

12TH GABRIEL NETWORK MEETING

MAY 31 – JUNE 2, 2023
YAOUNDÉ (CAMEROON)

Organized by the Mérieux Foundation and the Centre Pasteur of Cameroon
with the support of bioMérieux and Illumina



From May 31 to June 2, 2023, over 100 delegates representing researchers, physicians, specialists in laboratory diagnostics, academics, and scientists, coming from both the public and private sectors of 16 different countries, meet in person and online in Yaoundé, Cameroon, for the 12th GABRIEL network international meeting. In this newsletter you will find highlights of this meeting, including summaries of speeches and the key discussion.

The GABRIEL network international meetings have become a platform for members to share experiences, present new collaborative opportunities, review advances in quality assessment, and examine the most recent scientific research in infectious diseases. This year's program specifically addresses outbreaks and surveillance of emerging pathogens with a special focus on the African continent. Also discussed are topics related to infectious diseases, tuberculosis, antimicrobial resistance, and acute respiratory infections that have been presented in past meetings. This symposium provided an opportunity to identify the gaps and pitfalls that hamper accurate and effective diagnosis of infectious diseases and offers a knowledge-sharing platform for improved surveillance strategies and clinical management and prevention.

As in previous meetings, the program included the GABRIEL network 'Young Scientist Award', created to enable promising young scientists from low- and lower-middle-income countries to advance their careers by giving them the opportunity to present their research at international scientific meetings. Two winners were selected for this year's best presentations.

WELCOME ADDRESSES – MAY 31, 2023



Dr. Florence Komurian-Pradel, Manager of the GABRIEL network, in her welcome address, thanked the Centre Pasteur of Cameroon (CPC) for its support in organizing the 12th GABRIEL network international meeting. She highlighted the Mériem Foundation's top priority: its continuing support to scientific research on infectious diseases in developing and emerging countries. The specific mission of the GABRIEL network is to strengthen the

research capacity of the 21 member laboratories located in twenty countries and encourage researchers, physicians, and academicians from around the world to join hands in promoting scientific training and conducting joint research projects. Human capacity building within the GABRIEL network is conducted through practical and theoretical academic training, the provision of PhD grants, and webinars. The GABRIEL network provides support to a host of other South-South research projects dealing with acute respiratory infections, tuberculosis, COVID-19, and antimicrobial resistance, the topics of which range from vaccine impact studies to nosocomial transmissions.



Dr. Mirdad Kazanji, General Director of the Centre Pasteur in Yaoundé, Cameroon, spoke about the CPC's contributions to the fight against disease and the promotion of health and the prevention of international health risks in Central Africa through the monitoring of endemic and epidemic diseases, the pursuance of scientific research, and the training of health personnel. The CPC also conducts biological and epidemiological surveillance

activities and has established a national reputation as an internationally recognized scientific research institute. Dr. Kazanji gratefully acknowledges the CPC's fruitful collaboration with the GABRIEL network.

SYMPOSIUM DAY – MAY 31, 2023

SESSION I – Preparedness for outbreaks of emerging and re-emerging pathogens

Chaired by **Dr. Mirdad Kazanji**, Cameroon

Global outbreak response and innovations, a country-based strategy and 'One Health' framework



Dr. Pierre Formenty from the World Health Organization in Switzerland stated that emerging infectious diseases (EID) have been on the increase for the last 40 years. Microbes evolve. New threats emerge. The climate is changing. Our world is changing. In the face of this, we must examine key patterns at the human-animal interface, develop prevention and control through country-based strategies, and determine which R&D

products are the most effective to control major EID outbreaks, 80% of which occur in violent settings, such as in the Kivu in eastern Congo. Multisectoral collaboration is essential for prevention and control of disease, and country-based strategies as well. Lassa fever is an example whereby the development of a standardized training package for health care staff, with a focus on clinicians and nurses, is needed. Country capacity is essential to contain the spread of EIDs and this requires high-level government commitment and international collaboration. Detection and control of EIDs are major challenges because of the many factors that promote their transmission and obstruct control operations. There is a need to promote global public health to alleviate disease impact in vulnerable populations. New diagnostic techniques, vaccines, and therapeutics should improve medical interventions in areas of the world where access to care is difficult. Regional clinician and laboratory networks, such as GABRIEL, are vital players for the prevention of and response to disease outbreaks, as well as for the development of new R&D products through a 'One Health' approach.

Epidemic preparedness and response in Cameroon: state of progress and perspectives



Dr. Georges Alain Etoundi Mballa from the Ministry of Public Health of Cameroon began by presenting the Global Health Security Agenda (GHSA) as an international effort for infection prevention and control. At present, world health security is increasingly problematic due to the rapid growth of the world's population, global warming, emergence of new infectious pathogens, microbial resistance to antibiotics, greater international travel, as well as the threat of acts of bioterrorism. Cameroon is particularly exposed due to the number of epidemics in progress (cholera, meningitis, COVID-19, etc.).

In view of this, Cameroon has set up the Public Health Emergency Operations Coordination Center, abbreviated CCOUSP, as a structure for the coordination of health emergencies. It ensures the immediate availability of resources and capacity building for public health emergency responses. The center serves as a framework for consultation between the various national and international actors involved in the management of emergencies and the coordination of related interventions. The center has achieved remarkable results in the control of outbreaks of the influenza A virus H5N1, emergency operations in response to a rail accident, medical coverage during sporting events, suspected cases of meningitis among prison inmates, coordination of treatment against AIDS, control of monkeypox, threats of secondary blindness in hospitalized infants, control of COVID-19. These success stories are extremely encouraging for the development of future public health initiatives.

Outbreaks of emerging and re-emerging pathogens in Africa: the case of Ebola for response preparedness and implementation of medical countermeasures



Dr. Daniel Mukadi, Regional Director of the National Institute of Biomedical Research (INRB) in the Democratic Republic of Congo, presented the medical countermeasures tools available to conduct a successful Ebola Virus Disease (EVD). The goal of the sequencing tool is set to predict pathogen behavior, identify the at-risk populations, and evaluate the efficiency of medical countermeasures which comprise vaccines (rVSV-ZEBOV-GP, Ad26.ZEBOV GP, and MVA-BN-Filo) and specific therapeutics. At present, additional resources are needed for epidemiological and biological surveillance of EVD that include sample collection, packaging and transport, as well as qualified trials, biosafety and biosecurity measures, and qualified local health workers.

Translational research was carried out during recent EVD outbreaks in DRC, notably through clinical trials, to assess the effectiveness and safety of Ebola vaccines and therapeutics and to determine the contribution of the serology on the management of patients discharged as EVD non-case after EVD RT-PCR.

SESSION II – Surveillance of emerging pathogens at the human-animal interface

Chaired by **Dr. Francine Ntoumi**, Republic of Congo

Evolution and epidemiology of emerging viruses from animal reservoirs



Dr. Jan Felix Drexler, a virologist at Charité University in Germany, pointed out that among new disease-causing pathogens, at least 60% originate from animals such as bats, whose special immune system qualifies them as reservoirs for SARS-related viruses. Bats and rodents are ecologically relevant, and other animals are involved in the emergence of arboviruses because of a complex interplay between vector mobility, human mobility, viral adaptation, and livestock rearing. Evolution of infection patterns is occurring in animal reservoirs, as noted, for example, in chronic HBV infections in donkeys.

The Zika virus is also of interest in terms of possible T cell-mediated cross-protection with the dengue virus, as model testing has demonstrated protection from congenital Zika syndrome through DENV immunity. In addition, it has been reported that a Zika virus infection enhances the future risk of severe dengue disease.

