Overview of Zoonotic Infections from Fish and Shellfish

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Workshop Purpose

- **Provide an overview of zoonotic disease agents arising from fish and shellfish**
- **Highlight constraints in the determination of zoonotic disease from fishery products**
- **Provide preventative and remedial measures for aquaculturists, processors and consumers**
- **Generate awareness and interest in reporting/publishing zoonotic cases.**

Determination of zoonotic disease incidence from fishery products

- **Constraints**
  - **No cross disciplinary coordination of data sharing, research, and reporting between human and animal health professionals regarding health outcomes in animal and humans**

  Two bodies of literature-fish vs human health

  Limitations of study methods to evaluate clear linkages to human health

  Inadequate key words to search for zoonosis concept

Rabinowitz et al 2005 Animals as sentinels of human enviromental health hazards: An evidence based analysis, EcoHealth 2, 26-37

Determination of zoonotic disease incidence from fishery products

- **Constraints**
  - **Lack of commodity driven summaries by etiology in reports**
  - **variability of reporting between different countries (EFSA vs CDC)-different commodities**
  - **Disease incidence likely under-reported due to transience of the disease or lack of reporting mechanisms**
  - **No correlation between surveillence data and out breaks- (different surveillence criteria)**

Topically Acquired (Contact) Zoonosis

Acquired through water contact, stings, bites, spine/pincer puncture or open wounds

- **Risk groups and activities**
  - **Recreational water related activities-swimming, fishing, boating**
  - **Ornamental fish farmers, hobbyists, and public display aquarists-handling**
  - **Fish Processors, chefs –handling**
  - **Consumers- handling**

Topically Acquired (Contact) Zoonosis

- Catfish spine/venomous injuries are most common
- 9 families of catfish from marine and freshwater habitats worldwide
- Complex puncture wounds often complicated by severe pain and infection

Blomkalns and Otten (1999) Catfish spine envenomation: a case report and literature review. Wilderness and Environmental Medicine, 10, 242-246

Topically Acquired (Contact) Zoonosis

No reported

- **Parasitic**
- **Viral**
- **Fungal**

zoonoses acquired through handling of aquatic organisms

Bacteria are the primary causative agents for zoonotic infections through a contact route

Topically Acquired (Contact) Zoonosis

Principal fish/shellfish pathogens

- **Gram positive**
  - ***Streptococcus iniae***
  - ***Mycobacterium spp.***
- **Gram negative**
  - ***Edwardsiella tarda***
  - ***Aeromonas hydrophilia***
  - ***Vibrio vulnificus* and *V. damsela***

"Indigenous zoonotic pathogens"capable of causing disease in both fish and humans

Fish → **Humans = Zoonotic**

Foodborne (Ingestion) Zoonosis

Acquired through consumption of mishandled, raw or improperly cooked seafood

- **Risk groups and activities**
  - **Consumers, Food processers**
  - **Usually in immunodeficient (young) or immunocompromised (old) hosts**

Topically Acquired & Foodborne Acquired principal fish pathogens

Some organisms can be acquired through either route

Aeromonas hydrophila

Edwardsiella tarda

Vibrio spp.

Topically Acquired & Foodborne Acquired principal fish pathogens

Principal conditions of disease transmission

- *Season*
- *Patients contact with fishery, product or environment*
- *Dietary habits*
- *Immune system of exposed individual*

Topically Acquired *S. iniae*

Demographics of patients w/ Streptococcus iniae infection (1991-2004)

Human clinical signs	Age	Fish Exposure	Country	Reference
(12) Hand cellulitis (9), Septicemia w/endocarditis, meningitis & knee arthritis-1	69	Tilapia puncture	Canada	Weinstein et al 2007
(2) Bacteremic cellulitis in leg, spinal osteomyelitis-	80	Yes handling no injury	Hong Kong	Lau et al 2003; 2006
(1) Spinal osteomyelitis (2) Limb cellulitis Thumb infection in chef	73 67 24	Yes, cuts Yes, prick Yes, pincer	Singapore	Koh et al 2004; 2009
(7) Sepsis, pneumonia, cellulitis, osteomyelitis, toxic shock	71	??	USA	Facklam et al 2005
(1) Fever, abdomen distension	51	Yes husband fishmonger	Taiwan	Sun et al 2007

