FINPHARM Closing Conference:
"Antibiotic Crises: A Global Ward Round"

For the past five years the FINPHARM team has been analysing case studies on the impact of financialization on the development and use of pharmaceuticals in several areas of global health significance. Our work on the antibiotics has brought us into collaboration with researchers around the world who have published on antibiotic crises. To close our project, we held a closing conference on October 25th 2024with contributions from across disciplines, including academics and practitioners, in order to continue to build a community of practice to work towards solutions to access, availability and appropriate use of these critical medicines. The discussions are summarised below:

Panel 1: Antibiotic Shortages and Infrastructures

Mingyuan Zhang, Researcher, Department of Community Medicine and Global Health, University of Oslo: "The role of China in today's global antibiotic manufacturing landscape and the impact on shortages"

A sociocultural anthropologist at the University of Oslo, Zhang shared insights from her research on antibiotic production and circulation across the Indian Ocean, with a focus on China's role in manufacturing antibiotics and active pharmaceutical ingredients (APIs). The project traces the movement of antibiotics from production in China, to formulation in India, and finally to consumption in Tanzania. The history and evolution of China's pharmaceutical industry is explored especially through the North China Pharmaceutical Company which was founded in 1953 with Soviet assistance. This company, which became a key producer of antibiotics in the 1950s and 1960s, remains one of China's largest manufacturers of APIs today. A key research method had been attending online pharmaceutical trade fairs which provided valuable insights into the global production and marketing of antibiotics and APIs, the competition between Chinese and Indian companies and the complex relationships between these two nations, where Indian companies both competed with and depended on Chinese-produced antibiotics. The project's findings illustrate how international trade regulations and national interests shaped the pharmaceutical industry. This research provided a nuanced understanding of pharmaceutical supply chains and their geopolitical implications, emphasizing the complexity of global antibiotic production and trade.

Anthony Rizk, Researcher, Global Health Center, Geneva Graduate Institute: "Lebanon's diasporic microbiology? Biorepositories as transnational infrastructures"

Completing his PhD in anthropology at the Geneva Graduate Institute, Rizk explored the complex role of biorepositories in the global antibiotic production and the development of medical technologies to address antimicrobial resistance (AMR). The research highlights how biorepositories—facilities where biological samples, including pathogens, are stored—serve as

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key infrastructures in the development of antibiotics, vaccines, and antimicrobial detection technologies. Pathogen samples are essential for testing the efficacy of these technologies, and biorepositories play a crucial role in ensuring access to these samples for research and development. Anthony contrasted global pathogen governance with the realities observed in Lebanon, where a lack of central public health infrastructure has led to a reliance on private, university-based microbiology laboratories. These laboratories, although conducting vital research, often lack the resources and support of a centralized public health laboratory, leading to inefficiencies in pathogen collection and storage. The absence of a national biorepository has resulted in Lebanese pathogens being stored abroad, particularly in institutions in France and the United States. This reliance on foreign biorepositories challenges assumptions about the global distribution of pathogen samples, especially in Global South countries like Lebanon. Anthony argues that the under-investigation of biorepositories as a critical infrastructure in antibiotic production could be a blind spot in the global supply chain and contribute to current challenges in AMR research.

Victor Secco, Researcher, Department of Philosophy and Cultural Heritage, Ca' Foscari University of Venice: "Financing phages in India: 'communist' viruses in antibiotic infrastructures"

