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Editorial: Outbreaks of Post-Pandemic Childhood Pneumonia and the Re-Emergence of Endemic Respiratory Infections

Dinah V. Parums, MD PhD

Science Editor, Medical Science Monitor, International Scientific Information, Inc., Melville, NY, USA

e-mail: dinah.v.parums@isi-science.com

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Abstract

In October and November 2023, hospitals in the major cities of Beijing and Liaoning in northern China reported a surge in cases of pneumonia in children, with some hospitals being overwhelmed by pediatric emergency admissions. Similar outbreaks of childhood pneumonia had been reported in the autumn of 2022 in Europe and North America. Therefore, increased reports of childhood pneumonia could be driven by post-pandemic changes in the pathogenesis of endemic respiratory infections other than COVID-19, including *Mycoplasma pneumoniae*, respiratory syncytial virus (RSV), and influenza, rather than emerging novel pathogens. However, the recent reports of increased hospitalizations for children with pneumonia warrant continued infection surveillance and monitoring to exclude new respiratory pathogens or more virulent variants of known pathogens, including SARS-CoV-2. This editorial aims to present what is known about the re-emergence of endemic respiratory infections, which may be the cause of the recently reported outbreaks of childhood pneumonia.

Keywords: *Mycoplasma pneumoniae* • Respiratory Syncytial Virus • Influenza • SARS-CoV-2 • Editorial

In October and November 2023, hospitals in the major cities of Beijing and Liaoning, northern China, which are almost 800 km apart, reported a surge in cases of pneumonia in children, with some hospitals being overwhelmed by pediatric emergency admissions [1,2]. On November 23, 2023, the WHO held a teleconference meeting with health officials from the Chinese Center for Disease Control and Prevention (CDC) and the Beijing Children's Hospital, facilitated by China's National Health Commission and the National Administration of Disease Control and Prevention [2]. Chinese health authorities informed the World Health Organization (WHO) that this was a seasonal peak in a trend of rising respiratory infections in children following the lifting of COVID-19 pandemic restrictions [2]. Within days of these reports, national and international medical authorities and news reports began to speculate on the cause of these outbreaks of pneumonia in children, even though similar outbreaks of childhood pneumonia had been reported in the autumn of 2022 in Europe and North America. However, there are some differences in the presentation of these recent cases, and the cause or cause or causes remain to be determined.

Initial international review and evaluation came from the Program for Monitoring Emerging Diseases (ProMED) and the WHO. ProMED is an emerging infectious disease surveillance service organized by the International Society for Infectious Diseases (ISID), which has been active for more than 25 years [3,4]. ProMED provided an early initial report of the outbreaks of COVID-19 in Wuhan, China, in late 2019 [4]. On

November 25, 2023, ProMED highlighted that children were presenting to hospital without cough or typical symptoms of pneumonia but with high fever and pulmonary nodules on imaging, rather than patchy lung consolidation [5]. ProMED commented on the large number of affected children, the speed of presentation, and the localization of cases to two main cities, and suggested that they are cases of community-acquired pneumonia due to exposure in schools [5]. The WHO and ProMED have clarified that it is too early to project whether this could be the start of another possible pandemic [2,5]. However, because the clinical presentation of these new cases of pediatric pneumonia is unusual, and large numbers of children have been affected in such a short time, identifying the infectious cause or causes is a matter of urgency [5].

Pneumonia in neonates and infants is a recognized cause of hospital-acquired pneumonia or an opportunistic infection in infants with comorbidities that include immune suppression [6]. In children aged 5 years or more and those of school age, community-acquired pneumonia can be due to bacteria, viruses, or *Mycoplasma pneumoniae* [6]. In children who are hospitalized with community-acquired pneumonia, the causative infectious organism is only identified in up to 80% of cases [6]. In up to 60% of cases, childhood pneumonia is due to pyogenic bacteria, mainly *Streptococcus pneumoniae*, which can be easily identified by sputum microbiology and culture [6]. Atypical pneumonia due to *Mycoplasma pneumoniae* is more challenging to diagnose and may occur in combination with

viral pneumonia due to adenovirus, RSV, influenza, or SARS-CoV-2 infection [7]. Seasonal respiratory infections, including *Mycoplasma pneumoniae*, RSV, and influenza, can affect children more severely than adults [7]. Also, new variants of SARS-CoV-2 and influenza virus continue to emerge and may co-exist with RSV in children [6].

These recent reports of pneumonia in children, hospitalized with atypical symptoms and signs, have directed attention to *Mycoplasma pneumoniae*, alone or in combination with RSV or SARS-CoV-2, as the cause of the outbreaks [1,2]. On November 23, 2023, Meyer Sauter and Beeton, on behalf of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Study Group for Mycoplasma and Chlamydia Infections (ESGMAC) and the ESGMAC *Mycoplasma pneumoniae* Surveillance (MAPS) study group, published a rapid commentary on the possible cause of these cases [7]. *Mycoplasma pneumoniae* is a common cause of community-acquired pneumonia that shows a pattern of infection outbreaks annually or every few years [7]. The infectious organism is atypical as it is one of the smallest and slowest self-replicating organisms, is transmitted by close contact, and generates a cell-mediated immune response [7].

