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Comprehension Review

Review on Auromanes Disease

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Introduction

The genus *Aeromonas* consists of Gram-negative, oxidase positive bacilli that are considered of aquatic environments and are commonly isolated from clinical and environmental samples. Typical habitats for these bacteria are freshwater (ground water, lakes, rivers and reservoirs), chlorinated and un-treated drinking water, bottled water, swimming pools, wastewater, reclaimed waters, brackish waters, and seawater. *Aeromonas* spp. Can produce several diseases in wild and farmed freshwater and marine fish species impacting the economy of the aquaculture sector. Most common human clinical presentations of *Aeromonas* infections are diarrhea, wound and soft-tissue infections and bacteremia. Many infections are related to water exposure (traumatic accidents, near drowning, natural disasters. The most common species of aeromones are *A. hydrophila, A. caviae, A. veronii* and *A. dhakensis*. (Figueras Salvat, M.J. and Ashbolt, N. 2019. *Aeromonas.* In: J.B. Rose and B. Jiménez-Cisneros, (eds) Global Water Pathogen Project).

The members of the *Aeromonas* genus are ubiquitous, waterborne bacteria. They have been isolated from marine waters, rivers, lakes, swamps, sediments, chlorine water, water distribution systems, drinking water and residual waters; different types of food, such as meat, fish, seafood, vegetables, and processed foods. *Aeromonas* strains are predominantly pathogenic to poikilothermic animals, and the mesophilic strains are emerging as important pathogens in humans, causing a variety of extraintestinal and systemic infections as well as gastrointestinal infections. The most commonly described disease caused by *Aeromonas* is the gastroenteritis; however, no adequate animal model is available to reproduce this illness caused by *Aeromonas*. The main pathogenic factors associated with *Aeromonas* are: surface polysaccharides (capsule, lipopolysaccharide, and glucan), S-layers, iron-binding systems, exotoxins and extracellular enzymes, secretion systems, fimbriae and other nonfilamentous adhesins, motility and flagella (J. M. Tom´as, 2012, The Main *Aeromonas* Pathogenic Factors, Departament to Microbiologia, Universidad de Barcelona, Diagonal 643, 08071 Barcelona, Spain.

Taxonomy and classification

Aeromonads were divided into two major groups based on physiological properties and host range until the late 1970s. Motile aeromonads grow at optimum temperature of 35–37°C and those predicted to cause human infections were recognized to be *A. hydrophila*. Nonmotile aeromonad which grows at 22–28°C and causes infections in fishes is called *Aeromonas salmonicida*. Phenotypic markers for their differentiation include optimum growth temperature, motility, production of indole, and elaboration of melanin like pigment on tyrosine agar [1]. Thereafter, the genus *Aeromonas* has advanced with the addition of new species and the re classification of pre existing taxa [2]. In the past, *Aeromonas* species were placed alongside *Vibrio* species and *Plesiomonas shigelloides* in the family *Vibrionaceae*. However, genetic studies provide enough facts to support the placement of aeromonads in a family of their own called *Aeromonadaceae* [3].

The current classification of the genus *Aeromonas* is based on DNA-DNA hybridization and 16S ribosomal DNA relatedness, and the genera of the family *Aeromonadaceae* now include *Oceanimonas*, *Aeromonas*, *Tolumonas* (*incertae sedis*), and *Oceanisphaera* [4]. The existing genomospecies and phenospecies within the genus *Aeromonas* are as listed in Table below.

Biology of the disease

The *Aeromonas* are aquatic bacteria that are often associated with diarrhoea. However, their precise role in the etiology of gastrointestinal illness is unclear. Most species are motile due to the presence of flagella. *Aeromonas* spp. are widely distributed in stagnant and flowing fresh water, in saltwater that interfaces with fresh water, in fish tanks, water supplies and in sewage, with densities ranging from <1 to>1000/ml. Strains within each *Aeromonas* species, including *A. hydrophilia,* are commonly divided into two groups based on their temperature requirements for growth. The First one is *Psychrophilic* strains have an optimum growth temperature of between 15 and 20°C and may grow at temperatures as low as 0-5°C. The second one is *Mesophilic* strains have an optimum growth temperature of around 35°C and can grow at temperatures as high as 40-45°C, but generally will not grow below 10°C. There is evidence to suggest that those strains best adapted to grow at low temperatures are more commonly pathogens of fish and not humans [5].

