supply chains for essential goods, investing in local healthcare infrastructure, ensuring equitable resource distribution, and fostering public health partnerships that promote universal access to healthcare.

Session III – Critical research conducted in the context of emerging diseases

Chaired by Dr. Firdausi Qadri, Bangladesh

Dr. Branagh Crealock-Ashurst from the Pandemic Science Institute, UK, described the PEARLES framework as an analytical tool used in clinical research to address challenges in the response to infectious disease outbreaks. The PEARLES acronym represents the Political, Economic, Administrative, Regulatory, Logistical, Ethical, and Social

domains. This initiative aims to identify and reduce barriers to clinical research, enabling greater progress in responding to health emergencies. These mainly concern:

- Political factors that are related to research and associated with public engagement and coordination between governments and global organizations. Challenges lie in addressing the public's mistrust of health authorities and misconceptions about their policies.
- Economic considerations that bear on the costs for trials, scientific research, human resource matters, and vaccine development.
- Administrative challenges that address procedural bottlenecks in research approvals, data protection requirements, and limited availability of skilled personnel.
- Regulatory matters that concern the processes required by government bodies for trial standardization and medical product approval.
- Logistical aspects that include the implementation of digital technology, the efficient maintenance of supply chains, and management of operational matters. The readiness of basic health facilities to keep pace with a disease outbreak is also a critical logistical component.
- Ethical considerations that emphasize the maintenance of research integrity and equity, guided by ethical regulations at local, national, and international levels. The development of protocols for obtaining patient consent and building ethical human resource capacities is vitally important.
- Social dynamics that cover collective behavior, communications, and interactions between social groups and individuals. Public trust and community engagement are fostered by reducing the stigma of disease and preventing the spread of rumors.

The COVID-19 pandemic drew attention to the role of politics in shaping public perceptions of health policies and driving research responses. However, it also exposed significant gaps that include the absence of pre-planned research methodologies for emergencies, and delays in obtaining regulatory approvals. These challenges were particularly pronounced in low- and middle-income countries (LMICs).

Clinical study design in the context of emerging infectious diseases

Prof. Rodolphe Thiebaut from the University of Bordeaux, France, highlighted the critical need to identify the most suitable study design for evaluating vaccines and treatments during a disease outbreak. Determining the most appropriate protocol to adopt during initial trials is a key consideration. Is a control group needed? Is a placebo group ethically acceptable? Are cluster trials and wedge trials effective approaches? Will a ring vaccination strategy be effective?

Examples have been shown through Ebola vaccine development. The IMI2 EBOVAC2 and PREVAC (Partnership for Research on Ebola Vaccination) are research initiative aimed at assessing the safety, efficacy, and immune response of candidate Ebola vaccines. They illustrate how mathematical modeling and immunobridging, a method based on immune response data, allow to help for accelerating the development of vaccines.

Inequities between HICSs and LMICs in addressing new epidemics

Dr. Cheleka Mpande from WHO in Switzerland spoke about global health inequalities between HICs and LMICs that were exacerbated during COVID-19 and monkeypox health emergencies. While HICs provide better medical access to their population, LMICs must cope with barriers such as limited research capacity, inadequate healthcare infrastructures, and reliance on foreign aid. The dominance of pharmaceutical R&D driven by HICs often overlooks the capacities of LMICs, leading to products that are poorly suited to their needs. For instance, mRNA vaccines requiring ultra-cold storage highlighted this mismatch. To address these inequities, global collaboration and equitable resource distribution must be strengthened, ensuring that health solutions are tailored to the specific challenges faced by LMICs.

LMICs receive only 0.2% of global health research funding and experience significant disparities in human resources, with 56 times fewer researchers per capita compared to HICs. Limited access to higher education institutions further restricts their research capacity, and many nations fall short of meeting global health R&D spending targets. These challenges exacerbate inequalities in healthcare advancements and resource allocation.

During pandemics, LMICs often experience delayed access to vaccines, relying on donations or COVAX—both frequently influenced by geopolitical vaccine diplomacy—underscoring global inequities.

Strengthening health systems requires geo-diversification in medical countermeasures through local and global R&D, knowledge sharing, and innovative technology transfer. Establishing mRNA R&D and manufacturing in LMICs demands substantial investment in supply chains, regulation and long-term policy support. Building a R&D ecosystem requires infrastructure, workforce development and training programs, and international collaboration on regionally important diseases. The Global Lipid Consortium promotes mRNA research by optimizing manufacturing and accelerating novel applications like chikungunya and HPV vaccines.

These initiatives seek to strengthen the R&D capacity of LMICs and integrate them into global networks for medical innovation and production.

Open discussion

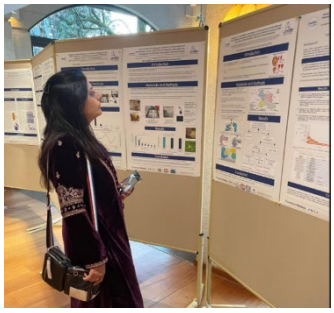
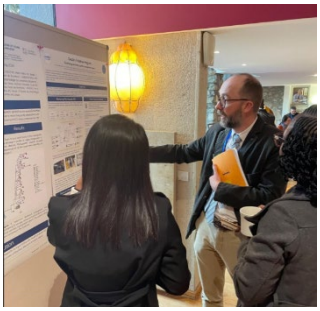
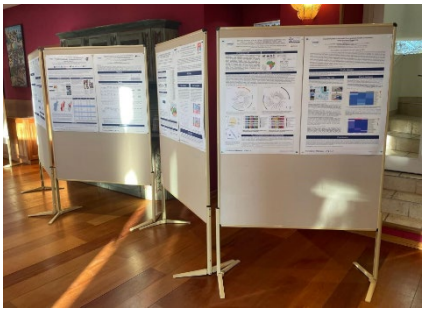
Chaired by Dr. Marianne Abifadel, Lebanon, and Dr. Florence Komurian-Pradel, France, with the following panelists: Dr. Marilda Siqueira (Brazil), Prof. Daniel Mukadi (Democratic Republic of Congo), Dr. Firdausi Qadri (Bangladesh), Dr. Marianne Abi Fadel (Lebanon), and Prof. Luc Samison (Madagascar)

The discussion centered on two critical questions: What is the role for the GABRIEL network in the context of outbreaks? And are the GABRIEL members strong enough to contribute to new challenges?

In response to these questions, the panelists and members of the audience expressed the following:

- The COVID-19 pandemic brought out challenges in disease identification and underscored the global shortage of critical capacities. We must address these issues collaboratively and seek greater funding through partnership-building. GABRIEL cannot tackle such massive tasks alone. In 2025, we should look toward integrating artificial intelligence and machine learning to ensure that we can keep abreast of the latest technology that /might have a positive effect on public health.
- More frequent meetings would serve to share our experience on specific research matters and determine whether current strategies suffice or require adjustments for faster and more effective responses.
- The GABRIEL network remains largely unknown in Africa, and there is a limited exchange of scientists within the network. In the event of a new pandemic, GABRIEL could play a critical role in supporting scientists to assess and understand the impact in affected countries and ensure a coordinated response.
- The GABRIEL network has built the strength to address new challenges through strong relationships between researchers, improved infrastructure, and quality management.
- The COVID-19 pandemic drew attention to the critical importance of building local health capacities with a holistic approach that accounts for genetic specificities, community disease profiles, and underlying chronic conditions like diabetes. By focusing on targeted training in disease sequencing and on local epidemiological environments, communities can develop adaptive health strategies that tackle malnutrition and chronic disease vulnerabilities. A localized approach enables tailored interventions that recognize the unique genetic and environmental factors influencing disease transmission and health outcomes. In Africa, fostering local participation has been crucial to ensure that solutions are tailored to regional needs.

