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Advances in listeria monocytogenes, infectivity and pathogenesis

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ABSTRACT

Listeria monocytogenes is a food borne pathogen with the ability to exist and thrive in diverse environments. Its evolution from the food environment into the gastrointestinal tract initiates a development that could culminate in pervasive systemic infection. *Listeria monocytogenes* has over the years surfaced as an astoundingly tractable pathogen surpassing the fundamental aspects of intracellular pathogenesis, cell biology, and natural as well as acquired immunity. To facilitate its intracellular existence, *Listeria monocytogenes* has developed several mechanisms of exploiting the host processes thus multiplying and spreading from one cell to another without damagingthe host cells. This paper will discuss the microbiological processes, molecular mechanisms and the molecular determinants of Listeria pathogenicity (virulence) and their mechanism of action. It will also look at the current knowledge on the pathophysiology of listeriosis, the cell biology and host cell responses to Listeria infection. An appreciation of the survival mechanisms of the pathogen in unfavorable environments is suitable to enlighten future designs of modern prophylactic approaches seeking to exploit particular pharmabiotics (i.e. prebiotics, probiotics, or phages).

KEYWORDS

Listeria monocytogenes;
Pathogen;
Infection;
Pathogenicity.

INTRODUCTION

sListeria monocytogenes is classified as a ubiquitous fast growing Gram-positive bacteria commonly found in food environments. The pathogen has abiological niche as well as host range. Infection in animals and humans alike finds its roots via contaminated food in most cases leading to severe, often deadly illness. The invasive nature of human being listeriosis illness mainly affects low immunity persons, neonates, the elderly, as well as pregnant women. The symptoms include meningitis and septicemia for non-pregnant persons, premature labor, neonatal septicemia, fetal loss, and meningitis in pregnant individuals with soaring case-fatality proportions of about 20–30%. Estimates by the Centers for Disease Control and Prevention (CDC) indicate that about 1600 Inv listeriosis occurrences are reported in the United States with 255 Fatalities happening each year[42].

The pathogen persists to trigger widespread epidemics from consumable food supplies and signifies a considerable basis of food-substancemortality. The pathogen thrives in the ecology; as a saprophyte hence can get into the human food chain directly or via infection and carriage in plow animals (zoonotic

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illness). Listeria possesses several molecular mechanisms that help them in adapting to various phases of the pathogenic cycle[19].

Pathogenic bacteria employ several mechanisms in causing sickness in human hosts. Bacterial pathogens possess a diverse range of molecules for binding host unit targets to facilitate diverse host reactions. The molecular approaches employed by bacteria in the interaction with hosts may be distinct to particular pathogens or limited across numerous diverse species. Capability to fighting illness is the recognizable proof and portrayal of all these different methodologies. The accessibility of comprehensive genome sequences for various pathogens combined with bioinformatics will prompt huge advances toward this objective[17].

Infectious ailments top the list of diseases causing deaths across the globe. The emergence of new infectious ailments coupled with re-emergence of fatal ailments as well as the escalating dominance of resilient antimicrobial strains; present an alarming risk to public welfare and health. Of late, considerable proof has surfaced indicating that patently various microbial pathogens utilize conventional methods in causing infection and illness. For instance, most different bacterial pathogens utilize mechanisms as per their capabilities to bond, attack and trigger harm to host tissues and cells, in addition to surviving host resistance and launch infection. Most occurrences of infection seem to be linked to the gaining of huge virulence genes blocks from a universal microbial ancestor, which is spread to additional bacteria utilizing parallel transfer. This parallel transmission of huge tracks of virulence carriers is proportionally accredited to the steady surfacing of new species in bacterial pathogens, most that are resilient to numerous antibiotics[43].

In reality, the antibiotic resilience of pathogens is emerging among the most crucial problems facing critical healthcare practitioners. A more absolute understanding of the main topics into microbial pathogenicity is fundamental in comprehending microbial virulence of molecular mechanisms, as well as in developing novel vaccines with therapeutic approaches for improved prevention and remedy of infectious illnesses. While it is afar the scale of this journal to confer in-depth particulars of molecular means in bacterial pathogenesis, the study concentrates on several mechanisms employed by bacterial pathogens in causing infectious sickness[19].