The role of the laboratory in the surveillance of emerging pathogens: the case of monkeypox



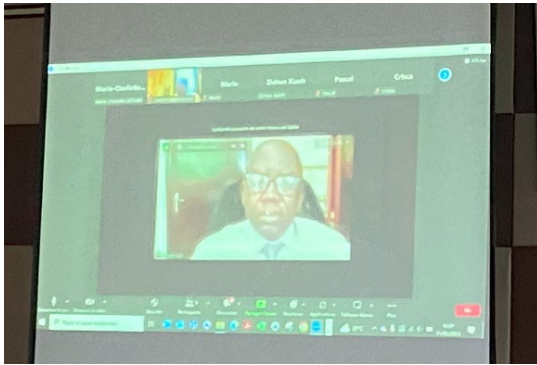
Prof. Richard Njouom, Director of the virological department of the Centre Pasteur of Cameroon, presented the CPC as Cameroon's national reference laboratory for monkeypox. Regarding the role of the laboratory during an outbreak of monkeypox (Mpox), Prof Njouom says that the laboratory is a leading player in the discovery, prevention, and control of the monkeypox epidemic in

human and animal populations. In the management of these outbreaks, the laboratory intervenes in the rapid identification and characterization of MPXV, a fundamental step for declaring an epidemic and triggering appropriate responses. The laboratory also can provide evidence showing that MPXV has stopped circulating in the population or that a level of immunity has been acquired after vaccination.

Currently, the CPC has the technical capacity to diagnose Mpox infections using the PCR technique. However, the main challenge facing Cameroon in diagnosing Mpox is the insufficient decentralization of diagnostic procedures in the field because infections occur in difficult-to-reach rural areas where health care facilities lack refrigerators or a reliable power supply to keep the specimens viable until they are transported for testing. As a result, more laboratories with the ability to detect MPXV illnesses are required, along with more skilled medical personnel for specimen collection, handling, and testing. Due to insufficient

disease monitoring systems, inadequate laboratory equipment, and a lack of information about monkeypox, there are worries about Cameroon's capacity to identify and treat the virus among health care workers and communities. Cameroon should take advantage of the COVID-19 molecular laboratories now present in all the ten regions of the country to strengthen its capacities.

Monkeypox in the Central African Republic: lessons learned



Dr. Emmanuel Nakoune from Institut Pasteur in Bangui, Central African Republic, spoke about the recent alarming rise in human monkeypox cases in the CAR and its potential for further spread across a wide geographical area. Human-to-human viral transmission seems to occur through direct contact with lesions or respiratory droplets, or through indirect environmental contact. Although the reservoir host of MPXV has not been definitively identified, many

mammalian species are naturally infected with the virus.

The AFRIPOX project takes the 'One Health' approach to characterize animal reservoirs of the monkeypox virus and their ecological habitats. It should shed light on the interactions between humans and these reservoirs to identify practices that can prevent zoonotic viral transmission. This can be achieved by combining research techniques in zoology (animal reservoirs and host identification), virology (molecular diagnostics and sequencing), epidemiology (transmission, understanding of origin), ecology (environmental atlas, climate profile, human activities, ethnohistorical study of local ecological and social changes), and anthropology (illness, formal health care workers, traditional healers, former patients).

Looking towards the future, we must train staff to strengthen national surveillance and patient management, support countries in the sub-region to develop cross-border exchange and extend the compassionate use of Tecovirimat® to southeastern CAR.

Round Table: Early warning systems for emerging pathogens at the human-animal interface



Dr. Jan Felix Drexler, Dr. Richard Njouom, Dr. Emmanuel Nakoune, and Dr. Yazdan Yazdanpanah (from the Assistance publique/Hôpitaux de Paris) led a round table discussion with members of the audience on the means to prevent and control epidemics caused by emerging

pathogens. The following points were raised:

- The sharing of information, rapid response, and cooperation are vital considerations.

- An epidemic is unstoppable. International borders in Africa, being porous, do not act as barriers to people's movements; transnational cooperation for the surveillance and control of epidemics must be ensured without any loss of efficiency.
- A regional holistic perspective must be adopted to develop regional hubs, set up preparedness, study the social and economic dynamics in relation to an epidemic.
- Human pathogens circulate in animal reservoirs, often in remote areas of Africa, where there are insufficient health structures to detect pathogenic microorganisms and prepare an adequate response.
- We must not underestimate the complexity of epidemic crises. Given their many factors, we must establish our priorities well in advance.
- Donors look for a positive impact in return for their money. Neglected diseases require funding as well.
- WHO recognizes that pathogens should be considered a priority especially in areas where they have emerged.
- The weakest link in research is the neglect of animal diseases. Vaccine programs and patterns of human mortality rates have been top priorities, but little has been accomplished in the past 20 years relative to animal diseases. Funding is essentially dedicated to health research for people, but too little for animals, thus resulting in creating a certain amount of bias.
- We must be cautious about competing for funding when supporting research networks.
- In trying to adopt a health strategy for Cameroon, reaching a consensus within the government is a challenging problem.

SESSION III – Surveillance of vector-borne diseases

Chaired by **Dr. Graciela Russomando**, Paraguay

Vector-borne diseases in the context of global changes



Dr. Anna-Bella Failloux from Institut Pasteur in France, mentioned that 75% of emerging infectious diseases are zoonoses and that 60% of infectious diseases are spread from animals. These percentages are on the increase. Ruminants, carnivores, rodents, birds, and primates constitute the five major animal categories that have transmitted pathogens to human populations.

Most recent epidemics are associated with two main mosquito species *Aedes aegypti* and *Aedes albopictus*, which are the vectors of the arboviruses causing yellow fever, chikungunya, zika and dengue. The vectorial system is complex and relies on multiple components:

- infection, density, and distribution of animal reservoirs,
- distribution, abundance, dispersal, survival, infection of vectors,
- distribution and susceptibility of humans

- contacts between the animal reservoir and the vector and between the vector and humans

Arboviruses cause more serious symptoms in immunologically naïve non-African populations. Malaria and many neglected tropical diseases in Africa attract more attention than Aedes-borne diseases.

Human activities and climate change affect vector-borne diseases. Climate change affects the life cycle of mosquitoes. Following a yellow fever epidemic in Angola, Chinese workers repatriated to China with a confirmed infection. Due to the growing presence of the vector, *A. aegypti* in Asia is becoming increasingly resistant to insecticides. There is now a high risk of the spread of yellow fever in the population.

Genetic drivers of insecticide resistance in African malaria vectors: impact on bednet efficacy



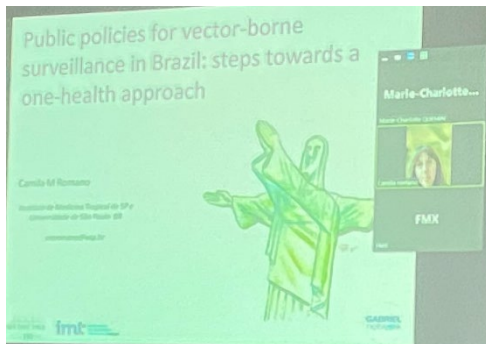
Dr. Charles Wondji, from the Centre for Research in Infectious Disease in Cameroon, spoke about the critical importance of managing insecticide resistance, because vector control is a key component of malaria prevention. The insecticides available to control public health pests are limited to four classes: organochlorines, organophosphates, carbamates, pyrethroids. Pyrethroid resistance could cause up to 260,000 deaths per year if nothing is done. Planning an insecticide strategy in malaria endemic countries should comprise the development of new vector control tools and fundamental research into insecticide resistance.

