



Pantoea Agglomerans: An Emerging Pathogen in Hospitals and Foods, A Narrative Review

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ABSTRACT

Introduction: *Pantoea agglomerans* is recognized as an opportunistic pathogen with a significant impact on human health. Despite its ubiquity in various environmental sources, its role in nosocomial infections and the potential for antibiotic resistance necessitate a thorough investigation. This study aims to investigate the evolutionary history and identify various aspects of the bacterium, *P. agglomerans*. A comprehensive review of literature from 1994 to March 2022 was conducted to elucidate the evolutionary trajectory of the *Pantoea* genus. Key search terms included "Pantoea," "P. agglomerans," "Enterobacter," and "E. agglomerans." This study prioritizes human-related research, adhering to strict inclusion and exclusion criteria.

Methods: A comprehensive review of literature from 1994 to March 2022 was conducted to elucidate the evolutionary trajectory of the *Pantoea* genus. Key search terms included «*Pantoea*,» «*P. agglomerans*,» «*Enterobacter*,» and «*E. agglomerans*.» This study prioritizes human-related research, adhering to strict inclusion and exclusion criteria.

Results: The results demonstrate that *P. agglomerans* are susceptible to imipenem, fluoroquinolones, aminoglycosides, broad-spectrum cephalosporins, and trimethoprim-sulfamethoxazole. Preventive strategies, particularly in hospital environments, are crucial to control the spread of this pathogen. These include stringent infection control practices, alcohol-based hand sanitizers, comprehensive hand hygiene education, and robust hospital-based surveillance protocols.

Conclusion: This study underscores the importance of advanced molecular diagnostic techniques in accurately identifying *P. agglomerans*. The findings also highlight the critical role of effective antibiotic therapy and rigorous infection control measures in managing and preventing *P. agglomerans* infections. Continuous surveillance and further research are essential to develop advanced diagnostic and therapeutic strategies, ensuring better clinical management and preventing infections caused by this pathogen.

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Introduction

Pantoea agglomerans which is one member of the *Enterobacteriaceae*, is characterized as a Gram-negative rod (1). Within this taxonomic

classification, *P. agglomerans* exhibits motility, lacks sporulation, and presents as a Gram-negative, aerobic, peritrichous bacillus. Notably,

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when cultivated in liquid media, *P. agglomerans* can generate sausage-shaped aggregations or symplasmata, comprising chains of spherical bodies measuring 7-13 μm in diameter, nested within a matrix (2). The terminology "Pantoea" originates from the Greek term "pantoios," signifying "of all sorts and sources," a reflection of the diverse geographic and ecological reservoirs from which these bacteria emerge (3). The specific epithet "agglomerans" pertains to the propensity of certain anaerobic strains to form bacterial aggregates encased within a translucent sheath (4). Moreover, the genomic G+C content of *P. agglomerans* DNA ranges between 55.1-56.8 (Tm). In recent taxonomic revisions, *Enterobacter agglomerans* and related taxa within the "*E. agglomerans* group" have undergone reclassification into the genus *Pantoea* (5). The establishment of the genus *Pantoea* dates back to 1989, with its type species designated as *P. agglomerans* (6). The assemblage known as the *E. agglomerans* group exhibits a heterogeneous and intricate nature, with several species being proposed to encompass strains formerly classified within this taxon. Notably, *E. agglomerans* and various species within the *E. agglomerans* complex form a distinct cluster separate from *E. cloacae* (7). The designation "*E. agglomerans* complex" encompasses a considerable number -20 to 40 genomic groups or phenons. Beyond this genomic diversity, strains within this complex lack close genetic relatedness to *E. cloacae* based on DNA hybridization studies. Certain members of this complex have been allocated to novel genera, such as *Rahnella aquatilis*, *Ewingella americana*, and *Leclercia adecarboxylata*. Notably, the proposal of the genus *Pantoea* has been set forth for various clusters within the *E. agglomerans* complex (8-10). The genus *Pantoea* can be categorized into two distinct groups of species: (1) the "Japanese" group, comprising *P. citrea*, *P. punctata*, and *P. terrea*, and (2) the *Pantoea* core group, encompassing *P. agglomerans*, *P. dispersa*, *P. ananatis*, and *P. stewartii* (11). The core group of species demonstrates the ability to utilize d-alanine, l-alanine, myo-inositol, dl-lactate, 1-O-methyl-b-d-glucoside, and l-serine as sole carbon sources. In contrast, the "Japanese" group lacks this capability. Moreover, two species within the "Japanese" group cannot utilize l-arabinose and d-mannitol, whereas all species within the core group exhibit proficiency in metabolizing these carbohydrates. Enzymatic assays reveal that all three species within the "Japanese" group exhibit positivity for the enzyme 2-ketogluconate dehydrogenase, with two species also testing positive for arginine dihydrolase activity. In

contrast, species within the core group yield negative results for both enzymatic activities (11,12). This study aimed to comprehensively investigate the evolutionary history of the *Pantoea* genus, with a specific focus on *P. agglomerans*. The study prioritizes human-related research, adhering to rigorous inclusion and exclusion criteria. This article emphasizes the importance of advanced molecular diagnostic techniques, effective antibiotic therapy, and robust infection control measures in the management and prevention of *P. agglomerans* infections.

