CarbaCamp

Assessment of phenotypic carbapenem susceptibility and genomic epidemiology of *Campylobacter* from animal, food and human domains

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17th EURL-AR workshop 2023 (virtual)
24-05-2023

Background

2018

Evidence of carbapenem non-susceptibility in *Campylobacter* in humans

- Hagiya et al.,2018
- Lehours et al. 2018

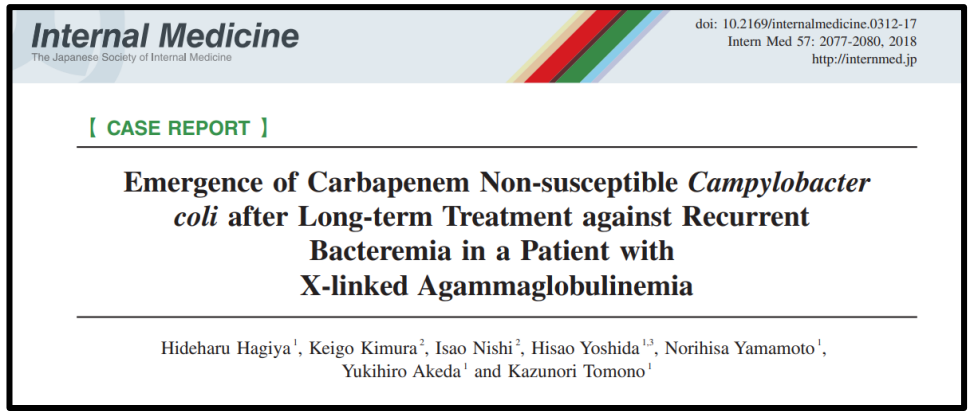
2020

ETP resistance included in the AMR monitoring of *Campylobacter*, by the Commission Implementing Decision (EU) 2020/1729

- Range 0.125 – 4 mg/L
- ECOFF = 0.5 mg/L

Disagreement on ECOFF:

- No ECOFF by EUCAST
- CLSI (M100-S32) recommends using the breakpoint of 16 mg/L for imipenem and meropenem (defined for other non-Enterobacteriaceae).
- Breakpoint of 1 mg/L is proposed by Comité de l'Antibiogramme de la Société Française de Microbiologie (CASFM) 2018 for ETP.



Internal Medicine
The Japanese Society of Internal Medicine

doi: 10.2169/internalmedicine.0312-17
Intern Med 57: 2077-2080, 2018
http://internmed.jp

【 CASE REPORT 】

Emergence of Carbapenem Non-susceptible *Campylobacter coli* after Long-term Treatment against Recurrent Bacteremia in a Patient with X-linked Agammaglobulinemia

Hideharu Hagiya[1], Keigo Kimura[2], Isao Nishi[2], Hisao Yoshida[1,3], Norihisa Yamamoto[1], Yukihiro Akeda[1] and Kazunori Tomono[1]

Recurrent *Campylobacter jejuni* infections with *in vivo* selection of resistance to macrolides and carbapenems: molecular characterisation of resistance determinants

Philippe Lehours[1], Monica Oleastro[2], Alexandra Nunes[2], Nadia Liassine[3], David M Lowe[4], Gauri Godbole[5]

1-French National Reference Center for Campylobacters and Helicobacters in Bordeaux (CNRCH), University Hospital of Bordeaux, France, 2-National Reference Laboratory for Gastrointestinal Infections and Bioinformatics Unit, National Institute of Health, Portugal, 3-Laboratoire Dianalabs, Geneva, Switzerland, 4-Department of Immunology, Royal Free Hospital, London UK, 5-Reference Microbiology, National Infection Service, Public Health England, UK

ECCMID 28th, European Congress of Clinical Microbiology and Infectious Diseases, MADRID 21-24 April 2018.

