



SPECIAL REPORT

10th GABRIEL MEETING June 17-20, 2019



*Université Saint-Joseph de Beyrouth Auditorium
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Campus de l'Innovation et du Sport,
Rue Damas, Beirut*



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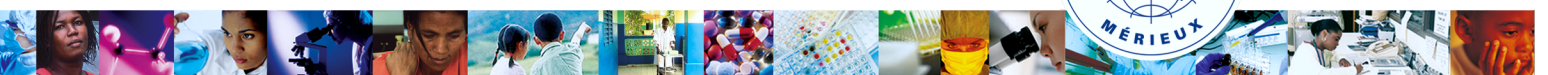
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Special Report

From June 17 to 20, 2019, over 100 researchers, physicians, specialists in laboratory diagnostics, academics, and scientists, arriving from both the public and private sectors of over 20 countries, convened at the Saint Joseph University of Beirut, Lebanon, for GABRIEL network's tenth international meeting. This special report provides highlights of this meeting, including summaries of speeches and the main points of discussion.

The first day of the assembly was devoted to the symposium, "Hot Topics in Infectious Diseases", with specialists speaking about advances in antimicrobial resistance, tuberculosis and pneumonia, and the role of infectious agents in chronic diseases. The symposium was an opportunity to identify the gaps and pitfalls that hamper accurate and effective diagnosis of these diseases, and to provide a knowledge-sharing platform where improved surveillance strategies and clinical management could be discussed.

The international GABRIEL meetings have become the occasion for members to share experiences, present new collaborative opportunities, review advances in quality assessment, and examine the latest scientific research in infectious diseases. This year's program included presentations on tuberculosis, antimicrobial resistance, fevers, and acute respiratory infections. As these diseases exhibit high serological complexity, making accurate diagnosis a true challenge, they are raising increased concern for global public health.

As in prior years' meetings, the program included the "GABRIEL Young Scientists Award", created to help boost the career development of promising young scientists from low- and lower-middle income countries 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

Prof. Marianne Abi Fadel from the Saint Joseph University of Beirut and **Prof. Monzer Hamze** from the Lebanese University welcomed the participants and thanked them for their presence at the symposium and the GABRIEL network meeting.

As part of its activities, Saint Joseph University considers scientific research a priority, as demonstrated by its Rodolphe Mérieux Laboratory whose activities are integrated in the School of Pharmacy degree programs. As for the Lebanese University, it is the sole public institution for higher learning in Lebanon, and it offers the broadest range of PhD programs in the country.

Dr. Florence Komurian-Pradel, Head Manager of the GABRIEL network, and **Dr. Hubert Endtz**, Scientific Director of the Mérieux Foundation, welcomed the participants to the symposium, which was organized with the Saint Joseph University of Beirut and the Lebanese University as part of the meeting. Continuing its support to scientific research on infectious diseases in developing and emerging countries is a top priority for the Mérieux Foundation. The specific mission of GABRIEL is to strengthen the research capacities of local laboratories in its now twenty member countries and to encourage researchers, physicians, and academics from around the world join forces in promoting scientific training and conducting joint research projects.



SYMPOSIUM ON “HOT TOPICS IN INFECTIOUS DISEASES”

SESSION I – AMR: New Perspectives and Interventions

Chaired by Dr. Zahi Helou, Lebanese Society for Diseases and Clinical Microbiology, and Dr. Shakeel Ahmed, BITID, Bangladesh

Global AMR: The role of WHO in Lebanon for AMR prevention and control

Dr. Alissar Rady from the World Health Organization, Lebanon, began with a review of Sustainable Development Goals, whose theme, “No One Left Behind”, reflects the pledge of the international community to identify and lift up those who are the most vulnerable and the furthest behind. It represents a commitment to promote healthy lives and wellbeing at all ages and for all.

Honoring this pledge, WHO takes a One Health approach that calls upon the human, animal and environmental health sectors to cross professional, disciplinary and institutional boundaries and to work in a more integrated fashion. This includes close collaboration with the FAO and the OIE to agree on an operational definition of One Health among key global institutions; WHO also calls under the Global AMR plan, to collectively work in line with the global AMR strategic objectives, namely:

- to improve awareness and understanding of antimicrobial resistance,
- to strengthen surveillance and research,
- to reduce the incidence of infections,
- to optimize the use of antimicrobial medicines,
- to ensure sustainable investment in countering antimicrobial resistance.

This initiative seeks to tackle the growing problem of resistance to antibiotics through effective communication, education, and training.

WHO fully supports Lebanon’s National Committee Against Antimicrobial Resistance in its actions to meet the objectives set by global institutions. Since 2013, WHO has been actively supporting the MOPH and National AMR committee; accordingly, three AMR prevention media campaigns have been organized, proficiency microbiology lab testing is supported with the USJ reference lab, and a national Plan of Action is developed, with its 5 main areas of intervention: awareness/education, surveillance, infection control, rational use of antibiotics, and research.

Limiting the in-hospital spread of MDRO – How to move on?

Prof. Jean Ralph Zahar from Université Paris XIII described the endemic spread of multidrug-resistant organisms throughout the world, due in large part to the growing amount of intercontinental travel of people infected with AMR microorganisms. The resistance of carbapenem-producing *Enterobacteriaceae* (CPE) is also intensifying.

In the wake of this trend, the French Council for Public Health issued the following recommendations with a view to check the spread of CPE:

- to isolate patients and health workers,
- to halt the hospital admission and transfer of infected patients,
- to identify contact patients subject to secondary acquisition of an infection, and
- to monitor antibiotic therapy.



These recommendations were based on the results of an Israeli nationwide intervention that was aimed at containing the spread of *K. pneumoniae*, a CPE that had been established as an important nosocomial pathogen. Patient-to-patient transmission via the non-sterilized hands of healthcare workers has been the main route for the spread of MDRO in acute-care settings. As part of this intervention, compliance with national guidelines on prevention was examined on-site at healthcare facilities, the number of infected carriers and their isolation status was routinely reported, and a communication network was set up to report on identified carriers, contact tracing, and screening. As a result of these measures, nosocomial CPE acquisition in acute-care facilities sharply declined.

Guidelines for containing the spread of CPE are guided by epidemiological reasons related to the high risk of CPE being disseminated outside of the hospital environment leading to secondary infections, thus aggravating the risk for antibiotic failure. Concerted action must be undertaken to identify risk factors associated with hospital-acquired infections, to develop new diagnostic methods, and to extend surveillance to other classes of antibiotics – not only to carbapenems.

Hospital-acquired infections: surveillance and protection

Dr. Christelle Elias from the Hospices Civils de Lyon began her talk by explaining that healthcare-associated infections (HAIs) are infections contracted by patients (or healthcare workers, or visitors) in a healthcare facility. An estimated 8.9 million cases occurred in the EU in 2016 and 2017 affecting one out of 15 hospital patients. One-third of the bacteria responsible for HAIs are antibiotic-resistant.

In a survey of infection surveillance, the CDC launched the Study in the Efficacy of Nosocomial Infection Control (SENIC project) to determine whether infection surveillance and control programs indeed lower the rate of nosocomial infections. In the EU, the surveillance of antimicrobial consumption, of antimicrobial resistance, and of HAIs has been carried out by the European Surveillance System. The European Center for Disease Prevention and Control has conducted point prevalence surveys on infected patients, HAIs, and on the use of antibiotics in European acute-care hospitals, and has classified them according to the sites of infection and to the types of health-care facilities, risk factors, and pathogens. The findings from these surveys should serve as an educational tool for healthcare workers. They also can estimate the burden of HAIs and the trends for future benchmarking. However, the quality of data obtained has been questioned as they tend to be inaccurate and fail to take certain long-lasting infections into account.

Measures have been recommended to prevent and control HAIs. These include the application of standard and complementary sanitary precautions, screening for MDRO carriage or infection, the isolation of carriers/infected patients, antimicrobial management programs, the training of healthcare staff, and communication to patients on HAI prevention.



AMR in a One Health approach

Dr. Jean-Yves Madec from ANSES, France, explained that AMR *Enterobacteriaceae* are currently a threatening One Health issue that affects more than one billion people worldwide. The proportion of ESBL carriage has increased everywhere across the globe. Colonization rates in American and European communities range from 2 to 4%, whereas those in the eastern Mediterranean and Southeast Asia reach 50% and 70%, respectively. AMR transfer through food is a One Health issue of major concern, with numerous examples. A high prevalence of ESBL *E. coli* has been reported in cattle, in milk, and in water sources in Lebanon. They have been detected in mussels and other seafood in markets in Tunisia. Food sold by vendors in Algeria has also been reported to contain ESBL-positive *K. pneumoniae*.

AMR plasmids have been recognized as important vectors of AMR. A huge diversity of AMR plasmids has been reported in food reservoirs that include both food-producing animals and food products. These AMR plasmids confer resistances to major antibiotics, such as extended-spectrum cephalosporins, carbapenems, or colistin. These plasmids are often multidrug-resistant and their dissemination can be driven by the selective pressure exerted by any of the antibiotics concerned. Also, AMR plasmids carry numerous other genes conferring vital properties to the bacterial cell, and can evolve to generate hybrid plasmids, thus making the epidemiological patterns of AMR plasmids in food a moving picture.

In a One Health perspective, it is urgent to limit the spread AMR by reconsidering the massive use of antibiotics worldwide

ESBL *E. coli* surveillance in Madagascar: a One Health approach

Prof. Luc Hervé Samison from the Center of Infectiology Charles Mérieux, Madagascar, spoke about one of WHO's research projects on antimicrobial resistance called Tricycle, which aims to advance standardized AMR surveillance worldwide. ESBL *E. coli* is one of the eight human pathogens posing the greatest threats to public health.

