Verotoxin producing *Escherichia coli* (VTEC)

Discontools:

Joint Meeting of Working Package 2 and 3 – Prioritisation & Gap Analysis, Monday, 10th May 2010

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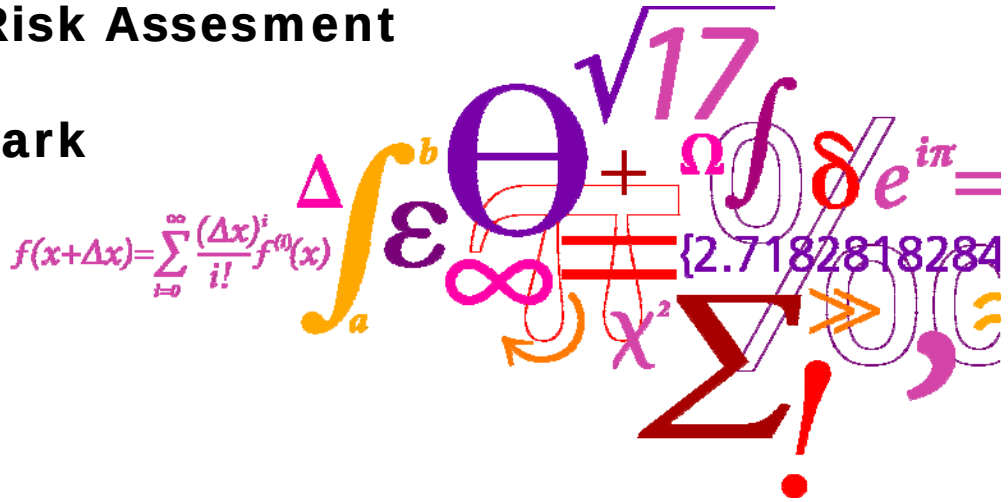


DTU Food
National Food Institute

Verocytotoxin/Shiga toxin-producing *Escherichia coli* (VTEC/STEC) Expert Group

Coordinator: Alfredo Caprioli, Istituto Superiore di Sanità, Community Reference Laboratory for *E. coli*, Rome, Italy

	Field	Expert
1	Laboratory diagnostics, animals	**John M. Fairbrother**, OIE Reference Laboratory for *Escherichia coli,* Faculté de médecine vétérinaire, Université de Montréal, Saint-Hyacinthe, Canada
2	Laboratory, pathogenesis, animal colonization	**Roberto M. La Ragione**, Veterinary Laboratories Agency (Weybridge), UK, Med-Vet-Net Deputy Coordinator
3	Laboratory, pathogenesis, animal colonization	**Lothar H. Wieler**, Veterinary Faculty, Freie University Berlin, Germany
4	Laboratory, animal colonization, farm ecology	**Jeffrey T. LeJeune**, Ohio Agricultural Research and Development Center, US
5	Food Microbiology	**Jeppe Boel**, National Food Institute , Technical University of Denmark, Copenhagen, Denmark
6	Epidemiology, burden of human disease (HUS) estimation, risk factors	**Gaia Scavia**, Dept. Veterinary Public Health, Istituto Superiore di Sanità, Rome, Italy

Escherichia coli

- **Normal bacteria in warm-blooded animals and humans**
- **Normal bacteria in many types of raw food**

