LA RESISTENCIA A LOS ANTIBIÓTICOS EN ECOSISTEMAS NATURALES NO CLÍNICOS: UNA SITUACIÓN DE IDA Y VUELTA

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Ecosistemas naturales como origen de los antibióticos

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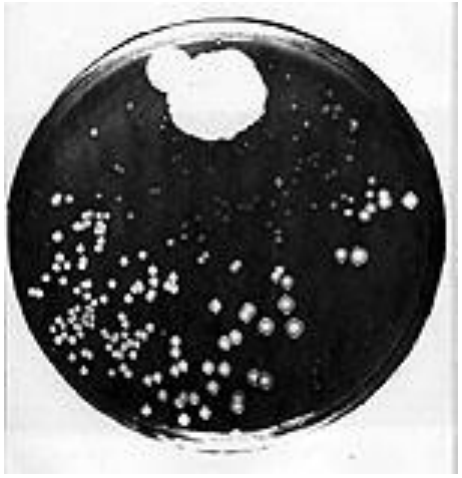


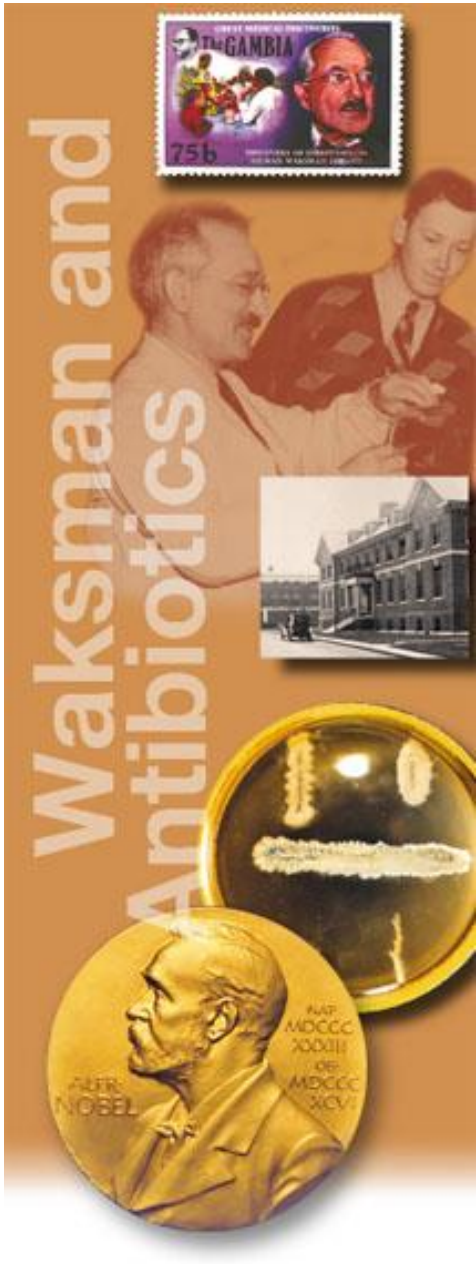
Las razones ecológicas para buscar antibióticos en ecosistemas naturales

THE SOIL AS A SOURCE OF MICROORGANISMS ANTAGONISTIC TO DISEASE-PRODUCING BACTERIA

SELMAN A. WAKSMAN AND H. BOYD WOODRUFF

J Bacteriol. 1940 40: 581–600

Bacteria pathogenic for man and animals find their way to the soil, either in the excreta of the hosts or in their remains. If one considers the period for which animals and plants have existed on this planet and the great numbers of disease-producing microbes that must have thus gained entrance into the soil, one can only wonder that the soil harbors so few bacteria capable of causing infectious diseases in man and in animals. One hardly thinks of the soil as a source of epidemics. What has become of all the bacteria causing typhoid, dysentery, cholera, diphtheria, pneumonia, bubonic plague, tuberculosis, leprosy, and numerous others? This question was first raised by medical bacteriologists in the eighties of the last century. The soil was searched for bacterial agents of infectious diseases, until the conclusion was reached that these do not survive long in the soil. It was suggested that the cause of the disappearance of these disease- producing organisms in the soil is to be looked for among the soil-inhabiting microbes, antagonistic to the pathogens and bringing about their rapid destruction in the soil.



Resistencia a los antibióticos: una respuesta para evitar ser desplazado del habitat

No. 3713. DEC. 28, 1940 NATURE 837

LETTERS TO THE EDITORS

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IN THE PRESENT CIRCUMSTANCES, PROOFS OF "LETTERS" WILL NOT BE SUBMITTED TO CORRESPONDENTS OUTSIDE GREAT BRITAIN.

An Enzyme from Bacteria able to Destroy Penicillin

FLEMING[1] noted that the growth of *B. coli* and a number of other bacteria belonging to the coli-typhoid group was not inhibited by penicillin. This observation has been confirmed. Further work has been done to find the cause of the resistance of these organisms to the action of penicillin.

An extract of *B. coli* was made by crushing a suspension of the organisms in the bacterial crushing mill of Booth and Green[2]. This extract was found to contain a substance destroying the growth-inhibiting property of penicillin. The destruction took place on incubating the penicillin preparation with the bacterial extract at 37°, or at room temperature for a longer time. The following is a typical experiment showing the penicillin-destroying effect of *B. coli* extracts. A solution of 1 mgm. penicillin in 0·8 c.c. of water was incubated with 0·2 c.c. of centrifuged and dialysed bacterial extract at 37° for 3 hours, in the presence of ether, and a control solution of penicillin of equal concentration was incubated without enzyme for the same time. (The penicillin used was extracted from cultures of *Penicillium notatum* by a method to be described in detail later. It possessed a degree of purity similar to that of the samples used in the chemotherapeutic experiments recorded in a preliminary report[3].) The growth-inhibiting activity of the solutions was then tested quantitatively on agar plates against *Staphylococcus aureus*. The penicillin solution incubated with the enzyme had entirely lost its growth-inhibiting activity, whereas the control solution had retained its full strength.

The conclusion that the active substance is an enzyme is drawn from the fact that it is destroyed by heating at 90° for 5 minutes and by incubation with papain activated with potassium cyanide at pH 6, and that it is non-dialysable through 'Cellophane' membranes. It can be precipitated by 2 volumes of alcohol, but much of its activity is lost during this operation. The activity of the enzyme, which we term penicillinase, is slight at pH 6, but increases considerably towards the alkaline range of pH. It is very active at pH 8 and 9. Higher pH's could not be tested as penicillin is unstable above pH 9.

