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Legionnaire's looms: Europe's wake-up call to enhance vigilance in detection and reporting

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Legionellosis is a broad collective term encompassing all infections caused by members of the genus *Legionella*, including Legionnaires' Disease (LD; severe form), non-pneumonia Pontiac fever (mild form), and Pittsburgh pneumonia [1]. Legionnaires' disease, the most reported form, is caused by *Legionella pneumophila*, a gram-negative proteobacteria that is commonly found in warm locations (25–45 °C) within urban plumbing systems and freshwater environments [2,3]. The bacterium typically replicates within its protozoan host, the free-living aquatic amoebae, but has also been described as a bacterium associated with biofilms [4]. Human infection is mediated by inhalation of contaminated water aerosols from showers, humidifiers, air conditioners, fountains, respiratory devices, and spas.

In recent years, the European Centre for Disease Prevention and Control (ECDC) has noted an increase in the number of reported *Legionella* outbreaks and the number of confirmed cases in its member countries (Fig. 1). Between 2015 and 2021, the ECDC reported 127 outbreaks that were either community- or hospital-acquired in the European Union/European Economic Area (EU/EEA) region. Most outbreaks, defined as two or more cases linked by time and place of illness onset with suspicion of a common source of infection or history of travel, were sporadic and community acquired [5]. Among those with identified sources, 23 have been linked to hospitals and six to geriatric centres. Typically, outbreaks have been confined to Western European nations such as France, Germany, Italy, the Netherlands, Portugal, Spain, and the United Kingdom. This makes the recent outbreak that was reported in Poland in 2023 noteworthy since such an incidence has not been recorded in the country before (at least in the recent past).

1. The Polish outbreak, 2023

In mid-August 2023, the Polish authorities reported a suspected cluster of community-acquired pneumonia cases in the southeastern province of Podkarpackie, located near the Polish-Ukrainian border [6]. The State District Sanitary Inspector's data revealed an outbreak of *Legionella pneumophila* infections on July 3rd, 2023, with the highest incidence observed from August 12th to 16th, 2023. The latest case was reported on September 6th, 2023 [7]. As of September 11, 2023, a total of 166 cases were confirmed positive for *Legionella* infection through laboratory testing. All identified patients were hospitalized, with 23 deaths reported (12 female and 13 male patients aged 55–98 years; all presenting with comorbidities), resulting in a case fatality rate of 14 % [6]. Among the confirmed cases, 67 % of patients were residents of Rzeszów city, while 23 % were residents of Rzeszów county. The remaining 10 % of cases were reported from other counties.

These figures are atypical and exceed the preceding years' epidemiological reports. Poland documented 255 cases of Legionellosis from 2018 to 2021. Among them, 92.5 % were of LD, and 7.5 % were of Pontiac fever, with an 11 % estimated case fatality rate [8,9]. Globally, *Legionella* infections account for approximately 4.6 % of all community-acquired pneumonia cases with an estimated incidence rate of 2.8 cases per 100,000 population [10]. However, the number of reported cases worldwide is underreported, particularly in low- and middle-income countries, leading to an underestimation of true disease incidence and prevalence. Within the EU/EEA region, the ECDC reported that the case notification rate remained below 1 case per 100,000 population in 11 countries (including Poland) for the year 2021 [5].

2. Clinical diagnosis and treatment

Although *Legionella* inhalation or aspiration is not pathogenic as such, it can be fatal in older adults, particularly in males over 50 years of age, smokers, and individuals with chronic conditions or immunosuppression [2,3]. Clinical diagnosis for LD is usually guided by a combination of epidemiological, microbiological, clinical, and radiological investigations [11]. Given the sporadic nature of the cases and the acutely progressive course of disease, identifying the diagnosis in a