Our current study was designed to assess the prevalence of ESBL *E. coli* in three sectors, human, animal, and the environment, and collect demographic data on antibiotic consumption in Madagascar. The human aspect of this study consisted in fecal sampling from hospitalized patients and pregnant women in the community. From these samples, isolated microorganisms were tested on antibiotic resistance by standard procedures of culture and antibiotic susceptibility testing in seven different laboratories. The results revealed that 39% of pregnant women were carriers of ESBL *E. coli*. As for the food chain aspect of the study, samples from chicken ceca from poultry bought at local markets were tested, revealing that the prevalence of ESBL *E. coli* in the chickens was about 56%. As for ESBL *E. coli* in the natural environment, water samples were taken from a river at several upstream and downstream sites. Colony-forming units of ESBL *E. coli* were more concentrated in downstream, waste, and slaughterhouse waters.

Recognizing that AMR is a major public health threat today, we conclude that the results from our study confirm that AMR is widespread in Madagascar and that resistance control should be the target of concerted action.



Role of vaccines in the fight against antimicrobial resistance in Lebanon

Dr. Randa Hamadeh from the Lebanese Ministry of Public Health reported that AMR infections account for the death of over 700,000 people each year in the world, more than those caused by tetanus, cholera, and measles combined.

In May 2015, the World Health Assembly of WHO adopted a global action plan on AMR with five main objectives: 1) to improve awareness of AMR through effective communication, education, and training, 2) to strengthen knowledge through surveillance and research, 3) to reduce the incidence of infection through sanitation, hygiene, and infection prevention measures, 4) to optimize the use of antibiotics, and 5) to develop the economic case for sustainable investment in new medicines, diagnostic tools, and vaccines.

The Lebanese Expanded Program on Immunization provides free immunization to all children in the 228 public health centers and 600 dispensaries around the country. The WHO-prequalified vaccines for ten communicable diseases are provided for by the Ministry of Public Health. The goal of this program is to reach a vaccination coverage of 98% in each district, to make Lebanon measles- and rubella- free by the year 2020, and to keep Lebanon polio-free. Despite these challenges, Lebanon has maintained a high vaccination coverage over the years. It has managed to remain polio-free for the past 15 years ever since IPV was initially introduced in 2011 in a national polio campaign. OPV, IPV, measles and MMR have been administered at all vaccination centers on border sites and in UNHCR registration centers. The PCV13 vaccine can prevent and reduce incidents of *S. pneumoniae* infections and thus mitigate the overuse of antibiotics leading to AMR.

Challenges still remain. Disease prevention among refugees has been a problem, as well as the poor retention by parents of their children's vaccination history. Also, some parents flatly reject vaccination for their children. At the program level, population counts need to be updated, and human and financial resources need to be coordinated at national and local levels.

INAUGURAL CEREMONY

Chaired by [Dr. Josette Najjar-Pellet](#), Mériex Foundation, Lebanon, in the presence of [Dr. Jamil Jabak](#), His Excellency the Lebanese Minister of Public Health

In her welcome address, **Prof. Marianne Abi Fadel**, Dean of the School of Pharmacy of Saint Joseph University of Beirut, spoke about the valuable exchanges of scientific knowledge taking place between the Mériex Foundation and Saint Joseph University as part of the combat against tuberculosis and other infectious diseases in the world. **Prof. Hubert Endtz**, Scientific Director of the Mériex Foundation, gave homage to Prof. Ogobara Doumbo, the Malian medical researcher who was a former member of the Mériex Foundation's Scientific Committee and who was recognized as an inspirational global leader in malaria research. The Mériex Foundation is committed to strengthening the laboratory capacities and the quality of clinical laboratory platforms in developing countries that are part of national healthcare systems. Enhancing local research capabilities and competencies will be attained by training young researchers and by



developing collaborative research and educational programs. **Prof. Hervé Sabourin**, Middle East Regional Director of the Agence Universitaire de la Francophonie, expressed satisfaction at providing French-speaking scientists a platform, such as the GABRIEL network, to promote scientific research in French in symposia and conferences, and in doctoral meetings and public health initiatives in partnership with institutions of higher education, like the Saint Joseph University. **Prof. Salim Daccache s.j.**, Rector of the Saint Joseph University, spoke of the challenges of bringing answers to these issues. Refugee camps and overpopulated cities are fertile ground for disease outbreaks.

Challenges of conduct medical research in countries in crisis: the example of Haiti

Jean William Pape, MD

Howard and Carol Holtzmann Professor of Clinical Medicine, Center for Global Health, Division of Infectious Diseases, Department of Medicine, Weill Cornell Medical College, New York, New York, USA

Director, The GHESKIO Centers, Port-au-Prince, Haiti

This presentation covered Haiti's multiple multidimensional crises since its independence in 1804 and the measures taken by the GHESKIO Centers to help Haitians overcome the resulting hardships that they have had to endure.

Haiti is the poorest nation of the Western Hemisphere with an economy that has stagnated for the past 30 years while the population has increased by 60%. Five major factors account for the country's persistent poverty:

- First Haiti's deliberate isolation by the major colonialist powers; because Haiti was the first country to break the chains of slavery, it was seen as the bad example and therefore was totally isolated by the major world powers. Up to the present times the country remains isolated by its geographic location, culture and language in a region dominated by Spanish and English influences.
- Haiti's historical external debt is perhaps the most significant blow to the economy. Although Haiti won its independence by defeating the army of Bonaparte, [France](#), with the complicity of its allies, demanded that the newly formed country pay the French government and French slaveholders the modern equivalent of US\$21 billion dollars. This independence debt was financed by French banks and the American [Citibank](#), and finally paid off in 1947.
- The third factor that impacted on the economy is the early and persistent divisions among Haitians that led to the 20-year United States occupation of 1915. After the 29 year of the Duvalier regime (father and son) that ended in 1986, the country had 22 governments including a US embargo that made the country lose US\$ 8 billion dollars, and 3 UN occupations up to the present day (Minijust).



- The fourth factor is the fact that Haiti is the 6th most ecologically fragile country in the world. From 1996 to 2015 the UN conducted a study to identify all natural disasters that occurred in the world and their impact. They identified 7,000 events that resulted in the death of 1.35 million people and 1/6 of all the deaths occurred in Haiti, a country of 11 million. During that 20-year study span, Haiti was subject to numerous hurricanes and floods but it is the 2010 earthquake, the worst in the world in over one century, that accounted for the greatest number of deaths: over 200,000, most in the capital city of Port-au-Prince. This UN evaluation did not take into account Hurricane Matthews in 2016 that ravaged the South of Haiti causing over 1,000 deaths and 6 US\$ billion dollars in damage.
- The fifth factor is the AIDS and cholera epidemics. Haiti had the highest HIV prevalence outside of Africa. For at least 15 years, AIDS was the major killer of adults, especially striking those in the workforce. The cholera epidemic started in 2010, the same year as the earthquake. As it was the country's first cholera attack, those affected had no immunity and it caused at least 10,000 deaths.

GHESKIO's principles are centered on its capacity to address the public health issues affecting the lives of vulnerable populations and on providing, over the long term, the resources needed to develop their capacity to overcome their distress. Free access to care, an ethical approach, and community involvement have been the keystones of its policy from the very start.

In 1980, Dr. Pape returned to Haiti to conduct research on the causes of infantile diarrhea, the major killer of children in Haiti and other developed countries. He introduced at the State university hospital the treatment by oral rehydration and the proper evaluation and monitoring of dehydrated children. The mortality rate dropped rapidly from over 40% to less than 1%. In 1982, a national program to control infantile diarrhea was created by the Ministry of Health with Pape's unit as the national training center. Over 14,000 health care workers were trained as well as over 155,000 parents. Each of the country's 10 department had a Diarrhea Treatment Center. As a result, the national infantile mortality dropped steadily from 144/1,000 in 1982 to 57/1,000 in 2008.

As Pape was perceived as an expert in diarrheal diseases he was asked to consult on adult patients with diarrhea admitted to the same hospital. They turned out to be the first AIDS cases. At the time the term AIDS did not exist. Patients presented with Kaposi's sarcoma or opportunistic infections. Hence the GHESKIO's French acronym that stands for Haitian Study Group on Kaposi's sarcoma and opportunistic infections.

In 1982, the GHESKIO Centers were founded as one of the first institutions in the world engaged in the fight against AIDS with a tripartite mission of research, training and patient care. Since its inception, GHESKIO has partnered with the Ministry of Health, Cornell University and the Mérioux Foundation. GHESKIO's mission expanded beyond AIDS to TB, other sexually transmitted infections, cholera and other diarrheal diseases, dengue, chronic diseases (cancer and cardiovascular disease) and global health. GHESKIO has received continuous research support from the US National Institutes of Health (NIH) since 1983 and the Fogarty International Center since 1993. The objective of GHESKIO has been to develop public health models based on successful outcomes of research projects that can be scaled-up at the national level and beyond.



