

Epidemiological Alert Anticipation of the onset of respiratory virus season

22 September 2023

Several countries from the southern hemisphere have been reporting an early start of the increase of acute respiratory infection during the recent 2023 season of circulation of respiratory viruses, suggesting a shift of seasonal pattern observed prior to the COVID-19 pandemic. Given this situation, the Pan American Health Organization / World Health Organization (PAHO/WHO) recommends that Member States of the northern hemisphere adjust prevention and control plans for respiratory virus epidemics to face an early onset of increased respiratory activity and a possible overload of health services. Measures for the prevention and control of respiratory virus infections should include early diagnosis and adequate clinical management, mainly among populations at high risk of presenting with severe disease, and ensuring respiratory virus vaccination, high vaccination coverage in high-risk groups, the adequate provision and organization of health services, strict compliance with infection prevention control measures, an adequate supply of antivirals, and well as effective risk communication for the public and healthcare professionals.

Situation Summary in the Region

In the most recent season of increased circulation of respiratory viruses in the southern hemisphere, several countries reported an early onset of increase cases and hospitalizations due to respiratory viruses. The situations faced by Argentina, Brazil, Chile, Paraguay, and Uruguay (cited in alphabetical order) are summarized (1). In addition, in the northern hemisphere, an advisory alerting all health professionals about the anticipated onset of increased respiratory syncytial virus (RSV) in the United States of America was issued by national authorities on 5 September 2023, specifically concerning southeast areas of the country (2).

The early onset of influenza and RSV circulation observed in the 2023 season, in some countries in the southern hemisphere, suggests a shift of the seasonal pattern observed in seasons prior to the COVID-19 pandemic and could be repeated in the current season in the northern hemisphere. This requires routine surveillance systems to have the capacity to detect changes in trends, while simultaneously requiring the capacity of rapid response from the health service to organize the flow of patients and provide adequate patient care management.

The following is a summary of the situation in select countries in the Region of the Americas.

In **Argentina**, the epidemic threshold for cases of influenza-like illness (ILI) began in epidemiological week (EW) 7 of 2023 and reached alert levels in EW 13 of 2023. An increase in pneumonia cases began in EW 8 of 2023, reaching outbreak levels in EW 20 and 21. Bronchiolitis cases began to increase in EW 10, reaching alert levels between EW 17 and EW 22, with the highest number of cases reported in EW 21. Influenza A cases started to increase in EW 18 of 2023 through EW 27, with the increase primarily cases of influenza A(H1N1)pdm09.

In 2023, an early onset of RSV activity was observed, as well as an early peak in bronchiolitis notifications (approximately 3-4 weeks earlier than that reported in prior years). A similar behavior was observed in relation to pneumonia, with a faster rise in cases compared to prior years, and a maximum level of cases reached a few weeks earlier than expected. Among those hospitalized, the highest proportion of RSV-positive cases was reported in children under 5 years of age, particularly in children under 1 year of age. Positive detections for influenza predominated in children under 5 years of age, followed by the 5- to 9-year-old group (3,4).

In **Brazil**, the onset of the increase in circulation of influenza and other respiratory viruses in 2023 occurred in EW 5. The southern and central-western regions were those that initially recorded the highest hospitalization rates. The largest proportion of hospitalized cases in children under 5 years of age was associated with RSV. As a result of this situation, between May and July 2023, seven states (Acre, Amapá, Paraíba, Pernambuco, Piauí, Rio Grande do Sul, and Santa Catarina) and one municipality (Boa Vista in Roraima State) declared a public health emergency due to the increase in cases that led to a significant increase in hospitalization rates.

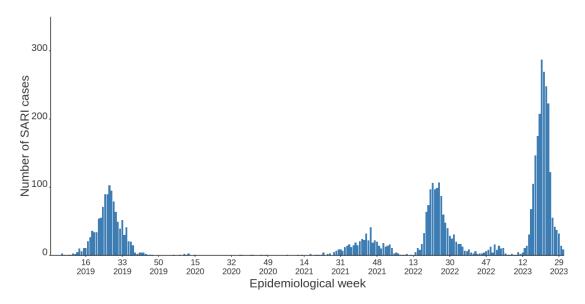
The onset of the increase in cases in Brazil occurred several weeks before the occurrence of the increase in prior years in which increases were reported between EW 10 and 21. In EW 11 of 2023, there was a notable increase of hospitalized cases due to influenza which peaked between EW 18 and 20; the hospitalized were mostly adults (20 to 59 years) and older people (60 years or older) (5).

