

## *Cupriavidus pauculus* as an Emerging Pathogen: A Mini-Review of Reported Incidents Associated with its Infection

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### Abstract

*Cupriavidus pauculus* infections have become increasingly associated among immunocompromised and immunocompetent patients. We summarize recent and past incidents reported as such since 1985 in order to emphasize significance in its awareness as an emerging pathogenic organism.

**Keywords:** *Cupriavidus pauculus*; Pathogen; Infection

### Introduction

*Cupriavidus pauculus* was formerly classified as CDC group IV c-2, *Ralstonia paucula* and then as *Wautersia paucula* [1]. *C. pauculus* is a Gram-negative mesophilic bacillus, motile, aerobic, non-spore-forming rod bacteria. It is catalase and oxidase positive, as well as a non-lactose fermenter on MacConkey agar. This species is widely distributed in nature, especially in water and soil [1,5]. *C. pauculus* can cause infections not only in immunocompromised patients with underlying diseases such as malignancies and AIDS but also in otherwise healthy people [2,10].

As such, it can be an opportunistic pathogen in the hospital setting and may potentiate outbreaks, especially in intensive care units. Water, including tap and bottled water, has been suspected to be a potential source of contamination [5,6]. *C. pauculus* has been implicated in several types of infectious pathologies, including bacteremia, community and hospital acquired pneumonias, tenosynovitis, peritonitis, meningitis, corneal ulcer, and septicemia from different parts of the world including, but not limited to, USA, France, India, and Turkey [2,5,21]. In our previous report in The Journal of Infection in Developing Countries, we documented the first case of pneumonia caused by this species in an infant in the Gulf Cooperation Council (April 2017) [3]. This patient, born with multiple congenital abnormalities, developed recurrent chest infection requiring multiple hospitalizations. During prolonged PICU stay, *C. pauculus* was identified as the pathogen in question which was confirmed by 16SrRNA sequencing.

In this mini-review, we summarize all the cases that has been reported in English literature since 1985 to the purpose of heightening attention to various infection types associated with this species.

### Review of incidents

The total reported patients infected with this species were 32 in both pediatric and adult ages, the youngest of which was 6 days old. The oldest reported was 77 years old, although one patient's case was reported without mentioning the age. *Cupriavidus pauculus* was noted to affect more males than compared to females, 18 patients reported as males compared to 8 patients reported as female. The other 6 cases were reported without mentioning gender of each.

Age	Gender	Country	Risk factors/ Comorbidity	Clinical Diagnosis/ Presentation	Sample Positive	Outcome	Reference
6 days	Male	India	Newborn/immunity naive	Fever, seizure, meningitis	CSF, blood	Improved	[2]
1 year	Male	Saudi Arabia	ESRD, GERD, Hypotonia	Pneumonia, intubated	Sputum specimen ETT	Improved	[3]
67 years	Male	Romania	Seizures, Alzheimer disease	RDS, pneumonia, intubated	Blood	Died	[4]
16 days	Male	Turkey	Newborn/Immunity naive	Community acquired pneumonia	Blood	Improved	[5]
28 years	Female	Texas, USA	Immunocompromised, Hemodialysis	Osteomyelitis, arthritis	Joint aspiration	Improved	[26]
15 months	Male	Minnesota, USA	Hypoplastic left heart syndrome	RDS, ECMO	Blood, ECMO equipment	Improved	[7]
4 months	Male	Arkansas, USA	none, healthy	Cardiogenic shock, ECMO	Blood, ECMO equipment	Improved	[7]
3 years	Male	Arkansas, USA	Shone's Complex	Sever Congestive heart failure	Blood, ECMO equipment	Improved	[7]
Term, newborn	Male	Arkansas, USA	Hypoplastic left heart syndrome	Norwood Procedure, ECMO	Blood, ECMO equipment	Died	[7]
16 months	Male	Arkansas, USA	Double Outlet Right Ventricle	ECMO, Fever	Blood, ECMO equipment	Improved	[7]
8 years	Female	Baltimore, USA	AML, immunocompromised	Pneumonia, intubated, sepsis	Blood, ETT	Died	[8]
29 years	Female	Colorado, USA	Congenital heart disease, ICD	ICD pocket infection	ICD Pocket	Improved	[9]
36 years	Male	Spain	Leukemia, stem cell transplant	Fever, sepsis	Blood	Improved	[10]
30 years	Male	Chicago, USA	AIDS, central line	Recurrent bacteremia	Blood, central line	Improved	[11]
20 years	Male	Barcelona, Spain	Testicular cancer, chemotherapy	Fever, sepsis	Blood, central line	Improved	[12]
55 years	Male	Boston, USA	Severe peripheral vascular disease	Plantar abscess on the left foot, septicemia	Blood	Improved	[13]
1 month	NA	Paris, France	Jejunal atresia	Septicemia	Blood, central line	Improved	[14]
11 years	NA	Paris, France	Nasopharyngeal carcinoma	Bacteremia	Blood, central line	Improved	[14]
3 months	NA	Paris, France	Immunodeficiency	Bacteremia	Blood, central line	Improved	[14]
11 years	NA	Paris, France	Lymphoma	Bacteremia	Blood, central line	Improved	[14]