- Our digital presence and communication strategy should lead us to develop a specific website for the network, set up social media channels, and develop open-source software and informatics platforms for collaborative knowledge dissemination. By leveraging members' diverse expertise across different domains, we can facilitate cross-disciplinary information exchange, enable comparative analysis between infectious and chronic disease research, and enhance collective research capacities through shared insights and experiences.

Question: What are the main barriers/weaknesses that impede countries from responding to outbreaks?

- Effective research collaboration requires strategic funding, capacity building, and data-sharing with health authorities. By fostering systematic collaboration, strengthening inter-laboratory connections, and developing a consistent publication strategy, our research network can establish greater visibility, credibility, and impact in addressing complex health challenges through shared scientific knowledge and resources.

Oral poster presentations

Chaired by Suruchi Shukla, India and Monzer Hamze, Lebanon

Chromoblastomycosis, sporotrichosis in Madagascar: an update on epidemiology, clinical presentation and molecular diagnosis

Dr. Tahinamandranto Rasamoelina from the Charles Mérieux Center for Infectious Disease of the Antananarivo University, Madagascar, described chromoblastomycosis (CBM) as a chronic skin fungal infections caused by a specific fungal species found in the soil and vegetation. It occurs mainly in tropical and subtropical regions. The infection can be disfiguring, causing wart-like lesions of the skin which gradually spread to adjacent areas. Sporotrichosis (SPT) is another skin infection caused by the inoculation of a fungus species. These two skin diseases are on the WHO list of neglected tropical diseases. The epidemiology has not been recently described in literature.

Our current investigation aims to develop molecular tools for pathogen identification of these diseases. It is designed to set up a permanent clinical-biological network that can confirm diagnosis and ensure targeted patient care.

Our results show that CBM and SPT are widespread and may be presently extending across Madagascar. Male agricultural workers are the most affected by both infections. Among the 450 recruited cases of our study, 33.5% were suspected of having CBM and presented crusted, verrucous tumoral lesions. In addition, 23.8% of those suspected of having SPT presented ulcerative and nodular lesions of the lymphatic system of the lower limbs.

The clinical knowledge gained during this study with the aid of a reliable PCR tool will help the national authorities to set up a proper control and prevention program.

The longitudinal landscape of immune reconstitution after acute SARS-CoV-2 infection of single-cell resolution

Dr. Zichun Xiang of the Chinese Academy of Medical Sciences in Beijing described the complex heterogeneity of post-acute sequelae (PASC) of COVID-19. Its most prevalent manifestations are immune dysregulation, microbial dysbiosis, endothelial abnormalities, and dysfunctional neurological signaling.

The study was conducted to identify core cell subsets that drive the long COVID inflammatory response and discover intervention targets for PASC. Single-cell RNA sequencing and cytokine assays were utilized to investigate longitudinal immune changes. Enrichment analysis revealed longitudinal changes with megakaryocytes, dendritic cells, and natural killer cells gradually recovering, while subsets of T cells, monocytes, and plasma cells remained abnormal, even one year later.

Our results show that the process from acute SARS-CoV-2 infection to the condition one year after recovery was characterized by multidimensional single-cell resolution without the interference of vaccination or re-infection. Findings reveal the long-term variable nature of COVID-19 immune reconstitution and suggest that CDKN1C+ nonclassical monocytes are potential biomarkers and treatment targets for PASC.

Epidemiological profile of patients with delta hepatitis and molecular characterization of the HDV virus, Rio Branco, Brazil

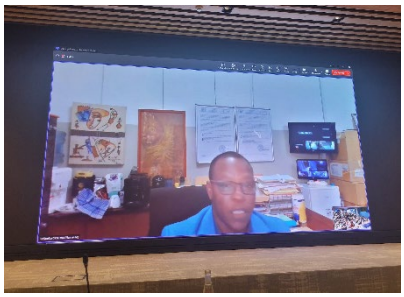
Dr. Rutilene Barbosa Souza from Center of Infectiology Charles Mérieux in Brazil stated that hepatitis D, caused by the HDV virus, is endemic in the Amazon region of South America and closely linked to hepatitis B virus (HBV) infection. Indigenous riverside populations are particularly vulnerable to this disease.

The study aimed to quantitatively diagnose HDV by measuring the viral load in hepatitis D carriers in the Acre region of Brazil.

Biological samples were collected, and viral RNA was extracted through automated methods. HDV-RNA was then amplified, sequenced, and analyzed using bioinformatics tools.

The results revealed that HDV-3 was the predominant genotype, exhibiting significant genetic variability. This research provides a valuable resource for managing chronic hepatitis D, offering crucial insights for patients and physicians to better understand the stages and progression of HDV infection.

Spatio-temporal distribution of human population-bearing antibodies against five viral hemorrhagic-fever viruses in urban and peri-urban areas of Bamako in Mali



Prof. Bourema Kouriba from the Charles Mérieux Center of Infectiology, Mali, described viral hemorrhagic fevers (VHFs) as a global health threat, especially in Mali, a country with significant human activity and trade. There is limited data on asymptomatic carriers of hemorrhagic fever viruses, which may significantly contribute to disease transmission.

In 2023, a cross-sectional study was conducted in Bamako's urban and peri-urban areas to assess human seroprevalence of hemorrhagic fever viruses and map the geographical distribution of antibody carriers.

Venous blood samples were collected from asymptomatic individuals at various sites. IgM and IgG specific to Rift Valley fever virus, Crimean-Congo hemorrhagic fever virus, Ebola virus, Lassa hemorrhagic virus, and hantavirus were tested using Luminex technology (MAGPIX®).

Antibodies against all five viruses were identified. The highest IgG seroprevalence was observed for Rift Valley fever in abattoir samples, Crimean-Congo hemorrhagic fever in livestock market and farm samples, and Ebola in farm samples. The highest IgM seroprevalence was observed for Rift Valley fever in livestock market samples.

These findings reveal that the hemorrhagic fever virus circulates in exposed asymptomatic humans as do the risks of disease transmission in urban and peri-urban areas. Enhanced surveillance of these viruses in humans, animals, and the environment is urgently needed in Mali.

Challenges to hepatitis C testing and treatment in a rural setting of Lao PDR

Dr. Phimpha Paboriboune from the Center Infectiology Lao-Christophe Mérieux Center, mentioned that the Asia-Pacific region bears over 45% of the global viral hepatitis burden. In Lao PDR, the prevalence of HCV exposure averages around 2% across the country, but the rural Samuoi district in Saravane province reports a strikingly high rate of 24.4% among adults over 30, underscoring the urgency of addressing the disease. Direct-acting antivirals are highly effective in treating the prevalent genotype 6. However, more than 40% of patients miss doses during treatment, which increases the chance of treatment failure and highlighting significant challenges in ensuring compliance.