In **Chile**, between EW 13 and EW 22 of 2023, there was an abrupt and significant increase in severe acute respiratory infection (SARI) cases associated with RSV being the largest increase in cases reported in the last 5 years (**Figure 1**). The largest number of cases were reported in EW 21 of 2023, five weeks prior to what was observed in previous years (6).

The increase in cases occurred in a very short period of time, leading to an increased demand on establishments of higher levels of emergency care and increase of hospitalizations due to respiratory conditions during an earlier period in comparison to pre-pandemic years and there was increased provision of pediatric intensive care beds to attend to the large flow of patients (**Figure 2**) (7).

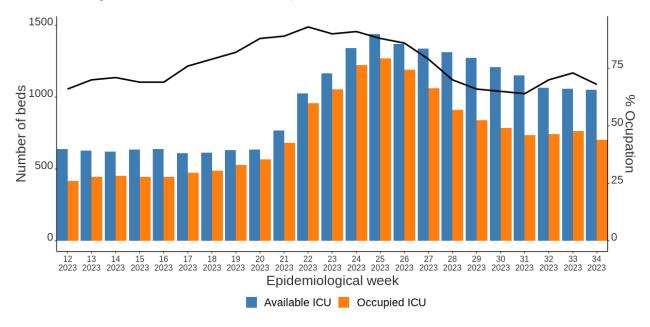
The greatest proportion of cases was reported among the age groups of one to four years old and children under one year old.

Figure 1. Severe acute respiratory infection (SARI) cases associated with RSV in sentinel hospitals by EW. Chile, 2019 to 2023 (until EW 36 of 2023)



Source: Adapted from Ministry of Health of Chile, Epidemiology Department. SARI Sentinel Surveillance Report. Santiago: MINSAL; 2023 [cited 19 September 2023]. Available from: http://epi.minsal.cl/

Figure 2. Availability and occupancy percentage of pediatric intensive care unit (ICU) beds of the Chile Integrated Assistance Network System, EW 12 to EW 34 of 2023.



Source: Adapted from Chile Ministry of Health. Daily Report - Respiratory Viruses Winter Campaign. Santiago: MINSAL; 2023 [cited 19 September 2023]. Available from: https://www.minsal.cl/informe-virus-respiratorios-campana-invierno-2023

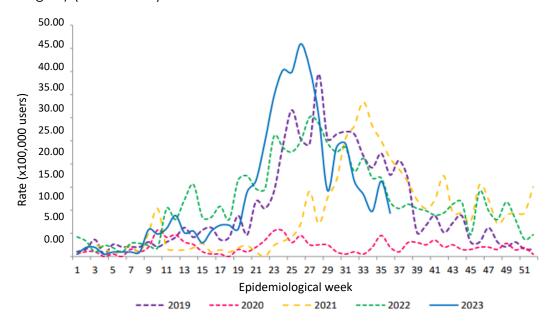
In **Paraguay**, EW 13 of 2023 saw the onset of increasing RSV cases among persons hospitalized with severe acute respiratory infection (SARI) as reported in sentinel centers; in contrast prior years had documented this increase as occurring around EW 16. In 2023, the peak of RSV associated hospitalized cases occurred between EW 21 and EW 27.

Between EW 1 to EW 35 of 2023, 1,384 RSV related hospitalizations were reported, of which 202 (15%) were in the Intensive Care Unit (ICU). The highest number of hospitalizations was reported in EW 24. The age group under 5-years of age represents the majority of hospitalized cases (87%). The average hospitalization stays were 7 days long (range 0 to 69 days). The onset of increased SARI activity was reported in EW 20 followed by a sustained increase in SARI cases and an increase in SARS-CoV-2 associated hospitalizations onset in EW 26 of 2023 (8).

