ANTIBIOTIC RESISTANCE GENES (ARG) IN AQUACULTURE:

ENVIRONMENTAL HOTSPOTS AND PUBLIC HEALTH IMPLICATIONS

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Fish Farm Waters & Effluents

Regular antibiotic use (prophylactic or therapeutic) in densely stocked fish generates low-level antibiotic residues in water. These sub-therapeutic concentrations exert selective pressure for resistant bacteria and stimulate horizontal gene transfer in the microbiome. Effluent water from farms is a conduit for ARGs into surrounding rivers or coastal areas.

Sediments

Pond and seafloor sediments under or near fish farms accumulate uneaten feed, fish excreta, and antibiotic residues. Sediments thus become long-term reservoirs of antibiotics and ARGs. Studies in Europe have shown antibiotic concentrations and ARG abundance in farm sediments far exceed those in the water column. Notably, ARGs can persist in sediments even after active antibiotic use ceases.

Biofilms:

Aquaculture systems develop biofilms on tank walls, nets, and equipment. Biofilms can harbor diverse bacteria (including opportunistic fish pathogens) in a protected matrix, allowing ARG-carrying strains to persist long-term. Importantly, biofilms facilitate plasmid transfer and gene exchange between co-resident bacteria. Because biofilm communities are tough to eradicate, they can become chronic sources of ARGs in farms

ENVIRONMENTAL FACTORS AMPLIFYING RESISTANCE SELECTION

Temperature & Bacterial Growth

Warm water temperatures (as encountered in summer or in tropical aquaculture) **accelerate bacterial metabolism and reproduction**. Therefore warmer climates (and seasonal warming) tend to have higher baseline levels of resistance in farm environments, likely due to more rapid gene transfer and mutation, as well as more frequent disease outbreaks (necessitating more drug use).

Seasonal Effects

Studies have observed that **resistance gene abundance often peaks in warmer months**. Heat amplifies selection pressure or bacterial stress responses that favor resistant strains. Similarly, climate warming can contribute to the onset of antibiotic resistance, exacerbating the issue in an already warm region. Fish in **warmer water** may also experience **more stress and pathogen load**, leading to more frequent use of antibiotics and thus a feedback loop of resistance selection.

Other Environmental Factors

High organic matter can increase microbial density , while sunlight/UV in shallow ponds might degrade some antibiotics but also induce SOS responses in bacteria that enhance mutation and gene uptake. **Low water exchange rates** (as in enclosed ponds) means longer exposure of bacteria to any given antibiotic and more time for gene transfer, whereas high exchange (open net pens) can spread ARGs to the broader environment but may lower on-site selection pressure.

Antibiotic(s) & Tested Bacteria	Observed Resistance Rate(s)	Aquaculture Context (Location, Species)
Tetracycline; Trimethoprim–sulfadiazine; Trimethoprim (Vibrio spp.)	17% (Tet); 7% (TPS); 2% (TMP) resistant	Marine fish farms along Adriatic coast (Italy) – *Vibrio* isolates from farm water
Multiple antibiotics (penicillins, sulfonamides, macrolides, etc.) – *Aeromonas spp.*	~100% of isolates multi-drug resistant (resistant to ≥5 drug classes)	Semi-intensive seabream farm, Tyrrhenian coast (Italy) – *Aeromonas* from fish showed near-universal resistance to sulfadiazine, amoxicillin, ampicillin, erythromycin, cephalothin, streptomycin, trimethoprim, etc.
Oxytetracycline (OTC) (various bacteria)	Up to 50% of isolates resistant in certain farm zones	Intensive marine farms (Italy, Adriatic) – High tetracycline resistance in bacteria from fish farm sites (versus lower rates offshore). Reflects heavy OTC use historically in Mediterranean aquaculture.
Flumequine (quinolone)	Low resistance (<1%) – e.g. 0.3% of isolates resistant	Adriatic Sea cage farms (Italy) – Resistance to flumequine remained very low (0–0.3%) in native marine bacteriaconsistent with more restricted use of flumequine.
Ertapenem, Meropenem (carbapenems; *Enterobacter* and *Pseudomonas* spp.)	Detected presence of resistance (isolates resistant to both)	Sea bream aquaculture site (Portugal) – >100 bacterial isolates screened; notably, some *Enterobacter* and *Pseudomonas* from farmed fish were found resistant to the carbapenems ertapenem and meropenem. These are clinically critical antibiotics not used in aquaculture, indicating ARG ingress from environmental sources or co-selection.
Sulfonamides & Trimethoprim (various bacteria)	~20–30% of isolates resistant (typical ranges)	Freshwater trout farms (France, USA) – Common use of potentiated sulfonamides leads to persistent moderate resistance rates in Aeromonas and Flavobacterium spp. (e.g. ~25% non-susceptible)