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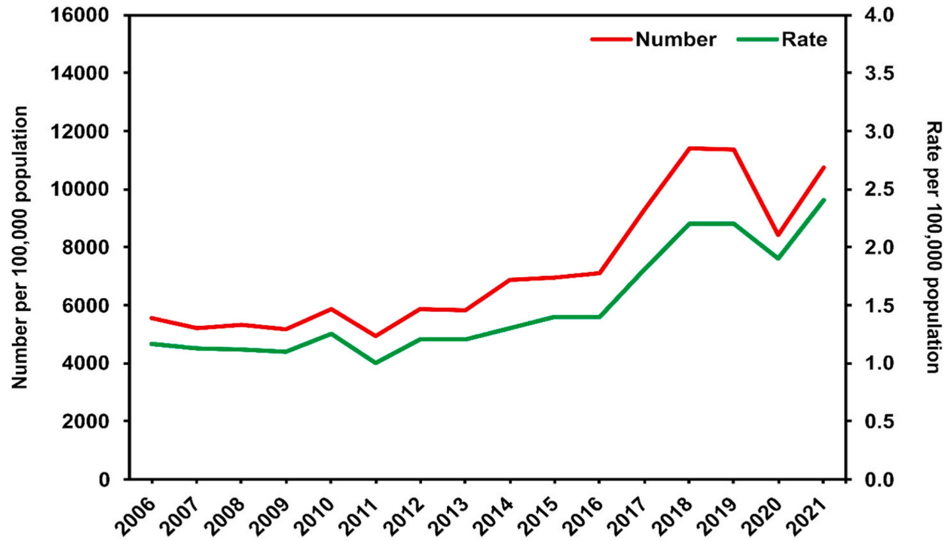

Fig. 1. Total number and rate of Legionnaires' disease cases per 100,000 population in the European Union/European Economic Area (EU/EEA) as compiled from ECDC annual epidemiological reports. Note that the United Kingdom (UK) withdrew from the EU in 2020 and hence the data presented here excludes data from the UK for 2020–2021 period.

timely manner is critical for effective patient management. Increased rainfall and higher temperatures have been shown to have a positive correlation with the incidence of LD. A recent systematic review found that the impact of precipitation can be observed with a two-week lag period preceding disease onset, while warmer temperatures (especially during June to October period) are associated with a lag period of nine weeks [12]. Contact tracing is aided by the fact that possible sources of contact are usually identified retrospectively through patient history including travel to regions with reported outbreaks. An incubation period of 2–14 days is typically used in case definitions, and recent evidence suggests that approximately 89 % of all cases develop symptoms within 2–10 days of exposure [13].

Microbiological detection of the bacteria is largely based on the results of the urine-antigen testing, a point-of-care first-line screening method that detects the lipopolysaccharides in the bacteria's cell wall [1]. However, the ability of the test to detect only *Legionella pneumophila* serogroup 1 (Table 1) and its variation in sensitivity (50–80 %; median 75 %) depending on the severity of the disease has limited its use to the acute phase of outbreak detection or in patients with severe community acquired pneumonia [1,11]. Isolation of bacteria on culture remains the gold standard for detection that aids antimicrobial resistance testing and serogroup identification [14]. Nonetheless, requirements of non-standard specific growth media – buffered activated charcoal yeast extract (BCYE) – and long incubation periods of up to two weeks limit its utility in quick diagnostics [14].

Moreover, cultures collected from outside the airways are rarely positive, and cultures collected from the lower airways are susceptible to contamination by oropharyngeal flora, requiring additional acidic pretreatment. Nucleic acid-based polymerase chain reaction (PCR) tests offer superior detection capabilities, but their usefulness is limited by the requirement for personnel with relevant expertise. According to ECDC's 2021 Annual Epidemiological Report, 89 % of all cases were detected through urinary antigen tests, while only 11 % were identified through culturing. PCR testing was used on only 12 % of all samples [5], highlighting the under-utilization of the technique among member states. In the recent Polish outbreak, a case report mentioned the use of both PCR and urinary antigen tests for confirmation of *Legionella* infection in a 53-year-old patient [9].

Table 1
Most common *Legionella pneumophilia* serogroups (% of all reported cases to ECDC) in EU/EEA for 2017–2021.*

Serogroup	2017	2018	2019	2020	2021
Lp1	79 %	85 %	83 %	83 %	82 %
Lp3	No information	3 %	3 %	3 %	4 %
Lp6	No information	1 %	2 %	2 %	1 %
Serogroup unknown	No information	7 %	7 %	8 %	9 %

* Data source - European Centre for Disease Prevention and Control (ECDC) annual epidemiological reports.