The high adherence (98%) to drug treatment has led to a 96% sustained viral response rate. However, the 20% loss to follow-up constitutes one of the barriers to HCV testing and treatment in rural areas, emphasizing the need to improve compliance in resource-constrained settings.

WHO-recommends a simplified, decentralized treatment for HCV diagnosis which aligns with the Lao National Strategic Plan on viral hepatitis. Scalable interventions are needed to improve access to testing and therapy, particularly in remote areas. We seek to provide insights into improving treatment outcomes and define the barriers to improved HCV management.

Characterization of microbial communities in aquatic environment using nanopore sequencing

Assist. Prof. Chan Leakhena Phoeung from the Rodolphe Mérieux Laboratory of the University of Health Sciences in Cambodia, explained that bioaerosols containing bacteria, fungi, viruses, and other microbial entities are ubiquitous in both natural and human living environments. Inhaling the bioaerosols carrying pathogenic microorganisms can cause serious diseases such as respiratory infections, etc.

Our study aimed to assess the impact of an aquatic environment as a potential source of bioaerosols that could pose a health risk to the surrounding population.

We examined common potential bacterial pathogens at the genus and species levels in various water environments. Water samples were collected from selected flooded

areas in Phnom Penh for preliminary analysis with the aid of DNA extraction and 16S rRNA gene amplification.

Using ONT sequencing analysis, we identified multiple bacterial species, some of which are hard to detect with conventional culture. The clustering of similar microbial profiles in the riverbank and market areas points to potential links between environmental factors and bacterial distribution. At the species level, *Klebsiella pneumoniae* and *Aeromonas hydrophila* were found to thrive close to dwellings, thus raising concerns about potential health threats.

GABRIEL INTERNATIONAL MEETING – NOVEMBER 28-29, 2024

The GABRIEL network: main achievements

Dr. Florence Komurian-Pradel, Manager of the GABRIEL network, highlighted the Mérieux Foundation's commitment to advancing infectious disease research throughout its 22 member laboratories in 16 developing and emerging countries.

The Center of Infectiology Charles Mérieux in Rio Branco, Acre, Brazil, recently joined as the network's 22nd member. During the COVID-19 pandemic, the Rodolphe Mérieux Laboratory located in Acre conducted over 80,000 tests. The center has supported public health initiatives in the region and now develops research on hepatitis delta virus, highly endemic in the Amazon.

GABRIEL is dedicated to enhancing research capacity and fostering global collaboration among researchers, physicians, and academicians. Its mission includes promoting scientific training and joint research initiatives, supported through academic programs, PhD grants, and webinars.

The network supports numerous South-South research projects addressing critical topics such as acute respiratory infections, tuberculosis, antimicrobial resistance, and emerging pathogens. It is also involved in the evaluation of vaccine impact and investigations of nosocomial infections.

Additionally, the Christophe Merieux Laboratory recently organized a workshop in Beijing, focused on advanced techniques for respiratory pathogen identification. Two new collaborative projects are underway: between CML and Ideshi and another between CML and Fiocruz. These projects aim to explore the respiratory microbiome diversity and risks in upper acute respiratory tract infections post-COVID-19, and to identify biomarkers associated with the severity and diagnosis of respiratory syncytial virus infection, respectively.

A focus on bioinformatics within GABRIEL

Mrs Emilie Westeel from the Mérieux Foundation presented the role of bioinformatics and biostatistics in strengthening capacities within the GABRIEL network. Her work focuses on genomic data analysis, workflow development, training and biostatistics, with applications in bacterial and viral sequencing.

The Foundation is expanding its training initiatives, including hands-on course and the INSEQBIN online program, which has already attracted 700+ participants from 49 countries. Emilie Westeel also highlighted the EQA program which assesses GABRIEL laboratories ability to analyze multi-drug resistant *E.coli* sequencing data. She emphasized the importance of collaboration and knowledge sharing to support the growing bioinformatics needs within the network.

Session I – Antimicrobial resistance

Chaired by Dr. Florence Komurian-Pradel, France, and Dr. Abdoul-Salam Ouedraogo, Burkina Faso

Presentation of the Mérieux Foundation's AMR program

Dr. Florence Komurian-Pradel emphasized that the spread of antimicrobial resistance (AMR) is among the top ten global public health threats. LMICs are particularly vulnerable to this "silent epidemic" due to their limited access to diagnostics, weak surveillance systems, and inadequate infection prevention and control measures.

To address these challenges, the Mérieux Foundation has launched several initiatives, including:

- strengthening diagnostic and laboratory capacities,
- improving surveillance systems,
- knowledge sharing

The One Health approach plays a critical role in addressing AMR by integrating work across human, animal, and environmental health sectors. Targeted initiatives and capacity-building programs have been set up to assess AMR prevalence and transmission. Key efforts include:

- scaling up the Tricycle project, to assess AMR prevalence in humans, animals & environment through analysis of ESBL *E. coli* and CPE
- investigating the pets as risk factors for ESBL-*E. coli* carriage
- developing tools for collecting, analyzing, sharing, and disseminating data and the establishment of an AMR Data Science Center
- developing expertise in next-generation sequencing and bioinformatics to support AMR research and response.

AMR surveillance with “One Health Approach” – AMR surveillance in human households and pets: what role do they play in transmission routes?

Study sites in Bangladesh

Transmission of Extended-spectrum beta-lactamases (ESBL) *E. coli* in pregnant women through exposure to companion animals

Mrs Sanchita Kar from the Institute for Developing Science and Health Initiative, Bangladesh, explained that the high carriage rate of ESBL *E. coli* in pregnant women poses a potential health risk, as AMR bacteria may be transmitted to newborns, increasing the risk of neonatal sepsis.

Given that companion animals are important reservoirs of AMR, the overall aim of the study was to assess the risk of ESBL *E. coli* transmission in pregnant women exposed to pets (dogs and cats). The study also sought to characterize resistance factors and evaluate the phylogenetic relationships among these ESBL *E. coli* isolates.

From fecal samples collected from pregnant women and household animals, we isolated bacterial colonies from culture, performed biochemical tests, synergy testing, and whole genome sequencing.

We compared ESBL *E. coli* genome, mobile genetic elements, core and plasmid-associated AMR genes, including ESBL genes, as well as a virulence factors specific to each host. A wide range of chromosomal antibiotic resistance genes were found among ESBL isolates, as well as a large variety of plasmids and plasmid-mediated virulence genes across all paired human and animal isolates. Phylogenetic analysis revealed a distinct clade of isolates carrying more resistance and virulence genes, irrespective of host origin.

Notably, the high carriage of rate of ESBL-producing *E. coli* in pregnant women remained consistent, regardless of whether they had companion animals or not.

Study sites in Brazil

Prevalence of Escherichia coli carrying extended spectrum β-lactamase in companion animals and pregnant women in São Paulo, Brazil

Dr. Silvia Costa from University of Sao Paulo, Brazil, reported that 6.29% of companion animals may carry ESBL *E. coli*, making household pets potential reservoirs of bacteria transmissible to humans. Pregnant women carrying ESBL *E. coli* face a risk of infection and may transmit these organisms to their newborns.