Listeriosis

Listeria monocytogenes is described as the underlying agent causing the ailment Listeriosis, a zoonotic disease affecting both human beings and animals. Listeriosis, though has long incubation periods making it hard to trail the cause of an epidemic. An estimated 5% of all fit humans host *Listeria monocytogenes* thrive within the gastrointestinal tract. The gastrointestinal tract is bile-rich and thus provides a favorable environment for the thriving of *Listeria monocytogenes*[17]. Humans get rid of the microbes in their fecal waste and often no symptoms of sickness are noticeable[45]. This pathogenic bacterium is fit for intersection of the epithelial walls making it possible for bacterial reproduction, which is many at time influenced by certain host conditions. Persons at risk of Listeriosis consist of a distinct high-risk set comprising of neonates, pregnant women, and low immunity adults[24].

GROWTH AND CONTROL OF LISTERIA MONOCYTOGENES

Growth

Listeria monocytogenes is favored by several conditions that make it thrive and multiply easily. The conditions are: pH 7.0, range 4.4-9.4, temperature 37°C-45 °C, range -1.5, atmosphere microaerophilic conditions at approximately 30% CO2, least water activity of 0.92 (≡11.5 % NaCl)[41].

Survival

Listeria monocytogenes thrives well at freezing temperatures, but the atmosphere does not influence the survival[27].

Inactivation

Listeria monocytogenes is inactivated rapidly by temperatures beyond 70oC, and pH levels below 4.4 and depending on temperatures and acidulates. High temperature favors the process, and

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macrobiotic acids appear more efficient as opposed to mineral acids[43]. The pathogen is capable of being viable for a long time under a dry environment[27].

Pathogenesis of listeria monocytogenesis

Listeria, a facultative intracellular pathogen, is primarily found in decomposing vegetable as well as soil and matter. In adults, most Listeria diseases arise from the oral intake and succeeding intestinal mucosal infiltration as well as systemic infection. *Listeria monocytogenes* is an extremely insidious intracellular pathogen[42]. Macrophages vigorously consume *Listeria monocytogenes*[1]. This internalization of bacteria is initiated by *Listeria monocytogenes*. The pathogen occurs in a vacuole that is afterward lysed by microbes facilitating its diversion in the cytoplasm of cells of the hosts. The bacteria later polymerize actin threads on one end forming elongated actin tails that drive it in the cytoplasm. Membrane proteins InlA and InlB promote this attack and survival[41]. The enforced phagocytosis transports *Listeria monocytogenes* to host cells enclosed in vacuoles, hence the escape of bacteria via protein hemolysin listeriolysin O (LLO). *Listeria monocytogenes* genes that take part in the intracellular phase are a group known as PrfA-reliant gene mass and are found in the chromosome. The genes are; plcA, plcB, actA, hly, prfA and mpl[24]

Mechanisms of bacterial pathogenicity

Pathogenic bacteria employ several mechanisms in causing disease to human hosts. They express a broad variety of molecules, which bind host unit targets thereby facilitating multiple diverse host responses. The molecular modes employed by bacteria in their interaction with the person are distinctive to particular pathogens and limited across numerous different species. The solution to fighting bacterial-related sickness is by identifying and categorizing all the various strategies used by the bacteria. The accessibility of absolute genome cycles for different bacterial pathogens in addition to bioinformatics will result in significant developments in achieving this goal[40].

ALTERATION MECHANISMS OF LISTERIA MONOCYTOGENES

Alteration to Low pH

In the course of passage through the gastrointestinal tract of humans, the *Listeria monocytogenes* comes across low pH surroundings in both the duodenum and stomach[1]. In humans, the low stomach pH offers a considerable hindrance to *Listeria monocytogenes* disease. Patients on gastric acid (such as proton drive inhibitors) reduction medications are more susceptible to infection. Listeria possesses several systems for the regulation of intracellular pH in case of contact with acidic environments[19].

Glutamate decarboxylase (GAD) tract plays a vital role in mediating pH homeostasis. In L. monocytogenes, the tract is compound and consists of three-glutamate decarboxylase enzymes (GadD1, GadD2 and GadD3) coupled with two glutamate antiporters (GadT1 and GadT2)[9]. In fact, gadT1, as well as gadD1 genes, are noticeable on the five-gene strain survival islet (SSI-1)[36], containing genes for encoding putative penicillin. This allows utmost bile tolerance[5].

The GABA has known to accumulate in the pathogen in the influence of minimum growth conditions making it thrive in almost all environments. Actually, during the colonization the gastrointestinal tract, all the GAD tract elements in listeria undergo transcriptional up regulation[1]. The L. monocytogenes subspecies as well possess an arginine deiminase (ADI) passage as well as an agmantine (AgDI) deiminase system hence contributing to pH homeostasis[39].

