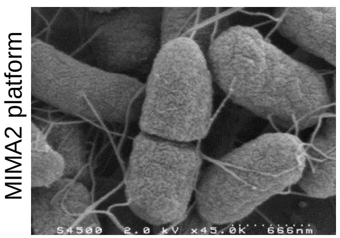
Emerging microbiological hazards bring new challenges to food safety



MIMA2 platform

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Introduction

Food Law Food operators shall not place unsafe foods on the market

5,196 foodborne outbreaks in Europe in 2013

43,183 human cases, 11 deaths

Why?

Mistakes

Contaminated raw materials — **Raw materials**

Mistakes during food preparation

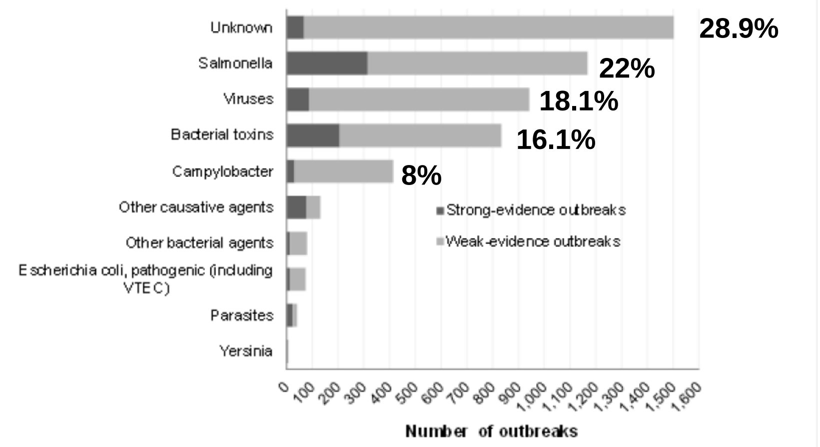
Contamination by staff

Contamination of equipment surfaces — **Food transformation**

Duration of preservation — **Storage (delivery/consumer's)**

Conditions of preservation (compromised temperature)

Safe food



Bacterial toxins include toxins produced by *Bacillus*, *Clostridium* and *Staphylococcus*. Food-borne viruses include calicivirus, hepatitis A virus, flavivirus, rotavirus and other unspecified viruses. Other causative agents include mushroom toxins, marine biotoxins, histamine, mycotoxins and escolar fish (wax esters). Parasites include primarily *Trichinella*, but also *Cryptosporidium*, *Giardia* and other unspecified parasites. Other bacterial agents include *Listeria*, *Brucella*, *Shigella*, *Vibrio* and other unspecified bacterial agents. In this figure, the category 'Pathogenic *Escherichia coli* (including VTEC)' also includes one strong-evidence outbreak due to pathogenic *E. coli* other than VTEC.

Figure 2. Distribution of all food-borne outbreaks per causative agent in the EU, 2013

(EFSA Journal 2015)

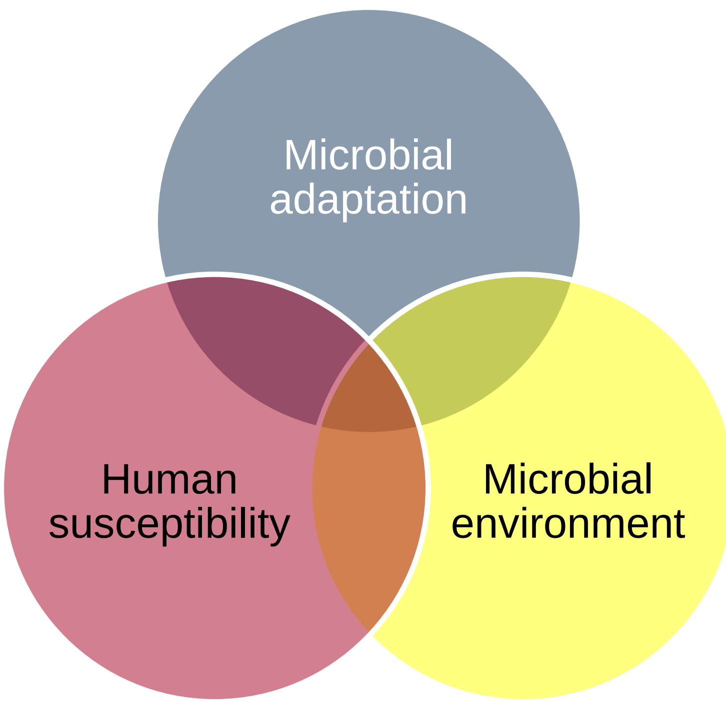
Emerging risks without relevant control measures

Introduction

Emerging infectious disease

- New (unknown) disease that emerge among the population
- Rapid increase of incidence or dissemination of an already known disease

Emergence of infectious disease is multifactorial



Time scale

low — **Speed of change** — **high**

Climatic disorders — Plasmid transfer

Spatial scale

restricted — **diffusion** — **large**

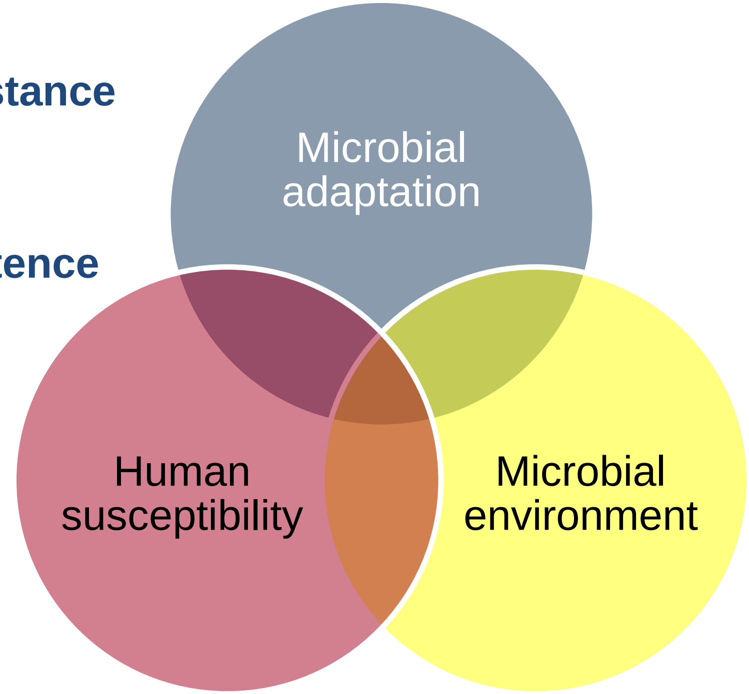
Plasmid transfer — Globalization of trade