This necessitates addressing key questions such as:

- What is the genetic basis of resistance and its evolution across African vectors?
- What are the causative mutations driving resistance?
- Can we design simple DNA-based diagnostic assays to track the spread of resistance?
- What is the impact of resistance on the efficacy of insecticide-based interventions and malaria transmission?

Multiple mechanisms have been identified in insecticide resistance: point mutations in coding regions, mutations in cis/trans regulatory loci, and variants in transcription factors. Structural variations in metabolic resistance refer to large-scale structural differences in the genomic DNA that are inherited and polymorphic in a species. They stem from chromosomal rearrangement – deletion, duplication, novel sequence insertion or inversion. Progress made into the molecular and genomics basis of resistance has recently allowed to design simple DNA-based tools to detect, track and assess the impact of resistance on insecticide-based interventions such as bednets.

Public policies for vector-borne surveillance in Brazil: steps towards a One Health approach



Dr. Camila Romano from the Instituto de Medicina Tropical da Faculdade de Medicina, University of São Paulo, Brazil, spoke about seasonally arbovirus outbreaks of dengue, chikungunya, zika, and yellow fever in Brazil that affect the most underprivileged. As for malaria, gold mining and deforestation in indigenous lands in the Amazon region of Brazil have severely exacerbated the spread of the vector-born disease.

The National Dengue Control Plan was created in 2002 to reduce the infestation of *Aedes aegypti*, and the resulting incidence of dengue hemorrhagic fever. The plan was expanded in 2016 and 2017 to include the recently emerged ZIKV and CHKV in the country. Currently the arbovirus surveillance program is designed to:

- monitor and reduce the risk of local epidemics,
- strengthen vector control,
- prevent and prepare for pandemics, and
- enhance innovation and build partnerships.

Various tools for vector control are now being studied:

- release of mosquitoes with *Wolbachia* into the wild to reduce the numbers of *Aedes aegypti*,
- use of biological larvicides that avoid resistance caused by chemical larvicides,
- use of male transgenic “sterile” *Aedes* insects that mate with wild female mosquitoes, transmitting the self-limiting gene to the offspring that ultimately die before reaching adulthood.

The fight against vector-borne diseases is a battle that should involve competent authorities, politicians, health professionals, science, and the population. In this regard, Brazil is committed to promoting integrated public policies.

SESSION IV – Surveillance of neglected diseases

Chaired by **Dr. Sara Eyangoh**, Cameroon

Onchocerciasis elimination in Central Africa: successes and challenges in scaling up alternative and innovative strategies



Prof. Joseph Kamgno from the Higher Institute for Scientific and Medical Research (ISM), Centre de Recherche sur les Filarioses et d'autres Maladies Tropicales (CRFILMT), in Cameroon formally spoke about onchocerciasis or river blindness caused by *Onchocerca volvulus* and transmitted by black flies of the genus *Simulium*. He described clinical presentation, the complications, and socioeconomic consequences of onchocerciasis. Concerning the fight against this disease, control started in West Africa with chemical vector control under the WHO Onchocerciasis Control Program (1974 – 2002). With the discovery of the efficacy of Ivermectin (Mectizan®) on *O. Voluvulus*, the

marketing autorisation in 1987 and the Donation, WHO put in place between 1995 and 2015, the African Program for Onchocerciasis Control with the Community Directed Treatment with Ivermectin that was the main strategy for onchocerciasis control. This strategy improved considerably the treatment coverages with significant impact of the level of endemicity and transmission. Some foci were almost eliminated in West Africa.

Despite the important progress made, the infection is persisting in certain foci due to poor drug coverages, the fear of Severe Adverse Events (SAEs) and a significant proportion of systematic non-compliers. The SAEs occur in some patients heavily infected by another filaria called loiasis endemic in Central Africa. The main strategy for the prevention of these SAEs is the Test and not Treat with systematic tests for loiasis using the LoaScope. The LoaScope allows the quantitative diagnosis of Loiasis in less than 3 minutes. The other challenge for onchocerciasis elimination is the lack of funding for the development of macrofilaricidal drugs and proper diagnostic tools. Vector control is an efficient strategy although the cost is higher due to the weekly use of larvicides and environmental impact. An alternative to chemical-based products is slash and clear, a community-based environment-friendly form of vector control that is under development.

Laboratory network as a strategy for NTDs integration management: case of Buruli ulcer



Dr. Sara Eyangoh from the Pasteur Centre of Cameroon described the Buruli ulcer as a neglected tropical skin disease that is caused by *Mycobacterium ulcerans* and results in massive tissue loss. The first sign of Buruli ulcer is a painless swollen bump on the arm or leg or a more widespread swelling under the skin. The mode of transmission is unclear and difficult to describe,

BU-LABNET (Buruli Ulcer Laboratory Network), a laboratory network comprising 13 laboratories from 9 countries, is a new program model for external quality assessment of PCR based diagnostics in endemic African countries for Buruli ulcer. Through the harmonization of SOPs, increased mean accuracy for PCR diagnosis has risen from 89.29% to 96.71% in the external quality assessment program. Harmonization of procedures is essential to improve diagnostic quality. Extending BU-LABNET is planned to extend SOP harmonization to the case management of other skin NTDs, such as yaws, leprosy, mycetoma, and leishmaniasis.

Challenges on leprosy surveillance in a low-resource country



Dr. Luc Samison from the Charles Mérieux Center of Infectious Disease in Madagascar stated that although Madagascar's Strategic National Plans announced that leprosy would be eradicated in 2006, 1,500 to 2,000 new cases are diagnosed each year. Madagascar's fight against leprosy comprises two main efforts: diagnosis and treatment of simple leprosy cases, and disability prevention and physical rehabilitation. Laboratory activities include genomic surveillance and immunology.

Prevalence and incidence of leprosy are overestimated in Madagascar, since 20% of clinical cases are negative according to the results of a laboratory exam. Recognizing the signs and symptoms of leprosy is challenging, especially in the early stages of the disease. Human migration has contributed to the emergence of different genotypes of *M. leprae*.

Immunity in the Malagasy population against leprosy has not been fully investigated. Improved diagnostic tools that facilitate diagnosis of leprosy are urgently needed. The follow-up of patients receiving multidrug therapy (MDT) is inadequate. MDT does not suffice to eliminate leprosy. Due to inadequate patient follow-up, relapsed leprosy patients treated with MDT has been less documented in Madagascar.

The mode of transmission of leprosy is not well known. Its spread occurs after prolonged contact with infected patients from environmental sources. Seroprevalence in children reflects a recent infection of leprosy and is an indicator that helps to understand the transmission chain in endemic regions.

Impact of climate change on vectors and vector-borne diseases



Dr. Florence Fouque from the World Health Organization in Switzerland, spoke about the impact of climate variables on vector distribution and life cycles. Changes in temperatures affect the survival of vectors, their breeding and geographical distribution, as well as their host-seeking and biting behaviors, host availability and transmission capacity. Changes in rainfall affect breeding and survival and changes in the wind can affect their dispersal.

Research has been conducted on the impact of climate on tsetse flies in east and south Africa. In the Zambezi valley, for example, studies have shown the tsetse densities decrease as temperatures increase but in more northern areas in Tanzania, rise of temperatures does not lead to a decrease in tsetse densities but more in changes in local geographical distribution. In Nepal, the rise in of temperatures has spread dengue fever northwards in the country. In Uganda, flooding has resulted in an increase of malaria incidence.

The effects of climatic changes do depend not only on biological factors, but, significantly, also on socio-economic factors such as migration of people. The capacity of health systems to appropriately adapt, allocate scarce resources, and gain support from the global community, will determine how resilient health systems are to the effects of climate change.