Alteration to bile acids

The Bile acids are manufactured in the liver from cholesterol, accumulated in the gall bladder and flow in the esophagus in a postprandial manner[39]. These acids may interrupt the membrane structure of bacteria thereby dissociating membrane proteins and eventually inducing DNA damage[38]. A recent study by Payne et al. (2013) confirmed these results during the analysis of proteome in L. monocytogenes in the presence of bile acids in anaerobic conditions[35].

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The study revealed changes in the proteins linked with the DNA repair, chaperone action as well as oxidative strain reactions comprising of increased heights of DNA disparity repair proteins, DnaK as well as the excinuclease ABC protein (UvrABC)[5].

Likewise, previous tests on the transcriptomic reaction of L. monocytogenes to mammalian bile have presented insights into the way bile can play the role of a particular signal through gastrointestinal transit[37]. The study revealed that bile contact controls several virulence features in L.monocytogenes. The work specifically the work recognized a TetR-type controller (BrtA) which senses bile (particularly the bile acid cholic acid); regulating the effect of the multidrug resistance (MDR) efflux pumps (MdrT and MdrM) which intervene in gall bladder/liver colonization as well as bile tolerance[36]. This finding is mainly pertinent given the greater task of MdrM/T of intervening emission of cyclic-di-AMP, an indication molecule for triggering STING-dependent creation of interferon-beta in addition to promoting in vivo endurance of the bacteria[5].

Recent work suggests that Sigma B and bile salt hydrolyses (BSH) are not vital for the thriving of L. monocytogenes in murine gall bladder[14], and pathogen relies on expression of channels necessary for nutrient gaining and/or the fusion of single bio-molecules[7].

Stress adaptation

Due to the proof of transient fecal nature of L. monocytogenes, there is a possibility the bacteria is the most undisputed allochthonous carrier in human being gut as opposed to autochthonous commensal. Most listeria genes are positively affected by the microbiota and usually necessitate the adjustment to gut surrounding[34]. They comprise of genes encoding routes normally involved in propanediol and ethanolamine metabolism as noticed in gastrointestinal thriving of Listeria and other pathogens. Practical genetic methods have been used in determining fundamental systems necessary for survival in the gastrointestinal tract. Preceding studies used mariner transposon-related mutagenesis method in identifying the loci taking part in the gastrointestinal cycle of L. monocytogenes infectivity[10].

Food matrix effects on listeria monocytogenes

Moderately few investigations have analyzed the effect of food matrix on succeeding infectious capability in L. monocytogenes[2]. Preceding physiological research has entailed that extracellular glutamate levels that acts as substrate for the GAD tract or carnitine that is absorbed mainly by OpuC carrier might possess the potential of influencing infectivity of gastrointestinal tract[3]. Moreover, salt or acid adaptation in the course of growth of food can influence the strain hardening of the pathogen, promoting subsequent thriving in the gut[33]. Both proteomic and transcriptomic methods are being exploited to enhance the understanding of molecular mechanisms strengthening cross-adaptation to diverse stresses. In addition to the interaction of various regulatory networks[26].

Existence of listeria monocytogenes as a food borne bacterium

Alterations in the production of food coupled with escalating demands of the society have amplified the food borne sickness incidences[32]. *Listeria monocytogenes* ability to multiply difficult to control during food processing is that it can multiply under a broad temperature range; even refrigerator temperature renders it complex to manage in processing food. Research has revealed that in nature, sheep are major carriers of Listeria[32].

Influence of microbiota on listeria colonization

L. monocytogenes is a tractable and painstaking target in the demonstration of the hindrance influence of probiotics commensal on infection or colonization[2]. In vitro unit culture, research reveals that cell attack by L. monocytogenes is restrained by various commensal pathogens[4]. Analyzes through germ-free rats also evidently reveal the importance of gastrointestinal microbiota as a hindrance to an infection caused by the pathogen[12]. Probiotics commensal defend gastrointestinal pathogens through several mechanisms such as immune modulation, enrichment of epithelial wall, bacterial indication events (such as quorum sensing) and direct antagonism[31]. Investigations have been done on several of these possible mechanisms of Listeria oral con-

tagion models. Research reveals that bacteriocin creation in situ offers a mechanistic ground through which microbiota defends against food bornepathogen[40].

