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#### Review

## A review of *Listeria monocytogenes*: An update on outbreaks, virulence, dose-response, ecology, and risk assessments



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#### ABSTRACT

Improved control measures starting in the 1990s have greatly reduced the prevalence of L. monocytogenes in many food categories, particularly in meats and meat products. However, the rate of listeriosis has remained constant during the last decade and the more severe, systemic (invasive) form of listeriosis is now recognized as occurring more frequently in small outbreaks than previously recognized. This review addresses the recent advances in epidemiology and virulence, in growth and modelling, and insights from the risk assessments. Recognition of recent outbreaks from food vehicles not traditionally associated with L. monocytogenes (celery, cantaloupe, mung bean sprouts, stone fruits, caramel apples and ice cream) was facilitated by PFGE and, increasingly, whole genome sequencing. The Key Events framework, an understanding of the key individual biochemical steps from ingestion to infection, provides a structure for relating new knowledge on strain variability, mutations, and host susceptibility to the probability of illness. Guidance for determination of the growth/no growth potential of a food has been issued by several regulatory authorities and the risk assessments indicate that prevention of growth remains a principle control element. The recognition of biofilm formation and the possible existence of dormant, non-dividing persister cells will require additional attention. The recent outbreaks underscored the individual characteristics of specific foods (melons vs all fruit; microenvironments in the caramel apples) and raised questions about the current understanding of infectivity of lower doses and the susceptibility of specific individuals. Advances have been made in these areas, but further research is clearly necessary to control this pathogen.

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#### **Contents**

1.	Introd	duction		
		Purpose of workshop and this paper		
3.		Recent advances in epidemiology and virulence		
		Recent advances in growth & modelling		
		Insights from risk assessments		
	Recent advances in epidemiology, virulence and dose response			
		WGS/PFGE and impact on outbreak identification and strain traceability		
		Food vehicles and outbreaks		
	3.2.	3.2.1. The European Union		
		3.2.1 IIS outbreaks		

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	Strain variation & virulence	4	
		3.3.1. Strain variation in tolerance to quaternary ammonium disinfectants and to phage	4
		3.3.2. Mutations in inIA, premature stop codon and virulence	4
		3.3.3. Pathogenesis models	5
		3.3.4. Key events framework	
4.	Recen	nt advances in ecology, persistence and growth	
	4.1.	Ecology of growth and survival	5
	4.2.	Persistence of cells in food environments	6
	4.3.	Defining growth/no growth conditions	
5.	Insigh	hts from risk assessments	. 8
	5.1.	Background	8
	5.2.	FAO/WHO - 2004	8
	5.3.	FSIS – 2010 and follow-up risk assessments	9
	5.4.	Dose-response modelling	9
6.	Resea	arch and data needs	. 9
	6.1.	Outbreaks and virulence	
	6.2.	Ecology and persistence	9
	6.3.	Risk assessment and dose response	. 10
7.	Concl	lusions	10
	Fundi	ing	11
	Ackno	owledgements	. 11
		ences	

#### 1. Introduction

Listeria monocytogenes remains a significant cause of foodborne illness. Even though the illness is in most cases expressed as a mild, febrile illness, it can also present as systemic (invasive) listeriosis with more severe symptoms and high hospitalization and case fatality rates. The incidence of listeriosis is low in the general population despite the wide distribution of the microorganism in the environment and the relatively high frequency of isolation in foods. The incidence of systemic listeriosis is much higher in susceptible populations, including pregnant women, the elderly and individuals with compromised immune systems.

Improved control measures starting in the 1990s have greatly reduced the prevalence of *L. monocytogenes* in many food categories, particularly in meats and meat products. However, the rate of illness has remained constant during the last decade. Furthermore recent outbreaks have challenged the conclusions of existing risk assessments and our understanding of the influence of virulence, host and food matrix on foodborne illness.

*L. monocytogenes* is widespread in the environment, and control of *Listeria* in food production facilities requires constant focus by risk managers. Therefore, better understanding of the characteristics of the microorganism, environmental impact, and interactions of virulence factors with host susceptibilities is necessary to devise better control measures to reduce the incidence of listeriosis.

#### 2. Purpose of workshop and this paper

A workshop was hosted by the Joint Institute of Food Safety and Applied Nutrition (JIFSAN), University of Maryland and the Grocery Manufacturers Association Science and Education Foundation at the Greenbelt Marriott Hotel, Greenbelt, MD on *June 16-18th 2015*. The purpose of this workshop was to facilitate a discussion amongst experts to evaluate the latest information on risk factors of *L. monocytogenes*, to determine what additional information is needed to answer remaining questions on *L. monocytogenes* risks, and to facilitate the development of effective risk management strategies. In 2011, the Interagency Risk Assessment Consortium (IRAC) and the Joint Institute for Food Safety and Applied Nutrition (JIFSAN) sponsored a workshop that summarized the state of

knowledge at that time about *L. monocytogenes* and foodborne listeriosis, and identified additional information that would be needed to improve assessment of *L. monocytogenes* risk (Hoelzer et al., 2013).

The 2015 workshop reviewed advances in our understanding to see if we addressed the gaps identified in the 2011 workshop and to see if there were any new information needs. The workshop asked additional questions that could be important to risk managers. Specific areas of interest were factors impacting virulence, criteria to evaluate whether a foodstuff supports the growth of *Listeria*, reviewing knowledge gained from recent outbreaks, evaluating the scope of existing risk assessments to determine what additional questions are relevant for risk managers (i.e. U.S. FDA/FSIS, 2003; FAO/WHO, 2004ab; U.S. FDA/FSIS, 2010).

The workshop participants addressed questions in three areas:

#### 2.1. Recent advances in epidemiology and virulence

What do the recent outbreaks from food vehicles not traditionally associated with listeriosis tell us? Do differences among strains have an impact on virulence of specific immunocompromised subpopulations? What has been the impact of genetic tools such as Whole Genome Sequencing (WGS) and Pulsed field gel electrophoresis (PFGE) on outbreak identification and strain traceability?

#### 2.2. Recent advances in growth & modelling

Based upon current understanding of public health impact, are any changes needed to the current approaches or focus on the management of the manufacturing of products in which *L. monocytogenes* cannot grow? Do we fully understand the ecology of growth and survival; in particular, are the definition criteria to define "products in which *L. monocytogenes* cannot grow" clear and scientifically sound? Can persister cells, which have enhanced survival capabilities, be present in foods?

#### 2.3. Insights from risk assessments

Do recent incident/case investigations raise concerns about

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