Secco's research explores bacteriophages and their potential as an alternative to antibiotics in treating antibiotic-resistant infections, particularly in the context of India. Bacteriophages, discovered in the early 20th century, were initially proposed as a treatment for bacterial diseases. However, their development was overshadowed by the rise of antibiotics following World War II. Despite early clinical trials, notably in India, phage therapy did not gain widespread traction, particularly in Western medicine, due to antibiotics' industrial scalability and geopolitical tensions during the Cold War. In contrast, the Soviet Union continued to research and use phages, with centers of expertise like the Eliava Phage Therapy Center in Georgia. The research further examines the resurgence of interest in phage therapy in the 21st century, spurred by the rise of antimicrobial resistance (AMR). Secco's fieldwork with microbiologists in India focused on the Ganges River, where contaminated waters serve as a rich source of natural phages targeting antibiotic-resistant bacteria. Further fieldwork with a biotech company in South India demonstrates the difficulties in patenting phages as natural entities. The research highlights the tension between the narrow-spectrum nature of phages and the industrial demands of modern pharmaceuticals, addressing the financialization, regulation, and commercialization of phage therapy within the global healthcare system.

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Panel 2: AMR in Conflict

Antoine Abou Fayad, Associate Professor, Department of Experimental Pathology, Immunology and Microbiology, American University of Beirut: "Armed conflict as an under-investigated pathway for AMR with growing significance"

Antimicrobial resistance (AMR) is a growing concern in conflict zones, where various factors combine to exacerbate the spread of resistant bacteria. One significant driver is the lack of surveillance before, during, and after conflicts, which limits understanding of AMR prevalence and hinders the ability to anticipate its escalation. In regions like the Eastern Mediterranean, surveillance is either minimal or absent, with countries like Lebanon and Egypt struggling with data collection due to limited resources or governmental control. Furthermore, the misidentification of pathogens due to inadequate laboratory capacity and a shortage of skilled healthcare workers worsens the situation. Fayad's research focuses on heavy metal contamination, a major factor contributing to AMR in conflict settings. Research in Lebanon, following the 2006 war, found that bacteria exposed to these metals developed resistance not only to the metals themselves but also to critical antibiotics like colistin. This phenomenon, known as cross-resistance, occurs when bacteria develop resistance mechanisms that protect them against both heavy metals and antibiotics. The interaction between heavy metals and antibiotics in conflict settings poses a dual threat, potentially accelerating the spread of multidrug-resistant pathogens. Research efforts are ongoing to identify the molecular mechanisms driving this resistance, with current conflicts providing a valuable opportunity for sampling and deeper investigation into the links between environmental contaminants, AMR, and public health outcomes.

Aula Abbara, Consultant in Infectious Diseases and Honorary Senior Clinical Lecturer at Imperial College, London: "AMR, conflict and humanitarian healthcare"

In recent years, discussions about antimicrobial resistance (AMR) in conflict-affected regions have evolved, with particular focus on the Western Asia and North Africa (WANA) region. Key experts have come together to explore how conflict, alongside environmental instability and other crises like climate change and displacement, intersects with AMR. The discussion centers on how conflicts in countries such as Syria, Gaza, Yemen, and Sudan exacerbate the challenges of antimicrobial stewardship, infection control, and healthcare access. Efforts to address AMR in these settings are ongoing but face significant challenges, including a lack of reliable data, underfunded health systems, and the continuous destruction of medical facilities in conflict zones. Abbara demonstrated several innovations in diagnostics, such as mini-laboratories and AI-assisted tools to support microbiology in these crisis zones, which are being developed and deployed to mitigate these issues. However, addressing AMR requires a holistic approach, involving multi-stakeholder collaboration across health, environmental, and political sectors. Moreover, it is crucial to consider the human and social aspects of AMR, including how displaced populations and vulnerable groups interact with antibiotics, as well as the broader impacts of climate change on the spread of resistance.