The mechanism of the enzymatic inactivation of penicillin is being studied. No oxygen uptake occurs during the reaction, and the inactivation proceeds with equal facility under aerobic and anaerobic conditions. No appearance of acid groups could be detected by pH measurement with the hydrogen electrode. Extracts of a number of other micro-organisms, made by crushing the bacteria in the bacterial grinding mill, were tested for penicillinase. The enzyme was absent from extracts of the penicillin-sensitive *Staphylococcus aureus*, of yeast and of *Penicillium notatum*. It was present in a Gram-negative rod, insensitive to penicillin, found as a contaminant of some Penicillium cultures. Unlike *B. coli*, it was not necessary to crush the organism in the bacterial mill in order to obtain the enzyme from it; the latter appeared in the culture fluid. The enzyme was also found in *M. lysodeikticus*, an organism sensitive to the action of penicillin, though less so than *Staphylococcus aureus*. Thus, the presence or absence of the enzyme in a bacterium may not be the sole factor determining its insensitivity or sensitivity to penicillin.

The tissue extracts and tissue autolysates that have been tested were found to be without action on the growth-inhibiting power of penicillin. Prof. A. D. Gardner has found staphylococcal pus to be devoid of inhibiting action, but has demonstrated a slight inhibition by the pus from a case of *B. coli* cystitis. The bacteriostatic action of the sulphonamide drugs is known to be inhibited in the presence of tissue constituents and pus[4]. That the anti-bacterial activity of penicillin is not affected under these conditions gives this substance a definite advantage over the sulphonamide drugs from the chemotherapeutic point of view. The fact that a number of bacteria contain an enzyme acting on penicillin points to the possibility that this substance may have a function in their metabolism.

E. P. ABRAHAM.
E. CHAIN.

Sir William Dunn School of Pathology,
Oxford.
Dec. 5.

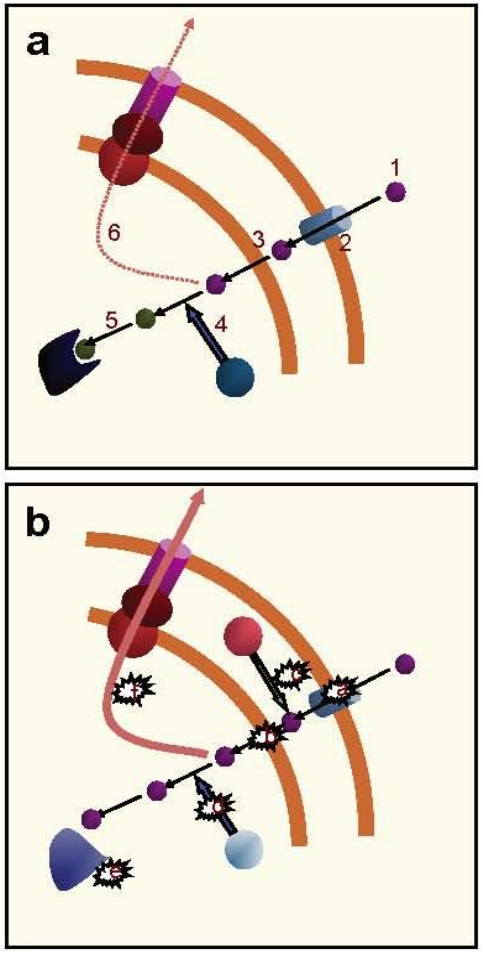
[1] Fleming, A., *Brit. J. Exp. Path.*, **10**, 226 (1929).
[2] Booth, V. H., and Green, D. E., *Biochem. J.*, **25**, 453 (1931).
[3] Chain, E., Florey, H. W., Gardner, A. D., Heatley, N. G., Jennings, M. A., Orr-Ewing, J., and Sanders, A. G., *Lancet*, 226 (1940).
[4] Maxted, C., *J. Exp. Med.*, **72**, 317 (1940).

Proc. Nat. Acad. Sci. USA Vol. 70 pp. 2276-2280,1973 Aminoglycoside Antibiotic-Inactivating Enzymes in Actinomycetes Similar to Those Present in Clinical Isolates of Antibiotic-Resistant Bacteria
RAOUL BENVENISTE AND JULIAN DAVIES

The metabolic role of the aminoglycoside-modifying enzymes in actinomycetes is not known. Miller and Walker have postulated that **phosphorylated streptomycin might be important as a metabolic precursor** of streptomycin or to **detoxify the antibiotic** (7). The enzymes might also be required for transport of these antibiotics in or out of the cell. Alternatively, they may have nothing to do with antibiotic biosynthesis and may play a role in another biosynthetic process.

Nothing is known about the origin of R factors. The Watanabe hypothesis (4) provides a simple molecular mechanism for their origin, but we can only speculate on the environmental and evolutionary factors that play a role in their formation and maintenance. **Their presence does not seem to require the extensive use of a selective antibiotic environment since Gardner et al. (21) have found R factors in an "antibiotic virgin population" in the Solomon Islands.**

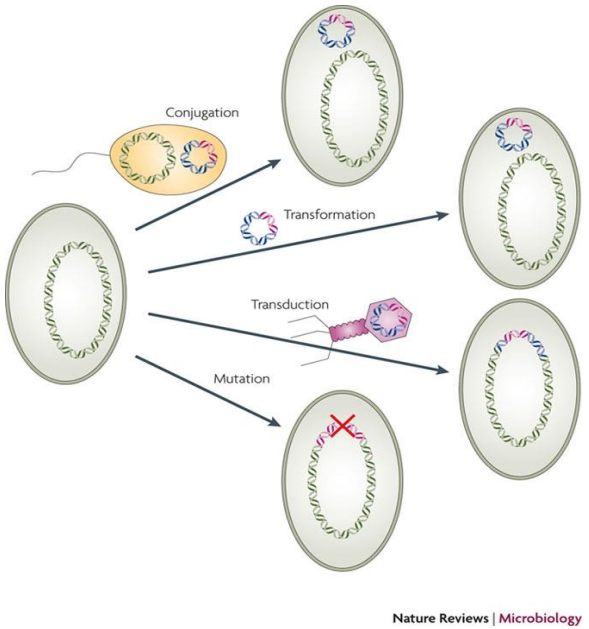
Mecanismos de acción y resistencia a los antibióticos



Resistencia es tan solo un problema clásico de equilibrio químico:

Cuando la concentración del antibiótico no es suficiente para inhibir de modo eficaz la actividad del blanco bacteriano.

Esta situación puede darse, bien reduciendo la concentración del antibiótico, bien modificando el blanco de modo que la afinidad del antibiótico quede disminuída.