To assess the risk of ESBL *E. coli* transmission in pregnant women from exposure to dogs and cats, we conducted a longitudinal study of ESBL *E. coli* carriage. We characterized resistance factors and evaluated the phylogenetic relationships among ESBL *E. coli* isolates from pregnant women and their household pets.

Rectal swabs were collected from pregnant women who live both with and without pets, and fecal samples were obtained from their pets. The samples were screened for ESBL *E. coli* and further analyzed using whole-genome sequencing and pulsed-field gel electrophoresis.

Preliminary results showed that pregnant women with pets were more frequently carriers of ESBL *E. coli* at six and nine months of pregnancy compared to those without pets. Additionally, households without electric water filters and those using untreated water had a higher prevalence of *E. coli* carriage.

This study underscores the importance of antimicrobial stewardship in veterinary medicine and highlights the need for antimicrobial resistance surveillance programs focused on companion animals.

Study sites in Paraguay

AMR surveillance with “One Health Approach” - AMR surveillance in human households and pets: what role do they play in transmission routes?

Dr. Rosa Guillen from the Instituto de Investigaciones en Ciencias de la Salud in Paraguay detailed a study aimed at determining the prevalence of ESBL *E. coli* among pregnant women. Participants were interviewed to create a candidate database, and fecal samples were collected from both the women and their pets. Laboratory procedures included bacterial culture, species identification, and confirmation of the ESBL phenotype. Bacterial DNA was subsequently extracted and quantified, with whole-genome sequencing conducted at Seqcenter to examine the genetic characteristics of the isolates.

In the study group, 80% of pregnant women had one to two pets, with 90% reporting close contact with their animals. Notably, 80% of households lacked a designated litter box for pet excrement disposal, and 35% of the women were directly involved in bathing their pets. Only 5% of participants shared their rooms with their pets. On the positive side, 95% of pets received regular vaccinations, and 80% had at least two veterinary visits per year. However, only 5% of the pets had undergone antibiotic treatment in the past six months.

The study will ultimately be completed with a bioinformatics analysis and an investigation of the bacterial strains.

AMR in the environment: assessment of the impact of wastewater on the spread of multi-drug-resistant bacteria in Cameroon

Dr. Pierrette Simo from the Centre Pasteur du Cameroun explained that wastewater is a complex matrix rich in chemical and biological markers of human activity, making it a valuable resource for understanding public health and environmental risks. In Cameroon, wastewater is a critical contributor to the spread of antimicrobial resistance (AMR) in the environment, with a high prevalence of multidrug-resistant bacteria such as *E. coli*, *K. pneumoniae*, and *Staphylococcus spp*. As elsewhere in LMICs, it is alarming to note that part of the population uses river water, often without any cognizance of the health risks.

Resistance to common antibiotics like beta-lactams and fluoroquinolones is alarmingly high in Cameroon wastewater, compounded by the widespread presence of AMR genes, including ESBLs, blaAIM-1, and blaGES-21, along with diverse plasmid replicons. A metagenomic surveillance project involving 757 sewage samples revealed a significant diversity and abundance of AMR determinants in wastewater. Despite this, AMR data in environmental settings remains limited, highlighting an urgent need for collaborative efforts to establish AMR surveillance and implement wastewater treatment systems.

Three projects in Cameroon focus on studying AMR in the environment, funded by the Contract Plan Fund and the Mérieux Foundation.

The first project, a multi-center evaluation, examines the impact of the COVID-19 pandemic on the spread of antimicrobial and biocide resistance in wastewater.

The second, the SARA Project, investigates the prevalence of ESBL *E. coli* in urban wastewater from human and animal sources with the application of a One Health AMR approach.

Lastly, a metagenomic analysis of hospital effluents assesses AMR determinants in healthcare facilities caring for COVID-19 patients. Hospital and urban wastewaters are highly significant sources for antibiotic resistant bacteria and determinants in Cameroon. This highlights the urgent need to implement antimicrobial stewardship programs and improve infection surveillance practices in hospitals.

Improving the data collection and sharing: Data Center for AMR in Madagascar and Burkina Faso

Dr. Luc Samison from the Charles Merieux Center of Infectious Disease, Madagascar, and Prof. Abdoul Salam Ouedraogo from the CHU Souro Sanou, Burkina Faso, stressed the vital need to improve the quality of AMR surveillance in both Madagascar and Burkina Faso. The ongoing project has four main deliverables:

- implementation of sustainable surveillance tools supporting active AMR surveillance,
- launch of a new generation of Data Science Centers,
- demonstration of the real-time digital platform to stakeholders,
- design of the Data Science Centers for integration into national AMR surveillance systems with potential replication in other LMICs.

Stakeholders have agreed to strengthen data sharing and governance processes in an effort to support antimicrobial resistance research. These stakeholders include the Ministries of Public Health, Agriculture, Environment, and Water; national pharmaceutical regulators; One Health secretariats; multisectoral AMR coordination committees; and international organizations like WHO and FAO.

AMR surveillance data from sentinel laboratories and research projects will be centralized. This data records information on antimicrobial consumption, residues in food, and resistance profiles. The IT department in each country will oversee server management and database updates under the Ministry of Public Health. A second stakeholders' meeting will review beta versions of the Data Science Centers, specifications, and monitoring tools. Agreements on data sharing and use will be finalized, ensuring secure management, dissemination, and validation of the AMR surveillance tool, advancing governance, and fostering research collaboration.

Session II – Acute Respiratory Infection – Meningitis

Chaired by Dr. Valentina Picot and Pr. Philippe Vanhems, France

Dr. Valentina Picot from the Mérieux Foundation presented the Foundation's Acute Respiratory Infection/Meningo-Encephalitis (AIR/ME) program, which aims to establish research collaborations and interventions in combating infectious diseases.

Ongoing projects include investigations on PCV II in Cambodia, pneumonia diagnosis in Cox's Bazar, Bangladesh,

and meningitis diagnosis in the Côte d'Ivoire and Burkina Faso. The program emphasizes capacity-building through project-based training, technology transfer, clinical research management, pneumonia care-seeking behavior training, vaccine and vaccinology courses, and other specialized programs covering AMR and epidemiology.

Additionally, the AIR/ME initiative fosters awareness and advocacy for pneumonia and meningitis through activities such as Pneumonia World Day, the Global Pneumonia Forum, PCV vaccine introduction, facilitating data sharing with governments, and scientific publications.

Improving diagnosis and case management of childhood pneumonia in limited-resource settings

Dr. Rofiqur Rahman from the Institute for Developing Science and Health Initiatives in Bangladesh spoke about the plight of the Rohingya refugees who have been driven to migrate to Bangladesh and now reside in 33 highly congested camps. These camps suffer from inadequate health infrastructure, insufficient access to clean water, and poor sanitation and hygiene. Refugees often arrive with injuries, low immunization coverage, and high rates of malnutrition, while also requiring reproductive health care and psycho-social support. They face significant risks of deadly disease outbreaks, including both vaccine-preventable diseases like measles and diphtheria, and water-borne diseases such as diarrhea and hepatitis.

Acute respiratory infections, malaria, and dengue are widespread. The lack of essential tools like oximeters further complicates the management of critical living conditions. There is an urgent need as well to improve diagnosis and case management of childhood pneumonia. This requires clinical assessment guidelines supported by decentralized diagnostic tools and point-of-care tests.