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Feb. 2023

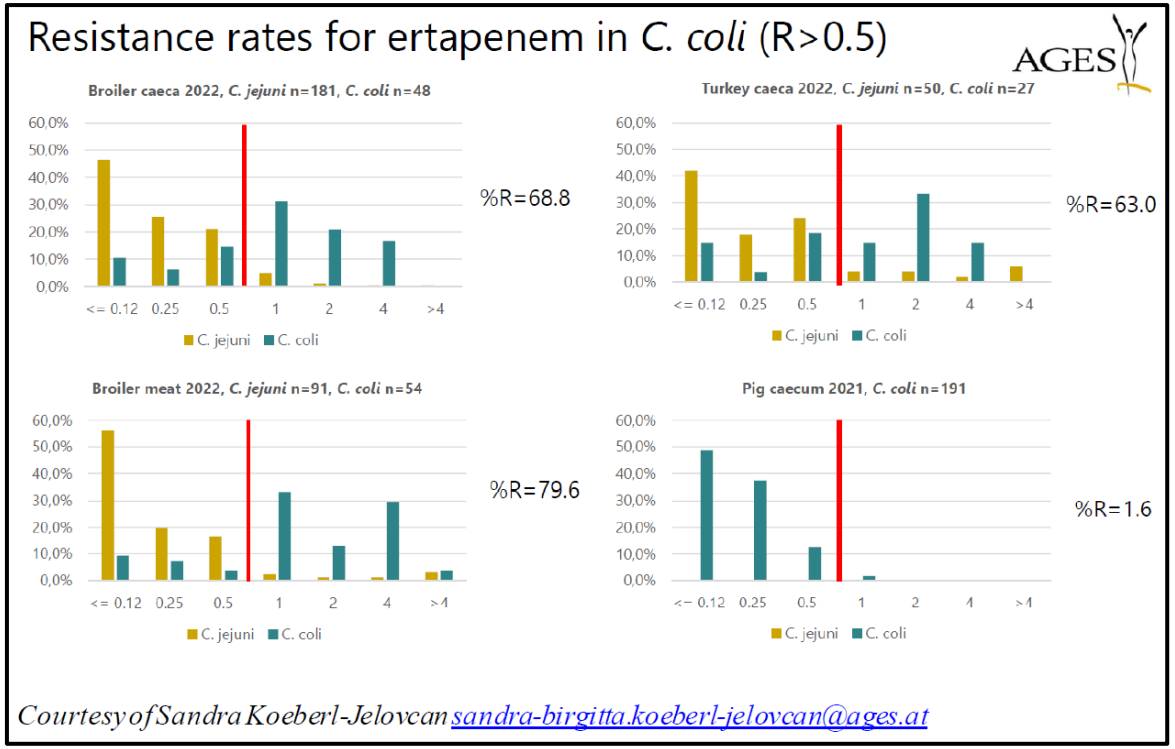
Observations from the Austrian Agency for Health and Food Safety (AGES) shared with the EURL-AMR:

- High rates for ETP non-susceptible Campylobacter from food animals
- Possible different wild-type distributions between C. jejuni and C. coli.

Mar. 2023

EURL-AMR organized a webinar with the EURL network, EFSA and ECDC. Data discussed within the network and:

- Dr. Philippe Lehours, University of Bordeaux, PU-PH, Bordeaux, France, an expert in AMR as well as with
- EFSA
- ECDC
- subsequently by the European Committee on Antimicrobial Susceptibility Testing (EUCAST).



Courtesy of Sandra Koeberl-Jelovcan sandra-birgitta.koeberl-jelovcan@ages.at

CarbaCamp project

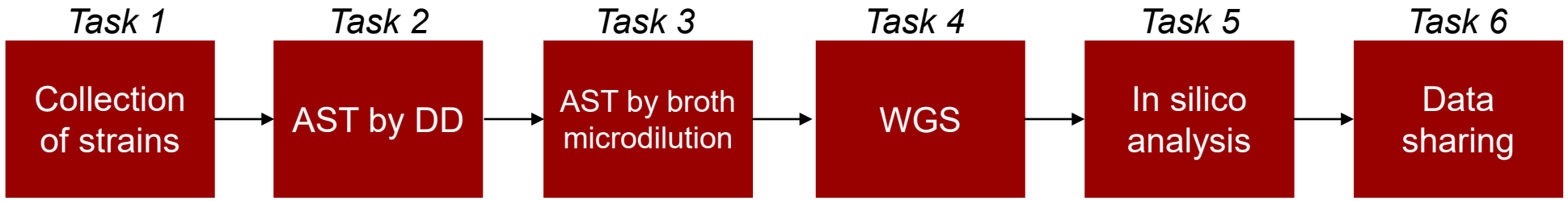
Main questions emerged from the webinar:

- Is the present ECOFF for ETP set correctly ?
- Is ETP the best carbapenem for the tests ?
- What is the effect of using EUCAST versus CLSI recommended media for AST?
- Are there any differences in the wild-type populations between animal types and between species?
- Can a resistance mechanism be identified as responsible for the higher MIC levels ?