Martínez, J. L., Baquero, F., Andersson, D. I. (2011) Current Opinion in Pharmacology. 5: 439-445.

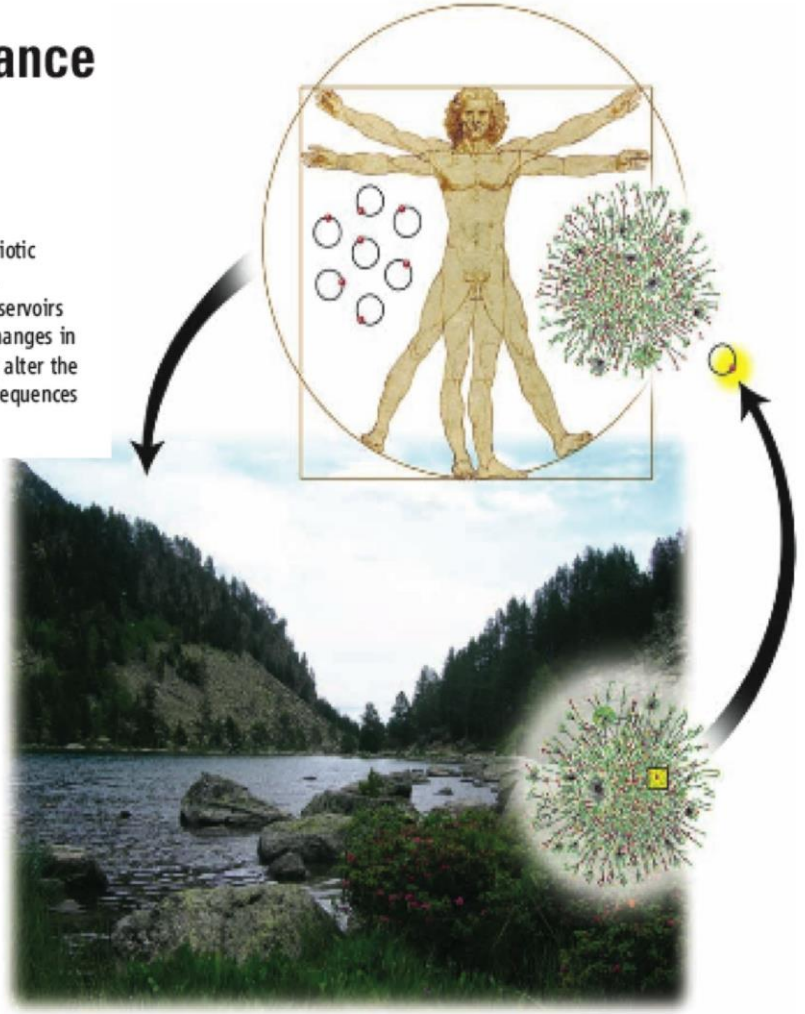
Los ecosistemas naturales son el origen de la mayoría de los genes de resistencias adquiridos por las bacterias patógenas e intervienen en su diseminación

PERSPECTIVE

Antibiotics and Antibiotic Resistance Genes in Natural Environments

José L. Martínez*

The large majority of antibiotics currently used for treating infections and the antibiotic resistance genes acquired by human pathogens each have an environmental origin. Recent work indicates that the function of these elements in their environmental reservoirs may be very distinct from the "weapon-shield" role they play in clinical settings. Changes in natural ecosystems, including the release of large amounts of antimicrobials, might alter the population dynamics of microorganisms, including selection of resistance, with consequences for human health that are difficult to predict.



Los genes de resistencia están presentes en todos los ecosistemas

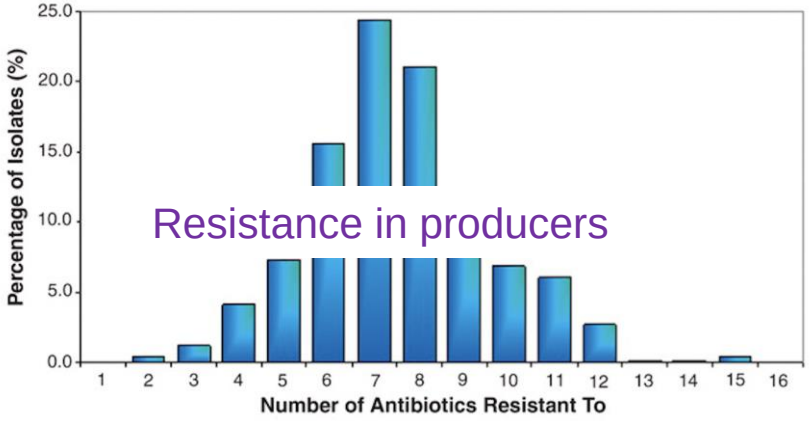
The Shared Antibiotic Resistome of Soil Bacteria and Human Pathogens

Kevin J. Forsberg,[1*] Alejandro Reyes,[1*] Bin Wang,[1,2] Elizabeth M. Selleck,[3] Morten O. A. Sommer,[4,5]† Gautam Dantas[1,2]†

OPEN ACCESS Freely available online

The Culturable Soil Antibiotic of Multi-Drug Resistant Bacte

Fiona Walsh*, Brion Duffy



2444–2447
ccess publication 4 August 2011

Journal of Antimicrobial Chemotherapy

as vehicles of the resistome in cystic fibrosis

olain*, Laura Fancello, Christelle Desnues and Didier Raoult

Microb Ecol (2013) 65:975–981
DOI 10.1007/s00248-013-0187-2

MICROBIOLOGY OF AQUATIC SYSTEMS

Marine Sediment Bacteria Harbor Antibiotic Resistance Genes Highly Similar to Those Found in Human Pathogens

Jing Yang · Chao Wang · Chang Shu · Li Liu · Jianing Geng · Songnian Hu · Jie Feng

Sampling the Antibiotic Resistome

Vanessa M. D'Costa,[1] Katherine M. McGrann,[1] Donald W. Hughes,[2] Gerard D. Wright[1*]

Functional Characterization of the Antibiotic Resistance Reservoir in the Human Microflora