THE GABRIEL NETWORK MEETING – JUNE 1, 2023

Main achievements



Dr. Florence Komurian-Pradel from the Mériex Foundation described GABRIEL as a worldwide network of 21 research institutions located in 16 lower-middle-income countries. Its mission is to improve laboratory- and hospital-based disease surveillance and research capacity for infectious diseases that have severely impacted public health, strengthen the capacity to conduct clinical research by enhancing local expertise, and foster assessment of novel

diagnostic tools. In 2022, GABRIEL welcomed as a new member the Fondation Congolaise pour la Recherche Médicale (FCRM) located in Brazzaville, Republic of Congo.

GABRIEL expertise and resources are organized to structure the network around expert centers on thematic areas and to construct a communication strategy around the thematic sub-networks for greater visibility, partnership-building, and fundraising. This includes:

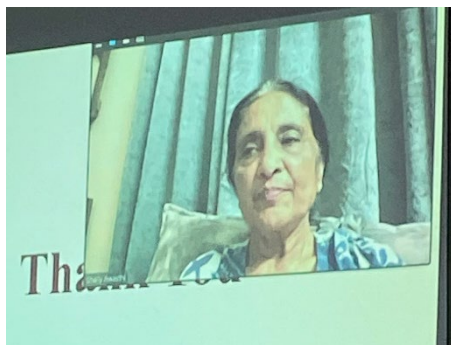
- primary and secondary activities of diagnosis, basic and clinical research, disease surveillance, training,
- transversal activities of quality assurance, biobanking, data collection,
- research projects on topics covering respiratory infections, tuberculosis, AMR, and emerging pathogens,

- expertise through the activities of reference laboratories, membership in international networks, etc.,
- human resources, and
- technical platforms.

SESSION I – ACUTE RESPIRATORY INFECTIONS

Chaired by **Dr. Valentina Picot**, France and **Dr. Firdausi Qadri**, Bangladesh

Effectiveness of 13-valent pneumococcal conjugate vaccine on radiological primary end-point pneumonia in Northern India



Dr. Shally Awasthi from King George's Medical University, Lucknow, India, presented community-acquired pneumonia (CAP) as a leading cause of the mortality of under-five-years-of-age children in India. The pneumococcal conjugate vaccine (PCV) against CAP recommended by WHO, has been included in India's national immunization program since 2017/2018. The primary objective of the study is to evaluate the effectiveness of PCV13 on chest radiograph (CXR)-

confirmed pneumonia in children hospitalized with WHO-defined severe CAP, and to compare hospital mortality with patients with primary endpoint pneumonia with or without other infiltrates (PEP±OI). This is a prospective hospital-based surveillance analysis.

In this prospective, multi-site, test negative study, we found that exposure to PCV13 had significantly reduced the odds of seeing PEP±OI on chest x-rays. Adjusted vaccine effectiveness was found to be 31.0% in children aged 2 to 23 months. Our case control was a Gambian study that reported vaccine effectiveness of 28% in children aged 2 to 59 months. Chest x-rays were evaluated by a panel of trained external radiologists using standard WHO-methodology of chest x-ray interpretation. The study therefore had internal as well as external validity and can be compared to studies that have used a similar methodology.

Multi-country pneumococcal colonization research, the example of Cambodia



Dr. Chan Leakhena Phoeung, Director of the Rodolphe Mérieux Laboratory in Cambodia, spoke about Cambodia's recent PCV13 vaccination program of newborns in 2015. A study carried out on the serotype distribution of clinical *Streptococcus pneumoniae* isolates before PCV13 was introduced in the national pediatric immunization program. All major microbiological laboratories in Cambodia were contacted for the purpose of identifying stored isolates of *S.*

pneumoniae from samples taken from patients with pneumococcal diseases before January 2015. We determined that in our study population, the pneumococcal carriage number among the children and the parents/guardians recruited in the study were 31.5%

and 8.4% respectively. We determined serotype distribution per sample and antimicrobial sensitivity of isolates according to vaccine coverage of serotypes.

The prevalence of PCV13 vaccine-type colonization among children was 77.4% at the age of 0-11 months, 63.0% (34/51) at age of 11-24 months, and 23.8% at the age of over 24 months.

This study provides baseline information on the prevalence of colonization, overall and with vaccine serotypes, after the introduction of PCV13 in Cambodia and should help in the surveillance of the impact of this type of vaccination in the future.

Characteristics of COVID-19 patients at admission and factors associated with clinical severity in low and middle-income countries: an observational hospital-based study



Dr. Mitra Saadatian-Elahi from the Hospices Civils de Lyon, France, spoke about the Noso-Cor project, an international seven-country observational, prospective, hospital-based multicentric study, whose objectives are i) to describe and compare clinical characteristics and outcomes of community/hospital acquired COVID-19 patients, ii) estimate mortality rates according to clinical features at admission, comorbidities, type of ward and community versus hospital-acquired infection, and iii) identify factors associated with the risk of ICU admission in community/hospital acquired COVID-19 patients. The study population was composed of relatively young patients.

The results showed that the mortality rate was the highest in Guinea, most probably due to the older age of patients and the greater number of existing comorbidities. Underlying cardiovascular diseases were a risk factor of COVID-19 severity, as was the male gender. The most frequently reported symptoms were those reported in older populations in developed countries.

The results also showed that there is a need for accelerated response mechanisms, often not in place, and that case definition is not fixed and changes due to the novelty of the disease. RT-PCR capacity testing has not been available in several countries since the beginning of the pandemic.

Epidemiology and serotype distribution of *Streptococcus pneumoniae* among influenza-like illness cases in metropolitan Vientiane, Lao PDR: a community-based cohort study



Dr. Valentina Picot from the Mérieux Foundation, France, presented the LaCoRis project as a community-based cohort study whose purpose was the active monitoring of the etiology and burden of influenza-like illness (ILI) among residents in metropolitan Vientiane, Laos, from 2015 to 2020. It assessed the prevalence, risk factors, and serotype distribution of *S. pneumoniae* carriage among ILI cases. The 13-valent pneumococcal conjugate vaccine (PCV13) was introduced among infants in October 2013.

We found that among 1,621 ILI cases, 16.6% tested positive for nasopharyngeal pneumococcal carriage, with the highest prevalence (55.4%) in children under 5 years. Pneumococcal carriage was significantly associated with concurrent detection of *Hemophilus influenzae* and exposure to household cigarette smoke. PCV13 serotypes accounted for 37.8% of all pneumococcal isolates.

According to the results of this study (*Front Public Health* 2023 Apr 20;11:1124016. doi: 10.3389/fpubh.2023.1124016), we can conclude that community-based surveillance of *S. pneumoniae* among ILI cases must complement surveillance at healthcare facilities to give a more complete picture of pneumococcal carriage. Our findings add also to the growing body of knowledge regarding the impact of PCV13 introduction on circulating serotypes and their prospective replacement.

Bacterial and viral etiology of acute respiratory infection among the Forcibly Displaced Myanmar Nationals (FDMNs) in the fragile setting in Cox's Bazar – a prospective case-control study



Dr. Abu Bakar Siddik, Senior Research Officer from the Institute for Developing Science and Health Initiatives, Bangladesh, described the Rohingya (FDMNs) as a refugee population forcibly displaced from Myanmar, the majority of whom have settled in Cox's Bazar, Bangladesh. They generally suffer from pneumonia, respiratory infections, diarrheal diseases, skin diseases, viral fevers, mental health disorders, COPD, pregnancy complications etc.