The main objective of the study is to evaluate the clinical value and patient outcome of reinforcing childhood pneumonia diagnosis capacities in resource-limited settings. Increasing immunization coverage is critical, however there is limited data on circulating *S. pneumoniae* serotypes. NPS samples were collected from Rohingya children with moderate to severe pneumonia presenting cough, dyspnea, tachycardia, and danger signs such as coma, convulsions, inability to drink or breastfeed, hypoxemia, and tachypnoea.

This study also evaluates the effectiveness of integrating oximeters and automated RR counters, along with comprehensive training for healthcare professionals in managing severe pneumonia among children under five. This requires an estimate of the prevalence of *S. pneumoniae* serotypes in healthy children and adult caregivers.

Expected outcomes should improve diagnostic accuracy with point-of-care tools to assure better pneumonia case management and reduce child morbidity and mortality.

Critical epidemiological data on *S. pneumoniae* serotypes should help guide PCV strategies.

Role of bacteria and their antimicrobial resistance pattern in community-acquired pneumonia in Dhaka, Bangladesh

Mr. Abu Bakar Siddik from the Institute for Developing Science and Health Initiatives in Bangladesh, emphasized that pneumonia remains the leading infectious cause of mortality worldwide. Community-Acquired Pneumonia (CAP) poses a significant global health burden, particularly affecting children under five and individuals over 60. While its etiology includes both bacterial and viral pathogens, *S. pneumoniae* accounts for approximately two-thirds of bacterial pneumonia cases. However, the diversity of *S. pneumoniae* serotypes, alongside the rise of non-PCV serotypes, presents new challenges. Antimicrobial resistance (AMR) has further complicated treatment due to irrational antibiotic use.

The study conducted at the Dhaka Medical College Hospital aimed to determine nasopharyngeal colonization rates in CAP patients, characterize *S. pneumoniae* serotypes, analyze phenotypic AMR patterns, and investigate the relationship between blood biomarkers and pneumonia etiology.

The findings revealed a higher burden of *S. pneumoniae* and RSV in children under five, with the 19A serotype emerging as a significant concern due to its elevated resistance to penicillin and macrolides. Although susceptibility patterns for *S. pneumoniae* and H. influenzae were identified, conclusions regarding biomarkers and NP culture were inconclusive.

These findings highlight the critical need for targeted interventions to address AMR and evolving serotype prevalence.

A multi-country randomized control trial to evaluate the clinical impact of a point of care diagnosis panel vs. standard of care for the diagnosis of meningitis in children under five years of age

Dr. Sita Savané from the National Institute of Public Hygiene in the Côte d'Ivoire and **Dr. Odilon Kabore** from the CHU Souru Sanou, Burkina Faso, described the ongoing bi-country epidemiological survey of meningitis/encephalitis (ME) in a targeted population of hospital patients.

The study aims to evaluate the clinical value of implementing a rapid diagnostic package compared to sole standard of care for the ME diagnosis of young children admitted to participating hospitals. A key focus is to assess the diagnostic accuracy of the ME panel against conventional cerebral spinal fluid (CSF) cytology and culture. The health economics and outcomes (HEOR) research of these diagnostic interventions is being explored in an effort to strengthen clinical research and diagnostics with the ultimate goal of eradicating meningitis by 2030.

Children under five years old admitted to hospitals with suspected ME were screened based on specific selection criteria. The BioFire ME Panel has been instrumental in identifying the etiology of ME, enabling clinicians to optimize treatment strategies (in viral etiologies detected only with Biofire). For example, a 21-month-old child who tested positive for H. influenzae via both BioFire and culture was successfully treated with ciprofloxacin, guided by antibiogram results made possible through early detection by BioFire.

However, the BioFire panel does not handle certain other pathogens which are endemic in the region. Challenges in differentiating meningitis from neurological malaria contribute to a high rate of negative results, alongside pre-hospital antimicrobial use resulting in clear CSF samples.

Despite these challenges, the BioFire ME Panel has demonstrated its value through its speed, accuracy, and ability to identify probable pathogens, optimizing antimicrobial use. Future studies should explore pathogens not currently covered by the BioFire panel, such as Plasmodium and Mycobacterium, and include patients over five years old to better target meningococcal infections.

Round table on RSV disease

Moderator: Dr. Marilda Siqueira

Global burden of RSV disease

Dr. Thomas Williams, research fellow at the University of Edinburgh, explained that the Respiratory Syncytial Virus (RSV) poses a significant global health burden, particularly among children under five years of age, accounting for one in every 28 deaths in this age group. Alarmingly, nearly 98% of pediatric RSV-related mortality occurs in LMICs economies, with the highest risk seen in infants younger than six months.

Establishing the true burden of RSV is challenging due to varying diagnostic methods that include rRT-PCR, point-of-care testing (POCT), and lateral flow tests (LFTs), as well as difficulties in measuring cases not tested, such as those in emergency departments or primary care. Coding disparities, with terms like “bronchiolitis,” “lower respiratory tract infection,” “ARI,” or “viral wheeze,” further complicate accurate burden estimation.

A multidisciplinary and international approach is needed to address these knowledge gaps, especially as numerous RSV vaccines and therapeutics are under development. Future research must focus on a more granular understanding of the global RSV burden across all age groups and assess the impact of interventions, including genomic epidemiology in order to evaluate whether RSV genetic variability could influence vaccine effectiveness. Ultimately, while RSV imposes a profound burden in hospital settings, greater efforts are needed to uncover its impact beyond hospital admissions.

Introduction of RSV Vaccines: Clinical impact, emerging therapies, and vaccination strategies

Dr. Erin Sparrow from WHO in Switzerland, mentioned that after more than 60 years of research, two RSV immunization products for early infancy have been licensed: a long-acting monoclonal antibody (Nirsevimab) given to infants and a bivalent stabilized RSV pre-fusion protein vaccine given during pregnancy to protect infants via maternal antibodies. These products are being implemented in several countries using varying strategies: some, like in Spain, focus on monoclonal antibodies; others, like in Argentina, prioritize maternal immunization; and some, like in the USA, use both approaches. Recommendations differ by country regarding which infants receive monoclonal antibodies, the timing of maternal vaccination, and gestational age criteria.

Nirsevimab has been shown to offer clinical protection against RSV-associated lower respiratory tract infections for at least 150 days in infants. Meanwhile, the maternal RSVPreF vaccine boosts antibody transfer during pregnancy, protecting infants until six months of age.

Efforts to enhance access to RSV immunization products in LMICs include an RSV maternal immunization impact study in Ghana, Kenya, South Africa, and The Gambia, to assess public health impact and investigate preterm birth signals. GAVI, the vaccine alliance, is set to confirm support for RSV products, with maternal vaccines already having a price commitment and a multi-dose vial presentation. WHO plans to assist country decision-making through RSV workshops and tools, introduction manuals, effectiveness protocols, and post-introduction evaluation tools.