In 1982, GHESKIO met its first challenge: HIV and AIDS. The history of AIDS in Haiti is inseparable to that of GHESKIO. GHESKIO conducted pertinent studies on the definition of the new syndrome, the occurrence of opportunistic infections and their treatment, the modes of transmission of this new infection, its association with tuberculosis and other diseases, the screening of persons at risk. In 1983, the US Centers for Disease Control singled out Haitians as a risk factor for AIDS, known as the “4 H disease”, for homosexuals, heroin addicts, hemophiliacs and Haitians. This impacted negatively the economy as it destroyed tourism and affected Haitian export products. It also led to widespread discrimination and stigmatization of all Haitians. GHESKIO conducted studies that showed that Haitians had the same risk factors as Americans. In 1986 when AIDS was spread all over the world and the damage was already done, the CDC removed Haitians from the risk group for AIDS. GHESKIO published excellent outcomes of 1,000 patients placed on HAART in 1993 with follow-up at 1, 5 and 10 years comparable to patients treated in the USA. A GHESKIO NIH-sponsored clinical trial (CIPRA) provided data to start ART treatment early as patients who started at the WHO CD4 counts of <math><200/\text{mm}^3</math> had 4 times more TB and deaths. Another GHESKIO study showed that starting ART the same day a patient tested positive for HIV was beneficial leading the WHO to adapt this test and treat strategy. GHESKIO showed that HIV-infected patients were ten times more likely to develop active TB and that prophylaxis with isoniazid can prevent the occurrence of TB. This is one of the most cost-effective strategies for AIDS control. GHESKIO developed new models for the treatment of multiple drug resistant TB with excellent results. GHESKIO introduced new algorithms to treat patients with STI that have been used at the national level. GHESKIO also tackled the problem of congenital syphilis, and through monitoring, rapid testing, and a prevention program, it has successfully reduced the number of cases in the country. Children are particularly vulnerable when infected by HIV. GHESKIO showed that a strategy using a mother’s club method where women discuss best ways to keep their child healthy, and plum peanuts can reverse the course of stunting and wasting.

In 2010, the severe earthquake that shook Port-au-Prince shattered the lives of over 2 million persons, the economy was ruined, city buildings collapsed, and public access to health care, to food and water, and social services was left in disarray. Homeless refugees set up tent cities in all open spaces as temporary housing that ended up lasting much longer than planned. In the face of this dire situation, GHESKIO rose to the challenge. Hospital care was provided to the injured, vaccination campaigns were launched as preventive measures against disease outbreaks, committees were set up for coordination in the refugee camps, access to fresh water was made available, GHESKIO staff personnel were sent into the camps to survey the population and check the spread of communicable diseases, etc.

Also, in 2010, a cholera epidemic broke out in the slums, presumably originating from an infection transmitted by UN staff. GHESKIO immediately took action, set up a treatment center and a sanitary station with chlorinated water, provided educational sessions to the population to explain disease prevention, and set up an anti-cholera vaccination program, that contributed to quelling the outbreak.

In the last ten years, tremendous progress has been achieved in reducing mortality caused by HIV/AIDS. With hundreds of publications in peer-reviewed journals, conclusions and recommendations from research at GHESKIO have influenced global guidelines, including WHO



guidelines on when to start antiretroviral therapy in low-income settings. Despite providing clinical care only in Haiti, GHESKIO's reach is definitively global. There are over 100,000 patients on ART in Haiti and about one third are treated in the GHESKIO network making this institution one of the largest treatment centers for AIDS in the Americas. With almost 3,000 new TB patients treated per year, it is also one of the largest TB treatment centers in the region. GHESKIO is also the largest postgraduate training center for health professionals. Since 1992, GHESKIO has provided training to approximately 4,000 physicians, 6,000 nurses and nurse's assistants, 2,000 laboratory technicians, and 1,500 social workers. The number of community health workers trained is over 450,000. GHESKIO established the nation's first Masters in Public Health program and Nurse Practitioner programs in Haiti. For 2 decades, HIV/AIDS was the first cause of mortality in Haiti. It is now the 7th cause of death accounting for 5.5% of all deaths. The national HIV prevalence decreased from 6.2% to 2.0%. Adolescents, sex workers and MSMs are the main AIDS challenges.

Cardiovascular disease is now the first cause of mortality in Haiti accounting for 28% of all deaths. To meet this new challenge, in 2018, GHESKIO opened a cardiovascular center to treat and care for patients diagnosed with or at risk for cardiovascular disease (CVD), at no cost to patients.

GHESKIO can attribute its successes to many factors:

- efficient teamwork,
- support from national and international partners,
- a wide range of services in research, education, and health care,
- synergy with the community and local institutions,
- participation in international research projects,
- macro- and micro-contingency planning,
- internal growth of its structures and facilities,
- investment in laboratory capacities,
- data collection,
- ethical principles.

In summary, to operate successfully in a country subject to recurrent crises, a health institution should be able to:

- define the country's public health problems,
- be credible,
- operate beyond the reach of political factions,
- get the local community involved,
- garner the support of local (and international) institutions,
- be based on ethical principles,
- formulate a plan for at least the next five years,
- offer course in health care to patients,
- allow volunteer work and input from patients,
- have strong leadership that sets the example,
- manage issues from both a broad and a narrow scale,
- plan ahead,
- review and seek to improve action plans after each crisis resolution,
- allow staff to gain greater expertise and set the stage for a new generation of dedicated and qualified staff.



SESSION II – Pneumonia and Vulnerable Populations

Chaired by Dr. Firdausi Qadri, Bangladesh, and Prof. Hubert Endtz, France

***Streptococcus pneumoniae* in Lebanon: what has been published in the 21st century**

Dr. Rima Moghnieh from the Lebanese Society for Infectious Diseases and Clinical Microbiology presented a literature review of published articles from Lebanon on *S. pneumoniae*, describing the country's pneumococcal disease burden and mortality with graphs indicating:

- clinical presentation of the disease,
- the serotype distribution of the bacterium,
- its antibiotic susceptibility,
- molecular mechanisms of antibiotic resistance,
- effects of comorbidities on mortality,
- the invasiveness of infections,
- vaccination eligibility and status and WHO/CDC recommendations.

This literature review was carried out selectively, taking into account inclusion criteria - articles mentioning *S. pneumoniae* in Lebanon - and exclusion criteria - articles with no mention of data on clinical presentation, epidemiology, vaccines/serotypes, ABX susceptibility, or molecular mechanisms of resistance.

This study has provided an overall picture of the epidemiological profile of the pneumococcus in Lebanon. *S. pneumoniae* imposes a substantial morbidity burden in Lebanon. Its susceptibility to penicillin should be interpreted with caution, because around 15% of pneumococcal infections are resistant to penicillin. Resistance to macrolides is around 45%, and to quinolones is very low (1-2%), however, MDR strains are appearing. The adult vaccination program is presently suboptimal.

Investigating Pneumonia Etiology Among Refugees and the Lebanese population (PEARL)

Dr. Thomas Kesteman from the Mérieux Foundation, Lebanon, presented the PEARL project, the main objective of which was to estimate the proportion of community-acquired pneumonia attributable to specific viral and bacterial pathogens in the refugee and resident populations of Lebanon.

This multicenter prospective case-control study determined the attributable fraction of each causative microorganism according to the age of the individuals, the years of incidence, and the severity of the cases. Individuals from all age groups with lower respiratory tract infection (LRTI) meeting the inclusion criteria have been recruited at four primary health care centers. Biological testing was carried out on samples from nasopharyngeal swabs, blood, sputum and urine.



The results reveal that viruses account for 81% of LRTI (top 5 pathogens: influenza, RSV, rhinovirus, parainfluenza, coronavirus), that 43% of pathogens were vaccine preventable, and that 9% of LRTI were attributable to atypical bacteria. Antibiotic treatment poorly matched the susceptibility profile of etiological agents, especially atypical bacteria.

This study should lead to steps that can be undertaken to reduce the morbidity of LRTI and guide health interventions targeting Syrian refugees, such as immunization campaigns or adapted treatment guidelines.

Transcriptomics to distinguish viral and bacterial infection: preliminary results

Dr. Asuncion Mejias from the Nationwide Children's Hospital, USA, began her talk by highlighting the challenges in pediatric pneumonia. One of the main problems that pediatricians face in children with community-acquired pneumonia, is the identification of the etiologic agent (virus or bacteria) causing the disease at least 30% of children. So, when do we start antibiotic treatment?

The need to start prompt antimicrobial therapy to control a mild infection before it progresses to a more severe form must be balanced with a wise use of antibiotics. In addition, the identification of the infectious agent often remains inadequate, especially when the microorganism is not present in the blood or any other accessible tissue or when detection by molecular techniques may not be sensitive enough to differentiate between infection or colonization. To this end, the analysis of the host response can be used as an alternative approach to identify the causative agent of pneumonia and to differentiate between viral and bacterial infections, potentially helping in the management of pediatric pneumonia. We tested the hypothesis of whether leukocytes isolated from peripheral blood in pediatric patients with different infections carry unique transcriptional profiles that permit pathogen discrimination and thus patient classification. We set out to determine if this was the case for respiratory viruses confined to the respiratory tract (i.e. not present in the blood), and defined the specific host immune response to different respiratory viral infections including those caused by respiratory syncytial virus (RSV) or rhinovirus. RSV remains the number one cause of pneumonia in children < 5 years of age, in both high and low-middle income countries. By analyzing the global host immune response, we identified a molecular score in infants with RSV lower respiratory tract infection that significantly correlated with acute clinical disease severity and predicted duration of hospitalization. This was the first evidence that gene expression patterns analyzed in blood leukocytes can be tied to RSV disease severity. This tool has the potential to help classifying patients according to disease severity in the clinical setting and possibly predict outcomes, including response to therapy. In conclusion, host responses can be measured and are specific according to the infecting pathogen. Transcriptomics is a promising technology to improve the diagnosis and the assessment of disease severity in pediatric pneumonia.



