Campylobacter: 4 decades of diarrhea

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Outline

- *Campylobacter* - some facts
- *Campylobacter* lab-methods
- Source attribution
- *Campylobacter* in Europe
- Control options and expected effects
- Potential approach to reduce the burden
- Take home messages
THE GLOBAL VIEW OF CAMPYLOBACTERIOSIS

REPORT OF AN EXPERT CONSULTATION

UTRECHT, NETHERLANDS, 9-11 JULY 2012
Campylobacter

- Sensitive for heat, dryness, disinfection,…
- Many (all?) animal species are asymptomatic carrier of *Campylobacter*
- …
Campylobacter 24 species

- *C. jejuni* (92% of gastro-intestinal infections)
- *C. coli* (5% of gastro-intestinal infections)
- *C. lari*
- *C. upsaliensis*
- *C. fetus* (blood cultures - systemic)
- ......
The importance of *Campylobacter* for humans

- *Campylobacter jejuni/coli* is the most common cause of bacterial intestinal disease in Europe (self-limiting)
  - Estimated at 10 million cases per year in EU (costs: 2.4 billion)

- Serious outcome
  - 35-45 per 100,000 ill (EU); 3.5-4.0 hospitalized; 0.15-0.30 fatal

- Sequelae
  - Guillain Barré Syndrome, Irritable Bowel Syndrome, Reactive Arthritis
    => contributing heavily to the burden of illness

- Largest part of the world: no data

- Difference in epidemiology between developing and industrialized countries
Campylobacteriosis

- Outbreaks are rare compared to *Salmonella*

- Even low doses has an high probability of infection

- Sepsis and extra-intestinal infections are rare
Focus on *C. jejuni* / *C. coli* (with routine media no differentiation between these 2 species)
Detection of *Campylobacter*

Clinical stool samples: direct plating

Blood samples: enrichment in blood culture media (more than *Campylobacter* only)

Meat/carcass samples: enrichment
Trouble shooting

- For stools: has the patient been treated?
- Quality of your sample (don’t them allow to dry; use transport media)
- Overgrowth of contaminants
  - Increasingly a problem with ESBL producing gram-negative bacteria
  - Is your agar of good quality?
- Experience
Campylobacter?  ISO-standard

- Morphology & motility
- Morphology in Gram staining
- Oxidase
- Lactose
- Sucrose
- Gas
- Catalase
- Hippurate hydrolysis
- Hydrolysis of indoxyl acetate
To prevent lots of confusion...

...use PCR to confirm *C. jejuni* and *C. coli*
Culture independent diagnostic tests (CIDTs)

- Make sure that you use validated tests!
- No isolation of strains: no data on species and antimicrobial susceptibility
What if you have an isolate?

- In a clinical setting: antimicrobial susceptibility testing
  - Report species and susceptibility to clinician

- For surveillance/epidemiology
What if you have an isolate?

- In a clinical setting: antimicrobial susceptibility testing
  - Report species and susceptibility to clinician

- For surveillance/epidemiology
  - No other typing methods than MLST (or Whole Genome Sequencing)!!
  - Antimicrobial susceptibility
SCIENTIFIC REPORT OF EFSA AND ECDC

The European Union Summary Report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2011

European Food Safety Authority

European Centre for Disease Prevention and Control

European Food Safety Authority (EFSA), Parma, Italy

European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden
Figure CA17. Spatial distribution of ciprofloxacin resistance among Campylobacter jejuni from Gallus gallus in countries reporting MIC data in 2011.
Figure CA18. Spatial distribution of erythromycin resistance among Campylobacter jejuni from Gallus gallus in countries reporting MIC data in 2011.
Figure CA10. Trends in erythromycin resistance in Campylobacter jejuni from Gallus gallus in reporting MSs and non-MSs, 2005–2011, quantitative data
### Table CA7. Antimicrobial resistance in Campylobacter spp. reported to be acquired within the EU and in other geographical regions in 2011, using clinical breakpoints

<table>
<thead>
<tr>
<th>Country</th>
<th>Amoxicillin</th>
<th>Ampicillin</th>
<th>Ciprofloxacin</th>
<th>Erythromycin</th>
<th>Gentamicin</th>
<th>Nalidixic Acid</th>
<th>Tetracyclines</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>% Res</td>
<td>N</td>
<td>% Res</td>
<td>N</td>
<td>% Res</td>
<td>N</td>
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<tr>
<td>Europe (EU/EEA Countries)</td>
<td>1,280</td>
<td>1.9</td>
<td>1,472</td>
<td>34.2</td>
<td>9,864</td>
<td>46.6</td>
<td>9,423</td>
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<tr>
<td></td>
<td>1,411</td>
<td>0.6</td>
<td>3,379</td>
<td>49.9</td>
<td>4,499</td>
<td>26.4</td>
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<td>Europe (non-EU/EEA Countries)</td>
<td>2</td>
<td>NA</td>
<td>3</td>
<td>NA</td>
<td>7</td>
<td>NA</td>
<td>2</td>
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<td></td>
<td>No Observations</td>
<td></td>
<td>3</td>
<td>NA</td>
<td></td>
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<tr>
<td>Africa</td>
<td>1</td>
<td>NA</td>
<td>2</td>
<td>NA</td>
<td>40</td>
<td>67.5</td>
<td>39</td>
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<tr>
<td></td>
<td>21</td>
<td>57.1</td>
<td>11</td>
<td>54.5</td>
<td></td>
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<tr>
<td>Asia</td>
<td>4</td>
<td>NA</td>
<td>7</td>
<td>NA</td>
<td>90</td>
<td>84.4</td>
<td>91</td>
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<tr>
<td></td>
<td>50</td>
<td>84.0</td>
<td>15</td>
<td>46.7</td>
<td></td>
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<td></td>
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<tr>
<td>Northern &amp; Central America</td>
<td>No Observations</td>
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<td>No Observations</td>
<td>NA</td>
<td>9</td>
<td>NA</td>
<td>No Observations</td>
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<tr>
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<td>No Observations</td>
<td></td>
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<td>4</td>
<td>NA</td>
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<tr>
<td></td>
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<td></td>
<td>No Observations</td>
<td>2</td>
<td>NA</td>
<td>No Observations</td>
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<tr>
<td>Oceania</td>
<td>No Observations</td>
<td></td>
<td>No Observations</td>
<td>7</td>
<td>NA</td>
<td>No Observations</td>
<td></td>
</tr>
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N = number of isolates tested.
% Res = percentage of resistant isolates.
NA = not applicable, if fewer than 10 isolates were tested, resistance was not calculated.
Clinical relevance of resistance in Campylobacter
Can we estimate the attribution from the different sources to human campylobacteriosis? and estimate the expected impact of control measures?
# Human illness source attribution methods

