Antibiotics in the environment D. G. JOAKIM LARSSON Department of Infectious Diseases, Institute for Biomedicine, The Sahlgrenska Academy at the University of Gothenburg, Guldhedsgatan 10, SE-413 46, Gothenburg, Sweden Abstract: Molecules with antibiotic properties, produced by various microbes, have been around long before mankind recognized their usefulness in preventing and treating bacterial infections.Ashbolt NJ, Amezquita A, Backhaus T, Borriello SP, Brandt KK, Collignon P, et al. Human health risk assessment (HHRA) for environmental development and transfer of antibiotic resistance.As feces often contain antibiotic-resistant bacteria as well as antibiotic residues, it is difficult to assign with certainty increased abundances of resistance genes to the contamination by antibiotics in the field o The changes over time may be due to the accumulation of more and more selective agents in the soil, but also because of years of amendment with manure from animals that over time contains more and more resistance genes as result of generations of antibiotic use on farms and selection within the intestines of farm animals, rather than within the soil.Such co-selection between different antibiotics is an important driver behind multi- resistance development in pathogens o Metals and antibacterial biocides are other classes of compounds that have the ability to co-select for antibiotic resistance Conclusion : o Given what is at stake, the precautionary principle can be invoked in order to reduce risks with environ- mental antibiotic contamination also in the absence of final evidence that it ultimately results in more infections with resistant bacterial pathogens.The concentrations found in manure or manure-amended soils are often considerably higher than those found in aquatic environments .The same holds true for sludge generated in municipal sewage treatment plants .However, many antibiotics tend to bind strongly to particles, and only a fraction of the total amounts is probably bioactive.Micro- organisms in farmland soil are crucial for e.g. nitrogen fixation and other nutrient fluxes, and there is a potential for antibiotics to disrupt such processes, however, there is no clear evidence for disturbed ecosystem services in soil communities due to antibiotic exposure given the prevailing exposure levels documented in the field.o Even releases of pathogenic bacteria containing integrons, capable of capturing and expressing arrays of genes, may conceivably accelerate the development of resistance by providing increased possibilities to probe the environmental resistance for novel resistance genes not yet encountered in the clinic References: 1.Sim WJ, Lee JW, Lee ES, Shinb SK, Hwang SR, Oh JE. Occurrence and distribution of pharmaceuticals in wastewater from households, livestock farms, hospitals and pharmaceu- tical manufactures.Phillips PJ, Smith SG, Kolpin DW, Zaugg SD, Buxton HT, Furlong ET, et al. Pharmaceutical formulation facilities as sources of opioids and other pharmaceuticals to wastewater treat- ment plant effluents.Ye Z, Weinberg HS, Meyer MT. Trace analysis of trimeth- oprim and sulfonamide, macrolide, quinolone, and tetracy- cline antibiotics in chlorinated drinking water using liquid chromatography electrospray tandem mass spectrometry.Gaze WH, Krone SM, Larsson DGJ, Li XZ, Robinson JA, Simonet P, et al. Influence of humans on evolution and mobilization of environmental antibiotic resistome.Kristiansson E, Fick J, Janzon A, Grabic R, Rutgersson C, Weidegard B, et al. Pyrosequencing of antibiotic-contaminatedriver sediments reveals high levels of resistance and genetransfer elements.Wellington EMH, Boxall ABA, Cross P, Feil EJ, Gaze WH, Hawkey PM, et al. The role of the natural environment in the emergence of antibiotic resistance in Gram-negative bacteria.Some antibiotics are easily degraded, such as penicillins, whereas others are considerably more persistent, such as fluoroquino -lones and tetracyclines, thus allowing them to prevail for longer times in the environment, to spread further, and to accumulate to higher concentrations.In most high-income countries with well-developed sewage infrastructure, discharge to the environment is reduced, but microbial communities within the treatment plants can nevertheless be exposed to mg/L concentrations of selected antibiotics .Again, to date, concentration of antibiotics found in municipal sewage treatment plants do not appear to be sufficient to reduce their treatment efficiency; however, for treatment plants receiving highly contaminated waste from manufacturing of antibiotics, the exposure levels and thus the risks for disturbed function can be quite different.Many of the mobile resistance genes we face in pathogens in the clinic today have their origin in harmless bacteria in and around us .The environmental microbiome represents a much greater diversity than those micro-organisms that thrive in or on our bodies.Pruden A, Larsson DGJ, Amezquita A, Collignon P, Brandt KK, Graham DW, et al. Management options for reducing the release of antibiotics and antibiotic resistance genes to the environment.Lemus JA, Blanco G, Grande J, Arroyo B, Garcia- Montijano M, Martinez F. Antibiotics threaten wildlife: circulating quinolone residues and disease in avian scavengers.Finley RL, Collignon P, Larsson DGJ, McEwen SA, Li X-Z, Gaze WH, et al. The scourge of antibiotic resistance: the important role of the environment.As a consequence, entire bacterial communities became exposed to unprecedented antibiotic selection pressures, which in turn led to the rapid resistance development we are facing today among many pathogens , other environments, outside of our bodies, may also be exposed to antibiotics through different routes, most often unintentionally.In principle, the transfer of a novel resistance gene or resistance vector to a pathogen colonizing a human being only needs to happen once in one place on our planet, as our heavy use of antibiotics, lack of sufficient hygiene, Such crucial gene transfer events may take place in the external environment, in ani mals or inside our bodies, in one or several steps.Forsberg KJ, Reyes A, Wang B, Selleck EM, Sommer MOA, Dantas G. The shared antibiotic resistome of soil bacteria and human pathogens.Resistant bacteria as well as selected resistance genes appear to increase or decrease in relative numbers between influents and effluents of sewage treatment plants in a rather non-predictable manner.Babic S, Mutavdzic D, Asperger D, Horvat AJM, Kastelan- Macan M. Determination of veterinary pharmaceuticals in production wastewater by HPTLC-videodensitometry.Boxall ABA, Rudd MA, Brooks BW, Caldwell DJ, Choi K, Hickmann S, et al. Pharmaceuticals and personal care pro- ducts in the environment: what are the big questions?The external environment also provides unique opportunities for genetic recombination and thus the creation of novel vectors for genes already circulating in pathogens.Arenas and conditions that favor such recombination and transfer events are not clear, but an added selection pressure from antibiotics, increasing the available pool of resistance genes and selecting for bacteria acquiring resistance genes through horizontal gene transfer, is an obvious risk factor.Importantly, not only discharges of antibiotics need to be controlled, but also antibiotic-resistant bacteria that might develop and become enriched within e.g. industrial processes.In the twentieth century we began mass-producing antibiotics, mainly synthetic derivatives of naturally produced antibiotic molecules, but also a few entirely synthetic compounds.There are concerns that increased selection pressures from antibiotics in the environment can contribute to the recruitment of resistance factors from the environmental resistome to human

pathogens.It has now become clear that man-made antibiotics can enter the environment in many ways, from the production of active pharmaceutical ingredients, through the excretion of residues after usage or through discarding, unused medicines .In surface waters receiving municipal waste-water, concentrations of antibiotics rarely exceed 1 mg/L, but are more regularly in the low ng/L range.Berlin, Heidelberg: Springer-Verlag;
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