Introduction

new virulence factors

new genes of resistance

adaptation to industrial environments and persistence



Climatic disorders

Agricultural practices

Modes of preservation

The elderly

Immunocompromised or chronically sick people

Modes of consumption

Trade and exchanges

A bit of history

Emergence of new hazards

Plague, cholera, dysentery (huge epidemics)

Typhoïd fever, bovine tuberculosis

Middle ages

1rst half of 20th century

Psychrotrophic bacteria because of generalization of refrigeration

- ***Yersinia enterocolitica*** **(1970)**
- ***Listeria monocytogenes*** **(1990)**
- ***Clostridium botulinum type E***

Disinfection of drinking water, sewage treatment, and milk pasteurization

50’: Refrigeration for food preservation

Zoonotic agents (transmission from animal to human)

- ***Campylobacter*** **(1980)**
- ***E.coli*** **EHEC (1980)**
- ***Vibrio parahaemolyticus*** **(1990)**

Microbial adaptation

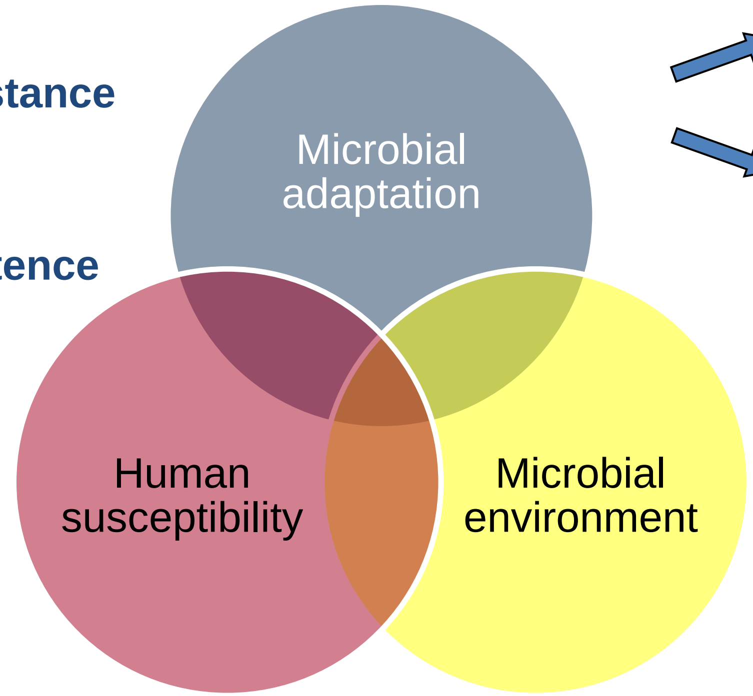
New pathogen

- **Newly identified pathogen** — Parasite *Cyclospora cayetanensis*
- **Pathogen that becomes more virulent or more resistant**

new virulence factors

new genes of resistance

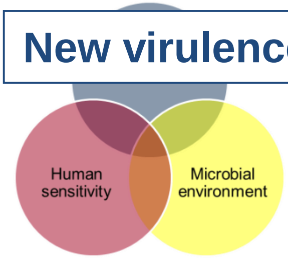
adaptation to industrial environments and persistence



- **Genetic changes**
- **Phenotypic changes**

Microbial adaptation

New virulence factors



1982: Foodborne infection by *E. coli* O157:H7 in USA

children with hemolytic and uremic syndrom (HUS)

Origin : minced beef (hamburgers)