Sources:
(1) Labella, A., Gennari, M., Ghidini, V., Trento, I., Manfrin, A., Borrego, J. J., & Lleò, M. M. (2013). High incidence of antibiotic multi-resistant bacteria in coastal areas dedicated to fish farming. Marine Pollution Bulletin, 70(1–2), 197–203.
(2) Henriques, I., Alves, A., Chouchane, S., Machado, A. L., & Almeida, A. (2018). Frequent detection of carbapenem-resistant bacteria in coastal marine environments: A potential impact of untreated effluents. Marine Pollution Bulletin, 135, 131–135
(3) Pepi M, Focardi S. Antibiotic-Resistant Bacteria in Aquaculture and Climate Change: A Challenge for Health in the Mediterranean Area. Int J Environ Res Public Health. 2021 May 26;18(11):5723. doi: 10.3390/ijerph18115723. PMID: 34073520; PMCID: PMC8198758.
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INTRODUCTION

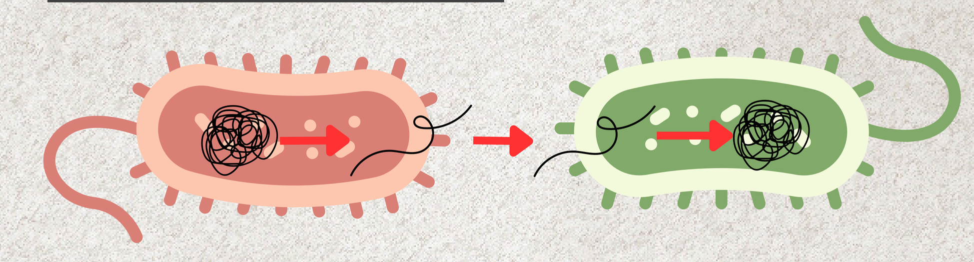
Growing concern of antibiotic resistance globally

Fish farming as an emerging hotspot for ARG (Antibiotic Resistance Genes) proliferation

Relevance to environmental safety and public health

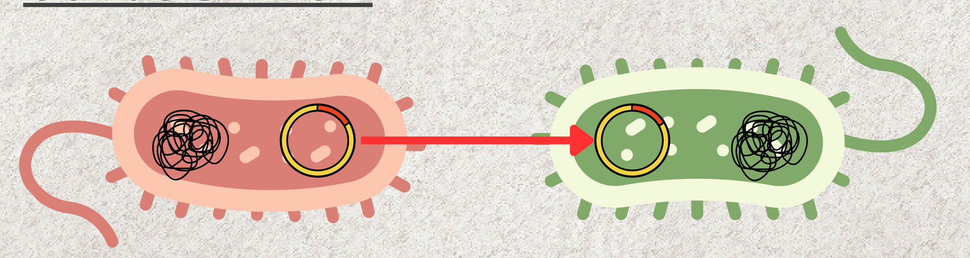
HORIZONTAL GENE TRANSFER (HGT)

TRANSFORMATION



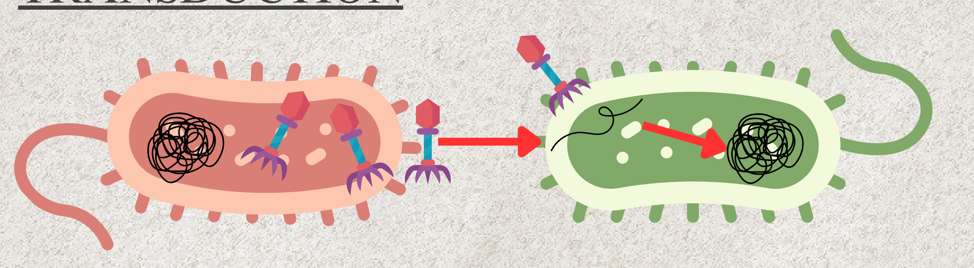
Introduction, uptake and expression of foreign genetic material

CONJUGATION



Transfer of DNA via a plasmid from a donor cell to a recipient cell

TRANSDUCTION



Bacterial DNA is moved from one bacterium to another by a virus

Relevance to environmental safety and **mobile genetic elements** create a network for ARG exchange in aquaculture. Plasmids transfer ARGs across species boundaries in water and biofilms; integrons collect multiple resistance genes and spread them as cassettes; transposons hop ARGs into new genomic contexts.

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