In **Uruguay**, the increase in respiratory infections began in EW 17 of 2023. While the behavior of respiratory viruses in people over 15 years of age has been similar to that reported in the years prior to the COVID-19 pandemic, an increase of cases among children under 15 years of age, onset in EW 20 continuing through EW 28 of 2023; a higher and slightly earlier peak was reached than that reported in previous years. The viruses circulating in the greatest proportion were RSV, followed by influenza A(H1N1)pdm09, SARS-CoV-2, and Influenza B.

Up to EW 35 of 2023, emergency service medical consultations related to acute respiratory infection were predominantly among children under 15 years of age, with the onset of increased consultations for that age group occurring EW 16 of 2023 (9).

Figure 3. Cumulative SARI incidence among children under 15 years of age in sentinel centers, by EW. Uruguay (2019 – 2023).



Source: Adapted from Uruguay Ministry of Public Health. Uruguay – Acute Respiratory Infections EW 36 Update, 11 September 2023. Montevideo: MINSAL; 2023. Available from: https://www.gub.uy/ministerio-salud-publica/files/documentos/noticias/Infografia%20respiratorio%20110923.pdf

In the northern hemisphere, the **United States of America** issued a health advisory on 5 September 2023 through the US Centers for Disease Control and Prevention (US CDC) Health Alert Network (HAN) to alert doctors and caregivers about the increase in RSV activity in some

areas of the southeastern United States in recent weeks. The increase suggests a change from the seasonal RSV trends observed before the COVID-19 pandemic.

In the United States, the historically the increase in RSV cases was recorded in the fall with peaks in the winter. However, this increase pattern seems to have altered, since the COVID-19 pandemic, with an increase in cases beginning in summer and peaks occurring in autumn months (October and November). While the seasonal pattern of RSV activity has changed, the geographic pattern appears to have remained the same, with cases beginning in the state of Florida and the southeast before spreading to the northern and western United States. Historically, these regional increases correlate with the onset of the national RSV season, with increased RSV activity spreading to the north and west of the country over the 2 to 3 months following the onset. RSV can cause serious illness in infants, young children, and older adults (2).

Recommendations

Following is a summary of the key recommendations on surveillance, clinical management and prophylaxis, risk communication, and vaccination.

Surveillance

PAHO/WHO recommends Member States integrate surveillance of influenza, RSV, SARS-CoV-2, and other respiratory viruses into existing national platforms and report surveillance data weekly through the FluNET and PAHO/WHO FluID.

Member States are recommended to continue strengthening influenza like illness (ILI) sentinel surveillance and prioritize severe acute respiratory illness (SARI) sentinel surveillance by complementing it with other surveillance strategies to monitor epidemiological changes and viral circulation trends to evaluate transmission patterns, clinical severity, the impact on the health system and society, and identify risk groups for developing associated respiratory complications (10).

PAHO/WHO recommends Member States implement event-based surveillance to accompany indicator-based surveillance. Event-based surveillance is the organized and rapid capture of information about events that may pose a potential risk to public health. The information may come from rumors and other ad-hoc reports transmitted through formal (pre-established routine information systems) or informal -not pre-established routine information systems (i.e., media, direct communication from health care workers, or non-governmental organizations) channels. Event-based surveillance is a functional component of the early warning and response mechanism (11).

Respiratory events that are unusual should be investigated and reported in accordance with the International Health Regulations (12). Unusual events include cases with atypical clinical progression; acute respiratory infection associated with animal disease exposure or observed in travelers to areas prone to novel influenza virus emergence; SARI among health care professionals; or clusters of respiratory viral infections outside the regular circulation season.

As part of routine respiratory surveillance and for the etiological confirmation of unusual cases, nasopharyngeal and oropharyngeal specimens (or bronchial lavage in severe cases) should be obtained to detect respiratory viruses. Laboratory analysis of the most severe cases should always be prioritized, especially those admitted to ICU and fatal cases (deaths), where

processing tissue samples from the respiratory tract is also recommended when available. All biosafety measures for respiratory pathogens should be granted. The technical guidelines and diagnostic algorithms of the National Influenza Center or the national reference laboratory responsible for laboratory surveillance should be followed. The recommended testing algorithms for influenza, RSV and SARS-CoV-2 are available online from PAHO/WHO (13).