Bovine

20 to 80% are carriers of STEC

5 to 20% are carriers of EHEC

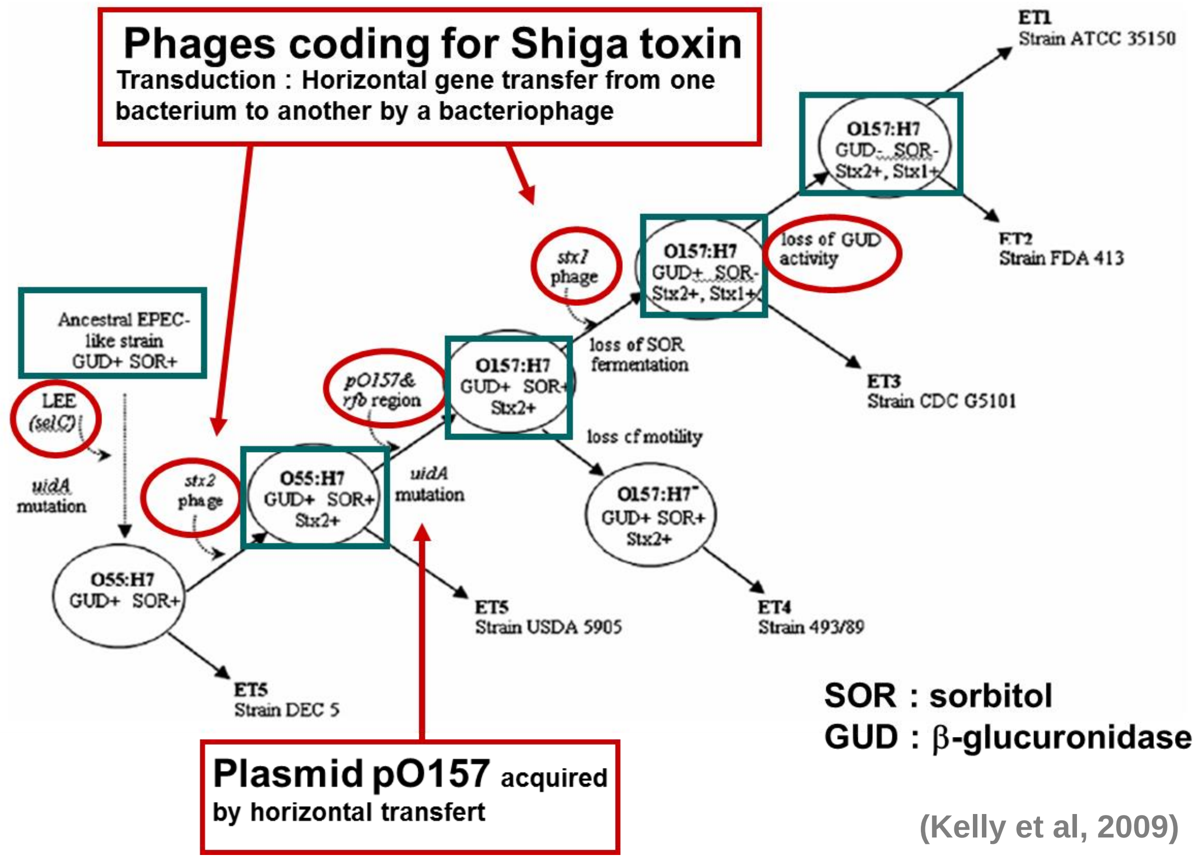
STEC

Shiga-toxin producing *E.coli*

EHEC

Enterohaemorrhagic *E.coli*

Evolution of EHEC O157: H7 from an non-toxigenic ancestor



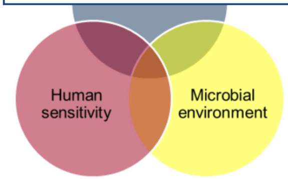
SOR : sorbitol

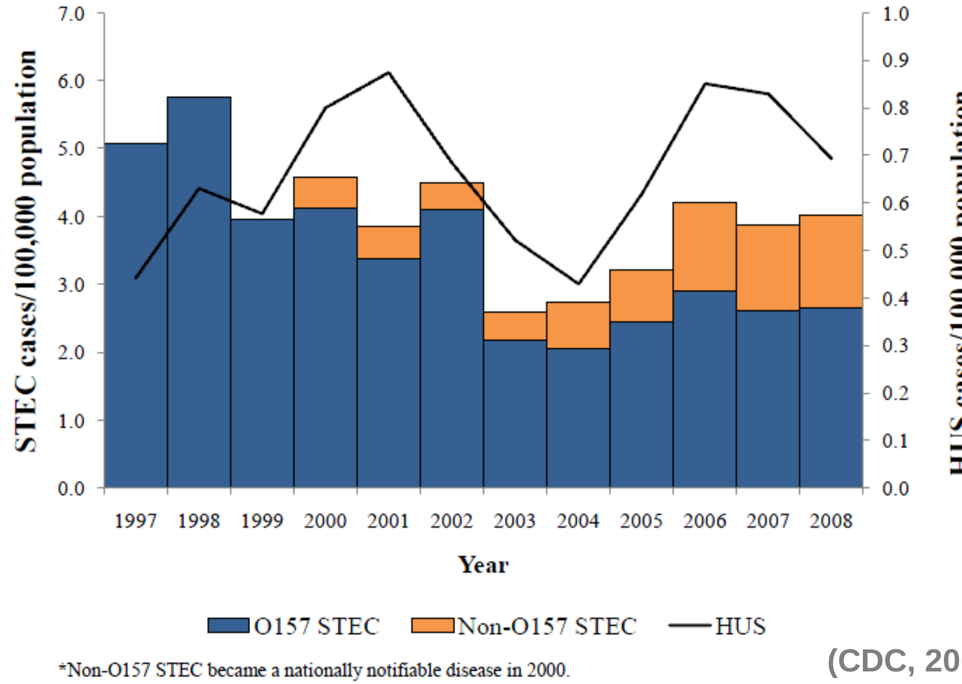
GUD : β-glucuronidase

(Kelly et al, 2009)

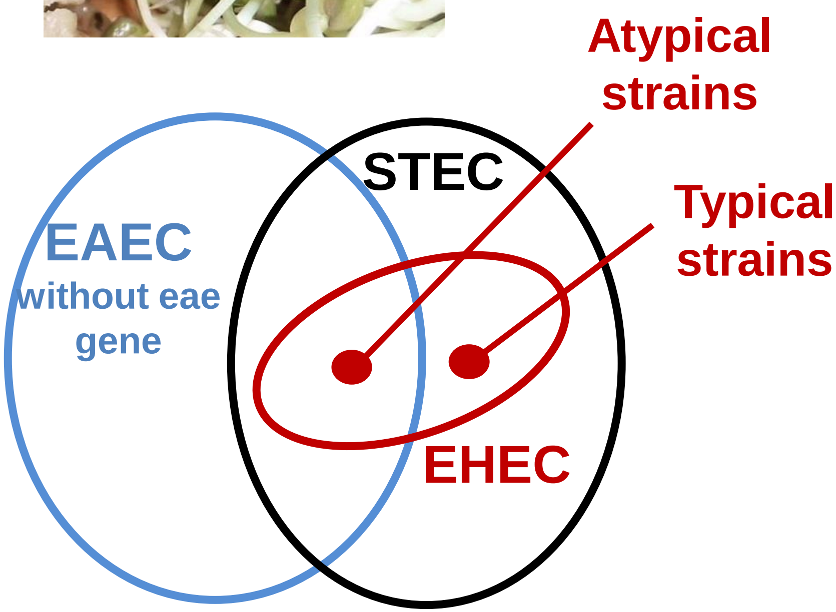
Microbial adaptation

New virulence factors





(CDC, 2009)



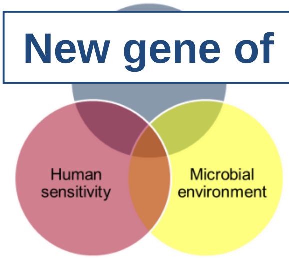
2011: Foodborne infection by *E. coli* O104:H4 in Germany

Over 4000 diseases, with 850 hemolytic and uremic syndrom (HUS), mostly adults
Origin : not cucumber but fenugreek sprouted seeds