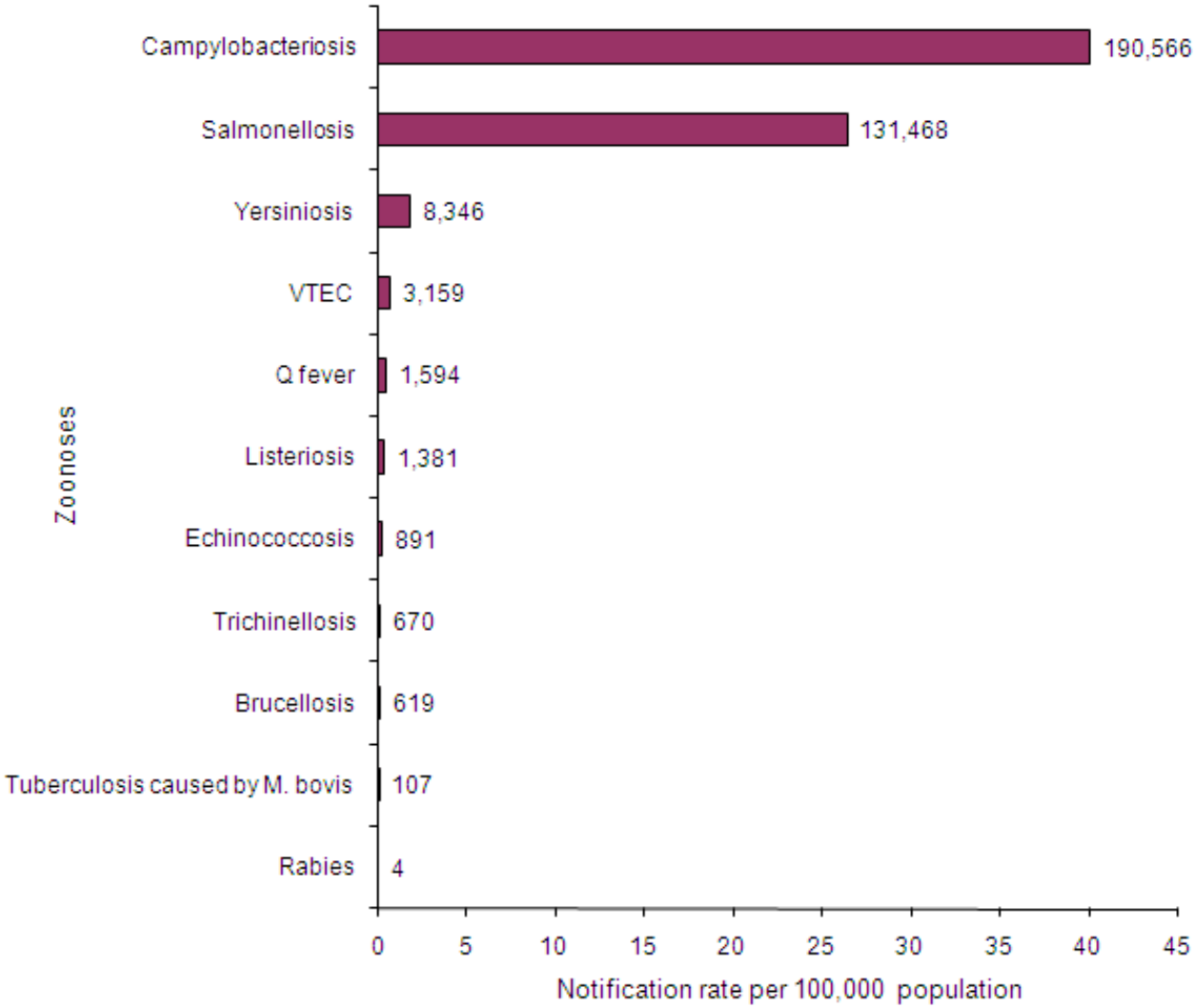
Human diarrhoeageic *E. coli*

”Non-zoonotic”