Materials and Method

A comprehensive narrative review of the literature from 1994 to August 2019 was conducted to elucidate the evolutionary trajectory of the *Pantoea* genus. This timeline underwent meticulous scrutiny prior to publication and was subsequently updated to encompass data up to March 2022. The principal research methodology entailed an exhaustive online inquiry conducted in September 2019 utilizing databases such as Google Scholar and PubMed. Key search terms employed included "*Pantoea*," "*P. agglomerans*," "*Enterobacter*," and "*E. agglomerans*." Applying evidence-based medicine competencies guided the formulation of inclusion and exclusion criteria. These competencies encompass the identification of pertinent issues, retrieval of relevant literature, and critical appraisal thereof, culminating in the synthesis of gathered information. Preference was given to studies involving human models.

Inclusion criteria:

1. Inclusion of at least two of the designated search terms in the title or abstract OR
2. A substantial amount of discussion (spanning at least two pages) on at least two search terms should be included within the body of the publication. OR
3. Papers that addressed at least two search terms thematically, regardless of whether they were explicitly stated.

Exclusion criteria:

1. Exclusion of papers published over 25 years prior to the search period (i.e., before 1994)
2. Exclusion of meta-analyses or systematic reviews published over a decade prior to the search period (i.e., before 2009)
3. Exclusion of papers focusing solely on a single search term failing to meet the aforementioned inclusion criteria
4. Exclusion of papers addressing one or more search terms primarily concerned with alternative forms of drug resistance or other bacterial species (e.g., methicillin-resistant *Staphylococcus aureus*).

Results & Discussion

Upon reviewing various articles, the gathered information was categorized and discussed under the following sections.

Epidemiology

In terms of epidemiology, *P. agglomerans* is ubiquitously present as an environmental commensal, inhabiting diverse niches such as fruits, vegetables, and aqueous environments like toilet water, and sporadically manifests as an opportunistic pathogen, particularly implicated in intravenous (IV) catheter-associated infections, wound infections, and bacteremia, as well as endocarditis among intravenous drug users (IVDUs) (17,36). The prevalence and distribution of microbial communities on fresh fruits and vegetables exhibit considerable variability contingent upon factors such as the specific produce type and the extent of post-harvest processing (37,38). Notably, *P. agglomerans* emerges as a prominent constituent of the epiphytic microflora inhabiting numerous vegetables, owing partly to its adeptness in outcompeting indigenous microbial populations, possibly attributable to its synthesis of potent antimicrobial agents (17,36).

Reservoirs

P. agglomerans, an opportunistic pathogen, has been sporadically linked to disease etiology. Its presence has been documented in bodily fluids such as blood, wounds, internal organs, and urine (18). Additionally, *P. agglomerans* exhibits widespread environmental distribution, being commonly identified in food items, floral arrangements, seeds, vegetables, water reservoirs, soil matrices, and diverse plant species. Its clinical significance stems from its capacity to incite endogenous nosocomial infections, thereby posing a considerable threat within healthcare facilities (19). Hospitalized cohorts are particularly vulnerable to outbreaks facilitated by *P. agglomerans*, which may arise due to their adeptness in thriving within commercial infusion solutions. Such outbreaks not only heighten patient susceptibility to infection but also strain healthcare infrastructures, potentially impeding hospitals (18,20). Although nosocomial incidents involving *P. agglomerans* are infrequently reported, certain risk factors predispose individuals to acquiring infections, including the complexity of intravenous hydration compositions, as well as medication handling practices. Investigation into a specific outbreak attributed its origin to a transfer tube, suggesting potential contamination via staff contact (18).

Notably, certain *P. agglomerans* isolates exhibit an animal origin, with documented pathogenicity encompassing gall formation on *Wisteria japonica* and *W. floribunda*, as well as stalk and leaf necrosis on onion plants, and gall formation on *Gypsophyla paniculata* (17).

Metabolism

The species exhibits all the phenotypic traits characteristic of the genus *Pantoea*. Specifically, *P. agglomerans* displayed a notably faster growth rate in a 5% dextrose solution at 25°C compared to other members within the *Enterobacteriaceae* family (13). Strains of *P. agglomerans* demonstrated robust growth on nutrient agar at 30°C, while growth was inhibited at 44°C. Some strains exhibited diminished growth rates at temperatures of 40 or 41°C. The biochemical profiles are detailed in Table 1 (14). The phenotypic profiling of *P. agglomerans* isolates from various geographical locales, encompassing samples from animals, plants, and clinical sources, has been systematically conducted. Notably, the Voges-Proskauer (VP) test yielded negative results, while the Methyl Red (MR) test was positive when *P. agglomerans* strains were examined at 31°C, although VP positivity was often observed at 30°C (15). Furthermore, none of the strains displayed ornithine decarboxylase activity (16). *P. agglomerans* isolates exhibit the capability to mitigate environmental contamination by oxidizing H₂ or acetate to reduce highly toxic metals, including Cr(VI), Mn(IV), and Fe(III) (17).