Topically Acquired *S. iniae*

Demographics of patients w/ Streptococcus iniae infection (1991-2004)

SUMMARY

- **26 reported cases**
- **Asian (22; 85%)**
- **Age (range 40-88;mean 70)**
- **Exposure to/handling fresh fish (15; 58%-42% unknown),**
- **Underlying conditions (35%) Unknown (42%)**
  - **Chronic rheumatic heart disease, osteoarthritis**
  - **Hypertrophic obstructive cardiomyopathy and duodenal ulcer and gallstones**
  - **Diabetes mellitus, hepatitis C related liver cirrhosis**
  - **Alcoholism**
  - **Hypertension, hypothyroidism**
  - **Partial masectomy**
- **Antibiotics administered:**

  ß-lactam antibiotics (penicillin, ampicillin, erythromycin, cefuroxime)

  Clindamycin, Romet, Tetracycline, Fluoroquinolones

Topically Acquired *S. iniae*

Constraints for diagnosis and link to seafood

- **Not identified by conventional identification systems in a diagnostic/clinical microbiological laboratory**
- **Little surveillance of *Streptococci* isolated from wounds, tissues**
- **Clinicians failure to derive history of fish exposure**

Prevention

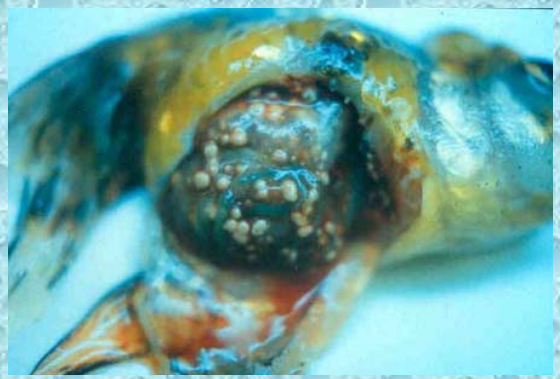
Protective equipment used when cleaning raw seafood

Prevalance of *S. iniae* potentially underestimated, particularly in Asian populations

Topically Acquired *Mycobacterium* spp.

Non-tuberculous myco (NTM) not *M. tuberculosis* and *M. leprae*

- **Currently, 120 recognized *Mycobacterium* spp.**
- **> 167 species of fish susceptible**
- **Worldwide distribution**
- **Synonyms- “swimming pool granuloma”, “fish tank granuloma”, fish handlers/fanciers disease, Fish TB”**



Topically Acquired *Mycobacterium* spp. with zoonotic potential

Species	Fish species	Region	Identification Reference
M. marinum	Saltwater	Worldwide	*Nichols et al 2004
M. chelonae	Salmonids	Pacific	Decostere et al 2004
M. fortuitum	Silver mullet	Venezuela	Perez et al 2001
	Review		Frerichs 1993/Chinabut 1999
M. absscessus	Silver mullet	Venezuela	Perez et al 2001
M. interjectum	Striped bass	USA-CB	Rhodes et al 2004
M. scrofulaceum	Striped bass	USA-PNW	Landsdell et al 1993
M. szulgai	Striped bass	USA-CB	Rhodes et al 2004
M. similae	Striped bass	USA-PNW	Landsdell et al 2003
M. triplex-like	Striped bass	USA-CB	Rhodes et al 2004

*Nichols et al 2004. Introduction. In: Pathogenic Mycobacteria in Water: A Guide to Public Health Consequences, Monitoring, and Management (ed. S. Pedley, J. Bartram, G. Rees, A. Dufour &J. Cotruvo) pp. 1-14. World Health Organization, IWA Publishing, London.

Topically Acquired *Mycobacterium* spp.

