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Meeting Report

Melioidosis in Africa: Time to Raise Awareness and Build Capacity for Its Detection, Diagnosis, and Treatment

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Abstract. Melioidosis is a tropical infectious disease caused by the soil-dwelling bacterium *Burkholderia pseudomallei* with a mortality of up to 50% in low resource settings. Only a few cases have been reported from African countries. However, studies on the global burden of melioidosis showed that Africa holds a significant unrecognized disease burden, with Nigeria being at the top of the list. The first World Health Organization African Melioidosis Workshop was organized in Lagos, Nigeria, with representatives of health authorities, microbiology laboratories, and clinical centers from across the continent. Dedicated hands-on training was given on laboratory diagnostics of *B. pseudomallei*. This report summarises the meeting objectives, including raising awareness of melioidosis and building capacity for the detection, diagnosis, biosafety, treatment, and prevention across Africa. Further, collaboration with regional and international experts provided a platform for sharing ideas on best practices.

Melioidosis, an infectious disease caused by the soil-dwelling gram-negative bacterium and tier 1 select agent *Burkholderia pseudomallei*, is characterized by sepsis, pneumonia, or localized abscesses. Melioidosis has a case fatality rate of 10–50%,[1] and individuals who are in regular contact with soil and water are at risk, such as rice farmers.[2,3] Diabetes mellitus is the main risk factor and can increase the risk of someone acquiring melioidosis by at least 12-fold.[4,5] Melioidosis is a well-known disease with a highly detrimental impact on society in the endemic hotspots of Northern Australia and large parts of Southeast Asia.[4,6] However, there is an urgent need to expand our knowledge on melioidosis beyond those geographic areas. It is estimated that melioidosis is grossly underreported in the 45 countries known to be endemic,[7] and probably endemic in a further 34 countries that have never reported the disease.[7] A recent modeling study estimated the global burden of melioidosis to be around 4.6 million disability-adjusted life years (DALYs) annually, corresponding to 84 DALYs per 100,000 population.[8] The global burden of melioidosis expressed in DALYs is higher than dengue, schistosomiasis, or intestinal nematode infections.[8] With the growing global pandemic of diabetes, the global burden of melioidosis is only expected to increase, especially as four-fifth of diabetic patients currently live in low- and middle-income countries.[3,9,10] Not surprisingly, there is a growing understanding that melioidosis needs to be recognized as a significant neglected tropical disease (NTD).[8,11,12]

In Africa, recent isolated human melioidosis cases have been reported from Gabon,[13] Cameroon,[14] The Gambia,[15] Kenya,[16] Malawi,[17] Madagascar,[18] Eritrea,[19] Congo,[20] and Nigeria.[21–23] Earlier, there have been reports of *B. pseudomallei* infections in animals from Niger,[24] Burkina Faso,[25] Chad,[26] and South Africa.[27] These scattered case reports could very well represent only "the Tip of the Iceberg."[28,29] For example, a prospective study performed in Lambaréné, Gabon, which involved both environmental sampling, population serology testing as well as a clinical study in a referral center, did identify a novel *B. pseudomallei* sequence type that caused lethal septic shock in a 62-year-old lady. The identified *B. pseudomallei* sequence type was revealed to be abundantly present in the soil around Lambaréné.[13] These data suggest that *B. pseudomallei* is probably present in large parts of Africa but underreported because of a lack of awareness and diagnostic facilities.[28,29] Nigeria is thought to be the country most affected by melioidosis on the African continent given the size of its population, the high prevalence of diabetes, and favorable climatological circumstances. This African country is estimated to be among the top five countries with the highest melioidosis burden worldwide with 237 DALYs per 100,000 people.[8] It has been estimated that each year around 13,000 Nigerians suffer from this disease of which the majority will not survive.[7] Therefore, the first WHO-sponsored African Melioidosis Workshop on March 27 and 28, 2019 was held in Lagos, Nigeria. The WHO, Nigeria, hosted this workshop in collaboration with the Lagos University Teaching Hospital and the College of Medicine–University of Lagos (LUTH/CMUL).