Infections caused by *P. agglomerans*

P. agglomerans is the preeminent species within the diverse genus *Pantoea*, garnering considerable clinical significance and frequent isolation. Nonetheless, its attribution as a human pathogen remains contentious due to taxonomic ambiguities and scant data on spontaneous infections instigated by this microorganism (21). Notably, in the early 1970s, *P. agglomerans* precipitated a nationwide septicemia outbreak from contaminated intravenous fluids (22). Subsequent occurrences include its detection in blood samples amidst outbreaks linked to tainted medical apparatus and intravenous substances. *Pantoea* species, including *P. agglomerans*, inhabit various niches such as soil, plants, and fecal matter, where they may assume commensal or pathogenic roles. Incidences of soft tissue or osteoarticular infections following vegetative penetrating trauma have been documented (23). Moreover, *P. agglomerans* bacteremia has been associated with contaminated blood products,

Table 1. The general types of chemical tests used for the detection of the *P. agglomerans*

Characteristic	Result
Motility (36°C)	+
Yellow pigment	d
Indole production	-
Malonate (Leifson)	+
beta-Xylosidase test	d
Voges-Prokauer	+
Gelatin hydrolysis at 22°C	(+)
Arginine dihydrolase	-
Phenylalanine deaminase	d
Glucose dehydrogenase	+
Gluconate dehydrogenase	+
2-ketogluconate dehydrogenase	-
Esculin hydrolysis	+
Nitrate reduced	+
ONPG hydrolyzed	+
Acid from:	
_l -Arabinose	+
_D -Arabitol	+
Cellobiose	d
Dulcitol	-
meso-Erythritol	-
Glycerol	(d)
myo-Inositol	(d)
Lactose	d
Maltose	+
d-Mannitol	+
Melibiose	-
Raffinose	(d)
_l -Rhamnose	+
Salicin	+
d-Sorbitol	-
Sucrose	+
Trehalose	+
_D -Xylose	+
Utilization of:	
trans-Aconitate	+
Adonitol	-
L-Arabinose	+
_D -Arabitol	+
_l -Arabitol	-
Betaine	-
Cellobiose	(d)
Citrate	d
Dulcitol	-
meso-Erythritol	-
L-Fucose	-
_D -Galacturonate	(+)
Gentiobiose	-
_D -Gluconate	(+)
myo-Inositol	+
5-Ketogluconate	-
Lactose	-
Lactulose	-
_D -Malate	(+)
Maltose	(+)
Maltotriose	(+)
_D -Melibiose	-
1-O-Methyl--galactoside	-
3-O-Methyl-d-glucose	-
1-O-Methyl-b-d-glucoside	(+)

Protocatechuate	-
Quinate	-
_D -Raffinose	-
_l -Rhamnose	+
_D -Saccharate	(+)
_D -Sorbitol	-
Sucrose	(+)
_D -Tagatose	-
_D -Tartrate	(+)
_l -Tartrate	-
meso-Tartrate	(+)
Trigonelline	-
Xylitol	-
_D -Xylose	+

Symbols: +, 90–100% of strains positive in 1–2 days; (+), 90–100% of strains positive in 1–4 days; -, 90–100% of strains negative in 4 days; d, positive in 1–4 days; (d), positive in 3–4 days

propofol anesthesia, total parenteral nutrition, and intravenous fluids (23). Although infections attributed to *P. agglomerans* are infrequent in pediatric populations, sporadic bloodstream, soft tissue, and osteoarticular infections have been reported (23). Particularly in children with central venous catheters, *P. agglomerans* bacteremia may manifest concomitantly with other conventional pathogens. Diagnosing bone and joint infections, notably chronic osteomyelitis, attributable to this bacterium is often impeded by limited clinical suspicion and its insidious presentation. Notably, trauma involving soil-laden objects or vegetation should prompt consideration of *P. agglomerans* as the etiological agent (23–25). *P. agglomerans* boasts diverse potential applications, including its utility as a reservoir for anticancer lipopolysaccharides and as a biocontrol agent against plant diseases, fostering interest among researchers and stakeholders (26–29). Certain studies have illuminated associations between *P. agglomerans* bacteremia and predisposing factors such as blood group A, antacid therapy, and upper gastrointestinal ailments (7). However, even in immunocompromised individuals, infections induced by this bacterium exhibit mild clinical courses and favorable prognoses. Polymicrobial infections often feature *P. agglomerans* alongside established pathogens (7).