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14 years	NA	Paris, France	Leukemia	Bacteremia	Blood, central line	Improved	[14]
37 years	Male	Israel	Plasma cell leukemia	Fever, myalgia, rigors, sepsis	Blood, central line	Improved	[15]
58 years	Male	Spain	CAPD	Peritonitis	Blood, central line	Improved	[16]
10 years	Female	Spain	ALL, Hickman Catheter	Sepsis	Blood	Improved	[17]
77 years	Male	Brazil	Immunocompromised, NHL, Catheter	Sepsis	Blood	Improved	[18]
73 years	Female	France	None, Healthy	Tenosynovitis	Wound	Improved	[19]
53 years	Male	NA	Chronic renal failure, DM	Peritonitis	Peritoneal Catheter	Improved	[20]
6 months	Female	Houston, USA	None, Healthy	Bacteremia	Blood	Improved	[21]
71 years	Female	Spain	ALL	Sepsis	Blood	Improved	[22]
37 years	Male	Argentina	CKD, Hemodialysis	Sepsis	Blood	Improved	[23]
26 years	Female	South Korea	Community lens solution	Corneal Ulcer	Corneal scrapping	Improved	[24]
NA	NA	Spain	Ventilated ICU	NA	Tracheal aspirate	NA	[25]

**Table 1:** Log of presentations associated with *C. paucula* infections.

The species was noted to affect both immunocompetent patients and immunocompromised patients. Specifically, 17 patients were known with compromised immunity that further risked development of this infection.

The majority of the infected cases were concurrently undergoing chemotherapy, along with maintaining central lines, for oncologic disease. This review reported 10 diagnosed with malignancies. In addition, seven affected patients suffering from diseases, aside from cancers, that may have compromised immunity and hence increase infection risk. Five were known suffering from end-stage renal disease. Four of these cases were on hemodialysis, and one was on continuous ambulatory peritoneal dialysis (CAPD). One reported adult patient was also diagnosed with AIDS with a kept central line. Another adult patient was diagnosed with primary immunodeficiency disease. Nine comorbidities, as risk factors for infection with *Cupriavidus pauculus*, were identified in this literature review. Congenital heart disease was reported in five cases, consisting of four pediatric cases and one adult.

Other comorbidities as risk factors included the following:

- One reported adult patient with seizures and Alzheimer’s.
- One reported adult patient with severe peripheral vascular disease.
- One reported patient kept under ventilation in ICU
- One reported pediatric age with jejunal atresia.

*C. pauculus* infection was reported in 6 patients, whose immune systems were known as competent. This consisted of 2 newborns, 2 pediatric cases and 2 adults.

Most of these reported patients presented to the hospital initially with signs and symptoms of sepsis, and some patients presented to the hospital with pneumonia and RDS requiring intubation or ECMO.

Of the 6 cases, one 6-day old newborn presented with fever, seizures and meningitis.

A four-month old baby boy, previously otherwise healthy, presented with signs and symptoms of cardiogenic shock that required using ECMO for management.

## **Discussion**

This species was isolated from different sample sites of the reported cases including blood, central lines, peritoneal catheter, sputum, tracheal aspirate, and ECMO equipment.

In addition, it was isolated from CSF and infected sites of joint aspirate, ICD pocket, wounds, and corneal scraping. All reported cases stated that patients were treated in the hospital with different kinds of IV antibiotics, including tobramycin, cefazolin, trimethoprim/sulphamethoxazole, ceftazidime, gentamycin, ceftriaxone, amikacin, ceftazidime and ceftizoxime.

All mentioned patients reported improvement except for three patients that died.

Two of the deceased were one newborn with hypoplastic left heart, post-surgical and ECMO treatment, and one 8-year-old with AML and undergoing chemotherapy.

From this review, we learned that *Cupriavidus pauculus* may cause a wide range of serious infections, although initial reports were of those affected individuals with compromised immunity due to cancers, with hemodialysis, or with congenital anomalies corrected through surgery. To our current understanding, general awareness of infectious disease involving this species has increased to identify healthy individuals in all ages that possibly may acquire *Cupriavidus pauculus* infections to then present as pneumonia, sepsis, meningitis, bacteremia and cardiogenic shock.

As such, *C. pauculus* is furthermore sensitive to a wide range of antibiotics. Thus, the majority of patients recovered with antibiotic treatment. Although few did not survive, these were particularly among those in the precarious setting of intensive care units.

## **Conclusions**

This compilation of incidents indicates the need for greater awareness of *C. pauculus* as a pathogen gaining notoriety since the past 3 decades. To our current knowledge, infection by this species, while treatable for many, still potentiates complications in both the hospital and general surroundings. Hence, this warrants further research into its parameters for pathogenicity, precise pharmacologic susceptibilities, and otherwise.

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