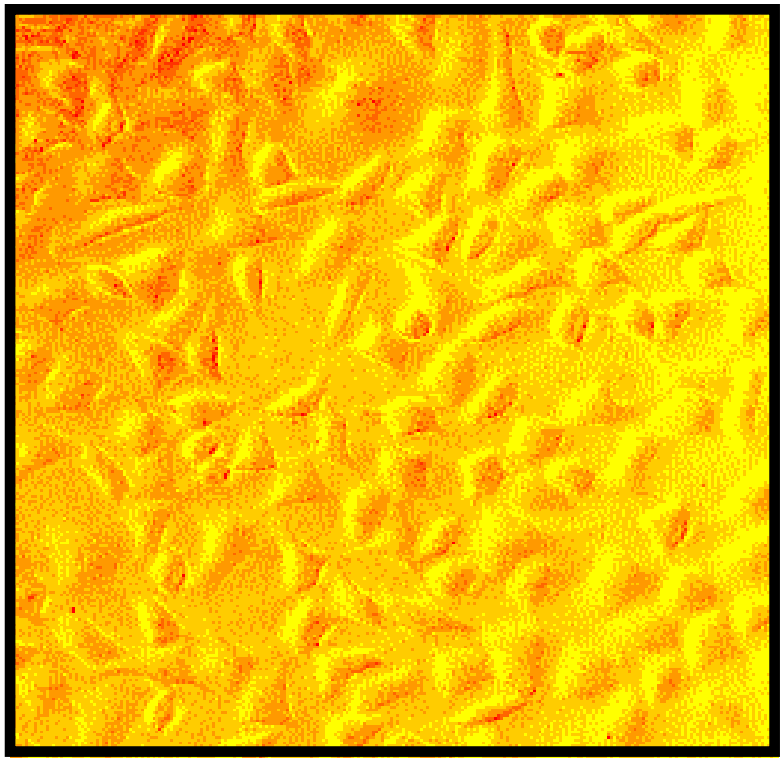
EnteroPatogenic *E. coli* (EPEC)
EnteroToxin producing *E. coli* (ETEC)
EnteroInvasive *E. coli* (EIEC)
***EnteroAggregative E. coli* (EAggEC)**
***Diffusely Adherent E. coli* (DAEC)**

"Zoonotic” **Verocytotoxin producing *E. coli* (VTEC)**
Shiga toxin producing *E. coli* (STEC)
(Enterohamorrhagic *E. coli* (EHEC))

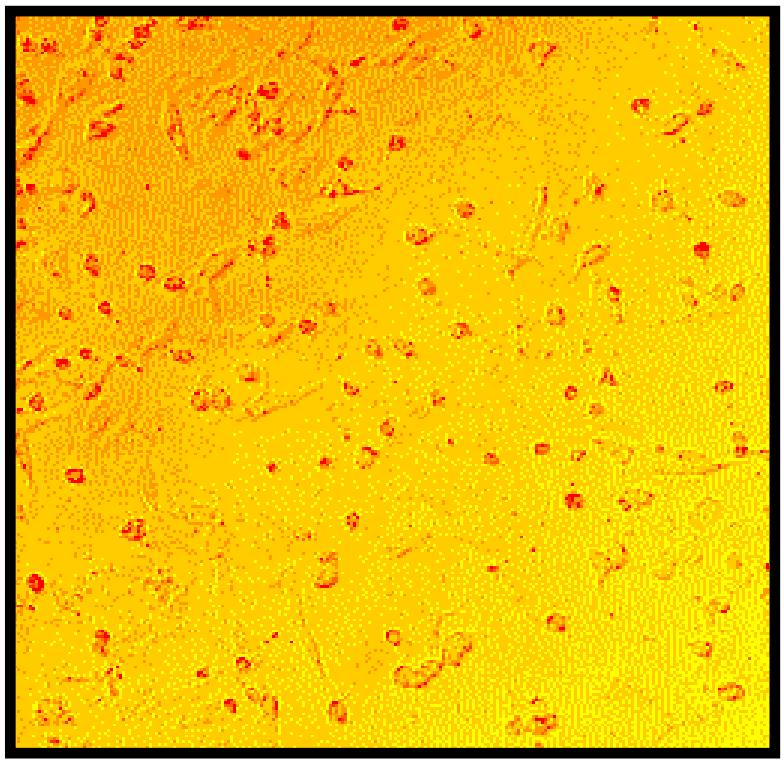
Reported notification zoonoses rates in confirmed human cases in the EU, 2008, EFSA zoonosis report



1977: Konowalchuk *et al.* discoveres a cytotoxin that kills Verocells, a kidney cell line from the Green African Vero monkey