Young Scientist Award Session

Chaired by Graciela Russomando, Paraguay and Chan Leakhena Phoeung, Cambodia

Innovating extrapulmonary tuberculosis care with RISK6 Transcriptomic Signature: diagnosis and treatment monitoring

Mr. Ashabul Islam from icddr, b (International Centre for Diarrheal Disease Research, Bangladesh) highlighted several clinical challenges in diagnosing and managing extrapulmonary tuberculosis (EPTB), including diverse and nonspecific symptoms, difficulties accessing infected sites, and challenges in obtaining definitive diagnoses. EPTB testing often requires specialized processing techniques and lacks reliable methods to monitor treatment progression.

A promising solution is the RISK6 transcriptomic signature, a blood-based, specimen-free biomarker based on the expression levels of six host genes in blood samples. Unlike traditional methods requiring respiratory or tissue specimens, RISK6 simplifies diagnosis through a minimally invasive blood test. It is capable of triage, diagnosis, and treatment monitoring.

The primary objective of our study was to assess the performance of RISK6 in diagnosing extrapulmonary TB (EPTB) and to evaluate its treatment monitoring capability .

Confirmed and unconfirmed EPTB cases were categorised using RISK6 scores and compared to reference testing (GeneXpert, Culture, AFB, clinical diagnosis). RISK6 demonstrated excellent agreement with reference testing and exhibited high positive and negative predictive values. Furthermore, RISK6 scores decreased with treatment progression, supporting its potential for treatment monitoring.

In conclusion, the findings suggested that RISK6 has the potential to be a valuable addition to EPTB care, improving diagnostic accuracy and treatment tracking.

Analysis of the SARS-CoV-2 mutational profile in immunocompromised individuals with prolonged viral shedding

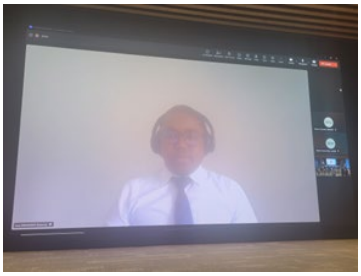
Ms. Elisa Cavalcante Pereira from the National Influenza Center (NIC), FIOCRUZ, Brazil, explained that the COVID-19 pandemic waves in Brazil were heavily affected by the emergence of new SARS-CoV-2 lineages and variants driven by the variability of SARS-CoV-2 and its intra-host evolution during acute infections. Immunocompromised individuals, in particular, represent a unique opportunity in understanding the natural history of COVID-19, as they often suffer from persistent infections that can lead to the development of new variants, increased virulence, and immune escape.

This study aimed to explore the SARS-CoV-2 mutational profile, focusing on intra-host single nucleotide variants (iSNVs) in immunocompromised individuals with prolonged viral shedding. It also explores how such conditions influence viral evolution. The duration of an infection seems to influence iSNV accumulation, though it is not the sole determining factor. Tracking iSNV accumulation is essential for understanding how pathogens evolve within a host, offering valuable insights into mechanisms such as immune evasion, drug resistance, and transmission potential.

Patient nasopharyngeal samples were analyzed by RT-PCR, whole-genome sequencing, genome assembly, phylogenetic analysis, and virus isolation in a BSL-3 facility. We examined the dynamics of iSNVs and their accumulation over time. The cycle threshold (Ct) values measuring the concentration of viral genetic material were determined from RT-PCR and provided insights into viral load, where low Ct values indicate high potential infectivity.

Our findings highlight the role of prolonged infection in shaping viral evolution. Notably, we identified the FLip S:L455F mutation in a BA.1 sample, underscoring the critical importance of enhanced genomic surveillance to prevent reintroduction of viral lineages and the emergence of more transmissible and immune-evasive variants. Such surveillance offers vital insights into mechanisms of immune evasion, drug resistance, and transmission potential, helping us understand how variants of concern arise and evolve.

Evaluation of primary resistance to anti-leprous drugs in Miandrivazo, Madagascar



Mr. Luca Maharavo from the Charles Merieux Center of Infectious Disease in Madagascar described leprosy as a chronic tropical infectious skin disease that remains endemic in Madagascar, with approximately 1,500 new cases reported annually. While treatment involves a standardized multidrug therapy (MDT) protocol using

Dapsone, Rifampicin, and Clofazimine, there are growing concerns about antimicrobial resistance (AMR) which necessitate targeted surveillance. WHO's guide for AMR in leprosy highlights the critical role of MDT in combating leprosy and underscores the importance of molecular methods to detect drug resistance by identifying mutations in resistance-associated genes: rpoB for Rifampicin, folP1 for Dapsone, and gyrA for Clofazimine.

Madagascar faces challenges in implementing these recommendations due to limited laboratory capacity and the absence of comprehensive surveys. To address this, our study conducted in Miandrivazo district aims to assess primary drug resistance in M. leprae, refine WHO surveillance guidelines to fit local conditions, and establish qPCR-RLEP at CICM Madagascar for detecting and quantifying M. leprae.

Samples were collected via door-to-door screenings and processed at the CICM laboratory using DNA extracted from skin biopsies. Resistance genes were identified

using methods such as the line probe assay, PCR DNA sequencing (targeting rpoB, folP1, gyrA, and the Malagasy-specific ml2446 locus), and the Deeplex Myc-Lep test, which also detects additional resistance markers and genotypic variations. This study represents a critical step toward building local capacity for effective surveillance of drug resistance in leprosy.

Genomic characterization of *Streptococcus pneumoniae* from pediatric patients reveals high prevalence of macrolide-Resistant non-PCV10 serotypes in Bangladesh

Mr. Mahin Hasan from the Institute for Developing Science and Health Initiatives, Bangladesh, highlighted the global and regional burden of *Streptococcus pneumoniae* (*S. Pneumoniae*), a leading bacterial cause of community-acquired pneumonia (CAP) and a significant contributor to morbidity and mortality in children under five. *S. Pneumoniae* has been listed by WHO as a 2024 Priority Pathogen due to its rising global threat, fueled by antimicrobial resistance (AMR) and serotype diversity. The Pneumococcal Conjugate Vaccine (PCV) provides protection against selected serotypes. However, the emergence of non-vaccine serotypes and antibiotic-resistant *S. Pneumoni*ae strains has led to greater healthcare costs and increased mortality rates. As *S. Pneumoniae* strains evolve considerably over large geographical areas, regional surveillance efforts should focus on developing tailored treatment and vaccine strategies.

Our study was conducted to track the emergence of *S. Pneumoniae* serotype 19A, identify antibiotic resistance genes and plasmids, and analyze evolutionary changes. Nasopharyngeal swabs from CAP patients were examined using PCR assays, whole-genome sequencing (WGS), and bioinformatics tools. The results revealed diverse serotypes, with non-PCV10 types dominating, and 19A being the most prevalent.

Future research aims to sequence more isolates, observe serotype shifts, explore genetic mutations linked to phenotypic plasticity, and make use of metagenomics to understand how the 19A serotype affects host flora. This work underscores the need for continued genomic surveillance to combat the evolving threat of *S. Pneumoniae.*

Low prevalence of transmitted drug resistance and high HIV type-1 subtype genetic diversity among treatment-naïve people living with HIV in Madagascar

Mr. Fetra Angelot Rakotomalala from the Charles Merieux Center of Infectious Diseases, Madagascar, pointed out that globally, 39.9 million people are living with HIV, with 1.3 million new infections and 630,000 AIDS-related deaths reported annually. In Madagascar, where HIV prevalence is estimated at 0.4% in the general population, stigma remains high, and HIV infections are often detected at advanced

stages. Limited data on genetic diversity and transmitted drug resistance (TDR) in Madagascar hinder effective management of the epidemic, despite HIV being among the top ten leading causes of death in the country.