Undetermined zoonotic potential and infrequent isolation

Species	Fish species	Region	Identification Reference
*M. chesapeaki**	Striped bass	USA	Heckert et al 2001
M. montefiorense	Moray eels (W&C)	USA	Herbst et al 2001
M. shottsii	Striped bass	USA	Rhodes et al 2001
M. pseudoshottsii	Striped bass	USA	Rhodes et al 2005

* Growth at 37°

Topically Acquired *Mycobacterium marinum*

Clinical effects	Antibiotic trt	Reference	Region
Granulomatous inflammation, Nodular or diffuse granulomas of the skin, subcutaneous tissues and tendon sheaths of fingers and hands	Minocycline Tetracycline Romet Rifampicin Ethambutol	Lehane & Rawlin 2000 Durborow 1999 Huminer et al 1989 Lahey 2003	Worldwide
Invasive Septic arthritis & osteomyelitis in immunocompromised hosts			

Mycobacterium marinum in the USA

Laboratory-confirmed cases of *Mycobacterium marinum* in the five regions of the United States (40 states reporting), by year, 1993–1996a

	No. cases (%)			
Region	1993	1994	1995	1996
Northeast	21 (14)	40 (22)	34 (23)	28 (18)
Southeast	58 (38)	66 (37)	41 (28)	64 (41)
North central	43 (28)	38 (21)	27 (27)	38 (24)
South central	17 (11)	17 (10)	17 (17)	14 (9)
Mountain	8 (5)	11 (6)	13 (13)	7 (5)
Pacific	5 (3)	7 (4)	15 (15)	6 (4)
Total	152	179	147	157

- The Centers for Disease Control and Prevention (CDC) now includes *Mycobacterium marinum* on its list of "*Emerging Infectious Diseases*."

Mycobacterium marinum-

- Novotny et al 2004 Fish: a potential source of bacterial pathogens for human beings. Vet Med-Czech, 49, 343-358
- 99 publications-653 cases between 1966-1996 Of 193 exposures w/ known infections
  - 49% assoc. w/ aquarium exposure
  - 27% w/ injury by aquarium fish
  - 9% w/ injury during bathing in seawater
- Aubruy 2002-(France) model survey
  - 63 cases between 1996-1998
  - 84% assoc.. w/ fish tank exposure
  - 95% patients infection assoc w/ upper limb
  - 29% of patients infection spread to deeper structures

Mycobacterium marinum-Invasive cases

- **Summary of invasive cases published since 1966 from MEDLINE searches (Lahey 2003)**
- **35 cases**
- **Age- mean 43**
- **Symptoms-tenosynovitis (60%), septic arthritis (17%), osteomyelitis (37%)**
- **Source of infection-water exposure/fish or shellfish injury**
- **Immune impairment-systemic steroids, chemotherapy, AIDS**
- **Time to diagnosis-17 months from symptom onset**
- **Duration of therapy-average 11.4 months surgery in 69% of cases**

Topically Acquired *Mycobacterium marinum*

Constraints for diagnosis and link to fishery products and prevalence

- Presentation insidious and non-specific
- Delay between onset of symptoms and medical consultation average 5 months
- Delay to definitive diagnosis of 4.4 weeks
- Poor growth at 37C so missed in hospital labs
- Clinicians failure to derive history of fish exposure

Topically Acquired *Mycobacterium marinum*

Prevention- Steps to reduce risks of infection:

People should avoid fresh or salt wate if there are open cuts, scrapes, or sores on their skin, especially in bodies of water where *Mycobacterium marinum* is known to subsist.

Persons with immunodeficiency shouldavoid handling any sort of fish or cleaning out fish tanks.

People should wear heavy, waterproof gloves while cleaning or processing fish cleaning home aquariums or fish tanks. Everyone should wash hands thoroughly with soap and water after fish processing.