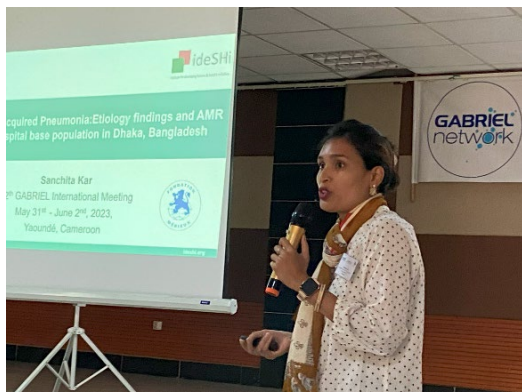
According to our research, viral pathogens such as ADVs, IFVs, and RSVs were the most observed in the ARI case group, as well as the number of viral co-infections. *S. pneumoniae* was the most detected bacterial pathogen, but serotype distribution patterns varied. The prevailing *S. pneumoniae* serotypes were 19A, 6A/B and 23F in the PCV-13 vaccinated group, whereas 13, 15B/C and 35B serotypes were the most common in the non-PCV-13 group, thus suggesting that a vaccination policy had been in place. Our study also suggests that the patterns of correlation with other pathogens and *S. pneumoniae*

serotypes may contribute to the development of the disease. However, further investigations are required to fully understand the mechanisms and consequences of such conditions.

A SARS-CoV-2 serology study was also conducted among the FDMNs in Cox's Bazar. It was found that antibody titer significantly decreased within 6 months both after a natural infection and a vaccination. However, vaccination boosted the antibody titers, underscoring its significance. No age-sex dependent variations were observed considering the antibody titer.

Antibody titer observed both in cases and RT-PCR negative households members indicate that there was a prior asymptomatic infection. SARS-CoV-2 related morbidity and mortality in such humanitarian crisis settings can be reduced by RT-PCR testing in addition to vaccination.

Community-Acquired Pneumonia: Etiology findings and AMR data from a hospital-based population in Dhaka, Bangladesh



Sanchita Kar from the Institute for Developing Science and Health Initiatives, Bangladesh, presented the study conducted to determine the bacterial etiology of community-acquired pneumonia (CAP) in Dhaka Medical College Hospital, Bangladesh. Its objectives were to characterize the *S. pneumoniae* serotypes among cases and control populations, perform phenotypic AMR characterization of bacterial etiology, and associate blood biomarkers with

etiological agent. From patient sputum and nasopharyngeal swabs, bacteria were cultured, and this was followed by PCR for pneumococcus serotyping and COVID testing. An antibiogram was also run for pneumococcus and other bacterial isolates. Inflammatory markers were checked from patient blood samples.

According to our findings, *S. pneumoniae* burden was higher in children under five years of age, whereas in adults, Gram negatives were predominant. *S. pneumoniae* serotype 19A showed elevated MIC value for penicillin, and macrolide resistance was high. However, at present, it is premature to make any conclusions on biomarkers in relation to NP/Sputum cultures. The sequencing of *S. pneumoniae* 19 A serotypes is projected.

SESSION II – ANTIMICROBIAL RESISTANCE

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

Multicenter evaluation of the impact of COVID-19 pandemic on the spread of antimicrobial and biocide resistance from wastewater to the environment



Dr. Ariane Nzouankeu from the Centre Pasteur of Cameroon pointed out that the misuse or overuse of antibiotics in humans and animals, as well as the release of untreated wastewater into the environment, are the primary causes of anti-microbial resistance.

The COV-AMR project involves multicenter collaboration between Cameroon, Brazil, and Madagascar. Its objectives are to evaluate the impact of the COVID-19 pandemic on the spread of antimicrobial resistance in the environment from the sewage of healthcare facilities whose patients have COVID-19. It also compares the abundance of antimicrobial and biocide-resistant bacteria and associated resistance factors and genes from different sampling sites. SARS-CoV-2 isolated from untreated wastewater and the levels of antibiotic residues were compared.

According to our findings, there was found to be a high rate of multidrug-resistant bacteria (*E. coli*, *K. pneumoniae* and *Enterococcus spp.*) at the hospital sites in the three countries. The bacteria carry a wide variety of antimicrobial resistance genes, most of which are borne by mobile genetic elements such as plasmids and integrons. No direct link was found between the SARS-Cov-2 detected and the diversity or relative abundance of antimicrobial and biocide resistance determinants. In Brazil the great diversity of antimicrobial residues and biocides are present in concentrations showing a high-risk quotient of resistance selection for bacteria present in the waters that were studied.

We draw the conclusion that the release of hospital sewage containing antimicrobial resistance determinants and antimicrobial residues in surface waters in the countries under study poses an environmental and human health risk in the three countries.

Strengthening Data Science Capacity in Madagascar and Burkina Faso: development of an AMR Data Center



Dr. Luc Samison from the Charles Mérieux Center of Infectious Disease, presented the data management of the Tricycle Protocol, involving three partners, the CICM and the University of Antananarivo in Madagascar, the Sourou Sanou University Teaching Hospital in Burkina Faso, and the Mérieux Foundation, which is to become the first pilot trans-African data center. As a new data science center, it will act as a sustainable surveillance mechanism, supporting active AMR surveillance in

Madagascar and Burkina Faso, and will be fully integrated into national AMR surveillance systems in other LMICs.

The plans for the upcoming months are i) the development of SOPs with Clinical Data Interchange Standards Consortium (CDISC) standards for data obtained from active AMR surveillance, ii) the design of the IT infrastructure and real-time digital platform, and iii) the presentation of the beta version of the data science center to the stakeholders.

This protocol, through the Mériex Foundation's LMIC laboratory capacity-building networks at the local, regional, and international levels, will use a multi-prolonged approach to communicate and disseminate project results. In addition, it will assure technology transfer, training, and knowledge-sharing among GABRIEL's 21 research institutions located in LMICs.

Capacity-building for the management, analysis, and use of integrated respiratory infection surveillance data in Burkina Faso



Dr. Isidore Traore from the Centre Hospitalier Universitaire Sourou Sanou in Burkina Faso described the AFROSCREEN Project that has carried out a situation analysis to integrate genomic surveillance of SARS-CoV2 into the existing national surveillance of respiratory infections. In the past, surveillance activities of these diseases were separate, as each had its own notification form, sample flow, and data management system.

Through our capacity-building activities, we have strengthened our surveillance of influenza-like illnesses by increasing the number of sentinel surveillance sites and integrating surveillance of COVID-19 and SARS-COV2 VOC and VOI. We have adapted the national COVID-19 database to provide a single database for COVID-19, Influenza-like illnesses, SARI surveillance, and added a metadata database for COVID-19, influenza-like syndrome, and severe acute respiratory infection. In addition, we have trained health workers at sentinel sites and laboratories on integrated surveillance and real-time data entry into the databases.

We now have a better capacity for advanced statistical analysis (temporo-spatial analysis) and we have set up a biological sample flow to enable all tests (screening, diagnosis, and genotyping with COVID-19 PCR, influenza PCR, and multiplex PCR (SARI), to be carried out on a single sample. This ongoing process is being used by the Ministry of Health to integrate surveillance of other respiratory infections, such as those caused by *Streptococcus pneumoniae*.

The Tricycle 'One Health' surveillance project in Antananarivo, Madagascar: evidence of ESBL *E. coli* strains and plasmid circulation between humans, chickens, and the environment



Dr. Milen Milenkov from the Mérieux Foundation, stated that antimicrobial resistance is a major public health threat, affecting not only humans, but also animals and the environment, with exchanges among the different sectors being incompletely described, particularly in low-income countries. The WHO has elaborated a surveillance protocol called “Tricycle” to address extended-spectrum beta-lactamase *E. coli* (ESBL) dissemination in these three sectors. Tricycle was carried out in Madagascar to

evaluate ESBL-*E. coli* prevalence and describe intra- and inter-sector transmission of ESBL-*E. coli* and associated plasmids.

