Can the Ocean Make You Sick

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ABSTRACT: It is fitting for the theme of IIFET 2000 "Microbehavior and Macroresults" that some of the smallest life forms on planet Earth (caliciviruses measuring 36 nanometers in diameter), which replicate only inside the living cells of their hosts, be examined. From their beginnings in this microscopic ecologic niche where they are spawned, caliciviruses spill forth into a variety of ocean reservoirs and then bridge the land-sea interface where they can have profound effects on a variety of diverse life forms including livestock and humans. Thus, from the intracellular microenvironment to the macroenvironmental issues involving seafood harvest, livestock production and consumer concerns of seafood and food safety to the societal processes of human diseases and their diagnosis and prevention, the very large footprints of the very tiny caliciviruses will be examined for their relevance and impact on broad issues relative to this session. These are the biological, environmental and social processes affected by this virus of ocean origin.

Keywords: calicivirus, ocean, livestock, human, diseases, IIFET.

Introduction

Viruses can, on occasion, have great plasticity in nature. Perhaps the best example of this is found within the genus Vesivirus of the family Caliciviridea. Members of this group move freely between mammalian, amphibian, and teleost hosts. Their primary reservoirs are in ocean species and they have been found in invertebrate filter feeders such as commercial shellfish as described in Smith, A.W (2000).

Biology of Caliciviruses

Caliciviruses are small, round, single stranded, linear, positive sense RNA viruses of about 8,000 bases having a characteristic "soccer ball" appearance. They are about 36 nanometers in diameter and derive their name from the cup shaped depressions on their surface. They are unique among viruses pathogenic for animals in that the capsid (outer protein coat) is made up of 180 molecules of a single structural protein species linked as dimmers to form 90 capsomeres having an arch-like morphology when viewed at a resolution of 23 angstroms using cryomicroscopy and computer imaging as demonstrated by Prasad, BVV, et al., (1994).

Understanding the ecologic adaptiveness of caliciviruses is based on various phenomena inherit in RNA replicative mechanisms. In higher orders RNA is produced off of DNA templates to code for proteins, but RNA does not store the genetic code of the species thus mistakes in RNA replicative sequences are dead-end, so-to-speak, while the genetic codes are stored in the very stable DNA sequences. DNA replicative mechanisms have inbuilt proofreading and repair mechanisms which are missing from RNA replication. By lacking this mechanism, the RNA caliciviruses generate between 1-10 mistakes for every virus replicate. By this means progeny viruses from a single parent are virtually all genetic variants, thus replicating RNA viruses do not form reproducible "species", but instead are referred to as "quasispecies" as outlined by Holland, J. (1993). This author goes even further to explain that small RNA viruses (such as caliciviruses) can have a base substitution in up to 50% of the base sequences and remain viable. Because caliciviruses have about 8,000 bases that means there are 4^{4000} possible viable variants. To summarize in lay terms, virtually every individual calicivirus replicate is a genetic variant from all others and there are more possible viable variants than there are grains of sand in all the deserts and oceans on planet earth.

Caliciviruses survive in nature by rapidly replicating to extremely high copy numbers of up to 10,000 viruses per infected cell after only 4 to 8 hours of incubation and there can be billions of infected cells per single organ system. This provides a mechanism for showering an ecosystem with large numbers of viable viruses each different, therefore theoretically adaptable to a new host.

In addition to their inherit flexibility and large "attack" numbers, caliciviruses are relatively stable in most environments. For example they can remain viable in 15° Celsius sea water for more than two weeks and for years if frozen or if held at 4° Celsius in a highly reduced environment.

The mechanisms whereby the disease causing caliciviruses gain such wide and diverse geographic dispersion can be understood by examining some aspects of their ecologic niches. First and foremost, they are contained in ocean reservoirs as described more fully by Smith, A.W. and Boyt, P.M. (1990) and Smith, A.W. (2000). Here they can be shed or released into the water

column by infected hosts and bubbles rising through that column can scrub virus particulates from the water then burst at the surface projecting virus laden droplets into the air where prevailing winds can transport them to new and distant locations. Fish and migratory birds and marine mammals have all been shown to be infected with disease causing caliciviruses, thus they can be transported throughout the oceans onto and across the land where new host species become exposed and infected. They can move by land, sea, or air.

There are over 40 neutralizing types (infection with one type does not protect against infection with any other type) and as shown in Table 1 a single type can infect at least 18 different species representing a host diversity extending from teleosts to humans.