Ensure habitual and adequate chlorination of swimming pools and fish tanks to kill any bacteria that may be present

Topically & Foodborne Acquired *Aeromonas hydrophilia*

Clinical effects	Antibiotic trt	Reference	Region
Cellulitis Muscle necrosis or septicemia*	Tetracycline Romet Chloramphenicol	Lehane & Rawlin 2000 Janda & Duffy 1998	Worldwide Fresh & Brackish

*Usually in immunodeficient (young) or immunocompromised (old) hosts

Isolates differ greatly in pathogenicity

Constraints to identification:

Variable growth at 37C (optimal 20-25 C) so missed in hospital labs

Possibility of mixed infections

Topically & Foodborne Acquired *Edwardsiella tarda*

Clinical effects	Antibiotic trt	Reference	Region
Soft tissue wound infections	Gentamycin	Lehane & Rawlin 2000	Fresh Marine
Arthritis Osteomyelitis	Amoxicillin	Ashford et al 1998	
Septicemia*, meningitis, cholecystitis	Romet	Janda & Abbott 1993	
Gastroenteritis, diarhea*			

*Serious infection in individuals w/ pre-existing disease- hepatic cirrhosis or increased availability of iron

Endemic in tropical, underdeveloped countries

Constraints to identification:

Lower incubation (optimal 22-26 C) so missed in hospital labs

Topically & Foodborne Acquired *Vibrio vulnificus & V. damsela*

Clinical effects	Antibiotic trt	Reference	Region
Cellulitis	Tetracycline	Lehane & Rawlin 2000	Estuarine Marine
Necrotizing fasciitis	Carbapenems		
Myositis	Quinolone		
Foodborne Septicemia*			

V. vunificus **accounts for approx. 95% of all deaths associated with seafood consumption in the US**

***Death can occur in individuals w/ chronic underlying conditions: Hemochromotosis, hepatic cirrhosis, immunosuppression, renal failure & diabetes**

Topically Acquired *Vibrio vulnificus & V. damsela*

Constraints to identification:

Specialized laboratory procedures for recovery of fish associated bacteria

Cultures from marine wounds on media used for standard samples recovers about 0.1-1% of marine bacteria

Salt supplementation of media, incubation at lower temperatures for longer are needed.

Prevention

Cook shellfish (clams, oysters, mussels) thoroughly

Don’t eat raw or unopened shellfish after cooking

Topically Acquired *Vibrio vulnificus & V. damsela*

Topical Prevention

Avoid exposure of open wounds or broken skin to warm marine or brackish waters or to raw shellfish harvested from such waters

Wear protective clothing when handling raw shellfish

Foodborne Prevention

Cook shellfish (clams, oysters, mussels) thoroughly

Don’t eat raw or unopened shellfish after cooking

Eat shellfish promptly after cooking and refrigerate leftovers

Avoid cross-contamination of cooked seafood with raw seafood

Foodborne (Ingestion) Zoonosis Resources

- *http://www.cdc.gov/foodborneoutbreaks/*

OutbreakNet Team: Foodborne Disease Surveillance and Outbreak Investigation Toolkit

Foodborne Disease Surveillance and Outbreak Investigation Toolkit

Case Report Form for Listeriosis

Guide to Confirming a Diagnosis in Foodborne Disease

Guidelines for specimen collection

Public Health Training Network

Reporting form for foodborne Disease Outbreaks Instructions

Vibrio Illnesses

Standard Questionaires

- *European Food Safety Authority*
- *World Health Organization*

Foodborne Ingestion Zoonoses Indigenous in shellfish

RNA viruses

Norovirues (Norwalk-like viruses)-Calcivirus

Foodborne outbreaks of norovirus occur most often when infected food handlers do not wash their hands properly after visiting the bathroom.

EU?

Noravirus outbreaks (cases)	All	Fish	Shellfish	
			crustacea	Mollusks
1998-2002	657 (27,171)	0	0	1
2006	505 (14,753)	2 (36)	1 (43)	1 (11)

Foodborne (Ingestion) Zoonosis
Non-indigenous fish pathogens

Principal pathogens

- ***Salmonella***
- ***Shigella***
- ***Listeria monocytogenes***
- ***Campylobacter jejuni***
- ***Escherichia coli***
- ***Staphylococcus aureus***

Foodborne (Ingestion) Zoonosis

- **“Determining the proportion of outbreak-associated cases of foodborne illness due to the various food commodities is an important step”**