Healty Verocells:



with Verotoxin

VCA positiv

VTEC

- > 100 different O:H serotypes identified as VTEC
- Varies in human pathogenic potential: harmless – fatal
- O157 (O157:H7/O157:H-) most important serogroup
- Other important serogroups: O26, O91, O103, O111, O145…

- Virulence factors:
  - VT production (VT1 and/or VT2)
  - Locus of Enterocyte Effacement (LEE): Type 3 secretion system, Intimin (*eae*), Tir, Esps etc.
  - Virulence plasmid Enterohaemolysin (*ehx*A, ToxB etc)
  - TCCP/espJ (non-LEE encoded type III effector protein)
  - Others EAST1 (toxin), Efa, SAA (adhesion factor)

VTEC clinical picture in humans

Onset of diarrhoea: Typically 2-4 days post ingestion

Watery diarrhoea 1-2 days
Abdominal cramps/light fever → Recovery

↓

Bloody diarrhoa 4-10 days
Severe abdominal cramps/no fever

↓

Haemolytic uremic Syndrome (HUS):
Characterized by acute renal failure, haemolytic anaemia
HUS develops in up to 10% of VTEC O157 patients

Fatality rates ranging from 1 to 5%

infectious dose of VTEC (O157; O111, O26) low, probably less than 100

VTEC serogroups in patients in Europe, 2008 (ECDC)

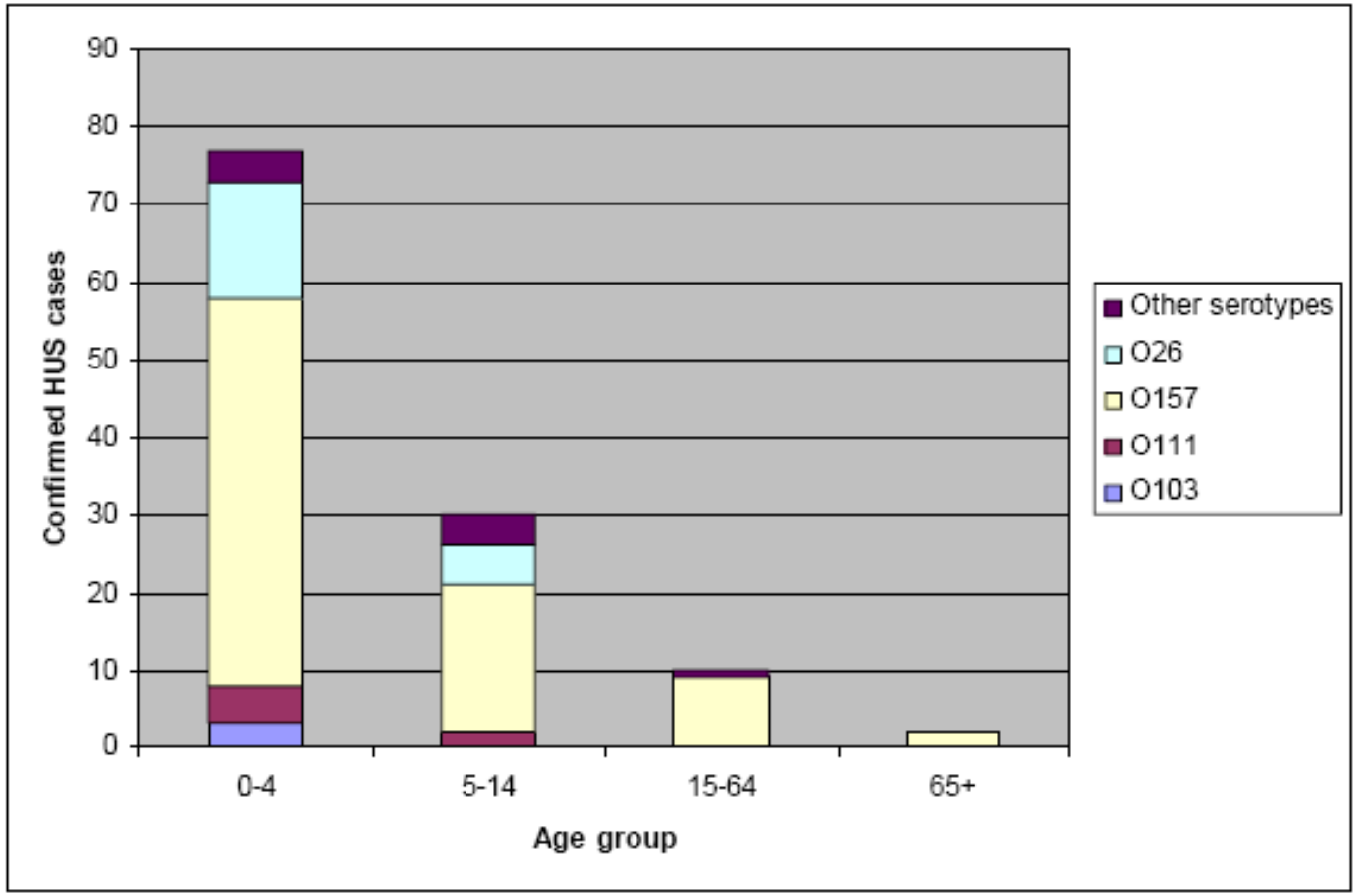
Table VT4. VTEC serogroups by country, 2008 (TESSy data)