Pathogenicity And Virulence Factors Lipopolysaccharide (LPS)

LPS constitutes the primary surface antigenic markers within Gram-negative bacterial entities, notably *P. agglomerans* (1). This molecule class assumes responsibility for the endotoxin activity inherent in Gram-negative organisms. Specifically, the lipid A moiety emerges as the

central constituent of LPS governing the clinical manifestations associated with endotoxin activity during *P. agglomerans*-induced sepsis. Such manifestations include hemorrhage, fever, shock, and vascular collapse. Additionally, endotoxin can instigate complement activation and precipitate disseminated intravascular coagulation (DIC) (1).

Ice nucleation activity

Regarding ice nucleation activity, *P. agglomerans* exhibits a distinctive capability in initiating the formation of ice nuclei, thereby fostering the creation of ice crystals. These ice crystals, even at relatively warm temperatures ranging from -2 to -5 degrees Celsius, can injure plant tissues, inducing frost damage (2,3). Notably, the ice nuclei generated by *P. agglomerans* are extruded from the bacterial outer membrane in the form of protein-laden vesicles, typically measuring 50-300 nanometers in diameter. These vesicular structures bear resemblance to previously described endotoxin-containing vesicles (3,7).

Hypersensitive response and pathogenicity (*hrp*) system: The process of gall formation by *P. agglomerans* pv. *Gypsophilae* is intricate and governed by several factors, notably including the quorum-sensing (QS) system, phytohormones, and the *hrp* system (30). The *hrp* system constitutes a cluster of genes encoding proteins pivotal for the bacterium's ability to infiltrate the host plant and induce disease. Phytohormones, plant-derived signaling molecules, can be generated either by the bacterium itself or by the infected host plant in reaction to the intrusion (31).

Plasmides

150 kb pPATH plasmid

The 150 kb pPATH plasmid harbored by *P. agglomerans* encompasses a pathogenicity island (PI) crucial for eliciting tumor formation across a spectrum of plant hosts (17).

Large *Pantoea* Plasmid (LPP-1)

The Large *Pantoea* Plasmid (LPP-1), ubiquitous among all identified *Pantoea* species, plays a fundamental role in various physiological processes of the bacterium. These encompass but are not limited to the assimilation of inorganic ions, the transport and breakdown of diverse substrates, host and environmental colonization, pathogenicity, antibiosis, and resistance to antibiotics and heavy metals. The functional repertoire of LPP-1 is contingent upon the specific *Pantoea* strain and species (17,32,33).

The type III secretion system (T3SS)

The T3SS is a pivotal pathogenicity factor of

P. agglomerans. Functioning as an extracellular apparatus, the T3SS is employed by numerous Gram-negative bacteria to transport effector proteins directly into the cytosol of both animal and plant cells via needle-like injectisomes or pili. These effector proteins play a critical role in manipulating host cell defenses, thereby facilitating successful colonization and proliferation of the pathogen. The presence of T3SS has been unequivocally identified within the *Pantoea* genus, encompassing *P. agglomerans* and its closely related counterpart *P. stewartii* subsp. *stewartii*, the etiological agent responsible for Stewart's bacterial wilt and leaf blight in maize. *Pantoea* species employ two distinct T3SS systems, designated as PSI-1 (*Pantoea* Secretion Island 1) and PSI-2, to achieve effective host colonization. Additionally, investigations have revealed the existence of a third T3SS system in *P. stewartii* subsp. *stewartii*, analogous to that observed in *Salmonella* spp., which has been designated as PSI-3. PSI-1 and PSI-2 are inherited vertically through evolutionary processes, while *Pantoea* species obtain PSI-3 horizontally through genetic exchange events with other members of the Enterobacteriaceae family, such as *Salmonella* spp. and *Yersinia* spp. This observation provides insights into the capacity of specific *Pantoea* strains to infect vertebrate animals and humans.

Immune response

The immune response elicited by *P. agglomerans* stems from the production of endotoxin, also called lipopolysaccharide (LPS), which serves as the predominant trigger for cytokine release by Gram-negative bacteria (34). Upon encountering this microbial stimulus, LPS interacts with cell receptors present on the host's macrophages, thereby instigating the activation of regulatory proteins, notably nuclear factor kappa B (NF- κ B). The engagement of LPS with its cognate receptors, including the CD receptors and Toll-like receptors (TLRs), orchestrates the formation of the LPS-binding protein complex on the cell surface and facilitates the transmission of the signaling cascade into the cellular milieu (35) "type": "article-journal", "volume": "288", "uris": ["http://www.mendeley.com/documents/?uuid=c22fd594-2e0f-4606-9aa5-0d5cd6ea4fcd"], "mendeley": {"formattedCitation": "(35. Through this intricate mechanism, LPS drives the initiation of the inflammatory response while concurrently activating the coagulation and complement cascades, culminating in the pathogenesis of adult respiratory distress syndrome (ARDS), DIC, and multiple organ dysfunction syndrome (MODS) (43).