Morten O. A. Sommer,*† Gautam Dantas,*†‡ George M. Church

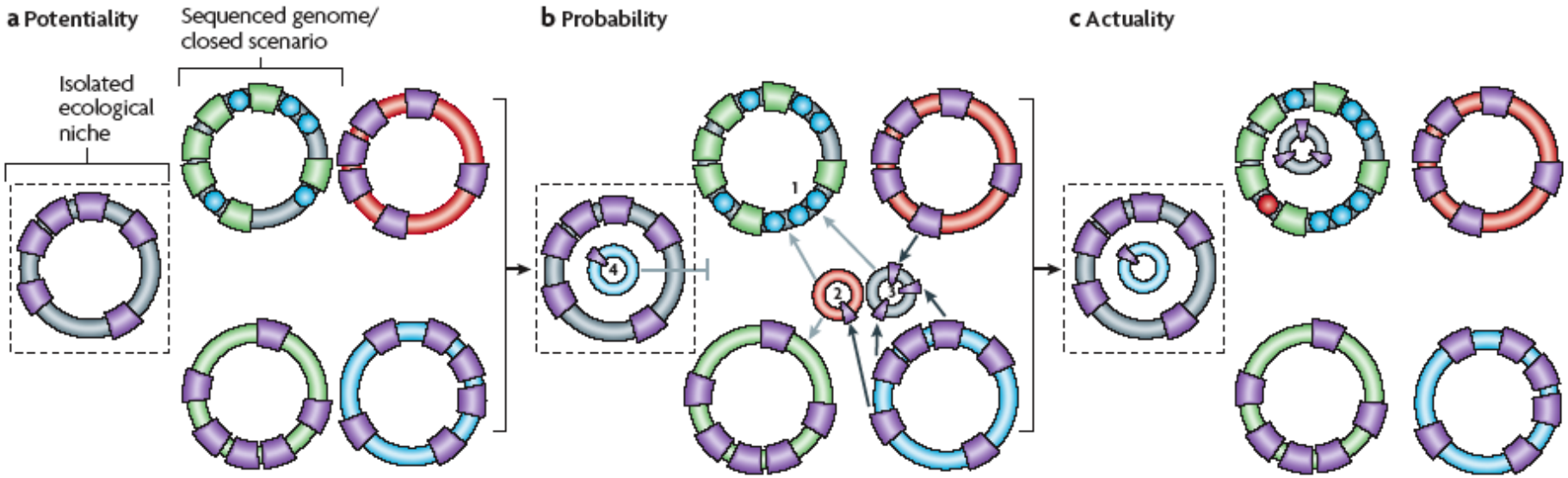
LETTER

doi:10.1038/nature12212

Antibiotic treatment expands the resistance reservoir and ecological network of the phage metagenome

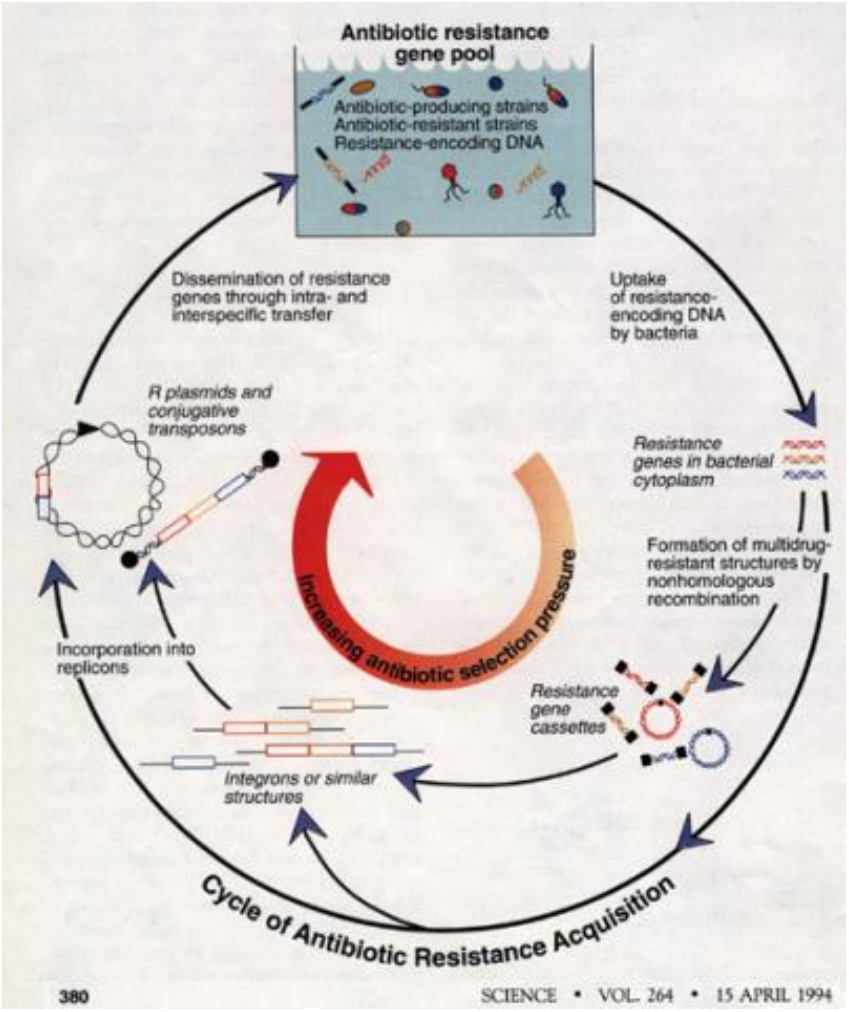
Sheetal R. Modi[1], Henry H. Lee[1]†, Catherine S. Spina[1,2,3] & James J. Collins[1,2,3]

Solo una pequeña parte de los genes que potencialmente pueden producir resistencia se encuentran en los patógenos humanos