Our study is being conducted to better characterize HIV infection. This is done by analyzing the genetic diversity of circulating strains and assessing TDR prevalence among treatment-naive people living with HIV. Phylogenetic analysis of 239 sequences revealed a high genetic diversity of HIV-1 with a predominance of subtype C, a variant prevalent in southern and eastern Africa. TDR was identified in treatment-naive people living with HIV, including a troubling prevalence among newborns due to mother-to-child transmission.

These findings emphasize the urgent need for enhanced surveillance. Demographic and health surveys are necessary to update prevalence data and acquired resistance profiles in people living with HIV.

Future investigations will include whole-genome sequencing of HIV-1 strains. The transfer of next-generation sequencing technology to our laboratory will help strengthen local capacity for comprehensive HIV management.

Session III – Tuberculosis

Chaired by Dr. Jonathan Hoffmann, France, and Dr. Zakir Hossain, Bangladesh

Presentation of the Mérieux Foundations's TB program

Dr. Jonathan Hoffmann described TB as the world's leading infectious disease killer, with 8.2 million new cases diagnosed in 2023, 12% of which are children. Despite the prevalence of TB, global funding for its prevention and care has decreased and remains far below target. Conventional TB diagnostic methods primarily rely on sputum-based microbiological analysis, highlighting the urgent need for non-sputum-based assays, especially to enhance case detection among children.

Mérieux Foundation's TB program aims to strengthen diagnostic and surveillance capacities of GABRIEL member laboratories, as demonstrated by initiatives in Lebanon, China, Lao PDR and Haïti. This TB program also promotes research and innovation, by identifying and evaluating alternatives to sputum-based tests, in line with WHO priorities. In this context, the TB program includes operational research projects such as the APRECIT project in Cameroon and Madagascar, designed to assess cost-effective and sustainable strategies for TB infection (latent TB) screening, the DEDICATE project for diagnosing childhood TB, and the EBC-LAM project in Bangladesh dedicated to exploring a breath-based test for TB detection.

A new project is to be implemented in Bangladesh (RISK4Kids), to assess the performance and positioning of innovative tools for differentiating TB from pneumonia in children under five years of age. This project will evaluate digital chest X-rays with computer-aided detection (AI module), RISK6 blood test as point of care diagnostic tool,

and smartphone cough recordings combined with an AI module. As near perspective, another operational research project will be developed and submitted for funding under the Initiative's call for proposals, aiming to enhance TB prevention, diagnosis, and management of drug resistance.

Strengthening diagnostic and epidemiological surveillance capacities

Improving TB diagnostics and surveillance among refugee populations in Lebanon

Dr. Josette Najjar-Pellet from the Mérieux Foundation in Lebanon presented key insights from the 2024 World Innovation Summit for Health (WISH), which emphasized the importance of incorporating regional perspectives when addressing global health challenges and translating research into actionable solutions.

Given its expertise in health, migration, and combating infectious diseases, and its strategic role in Lebanon, the Mérieux Foundation was invited to collaborate with WHO and the Qatar Foundation to prepare a comprehensive report. This report outlines strategic recommendations and policy proposals to tackle the obstacles to healthcare, particularly among refugees and migrants, whose dire living and working conditions, social stigma, cultural barriers, and limited access to healthcare exacerbate the spread and impact of TB.

The WISH report proposes innovative strategies to eliminate TB among these populations. Actions include ensuring universal health coverage, engaging civil society and NGOs to combat stigma and improve service delivery, strengthening surveillance systems for at-risk groups, and promoting research to enhance TB prevention, diagnosis, and care. These measures aim to bridge the equity gap and address the broader challenges threatening global health.

Multidrug-resistant tuberculosis in Lao PDR: characterization of primary and secondary resistance for improving the treatment of tuberculosis patients

Dr. Phitsada Siphanthong, MD, an IRD-ARTS PhD student supervised by the Institut de Recherche pour le Développement (IRD), the Center Infectiology Lao-Christophe Merieux (CILM), the National TB Center (NTC), and Mérieux Foundation, highlighted the growing challenge of tuberculosis (TB) drug resistance in Laos.

This issue is compounded by the country's geographic proximity to nations with a high prevalence of multidrug-resistant TB (MDR-TB). Contributing factors include delays in early diagnosis and

treatment, limited screening focused primarily on Rifampicin resistance, and an increased risk of secondary resistance, which exacerbates the circulation of MDR-TB strains within the population (primary resistance). Rapid, comprehensive molecular detection techniques are urgently needed to assess drug resistance effectively, both at the primary and secondary levels.

The objective of our study is to characterize primary and secondary drug resistance to improve TB treatment and develop innovative tools for enhanced treatment monitoring. Routine TB patient samples collected from diverse sites across Laos were analyzed for drug susceptibility, focusing on Rifampicin resistance and sensitivity. The findings indicate that Rifampicin resistance is present nationwide, with the highest prevalence in the northern regions, where 49% of samples tested positive. Diabetes emerged as a significant comorbidity, associated with 15% of cases, highlighting its role in promoting TB and drug resistance. Furthermore, the 15–34 age group, predominantly female, accounted for 53% of TB cases, reflecting Laos's youthful demographic and the potential for increased transmission through close contact and social interactions.

The rising prevalence of MDR-TB and quinolone resistance in secondary resistance cases underscores the urgent need for effective treatment monitoring and adherence strategies to curb the spread of drug-resistant TB. Alarmingly, pre-extensively drug-resistant TB (Pre-XDR), defined by resistance to Rifampicin and fluoroquinolones in primary resistance cases, has been detected, signaling the emergence of high-level resistance. Preliminary discrepancies in drug susceptibility testing are attributed to low bacterial concentrations or poor DNA quality. Efforts are ongoing to address these technical limitations and improve diagnostic accuracy.

This research highlights the critical need for tailored interventions to address TB drug resistance in Laos, leveraging improved diagnostics, treatment monitoring, and prevention strategies to mitigate the public health impact of MDR-TB.

Supporting local health authorities to define cost-effective TB screening and care strategies

Improving the management of latent tuberculosis infection in Cameroon and Madagascar (APRECIT project)

Dr. Valerie Donkeng-Donfack from the Centre Pasteur in Cameroon described the APRECIT project that aims to improve diagnosis and treatment of latent tuberculosis infection (LTBI) among high-risk populations in Cameroon and Madagascar with the ultimate goal of eliminating TB in these regions. A key focus is the systematic screening of household contacts for LTBI.

The main objective of the investigation is to compare the diagnostic value of two immunological tests for identifying LTBI: interferon gamma release assays (IGRAs), and the traditional tuberculin skin test (TST). Additionally,

the performance of both TST and IGRA in screening for TB infection was examined for the value in predicting the progression from latent to active TB.

We conducted a prospective observational and non-interventional cohort study in Cameroon and Madagascar to better understand LTBI among household contacts of active TB cases. This involved community-based identification, inclusion, and follow-up of 1,659 eligible household contacts over 18 months. Diagnostic methods were employed to assess TB infection, and comprehensive socio-demographic, environmental, and clinical data was collected.