EAEC strain has acquired the gene coding for the Shiga-toxin by horizontal transfer => New pathovar

Microbial adaptation

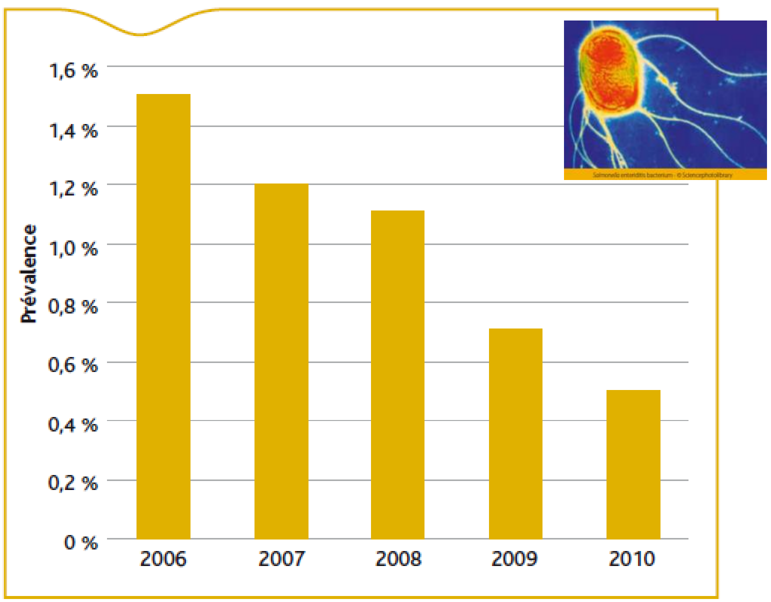
New gene of resistance



But emergence of new multi-drug resistant strains !

Global prevalence of *Salmonella* in foods decreases in France…

Prevalence : % of contaminated foods



(BEH 50, 2012)

Uses of antibiotics in veterinary medicine

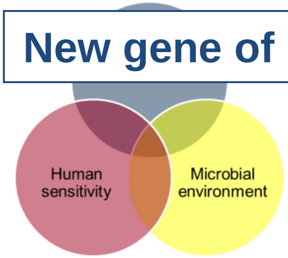
Affected animals

Therapeutic use	Metaphylaxis	Prophylaxis Preventive means	Growth factors
Affected animals	Clinical signs on some animals Certainty that the illness will extent to all the group	Unaffected animals but existence of a risk factor (eg: piglet weaning)	Healthy animals **forbidden in EU**

Healthy animals

Microbial adaptation

New gene of resistance



But emergence of new multi-drug resistant strains !

***Salmonella* Typhimurium DT 104**

Within human strains,

- More than 11% are now resistant to five antibiotics (ampicillin, chloramphenicol, streptomycin, sulfonamides, tetracycline)

- Some have also acquired resistance to the third generation of cephalosporine

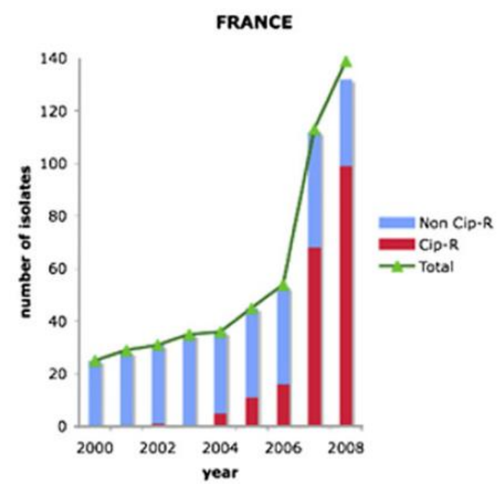
Appeared all over the word in 1990' except in Australia and New Zeeland (quarantine on imported animals)

(Velge et al, 2005)

***Salmonella* Kentucky**

Origin: Egypt (massive use of antibiotics)

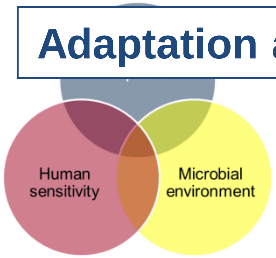
Poultry is the main vector of the strain



(Le Hello, 2011)

Microbial adaptation

Adaptation and persistence

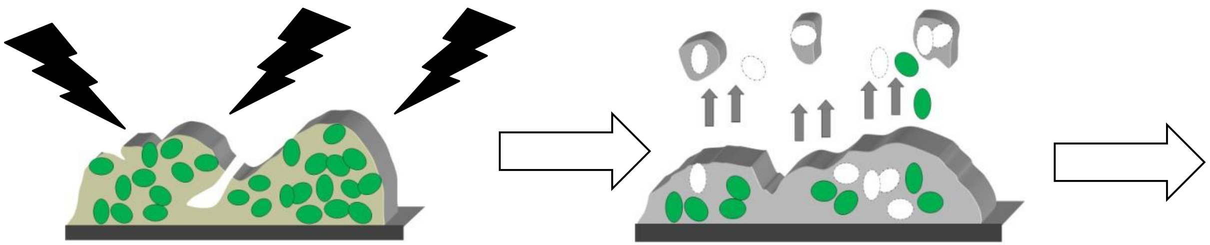


Bacterial stress, stress response, tolerance and persistence in food-processing environments

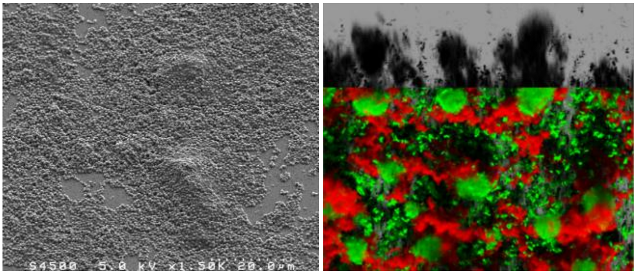
Heat, dehydration, disinfection, etc.