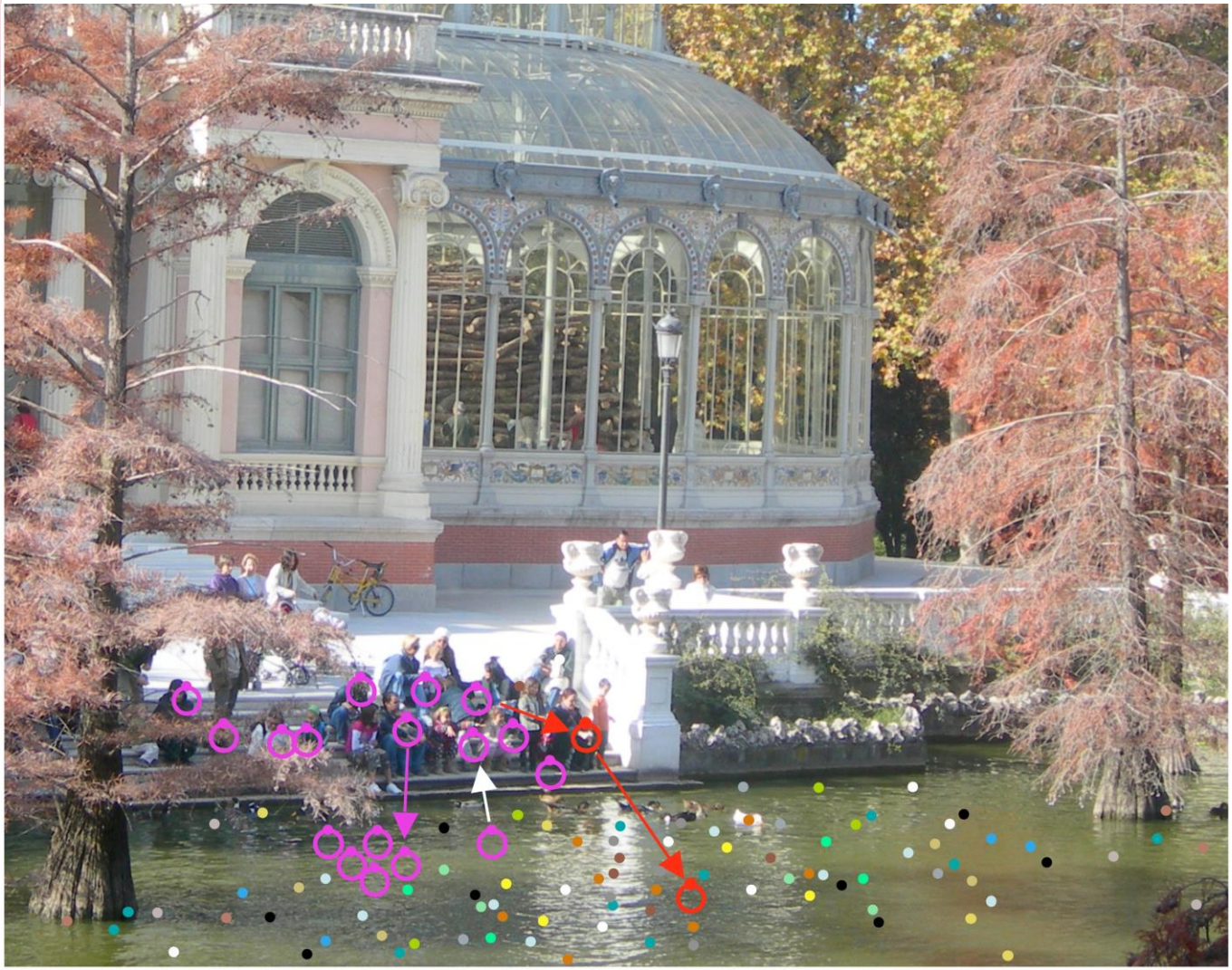


Martinez, J. L., F. Baquero & D. I. Andersson, (2007) Predicting antibiotic resistance. Nature Reviews in Microbiology 5: 958-965.
Martinez, J. L., F. Baquero & D. I. Andersson, (2011) Beyond serial passages: new methods for predicting the emergence of resistance to novel antibiotics. Curr Opin Pharmacol 11: 439-445.
Martínez JL., Coque, T., Baquero, F. What is a Resistance Gene? (2015) Ranking Risks on Resistomes. Nature Reviews in Microbiology 13: 116-123.

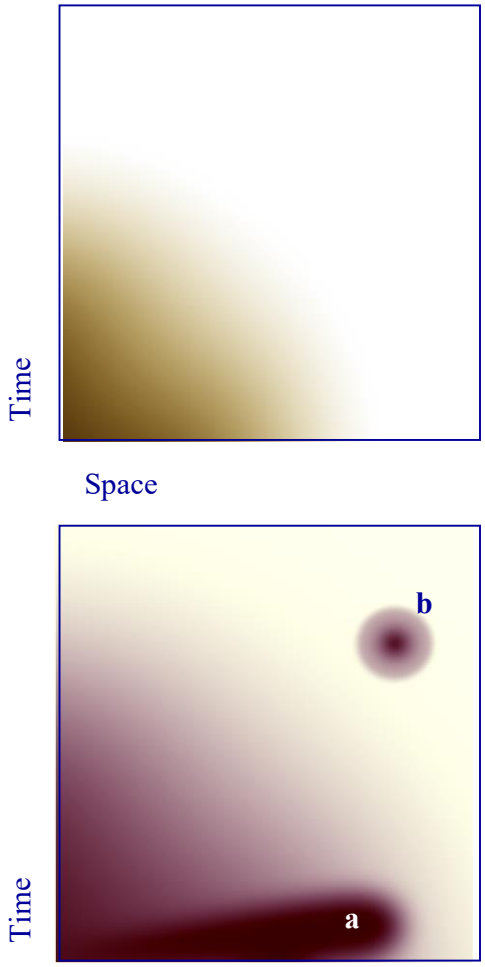
Solo una pequeña parte de los genes que potencialmente pueden producir resistencia se encuentran en los patógenos humanos: estructura jerárquica de la resistencia a los antibióticos



Diseminación de los genes de resistencia a los antibióticos: Retorno a ecosistemas naturales



Efecto auto-replicativo de la resistencia a los antibióticos



Unexpected Occurrence of Plasmid-mediated Quinolone Resistance Determinants in Environmental *Aeromonas* spp.

Vincent Cattoir,*†‡ Laurent Poirel,*† Camille Aubert,*† Claude-James Soussy,‡ and Patrice Nordmann*†

Emerging Infectious Diseases • ww

Journal of Antimicrobial Chemotherapy (2008) **62**, 948–950
doi:10.1093/jac/dkn341
Advance Access publication 3 September 2008

JAC

Plasmid-mediated quinolone resistance in *Aeromonas allosaccharophila* recovered from a Swiss lake