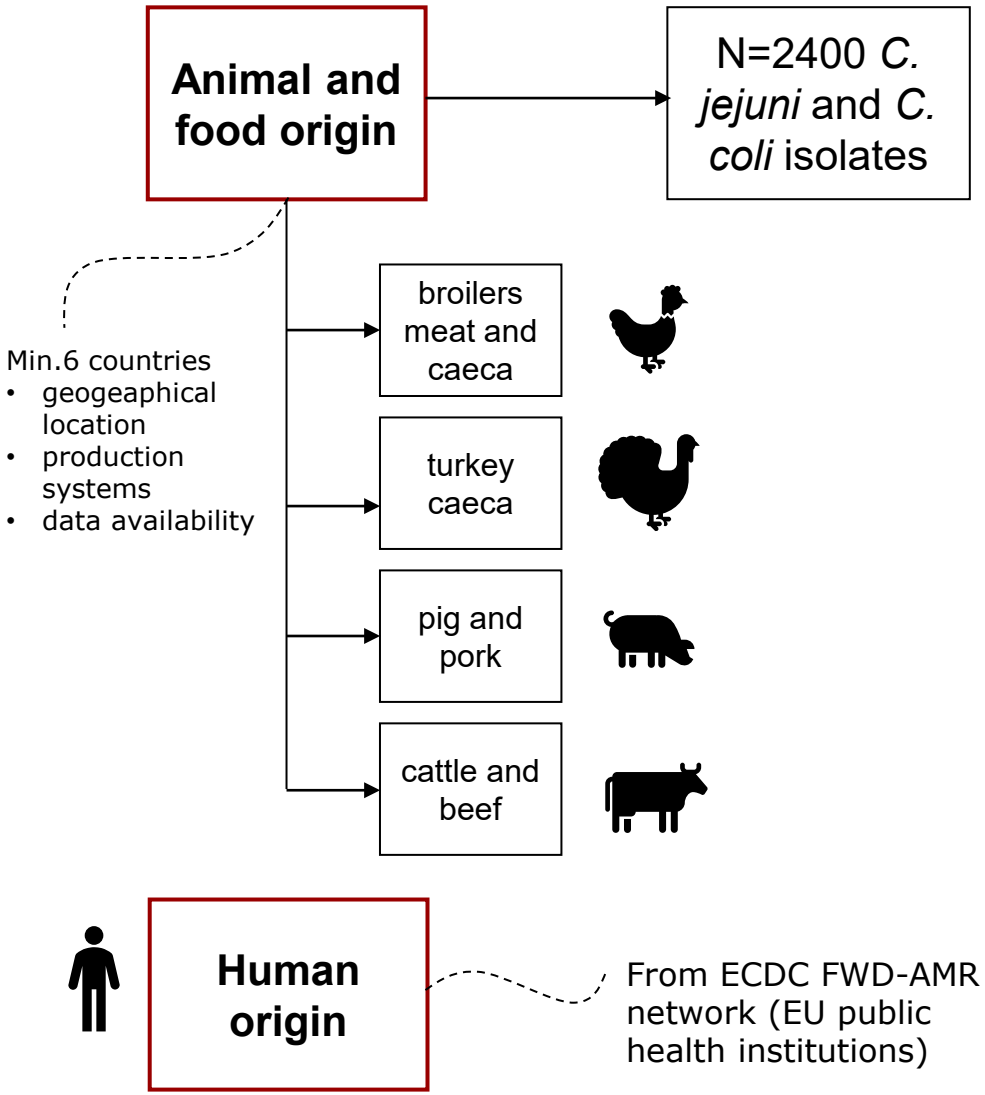
EFSA requested a proposal from the EURL AR with high priority to urgently address the issues.

"CarbaCamp"

- **Project duration:** 24 months from the kick-off meeting
- **Collaborator:** EUCAST Development Laboratory (EDL)
- **Project structured in 6 "Tasks"**



Task 1 – Collection of strains



⇒ strain collections from interested NRLs of the EURL AR network providing data to the EFSA surveillance of AMR.