Cellular death and stress of surviving cells

Response to stresses



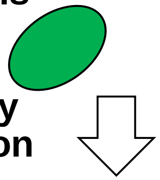
Biofilm state on surfaces



Stress proteins

rpoS

Membrane fatty acid composition



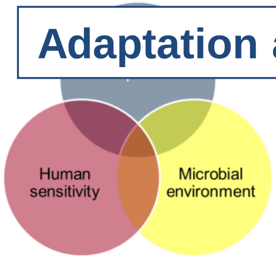
EPS overproduction

Problems for detection of stressed cells

Induced tolerance

Microbial adaptation

Adaptation and persistence



Pathogen persistence in environment

Persistence of *Salmonella* in the processing environment of a peanut butter factory

Used as ingredient in numerous processed products with long shelf-life (cookies, ice-creams, cereals, sweets, etc…)

Large scale outbreak in the USA in 2009 **(Nyachuba et al, 2010)**

Persistence of *L. monocytogenes* in a production plant of turkey

1 sporadic case in 1988 in Oklahoma (turkey sausage)

1 outbreak in 2000 in several American states (processed turkey)

12 years between both events

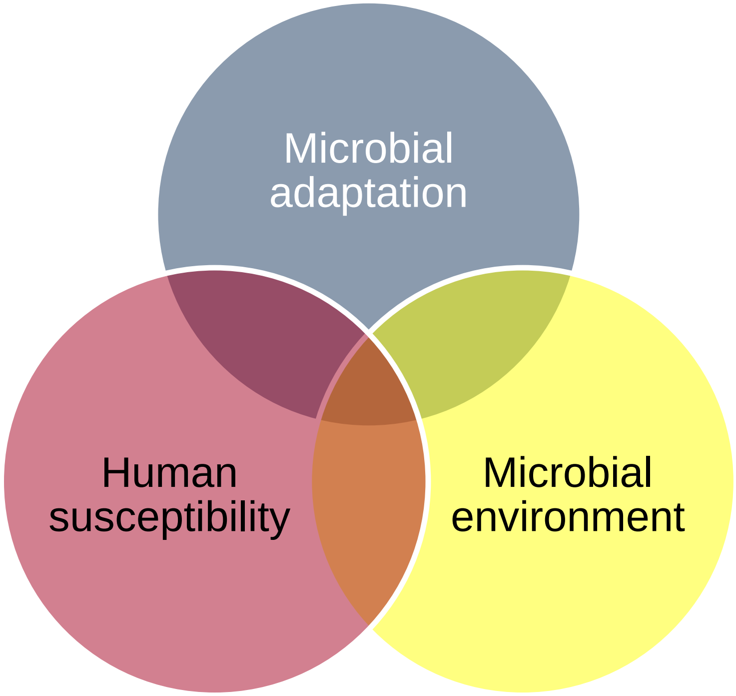
(Orsi et al, 2008)

Changes in microbial environment

Changes in microbial environment

Unusual transfer of contamination to foods

Unusual transfer of contamination to human beings



Climatic disorders

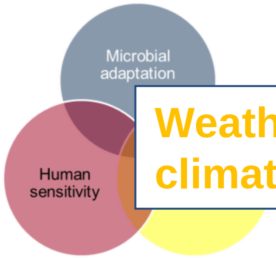
Agricultural practices

Modes of transformation and of preservation

Modes of consumption

Trade and exchanges

Changes in microbial environment



Weather conditions and climatic disorders

Seasonal increase in temperature

Increase of temperature in summer → 5-10% increase of Salmonellosis per °C of ambient temperature (Kovats, 2004)

→ Farmed animals carry more pathogenic agents (Hellberg & Chu, 2015)

Extreme weather conditions

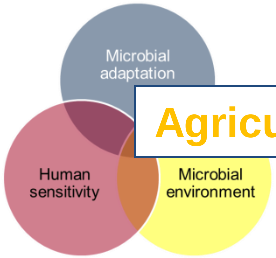
Water availability and quality

Flooding
- Wet environment → Mold development
- Waste water discharges by stormwater overflow → Shellfish contamination

Drought
- Migration of animals → Transfer of contamination in low prevalence areas
- Displacements of cultivation zones → Modifications of ecosystems

(Havelaar et al, 2010)

Changes in microbial environment



Agricultural practices

Farm organization

- **At the end of 2Oth century: increase of farm size**

Huge poultry farm

May to November 2010 in USA:
1939 salmonellosis due to shell eggs (15 millions of poultry)

(CDC, 2010)

Huge farm in fruit and vegetable sector

- **Today, more and more small organic and free-range farms**

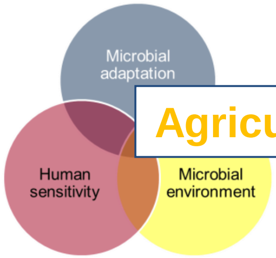
Ex: on 675 organic and non-organic pork farms:
Higher prevalence of *Salmonella* and *Toxoplasma* in organic farms – *Trichinella* detection

(Gebreyes et al, 2008)

Slaughterhouse organization

Collection of living cattle from farms to farms → Pathogen dissemination

Changes in microbial environment



Agricultural practices

Watering of crops with contaminated water

USA : Contamination of fresh raspberries produced in Guatemala by the parasite *Cyclospora cayetanensis*

(Ho, 2002)

Scandinavian countries: Frozen raspberries contaminated by Norovirus

(Skovgaard, 2007)

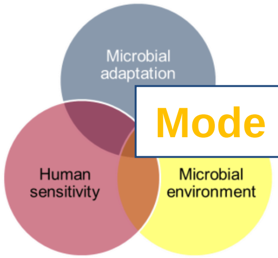
Use of sewage sludge as fertilizer

USA, Canada: Contamination of peppers and tomatoes by *Salmonella*

Outbreak of *Salmonella* Serotype Saintpaul Infections Associated with Multiple Raw Produce Items --- United States, 2008

Internalization of *Salmonella* during the formation of the fruit **(Zen, 2013)**