Diseases

P. agglomerans, while not characterized as an obligate pathogen of human, exhibits a proclivity for instigating opportunistic infections in human hosts, predominantly manifesting in two primary contexts: 1) hospital-acquired infections, and 2) wound infections associated with plant-derived materials. Notably, this bacterial species is implicated in a spectrum of infections occurring within both community and hospital settings, irrespective of the host's immunological status. These infections encompass a wide array of clinical presentations, including but not limited to septic arthritis or synovitis, endophthalmitis, corneal infiltrate, periostitis, endocarditis, osteomyelitis, tibial osteitis, tumor-like muscle cysts, bacteremia, septicemia in adult oncologic patients, infectious pneumonia, liver abscesses, and acute unilateral dacryocystitis (31, 49). Wound infections attributable to *P. agglomerans* commonly arise after skin lacerations or punctures inflicted by wooden splinters, plant thorns, or analogous plant-derived materials. Such injuries frequently occur during gardening, recreational activities, or agricultural pursuits, with the bacteria gaining ingress into the wound from the surface of the implicated plant (31, 50). Moreover, *P. agglomerans* has been identified as a constitutive component of the microbiota present in chronic periodontitis lesions, thereby posing an escalated risk for systemic infections, particularly among hospitalized and immunocompromised cohorts. Furthermore, it is noteworthy that *P. agglomerans* emerges as a relatively prevalent etiological agent of peritonitis among mature patients with renal failure undergoing peritoneal dialysis (31). The clinical presentations of infections attributed to *P. agglomerans* are heterogeneous and opportunistic, predominantly afflicting immunocompromised individuals. In most instances, the disease progresses mildly, and administration of appropriate antibiotic therapy culminates in complete recovery (4, 51). Instances of hospital-acquired infections stemming from *P. agglomerans*, wherein the source of contamination has been ascertained, encompass scenarios such as endocarditis in patients exhibiting mitral valve leaflet prolapse, septicemia subsequent to blood transfusion, septicemia in malignancy patients attributable to contaminated catheters, ventilator-associated pneumonia in individuals with chronic renal failure, and pneumonia in heart-lung transplant recipients post-transplantation (31, 52, 53). Notably, nosocomial septicemia instigated by *P. agglomerans*, boasting a mortality rate of 13.4%, has been traced back to factory-contaminated

screwcaps affixed to bottles containing intravenous fluids (31). Furthermore, instances of nosocomial sepsis attributed to *P. agglomerans* and *Enterobacter cloacae*, originating from screwcaps adorning bottles containing intravenous fluids, have been reported among infants and children, with a mortality rate of 6.3% (54). Additionally, septicemia coupled with respiratory failure, with an associated mortality rate of 87.5%, has been documented among neonates in intensive care units, purportedly stemming from parenteral nutrition solutions tainted with *Pantoea* spp. (55).

P. agglomerans in powdered infant formula (PIF) milk

P. agglomerans, a prevalent multidrug-resistant bacterium, poses a significant threat to the safety of PIF. Its robust viability and capacity for proliferation at ambient temperatures exacerbate the risk of contamination within PIF. Moreover, certain stressors, such as the pasteurization process, can induce a viable but non-culturable (VBNC) state in bacteria, further complicating detection and eradication efforts (1). Healthcare practitioners in neonatal units must recognize that PIF is inherently non-sterile and susceptible to bacterial colonization. The ingress of *P. agglomerans* into PIF primarily occurs through two avenues: intrinsic and extrinsic contamination. Intrinsic contamination arises from tainted ingredients introduced post-drying or from the processing milieu post-drying but pre-packaging. Conversely, extrinsic contamination arises during PIF reconstitution and handling processes. To mitigate the risk of PIF contamination, adherence to stringent good manufacturing practices (GMPs) is imperative. Such measures encompass the utilization of premium, adequately sanitized ingredients, maintaining hygienic processing environments, and the implementation of proper reconstitution and handling protocols (1).

Antimicrobial Resistance of *P. agglomerans*
Pantoea spp., notably *P. agglomerans*, exhibit significant resistance to first-generation cephalosporins primarily attributable to the expression of a beta-lactamase enzyme displaying predominant cephalosporinase activity. Moreover, a considerable proportion of these strains demonstrate resistance to chloramphenicol, streptomycin, and tetracycline (46).

Laboratory Detection

Culture And Biochemical-Based Identification:

The morphological characteristics of *Pantoea* spp. colonies are typically observed to possess a slight mucoid appearance, albeit with a relatively modest production of extracellular material. Notably, in *P. agglomerans*, the presence of an ochre or rusty yellow pigment is discernible. Extended incubation periods reveal the development of granular structures, denoted as symplasmata, alongside biconvex bodies exhibiting distinct margins, believed to signify downgrowths into the growth medium (47). Notably, *P. agglomerans* exhibits limited growth on MacConkey agar and does not elicit hemolysis on blood agar. Liquefaction of gelatin is typically initiated within a span of 6-10 days. Optimal growth is observed within the temperature range of 20°C to 37°C, with the latter being the preferred temperature for cultivation. Given the likelihood of encountering mixed microbial populations in clinical specimens, selective culture media are indispensable for isolating pertinent *Pantoea* species. Three principal categories of media are commonly employed for the retrieval of Enterobacteriaceae from such specimens, including nonselective media for initial isolation (e.g., blood agar), selective or differential agars (e.g., MacConkey and Hektoen enteric agars), and enrichment broths. Furthermore, *P. agglomerans* typically demonstrates resist Fosfomycin, thereby serving as a practical and straightforward test for the presumptive identification of this bacterium (47).