Table 1. Host Range for Calicivirus SMSV-5

Host	No. of species
Shellfish	3
Opal eye fish	
Seals	5
Swine	
Cattle	
Cetaceans	3
Horses	
Fox	
Monkeys	
Humans	

Environmental Issues

An appreciation for the known ocean distribution of the caliciviruses can be easily gained by viewing Table 1 and realizing that many of the species shown have very extensive migration cycles. For example male sperm whales are distributed globally with ranges extending to 55° latitude both North and South. Some California Grey whales will feed north of the Baring Straits then migrate into the Sea of Cortez for mating then return North each year. Some near-shore species may remain local for example, the opal eye perch and female California Sea Lions will not normally be found north of Point Conception California.

The distribution in livestock is not yet established on a global basis. However, in the United States where U.S. Department of Agriculture officials have since 1959 classed viruses of this groups Foreign Animal Disease Agents. Both cattle herds and swine have been and still are shown to be infected using the specific antibody tests and by our isolating from them caliciviruses which cause clinical cases of the Foreign Animal Disease, vesicular exanthema of swine. Table 2 provides a listing of virus types found since the date the virus was reported as eradicated from livestock to either elicit positive neutralizing antibody responses or positive viral shedding in agricultural species.

Table 2. Caliciviruses where neutralizing antibodies are seen in either cattle or swine.

VESV Types	SMSV Types
A_{48}	Types 1-13
B_{51}	Bovine calicivirus
I_{55}	

Waste disposal from agricultural livestock (primarily swine, dairy and beef cattle) production operations should be expected to provide environmental concerns for contaminated ground water and effluents leading to open waterways. These issues have gone essentially unaddressed as has the issue of caliciviruses in wastes from food processing including foods from livestock and those from ocean catches and aquaculture operations.

Social Processes

There are several societal issues that should be addressed. The first of these is the impact, if any, that can occur when fish or fish products contain caliciviruses that have previously gone unreported as potential livestock and human pathogens. It is not unrealistic to think that reporting the presence in U.S. livestock herds of caliciviruses which are the same as or are currently indistinguishable from a Foreign Animal Disease Agent could lead to trade issues both domestic and international. This would be especially true regarding exports when only the U.S. has acknowledged the presence of this agent class. The U.S. receives several billion dollars each year in revenues from cattle and cattle product exports, which have been traded seemingly without issues involving caliciviruses being addressed.

Perhaps more important from both a fisheries and production livestock view is the issue of food safety. Shellfish have long been known to be a common source of human infection from a related calicivirus, the Norwalk agent. However, the reporting that the caliciviruses of the genus Vesivirus are present in Teleosts and commercial shellfish as well as marine mammal carcasses that have been ground in a course burger stored frozen for a year then fed to and caused infection in susceptible animals suggests a variety of food safety issues. To see a listing of the diseases caused in animals viewed in this scenario as possible models for human disease see Table 3. The human health issues and implications have been discussed more fully by Smith, A.W., et al., (1998a and 1998b). The main lesson to be gained from this is that caliciviruses of ocean origin can find their way into our immediate environment, contaminate various foods, or animals we contact and we can become exposed then infected in a variety of ways. Our environment and our foods can all act as point sources of infection.

Table 3. Disease conditions Caused by Caliciviruses

*	Hepatitis
	Agalactia
*	Blistering
	Pheumonia
	Brain infections
	Myocarditis
	Muscle and Joint infection
*	Abortion

*Conditions in humans either caused by caliciviruses or evidence suggests causal association

However, there is now emerging evidence that human-to-human calicivirus transmission may also be occurring as shown in Table 4, which gives preliminary serologic results on human abortion and hepatitis.

Table 4. Human Disease (serologic Tests)

	No. Tested	No. Positive	Percent Positive	
Aborting Women	10	4	40%	
Normal Blood Donors	398	19	5%	
Donors with evidence of Hepatitis	197	16	8%	P=0.13
Developed Hepatitis after transfusion	32	7	22%	P=0.0016

Conclusions and Recommendations

Knowledge of pathogenic caliciviruses that infect fish, people and livestock can adversely affect perceptions of food/seafood safety and the marketability of these products. Presumably, the distribution of these agents is world wide involving all the continents as well as the oceans, but this is not yet confirmed. Reagents for testing blood samples as well as products to detect antibodies against caliciviruses or the presence of caliciviruses are being used and are being further refined at the Oregon State University Laboratory for Calicivirus Studies in collaboration with AVI BioPharma, Corvallis, Oregon. These can be made available on a research basis.

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