The melioidosis workshop was by invitation only and brought together key experts from clinical microbiology, infectious diseases, epidemiology, and public health authorities from countries including Nigeria, Ethiopia, the Democratic Republic of Congo, Vietnam, Austria, and The Netherlands (see Figure 1A). Dedicated sessions were organized for key

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laboratory technicians with experience in clinical microbiology and the culture and identification of microorganisms. The set objectives of this workshop were to 1) raise awareness of melioidosis and its causative agent *B. pseudomallei* in Africa with a focus on Nigeria; 2) build capacity for detection of *B. pseudomallei* in its possible natural habitats and clinical specimens; 3) bring together regional and international experts and stakeholders to share best practices for detection, laboratory-based diagnosis, biosafety and biosecurity, treatment, and prevention of melioidosis in Africa. The workshop consisted of lectures, a practical poster session, focus group (Figure 1B) discussions, and a laboratory practical (Figure 1C and D).

On the first day, the meeting commenced with a welcome speech by Professor Alani Akanmu, who introduced the regional/international experts on melioidosis, the participants, and the organizing committee and announced the overall learning objectives. Dhamari Naidoo (Technical Officer, WHO, Abuja, Nigeria) advised bridging the gaps between all stakeholders to reduce the burden of melioidosis in Africa. The Nigeria's honorable Minister of Health, Professor Isaac Adewole, who was ably represented by the Director General of the Nigerian Institute of Medical Research Professor Babatunde Salako, formally inaugurated the workshop. He highlighted the need to raise awareness of melioidosis and *B. pseudomallei*, to create and enhance best practices for prevention and expand the African Melioidosis Network (AMENET). In Session I (*the burden of melioidosis*), Dr. Emma Birnie (Amsterdam University Medical Centers, The Netherlands) explained the epidemiology and global burden of melioidosis. It is estimated that the African region, with 775,266 DALYs per year, accounts for the largest melioidosis burden after the South East Asia Region.[8] She emphasized the need for the WHO to include and recognize melioidosis officially as NTD. Next, Professor Joost Wiersinga (Amsterdam University Medical Centers, The Netherlands) discussed the history of melioidosis in Africa and described reported cases.[28,29] At the moment of this workshop, the only culture-positive case thought to have been acquired in Nigeria was a 46-year-old diabetic woman who sought treatment in St. Thomas Hospital, London, United Kingdom, after a 6-week visit to Sagamu, Ogun State, Nigeria. She had no history of travel outside the United Kingdom or Nigeria.[22] Next, Professor Ivo Steinmetz (University of Graz, Austria) presented on the worldwide ecology of *B. pseudomallei*, environmental conditions, and different soil surveillance approaches. In Session II (*melioidosis the disease*), Professor Wiersinga gave an overview of the clinical presentations and management, risk factors, and pathophysiology.[2,3] Subsequently, Professor Steinmetz explained new tools to unravel the disease burden, including a protein array assay for specific antibody detection[30] and

FIGURE 1. (**A**) Group photo of the First African Melioidosis Workshop at the Sheraton Hotel, Lagos, Nigeria, sponsored by the WHO. (**B**) Participants were divided into four groups during the focus group discussion. (**C**) Practical laboratory session provided a hands-on training. (**D**) Work during the practical laboratory session was performed with *Burkholderia thailandensis.* This figure appears in color at www.ajtmh.org.