Molecular Detection of *P. agglomerans*

The molecular detection of *P. agglomerans* involves the utilization of the 16S rRNA gene sequencing method, a technique acknowledged for its utility in the identification of the aforementioned bacterium (1). However, it is imperative to acknowledge that this method, while valuable, does not singularly confer a definitive diagnosis. Thus, complementary molecular-based approaches, such as whole-genome sequencing or multilocus sequence typing, are indispensable for achieving a more exhaustive comprehension of *P. agglomerans* (1).

Treatment of infection caused by *P. agglomerans*

Regarding treating infections induced by *P. agglomerans*, it is noteworthy that this bacterium generally exhibits susceptibility to a broad spectrum of antibiotics. Notably, these include but are not limited to imipenem, fluoroquinolones (e.g., ciprofloxacin and ofloxacin), aminoglycosides (e.g., amikacin,

gentamicin, and tobramycin), broad-spectrum cephalosporins, and trimethoprim-sulfamethoxazole (1,2).

Prevention Strategies

P. agglomerans and closely related species warrant classification as biosafety level 2 (BL2) organisms due to their potential health hazards arising from exposure to endotoxins and allergens, especially prevalent in agricultural settings (31). Deployment of alcohol-based hand sanitizers across all hospital units is recommended for healthcare personnel attending to inpatients. Moreover, institution-wide educational campaigns focusing on hand hygiene to curb nosocomial infections should be instituted. This initiative includes reinforcing the prohibition of eating and drinking in patient care zones among hospital staff. Intensifying hand hygiene practices constitutes a pivotal preventive strategy, necessitating augmented allocation of resources towards fostering and sustaining optimal hand hygiene adherence among hospital personnel. Furthermore, robust hospital-based surveillance and seamless collaboration between the infection control unit and microbiology laboratory are imperative (29).

Conclusion

In conclusion, this narrative review provides a comprehensive analysis of the molecular detection, treatment options, and prevention strategies for infections caused by *P. agglomerans*. Utilizing the 16S rRNA gene sequencing method has proven effective in identifying this bacterium; however, it should be supplemented with additional molecular techniques such as whole-genome sequencing or multilocus sequence typing for a more definitive diagnosis. The antibiotic susceptibility profile of *P. agglomerans* indicates a broad susceptibility to antibiotics including imipenem, fluoroquinolones, aminoglycosides, broad-spectrum cephalosporins, and trimethoprim-sulfamethoxazole. This highlights the potential for effective treatment using these antibiotics. Preventive measures are crucial, particularly in hospital settings, to mitigate the risk of nosocomial infections. The categorization of *P. agglomerans* as a biosafety level 2 bacterium underscores the need for stringent infection control practices. This includes using alcohol-based hand sanitizers, comprehensive hand hygiene education programs for healthcare workers, and strict adherence to hospital-based surveillance protocols. Enhanced collaboration between infection control units and microbiology laboratories is essential to

prevent outbreaks and ensure prompt response to any emerging threats.

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Conflict of interest

“The authors declare no competing interests”.