SESSION III – Tuberculosis and Humanitarian Crisis

Chaired by Dr. Hiam Yaacoub, Lebanon, and Dr. Nestani Tukvadze, Georgia

Tuberculosis: which role for a BSL3 in the Middle East?

Prof. Hechmi Louzir from the Pasteur Institute of Tunisia (IPT) began his speech with a description of the IPT's public health activities in Tunisia and its role as the Regional Training Center for the Eastern Mediterranean as well its role within the Pasteur International Network. The IPT also spearheads a wide variety of research projects through international multilateral or bilateral cooperation programs with the support of many funding agency, including EU, NIH, and WHO and other institutional partners.

One of the research projects on tuberculosis in Tunisia is currently attempting to decipher the molecular basis underlying the relative success of Haarlem and LAM genotypes of *M. tuberculosis* and is targeting the human FOXO3 transcription factor as a way to enhance BCG efficacy and potentiate the chemotherapy of TB. This is being achieved with cellular models to assess the role of FOXO3 on the macrophage response to mycobacterial infections.

The recent construction of a high-security BSL3 laboratory will significantly contribute to strengthening the research capabilities and diagnosis of TB, not only for the benefit of the IPT, but also in other laboratories. This essential need was filled with the generous support of the Mérieux Foundation.

Nationwide survey of anti-tuberculosis drug resistance in Lebanon (June 2016 – Nov. 2017)

Prof. Monzer Hamze from the Faculty of Public Health of the Lebanese University described the global tuberculosis epidemic that, with 10 million new cases in 2017, affects one-fourth of the world's population. In Lebanon, the risk of tuberculosis is 20 times greater than in the general population due to the effects of malnutrition and discontinuity of health services. The non-national Lebanese population is being increasingly affected.

The laboratory's current investigation on TB involves setting up and running a system for a Lebanon-wide sample collection program over a period of 18 months to determine the annual prevalence of TB with conventional and molecular tools. This procedure includes evaluating the prevalence of drug resistance in Lebanon with the use of Deeplex-MycTB and comparing the results with routine diagnostic tools. Another facet of the study is to determine the prevalence of *M. bovis* compared to *M. tuberculosis* complex, and evaluate the level of genetic diversity and molecular clustering of MTBC isolates.

The study resulted in a distribution map of bacteriologically confirmed TB cases in Lebanon and in a measure of mono- and poly-drug resistance rates.

Deeplex-MycTB, complemented by MIRU-VNTR typing, is used to detect *M. bovis* and to determine the prevalence of *M. bovis*-induced zoonotic TB in Lebanon.



Although the prevalence of rifampicin-resistant TB in Lebanon is relatively low (2.8%), this study reported for the first time the emergence of XDR-TB cases, some occurring among refugees and migrant workers. FQ resistance was tested in MDR cases (resistance to RIF and INH) and was shown to occur in 10% of non-MDR TB cases. The prevalence of zoonotic TB is not negligible in Lebanon.

Management of tuberculosis in a crisis context: the case of Haiti

Jean William Pape, MD

Howard and Carol Holtzmann Professor of Clinical Medicine, Center for Global Health, Division of Infectious Diseases, Department of Medicine, Weill Cornell Medical College, New York, New York, USA

Director, The GHESKIO Centers, Port-au-Prince, Haiti

This presentation described the crisis factors between 1979 and 2019 that have favored the spread of tuberculosis in Haiti.

In any country the following conditions favor the spread of TB: the inherent breakdown of the public health system, the poor management of prisons, natural disasters (major earthquakes/hurricanes) with capacity to disrupt public services and TB drugs' availability, overcrowding conditions, states of immunodeficiency associated with HIV, general poverty and malnutrition and food shortages. The immunodeficiency status of slum-dwellers is exacerbated by protein-energy malnutrition that compromises cell-mediated immunity and increases their susceptibility to more severe infections. The risk for TB increases 4- to 10-fold with a HIV/AIDS co-infection and is impacted by diabetes and CVD. All the TB-favoring conditions described above apply to Haiti.

After the earthquake, the spread of TB was favored by the pre-existing high background incidence of TB in the population. In Port-au-Prince, with 50% of all TB cases, hospitals and TB centers left in ruins, many TB patients were stranded without any access to medication. Prisons were damaged allowing TB-infected prisoners to escape. Most of those prisoners took refuge in "tent cities". Moreover, the risk for active TB increased for the thousands of slum-dwellers with malnutrition now living in overcrowding conditions in poorly ventilated tents. This was first noticed in Haiti by a fourfold increase in pediatric TB cases at the GHESKIO Centers.

The best way to control TB in crisis conditions is to put all the efforts to cut the chain of transmission. At the GHESKIO Centers, to control the chain of transmission we focus on early TB diagnosis and treatment (test and treat) and the active search of TB cases. GHESKIO has achieved a high treatment success rate of over 85%. Early prevention of TB by isoniazid prophylaxis is also important for people who are at high risk for TB and HIV. HIV-infected patients without active TB should be rapidly placed on HAART. In times of crisis, all potential active TB cases must be identified early (all those presenting with chronic cough) and isolated for rapid screening and treatment if needed. For us, the same-day diagnosis and treatment for TB has been a major contributing factor in successfully managing the disease.



All institutions must have a contingency plan for crisis. The contingency plan is built around the set-up of emergency medical teams, the availability of medications and lab reagents at all times, adequate vehicle transport, power generators, fuel, and power inverters with batteries. A policy for medications must be devised to channel supplies effectively.

At GHIESKO, experience has proven that to control TB in times of crisis, it is imperative to seek potential active TB cases, quickly isolate TB suspects, to diagnose them promptly and provide treatment as early as possible, and to prevent latent-TB patients from developing active TB. To achieve this, diagnostic methods, including radiology, microscopy, Xpert RIF, and mycobacterial culture, are used. Most importantly, it is important to develop a contingency plan that must be revised and improved each time large-scale natural disasters strike.

From diagnosis to the strengthening of the National TB Program: LRM expertise for better and rapid treatment strategies

Dr. Marianne Antar is the manager of the Rodolphe Mérieux Laboratory (RML) affiliated with the School of Pharmacy of the Saint Joseph University of Beirut. It was nominated National Tuberculosis Reference Laboratory in Lebanon, in accordance with the National Strategic Plan for eradication of tuberculosis.

Lebanon is a low TB-burden country with an estimated incidence rate of 12/100,000 and an estimated mortality rate of 0,95/100,000 in 2017. However, it is at amplified risk of increasing burden of tuberculosis due to the massive influx of Syrian refugees since 2012 and imported workforce over the past 11 years. Drug-resistant TB in 2018 has been estimated at 0.45% among new TB cases and 14.3% among previously treated TB cases.

The Rodolphe Mérieux Laboratory has a BSL-3 facility with biosafety and infrastructure requirements for performing the full range of diagnostic tests related to TB, such as identification of tuberculous and non-tuberculous mycobacteria, phenotypic and genotypic DST for *Mycobacterium tuberculosis*. As for XDR-TB, inactivated DNA patient samples and isolates are shipped to the CNR-MyRMA, Laboratoire de Bactériologie-Hygiène du CHU Pitié-Salpêtrière, in Paris. Deeplex®-Myc TB is performed to test 18 main gene targets associated with first- and second-line drug resistance. Screening for latent tuberculosis infection is performed in the Rodolphe Mérieux Laboratory using the WHO recommended method. The laboratory is currently working on the ISO 15189:2012 accreditation, related to requirements for quality and competence of medical laboratories.



SESSION IV – Infectious Events and Chronic Diseases

Chaired by Dr. Robert Sebbag, France, and Dr. Myrna Germanos, Lebanon

How the HIV/AIDS epidemic has changed the worldwide public health landscape

Dr. Robert Sebbag, a member of Merieux Foundation board, stated that for the first time at the G7, discussions have been held on the topic of global public health at a political level. The gap in health between countries of the North and the South, ravaged by the scourges of tuberculosis, malaria, and HIV (6 million cases in South Africa) point to the dire need of addressing both communicable and chronic health emergencies. Good health and wellbeing are one of the founding 17 Sustainable Development Goals. The private sector is doing its part – the Bill & Melinda Gates Foundation, the Clinton Foundation and many others. HIV's endemic situation in Africa has induced a strong awareness on public health in developing countries. And the 18 neglected tropical diseases listed by WHO, affecting 1.4 billion people, have been the target of high-level agreements designed to combat them, but calls have been made to prioritize diabetes and cardiovascular diseases instead. Mental health conditions, diseases of the nervous system, the stigmatization of epilepsy, etc. have gained greater attention. The heightened awareness of disease and of the quality of life is important, but diagnostics remain inadequate. In its recognition that health is a global issue, the Mériex Foundation is addressing these concerns.

Crosstalk between cardiovascular and infectious: special focus on cholesterol metabolism and PCSK9

Marianne Abi Fadel, Dean of the School of Pharmacy of Saint Joseph University of Beirut, explained that familial hypercholesterolemia (FH) is due to a greater accumulation of low-density lipoprotein cholesterol (LDL-C) leading to atherosclerosis. The frequency of FH is 1/300-1/500, with higher frequencies in some countries like Lebanon. FH can be caused by mutations in four known genes.

In 2003, Abifadel et al. (Nat. Genet. 34:154-156, 2003) discovered that PCSK9 was the third causal gene for autosomal dominant hypercholesterolemia by identifying the first gain-of-function mutations of PCSK9 in families suffering from the disease. The implication of PCSK9 in hypercholesterolemia has shed light on a new protagonist in cholesterol metabolism and cardiovascular diseases. Loss of function mutations in PCSK9 were also implicated in hypocholesterolemia. PCSK9 is now one of the most powerful therapeutic targets in LDL-C lowering. Anti-PCSK9 monoclonal antibodies reduce LDL-C levels by 50-60% and received FDA and European Medicines Agency approvals in 2015 on top of statin therapy.