Serological association of listeria species

Serology is typically an implement used in epidemiological studies. It involves analyzing the features and influence of serums (i.e. semen, blood sweat saliva as well as fecal matter) to identify the occurrence of antibodies counteracting a microorganism[5]. The species are serotyped based on flagella (H) and cellular (O) antigens. Serology is mostly used in cases where epidemiology is critical to case study or an epidemic[30]. A majority of *Listeria monocytogenes* isolates are serotyped through commercially existing sera, a serum containing antibodies Sera is serum that contains antibodies that have been acquired from an immunized animal through contagion with antigen-rich microorganisms or antigen injection[40].

Inhibiting the growth of listeria monocytogenes

To manage postproduction contagion of food produce, several research avenues have been discovered[6]. The employment of peril testing and critical regulatory point policies has permitted processors to recognize concern areas and find solutions to the problem[29]. Other techniques used for minimizing *Listeria monocytogenes* involve using minimal dose irradiation as well as high dose irradiation. Likewise, prevention of *Listeria monocytogenes* in juice concentrates has also been achieved[35].

Microbiology

Among all the Listeria species, *L. monocytogenes* mostly infects humans. Listeria is anaerobic in nature, beta-hemolytic, motile, short, non–spore-forming, gram-positive tail exhibiting typical low motility in light microscopy[7]. Listeria appears individually or as brief chains. On a Gram blot, Listeria resembles diphtheroids (Corynebacteria), pneumococci, enterococci, and can even be gram alterable making it difficult to differentiate from Haemophilus species. Listeria yields a typical form in blood agar and small portions of lucid beta-hemolysis covering each colony[28]. Listeria thrives properly at low temperatures (4°-10°C)[31].

Since the early seclusion and depiction at the beginning of 19th century *Listeria monocytogenes* has evolved to be of global prevalence and mostly linked with severe illness in a broad range of organisms, man included[8]. Our expertise on the bacterial pathogen, as well as the different types of listeriosis caused by it, has until of late been very limited[27]. However, the ongoing advances in bacterial typing, isolation methods, taxonomy, cell biology, and molecular biology have broadened our knowledge[26]. *Listeria monocytogenes* is an extremely flexible ecological bacterium with the ability to exist as either a plant saprophyte or an animal pathogen under the influence of a strong range of controlled virulence factors[18]. Most listeriosis cases are because of consumption of contaminated foodstuff[9]. Although several types of the disease are easily identifiable, including septicaemia and encephalitis, the epidemiological features as well as the pathogenesis of contagion in most ruminants continue to be inadequately understood[25]. The bacteria attack the tangential nerve cells therefore gaining direct access through the brain causing severe damage[10]. Therefore, this has been hypothesized as one of the unique traits of listeria virulence. Therefore, this calls for the invention of more relevant and viable sickness models to aid in the investigation of this phenomenon[18].

Control and treatment of listeria monocytogenes

Over the years, healthcare practitioners have worked tirelessly to find solutions to end the epidemic caused by *listeria monocytogenes*. Interim listeria measures have been introduced in concern to ready-to-consumer food products[24]. The meat and food industry has imposed post lethality Medicare as well as growth inhibitors on *listeria monocytogenes*, and uphold sanitation standards in the processing zones in an effort to control the spreading of the pathogens[23]. Case in point, the nutrition Safety and scrutiny Service in the United States' department of agriculture has issued new guidelines for the "Verification Procedures for the *Listeria monocytogenes* Regulation and Microbial Sampling of Ready-to-Eat (RTE) Products, which has to be

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followed in the control of *listeria monocytogenes*on all ready to consumed products[8].

Prevention of listeriosis as a foodborne disease demands the upholding of efficient sanitation standards on all food contact zones. Cossart (2011) once argued that Alcohol is a helpful topical sterilizer against *Listeria monocytogenes*. In addition, quaternary ammonium combined with alcohol can be effective as food zones sterilizer when used for prolonged periods. At home, precautionary measures need to be taken during food storage[22]. Food for refrigeration should be at temperatures below 4 °C as this would to inhibit bacterial growth. Contact surfaces ought to be clean and sterilized occasionally to prevent re-emergence and multiplication of *listeria monocytogenes*. In the food industry, the application of antimicrobials has become common[12]. These are agents used to inhibit the growth and possibly eliminate *listeria monocytogenes*[21]. The antimicrobial agents act in two ways; cidal or stasis mechanisms. Antimicrobials that utterly destroy and eliminate the pathogen are said to be cidal in nature. Those that only inhibit the growth of *listeria monocytogenes* are stasis antimicrobials. Too often, chemical reagents used in the control of listeriosis are cidal in nature and are meant to sterilize and disinfect food contact zones thereby killing all present microbes. For preservation purposes, the antimicrobials used are cidal that inhibit thriving of the bacteria, as opposed to stasis that may cause harm to the users [28].