Influenza-positive specimens from severe cases or those with unusual presentations must be sent to the PAHO/ WHO Collaborating Center at the United States Centers for Disease Control and Prevention (CDC) in Atlanta for further characterization, according to WHO guidelines (14). Influenza A samples, for which the virus subtype cannot be determined (those positive for Influenza A but where the PCR for subtyping is negative or inconclusive), should also be sent immediately to the PAHO/WHO CC at the US CDC (14).

Influenza-positive specimens from animals, must be sent to the PAHO/WHO Collaborating Center at St. Jude's Hospital in Memphis, Tennessee, in the United States, for further characterization.

Clinical management and prophylaxis

Recommendations for the clinical management of patients with severe respiratory disease indicated in previous PAHO/WHO guidelines and Epidemiological Alerts and Updates continue to apply (15). Groups at higher risk of developing influenza-associated complications include children less than two years of age; adults over 65 years; pregnant or post-partum women; people with underlying clinical morbidity (e.g., chronic lung disease, asthma, cardiovascular diseases, chronic kidney disease, chronic liver disease, diabetes mellitus, neurological conditions such as central nervous system injuries and delayed cognitive development); people with immunosuppression (e.g., HIV/AIDS or due to medications); and people with morbid obesity (body mass index greater than 40) (16).

Any person with severe or progressive clinical presentation of respiratory illness should be treated with antivirals as soon as influenza is suspected or treated according to the recent guidelines in case of COVID-19 is suspected (17). Treatment should be initiated even before having laboratory confirmation of respiratory infection as treatment is more successful if started early. In persons with suspected or confirmed influenza virus infection with or at risk of severe illness (i.e., including seasonal influenza, pandemic influenza and zoonotic influenza), we suggest administering oseltamivir as soon as possible. We suggest not administering inhaled zanamivir, inhaled laninamivir, intravenous peramivir, corticosteroids, passive immune therapy macrolide antibiotic for treatment of influenza (16).

In settings where batch RT-PCR or other rapid molecular influenza assays (with similar high sensitivity and high specificity) are available and results expected within 24 hours, we suggest a strategy of testing for influenza, treating with oseltamivir as soon as possible, and re-evaluating treatment when the test result is available.

In settings where batch RT-PCR or other rapid molecular influenza assays (with similar high sensitivity and high specificity) are not available to provide results within 24 hours, we suggest a strategy of not testing for influenza and treating with oseltamivir as soon as possible.

For more details consult the WHO Guidelines for the clinical management of severe illness from influenza virus infections (16) and the WHO Clinical care of severe acute respiratory infections – Tool kit (18).

Guidelines for the clinical management of COVID-19, including the use of Antivirals, Monoclonal Antibodies, and Other Interventions for the Management of COVID-19 Patients (17) are available through the PAHO/WHO Technical Documents on Coronavirus Disease (COVID-19) (19) and the WHO Clinical management of COVID-19 (20).

With regards RSV clinical management and prophylaxis, young infants are at higher risk for severe complications and hospitalization with RSV infection and represent the highest morbidity burden. Many risk factors for RSV infections are like those identified for all-causes lower respiratory tract infections. There are no effective treatment and supportive care remains the cornerstone of clinical management. Currently, RSV treatment is symptomatic with no effective antiviral drugs. Passive immunization with monoclonal antibodies -palivizumab- constitutes an appropriate intervention to reduce severe acute respiratory infection by RSV among at-risk infants (21).

Palivizumab prophylaxis is available for children <24 months at increased risk of severe RSV disease, as it was associated with a 43% rate reduction of RSV-related hospitalizations among children with hemodynamically significant congenital heart disease, and a reduction in recurrent wheezing. The cost and method of administration of the drug remain a challenge, although its cost-effectiveness is well-documented (21).