Studies have also shown that polymorphisms in PCSK9 may influence the course of malaria, since the proliferation and the infectivity of Plasmodium spp. partially depend on host cholesterol. It has been shown that hypocholesterolemia confers protection against malaria by reducing infectivity. In addition, pharmacological inhibition of PCSK9 improves survival and inflammation in murine polymicrobial peritonitis. PCSK9 is a critical regulator of the innate immune response and septic shock outcome. Indeed, it has been demonstrated that PCSK9 loss of function variants are associated with improved survival in septic shock patients and a decrease in inflammatory



cytokine response. Together, these results show that reduced PCSK9 function is associated with increased pathogen lipid clearance, a decreased inflammatory response, and improved septic shock outcome.

HIV infection, antiretroviral therapy and cardiovascular risk: the role of HDL particles

Dr. Petra El Khoury from the Saint Joseph University of Beirut began her talk by explaining the relationship between low density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C) and cardiovascular mortality.

The main anti-atherogenic function of HDL lies in the reverse cholesterol transport pathway. In the initial step, HDL particles stimulate the exit of cholesterol from foam macrophages in a process known as cholesterol efflux. Then, HDL particles transport cholesterol back to the liver for elimination. The capacity of HDL to remove cholesterol from macrophages is inversely associated with the severity of coronary artery disease.

Coronary heart disease rates are expected to be higher as the human immunodeficiency virus (HIV) population ages. Highly active antiretroviral therapy (HAART) has been associated with the occurrence of cardiovascular events in HIV-infected patients. However, endothelial dysfunction, immune activation, inflammation, and alterations in plasma lipids are dynamic features of both untreated HIV infection and atherosclerosis.

We evaluated in a large population, the effects of HIV infection, in the absence of antiretroviral therapy, on the capacity of plasma or isolated HDL particles to mediate cholesterol efflux from human macrophages and from various cellular models, each representative of one specific efflux pathway. Then we assessed the impact of the HAART regimen on HDL functionality. Untreated HIV-infected subjects, uninfected controls and a subset of HIV subjects receiving HAART were enrolled in this study. Plasma cholesterol efflux capacity was reduced in HIV patients as compared with controls. HIV infection reduced the capacity of HDL subfractions to promote cholesterol efflux from macrophages. We observed a reduced ABCA1-dependent efflux capacity of plasma from HIV-infected subjects. HAART administration restored the capacity of plasma from HIV patients to stimulate cholesterol efflux from human macrophages. Both intracellular and extracellular mechanisms of HIV interact together and favor the progression of atherosclerosis. During HIV infection, the capacity of whole plasma to remove cholesterol from macrophages is reduced, thus potentially contributing to the increased coronary heart disease in the HIV population.

HAART restores HDL-mediated cholesterol efflux from macrophages either directly by acting on its metabolism or indirectly by suppressing viral charge and thus eliminating HIV adverse effects on HDL functionality. We thus propose that the overall increase in cardiovascular risk in HIV-infected patients receiving HAART appears not to be associated with an alteration of the capacity of HDL particles to stimulate macrophage cholesterol efflux.



10th INTERNATIONAL GABRIEL MEETING

GABRIEL NETWORK UPDATE

Dr. Florence Komurian-Pradel from the Mérioux Foundation presented an update on GABRIEL membership applications. At present, 20 laboratories located in the Americas, Asia, Europe, and Africa are members of GABRIEL. Three other laboratories have expressed an interest in membership: the Tropical Medicine Institute of São Paulo, University of São Paulo, the Rodolphe Mérioux Laboratory in Rio Branco, Brazil, and the Pasteur Institute of Madagascar.

GABRIEL's ongoing research projects in the field of acute respiratory infections include studies on an ARI surveillance, pneumococcus epidemiology, ARI etiology among Rohingya refugees, and the discovery of new animal viruses.

As for tuberculosis, investigations are currently being conducted in France on the intra-host diversity and evolution of *Mtb*, on the molecular typing of circulating TB in Laos, on the transmission of drug-resistant TB in Georgia, and on biomarker research for improved efficacy of TB treatment (Bangladesh, Lebanon, Paraguay, Madagascar, Georgia, France). Community-based interventions on latent TB are being conducted in Cameroon and Madagascar, and biomarkers for the diagnosis and monitoring of treatment efficacy of leprosy in Madagascar. Antimicrobial resistance is another important research topic, as is typhoid diagnosis and the measure of disease burden in Africa.

New, in 2019, is the GABRIEL network's call for proposals, which aims to stimulate collaborative research with a focus on ARI, tuberculosis, and antimicrobial resistance.

The network's second main activity consists of strengthening the research capacity of laboratories through tutorial training, workshops, and e-learning modules, the most recent being devoted to biobanking.

The GABRIEL network is grateful to the various NGOs and private companies who provide their continuing support for the successful completion of these various undertakings.

SESSION I – Tuberculosis

Chaired by Dr. Sayera Banu, Bangladesh, and Dr. Juliet Bryant, France

Discovery of new biomarkers

Dr. Virginie Rozot from the South African Tuberculosis Vaccine Initiative discussed the importance of understanding latency spectrum from incipient, subclinical to active forms of tuberculosis (TB) on diagnostic strategies. The progression to TB is associated with sequential immune modulations that can be measured by following changes in blood transcriptomic signatures. These signatures can reveal incipient and subclinical TB far before the onset of disease and thus predict if a person is at risk of developing TB. Transcriptomic (and proteomic) risk signatures mostly detect inflammatory signals during disease progression.



To reach a point-of care level test, these signatures need to contain the least number of variables to improve cost effectiveness and implementation strategies. Application of these prognostic signatures to follow-up of treatment efficiency also shown positive results.

Prognosis, diagnosis and treatment efficiency signatures must be tested globally in different epidemiological and clinical settings. Prospective clinical validation in unselected populations is critical as well as testing in HIV+ population groups.

Advancing tuberculosis biomarker research through multicenter cohort studies in the GABRIEL network

Dr. Jonathan Hoffmann, France, presented the HINTT study, a multicentered evaluation of immunodiagnostic tools for monitoring tuberculosis treatment outcome. Its purpose is to improve TB diagnosis and treatment, and conduct advanced tuberculosis biomarker research. In this study, innovative approaches to diagnostics - HBHA-based IGRA, transcriptomics, proteomics and immunophenotyping – are being evaluated. Paraguay, Georgia, Paraguay, Bangladesh, and Madagascar are the participating countries.

Patients with bacteriologically confirmed tuberculosis received anti-TB treatment over the course of 6 months (for drug-susceptible TB patients) or 9 months (for drug resistant TB patients), after which time they were put under observation for an additional 2 months. Whole-blood samples have been collected, during, at the end of treatment, and during post-treatment and these were tested with QuantiFERON-TB Gold plus and recombinant *M. smegmatis* HBHA. Sputum sample smears have been examined and tested for drug susceptibility.

Dr. Khaja Mafij Uddin, Bangladesh, presented the preliminary results of the study conducted in Bangladesh. Challenges lay in the screening and enrollment of MDR patients and in the difficulty of following up patients after being treated and discharged from the hospital. Some patients were lost or dropped out of the study. The results of the study should provide information on disease interactions, immunology and impact of TB and diabetes in Bangladesh.

Dr. Graciela Russomando, Paraguay, explained that the preliminary results of the HINTT study were affected by the significant number of patients coming from prisons or having been addicted to alcohol or drugs. Data is being collected and prospectively a study on diabetes should also be conducted.

Paolo Ranaivomanana, from the Pasteur Institute in Madagascar, stated that there were 30,000 TB cases in Madagascar in 2017, many of which affecting diabetics, smokers, and alcohol abusers. Yet few have MDR-TB or are coinfecting with HIV. Challenges remain in coping with TB: deficiencies in the healthcare system, poverty and malnutrition of the population, unhealthy air in dwellings, poor diagnostic facilities. Furthermore, patients do not always comply with prescribed treatment. The HINTT TB study is still underway collecting results.



Dr. Nestani Tukvadze, from the National Center for Tuberculosis and Lung Diseases in Georgia, mentioned that in Georgia, treatment outcomes have improved in recent years through a patient-centered approach and with access to new types of treatments. However, Georgia is a high-burden MDR-TB country. Universal access to diagnosis and treatment of MDR- and XDR-TB are now available. The involvement of local NGOs in TB care, and improved access to TB prevention, diagnosis and treatment for hard-to-reach groups at high risk are the approaches being put into place.

Rim Bayaa, from the Lebanese University in collaboration with the University Claude Bernard-Lyon presented the preliminary results from the HINTT study in Lebanon. Although Lebanon is a low tuberculosis-burden country, the number of TB cases among migrant workers and Syrian refugees has been increasing.

From July 2018 until June 2019, only 50 confirmed TB cases were found, of which 21 having extra-pulmonary TB were excluded from our study. Of those remaining, two were excluded for diabetes, two for HIV and 16 for other reasons. We first compared the concentration of IFN-gamma secreted by T cells separately stimulated by TB1 and TB2 antigens at different time points. Not one drug-resistant TB case was detected.