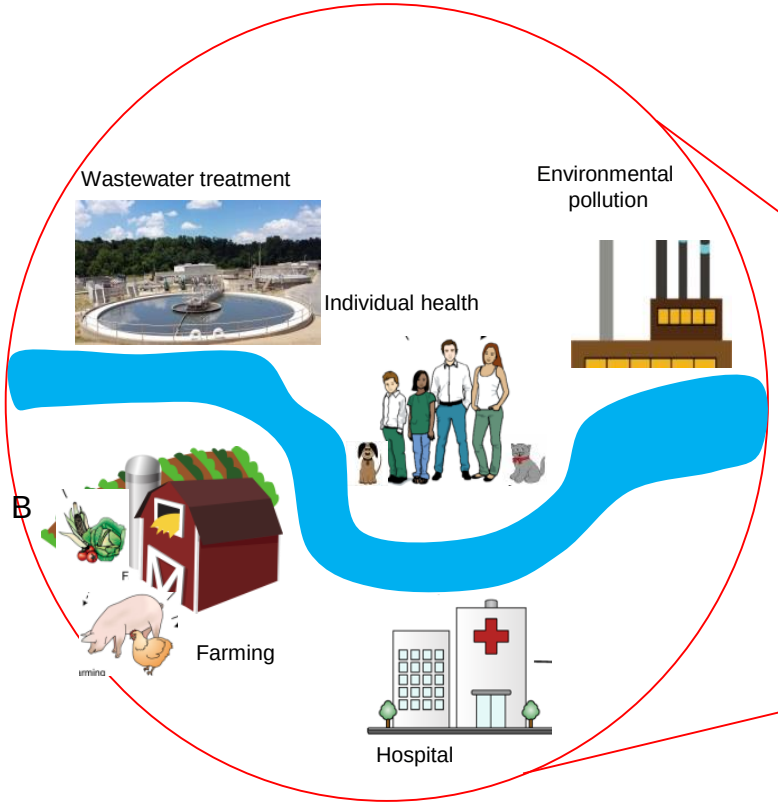
Renata Cristina Picão[1,2], Laurent Poirel[1], Antonella Demarta[3], Carla Sofia Ferreira Silva[1], Anna Rita Corvaglia[4], Orlando Petrini[3] and Patrice Nordmann[1]*

[1]*Service de Bactériologie-Virologie, INSERM U914 'Emerging Resistance to Antibiotics', Hôpital de Bicêtre, Assistance Publique/Hôpitaux de Paris, Faculté de Médecine et Université Paris Sud, K.-Bicêtre, France;* [2]*Laboratório ALERTA, Universidade Federal de São Paulo, São Paulo, Brazil;* [3]*Istituto Cantonale di Microbiologia, Bellinzona, Switzerland;* [4]*Centre Médical et Universitaire, Université de Genève, Geneva, Switzerland*

suggests that these genes may spread silently. In addition, the fact that the same mobile insertion cassette-associated *qnrS2* structure has been found in different *Aeromonas* species from aquatic environments from distantly related geographical areas may indicate that these PMQR determinants are widespread, at least in Europe. Our findings strengthen the possible role of *Aeromonas* spp. and of mobile insertion cassette-type structures as vehicles for the dissemination of quinolone resistance markers. They may be the link between the progenitor of QnrS proteins (Vibrionaceae) and enterobacterial clinical species such as *Salmonella*.

Martínez, J.L. (2009) Environmental Pollution 157:2893-902

Salud única y salud global: conceptos semejantes pero no exactamente iguales

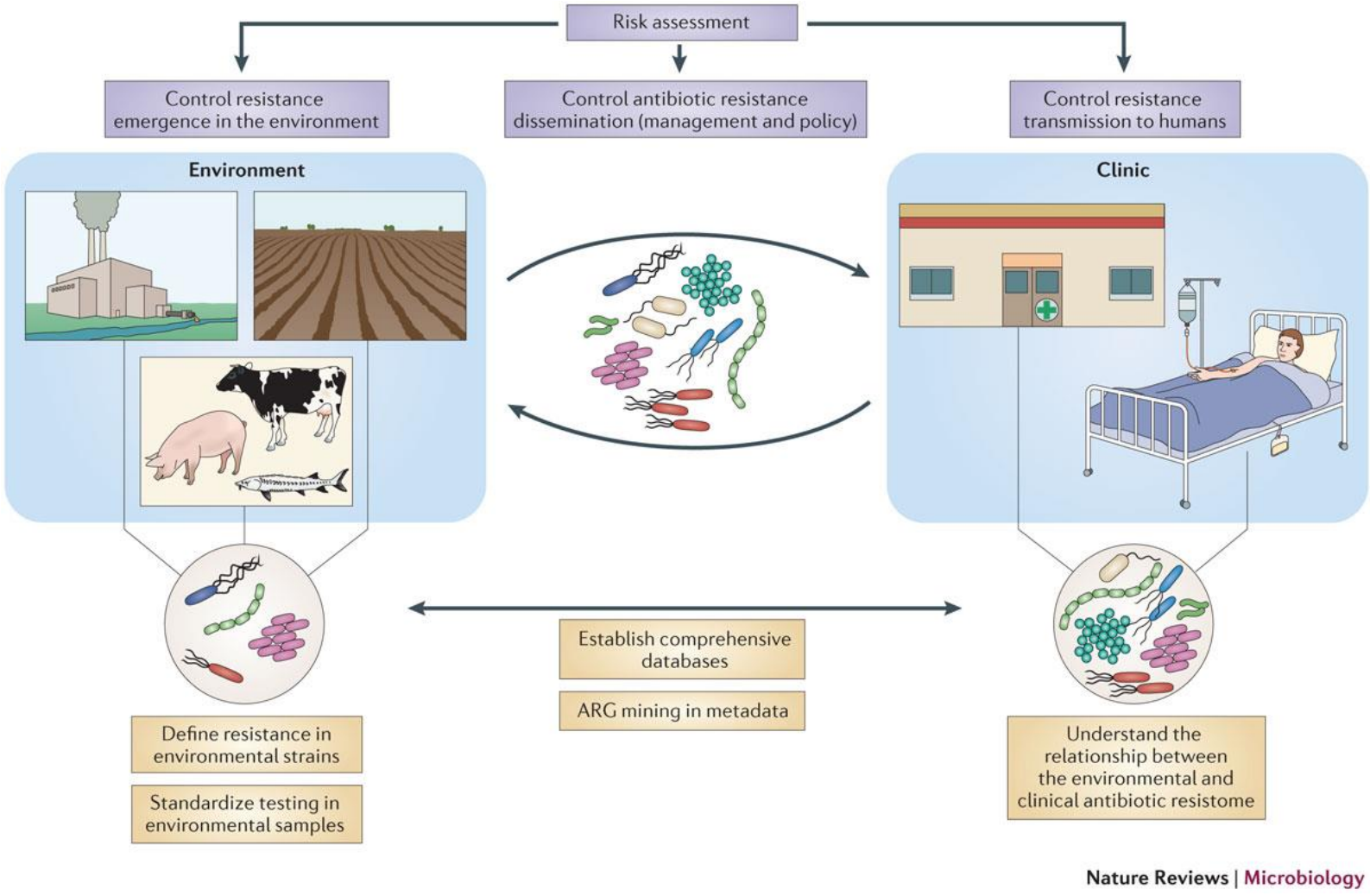


One Health(s)

Global Health

Hernando-Amado, S. Coque, T. M., Baquero. F., Martínez, J. L. Defining and combating antibiotic resistance from One-Health and Global-Health perspectives. Nature Microbiology 2019 Sep;4(9):1432-1442