The genus *Aeromonas* was re-categorized from the family Vibrionaceae to the family *Aeromonadaceae* in the mid-1980s, when phylogenetic evidence from molecular studies became available to support this distinction. The genus *Aeromonas* has been divided into two major groups [6]:

- Motile, mesophilic species, including eight that can cause disease in humans.
- Non-motile, psychrophilic species that generally cause disease only in fish. *Aeromona* species are oxidase positive and ferment glucose. The organisms grow at a range of Temperatures from 0 to 42ºC.

DNA hybridization group (HG)	Type strain/Reference	Genospecies	Phenospecies	Remarks
1*	ATCC 7966	*A. hydrophila*	*A. hydrophila*	Isolated from clinical specimens
1*	BCCM/LMG 19562	*A. hydrophila* subsp. *dhakensis*	*A.hydrophila* subsp. *dhakensis*	Isolated from clinical specimens
1*	BCCM/LMG 19707	*A. hydrophila* subsp. *ranae*	*A. hydrophila* subsp. *ranae*	Pathogenic for frogs
2*	ATCC 14715	*A. bestiarum*	*A. hydrophila like*	Isolated from clinical specimens
3*	ATCC 33658	*A. salmonicida*	*A. salmonicida* subsp. *salmonicida*	Nonmotile fish pathogen
3*	ATCC 33659	*A. salmonicida*	*A. salmonicida* subsp. *achromogenes*	Nonmotile fish pathogen
3*	ATCC 27013	*A. salmonicida*	*A. salmonicida* subsp. *masoucida*	Nonmotile fish pathogen
3*	ATCC 49393	*A. salmonicida*	*A. salmonicida* subsp. *smithia*	Nonmotile fish pathogen

Table 1

Carnahan and Joseph (2000)

Biochemical characteristics

Biochemical identification of Genomospecies of the Motile *Aeromonas.*

Species	$NO_3^- \rightarrow NO_2^-$	D-Glucose, gas	Indole	Arginine dihydrolase	Lysine decarboxylase	Ornithine decarboxylase	Esculin hydrolysis	NaCl tolerance 0%	NaCl tolerance 6%	Sucrose	D-Manitol	L-Arabinose	Salicin	Manose	β-hemolysis	Resistence to ampicilin[a]
Aeromonas hydrophila	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+
Aeromonas salmonicida	+	+	+	V	V	-	+	+	-	+	+	+	-	+	V	+
Aeromonas media	+	-	+	+	-	-	+	+	-	+	+	+	V	+	V	+
Aeromonas encheleia	+	V	+	+	-	-	+	+	-	+	+	-	+	+	V	+
Aeromonas allosaccharophila	+	V	+	+	+	-	V	+	-	+	+	V	-	+	V	+
Aeromonas eucrenophila	+	+	+	+	-	-	+	+	-	V	+	+	+	+	V	+
Aeromonas bestiarium	+	V	+	+	+	-	+	+	-	+	+	+	V	+	V	+
Aeromonas caviae	+	-	+	+	-	-	+	+	-	+	+	+	+	V	V	+
Aeromonas veronii sobria	+	V	+	+	+	-	-	+	-	+	+	-	-	+	+	+
Aeromonas veronii veronii	+	+	+	+	-	+	+	+	-	+	+	-	+	+	+	+
Aeromonas schubertii	+	-	-	+	+	-	-	+	-	-	-	-	-	+	V	+
Aeromonas jandaei	+	+	+	+	+	-	-	+	-	-	+	-	-	+	+	+
Aeromonas trota	+	V	+	+	+	-	-	+	-	V	V	-	-	+	V	-
Aeromonas popoffii	+	+	V	+	-	-	-	+	-	-	+	V	-	+	-	+
Aeromonas culicicola	+	+	+	+	+	-	-	+	-	+	+	-	-	+	+	+
Aeromonas simiae	+	-	-	+	+	-	V	+	-	+	-	-	-	+	-	+
Aeromonas molluscorum	+	-	-	+	-	-	+	+	-	+	+	+	+	+	nd	+
Aeromonas sobria	+	V	+	-	+	-	-	+	-	+	+	-	-	+	V	V

Source: Pidiyar and col., 2002; Abbott and col., 2003; Harf-Monteil and col., 2004
Note: (+) = .85% of positive strains; (-) = > 85% of negative strains; (V) = 50%; nd = not determined

Figure a: Biochemical characteristics of different species of Aeromonas.

