World Pneumonia Day 2024: Fighting Pneumonia and Antimicrobial Resistance

This is the age of omics, artificial intelligence, and precision medicine. However, despite the current advances in science and medicine, pneumonia, a treatable and preventable disease described since ancient times, continues to be a major cause of mortality all over the world (1). According to the 2021 Global Burden of Disease report, 2.1 million people died of pneumonia in that year (2); children under 5 years of age and adults over 70 years of age continued to be the most vulnerable populations, with more than 500,000 and 1 million pneumonia-related deaths, respectively (2). Added to the enormous burden of this pathology is the impact of antimicrobial resistance (AMR); according to the 2019 Global Burden of Disease report, 1.27 million deaths were attributable to bacterial AMR in that year (3), and one in five deaths caused by AMR occurred in children under 5 years of age. According to this report, six leading pathogens were responsible for almost 1 million deaths attributable to AMR, with *Streptococcus pneumoniae* being the most frequent pathogen identified in pneumonia and contributing to 16% of the deaths attributable to AMR (3).

The coronavirus disease (COVID-19) pandemic highlighted our vulnerabilities in the management of pneumonia and our low level of preparedness for pandemic situations worldwide (4) and drew attention to the impact of respiratory infections, the importance of early diagnosis and initiation of therapy, the vital role of oxygen in this global emergency, and the worldwide healthcare inequities. However, the scientific community also demonstrated its ability to respond to an emergency of this scale by developing new vaccines, rapid diagnostic tests, and clinical treatments in record time.

Two questions regarding the impact of pneumonia remain unanswered: first, why does pneumonia, a treatable and preventable disease, still have such a huge impact on global health? And second, how is it possible that pneumococcus was involved in 16% of the deaths attributable to AMR when we have effective pneumococcal vaccines? Maybe the answer to these questions is to be found in an article published in 2022 that focused on the shortcomings in child pneumonia research (5). The authors identified 20 research priorities in child pneumonia, the most important one being "to explore interventions to prevent neonatal pneumonia," reflecting the concern with the mortality due to the condition in newborns, as 47% of deaths in children 5 years of age or younger occur in this group. Similarly, new research finds that increasing the application of four pneumonia interventions (vaccination against *Haemophilus influenzae* B, pneumococcal conjugate vaccine [PCV], treatment with oral antibiotics, and targeted oxygen treatment of hypoxemia) to reach ⩾90% by 2030 could prevent half of the predicted deaths from pneumonia in children 5 years old or younger in Chad, Ethiopia, and Bangladesh, the countries with the highest rates of child mortality (6).

In fact, the Child Health and Mortality Prevention Surveillance network (7), a collaborative platform that conducts standardized, comprehensive, and high-quality surveillance of causes of child mortality in sub-Saharan Africa and Asia, reported that, in these high-mortality settings, infectious diseases continue to cause the most deaths in infants and children, often in conjunction with malnutrition. That study identified lower respiratory tract infections as the most common overall cause of death, occurring in almost half of all fatalities. The finding that pathogens such as *S. pneumoniae*, *Klebsiella pneumoniae*, and *H. influenzae* had an important impact as causes of infections demonstrated the gaps that still exist. Efforts to ensure that pneumonia vaccines achieve optimal coverage and avoid unjustified deaths are needed, despite the fact that the 2023 World Health Organization/UNICEF Estimates of National Immunization Coverage report (8) showed that more children are being immunized than ever before.

These positive results were achieved with the support of the Global Alliance for Vaccines and Immunization (9). However, the report also stressed there were approximately 11 million "zero-dose" children in Global Alliance for Vaccines and Immunization–supported countries in 2023, suggesting an increase of 0.5 million compared with 2022 (8). Ten countries account for 59% of zero-dose children, all of them countries with weak health systems or afflicted by conflict and humanitarian crises such as Sudan, Yemen, and Syria. The disruption caused by the pandemic also affected the low coverage (8), which in turn may explain the burden of AMR in these countries.

Reducing infection rates would help bring down the use of antimicrobial agents and therefore the risk of AMR. An effective way to achieve this is to implement vaccines for preventing infections, as shown in the recent One Health Trust report (10), which enumerated the benefits of vaccines against antimicrobial resistance: namely, the significant reduction in drug-resistant infections achieved by PCV, which limit the circulation of antibiotic-resistant pneumococcal serotypes; the positive impact on healthcare costs; and the decrease in the use of antimicrobial agents. One important example of the impact of immunization on reducing AMR is found in a study that investigated the effect of vaccination on antibiotic agent consumption in 18 low- and middle-income countries and reported that, at 70% coverage, PCV immunization in children 2 years of age and younger might avert 23.8 million antibiotic-treated acute respiratory infections every year (11).