Definición de "entidades de resistencia" para romper los puentes que permiten la diseminación de la resistencia a los antibióticos



Nature Reviews Microbiology **volume 13**, pages 310–317 (2015)

La polución es la mayor fuente de resistencia a los antibióticos en ecosistemas naturales

Fecal pollution can explain antibiotic resistance gene abundances in anthropogenically impacted environments

Antti Karkman [1,2,3], Katariina Pärnänen[4] & D.G.Joakim Larsson [1,2]

Discharge of treated sewage leads to release of antibiotic resistant bacteria, resistance genes and antibiotic residues to the environment. However, it is unclear whether increased abundance of antibiotic resistance genes in sewage and sewage-impacted environments is due to on-site selection pressure by residual antibiotics, or is simply a result of fecal contamination with resistant bacteria. Here we analyze relative resistance gene abundance and accompanying extent of fecal pollution in publicly available metagenomic data, using crAssphage sequences as a marker of human fecal contamination (crAssphage is a bacteriophage that is exceptionally abundant in, and specific to, human feces). We find that the presence of resistance genes can largely be explained by fecal pollution, with no clear signs of selection in the environment, with the exception of environments polluted by very high levels of antibiotics from manufacturing, where selection is evident. Our results demonstrate the necessity to take into account fecal pollution levels to avoid making erroneous assumptions regarding environmental selection of antibiotic resistance.

NATURE COMMUNICATIONS | (2019)10:80 | https://doi.org/10.1038/s41467-018-07992-3 | www.nature.com/naturecommunications

Sin embargo, bacterias de origen ambiental (en varios casos acuático), son el origen de genes de resistencia adquiridos por bacterias patógenas

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Aug. 2005, p. 3523–3525 Vol. 49, No. 8
0066-4804/05/$08.00+0 doi:10.1128/AAC.49.8.3523–3525.2005

Origin of Plasmid-Mediated Quinolone Resistance Determinant QnrA

Laurent Poirel,[1] Jose-Manuel Rodriguez-Martinez,[1,2] Hedi Mammeri,[1] Alain Liard,[1] and Patrice Nordmann[1]*

Service de Bactériologie-Virologie, Hôpital de Bicêtre, Assistance Publique/Hôpitaux de Paris, Faculté de Médecine Paris-Sud, Université Paris XI, 94275 K.-Bicêtre, France,[1] and University Hospital Virgen Macarena, University of Sevilla, Sevilla, Spain[2]

Received 15 March 2005/Returned for modification 19 April 2005/Accepted 21 May 2005

Plasmid-mediated resistance to quinolones is increasingly reported in studies of *Enterobacteriaceae*. Using a PCR-based strategy, a series of gram-negative species were screened for *qnrA*-like genes. *Shewanella algae*, an environmental species from marine and fresh water, was identified as its reservoir. This is a one of the very few examples of progenitor identification of an acquired antibiotic resistance gene.

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Sept. 2011, p. 4405–4407 Vol. 55, No. 9
0066-4804/11/$12.00 doi:10.1128/AAC.00681-11

Origin of OXA-181, an Emerging Carbapenem-Hydrolyzing Oxacillinase, as a Chromosomal Gene in *Shewanella xiamenensis*[▽]

Anaïs Potron, Laurent Poirel, and Patrice Nordmann*

Service de Bactériologie-Virologie, INSERM U914, Emerging Resistance to Antibiotics, Hôpital de Bicêtre, Assistance Publique/Hôpitaux de Paris, Faculté de Médecine, and Université Paris-Sud, 84275 Le Kremlin-Bicêtre, France

Received 17 May 2011/Returned for modification 22 June 2011/Accepted 26 June 2011

Plasmid-mediated carbapenem-hydrolyzing β-lactamases are becoming emerging threats with *Enterobacteriaceae*. In particular, the carbapenem-hydrolyzing class D β-lactamase OXA-48 and its derivative OXA-181 have been reported increasingly worldwide. Using a PCR-based strategy, environmental samples were screened for bla_{OXA-48}-like genes. *Shewanella xiamenensis*, an environmental species from marine and freshwater, was identified as the progenitor of the $bla_{OXA-181}$ gene. This work identifies the reservoir of an emerging carbapenemase gene that is clinically significant.

Tratamiento de aguas y su efecto en la diseminación de resistencia a los antibióticos

Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human health: an environmental point prevalence study

Timothy R Walsh, Janis Weeks, David M Livermore, Mark A Toleman

Summary

Background Not all patients infected with NDM-1-positive bacteria have a history of hospital admission in India, and extended-spectrum β-lactamases are known to be circulating in the Indian community. We therefore measured the prevalence of the NDM-1 gene in drinking water and seepage samples in New Delhi.

Methods Swabs absorbing about 100 µL of seepage water (ie, water pools in streets or rivulets) and 15 mL samples of public tap water were collected from sites within a 12 km radius of central New Delhi, with each site photographed and documented. Samples were transported to the UK and tested for the presence of the NDM-1 gene, bla_{NDM-1}, by PCR and DNA probing. As a control group, 100 µL sewage effluent samples were taken from the Cardiff Wastewater Treatment Works, Tremorfa, Wales. Bacteria from all samples were recovered and examined for bla_{NDM-1} by PCR and sequencing. We identified NDM-1-positive isolates, undertook susceptibility testing, and, where appropriate, typed the isolates. We undertook Inc typing on bla_{NDM-1}-positive plasmids. Transconjugants were created to assess plasmid transfer frequency and its relation to temperature.

Findings From Sept 26 to Oct 10, 2010, 171 seepage samples and 50 tap water samples from New Delhi and 70 sewage effluent samples from Cardiff Wastewater Treatment Works were collected. We detected bla_{NDM-1} in two of 50 drinking-water samples and 51 of 171 seepage samples from New Delhi; the gene was not found in any sample from Cardiff. Bacteria with bla_{NDM-1} were grown from 12 of 171 seepage samples and two of 50 water samples, and included 11 species in which NDM-1 has not previously been reported, including *Shigella boydii* and *Vibrio cholerae*. Carriage by enterobacteria, aeromonads, and *V cholera* was stable, generally transmissible, and associated with resistance patterns typical for NDM-1; carriage by non-fermenters was unstable in many cases and not associated with typical resistance. 20 strains of bacteria were found in the samples, 12 of which carried bla_{NDM-1} on plasmids, which ranged in size from 140 to 400 kb. Isolates of *Aeromonas caviae* and *V cholerae* carried bla_{NDM-1} on chromosomes. Conjugative transfer was more common at 30°C than at 25°C or 37°C.