Figure b

Host range

The motile *Aeromonas* appear worldwide. Their principal reservoir is in river and estuary waters, as well as in salt water where it meets fresh water. Population density is lower in highly saline waters and waters with limited dissolved oxygen. It has sometimes been possible to isolate *Aeromonas* from chlorinated water, including municipal water supplies. These bacteria are more prolific in summer than in winter. Aeromoniasis is primarily a disease that affects fish, amphibians, and reptiles. The disease is rare in wild or domestic mammals and birds. *A. hydrophila* is a recognized pathogen in fish, amphibians, and reptiles. The disease may occur individually or epidemically, particularly In fish-farming pools. The agent affects many fish species, particularly fresh water species. Its economic impact varies, but can be severe. Aeromoniasis due to *A. hydrophila* also causes significant illness in colonies of amphibians and reptiles bred for experimental purposes [7].

Transmission

The primary reservoir of *A. hydrophila* and *A. sobria* is fresh water in rivers, ponds, and lakes. It is also found in estuaries and in low-salinity salt water. Even treated municipal water supplies can contain *Aeromonas*.

It is difficult to understand why, since the bacteria are widely distributed in nature, water, animal feces, and foods of animal origin, and since they also multiply at refrigeration temperatures. The distribution of the agents in water reaches its highest level during the warm months, as does the disease. The situation seems to be different in tropical countries and fish are another reservoir, Water contaminated by virulent strains of *A. hydrophila* or *A. sobria* is the source of infection for man and other animals. Domestic animals, especially cattle and pigs, eliminate in their feces a large amount of *Aeromonas* that are probably of aquatic origin. Enteric disease occurs in normal children and the route of infection is through the mouth. Another one is Wounds becomes infected upon contact with water. Medicinal leeches can infect the wound they produce with the *Aeromonas* they harbor in their digestive tract and suckers. The most serious form of the disease, septicemia and its various organic complications, occurs in immunodeficient individuals and the route of infection is usually extra intestinal. Fish, amphibians, and reptiles—especially in intensive breeding programs—are infected through the mouth. The factors that contribute to infection are stress from Overpopulation, temperature changes, lack of hygiene, and inadequate feeding [7].

Horizontal transmission, close contact with infected individual, ingestion of bacterium, direct inoculation through wounds, especially from contaminated water and detritus. Snake mite (*Ophionyssus*, *natricis*) capable of transmitting bacteria [8].

Ecology and epidemiology

Mesophilic aeromonads have a global distribution and have been isolated from a variety of

Aquatic environments, including:

- Fresh water
- Estuarine (brackish) water
- Surface water, especially recreational
- Drinking water, including treated, well, and bottled Polluted waters
- Waste water effluent sludge

Aeromonads are not generally considered marine organisms, but can be found in marine systems that interface with fresh waters and can survive at all but the most extreme salt concentrations [9].

Usually they are not part of the groundwater bacterial population, which is generally poor in nutrients. In nutrient-rich waters, *Aeromonas* species can grow to large numbers and generally peak in the warmer temperatures of the summer months in temperate freshwater lakes and chlorinated drinking water [10].

Aeromonas species appear to tolerate polluted environments, including chemical pollution, although they are not considered to be of fecal origin [11]. The organism has also been isolated from retail produce sources and meat products [12]. Contact with any fresh or brackish water body is the most common source of human infection. The risk of infection can be reduced by caution in the setting of natural water sources (lakes, rivers, streams, ponds, bays), including minimizing the risk of traumatic wounds and avoiding oral ingestion, particularly during warmer summer months.

Pathogenesis

Aeromonas is said to be pathogenic because it possess all the requirements of pathogenic bacteria. It attaches and enters into host cells through production of flagella, pili and adhesins. Multiplication in host tissue is assisted by the production of siderophores and outer membrane proteins, while production of capsule, Slayer, lipopolysaccharide, and porins contributes to their resistance to host defenses mechanism. Enterotoxins, proteases, phospholipases, and hemolysins cause damage to host cells leading to cell death [13].