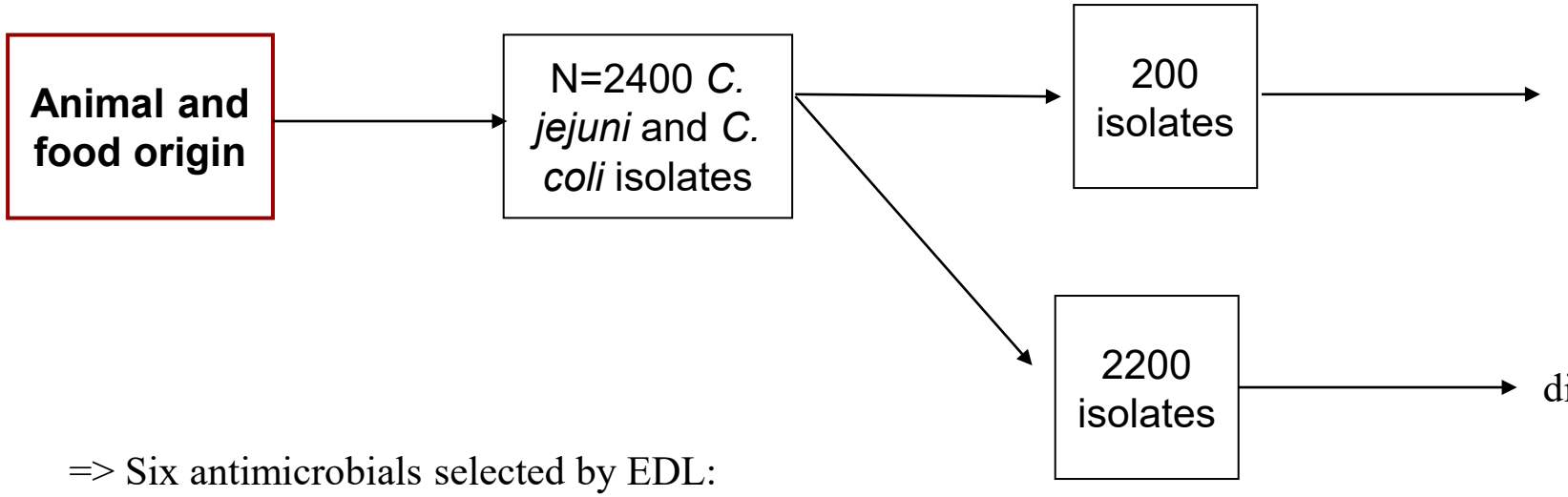
⇒ NRLs that have submitted most Campylobacter data of the four animal and food domains to the EFSA surveillance of AMR will be targeted (Survey)

⇒ The animal and food strain collection will be based obtaining a representative diversity of strains representing different MIC distributions against ETP ensuring isolates across the MIC range of 0.125 – 4 mg/L.

⇒ MTAs between DTU and NRLs

All strains shipped to DTU for analysis

Task 2 – AST by DD



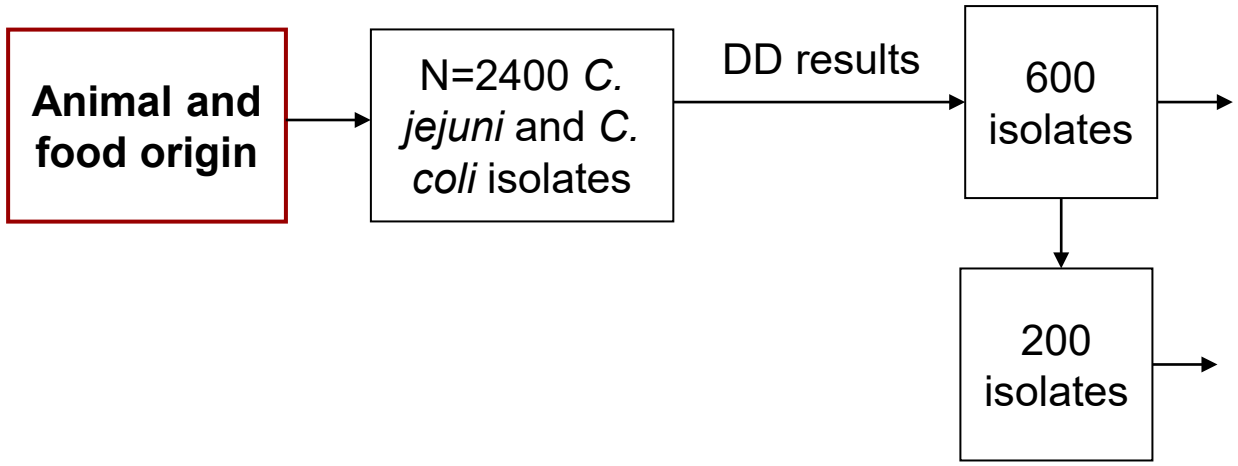
=> Six antimicrobials selected by EDL:

- Meropenem
- Ertapenem
- Imipenem
- Pefloxacin (screening for fluoroquinolone resistance)
- Erythromycin (screening for macrolid-resistance)
- Tetracycline.