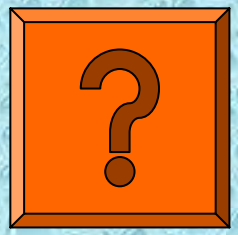
- **“Identification of particular food commodities causing outbreaks can help public health officials and the food industry to target control efforts from the farm to the table.”**

Foodborne disease outbreaks US 1998-2002 & 2006

Etiology	All outbreaks (cases)		Fish		Shellfish	
	1998-2002	2006				
Listeria	11 (256)	4 (10)	0	0	0	0
Vibrio parahemo	28 (625)	8 (322)	0	0	1(11)	7(303)
Bacillus cereus	37 (521)	31 (72)	0	0	1	0
Campylobacter	61 (1,440)	25 (301)	0	0	1	1(3)
Shigella	67 (3,677)	10 (185)	1	1 (8)	0	0
Staphylococcus	101 (2,766)	29 (428)	0	2 (4)	0	1(13)
Clostridium spp	142 (6,776)	34 (1,880)	0	0	2	1(55)
Salmonella	595 (16,821)	117 (3,296)	1	0	0	0

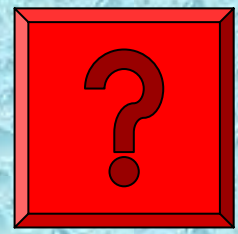
Trends and Sources of Zoonoses and Zoonotic Agents in the European Union in 2007- European Food Safety Authority

- Salmonella cases in humans (151,995) recorded in 2006 and 2007
- Listeriosis cases in humans (1,554 confirmed cases)
- A high fatality rate of 20%
- Detected above the legal safety limit 100 cfu/g in smoked fish and other ready-to-eat fishery products followed by ready-to-eat meat products and cheeses.
- Highest frequencies of samples above limits reported by Czech Republic in samples of smoked fish from processing and in samples from the Netherlands of smoked fish from retail
- http://enews.nieuwskiosk.nl/jump.aspx?i=541&e=6624&u=501206&li=60197&url=http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902267941.htm



Potential zoonosis

Lactococcus garvieae



Human Clinical effects	Antibiotic trt	Exposure
Fever & leg lesions	Penicillin	Yes-raw squid
Multiple organ failure	Died	Yes-grilled tilapia
Pain and fever	Cefazolin & gentamicin	?
Peritonitis	Piperacillin & amikacin	Yes-sashimi

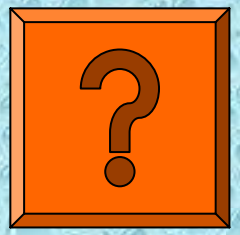
Disease associations between humans and fish unclear

- *Cases assoc w/season (June-Aug) w/ Increased incidence of L. garvieae in aquaculture farms*
- *All cases between 2000-2003 assoc w/ patients w/ gastrointestinal disorders*

Wang et al 2007. L. garvieae infections in humans: possible association w/aquaculture outbreaks. Int J of Clinical Practice, 61, 68-73.

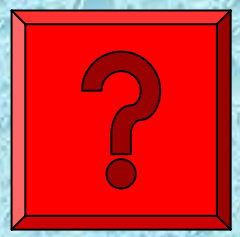
“Anthropogenic pathogens”

- Pathogens associated with humans and human activities and the environment
- Exploration of phylogenetic relationships and transmission studies
- Possibility that they are capable of infecting fish- GBS maybe an example



Streptococcus agalactiae zoonosis

Lancefield group B streptococcus (GBS)