Country	Serogroup										
	O157	NT	O26	O103	O145	O91	O111	O128	O146	O117	Other
Austria	22	37	3	0	1	0	1	0	1	0	4
Belgium[1]	55	3	7	1	0	1	8	2	1	2	23
Cyprus	0	2	0	0	0	0	0	0	0	0	0
Denmark	15	7	6	19	11	11	9	8	12	8	55
Estonia	3	0	0	0	0	0	0	0	0	0	0
Finland	2	6	0	0	0	0	0	0	0	0	0
France	42	28	12	0	0	0	1	2	0	0	0
Germany	59	576	64	45	22	30	11	11	9	1	48
Ireland	161	7	36	2	0	0	0	0	0	0	7
Italy	7	2	7	2	0	0	4	1	0	0	1
Luxembourg	1	0	0	0	0	0	2	0	0	0	1
Malta	8	0	0	0	0	0	0	0	0	0	0
Netherlands[2]	46	5	5	2	2	1	0	2	0	4	25
Poland	3	0	0	0	0	0	0	0	0	0	0
Romania	3	0	0	0	0	0	0	0	0	0	1
Slovakia	0	8	0	0	0	0	0	0	0	0	0
Slovenia	1	1	1	3	0	0	1	0	0	0	0
Spain	21	0	0	0	0	0	0	0	0	0	0
Sweden	75	134	24	13	10	7	6	2	2	5	26
United Kingdom	1,149	3	1	1	3	0	0	0	0	0	7
EU Total	**1,673**	**819**	**166**	**88**	**49**	**50**	**43**	**28**	**25**	**20**	**198**
Iceland	4	0	0	0	0	0	0	0	0	0	0
Norway	8	4	1	2	1	0	0	0	1	2	3

Note: In Belgium, laboratory data.

1. Cases of VTEC non-O157 cover only a part of the Netherlands (+/- 25%), as not all laboratories use methods aiming at detecting VTEC serotypes other than O157.

Haemolytic Uremic Syndrome (HUS) by age and serogroup in EU, 2008 (EFSA data)



Source: Belgium, Denmark, France, Germany, Ireland, Italy, Netherlands, Poland, Spain and United Kingdom (N=144).