As the world's population ages, infectious diseases such as pneumonia represent a huge burden, mainly because of the low vaccination rate in elderly individuals and the lack of awareness of the gravity of this infectious disease in this population. The susceptibility

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to infections in this population (12, 13) highlights the significant impact that vaccines may have in older populations, especially in view of the effect of immunosenescence on vaccine efficacy, and also because of the anticipated increase in the elderly population worldwide, which is forecast to reach 1.5 billion by 2050 (14).

It is also important to stress the potential of childhood immunization for reducing disease in older adults; for example, the indirect effect of PCV (i.e., reductions in adult cases and mortality through the prevention of transmission of disease-causing strains) is actually much larger than the direct effect of prevention in immunized adults (15). Importantly, attitudinal factors were the most consistently associated with vaccination status in older adults, suggesting that awareness and education campaigns might be key interventions for lowering the burden of immunization-preventable respiratory infections (16).

The development of new effective preventive interventions against RSV, which is currently a major cause of severe pneumonia in infants and an important cause of pneumonia in elderly individuals, is a key step in the fight against pneumonia. There are now three RSV vaccines for adults aged 60 years and older, a maternal vaccine, and a long-acting monoclonal antibody to protect against disease in infancy or early childhood throughout the RSV season; however, greater global availability and access is needed (17).

World Pneumonia Day, held annually on November 12, aims to raise global awareness of pneumonia and to encourage a global conversation focused on reducing the burden of pneumonia worldwide. To learn more about World Pneumonia Day and the activities planned, please visit https://stoppneumonia.org/latest/world-pneumonia-day/.

Clearly, we must continue with the implementation of effective interventions that help reduce the global burden of pneumonia, and we must invest in research especially focused on reducing risk factors for infection and mortality in the groups at greatest risk of death, namely those exposed to air pollution, malnutrition, tobacco smoking, and harmful working environments, and also those with limited access to health care and therefore have low rates of immunization and are unlikely to seek care or treatment. Above all, we must realize the importance of the role of healthcare workers, stakeholder authorities, and the general public in raising awareness of the impact of this disease that is currently the cause of more deaths than any other infectious disease. ■

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References

1. Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, *et al.* Diagnosis and treatment of adults with community-acquired pneumonia.