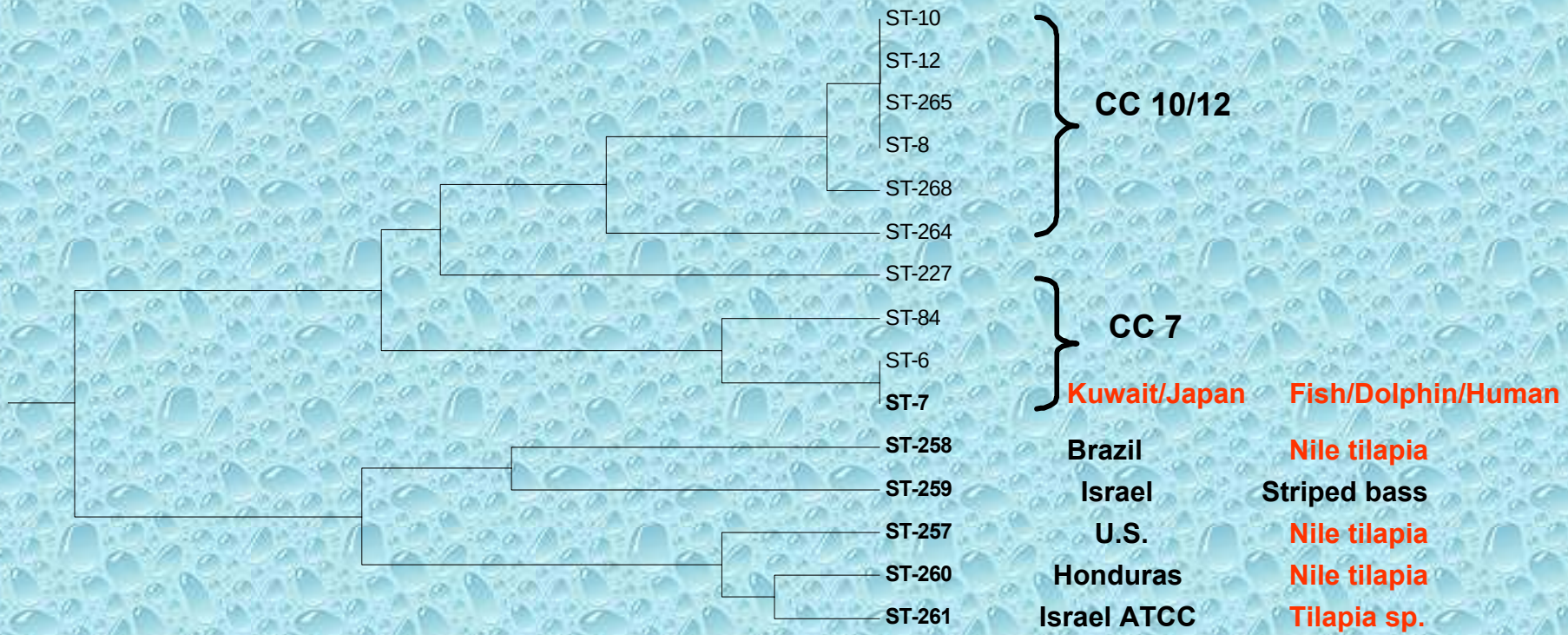
Human Clinical effects	Antibiotic trt	Reference	Region
None reported	Amoxicillin Bacitracin Choramphenicol Ciprofloxacin Clindamycin Erythromycin Oxytetracycline Penicillin Rifampin		

Human and bovine isolates resistant to vancomycin while aquatic isolates sensitive