References

- Mardaneh J, Dallal MMS. Isolation, identification and antimicrobial susceptibility of *Pantoea* (Enterobacter) agglomerans isolated from consumed powdered infant formula milk (PIF) in NICU ward: First report from Iran. *Iran J Microbiol*. 2013;5(3):263.D
- Dutkiewicz J, Mackiewicz B, Lemieszek MK, Golec M, Milanowski J. *Pantoea* agglomerans: a mysterious bacterium of evil and good. Part I. Deleterious effects: dust-borne endotoxins and allergens-focus on cotton dust. *Ann Agric Environ Med*. 2015;22(4).
- Kini K. *Pantoea* spp: a new bacterial threat to rice production in sub-Saharan Africa. Université Montpellier; AfricaRice (Abidjan); 2018.
- Dutkiewicz J, Mackiewicz B, Lemieszek MK, Golec M, Milanowski J. *Pantoea* agglomerans: a mysterious bacterium of evil and good. Part IV. Beneficial effects. *Ann Agric Environ Med*. 2016;23(2).
- Imhoff JF. Enterobacteriales. In: *Bergey's manual of systematic bacteriology*. Springer; 2005. p. 587-850.
- Delétoile A, Decré D, Courant S, Passet V, Audo J, Grimont P, et al. Phylogeny and identification of *Pantoea* species and typing of *Pantoea* agglomerans strains by multilocus gene sequencing. *J Clin Microbiol*. 2009;47(2):300-10.
- Cheng A, Liu C-Y, Tsai H-Y, Hsu M-S, Yang C-J, Huang Y-T, et al. Bacteremia caused by *Pantoea* agglomerans at a medical center in Taiwan, 2000-2010. *J Microbiol Immunol Infect*. 2013;46(3):187-94.
- Berner I, Konetschny-Rapp S, Jung G, Winkelmann G. Characterization of ferrioxamine E as the principal siderophore of *Erwinia herbicola* (Enterobacter agglomerans). *Biol Met*. 1988;1(1):51-6.
- Gavini F, Lefebvre B, Leclerc H. Etude taxonomique de souches appartenant ou apparentées au genre *Erwinia*, groupe *Herbicola*, et à l'espèce *Enterobacter agglomerans*. *Syst Appl Microbiol*. 1983;4(2):218-35.
- Verdonck L, Mergaert J, Rijckaert C, Swings J, Kersters K, De Ley J. Genus *Erwinia*: numerical analysis of phenotypic features. *Int J Syst Evol Microbiol*. 1987;37(1):4-18.
- Grimont PAD, Grimont F. Genus *Pantoea*, p 713-720. *Bergey's Man Syst Bacteriol*. 2005;2.
- Grimont PAD, Grimont F. Genus *Pantoea*, p 713-720. *Bergey's Man Syst Bacteriol*. 2005;2.
- Maki DG, Martin WT. Nationwide epidemic of septicemia caused by contaminated infusion products. IV. Growth of microbial pathogens in fluids for intravenous infusion. *J Infect Dis*. 1975;131(3):267-72.
- Lind E, Ursing J. Clinical strains of *Enterobacter agglomerans* (synonyms: *Erwinia herbicola*, *Erwinia milletiae*) identified by DNA-DNA-hybridization. *Acta Pathol Microbiol Scand Ser B Microbiol*. 1986;94(1-6):205-13.
- Lindh E, Frederiksen W. Ornithine decarboxylating strains of *Klebsiella pneumoniae* demonstrated by DNA-DNA hybridization. *APMIS*. 1990;98(1-6):358-62.
- Gavini F, Holmes B, Izard D, Beji A, Bernigaud A, Jakubczak E. Numerical taxonomy of *Pseudomonas alcaligenes*, *P. pseudoalcaligenes*, *P. mendocina*, *P. stutzeri*, and related bacteria. *Int J Syst Evol Microbiol*. 1989;39(2):135-44.
- Dutkiewicz J, Mackiewicz B, Lemieszek MK, Golec M, Milanowski J. *Pantoea* agglomerans: a mysterious bacterium of evil and good. Part III. Deleterious effects: infections of humans, animals and plants. *Ann Agric Environ Med*. 2016;23(2).
- Bicudo EL, Macedo VO, Carrara MA, Castro FFS, Rage RI. Nosocomial outbreak of *Pantoea* agglomerans in a pediatric urgent care center. *Brazilian J Infect Dis*. 2007;11(2):281-4.
- Gonçalves CR, Vaz TMI, Leite D, Pisani B, SIMÕES M, Prandi MAM, et al. Molecular epidemiology of a nosocomial outbreak due to *Enterobacter cloacae* and *Enterobacter agglomerans* in Campinas, São Paulo, Brazil. *Rev Inst Med Trop Sao Paulo*. 2000;42(1):1-7.
- Moosavi SM, Pouresmaeil O, Zandi H, Emadi S, Akhavan F, Toriki A, et al. The Evaluation of Antibiotic Resistance and *nalB* Mutants in *Pseudomonas eruginosa* Isolated from Burnt Patients of Shohada Mehrab Yazd Hospital Burn Ward. *Reports Biochem Mol Biol*. 2020;9(2):140.
- Soutar CD, Stavrinides J. Molecular validation of clinical *Pantoea* isolates identified by MALDI-TOF. *PLoS One*. 2019;14(11):e0224731.
- Kaur IP, Inkollu S, Prakash A, Gandhi H, Mughal MS, Du D. *Pantoea* agglomerans bacteremia: is it dangerous? *Case Rep Infect Dis*. 2020;2020.
- Tehrani HF, Barkhordari M, Safari Z, Voosough H. *Pantoea* Agglomerans, A Plant Pathogen Causing Human Disease. *Iran J Public Health*. 2014;43(2):199.
- Lau KK, Ault BH, Jones DP. Polymicrobial peritonitis including *Pantoea* agglomerans from teething on a catheter. *South Med J*. 2005;98(5):580-2.
- Liberto MC, Matera G, Puccio R, Lo Russo T, Colosimo E, Focà E. Six cases of sepsis caused by *Pantoea* agglomerans in a teaching hospital. *New Microbiol*. 2009;32(1):119.
- Nakata K, Inagawa H, Soma G-I. Lipopolysaccharide IP-PA1 from *Pantoea* agglomerans prevents suppression of macrophage function in stress-induced diseases. *Anticancer Res*. 2011;31(7):2437-40.
- Kohchi C, Inagawa H, Nishizawa T, Yamaguchi T, Nagai S, Soma G-I. Applications of lipopolysaccharide derived from *Pantoea* agglomerans (IP-PA1) for health care based on macrophage network theory. *J Biosci Bioeng*. 2006;102(6):485-96.
- Vincent K, Szabo RM. *Enterobacter agglomerans* osteomyelitis of the hand from a rose thorn: A case report. Vol. 11. Slack Incorporated Thorofare, NJ; 1988. p. 465-7.
- Uche A. *Pantoea* agglomerans bacteremia in a 65-year-old man with acute myeloid leukemia: case report and review. *South Med J*. 2008;101(1):102-3.
- Panijel M, Chalupowicz L, Sessa G, Manulis-Sasson S, Barash I. Global regulatory networks control the *hrp* regulon of the gall-forming bacterium *Pantoea* agglomerans pv. *gypsophilae*. *Mol plant-microbe Interact*. 2013;26(9):1031-43.
- Chalupowicz L, Manulis-Sasson S, Itkin M, Sacher A, Sessa G, Barash I. Quorum-sensing system affects gall development incited by *Pantoea* agglomerans pv. *gypsophilae*. *Mol plant-microbe Interact*. 2008;21(8):1094-105.
- De Maayer P, Chan W-Y, Blom J, Venter SN, Duffy B, Smits THM, et al. The large universal *Pantoea* plasmid LPP-1 plays a major role in biological and ecological diversification. *BMC Genomics*. 2012;13(1):1-12.
- Kirzinger MWB, Butz CJ, Stavrinides J. Inheritance of *Pantoea* type III secretion systems through both vertical and horizontal transfer. *Mol Genet genomics*. 2015;290(6):2075-88.
- Munford RS. Sensing gram-negative bacterial lipopolysaccharides: a human disease determinant?