An official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med* 2019;200:e45–e67.
2. Bender RG, Sirota SB, Swetschinski LR, Dominguez R-MV, Novotney A, Wool EE, *et al.* Global, regional, and national incidence and mortality burden of non-COVID-19 lower respiratory infections and aetiologies, 1990–2021: a systematic analysis from the Global Burden of Disease Study 2021. *Lancet Infect Dis* 2024;24:974–1002.
3. Murray CJL, Ikuta KS, Sharara F, Swetschinski L, Aguilar GR, Gray A, *et al.* Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet* 2022;399:629–655.
4. Churpek MM, Gupta S, Spicer AB, Parker WF, Fahrenbach J, Brenner SK, *et al.*; STOP-COVID Investigators. Hospital-level variation in death for critically ill patients with COVID-19. *Am J Respir Crit Care Med* 2021; 204:403–411.
5. King C, Baker K, Richardson S, Wharton-Smith A, Bakare AA, Jehan F, *et al.* Paediatric pneumonia research priorities in the context of COVID-19: an eDelphi study. *J Glob Health* 2022;12:09001.
6. Pfurtscheller T, Lam F, Shah R, Shohel R, Sans MS, Tounaikok N, *et al.* Predicting the potential impact of scaling up four pneumonia interventions on under-five pneumonia mortality: a prospective Lives Saved Tool (LiST) analysis for Bangladesh, Chad, and Ethiopia. *J Glob Health* 2024;14:04001.
7. Bassat Q, Blau DM, Ogbuanu IU, Samura S, Kaluma E, Bassey IA, *et al.*; Child Health and Mortality Prevention Surveillance (CHAMPS) Network. Causes of death among infants and children in the Child Health and Mortality Prevention Surveillance (CHAMPS) network. *JAMA Netw Open* 2023;6:e2322494.
8. World Health Organization. WHO/UNICEF estimates of national immunization coverage. Geneva, Switzerland: WHO; 2024 [updated 15 Jul 2024; accessed 2024 Aug 12] Available from: https://www.who.int/news-room/questions-and-answers/item/who-unicef-estimates-of-national-immunization-coverage.
9. GAVI Staff. Global immunisation in 2023: 7 things you need to know. Geneva, Switzerland: GAVI, The Vaccine Alliance; 2024 [updated 15 Jul 2024; accessed 2024 Aug 01] Available from: https://www.gavi.org/vaccineswork/global-immunisation-2023-7-things-you-need-know.
10. Kalanxhi E, Roberts N, Bahati F, Laxminarayan R. The value of vaccines to mitigate antimicrobial resistance—evidence from low- and middle-income countries. Washington, DC: One Health Trust; 2023 [updated 23 Oct 2023; accessed 2024 July 23] Available from: https://onehealthtrust.org/publications/reports/the-value-of-vaccines-to-mitigate-antimicrobial-resistance-evidence-from-low-and-middle-income-countries/.
11. Lewnard JA, Lo NC, Arinaminpathy N, Frost I, Laxminarayan R. Childhood vaccines and antibiotic use in low- and middle-income countries. *Nature* 2020;581:94–99.
12. Bosco E, van Aalst R, McConeghy KW, Silva J, Moyo P, Eliot MN, *et al.* Estimated cardiorespiratory hospitalizations attributable to influenza and respiratory syncytial virus among long-term care facility residents. *JAMA Netw Open* 2021;4:e2111806.
13. Ramirez J, Furmanek S, Chandler TR, Wiemken T, Peyrani P, Arnold F, *et al.*; The University of Louisville Pneumonia Study Group. Epidemiology of pneumococcal pneumonia in Louisville, Kentucky, and its estimated burden of disease in the United States. *Microorganisms* 2023;11:2813.
14. World Health Organization. Ageing and health. Geneva, Switzerland: WHO; 2024 [updated 1 Oct 2024; accessed 2024 Sep 01] Available from: https://www.who.int/news-room/fact-sheets/detail/ageing-and-health.
15. Kellner JD. Who benefits, and how much? Indirect effects of childhood pneumococcal vaccination in adults at increased risk of pneumococcal disease. *Clin Infect Dis* 2019;68:1374–1375.
16. Eiden AL, Barratt J, Nyaku MK. Drivers of and barriers to routine adult vaccination: a systematic literature review. *Hum Vaccin Immunother* 2022;18:2127290.
17. Cunningham S, Zar HJ. New interventions to prevent respiratory syncytial virus disease in infants—time for equitable global access. *Am J Respir Crit Care Med* 2023;207:1556–1557.

A Rising STAR in Chronic Obstructive Pulmonary Disease or More Deckchair Rearrangement?

In the 18th century, Carl Linne, the Swedish physician and botanist commonly referred to as Linnaeus, developed a rational system of classifying plants. This process of classifying organisms, initially on the basis of their physical attributes and now underpinned by scientifically robust studies of their phenotype and genotype, was of great interest to the Founding Fathers of the United States and has been a powerful tool for understanding disease. It was a logical step to use one or more of these defining features to evaluate the severity of a condition, as has been done in the case of patients with chronic obstructive pulmonary disease (COPD). Here spirometry has been the objective characteristic studied, and several arbitrary cut points based on the observed reduction in FEV_1 were selected to define the extent to which impaired lung mechanics and hence structural lung damage is present (1). These broad groupings define people with different clinical outcomes, especially for mortality, where FEV_1 percent predicted is still the strongest predictive variable (2, 3). For the last 25 years, the most widely adopted approach is that of the Global Initiative for Chronic Obstructive Lung Disease (GOLD), where COPD is defined by the presence of an FEV_1/FVC ratio of 0.7 (70% or less) and severity (or GOLD stage) is based on the FEV_1 percent predicted; GOLD 1 is an FEV_1 80% predicted or greater; GOLD 2, 79–50% predicted; GOLD 3, 49–30% predicted; and GOLD 4, below 30% predicted (4).

Recently, Bhatt and colleagues suggested an alternative approach that uses the defining characteristic of airflow obstruction to grade severity in their Staging of Airflow Obstruction by Ratio (STAR) system (5). Again, four grades were created, STAR 1 being a ratio of 60–70%; STAR 2, 50% to <60%; STAR 3, 40% to <50%; and STAR 4, <40%. They validated this system in the large COPDGene (Genetic Epidemiology of COPD Study) observational cohort and two COPD cohorts from Philadelphia, comprising a total of 12,149 individuals with detailed clinical data, and they compared the new system with the conventional GOLD grading. The system produced similar

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