Streptococcus agalactiae

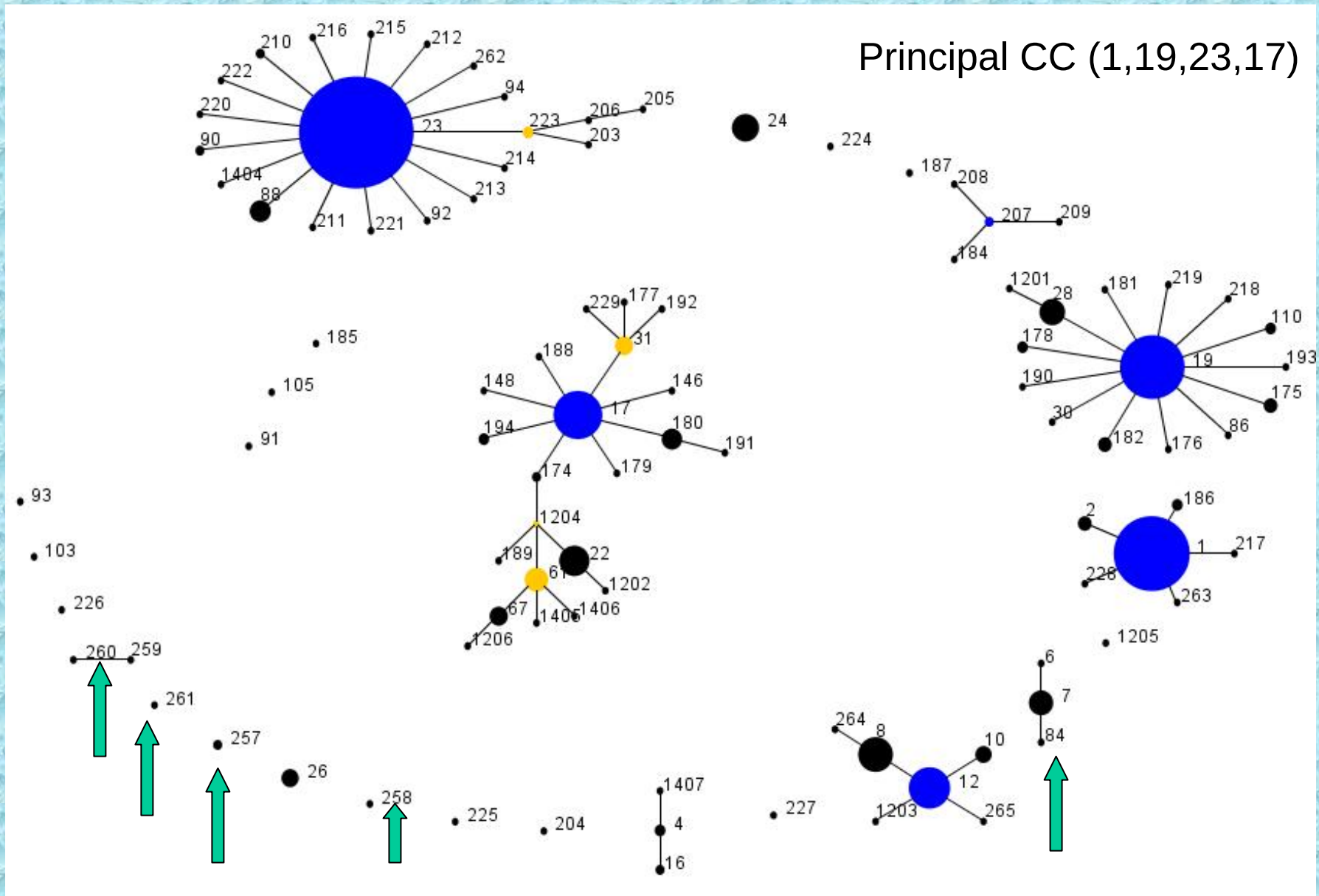
Lancefield group B streptococcus (GBS)