Main gaps – human infections

- ***Identification of the minimal set of virulence genes/factors ("virulome") required for causing severe disease in humans.***
- ***Better diagnostic methods for the identification of human VTEC infections.***
- ***Better surveillance systems, with inclusion of VTEC non-O157 and definition of the serotypes/clones associated with severe diseases (HUS and bloody diarrhea).***
- ***Estimation of the burden of VTEC infections, including costs, in the population; at present, it is available only for a few countries.***
- ***Estimation of the possible role of humans as a reservoir for sorbitol fermenting VTEC O157 and some VTEC non-O157 (eg, O26 VT2+ve) pathogenic clones?***
- ***Research on VT genetic variation and expression and on the diseases potential of the different toxin variants; mechanisms of VT blood transportation during HUS.***

VTEC – animal reservoirs

Ruminants (cattle, sheep, goat, deer)

VTEC does not affect animals (with a few exceptions)

Pigs and poultry: Not significant reservoirs

VTEC: human infection routes

Foods: Beef meat (minced)
unpasteurized milk and by-products
unpasteurized juice (cider)
Fresh produce incl. sprouts
All faecally contaminated products

Person to person transmission
Direct animal contact
Drinking water
Bathing (sea, lakes, swimming and paddling pools)

Both sporadic cases and large epidemic outbreaks
Most outbreaks caused by VTEC O157

Classical food borne VTEC outbreaks

Outbreak	Cases/No. of deaths	Source
’82 Oregon, USA O157	26/0	Hamburgers
’93 Washington, Idaho, California, Nevada, USA O157	700/4	Jack in the Box Hamburger
’96, Sakai, Japan O157	10.000/11	Sprouts
’96 Skotland O157	400/17	Butchers shop (catering - gravy)
06: Norway O103:H25	18 cases/1 10 HUS cases	Sausage made of sheep meat

Prevalence of VTEC in ruminants (cattle) and meat hereof – the rough picture

VTEC

Faeces: Up to 100%?
Hides at slaughter: Up to 100%
Fresh meat of bovine origin Up to 40%

VTEC O157

Faeces, typically 3-10% (variation 0-100%)
Hides at slaughter >10%-100%
Fresh meat of bovine origin 0-5%

Other important O-groups: (O26, O91, O111, O103, O145)

Sparse amount of data

Cattle and VTEC (O157)

- **VTEC incl. O157 can be isolated from most cattle herds**
- **No specific management factors have been identified to control the problem at herd level**
- **Shedding is intermittent**
- **Super shedders exists (>10E5 CFU per gram faeces)**

Animals: Control options?

- Tools to identify super shedders
- Vaccination
- Probiotics
- Phage therapy
- Antimicrobials