Rectal swabs from healthy pregnant women, cecal samples from farm chickens, surface water and wastewater were collected in Antananarivo and tested for ESBL-*E. coli*. Isolates were sequenced by short-(Illumina) and long-(Nanopore) read methods. Experiments include the phenotypic and molecular characterization of bacterial isolates, antibiotic susceptibility testing, the identification of phylogenetic groups, the search for resistance and virulence genes, point mutations, plasmid content, as well as the study of the genetic links between isolates of different origins.

The bacterial isolates showed considerable genetic diversity. Despite varying strain population structures, we detected a high ESBL-*E. coli* prevalence in healthy pregnant women, farm chickens, and the environment in Antananarivo. We observed the circulation of both ESBL-*E. coli* strains and ESBL-carrying plasmids in all three sectors. In order to restrict the spread of antibiotic resistance, and to limit the transmission of resistance between the three sectors urgent public health measures need to be undertaken.

Transmission of ESBL-*E. coli* in humans through exposure to companion animals



Dr. Nazareno Scaccia from the Instituto de Medicina Tropical da Faculdade de Medicina in Brazil raised the question whether companion animals can transmit ESBL *E. coli* to pregnant women. A pilot project carried out in Bangladesh, Brazil, and Paraguay, is evaluating the transmission of ESBL-*E. coli* in humans through exposure to companion animals. The objectives are to assess the risk of transmission of ESBL-*E. coli* in pregnant women through exposure to dogs and cats, perform a longitudinal study of ESBL-*E. coli* carriage in pregnant women and in companion animals (dogs and cats), and characterize resistance factors and evaluate phylogenetic relationship among ESBL-*E. coli* isolates from pregnant women and pets from the same household. Comparative whole genome sequence analysis of ESBL-*E. coli* is being carried out to infer the likely pathways of transmission and AMR characterization.

This study should provide data on the prevalence and persistence of ESBL-*E. coli* carriage in pregnant women and during delivery, and data on the molecular relationship of ESBL-*E. coli* strains isolated from pregnant women and companion animals from the same household.

SESSION III – CAPACITY BUILDING FOR THE SURVEILLANCE OF COVID-19 EMERGENCE OF VARIANTS

Chaired by **Richard Njouom**, Cameroon and **Tahinamandranto Rasamoelina**, Madagascar

The SARS-COV-2 Variants Surveillance Initiative in GABRIEL



Emilie Westeel from the Mérieux Foundation described the GABRIEL initiative to build SARS-CoV-2 variants surveillance capacities among the members of the GABRIEL network. PCR-screening and next generation sequencing have been implemented to identify and characterize SARS-COV-2 variants, along with a communication channel with the national health authorities for the reporting. The goal is to assist in the development of stronger national health systems and to position GABRIEL as a stakeholder in health crises.

SARS-CoV-2 variant surveillance in Bangladesh



Dr. Zannat Kawser from the Institute for Developing Science and Health initiatives (ideSHi) described the objectives of the SARS-CoV-2 variant survey: i) to evaluate the presence of VOCs and VOIs in specimens collected from different regions of Bangladesh, ii) to measure the variations in the proportion of VOCs and VOIs using PCR and NGS, and iii) to find epidemiological or clinical characteristics associated with the viral genetic background. In a CORAIL study we found that Omicron and Delta were the most common SARS-CoV-2 variants. We determined that a panel of multiplex, mutant-specific RT-PCR assays is the best compromise between cost,

turnaround time, and precision. Such a rapid and accessible method is essential in the context of pandemic response requiring rapid strain typing to guide both treatment decisions and public health measures,

This research provides cross-disciplinary collaboration opportunities for knowledge and the transfer of skills (Mérieux Foundation, ideSHi, BITID, IEDCR).

SARS-CoV-2 variant surveillance in Cameroon



Dr. Ronald Perraut from the Centre Pasteur of Cameroon described the impact of the AFCON mass-gathering event on the COVID-19 epidemic among the population of Garoua in Cameroon.

Following the Centre Pasteur's passive screening for COVID-19 variants, it was found that the football match did not trigger any increase of symptomatic cases 2 to 3 weeks after the event and beyond. The epidemic curve was not impacted and displayed similar profiles with those of neighboring countries.

Questions remain as to whether the population is naturally resistant and whether the immunity level is already high.

YOUNG SCIENTIST AWARD PRESENTATION – June 2, 2023

Chaired by **Dr. Graciela Russomando**, Paraguay and **Dr. Jean-Yves Madec**, France

As in previous years' meetings, the program included the "GABRIEL Young Scientist Award", created to enable promising young scientists from low- and lower-middle-income countries to advance their careers by allowing them to speak about their research at international scientific meetings. Two winners among the five following reports were selected for this year's best presentations.

Genomic surveillance of SARS-CoV-2 and other pathogens in the Republic of Congo



Claujeans Chastel Mfoutou Mapanguy from Fondation Congolaise pour la Recherche Médicale, Republic of Congo, presented the study whose aim was to carry out whole-genome sequencing of SARS-CoV-2 and other pathogens on blood and sputum samples collected from Congolese individuals.

The methods entailed the screening of 596 samples for SARS-CoV-2 using RT-PCR. Other pathogens such as *Plasmodium falciparum*, *M. tuberculosis* and Norovirus were also screened. The genomes were annotated and screened for mutations using applications pangolin and Genome detective. According

to the results, 396 SARS-CoV-2 genomes were successfully sequenced and submitted to the GSAID database. The Congolese SARS-CoV-2 sequences were shown to belong to lineage B1 and Nextclade 20A and 20C, which split them into distinct clusters, indicating two separate introductions of the virus into the Republic of Congo.

This study has helped monitor the spread of SARS-CoV-2 in the Republic of Congo and it should support the national containment strategies of the pandemic. The national genomic platform may be expanded to other circulating pathogens for surveillance, prevention, and response interventions.

Respiratory syncytial virus infection in persons with acute respiratory infections during the COVID-19 pandemic in Yaoundé, Cameroon: prevalence, genetic diversity, and risk factors



Moïse Henri Moumbeket Yifomnjou from the Centre Pasteur of Cameroon described the study whose aim was to determine the prevalence of RSV and other respiratory viruses in hospitalized and ambulatory patients with acute infections during the COVID-19 pandemic in Yaoundé, Cameroon, and assess the correlation between the various associated risk factors and the resulting respiratory infections. He described the different genotypes, sub-genotypes, and genetic lineages of the detected RSV strains. In addition, the

evolutionary dynamics of co-circulating RSV variants and the mechanisms of maintenance and propagation of this virus in Cameroon were studied.

Patients with SARS-CoV-2 and other respiratory viral infections were monitored for respiratory symptoms. Nasopharyngeal samples were tested for SARS-CoV-2, influenza, and respiratory syncytial virus (RSV) using real-time reverse-transcription polymerase chain reaction methods. Virus distribution and demographic data were analyzed with R version 2.15.1.

According to the study's findings, the overall viral detection rate was 32.5%, including 9.5% for RSV, 12.6% for influenza virus, and 12.8% for SARS-CoV-2. Co-infections were detected in 6.9% of positive cases. While RSV and influenza virus showed seasonal trends, SARS-CoV-2 was detected throughout the study period. We found that during COVID-19 pandemic, respiratory viruses play an important role in etiology of influenza-like illness in Cameroon,

Natural selection shapes the evolutionary pattern of SARS-CoV-2 Omicron in Bangladesh



Md Saikt Rahman representing the institute for developing Science and Health Initiatives in Bangladesh spoke about the evolutionary pattern of SARS-COV-2 Omicron VOC in the aspect of Bangladesh. Omicron possesses few characteristics mutations, especially in the S gene and Receptor Binding Domain (RBD) of the S gene, which increase the transmission and adaptability of the Omicron VOC. The purpose of this study was to understand the evolutionary pattern of Omicron VOC, predict its adaptation in Bangladesh, and identify positively selected sites related to Omicron adaptability by calculating the ratio of non-synonymous (dN) and synonymous (dS) mutation sites of SARS-COV-2 genome. Phylogenetic Analysis by Maximum Likelihood (PAML) which is used to study sequence evolution, was applied to calculate the position selection in

each protein-coding genes and also to calculate the disproportional selection pressure

among different domains of the S gene of Omicron. In determining the natural selection process acting on Omicron, it was found that S gene, M gene and ORF6 gene showed evidence of positive selection. Especially, S gene showed more confident evidence of positive selection.