Prospectively, additional TB patients should be enrolled for subsequent in-depth analyses with mass cytometry, Luminex, proteomics, transcriptomics for the identification of biomarkers that can be used to monitor treatment efficacy. From July 2018 till June 2019, only 50 confirmed TB cases were found, of which 21 having extra-pulmonary TB were excluded from our study. Of those remaining, two were excluded for diabetes, two for HIV and 16 for other reasons. We first compared the concentration of IFN-gamma secreted by T cells separately stimulated by TB1 and TB2 antigens at different time points. Not one drug-resistant TB case was detected.

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Exploring the immune landscape of tuberculosis patients to TB treatment

Carole Chedid from the Mérieux Foundation, France, spoke about the challenge of TB monitoring. Current methods are limited to microbiological techniques – microscopy and culture – and clinical assessment. There is a critical need for more specialized methods. One is high-dimension analysis using cytometry by time of flight (CyTOF): a classical cytometry injection system coupled with a mass spectrometry detection system (in lieu of fluorescence).

Testing involves whole blood sampling from patients who have been receiving anti-TB treatment from 6 to 22 months. White blood cells are extracted and shipped to Lyon for analysis. Cytometric immune modulations can be visualized over the duration of treatment with viSNE (visual Stochastic Network Embedding). This procedure provides a first overview of the abundance of the variations occurring during treatment. Also, different clusters (cell populations sharing a similar phenotype) can be observed varying during treatment. The result is superior in depth and data analysis performance to manual gating.



Further studies will be conducted to compare data obtained with that of healthy donors and latent-TB participants. Data from TB-antigen-stimulated cells and non-T cell populations should also be analyzed. Finally, findings will require validation with functional assays/*in vitro* modelling.

Cytometry can therefore help explore immune variations that will lead to identifying specific TB-associated cell populations that respond during treatment. Further work is needed to identify biomarkers (secreted molecules, circulating cell populations, etc.) usable in simpler, cost-effective experiments.

Management of latent TB infections within the community: a new research study within the GABRIEL network

Dr. Sara Eyangoh from the Centre Pasteur, Cameroon, explained that latent TB infections pose a real challenge in TB eradication programs. In Madagascar and Cameroon, where high TB incidence rates are reported, the screening of latent TB is not systematically performed.

The APRECIT project, “Evaluation de stratégies pour **Améliorer le dépistage et la PRise En Charge globale de l’Infection Tuberculeuse Latente au Cameroun et à Madagascar**”, is a multicenter project involving selected hospitals in Cameroon and Madagascar and designed to seek improved screening, treatment, and prevention of TB. In Cameroon and Madagascar, household primary contacts are the most at risk for contracting TB. The screening of latent TB is not carried out systematically.

Specifically, this project aims at evaluating the diagnostic and prognostic values of IGRA testing compared to IDR test when predicting a TB infection and its progression to active TB. It will also measure the efficacy of preventive treatment and the cost-effectiveness of community interventions. In addition, it will help evaluate the difference between a single-use or a combination of IGRA and/or IDR on intra-residential contacts of index cases of TB. This project should boost the local development of biological sample collection in association with the clinical data and epidemiological profile of subjects when investigating the prognostic value of new biomarkers.

As the project advances, new protocols and guidelines for community intervention will be prepared, along with training modules and other educational material.

SESSION II – AMR/Fever

Chaired by **Dr. Jean-Yves Madec, France, and Dr. Florence Komurian-Pradel, France**

Flow of AMR genes between humans, animals, and environment in Bamako, Mali

Dr. Bourèma Kouriba from the Charles Mérieux Center for Infectious Disease of Mali spoke about antimicrobial resistance that has become a global threat to human health. AMR has been especially aggravated in developing countries where antibiotic-control policies and adequate infrastructures are lacking. Multidrug-resistant bacteria have been proliferating in hospitals and more recently in the general population. Presently, AMR is responsible for 700,000 deaths per year, and in 2050 this figure could reach 10 million if no action is taken.



Antibiotics are being overused across the world. In Africa, they are sold illicitly or are overprescribed. In West Africa specifically, ceftriaxone, amoxicillin, amoxicillin-clavulanic acid, ciprofloxacin, and co-trimoxazole are the most commonly used antibiotics, both in hospitals and among outpatients. The struggle against AMR calls for novel tools which only can be found through a deeper understanding of the flow of AMR genes across the community.

Our present investigation, conducted with AMRIWA (a consortium in West Africa bringing together Burkina Faso, Ghana, and Benin) and with Finland, studies the flow of AMR genes in Mali so that the prevalence of AMR and the overuse of antibiotics in health centers in Mali can be examined. Using the One Health approach, environmental, microbiological, sociological, and medical parameters are taken into account to examine the development and the transfer of AMR genes through water, soil, animals, food, and humans.

Bacterial samples from humans, animals, water sources, and soils were tested by Epic PCR, qPCR array analysis, and deep sequencing to come up with heat maps displaying ESBL genes. AMR genes have been detected in virtually all human, environmental, and animal samples. Further studies are underway to study the overuse of antibiotics.

Antimicrobial resistance of bacterial pathogens isolated from patients with diarrhea and urinary tract infection

Dr. Shakeel Ahmed from BITID, Bangladesh, pointed out that antimicrobial resistance (AMR) is a growing global public health threat that is imposing serious consequences on the management of infectious diseases. The unreasonable use of antibiotics is the greatest driver of resistance due to the fact that some 50% of antibiotics are prescribed inappropriately, 50% of patients comply poorly with antibiotic therapy, and 50% of the world's population do not have access to essential antibiotics. In addition, in countries like Bangladesh, antimicrobials are readily available without a prescription or are prescribed by unqualified medical practitioners.

In Bangladesh, the 2016-to-2020 National Action Plan against AMR has been developed with the Institute of Epidemiology, Disease Control and Research. A surveillance system with ten sentinel sites has been set up across the country to monitor AMR so that appropriate remedial action can be taken. Specifically, this will be achieved by staffing microbiology laboratories with technicians skilled in performing standard bacterial culture and sensitivity testing, periodically developing antibiograms reflecting observed sensitivity patterns, devising and updating the Standard Treatment Guidelines of infectious diseases, and ensuring that good laboratory practices are implemented in microbiology laboratories to the extent that accreditation can be received.

Samples were taken from five clinical specimens: stool, urine, blood, sputum, swab/pus from wounds. Bacterial isolates were identified and tested for antibiotic susceptibility.

The results have been compiled according to type of sample, type of infection, age of the patient, distribution of enterobacteria and urinary tract pathogens, and resistance patterns to specific antibiotics. These findings will be useful to determine the action plan to be undertaken in the fight against AMR.



Next-Generation Sequencing application for AMR

Emilie Westeel from the Mérieux Foundation, France, explained that Next-Generation Sequencing (NGS) technologies are expected to play a crucial role in the surveillance of infectious diseases, since they can characterize genetic information underlying the virulence and antimicrobial resistance bacterial (AMR) properties. Due to growing AMR threats, monitoring the rise and spread of AMR organisms has become imperative. The accurate and rapid determination of antimicrobial resistance is crucial not only for the treatment of infections, but also for minimizing the risk of antibiotic abuse.

The objectives of our study were to investigate the genotypic diversity and AMR phenotypes of well-characterized *S. typhi* isolates from Bangladesh. In addition, the location of the resistance genes was identified and the phylogenetic relationships among the isolates examined and compared with those found in Nepal and Pakistan.

From our analyses, we indeed detected genotypic resistance patterns that matched laboratory-confirmed phenotypes for most *S. typhi* isolates. We also determined that the gene sequence and the genotype of the ceftriaxone-resistant isolate in Bangladesh was different from XDR isolates in Pakistan, possibly indicating independent origins. Resistance genes were described as being carried by plasmids, but also by genomic islands directly integrated in the chromosome.

The emergence and spread of XDR *S. typhi* strains reconfirm the necessity for preventive measures to control typhoid fever. Meanwhile, vaccine interventions are needed over the short term, and safe water and sanitation programs over the long term.

We also used NGS technology to study AMR *M. tuberculosis*, as it delivers a complete data set on genetic material in a sample more quickly and more cost-effectively than ever before.

The sequencing of genomes, and the plasmids they host, provide a view of the potential of antimicrobial activities in one single experiment. It is with this type of rapid detection and faster responses to outbreaks and emerging resistance, that we can contain and control the spread of AMR.

Funding landscape

Dr. Leticia Lobo from the Mérieux Foundation, France, said that several initiatives are underway in the fight against AMR: WHO's Global Action Plan against Bacterial Resistance, and the Global Antimicrobial Resistance Surveillance System, the European One Health Action Plan against bacterial resistance, the African Antimicrobial Resistance Surveillance Network, as well as other worldwide country-related initiatives.

The Joint Programming Initiative on Anti-microbial Resistance (JPIAMR) is a global collaborative platform engaging 27 nations to curb AMR through a One Health approach. The initiative coordinates national funding to support transnational research and activities within the six priority areas of the shared JPIAMR Strategic Research and Innovation Agenda – therapeutics, diagnostics, surveillance, transmission, environment, and interventions. The JPIAMR AMR R&D



investments dashboard is an interactive tool for exploring public investments in AMR research. Its users can consult national competitive grant data by agency, country, AMR research topics, and individual research projects.

Another resource is the World RePORT, an open-access, interactive mapping database project highlighting biomedical research investments and partnerships from some of the world's largest funding organizations, depicting both the organization funding the study, as well as the recipient.

The U.S. government's AMR Challenge is a yearlong effort to accelerate the fight against AMR across the globe. It is a way for governments, private companies, and non-governmental organizations worldwide to make formal commitments in the fight against antimicrobial resistance. Through its One Health approach, launched at the UN General Assembly in September 2018, the health of people has been recognized to be connected to animal health and environmental safety.