Some of these options could also be used on the abattoir

Main gaps Animal infections

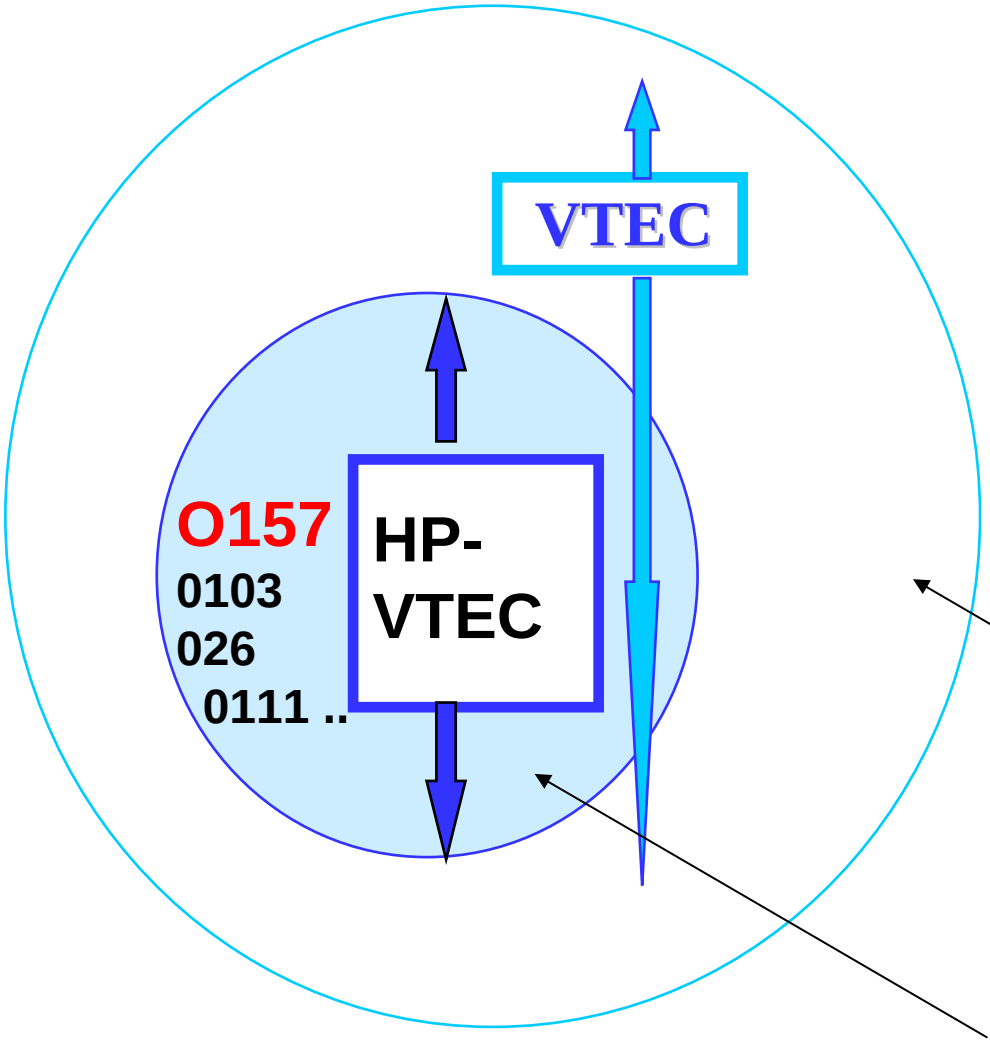
- ***In general, to extend the knowledge gained on VTEC O157 to the main pathogenic VTEC non-O157 serogroups.***
- ***Better understanding of colonization and persistence of VTEC O157 and non-O157 in ruminants.***
- ***Better understanding of the biology of the "super shedder" phenomenon and of the role of these subjects in the infection cycles.***
- ***Better understanding of the immune response in animals, particularly to bacterial structures that could represent vaccine components.***
- ***Reseach on inter- and intra-farm spread of VTEC: how he organism is spread between one farm to the other, and how animals are exposed within a single farm. Better understanding of the environmental survival.***
- ***Research on the use of probiotics and phage therapy to prevent colonization.***
- ***Modelling the cost/benefit of control measures in term of reduction of the burden of VTEC infections in humans.***

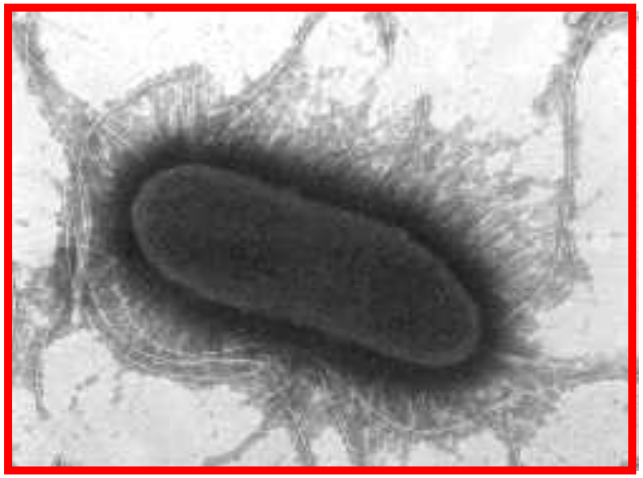
Main gaps: Food control

•Easy and rapid tests targeting the main VTEC non-O157 pathogenic serogroups are required. VTEC that are presumably poorly virulent to humans are abundant in animals and food, so the methods should be targeted to the serogroups/clones most associated with human disease.

•Role of vegetables: studies on the interaction between bacteria and plant organisms and models for crop contamination via manure and/or irrigation.

VTEC and Human Pathogenic VTEC?





Many food and animals isolates

Limited range of "seropathotypes"

Transmission of VTEC between reservoirs