We were able to conclude that natural selection is the driving force of Omicron evolution in Bangladesh, that the S gene is a focal point for natural selection, and that, in the future, accumulating naturally evolving beneficiary mutations, and future VOCs, could emerge. Future vaccine strategies should focus on those sites of natural selection and on heavily mutated Omicron strains.

Prevalence of isoniazid-resistant strains of *Mycobacterium tuberculosis* clinical isolates with unknown resistance mechanism in Cameroun



Nono Vanessa Ninkeh from the Centre Pasteur of Cameroon stated that the accumulation of spontaneous mutations at target genes has been considered the main cause of drug-resistant tuberculosis. In terms of rifampicin resistance, mutations at the RIF-resistant determining region of *rpoB* gene account for 96% of cases. On the other hand, the mechanism of resistance to isoniazid is complex with mutations conferring resistance occurring at *katG*, *inhA* promoter region, *oxyR-aphC*, *kasA*, and *ndh* genes. However, 20-30% INH-resistant strains lack these mutations at drug-target genes.

A question remains: are there isoniazid-resistant strains of *Mycobacterium tuberculosis* with unknown mechanism of resistance in Cameroon? In our research we attempt to describe the existence and prevalence of isoniazid-resistant strains of *M. tuberculosis* clinical isolates whose mechanism of resistance are unknown in Cameroon. We obtained a prevalence of 13.66% INH-resistant strains lacking mutations at the *katG* and *inhA* promoter genes. Thus, there is an urgent need to determine the mechanisms via which these strains confer resistance to isoniazid as this would help identify new therapeutic targets necessary for the development of new diagnostic assays and drugs, thus facilitating the management of isoniazid-drug resistant cases in Cameroon and beyond.

Assessment of neutralizing antibody responses to SARS-CoV-2 in the Bangladeshi population: a comparison between natural infection and vaccination with four different COVID-19 vaccines



Mohammad Kamruzzaman from the International Centre for Diarrheal Disease Research in Bangladesh, icddr, spoke about the COVID-19 situation in Bangladesh. He pointed out that 83% of the population has completed full dose regime of the vaccines available that include Covishield (ChAdOx1), Pfizer-BioNtech (BNT162b2), Moderna (mRNA-1273), Sinopharm (Vero cell-inactivated), Sinovac, Janssen (Johnson & Johnson). Neutralizing antibodies are known to be a useful correlate of protection for vaccine clinical trials and for population-level surveys.

A study was conducted on four groups of participants: i) those vaccinated with one of the first four vaccines mentioned and reportedly negative for SARS-CoV-2 during the follow up period, ii) those previously infected with SARS-CoV-2 and then vaccinated, iii) healthy controls tested negative for SARS-CoV-2 during enrollment, iv) unexposed pre-pandemic healthy controls.

The SARS-CoV-2 RBD specific IgG antibodies and spike-specific neutralizing antibody responses in COVID-19 infected individuals were measured.

It was found that vaccinated participants, regardless of whether they had prior COVID-19 infection or not, exhibited significantly higher levels of 50% neutralizing (NT50) titers when compared to the cohort of COVID-19 patients. In addition, neutralizing antibodies were significantly increased in COVID-19 patients at day 28 following the detection of the virus. Moderate to severe patients demonstrated higher NT50 and RBD-IgG titers compared to asymptomatic to mild patients, and persistent neutralizing antibody responses were observed five months after the initial dose of COVID-19 vaccination. Previously infected individuals exhibited higher NT50 levels compared to uninfected individuals at each time point for each vaccine group. Vaccinated participants displayed significantly higher NT50 titers compared to the cohort of COVID-19 patients.

SESSION IV – TUBERCULOSIS

Chaired by **Dr. Sayera Banu**, Bangladesh and **Dr. Jonathan Hoffmann**, France

Evaluation of screening and management strategies for TB infection in Madagascar and Cameroon



Dr. Valerie Donkeng from the Centre Pasteur of Cameroun stated that the COVID-19 pandemic has reversed years of progress made in the fight to end tuberculosis, and that TB deaths have increased since 2021 following years of decline in the preceding years. In addition, fewer people have received TB preventive treatment due to a shortage of available resources for TB services and TB R&D.

The APRECIT project is designed to evaluate various screening strategies and improve the overall program management of latent TB infections in Madagascar and Cameroon. It entails assessing a community intervention strategy for TB identification and management of household members and individuals in high-risk groups (children under the age of five and HIV-positive individuals) in a quantitative and cost-effective manner in accordance with WHO recommendations. Diagnostics are performed with two interferon-gamma-release assays (IGRA); Quantiferon gold plus and TSpot TB to identify amongst household contacts people with LTBI or not. All the household contacts were followed up to 18 months at four time points (months 0, 6, 12 and 18). The objective was to identify people with LTBI and to predict the progression from LTBI to active TB infection from a sensitivity/specificity and a cost/efficacy perspective.

At the community level, the initiatives include population sensitization, identification of intra-domiciliary contacts, screening of household contacts of active tuberculosis cases, referral of contacts with TB-suggestive symptoms to the health care facility for TB diagnosis, and initiation of preventive therapy.

The difficulty of bringing together all intra-domiciliary contacts for blood sampling, and the refusal of some participants to continue the study after the index cases have been cured can be mitigated by having project staff maintain regular contact with the families and re-sensitizing the participants in the project.

Evaluation of screening and management strategies for TB infection in Madagascar



Dr. Niaina Rakotosamimanana from the Institut Pasteur of Madagascar presented a study to actively detect latent TB infections (LTBI) in households in Madagascar, who will subsequently be monitored for up to 18 months. The objective is to assess the diagnostic value of immunodiagnostic tests used to identify LTBI, more specifically, the Tuberculin Skin Test (TST), and the Interferon-gamma release assays (IGRA): QuantiFERON®-TB Gold Plus and T-SPOT.TB®.

It was noted that the IGRA positivity increases with the age of the participants and that combining IGRA with TST more accurately measures the progression of TB. TST and TSPOT have better prognostic values for classifying TB progressors from inclusion.

The second part of the study consists of examining the accuracy of serological test using the Luminex for SARS-CoV-2 infection and determining the impact of a SARS-CoV-2 infection on the TB infection progression to active disease. There appears to be no association between SARS-CoV-2 infection and TB progression.

Further studies will be run to estimate the period of TB infection for better case management and to assess the cost-effectiveness of identifying active LTBI cases. In addition, biobanks including bacterial strains and cell transcriptomics are promising factors for exploratory investigation of TB biomarkers.

Clinical evaluation of non-sputum-based assays for childhood and extra-pulmonary TB



Dr. Mohammad. Khaja Mafij Uddin from the International Centre for Diarrheal Disease Research in Bangladesh spoke about the difficulty of diagnosing pulmonary TB in children (Ch-PTB). Extrapulmonary TB (EPTB), secondary manifestation of MTB infection that can affect any part of the body outside of the lungs. Invasive procedure makes sample collection difficult.