Current and recent opportunities for funding research on antimicrobial resistance and antimicrobial use include the Fleming Fund Grants (fellowships and mentoring). Major presently open call for proposals are from European funding: H2020 framework (Health, demographic change and wellbeing) and EDCTP, which funds research for prevention and treatment of poverty-related infectious diseases in sub-Saharan Africa.

SESSION III - Young Scientist Award Presentation

Chaired by Ana Tereza R. de Vasconcelos, Brazil, and Monidarin Chou, Cambodia, and headed by the Scientific Award Committee

Healthy carriage of resistance to colistin, extended-spectrum beta-lactamases and carbapenem in Lebanese workers

Ms. Hiba Al Mir from the Lebanese University and the University of Lyon presented her research on antimicrobial resistance (AMR). AMR is not confined to clinical settings, but has also extended into the community. Animals, as well as environment and foodstuffs, are potent reservoirs of AMR in Lebanon. And they are generally considered as a reservoir of MDR and XDR bacteria, particularly *Enterobacteriaceae*. A high number of studies have targeted the AMR crisis in Lebanon, as in other developing countries especially in clinical settings.

Extended-spectrum beta-lactamase (ESBL)- and carbapenemase-producing bacilli have been reported in humans in this country, but none are resistant to colistin mediated by *mcr-1* gene. Moreover, none of the conducted studies to date have described extra-hospital settings of human fecal carriage of resistant strains in the food sector.

We performed a longitudinal prospective study in Northern Lebanon to determine the prevalence of extended-spectrum cephalosporin-, carbapenem- and colistin-resistant bacteria in healthy workers in the food sector. We also wanted to characterize and genotype the resistance of these strains and determine the genetic supports involved.



Fecal samples were collected, resistant bacteria were isolated and tested for antibiotic susceptibility testing followed by molecular characterization of the bacterial clones and plasmids.

Our results are alarming in that they show a high carriage-prevalence of third-generation cephalosporin-resistance among healthy workers in the food sector in Lebanon. Carbapenem- and colistin-resistance were found in different individuals but prevalence rates were much lower than for ESBL carriage. We also reported for the first time the emergence of *mcr-1*-positive *Enterobacteriaceae* fecal carriage among healthy humans in Lebanon.

We hope that our findings highlight the national necessity to reevaluate effective antimicrobial stewardship, enhance national surveillance systems with harmonized global standards and promote public awareness programs in order to limit the spread of AMR in Lebanon.

Antibiotic resistance spectrum and detection of genes associated with resistance of aminoglycosides, macrolides and β -lactam groups of antibiotics in the clinical isolates of patients with ARI, typhoid, diarrheal, and wound infections

Dr. Golam Sarower Bhuyan from ideSHi, Bangladesh talked about the global crisis of antibiotic resistance and the absolute need for collecting data on the degree of prevalence, the distribution, and the impact of antibiotic-resistant microorganisms.

The aim of this investigation was to determine the resistance pattern of clinical isolates at three sites in Bangladesh, taken from samples of patients suffering from acute respiratory infections, enteric fever, wound Infections, or diarrheal disease. On these samples, the pathogenic organisms were isolated and their antibiotic sensitivity pattern was determined using disc diffusion method. Then molecular characterization of aminoglycosides was carried out, as well as the identification of extended spectrum of β -lactamase (ESBL) bacteria and macrolide-resistance genes in the isolates. This study should lead to a better understanding of the correlation between phenotype and genotype.

From the data obtained, antibiograms were drawn up corresponding to specific bacterial isolates identified and to a spectrum of multidrug resistance patterns. Findings indicate that the proportion of multi-drug resistant pathogens is the greatest in *K. pneumoniae*, *E. coli* and methicillin-resistant *S. aureus*. Nearly all bacteria were resistant to the macrolide group of antibiotics. Higher percentages of resistance genes are harbored by *K. pneumoniae*, *E. coli*, and *Pseudomonas* spp.

With a better understanding of the use of antibiotics and resistance and improved surveillance, the threat of widespread AMR can be contained.

Re-emergence and spread of the measles virus genotype D8 in Brazil, 2018

Dr. Paola Cristina Resende from the Oswaldo Cruz Institute, Brazil, pointed out that measles is a serious public health problem subject to major outbreaks throughout the world. During an infection, characterized by a rash, fever, cough, and runny nose, the measles virus can also trigger complications such as ear infections and diarrhea, and, in more severe cases, pneumonia or encephalitis, leading to permanent brain damage. Measles is preventable with a safe and



effective vaccine and the virus was declared to be eradicated in Brazil in 2000 and in 2016 the Americas received the WHO certification of Measles and Rubella elimination.

The objectives of the investigation were to use a genomic surveillance approach to examine which lineages were responsible for an outbreak that occurred in Brazil 2018-2019. The spread of the virus geographically and over time was also tracked. This was achieved by sequencing the 450N gene region to define the measles genotypes and exclude vaccinated cases, as well as the measles genome to define the lineages in the outbreak. The measles genome sequencing protocol was standardized using the MinION ONT platform.

From the findings obtained, it was possible to draw up an area map of the possible transmission routes of the measles virus in Brazil. This investigation of measles genomic data, a first in South America, should help improve the representativeness of Brazilian measles outbreaks and acquire obtain a better picture of the spread of the virus.

WHO encourages further sequencing of the measles genome so that the progression of further outbreaks can be checked and measles eradication programs can be properly monitored and assessed.

Influenza type A viral infection alters FLT3-L-dependent de novo generation of conventional dendritic cells that contributes to bacterial superinfection

Dr. Ranin Beshara from the Lebanese University spoke about *Myxovirus influenzae*, a ubiquitous, enveloped, single-stranded RNA virus. It mainly causes human upper and lower respiratory tract infections that can be severe in young children and the elderly. Annual epidemics are estimated to cause up to 650,000 deaths yearly.

An influenza A virus infection (IAV) increases susceptibility to secondary bacterial infections due to alterations of mechanical defenses in the function of innate and adaptive immune cells. Myeloid cells are mobilized from the bone marrow to the infected tissues in a process referred to as emergency myelopoiesis. A profound alteration in the pulmonary myeloid cell compartment is characterized by the recruitment of inflammatory myeloid cells. An IAV leads to reduced number of conventional dendritic cells in the lungs and severely impairs their differentiation in the bone marrow (DCpoiesis) for the benefit of monopoiesis. Overexpression of the Flt3-L gene during influenza augments the number of bone marrow dendritic cell progenitors and restores lung dendritic cell compartment. This feature is associated with a lowered number of lung inflammatory monocytes and reduced lung damages. This Flt3-L overexpression also partially protects against secondary pneumococcal infection characterized by reduced bacterial loads, improved pathological outcomes, and prolonged survival. These results provide new clues on the manner an IAV influences the differentiation of dendritic cells, and highlight the potential therapeutic value of Flt3-L in a disease that desperately requires improved treatment.

Future work will involve the study of the underlying mechanisms for decreased Flt3-L production upon IAV infection with questions on the apoptosis of lymphocytes B or of epithelial cells. In addition, underlying mechanisms of Flt3-L should be examined as a way of protecting against pneumonia, perhaps by the activation of neutrophils.



New Flt3-L injection protocols will be examined, as well as the Flt3-L quantification in blood serum from patients with IAV to check whether dendritic cell poiesis is altered. This should lead to a study of the impact of Flt3-L, in combination with GM-CSF or with antibiotics on secondary bacterial infections.

Role of VDR gene variants (Apal and FokI) in asthmatic children: a case-control study

Dr. Nidhi Awasthi, King George's Medical University, India, described bronchial asthma as a major chronic lung disease characterized by symptoms of recurrent attacks of breathlessness and wheezing and affecting 235 million persons worldwide.

The insufficiency of vitamin D is of great importance in the development of bronchial asthma in children. Gene polymorphism related to vitamin D metabolism and functional pathway can cause a lack of vitamin D leading to the onset of asthma. The aim of this study was to explore the correlation of two vitamin D receptor (VDR) gene polymorphisms, rs7975232 and rs2228570 in asthmatic children and controls.

Children aged 5-15 years, diagnosed as asthmatic according to GINA guidelines were selected for this study. Blood was collected, DNA extracted, and genotyping carried out on the specimens. From the gel pictures obtained, the frequency distributions of the rs7975232 and rs2228570 polymorphisms of the VDR gene were observed in the cases and controls.

Genotypic and allelic frequencies of the rs7975232 and rs2228570 polymorphisms were compared in asthma cases and controls. Forced expiratory volume levels were also compared. From the haplotype analysis of VDR gene polymorphisms in asthmatic cases and controls, the presence of the TA haplotype was found to lower the incidence of asthma, while patients having TC haplotype were found more prone towards asthma. Significant association of asthma was found with mutant A allele and heterozygote AC genotype of rs7975232.

To conclude, children with bronchial asthma are often accompanied by different degrees of changes in VDR gene polymorphism, which are negatively correlated with the severity of asthma. The level of vitamin D can result in a change in the disease, and therefore it is useful for properly determining the prognosis in children. A higher vitamin D level can thus guide clinical treatment.



SESSION IV- Acute Respiratory Infections

Chaired by Dr. Valentina Picot, France, and Dr. Jianwei Wang, China

RSV surveillance to prepare policies of RSV immunization

Dr. Fernando Do Couto Motta from the Oswaldo Cruz Institute, Brazil, described the respiratory syncytial virus (RSV) and its clinical impact worldwide. This virus is responsible for 3.4 million hospitalized cases and up to 200,000 deaths per year. In Brazil, RSV research has focused on developing diagnostic methods and on understanding the seasonality of the virus in different geographical regions. Further knowledge on the epidemiological patterns of the RSV is needed to better understand how patients may benefit the most from vaccines or antiviral treatment.