Several extracellular products are elaborated, including cytotoxic and cytotonic enterotoxins, hemolysins, and various hydrolytic enzymes. The occurrence of both Type II and Type III secretions systems has been demonstrated, including the presence of several virulence factors such as enolase. Some aeromonads produce a range of cell surface and secretory proteases that may augment their virulence [14].

It is well documented that a significant proportion of the *A. hydrophila* isolated from chlorinated and nonchlorinated water contained genes responsible for enterotoxigenic or cytotoxic activity [15]. Also, environmental temperature has been reported to be a parameter in the expression of virulence factors. *A. hydrophila* isolated from the environment produced significantly less enterotoxins when grown at 37^0C compared to 28^0C, while the clinical isolates examined produced more enterotoxins at 37^0C than at 28^0C [16].

Zoonotic potential of the disease

Animal-to-person transmission may occur through direct contact, or by ingestion of contaminated food products of animal origin.

Prevalence's in our country

In Ethiopia, some authors reported prevalence of *Aeromonas* species in fish samples. Nuru., *et al.* [17] reported 10.30% prevalence in fish from Lake Tana and Tesfaye., *et al.* [18] 7.80% from Lake Hayike.

Clinical infections

Diarrhea

Aeromonas spp are associated with a range of diarrheal presentations including: There have been two reports of *A. hydrophila* enterocolitis associated with the hemolytic uremic Syndrome (HUS) [19].

Wound infections

Aeromonas can cause mild to severe wound infections. Infection typically occurs on the extremities following traumatic aquatic injury. Such wound infections affect men three times more commonly than women. The most typical presentation is cellulitis. A case of nearly fatal necrotizing fasciitis from a traumatic leg wound

- Polluted waters
- Waste water effluent sludge [20].
- Acute, secretory diarrhea, often accompanied by vomiting
- Acute, dysenteric diarrhea with blood and mucus
- Chronic diarrhea, lasting more than 10 days
- Choleric diarrhea with "rice-water" stools

Incurred from contact with a fresh water river highlights the virulence potential of aeromonads to Cause serious disease [21]. *A. hydrophila*, *Aeromonas veronii*, and *Aeromonas schubertii* are the species most commonly isolated from wound infections [22].

Bacteremia

Sepsis with *Aeromonas* species is strongly associated with infection with *A. veronii* biovar sobria. These patients present with the classic signs and symptoms of gram-negative sepsis and may have gastrointestinal symptoms, including abdominal pain, nausea, vomiting, and diarrhea [23].

- **Fish**: Acute mortality, septicemia**,** erythema, exophthalmia, hemorrhages in skin, fins, muscle and oral cavity, with skin boils and ulceration. Fecal casts or bloody discharge from vents
- **Amphibians**: Acute mortality**,** septicemia, anorexia, ventral erythema with cutaneous hemorrhage especially ventral thighs, edema in subcutis, anasarca, hemorrhagic ulcerations of digit tips and jaw. May feature digital amputation due to vasoconstriction, secondary to septicemia.
- **Reptiles**: Acute mortality, septicemia, pneumonia, ulcerative stomatitis particularly in snakes, dermal ecchymoses, epidermal ulceration, anorexia, listless, labored respirations, harsh respiratory sounds, mouth gaping, steady decline in status, rule out predisposing or underlying environmental or host factors.
- **Waterfowl:** Upper respiratory tract infections, salpingitis, enteritis, septicemia, localized abscessation, and arthritis
- **Marine mammals**: Septicemia, pneumonia
- **Humans**: Gastroenteritis, watery diarrhea which can be chronic in nature, septicemia, pustular dermatitis, cellulitis, necrotizing fasciitis, pneumonia, peritonitis, cholecystitis, bacteremia and hepatitis (Infectious Disease Manual, edited 2019).

Diagnosis

- **Culture-Based Detection Methods:** Aeromonads grow on isolation media, and a huge number of selective and differential isolation media have been developed for the recovery of *Aeromonas* species from the environment, foods, and clinical specimens [24].
- **Molecular Detection and Identification Methods**: Polymerase chain reaction (PCR) methods have been developed to detect the presence of *Aeromonas* species in a wide range of samples. of *A. hydrophila* in raw milk [25].