Clinically and radiologically, the presentation of *Legionella*-associated pneumonia is indistinguishable from other causes of pneumonia. Moreover, there are no clinically significant distinctions in presentation between various *Legionella* species and serogroups [15]. Predominant unspecific symptoms involve fever, cough, fatigue, and dyspnoea. However, a registry audit comparing clinical symptoms between pneumonia associated with *Legionella* and non-*Legionella* species found significant associations (Fisher's Exact $P < 0.05$) between the cause of pneumonia and fever (>39 °C), hyponatremia (<133 mEq/L), and urine protein levels >30 [16]. Failure to response to beta-lactam monotherapy can also be suggestive of *Legionella* as the causative agent [9]. Extrapulmonary manifestations remain rarely reported and mostly in immunocompromised patients. On chest X-rays, pneumonia and unilobar patchy infiltrates (inflammatory lesions) progressing to consolidations may be seen.

Current treatment guidelines recommend the use of either fluoroquinolones like levofloxacin or macrolides like azithromycin as first-line options [17]. Recent systematic reviews and meta-analyses have demonstrated non-superiority of these agents in preventing mortality over each other [18,19], though fluoroquinolones may be associated with shorter length of hospital admission [20]. In the case reported from the Polish outbreak, the patient was initially treated with levofloxacin monotherapy before initiation of combination therapy with clarithromycin due to reappearance of fever and negative culture results [9]. Combination therapy with clarithromycin and levofloxacin has been shown to have *in-vitro* synergistic effects ($P < 0.001$) [21].

3. Future directions

Until September 20th, 2023, the State District Sanitary Inspector collected 257 samples of hot and cold water from the city's water supply system for testing. Out of those, 27 samples were found to be positive for *Legionella pneumophila* bacteria [7]. This has prompted the local authorities to open an investigation into intentional tampering of the city's water supply, though no such signs have been identified yet. The inspectorate has additionally, taken measures at the local level, such as conducting epidemiological interviews with patients and their families to rule out infections related to travel, providing enhanced surveillance of at-risk institutions like nursing homes, care facilities, hospitals, and group residences, and deactivating fountains and water curtains across the city [7]. The water supply network has also underwent disinfection and washing, coupled with a simultaneous increase in the levels of chlorine, ultraviolet radiation, and ozone used in water treatment to the maximum permissible values. Daily crisis team meetings are planned at the mayor's office.

Moving forward, it is essential for Poland and other EU member states to implement strict monitoring strategies in adherence to the EU directive 2020/2184 (On the quality of water intended for human consumption; dated December 16, 2020) [22,23]. Nonetheless, the Polish authorities have denied the failure to implement the EU directive as a potential cause of the current outbreak [24]. At the same time it is important to note that the World Health Organization (WHO) has identified *Legionella* as a major cause of waterborne illnesses in EU-member states, primarily resulting from contamination in domestic distribution systems [22]. Accordingly, the EU directive 2020/2184 requires that the concentration of *Legionella* for risk assessment in domestic distribution systems should be < 1000 CFU/L (colony forming units/litre). However, in cases of confirmed *Legionella* (along with species identification) infections and outbreaks, a lower threshold might be considered by the member states [22].

The rise in *Legionella* outbreaks throughout the EU/EEA region highlights the necessity for a unified public health strategy to combat the escalating hazard. This necessitates the development of capacity, employing relevant diagnostic testing, promptly reporting cases, public health education, and enforcing stringent water safety protocols in domestic water supply systems.

a. Ethics approval

Not Applicable. All data presented here as been sourced from open-source information with appropriate citations.

b. Data availability

All data presented here as been sourced from open-source information with appropriate citations.

c. Consent to publish

Not Applicable.

d. Funding

Not Applicable.

e. Conflict of interest

None to declare.

g. Author contributions

NJ conceptualized and prepared the present the initial draft of the editorial. NJ and AMK collected and analysed data. Both authors have read and agreed to the contents of the final draft for publication.

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