Between 2017 and 2020, the pre-pandemic incidence of *Mycoplasma pneumoniae* pneumonia was identified by polymerase chain reaction (PCR) testing as 8.61% [7]. In early 2020, the introduction of nonpharmaceutical interventions (social distancing and lockdown) during the COVID-19 pandemic abruptly ended epidemics of *Mycoplasma pneumoniae* pneumonia, which continued into 2021/22 [7]. The first global prospective surveillance study of *Mycoplasma pneumoniae* pneumonia, the ESGMAC MAPS study, commenced in April 2022 and identified a sustained and very low incidence of *Mycoplasma pneumoniae* pneumonia in the third year from the start of the COVID-19 pandemic, from April 2022 to March 2023 (0-82%) [7]. However, despite the low levels of infection detection, between January and March 2023, there was an increase in cases in some countries [7]. In the six months between April 1 and September 30, 2023, prospective surveillance data from 45 sites in 24 countries in Europe, Asia, Oceania, and the Americas identified the mean incidence of *Mycoplasma pneumoniae* has increased to 4.12% [7]. This degree of delayed re-emergence of infection is unique to this pathogen, although both *Mycobacterium tuberculosis* and *Bordetella pertussis* also show some delay [7]. Loss of cell-mediated herd immunity may account for the delayed re-emergence of *Mycoplasma pneumoniae* [7]. However, no re-emergence has been identified in northern European countries, including Norway, Germany, and Finland, where previous epidemics of *Mycoplasma pneumoniae* were reported in 2017/18 [7]. It is also possible that factors associated with this atypical pathogen might explain the delayed time interval between re-establishing *Mycoplasma pneumoniae* pneumonia within a population, including the

relatively low transmission rate and the long incubation period of between 1 and 3 weeks [7].

Studies in Europe have shown the consequences of the COVID-19 pandemic and the relaxation of social restrictions (nonpharmaceutical interventions) on the transmission of other respiratory viruses, particularly pediatric RSV and influenza [8]. At the beginning of 2020 in the southern hemisphere, the COVID-19 lockdown measures resulted in a winter season with a significant reduction in pediatric RSV and influenza [8]. Pandemic lockdowns in the northern hemisphere interrupted pediatric RSV and influenza transmission during winter 2020/21, which were then followed by delayed RSV peaks [8]. In late 2022, in the U.S., there was a similar surge in a cluster of common respiratory pathogens that resulted in reports in the U.S. media of healthcare services being overwhelmed by pediatric emergency hospital admissions [9]. This wave of respiratory infections in children coincided with lifting COVID-19 pandemic restrictions, including reopening schools [9]. On November 4, 2022, the Centers for Disease Control and Prevention (CDC) in the U.S. recommended that healthcare providers offer prompt influenza and SARS-CoV-2 vaccination to all eligible individuals aged 6 months and older who are not up to date with their vaccines to prevent hospitalization and mortality associated with these respiratory infections [10].

The COVID-19 pandemic and the social and medical strategies required to limit transmission and infections globally affected other respiratory virus infections [11]. Although there were reductions in respiratory virus infections, including by influenza virus and RSV at the onset of the pandemic, respiratory virus evolution and host immunity rely on maintaining a diverse viral genetic pool and host immune response [11]. The epidemiological and disease surveillance findings from Europe and the U.S. support the possibility that the surge in pediatric cases of pneumonia is due to pathogens affecting an immune-naïve population following the lifting of China's zero-COVID policy, which commenced in early 2023 [2,5,7,8,10]. The terms 'immunity debt' and 'immunity gap' have recently been proposed for the effects of societal lockdown or nonpharmaceutical interventions during the COVID-19 pandemic [12,13]. There is also the possibility of coinfection in children with variants of SARS-CoV-2 and RSV [14]. They also highlight the importance of continuing to implement global infection surveillance programs with viral whole genome sequencing, phylogenetic analysis, and open data sharing and maintaining vaccine development and use in the pediatric population.

Conclusions

Recent reports of outbreaks of childhood pneumonia in northern China could be driven by post-pandemic changes in the

pathogenesis of endemic respiratory infections other than COVID-19, in a similar way to outbreaks reported in the U.S. and Europe in late 2022. Epidemiological evidence supports that, rather than emerging novel respiratory pathogens that target children, it is more likely that one or more re-emerging infections, such as RSV, influenza, or *Mycoplasma pneumoniae*,

are the cause. However, recent reports of increased hospitalizations for children with pneumonia warrant continued infection surveillance and monitoring to exclude new respiratory pathogens or more virulent variants of known pathogens, including SARS-CoV-2.

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