Treatment of listeriosis in most cases involves the use of antibiotics. For non-invasive listeriosis, pathogens often stay in the digestive system and cause only slight symptoms that last for just a few days, and only need supportive care[10]. The fever and muscle pain that result are easily treated using over-the-counter prescriptions while the gastroenteritis and diarrhea are treated using more complex over-the-counter prescriptions[13]. However, for the invasive form of listeriosis, the pathogens spread into the central nervous system as well as the bloodstream, causing severe disease[14]. The treatment usually involves the intravenous administration of a high dosage of antimicrobials and requires in-patient facility care for close monitoring[19]. These antimicrobials include penicillin, ampicillin and amoxicillin depending on the severity of the infection. Patients with immune-compromised systems are often treated with more complex doses of antimicrobials and supplements for boosting their immunity. Quick arrest of listeria contagious is vital especially for pregnant and immune compromised persons[25].

Future perspective of listeria monocytogenes

What are the prospects on research in comprehending microbial pathogenesis and the mechanisms of survival of *listeria monocytogenes*? With the ongoing scientific developments, DNA sequencing, as well as microarray related gene extractions, scientists are likely to ascertain promptly the total genomic cycles of both the microbial pathogens and their hosts, and eventually assess the gene with a description of events following infection by *listeria monocytogenes*[25]. The use of these techniques on microbial pathogens genomes and the respective hosts, coupled with effective analytical methods as well as genome scale techniques for the study of gene representation, is transforming the advancement of novel techniques for identification, prognosis, as well as the clinical control of contagious disease[18]. In fact, the application of such technologies has resulted in the detection of common control mechanisms, secretory machinery, and homology amongst certain virulence molecules. In addition to these, recent use of high compactness genomic profiling in examining molecular responses of host cells on infection by several microbial pathogens will help elucidate the compound interactions between the pathogen and host throughout the infection course[17]. The accessibility of several absolute genome cycles of microbial pathogens has considerably played part in our awareness of the contagious disease cycle leading to the insight that most of such organisms make use of general mechanisms in causing infection and sickness[15].

It is predict that novel techniques and tactics will be applied in advancing the speed of eradicating microbial pathogenesis[16]. Although considerable improvements have been made to understand active interactions between the hosts and pathogens throughout the infection cycle, our knowledge of the pro-

cesses is however at its infancy[15]. As our basic understanding of ordinary subjects on microbial pathogenicity intensifies, it may be projected that the mechanisms, through which microbial disease can be managed using vaccines as well as other new therapeutic techniques, will minimize the probability and thus the effects of infectious sicknesses. Such improvements will offer the desperately desired novel medication for the rising dominance of fatal contagious diseases that have acquired manifold resistance towards antibiotics[13].

CONCLUSION

Listeria monocytogenes is one of the leading causes of contagious disease across the globe. *Listeria monocytogenes*, a foodborne pathogen, has been of alarm to ready-to-eat food manufacturers. The meat and food industry is a steadily advancing entity. Processors dynamically toil to uphold superior and safety in their products. This ever-present pathogen is capable of surviving and growing at diverse temperatures. This review focused on the mechanisms of survival of the pathogen, pathogenesis as well as novel advances in the epidemiology of *listeria monocytogenes*. *Listeria monocytogenes* is a gram-positive pathogen responsible for causing the contagious disease listeriosis. The pathogen has developed new mechanisms of surviving diverse environments, a situation that has proved difficult to control. Healthcare practitioners in collaboration with scientists are working round the clock in ensuring proper control and possibly elimination of contagious diseases.

Increased knowledge of the means through which L. monocytogenes adjusts to host cells and environments holds the potential of informing the advancement of new prevention and even treatment strategies. With the advancement in scientific research, healthcare practitioners and scientists are likely to find lasting solutions to end this menace. Antimicrobials coupled with other therapeutic methods are being put in place to control *listeria monocytogenes* before the situation gets out of hand. Although advances in pathogenesis are underway, much needs to be done if we are to win the fight against *listeria monocytogenes*. Awareness to the public through educative forums on protective measures to avoid spreading of the bacteria is essential in attaining a listeria free society. Technological innovations will help a great deal in this mission. Having been armed with enough insight into the mechanisms of *listeria monocytogenes*, pathogenesis and epidemiology, survival tactics, control and treatment of the pathogen, we are in a better position to prevent spreading of listeriosis by taking precautionary measures. In addition, we leave the task of finding lasting solutions to the scientists.

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