Recently, two RSV vaccines for older adults were approved by the US Food & Drug Administration (FDA) (22, 23) for use in the United States for the prevention of lower respiratory tract disease (LRTD) caused by RSV in individuals 60 years of age and older. In clinical randomized trials, the vaccines reduced the risk of developing RSV-associated LRTD by 66.7%-6% and reduced the risk of developing severe RSV-associated LRTD by 94.1% (22). Currently there has been a resurgence of vaccine development (vaccine candidates and long-lasting immunoprophylaxis with monoclonal antibodies) along with significant progress in the understanding of immune responses to RSV.

Key recommendations for RSV clinical management include (24, 25, 26):

- The diagnosis of bronchiolitis and assessment of disease severity should be based on history and physical examination. Laboratory and radiologic studies should not be routinely ordered for diagnosis.
- Risk factors for severe disease such as age less than 12 weeks, premature birth history (particularly under 32 weeks), underlying cardiopulmonary disease (including bronchopulmonary dysplasia and haemodynamically significant congenital heart disease), neuromuscular disorders, or immunodeficiency should be assessed when making decisions about evaluation and management of children with bronchiolitis.
- Bronchodilators (albuterol, salbutamol), epinephrine, and corticosteroids should not be administered to infants and children with the diagnosis of bronchiolitis. Likewise, nebulized hypertonic saline should not be administered to infants with the diagnosis of bronchiolitis in the emergency department. Nebulized hypertonic saline may be administered to infants and children hospitalized for bronchiolitis.
- Antibiotics should *not* be used in children with bronchiolitis unless there is a concomitant bacterial infection.

- Palivizumab prophylaxis should be administered during the first year of life to infants with hemodynamically significant heart disease or chronic lung disease of prematurity (<32 weeks gestation who require >21% O₂ for the first 28 days of life).
- To prevent the spread of respiratory syncytial virus (RSV), hands should be decontaminated before and after direct contact with patients, after contact with inanimate objects in vicinity of patient, and after removing gloves. Alcohol rubs are the preferred method for hand decontamination. Clinicians should educate personnel and family on hand sanitation.
- Infants should not be exposed to tobacco smoke.
- Exclusive breastfeeding for at least 6 months is recommended to decrease the morbidity of respiratory infections.

Risk Communication

Seasonal influenza is an acute viral infection that spreads easily from person to person. Seasonal influenza viruses circulate worldwide and can affect anyone from any age group. Vaccination prior to the start of seasonal virus circulation remains the best preventive measure against severe influenza.

The public should be informed that the main mode of transmission of influenza is by interpersonal contact. Hand washing is the most efficient way to decrease transmission. Knowledge about "respiratory etiquette" also helps to prevent transmission.

People with fever and respiratory symptoms should avoid going to workplaces or public places until the fever subsides. Similarly, school-age children with respiratory symptoms and / or fever should stay at home and not go to school.

To leverage on the knowledge that most of the public has acquired on respiratory disease prevention -brought by the COVID-19 pandemic-, and to prevent confusion and exercise effective communication, Member States should consider developing risk communications strategies and campaigns that integrate prevention messaging for respiratory viruses. Integration of communication is also advised for the promotion of influenza and COVID-19 vaccination.

Vaccination

Immunization is an important strategy for preventing severe outcomes of seasonal influenza and COVID-19, including hospitalizations and associated deaths.

PAHO/WHO recommends vaccination of groups at particular risk of severe disease, including older adults, people with underlying conditions, children under 59 months and pregnant individuals. Health workers are at increased risk of exposure and transmission of influenza and SARS-CoV-2 virus and therefore should also be prioritized.

Apart from vaccination, personal measures such as hand hygiene, physical distancing, respiratory etiquette, mask use, and staying home when sick, should be observed, which are effective in limiting respiratory viruses transmission (27).

Non pharmacological public health measures in populations

As recently evidenced during the COVID-19 pandemic, non-pharmacological public health measures complement the response to respiratory events.

For more details consult the WHO guidance on Non pharmaceutical public health measures for mitigating the risk and impact of epidemic and pandemic influenza (27) and the PAHO/WHO Guidance for implementing non-pharmacological public health measures in populations in situations of vulnerability in the context of COVID-19 (28).

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Surveillance

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