

# The role of wastewater in surveillance and emergence of antibiotic resistant bacteria

Akademisk avhandling som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Medicinargatan 3, den 17 juni, klockan 13:00.

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**Avhandlingen baseras på följande delarbeten**

**I. Population-level surveillance of antibiotic resistance in *Escherichia coli* through sewage analysis.**

Marion Hutinel, Patricia Maria Catharina Huijbers, Jerker Fick, Christina Åhrén, Dan Göran Joakim Larsson, and Carl-Fredrik Flach. *Eurosurveillance*, 2019, 24(37), 1800497

**II. Monitoring of hospital sewage shows both promise and limitations as an early-warning system for carbapenemase-producing Enterobacterales in a low-prevalence setting.**

Carl-Fredrik Flach, Marion Hutinel, Mohammad Razavi, Christina Åhrén, and Dan Göran Joakim Larsson. *Manuscript*.

**III. Antibiotic resistance genes of emerging concern in Swedish municipal and hospital wastewaters.**

Marion Hutinel, Dan Göran Joakim Larsson, and Carl-Fredrik Flach. *Manuscript*.

**IV. Investigating the effects of municipal and hospital wastewaters on horizontal gene transfer.**

Marion Hutinel, Jerker Fick, Dan Göran Joakim Larsson, and Carl-Fredrik Flach. *Environmental Pollution*, 2021, 276, 116733.

**SAHLGRENKA AKADEMIN  
INSTITUTIONEN FÖR BIOMEDICIN**



# The role of wastewater in surveillance and emergence of antibiotic resistant bacteria

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## Abstract

As antibiotic resistance spreads among bacterial pathogens, it reduces treatment options and increases treatment failures of infectious diseases. Strategies employed to reduce this spread or adapt to its consequences need to be based on reliable surveillance data which is lacking in many countries, often due to limited resources. Wastewater contains pooled excreted bacteria, including common pathogens such as *Escherichia coli*, from the population connected to the sewers. Hence, analysis of wastewater has the potential to be used as a resource-efficient surveillance system for antibiotic resistance. In the sewers, human-associated bacteria are also mixed with environmental bacteria and exposed to many substances known to induce horizontal gene transfer (HGT), a major driver for the acquisition of antibiotic resistance in bacteria. The studies presented in this thesis aimed to develop and assess several ways in which the analysis of wastewater samples could be used to provide clinically relevant antibiotic resistance data and evaluate the effects of wastewater on HGT.

The resistance rates of *E. coli* from wastewaters were determined. Additionally, the abundance of different carbapenemase-producing Enterobacterales (CPE) and antibiotic resistance genes (ARGs) were quantified in wastewater. Resistance rates in wastewater *E. coli* were strongly correlated with resistance rates in clinical isolates and the detection of CPE in wastewater was coherent with the detection of similar CPE in the contributing population. The concentrations of some carbapenemase genes (namely *bla*<sub>OXA-48</sub>, *bla*<sub>NDM</sub> and *bla*<sub>KPC</sub>) were in accordance with the occurrence of CPE carrying those genes in wastewater. Further, a rise of *bla*<sub>OXA-48</sub> in wastewater preceded detection of corresponding CPE in patients, indicating that monitoring of ARGs in wastewater could serve as an early warning system. Hence, it is noteworthy that many ARGs of emerging concern (*cftr*, *optrA*, *mcr-1*, *mcr-3*, *mcr-4*, *mcr-5*, *sul4* and *gar*), which have almost never been detected in Swedish clinical samples, were detected regularly in wastewater.

A HGT assay, where a recipient strain was mixed with a complex donor bacterial community, was used to measure the rate of acquisition of ARGs in the presence of wastewater. Municipal wastewater had no detectable effect on HGT but exposure to hospital wastewater could promote antibiotic resistance.

Overall, this thesis provides evidence supporting the use of antibiotic resistance data from wastewater analyses as a valuable complement to traditional clinical surveillance. Additionally, the thesis highlights a possible role of hospital wastewater in the emergence of antibiotic resistant bacteria.

**Keywords:** Antibiotic resistance, wastewater, sewage, surveillance, horizontal gene transfer

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