core genome multi-locus sequence typing for *B. pseudomallei*. In Session III (*epidemiological principles and studies on melioidosis*), Dr. Birnie presented the results of the seroepidemiological, prospective fever, and soil surveillance study conducted in Gabon[13] and the environmental surveillance study conducted in Sierra Leone.[31] Next, Professor Steinmetz, being the coordinator of the AMENET, gave a presentation about this collaborative effort between the European and African Union to improve health through an integrated microbiological, clinical, and environmental research approach (including African partner countries in Burkina Faso, Ghana, Ivory Coast, Madagascar, Ethiopia, and Congo).[29] Dr. Trinh Trung (Vietnam National University, Hanoi, Vietnam) presented recent progress after raising awareness of melioidosis in Vietnam.[32] He showed that one could learn from other resource-limited settings and introduced a simple laboratory algorithm to identify *B. pseudomallei* from clinical samples.[33] Although *B. pseudomallei* grows on blood and MacConkey agar, *B. pseudomallei* is often misidentified as *Pseudomonas* species or dismissed as a contaminant. In Session IV (*microbiological diagnosis of melioidosis*), there was time for an interactive poster session on laboratory diagnostics, preparation of selective media, morphology of *B. pseudomallei* and identification methods, and antibiotic susceptibility test. Finally, Professor Akin Osibogun (LUTH/CMUL, Lagos, Nigeria) introduced fundamental epidemiologic principles for monitoring emerging infectious diseases, such as sampling, testing, data collection and analysis, and disease prevention actions.

On the second day (Session V: *closing session*), Dr. Birnie presented the official kickoff of the pilot study *In Search of Melioidosis in Nigeria,* funded by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID). This study combines environmental, clinical and, seroepidemiological surveillance of *B. pseudomallei.* This project will provide the first insights into the prevalence of *B. pseudomallei* in Nigeria's soil and melioidosis infections. During the environmental sampling study after this workshop, we have discovered several potential *B. pseudomallei* soil isolates from Nigeria. Currently, we are analyzing and sequencing these strains. Next, Dr. Lorhen Akasa (University of Lagos, LUTH/CMUL, and African Sepsis Alliance representative) depicted a need for collaborative effort while advancing the fight against sepsis and melioidosis.[34] This is especially urgent as unrecognized melioidosis could very well be an essential cause of sepsis-associated mortality in Africa. In Session VI (*discussion*), Professor Akanmu chaired the focus group discussions (Figure 1B). Participants were divided into four groups to discuss 1) the challenges and awareness of melioidosis, 2) microbiology and laboratory detection of *B. pseudomallei*, 3) creation of regional and international collaborations, and 4) develop a sustainable funding plan for melioidosis detection in their respective institutions. The representatives of each group presented their experiences, ideas, and recommendations. The most common challenges mentioned were limited diagnostic facilities and resources and a lack of awareness of the disease and the causative agent. As a result, *B. pseudomallei* is most likely often misidentified. Moreover, most African countries have not enlisted melioidosis as a reportable disease. Possible collaboration efforts with the African Centers for Disease Control, WHO, and African Sepsis Alliance were discussed. Participants proposed the following action steps for Africa, starting in Nigeria: 1) determine the magnitude and burden of the disease; 2) continue to generate hospital data for better patient care; 3) and organize advocacy meetings with significant health stakeholders, such as the Ministry of Health, State Commissioners for Health, and major public health parastatals at both federal and state levels. In the afternoon, a selection of the participants joined the laboratory session (Figure 1C). This practical session provided hands-on training on basic microbiology for the isolation, identification, and characterization of *B. pseudomallei*. Work was performed with *Burkholderia thailandensis*, a less-virulent species that requires a lower biosafety level (BLS-2) (Figure 1D). The participants were trained to cascade the knowledge acquired during this workshop to their colleagues in various institutions. Participants were able to use the lectures presented in this workshop as a training guide.

In conclusion, this stimulating collaboration boosted the participating stakeholders' enthusiasm, and we therefore considered this first WHO African Melioidosis Workshop a success. Most of the participants heard for the first time about the importance of melioidosis and were keen to learn more. It is hoped that this will translate to better management of patients at risk of this infection in Nigeria. The workshop participants and organizers intend to organize similar workshops every 4 years in a different African country to ensure sustainability. By sharing knowledge about and experience with melioidosis, the aim is to improve the identification and reporting of melioidosis, clinical diagnosis, laboratory confirmation, treatment, and outcome in Africa. Possible collaboration partners include the African Centers for Disease Control, WHO, and African Sepsis Alliance, but additionally, it would be essential to join forces with Antimicrobial Resistance action plans. More data collection on the African continent using a One Health approach will contribute to a greater understanding of the global burden and will help to decrease morbidity and mortality of melioidosis.

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