- Infect Immun. 2008;76(2):454-65.
35. Fukata M, Michelsen KS, Eri R, Thomas LS, Hu B, Lukasek K, et al. Toll-like receptor-4 is required for intestinal response to epithelial injury and limiting bacterial translocation in a murine model of acute colitis. *Am J Physiol Liver Physiol.* 2005;288(5):G1055-65
 36. Strömqvist B, Edlund E, Lidgren L. A case of blackthorn synovitis. *Acta Orthop Scand.* 1985;56(4):342-3.
 37. Zagory D. Effects of post-processing handling and packaging on microbial populations. *Postharvest Biol Technol.* 1999;15(3):313-21.
 38. Nguyen-the C, Carlin F. The microbiology of minimally processed fresh fruits and vegetables. *Crit Rev Food Sci Nutr.* 1994;34(4):371-401.
 39. Rave O, Assous MV, Hashkes PJ, Lebel E, Hadas-Halpern I, Megged O. *Pantoea agglomerans* Foreign Body-Induced Septic Arthritis. *Pediatr Infect Dis J.* 2012;31(12):1311-2.
 40. Jain S, Bohra I, Mahajan R, Jain S, Chugh TD. *Pantoea agglomerans* infection behaving like a tumor after plant thorn injury: an unusual presentation. *Indian J Pathol Microbiol.* 2012;55(3):386-8.
 41. Habhab W, Blake PG. *Pantoea peritonitis*: not just a "thorny" problem. *Perit Dial Int.* 2008;28(4):430.
 42. Shubov A, Jagannathan P, Chin-Hong P V. *Pantoea agglomerans* pneumonia in a heart-lung transplant recipient: case report and a review of an emerging pathogen in immunocompromised hosts. *Transpl Infect Dis.* 2011;13(5):536-9.
 43. Kurşun O, Unal N, Cesur S, Altın N, Canbakan B, Argun C, et al. A case of ventilator-associated pneumonia due to *Pantoea agglomerans*. *Mikrobiyol Bul.* 2012;46(2):295-8.
 44. Matsaniotis NS, Syriopoulou VP, Theodoridou MC, Tzanetou KG, Mostrou GI. Enterobacter sepsis in infants and children due to contaminated intravenous fluids. *Infect Control Hosp Epidemiol.* 1984;5(10):471-7.
 45. Van Rostenberghe H, Noraida R, WI WP, Habsah H, Zeehaida M, AR R, et al. The clinical picture of neonatal infection with *Pantoea* species. *Jpn J Infect Dis.* 2006;59(2):120-1.
 46. Chen ChaoQiong CC, Xin KaiYun XK, Liu Hao LH, Cheng JuanLi CJ, Shen XiHui SX, Wang Yao WY, et al. *Pantoea alhagi*, a novel endophytic bacterium with ability to improve growth and drought tolerance in wheat. 2017
 47. Graham DC, Hodgkiss W. Identity of gram negative, yellow pigmented, fermentative bacteria isolated from plants and animals. *J Appl Microbiol.* 1967;30(1):175-89.