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Louis-Patrick Haraoui, Associate Professor, Department of Microbiology and Infectious Diseases, University of Sherbrooke and CIFAR Human and the Microbiome Program, Canada: "Identifying novel antibiotic resistant genes in the context of armed conflict"

Antimicrobial resistance (AMR) has become a major global challenge, with a growing recognition of environmental sources of resistance, particularly in the context of armed conflict. While much of the initial focus was on clinical settings, research over the past 15 years has revealed that the majority of antibiotic-resistant bacteria and resistance genes originate from environmental ecosystems such as soils, oceans, and water bodies, which are often exposed to pollutants like heavy metals and biocides. Bacteria in these environments adapt to these pollutants, leading to the development of resistance, which can later spread through bacterial genetic exchange. This makes the environment a significant driver of AMR. Haraoui shows how recent advancements in artificial intelligence (AI) and genomics are providing new opportunities to detect and prevent the spread of AMR. One AI-powered tool, AlphaFold, can predict the three-dimensional structure of proteins, including those associated with resistance. Combining comparative genomics with AI improves the ability to predict and detect new resistance genes before they spread into clinical settings. In a study focusing on a lake in Kolkata, India, Haraoui and his team use these tools to identify new resistance genes that could potentially spread to human pathogens. This approach also offers a potential solution to mitigating the environmental spread of AMR, particularly in conflict zones where environmental degradation could accelerate the emergence of new resistance genes. Civilian science, leveraging local communities, could play a critical role in monitoring and mitigating these risks.

Panel 3: Financialisation and the Antibiotic Pipeline

Nadya Wells, Senior Research Adviser, Global Health Centre, Geneva Graduate Institute (IHEID) and Faculty of Medicine, University of Geneva: "Novel insights from financial analysis of the failure to commercialize plazomicin"

Wells examines the financial challenges facing small and medium-sized enterprises (SMEs) in the antibiotic development pipeline. Using the case of Achaogen, a US-based biotech firm that developed the aminoglycoside plazomicin, the study focuses on the financial vulnerabilities of SMEs, a crucial driver of the antibiotic pipeline. Key findings include the stark contrast between the immense costs of antibiotic development and the minimal revenues generated. Achaogen faced escalating costs while struggling to generate sufficient revenue, exacerbated by pricing mechanisms that do not account for the unique needs of antibiotics. The study highlights that, for SMEs, capital markets play a significant role in financing development, with these companies relying on equity and debt financing to fund the commercialization stage. The paper argues that the current system of financing is inadequate, as the revenues from new antibiotics are too low to cover the necessary costs for commercialization. Furthermore, the study identifies the growing dependence on SMEs in the antibiotic pipeline, with 93% of late-stage antibiotics being developed by small biotech companies. The bankruptcy of Achaogen in 2019, followed by other

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SME failures, is portrayed as a warning signal that has diminished investor confidence in antibiotic development. The paper calls for greater recognition of the financial challenges SMEs face and advocates for more tailored financial support, such as cash flow guarantees or debt instruments, to help sustain the antibiotic pipeline. Solutions would need to include restoring confidence in the business model, creating mechanisms to support the long-term viability of antibiotics, and ensuring both high-income and low-income markets benefit from new treatments.

Keynote: ***Ryan Cirz, Chief Executive Officer, Revagenix, Inc.: "Financial Aspects of Antibiotic Development and Commercialization"***

Cirz highlights the complex challenges faced by plazomicin, an antibiotic developed to treat carbapenem-resistant Enterobacteriaceae (CRE). Despite showing promising clinical efficacy in trials, particularly in comparison to older drugs, the drug struggled to gain market traction due to the high costs associated with its development and the limited pricing flexibility in the global healthcare system. The financial model, based on recouping a $500 million development cost over 10 years, required pricing that would make the drug inaccessible to many patients. Even though plazomicin demonstrated clinical superiority in certain trials, the pricing model made sustainability difficult. The analysis underscores how pricing, patient numbers, treatment duration, and regulatory hurdles all interplay in determining whether a drug can become commercially viable. The development of plazomicin occurred within a larger context of stagnation in antibiotic innovation, particularly for gram-negative infections. The market for such antibiotics is constrained by high production costs, limited patient populations, and slow adoption by healthcare systems, compounded by the constant threat of generics entering after patent expiry. Ultimately, while plazomicin could have saved lives and addressed a critical need, the economic and market barriers led to its limited impact, raising broader questions about the sustainability of developing new antibiotics under current regulations

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