⇒ *C. jejuni* strain ATCC 33560 will be used for quality control.

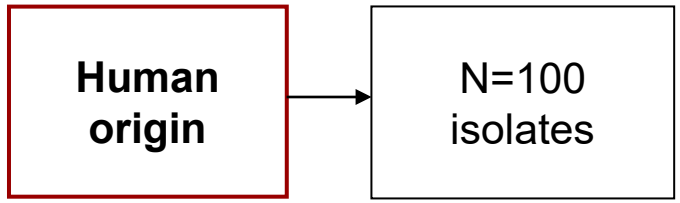
=> EUCAST DD protocol for *Campylobacter* (https://www.eucast.org/ast_of_bacteria/disk_diffusion_methodology) using Muller Hinton agar (MHF (EUCAST recommendation)) of two different suppliers e.g. Oxoid and BioRad

Task 3- AST by broth microdilution

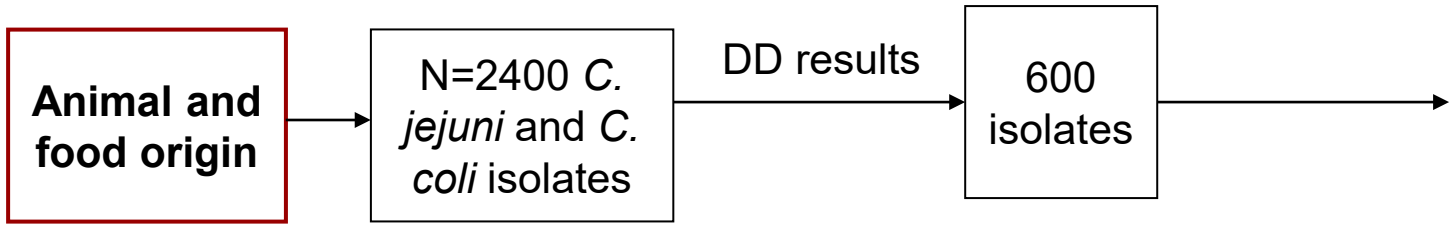


=> AST by broth microdilution
=> Custom sensititre plate design – 500 plates minimum order
⇒ Ertapenem, imipenem, and meropenem
⇒ range from 0.002 to 32 mg/L.
=> Half a plate for one strain => 300 plates for 600 isolates
=> MH-F (EUCAST recommendation)) of two different suppliers every second week following the EUCAST testing principle

test a subset of the same isolates using the MH+LHB (CLSI recommendations) broth in comparison to MH-F



Task 4&5- WGS and in silico analysis



Illumina technology using the standard EURL-AR WGS protocol

https://www.eurl-ar.eu/CustomerData/Files/Folders/34-wgs/628_protocol-for-wgs-v2-2.pdf

- presence of known antimicrobial determinants e.g. *bla*OXA and resistance mutations *por*A or *cme*ABC
- relevant epidemiological markers, and phylogeny using both a gene by gene; cgMLST and SNP approach based on the experience of the EFSA GenCamp project (https://www.efsa.europa.eu/en/supporting/pub/en-1398).
- In addition, the data will be further investigated to detect novelties explaining the non-susceptibility to carbapenems.
- All raw data of the study will be supplemented with additional *C. jejuni* and *C. coli* genomes from ENA

Expected Outcomes

- To determine the wildtype MIC distribution between *C. jejuni* and *C. coli* as well as between the four animal domains and in humans by disk diffusion and broth microdilution.
- To determine the comparability between the EUCAST and CLSI recommended media for MIC determination of *Campylobacter*.
- To determine the genomic diversity of susceptible and nonsusceptible *C. jejuni* and *C. coli* across the different animal species and humans in EU.
- To determine which of ertapenem, imipenem and meropenem would be most suitable for the monitoring of *Campylobacter*.
- To investigate potential resistance mechanism conferring nonsusceptibility to carbapenems as well as the role of blaOXA genes observed in *Campylobacter*.