Changes in microbial environment



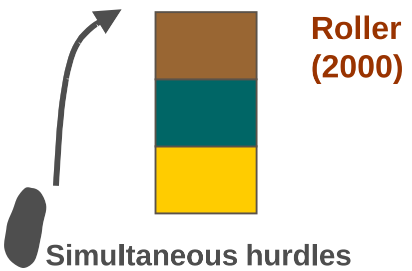
Mode of preservation

Consumers demand for ready-to-eat foods

« fresh » (minimally treated) but with long shelf-life…

Non-sterile food products can be preserved by combinations of hurdles such as:

- Mild thermal treatments (70-95°C),
- Refrigeration (<8°C)
- Packaging under vacuum or modified atmosphere
- Shelf-life (< 42 days)



➡ **Sensitive products to preservation failures (break in the cold chain)**

➡ **Psychrotrophic sporulating bacteria**

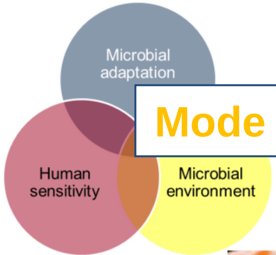
B. cereus

***C. botulinum* type E** Strictly anaerobic, able to growth until 2,5°C and to produce toxin until 6°C, contaminating fish

***C. botulinum* emergent risk in vacuum refrigerated fish products**

(Markland et al, 2013)

Changes in microbial environment



Mode of consumption

Consumption of exotic foods expands

Raw and/or smoked fish

- **Sushi, sashimi from Southeast Asia**
- **Ceviche from Peru**
- **Marinated herrings or anchories**

Anisakis risk in raw fish

Anisakis simplex

Prevalence

Found in all seas and oceans
Risk with farmed fish is near-zero

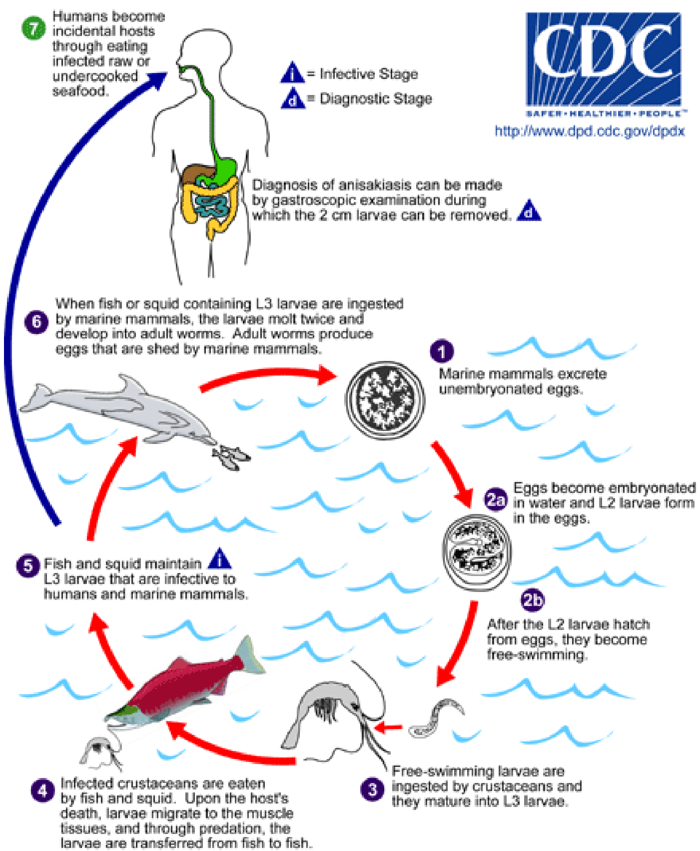
Effect on health

Gastroenteritis, gastro-allergic symptoms or skin allergy

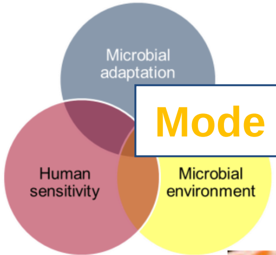
Preventive means

- Cooking
- Early evisceration, visual inspection
- Fish freezing is mandatory to sell raw fish products (at -20°C during at least 4 days in Europe) (R853/2004)

Life cycle of the parasite



Changes in microbial environment



Mode of consumption

Expansion of consumption of exotic foods

Raw and/or smoked fish

- **Sushi, sashimi from Southeast Asia**
- **Ceviche from Peru**
- **Marinated herrings or anchories**

Vibrio parahaemolyticus risk in raw fish

Highly virulent serotype O3:K6

Southeast Asia
↓
USA **1998**
↓
Chile **2004**
↓
Spain **2004**

Prevalence

Today present in many estuaries in the world (disseminated in ballast tanks of commercial boats)

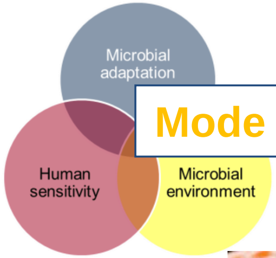
Characteristics:

Halophilic, can survive a long time in water at low temperature, is often associated with a wide variety of seafoods,
Destroyed by cooking (but not freezing)

Effect on health: gastroenteritis, possible sepsis for immunocompromised patients