Lack of specific clinical signs, collection and paucibacillary nature of the specimen make difficulties in diagnosis of EPTB and Ch-PTB. There is a crucial need of a non-sputum-based host biomarker capable of diagnosing TB and monitoring response to TB therapy. The purpose of this study is to evaluate diagnostic performances of Xpert-MTB-HR and RISK6 transcriptomic signature as innovative tools for diagnosis of

Ch-PTB and EPTB. In addition, we want to evaluate the use of Xpert-MTB-HR and RISK6 transcriptomic signature for treatment monitoring among Ch-PTB and EPTB patients. RISK6 is a PCR-based host-blood transcriptomic signature that has multiple applications for the

identification of at-risk individuals for incident disease, the screening of subclinical or clinical TB, and the monitoring of TB treatment. The study is currently in progress awaiting the completion of RISK6 signature analysis and the continuation of Xpert-HR-MTB-Prototype.

Evaluation of host plasma protein biomarkers for tuberculosis treatment monitoring in Paraguay



Dr. Graciela Russomando from the Instituto de Investigaciones en Ciencias de la Salud in Paraguay presented the Paraguayan results related to HINTT project whose main objective is the evaluation of blood-based biomarkers for monitoring tuberculosis treatment in five countries, including Paraguay.

Blood samples were collected at baseline (T₀), month-2 (T₁) and following 6-months treatment (T₂). Interferon-gamma release assays (in-house recombinant *Mycobacterium smegmatis* heparin-binding hemagglutinin-IGRA and QuantiFERON-TB Gold plus) were performed at each time points. A total of 20 blood-based biomarkers (17 Th1/Th17/Th2/Th9 cytokines levels and C1Q, C3 and C4) were evaluated in plasma samples stimulated with either rmsHBHA or TB2 (QuantiFERON-TB gold plus®) using an xMAP® assay. The complete blood count of each TB patient following TB treatment was assessed and considered in a combinatory analysis to identify and evaluate host protein signatures performances to differentiate an active pulmonary TB from a cured profile. We identified hematological and immunological patterns differentiating an active TB patient from a treated subject in non-stimulated and HBHA-stimulated samples, and we observed a correlation between biomarker expression dynamics and the bacterial load observed.

For the future we plan on identifying different subsets of memory T cells based on the expression of CCR7 and CD45RA genes, and to analyze their activation profiles (following HBHA stimulation). To identify natural killer (NK) cells, we will target populations that are negative for lineage markers (CD3, CD14 and CD19) and positive for CD56.

(*) This research was supported within the framework of the PROCIENCIA program of the National Council of Sciences and Technology of Paraguay (CONACYT) Project Number PINV18-1322

Plasma host protein signatures correlating with *Mycobacterium tuberculosis* activity prior to and during antituberculosis treatment



Dr. Mame Diarra Bousso Ndiaye from the Institut Pasteur, Madagascar, stated that the complexity of long-term treatment of TB often leads to a high number of patients quitting treatment and this can trigger the emergence of resistant strains of *M. tb*.

There is an urgent need to develop alternative tests for screening for TB using non-sputum samples, with a series of Target Product Profiles (TPPs) detailing the minimum and optimum criteria for diagnosing and monitoring response to TB treatment. It is therefore essential to develop new biomarker-based screening tests for tuberculosis using non-sputum samples.

Madagascar is one of the five countries participating in the HINTT project whose aim is to evaluate TB biomarkers for TB diagnosis and TB treatment monitoring. The objective of our study was to measure and compare the expression of a selected panel of human plasma proteins in TB patients throughout their anti-TB treatment, and in healthy donors to identify a putative host-protein signature useful for both TB diagnosis and treatment monitoring. Protein signatures were assessed using multiplex Luminex xMAP® to quantify the plasmatic levels in each group, as well as the protein levels at baseline and at three timepoints during the six-months ATB treatment.

In conclusion, the signature of four host markers, "ECM1-CLEC3B-IP10-SELL", appears to meet WHO recommendations for a non-sputum-based test for treatment follow-up. This can be validated in a larger cohort including other respiratory infections.

One of the main problems in TB research is the lack of translation from clinical research to commercially available clinical applications. It is therefore essential to move from basic research to operational research on tuberculosis.

YOUNG SCIENTIST AWARD CEREMONY

The GABRIEL Young Scientist Award is an important initiative for the future of science and an incentive for young researchers. Countries throughout the world need talented scientists who should be recognized as our future leaders in the fight against infectious diseases.

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, GABRIEL's jury composed **Dr. Jean-Yves Madec** (France), **Dr. Abdoul-Salam Ouedraogo** (Burkina Faso), **Dr. Graciela Russomando** (Paraguay), **Dr. Tahinamandranto Rasamoelina** (Madagascar), and **Dr. Daniel Mukadi** (Democratic Republic of Congo) decided to award the two prizes to:



Nono Vanessa Ninkeh (left) for her work on the natural selection and the evolutionary pattern of the Omicron variant in Bangladesh, and **Claujeans Chastel Mfoutou Mapanguy** for his research on the genomic surveillance of SARS-CoV-2 in the Republic of Congo.

The two winners were congratulated for their outstanding contribution to science.



CLOSE OF THE GABRIEL MEETING

Alain Mérieux concluded this twelfth edition of the GABRIEL network international meeting in Cameroon by thanking the organizers and all the participants for their generosity and their contribution to the meeting's success. He confirmed that the Mérieux Foundation's work remains focused on serving public health and setting up educational programs in all member countries, including Fondation Congolaise pour la Recherche Médicale in Brazzaville, Republic of Congo, which has joined the GABRIEL network as a new member.

He concluded "Today's global context is demanding and complex. Despite the lack of security, the violence, and the threats of war in many regions, the Mérieux Foundation is committed to reaching out even further afield with support in areas, such as child and maternity care, laboratory diagnostics, mental health, and epidemiology, just to name a few. Our hope is to overcome borders. This hope is a component of the Foundation's world vision. We must never lose sight of our mission: to share knowledge, to keep the laboratories at the core of our efforts and in line with our principles, and to make a true impact on public health, scientific innovation, relief to populations, and scientific career opportunities for the youth of the developing world. For these reasons, we are optimistic. There is always room for hope and cooperation wherever we may be. We are like bacteria: we adapt to our environment!"

List of acronyms

GABRIEL: Global Approach to Biological Research on Infectious Epidemics in Low-income countries

CPC: Centre Pasteur du Cameroun

INRB: Institute of Biomedical Research

CAR: Central African Republic

WHO: World Health Organization

ISM: Institute for Scientific and Medical Research

CRFILMT: Centre de Recherche sur les Filarioses et d'autres Maladies Tropicales

FCRM: Fondation Congolaise pour la Recherche Médicale

CICM: Centre d'Infectiologie Charles Mérieux

ideSHI: Institute for Developing Science and Health initiatives

BITID: Bangladesh Institute of Tropical and Infectious Diseases

Icddrb: International Centre for Diarrhoeal Disease Research, Bangladesh

EID: emerging infectious diseases

GHSA: Global Health Security Agenda

HBV: Hepatitis virus

EVD: Ebola Virus Disease

MPVX: monkeypox virus

MDT: multidrug therapy

CAP: community-acquired pneumonia

PCV: pneumococcal conjugate vaccine

AMR: Antimicrobial Resistance

LMIC: Low- and Middle-income Countries

ESBL: extended-spectrum beta-lactamase

RSV: respiratory syncytial virus

LTBI: latent tuberculosis infections

TST: Tuberculin Skin Test

EPTB: Extrapulmonary Tuberculosis

MTB: Mycobacterium tuberculosis