The community's low acceptance rate of tuberculosis preventive treatment is partly due to the six-month duration of treatment. Additionally, many parents refuse treatment for their children, believing they are healthy and not at risk. Furthermore, the inability to afford travel to treatment centers is an additional deterrent. These obstacles underscore the need for strategies to address logistical, financial, and perceptual barriers to improve treatment.

Moving forward, household contact surveys should be continued, and barriers to TPT acceptance must be overcome through community education and awareness campaigns. Overall, the APRECIT project has provided critical insights into community-based TB prevention and management, emphasizing the need for local engagement, better diagnostics, tailored interventions, and sustainable health systems and also has demonstrated that IGRAs and TST display significant prognosis values to early identify individuals at risk of developing active TB disease and the Combination of TST-14 and IGRA test (QFT or T-SPOT) results can help identify those at risk of developing TB disease and thus target TPT beneficiaries

Advancing science and innovation

Transcriptomic and phenotypic signatures of progression to TB disease among close contacts in Madagascar and Cameroon (APRECIT-BIS)

Dr. Niaina Rakotosamimanana from the Institut Pasteur of Madagascar emphasized the importance of providing preventive therapy to individuals at risk of having their latent TB progress to active disease as a result of a disruption to their immune system.

The APRECIT project focuses on enhancing the management of latent TB infections in Cameroon and Madagascar through improved screening and the use of immuno-diagnostic tests. Detecting and predicting the progression of TB involves characterizing reliable biomarkers that can identify individuals at various stages of TB, from latent infection to active disease. These biomarkers reflect the host's interaction with M.tb, offering insights into the mechanisms of infection control or disease progression.

Biobanks serve as repositories of biological samples, collected and preserved for future TB research. These aid in exploring diagnostic, prognostic, and therapeutic solutions that directly benefit TB control efforts.

RISK6, a PCR-based host-blood transcriptomic signature, offers versatile applications in TB management. It can identify individuals at risk of developing incident TB, serve as a screening tool for subclinical or clinical TB, and monitor the effectiveness of TB treatment. These findings support the integration of RISK6 into rapid, capillary blood-based point-of-care PCR devices, enabling prospective assessment in field studies.

T-cell activation serves as a valuable marker for characterizing specific recent immune responses against M.tb infection. Prior research highlights the diagnostic potential of measuring M.tb-specific T-cell activation through flow cytometry. This approach effectively differentiates M.tb infection from active TB disease and provides a method for monitoring treatment response.

Evaluation of LAM detection in exhaled-breath condensate samples for TB diagnosis in Bangladesh (EBC-LAM project)

Mr. Mohammad Khaja Mafij Uddin from the International Centre for Diarrheal Disease Research, Bangladesh, explained that exhaled breath condensate (EBC) has emerged as a diagnostic tool for tuberculosis (TB). EBC consists of aerosolized droplets and volatile compounds from the lower respiratory tract, containing biomarkers such as volatile and non-volatile organic compounds, metabolites, lipids, glycoconjugates, and proteins.

EBC, the liquid phase of exhaled air, is a valuable medium for analyzing disease-specific biomarkers. Mycobacterial lipoarabinomannan (LAM), a critical TB biomarker, is present in much higher concentrations in EBC than in urine. These molecules, key components of the mycobacterial envelope, play a crucial role in the pathogen's interaction with the host's immune system.

The objective of our study was to evaluate the combination of EBC samples and LAM as potential point-of-care (POC) assays for identifying TB patients. We used a LAM AG POC test to detect LAM in EBC and Urine samples and compared the efficacy of two breath sampling devices, Medivac and FIND.

The preliminary findings of the study revealed that LAM POC assays from EBC collected using FIND devices demonstrated higher sensitivity compared to Urine and EBC collected using Medivac devices. Furthermore, LAM POC sensitivity using EBC was higher among cases with low bacterial burden compared to LAM POC sensitivity using Urine, suggesting that LAM in EBC can be detectable in the early stages of the disease. Overall, EBC was found to be a promising candidate for TB screening.

Moving forward, we plan to quantify LAM in EBC using the dot-blot technique to gather additional evidence and use newer generations of TB LAM antigen tests to screen individuals at high risk of TB.

Diagnostic Accuracy of a blood transcriptomic signature for childhood TB (DEDICATE project)

Stéphane Pouzol from the Mérieux Foundation, France, spoke about the urgent need for fast, accurate, reliable, and affordable diagnostic tests for childhood TB. Access to quality diagnostic services remains limited in resource-limited settings, where the poor predictive value of TB symptoms further complicates early detection. Molecular tests often show suboptimal performance in diagnosing pediatric TB, contributing to missed cases. In fact, 55% of children with TB are not reported to national TB programs, highlighting the critical gap in the detection and reporting of this disease.

RISK6 is a rapid diagnostic scoring tool designed to assess the likelihood of TB and helps prioritize individuals who may require further diagnostic testing, thus improving the efficiency of TB screening in resource-limited settings.

Our study population was composed of children in the Dhaka Hospital in Bangladesh of whom 83% were under two years of age and subject to malnutrition. The RISK6 score taken from sputum and stool samples were significantly different between confirmed, unconfirmed, and unlikely TB cases when TB treatment was used as reference standard. The sensitivity of RISK6 was best when used alone or in combination for triaging purpose.

In modeling analysis, while RISK6 is not as cost-effective as the TST, it is still less expensive than chest X-ray. However, RISK6, either alone or in combination with other tests, demonstrated superior case identification rates in children, outperforming Xpert assays. Its ability to identify clinical cases makes it a useful triage test, and while TST remains the cost-effective single strategy for TB identification, combining it with RISK6 offers valuable prospects for enhancing TB detection and diagnosis.

Further evaluation of RISK6 is needed to determine the added value of the assay as a decision-support tool for healthcare personnel implementing the integrated treatment decision algorithms suggested by WHO for pulmonary TB in children.

GABRIEL Young Scientists Award ceremony

The Mérieux Foundation's GABRIEL Young Scientist Award is an important initiative for the future of science and an incentive for young researchers.

The two award winners were selected based on the interest, value, and public health relevance of their research, as well as on the quality of their presentations.

After careful deliberation, the members of the jury, Dr. Graciela Russomando, Pr. Philippe Vanhems, Dr. Cassia Mendez, Dr. Daniel Mukadi, and Dr. Chan Leakhena Phoeung decided to award the two prizes to:

Mr. Ashabul Islam, iccdr,b Bangladesh: "Innovating extrapulmonary tuberculosis care with RISK6 transcriptomic signature: diagnosis and treatment monitoring", and

Mr. Mahin Hasan, ideshi, Bangladesh: "Genomic characterization of Streptococcus pneumoniae from pediatric patients reveals high prevalence of macrolide-resistant non-PCV10 serotypes in Bangladesh".

Close of the GABRIEL meeting

Dr. Florence Komurian-Pradel concluded this year's edition of the GABRIEL International Meeting by expressing her gratitude to all participants for their valuable contributions. She emphasized that the Mérieux Foundation remains committed to advancing public health and implementing educational programs across all member countries. Dr. Pradel expressed anticipation for the next GABRIEL meeting, which is to be held in 18 months, and encouraged everyone to continue their excellent work.