Preventive means **Short shelf-life in raw fish products and storage below 5°C**

Changes in microbial environment



Mode of consumption

Expansion of consumption of exotic foods

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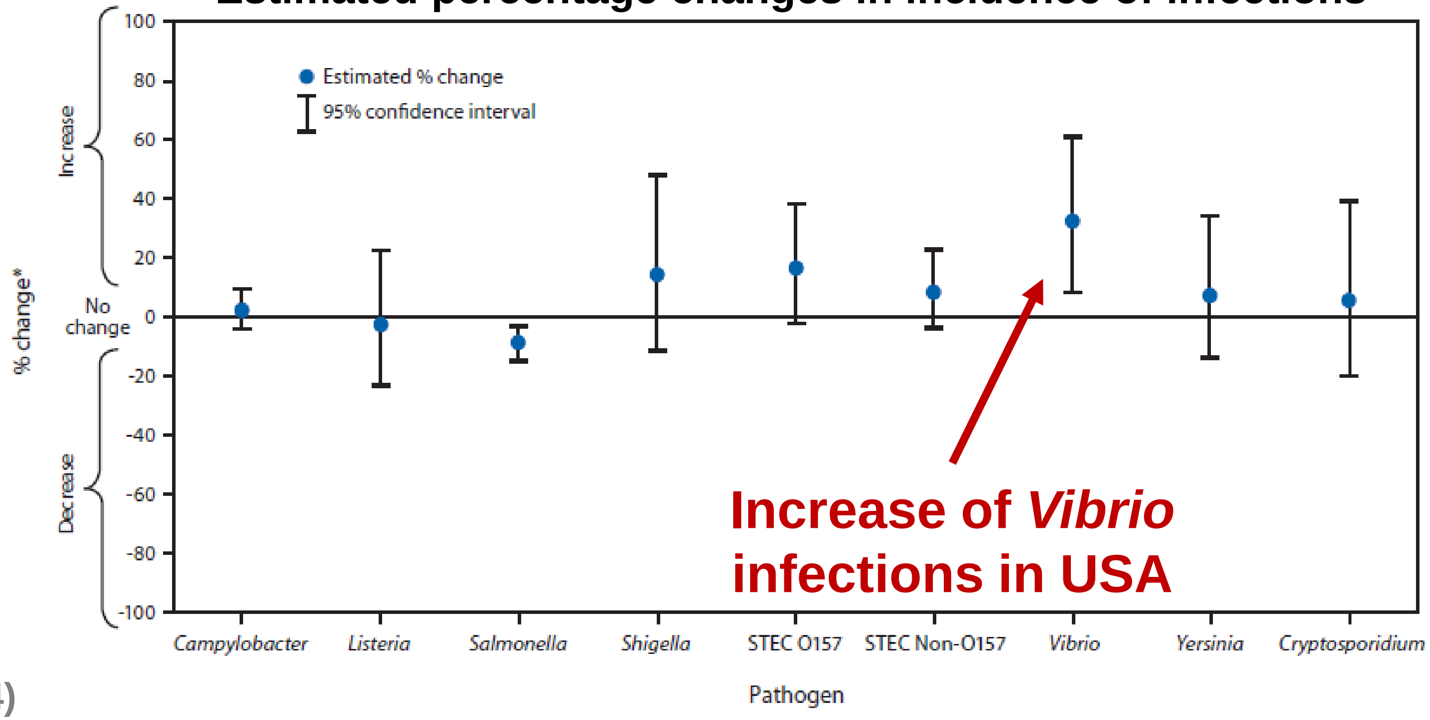
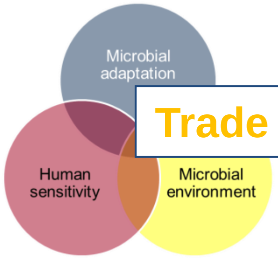
Estimated percentage changes in incidence of infections



(CDC, 2014)

Changes in microbial environment



Trade and exchange

Dissemination of pathogens though the globalization of exchanges

- Increase of exchanges of people, goods, animal and vegetable raw materials
- Agricultural and hygiene practices different between exporting and importing countries
- Different regulations for the use of antibiotics
- Pathogen detection and monitoring defective in some producing countries

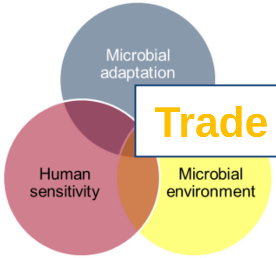
Dissemination of food poisonings all over the world

Formerly outbreaks were localized in the area of food production

Increase of falsely sporadic cases

Cases having the same origin (same product) but dispersed all over the world

Changes in microbial environment



Trade and exchange

Examples of worldwide dissemination of pathogens

Exotic fruit commercialization all over the word

1999, outbreak in 13 American states: *Salmonella* Newport in imported mangos from Brasil

2000, outbreaks in several American states: parasite Cyclospora in raspberries from Guatemala

(Sivapalasingam et al, 2003)

Cattle transportation

Salmonella Typhimurium DT 104 appeared all over the word except in Australia and in New Zealand because of the quarantine for imported animals

Boat circulation

Dissemination of *Vibrio parahaemolyticus* O3:K6 (in the 90s) from the southeast Asia and Japan to USA and Spain in ballast tanks of commercial boats

(Tauxe et al, 2002)

Human susceptibility

Susceptible people

Infants, pregnant women

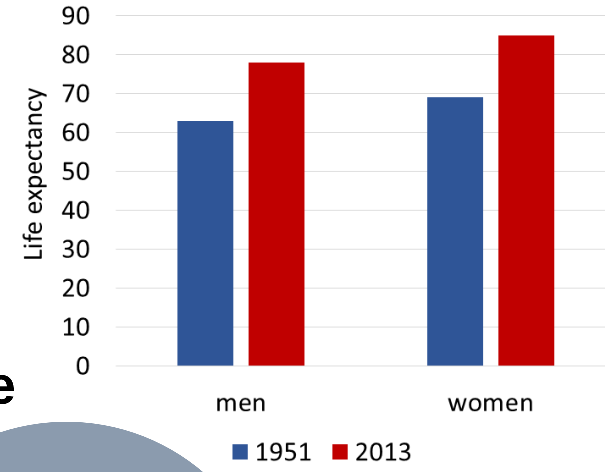
The elderly

Immunocompromised people
(AIDS, patients receiving treatment against cancer or immunosuppressive treatments (organ transplant)