Fish, Dolphin, human and bovine isolate relationship

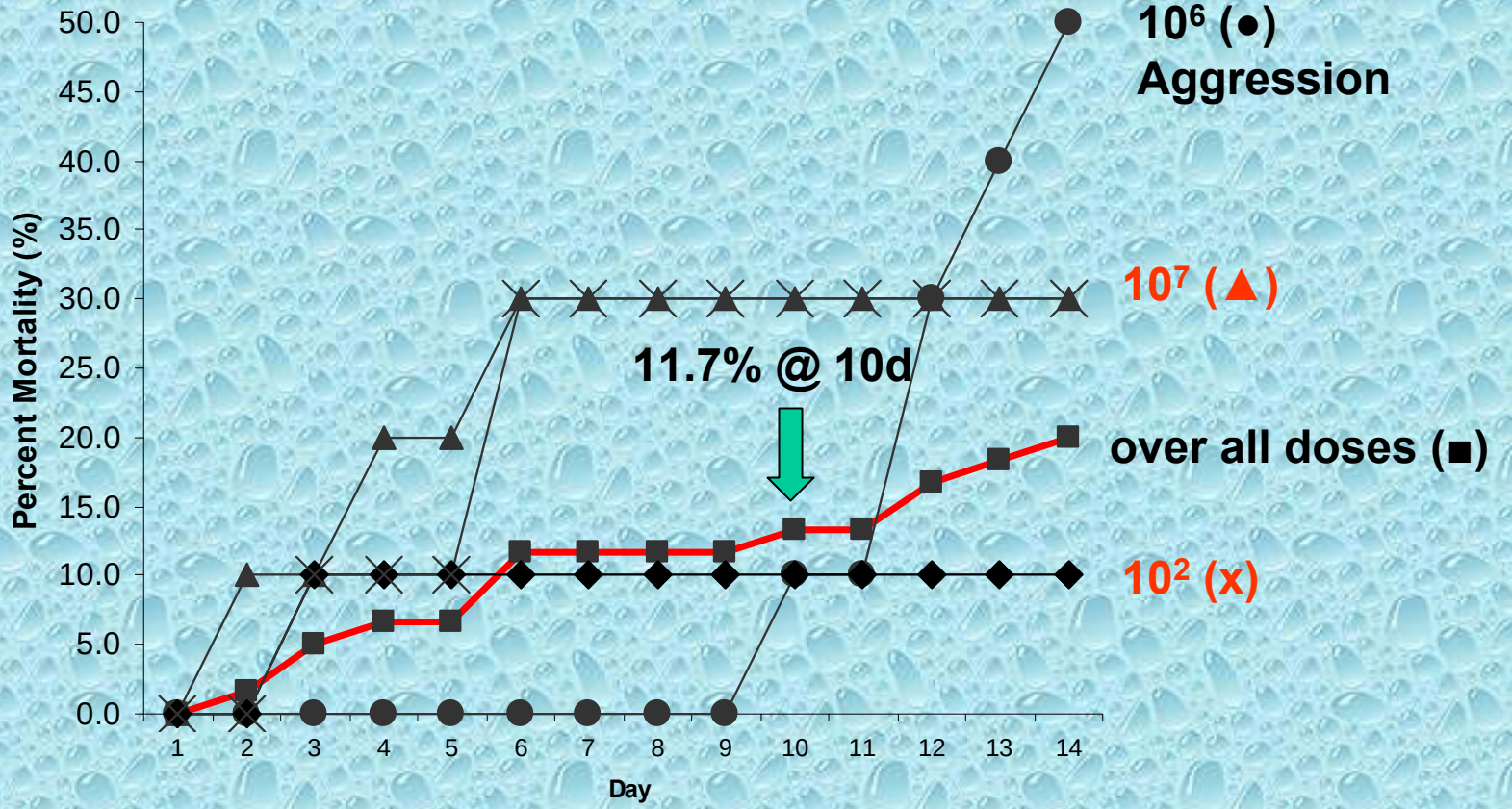


Dendrogram derived from unweighted pair group with arithmetric mean of concatenated sequences of the seven amplicons sequenced in the MLST analysis.

Sequence type (ST) Human, bovine, dolphin and piscine GBS strains (N=1150)



Cumulative % mortality of Nile tilapia from human isolate



Percent mortality of Nile Tilapia (n=60) over all doses (■) and percent mortality of 10 tilapia each challenged with a human *S. agalactiae* isolate (#510012) at 10^2 (x), 10^3 (⌛), 10^6 (●), and 10^7 (▲) cfu/fish.

S. agalactiae Mammalian isolates Experimental infectivity to Nile tilapia

Country	Host Origin	Dose cfu/fish	% Mortality	Reference
USA	Bovine	10^9-10^{10}	0	Garcia 2008
USA	Bovine	10^5 , 10^7	0	USDA unpublished
Kuwait	Bottlenose dolphin	1 x 10^7	90	Evans 2006c
Japan	Human	10^2-10^7	11.7	Evans et al 2008b

[1] Fish were challenged by IP injection with the specified isolate at the indicated doses and observed for mortalities for up to 14 days post-challenge.

Discussion points

- **Development of better and standardized reporting of zoonotic infections resulting from fishery-related activities**

- **Merger of fragmented scientific literature from both fisheries & human perspectives**