A major obstacle to RSV immunization is the onset of an RSV infection early in life when immune responses are not fully developed.

In 2015, WHO global RSV surveillance goals were devised with a RSV pilot network to:

- identify RSV seasonality in different countries and geographical regions,
- determine age and risk groups for severe RSV disease,
- estimate RSV out-patients, hospitalizations, and deaths,
- provide optimal case definitions for different high-risk age groups,
- standardize laboratory procedures and quality assurance,
- assess the incremental cost of testing RSV surveillance,
- provide evidence to inform global and national policy decisions,
- establish feasibility of the future global expansion of RSV surveillance.

Studies in Brazil have been conducted to determine the seasonality of the virus, its infection by age group and by temperature and precipitation records, and by genotype. Samples were collected in three Brazilian cities, covering distinct climates.

In the results obtained, the greatest percentage of RSV was found in pediatric samples. The correlation between humidity and virus circulation seems different in the NE of Brazil compared to cities in the South and Southeast.

G-gene sequencing analysis showed only one genotype for each RSV group, but within each genotype there was great diversity. Studies on Brazil's elderly population are still needed, as currently, these individuals are underrepresented. Further phylogenetic analyses should be conducted to compare samples from distinct regions.

Sero-epidemiological studies of RSV exposure: assay development

Dr. Marie Moroso from the Mériex Foundation, France, explained that an incomplete understanding of RSV disease and immunity is due to a lack of available large-scale data that is currently available in only a few countries and settings. Despite the major costs expended for health care, the low levels of recognition among government policymakers of this virus's pathogenicity points to the need for large-scale national surveillance systems to guide future



vaccine interventions. But first, further data must be collected on the burden of RSV diseases by age groups and key risk groups, on the geographical distribution of the virus, on seasonality patterns across the world, on viral parameters related to subtypes and genotypes, and on host immune responses. WHO has devised a strategy for global RSV surveillance with an extended SARI-case definition for hospital-based surveillance of severe RSV infections.

For vaccine development, serological assays need to be carried out. Also, the RSV must be tested by PCR, and the antibody response analyzed to measure levels specific to neutralizing antibody responses. Sero-epidemiological data should also improve the understanding of RSV's contribution to neonatal morbidity and mortality, and generate baseline data on RSV prevalence and incidence to inform future vaccine interventions.

Questions still remain on the ways to combine RSV studies with other public health interventions/surveillance platforms and with interactions between RSV severity and malnutrition, prematurity, co-morbidities with HIV/TB or other risk factors.

Comparative pneumococcal carriage investigation: a multicenter study

Dr. Shally Awasthi from King George's Medical University, India, and **Dr. Gabriela Russomando** from the Instituto de Investigaciones en Ciencias de la Salud, Paraguay, each spoke about the multicenter pneumococcal study. The primary objective is to measure pneumococcal colonization rates and predominant circulating serotypes among children and adults in diverse countries undergoing PCV introduction. This is to be achieved by quantifying pneumococcal nasopharyngeal colonization and serotype distribution across different epidemiological contexts in relation to:

- dosing schedule for PCV immunization
- vaccine product (PCV13, PCV-10, SIIIL-PCV10)

In addition, predisposing factors on carriage (e.g. age, family size, antimicrobial usage, infections within the family, primary care/school attendance) are to be assessed. *Pneumococcus* transmission and the impact of vaccine use on nasopharyngeal carriage rates from each country will be modelled in order to evaluate alternative and future immunization strategies (new formulations, different schedules, maternal immunization). Finally, a biorepository of respiratory specimens for use in future research investigations, e.g. evaluations of novel serotyping methods, will be established.

Specifically, in India, the Indian Council of Medical Research is undertaking a task force study on the etiology of childhood pneumonia, whose primary task is to estimate the relative prevalence of selected bacterial and viral pathogens in cases with clinically diagnosed community-acquired severe pneumonia and in healthy controls among children aged 29 to 59 months of age.

In Paraguay, the current project concerns the molecular identification, isolation, serotyping, and antimicrobial susceptibility of *S. pneumoniae* in a nasopharyngeal carriage study on children and adults. The results have yielded data on the vaccination status of children and also on *S. pneumoniae* risk factors and carriage detection by qPCR as a function of their age, home environment; etc. Antibiotic resistant profiles have been drawn up as well.



Acute respiratory infections etiology among displaced Rohingya settled in humanitarian refugee camps in Bangladesh

Dr. Firdausi Qadri from icddr,b, Bangladesh, said that ARIs account for high mortality and morbidity in the crisis-affected Rohingya refugee population. Other infectious diseases, including diarrheal diseases, febrile illnesses, measles/rubella, mumps, and diphtheria are also common in the Rohingya settlements near Cox's Bazar.

The LARI prospective case-control study is designed to estimate the proportion of LARI attributable to specific viral and bacterial pathogens, estimate the fraction of clinical pneumonia attributable to pathogens that are vaccine preventable (vaccines that are current or being developed), detect serotypes of *S. pneumoniae* in nasopharyngeal/nasal swabs and blood specimens, and assess putative risk factors for infection and/or disease. The Randomized Controlled Trial is to evaluate the impact of using a rapid diagnostic POC package on case management compared to routine practice, and to assess the diagnostic performance of a combination of host biomarkers in identifying individuals needing antibiotic treatment.

Rohingya subjects and controls were selected for sampling of blood, serum, sputum, urine, and nasopharyngeal swabbing. These specimens were tested by Triplex PCR and other techniques, and from these test results, a diagnostics algorithm was developed.

Data was collected from NP and blood culture results, from urine antibiotic sensitivity tests, and PCR on swabs and blood specimens.

Clinicians at the study sites are now beginning to prescribe fewer antibiotics based on the C-reactive protein results (in addition to judgement based on clinical presentation, pulse oxymetry and danger signs).

Etiology and risk assessment of community-acquired pneumonia

Dr. Jianwei Wang from the Chinese Academy of Medical Sciences provided an update on the results of the laboratory- and hospital-based longitudinal study on respiratory infections. He reported the prevalence, seasonality, and the risk factors associated with pediatric respiratory infections, particularly those caused by the RSV. He also presented data on the identification of host factors associated with RSV infections. PF4, a host factor, has been discovered to restrict RSV infections and it is a potential predictor of the severity of RSV infections.

Surveillance of severe acute respiratory infections

Dr. Mona Al Buaini from the Rafik Hariri University Hospital, Lebanon, stated that the surveillance of severe acute respiratory infections (SARI) in Lebanon was set up in 2014 in collaboration with WHO. An ongoing case investigation is being carried out at various sentinel sites whose objectives are to estimate the morbidity of SARIs, obtain demographical and clinical data, describe SARI cases by time, place, person, susceptibility, severity, identify circulating influenza strains novel viruses, and contribute to influenza surveillance conducted worldwide.



The results of this study have been shared with regional and global WHO databases. However, further investigation is needed to determine the burden of the diseases, compute incidence rates, and collect data on vaccine coverage and vaccine efficacy.

The SARI surveillance system is meant to identify the current disease patterns and follow epidemiological indicators, so that they can be measured against alert thresholds. A surveillance network should ideally prepare the way for combatting seasonal and/or pandemic influenza by establishing a national preparedness plan. This can be achieved by capacity-building in countries subject to epidemics and by conducting severity assessments that are crucial to alert people.

YOUNG SCIENTIST AWARD CEREMONY

Chaired by Cynthia-Maria Ghobril Andrea and Dr. Hubert Endtz

Sayera Banu, the President of the Scientific Award Committee, presented the GABRIEL Young Scientist Award as an important initiative for the future of science and an incentive for young researchers. Countries throughout the world are in need of talented scientists who should be recognized as the future leaders in the fight against infectious diseases.

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

After careful deliberation, the Scientific Award Committee decided to award the two prizes to:

- Ranin Beshara for her work on the relationship between influenza type A virus and bacterial superinfections,
- Paola Cristina Resende for her research on the measles virus in Brazil.

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



Close of the GABRIEL Meeting



Dr. Salim Daccache s.j., the Rector of the Saint Joseph University of Beirut, stated that the GABRIEL network has become a major player at the university, not only in terms of public health, but also as a community platform for sharing knowledge and carrying out research crucial to combating infectious diseases. The success of the PEARL project is an outstanding example. Thanks to the work of the GABRIEL network, the Ministry of Health of Lebanon declared on June 11 that the Rodolph Mérieux Laboratory is to be designated as a reference laboratory for tuberculosis, a recognition of its capacity to carry out diagnostics and train staff in laboratory techniques. These are huge tasks. He also thanked the university's School of Pharmacy and all those who collaborated on these initiatives, stating that their work will carry on.

Alain Mérieux, President of the Mérieux Foundation, brought this year's edition of the GABRIEL international meeting to a close with warm thanks extended to all the participants for their contribution. He expressed his heartfelt acknowledgement for the achievements of the Rodolph Mérieux Laboratory that have earned it national recognition in Lebanon.. He spoke about the foundation's work in the interest of public health, citing in particular the foundation's education programs in Haiti, Mali, Laos, and Madagascar. He mentioned the increasingly strong relations with the Pasteur Institute. He acknowledged that today's context is tough and complex. Some countries are not as secure as they used to be. He stated that the foundation must never lose sight of its mission to make a true impact on public health. He confirmed his optimism looking to the future and thanked the group for their work.