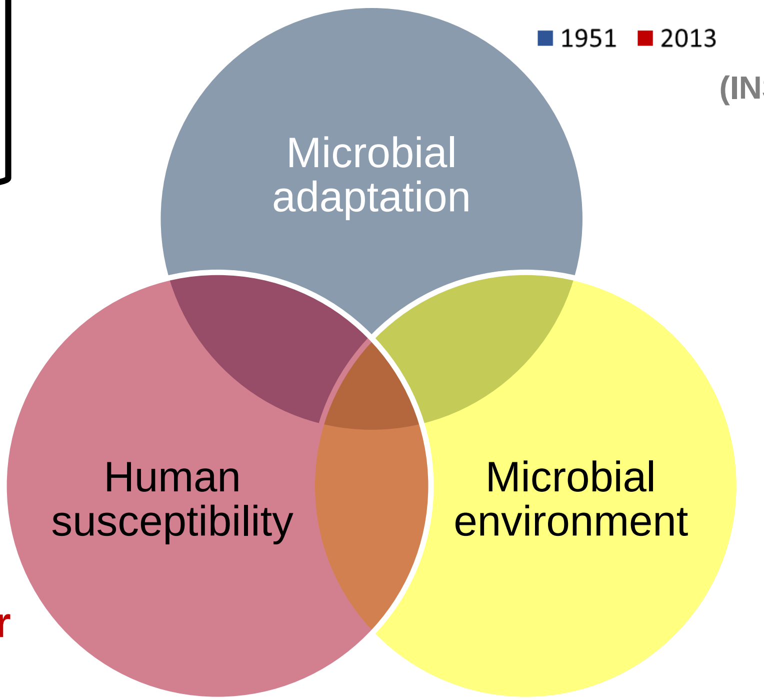
Patients with chronic diseases
(diabetes, disease of the intestinal tract)

Increase

Life expectancy increases



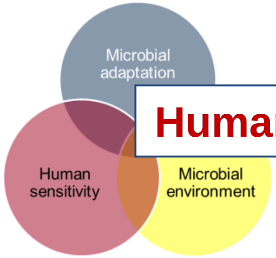
(INSEE, 2013)



The elderly

Immunocompromised or chronically sick people

Human susceptibility



Human susceptibility

Emergence of pathogens particularly virulent against susceptible people

Listeria monocytogenes (infants, pregnant women, elderly, immunocompromised people)
Vibrio vulnificus (sepsis in susceptible persons, 50% lethality)
Cronobacter sakazakii (septis in infants)

Relative susceptibility to *L. monocytogenes* for different sub-populations

Table 2 Relative susceptibilities for different sub-populations based on French epidemiological data.

Condition	Relative susceptibility
Transplant	2584
Cancer-Blood	1364
AIDS	865
Dialysis	476
Cancer-Pulmonary	229
Cancer-Gastrointestinal and liver	211
Non-cancer liver disease	143
Cancer-Bladder and prostate	112
Cancer-Gynaecological	66
Diabetes, insulin dependent	30
Diabetes, non-insulin dependent	25
Alcoholism	18
Over 65 years old	7.5
Less than 65 years, no other condition	1

RTE foods report (FAO)

The elderly are more susceptible to salmonellosis

In USA: Fatality rate of salmonellosis for elderly living in retirement homes is 7% (0,5% in the whole population)

(Alterkruse et al, 1997; Scallan et al, 2011)

Conclusion

Microbiological hazards are evolving

New infectious disease → **Quick solutions to detect, identify, characterize the microorganism and its mode of transmission** → **Quick proposal of control measures**

Characterization of an emerging hazard is necessary from:

Clinical point of view for sick person treatment:
What is the disease? What is the severity? Resistant to antibiotics? Treatment available?

Analytical point of view for quick detection and quick proposal of control measures:
Detection methods in food? Growth and resistance characteristics?

Epidemiologic point of view for evaluation of the impact on the whole population:
Infection occurrence? Reservoir and mode of transmission to humans? Infectious dose? Incubation period?

Conclusion

Multidisciplinary approach is now necessary to better manage food safety, to increase the efficiency of surveillance and to better understand the mechanisms of emergence

- **Technologies for real-time monitoring** (ex: temperature)

- **Genomic techniques**
fast detection and identification of pathogens

- **Predictive modeling for:**
  - microbial growth
  - epidemiology
  - dynamics of infectious diseases
  - source attribution
  - Risk assessment

Zero risk cannot be achieved

Improving food safety means reducing the risk and increasing the reactivity in case of epidemic

(McMeekin et al, 2010)

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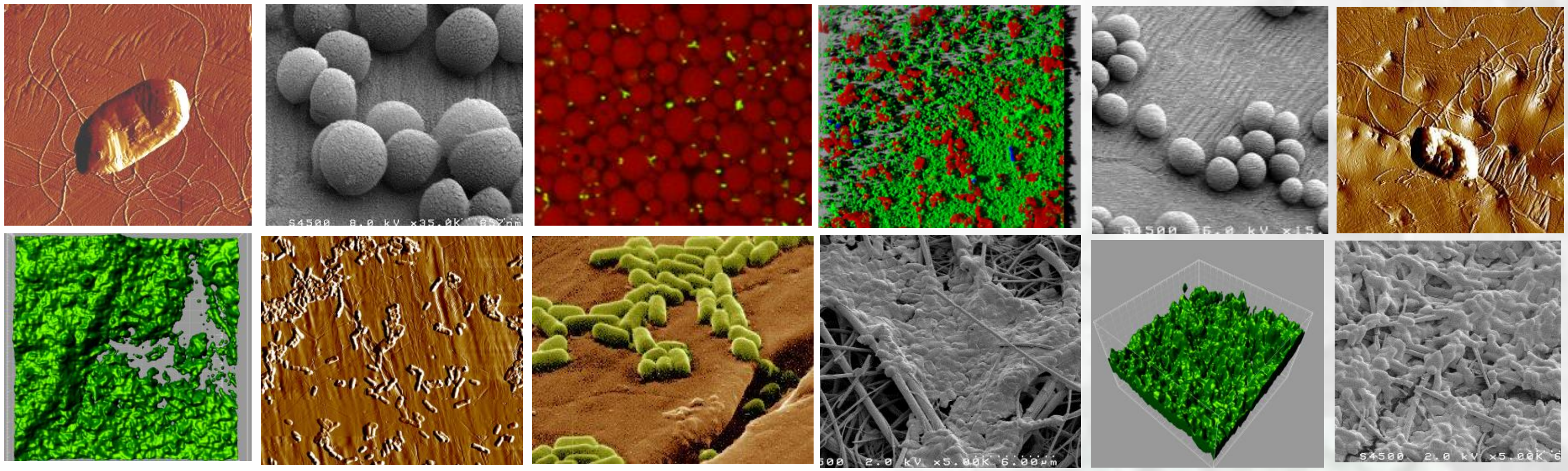
Conclusion



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Thank you for your attention !

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