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<th>Methods</th>
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<td>Microbial subtyping</td>
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<td>Analysis of sporadic cases</td>
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<tr>
<td>Intervention studies</td>
<td>Analysis of data from outbreak investigations</td>
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<td>Expert elicitation</td>
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Human illness source attribution methods

- Case control studies and outbreaks: 24-29% attributed to poultry meat
Human illness source attribution methods

Methodologies for attribution of human illness to specific sources

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The Dioxin Crisis as Experiment To Determine Poultry-Related Campylobacter Enteritis

Akke Vellinga and Frank Van Loock

Emerging Infectious Diseases • Vol. 8, No. 1, January 2002
Weekly number of cases campylobacteriosis

- **Observed**
- **Expected**
- **Tolerance**

Avian influenza outbreak

data from Wilfrid van Pelt, RIVM
Source attribution based on different approaches

- Case control studies and outbreaks: 24-29% attributed to poultry meat
- Intervention studies: 40% attributed to poultry meat
Human illness source attribution methods

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Multi Locus Sequencing Typing (MLST)

- DNA-sequence based method
- Strains from different sources (chicken, cattle, dog, human, pigs, environment)
- All information in 1 database (Oxford, UK)
- Mathematical modelling…..
- Outcome: what strains in humans are most likely from…..
Source attribution based on different approaches

- Case control studies and outbreaks: 24-29% attributed to poultry meat
- Intervention studies: 40% attributed to poultry meat
- Microbial subtyping (MLST): 50-80% attributed to poultry
Source attribution based on different approaches

- Case control studies and outbreaks: 24-29% attributed to poultry meat
- Intervention studies: 40% attributed to poultry meat
- Microbial subtyping (MLST): 50-80% attributed to poultry
The goal is to estimate the relative contribution (%) of different (amplifying) reservoirs for *Campylobacter* to human infections.

It provides no information on the transmission pathways by which *Campylobacter* arrives to humans from the different reservoirs.
Results – Source attribution

![Bar chart showing the proportion of cases attributed to different sources. The chart indicates that chicken has the highest proportion, followed by cattle, environment, sheep, and pig. The values are 0.663 for chicken, 0.207 for cattle, 0.101 for environment, 0.025 for sheep, and 0.003 for pig.]
Interventions

- Intervention in the poultry meat production chain can prevent potentially 30-40% of the human infections at meat consumption level.

- Intervention in the primary production can prevent potentially up to 80% of the human infections.
Novel approaches to control Campylobacter in primary poultry production

EU FP7 project, 2010-2015, 3 mill Euro

Hanne Rosenquist, Nicola Williams, Jaap Wagenaar, Mathilde Josefsen, Maarten Nauta, Mogens Madsen, Merete Hofshagen
Campylobacter in poultry
Campylobacter in poultry

- newly hatched chicks are Campylobacter free
- colonisation < 10 days rare - maternal immunity?
- colonisation is age dependent (organic production)
- up to $10^9$ cfu per gram cecal contents (amplification vessel)
- asymptomatic and lifelong for broilers, slight decline in older birds
- almost 100% of birds in a flock become positive within a few days
- strong seasonality
- only decline of counts after slaughterhouse
Campylobacter in Europe: EU data
Figure SU1. Reported notification rates of zoonoses in confirmed human cases in the EU, 2011

- Campylobacteriosis (N = 220,209)
- Salmonellosis (N = 95,548)
- VTEC (N = 9,485)
- Yersiniosis (N = 7,017)
- Listeriosis (N = 1,475)
- Echinococcosis (N = 781)
- Brucellosis (N = 330)
- Trichinellosis (N = 266)
- Tuberculosis caused by M. bovis (N = 132)
- Rabies (N = 1)

Notification rate per 100,000 population
Campylobacter trend EU
EU – baseline study in 2008

- Includes flocks and carcasses of broilers
- Objectives:
  - 'baseline' prevalence in all member states in ceca and carcasses (neck skins)
  - Enumeration of *Campylobacter* from neck skins
- Inclusion: 10,132 flocks in 561 slaughterhouses in 26 EU member states (+NO&CH)
Figure 3. Prevalence of *Campylobacter*-colonised broiler batches in the EU*, 2008

* Greece did not participate in the baseline survey and two non-MSs, Norway and Switzerland, participated.
Interventions in the poultry meat production chain