Isolation on routine media (heart infusion agar, blood agar, MacConkey, Tryptone soya agar) with subsequent identification, commercial systems, and molecular identification (amplified fragment length polymorphism (AFLP) analysis). Results must be taken in context of clinical signs and pathologic findings (Infectious Disease Manual, edited 2019).

These organisms are best identified using culture, Gram stain, and biochemical tests. Positive Oxidase reaction, growth in nutrient broth without NaCl, no growth in nutrient broth with 6%NaCl, Inability to grow on thiosulfate citrate bile sucrose agar and resistance to the vibriostatic Compound 0/129 help in the differentiation of *Aeromonadaceae* from *Vibrio* and *pleisiomonas genera*. The most common human pathogenic species (*Aeromonas caviae, A. hydrophilla*, and *A. Veronii biovar sobria*) can be differentiated based on the microbiological xaminations, including Voges–Proskauer test, fermentation of Larabinose, esculin hydrolysis, and gas production from Glucose [26].

Treatment

As highlighted previously, aeromonads are ubiquitous in many environmental waters. As a result, they are present in most source

waters used for drinking water production. The existing techniques used for treatment and disinfection are effective in minimizing the level of aeromonads in the finished drinking water. It has been reported that *A. hydrophila* is usually more susceptible to chlorine and mono chloramines than coliform [27].

Antimicrobial susceptibility

Clinical studies have demonstrated differences in antimicrobial susceptibility between species, highlighting the importance of both species identification and susceptibility testing for all isolates, particularly in the setting of serious infection. Most *Aeromonas* strains are resistant to penicillin, ampicillin, carbenicillin, and ticarcillin; most are susceptible totrimethoprim-sulfamethoxazole (TMP-SMX), fluoroquinolones, second and third generation cephalosporins, amino glycosides, carbapenems, chloramphenicol, and tetracycline's [28].

The most efficient approach for controlling *Aeromonas* growth is to limit the *Aeromonas* species entering the distribution system through effective treatment and maintenance, to maintain temperatures below 14°C, to provide free-chlorine residuals above 0.1–0.2mg/L, and to limit the levels of organic carbon compounds in the water. However, it is difficult to manage its growth in bio films. Rehydration therapy is adequate intervention in most pediatric cases of gastroenteritis and watery diarrhea caused by *Aeromonas* species [29].

Draining obstructions and antibiotic therapy are effective in the management of infection in patients with acute suppurative cholangitis. Surgical intervention might be necessary in cases of necrotizing fasciitis. In addition, cellutis may require debridement, and abscesses may require draining. Gastrointestinal infections caused by aeromonads are generally self-limiting, and antibiotic therapy is required only in prolonged cases in immunocompromised hosts. Antimicrobials are employed for only severe and unresponsive cases of *Aeromonas* gastroenteritis [30,31].

Antibiotic selection is dependent on susceptibility testing. In general, these bacteria are susceptible to amino glycosides, extended spectrum cephalosporin's, azithromycin, mono bactams, nitro furans, extended spectrum penicillin's, phenicols, fluoro quinolones, and tetracycline's, with variable susceptibility to potentiated antifolates (trimethoprim-sulfas). *Aeromonas* spp. produces strong *B*-lactamases, so they resistant to narrow spectrum penicillins (e. g. amoxicillin, ampicillin, penicillin) and cephalosporin's (e.g. cefoxitin), sulfamethoxazole, erythromycin, and clarithromycin (Infectious Disease Manual, edited 2019).

Prevention and control

Ubiquitous in environment and may comprise part of the normal intestinal flora. Opportunistic infection In species other than fish, infections are often opportunistic or secondary to debilitation or immunosuppression. Maintain good environmental hygiene, water quality and optimal husbandry conditions; ultraviolet irradiation or ozonation of water sources; proper food storage and follow safe cooking and thawing recommendation; follow all wound care procedures recommended by veterinarian or physician; practice good hygiene; wash hands often. Prevention through good environmental and personal hygiene practices, optimal husbandry, UV irradiation or ozonation of water; vaccination for *Aeromonas salmonicida* (Infectious Disease Manual, edited 2019).

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