Interpretation The presence of NDM-1 β-lactamase-producing bacteria in environmental samples in New Delhi has important implications for people living in the city who are reliant on public water and sanitation facilities. International surveillance of resistance, incorporating environmental sampling as well as examination of clinical isolates, needs to be established as a priority.

Lancet Infect Dis 2011; 11: 355–62

Published Online
April 7, 2011
DOI:10.1016/S1473-3099(11)70059-7

See Comment page 334

Department of Infection, Immunity and Biochemistry, School of Medicine, Cardiff University, Heath Park, Cardiff, UK (Prof T R Walsh PhD, J Weeks BSc, M A Toleman PhD); **University of Queensland Centre for Clinical Research, University of Queensland, Brisbane, Australia** (Prof T R Walsh); **and Health Protection Agency Microbiology Services, Colindale, London, UK** (D M Livermore PhD)

Correspondence to:
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t.r.walsh@uq.edu.au

Plantas de tratamiento de aguas como lugar para analizar de modo global la resistencia a los antibióticos de una ciudad

SCIENCE ADVANCES | RESEARCH ARTICLE

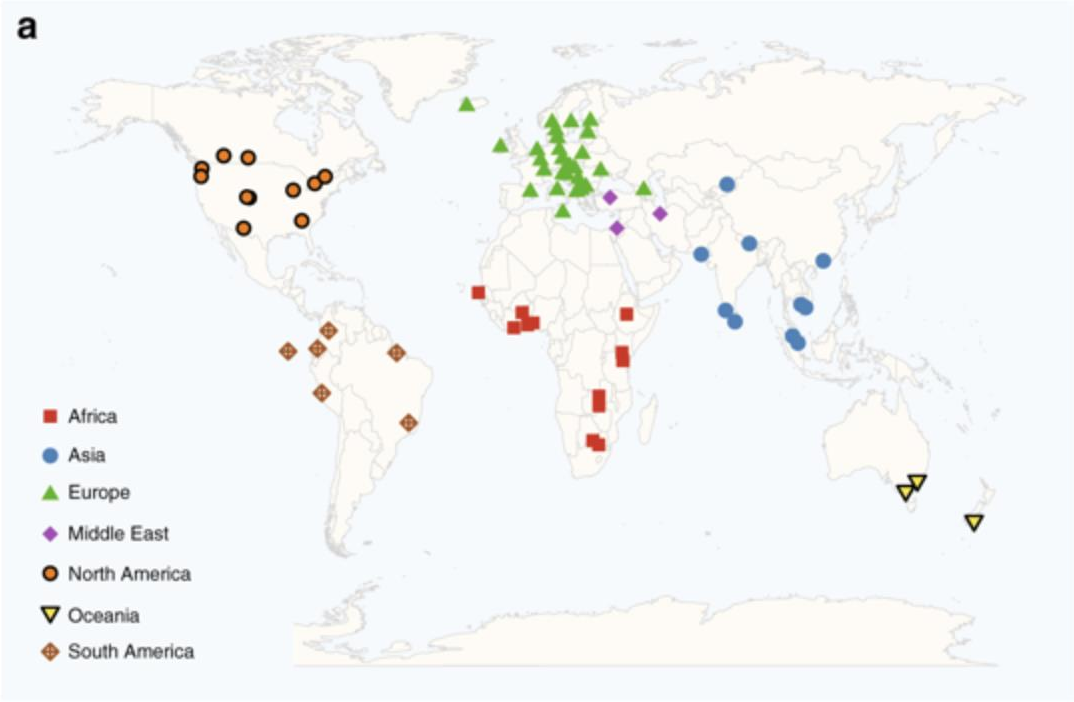
HEALTH AND MEDICINE

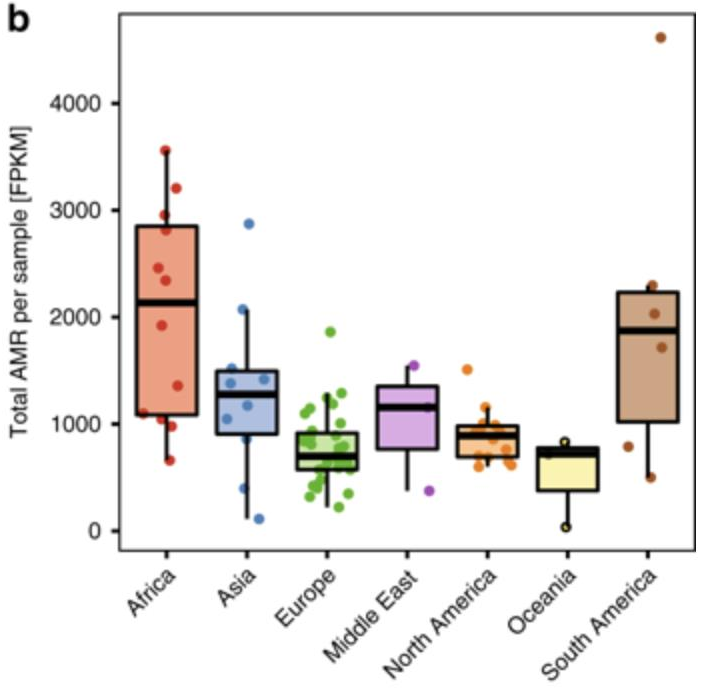
Antibiotic resistance in European wastewater treatment plants mirrors the pattern of clinical antibiotic resistance prevalence

Katariina M. M. Pärnänen[1]*, Carlos Narciso-da-Rocha[2]*, David Kneis[3]*, Thomas U. Berendonk[3], Damiano Cacace[3], Thi Thuy Do[4], Christian Elpers[5], Despo Fatta-Kassinos[6], Isabel Henriques[7], Thomas Jaeger[8], Antti Karkman[1], Jose Luis Martinez[9], Stella G. Michael[6], Irene Michael-Kordatou[6], Kristin O'Sullivan[10], Sara Rodriguez-Mozaz[11], Thomas Schwartz[8], Hongjie Sheng[12,13], Henning Sørum[10], Robert D. Stedtfeld[13], James M. Tiedje[14], Saulo Varela Della Giustina[11], Fiona Walsh[4], Ivone Vaz-Moreira[2], Marko Virta[1†], Célia M. Manaia[2†]

Integrated antibiotic resistance (AR) surveillance is one of the objectives of the World Health Organization global action plan on antimicrobial resistance. Urban wastewater treatment plants (UWTPs) are among the most important receptors and sources of environmental AR. On the basis of the consistent observation of an increasing north-to-south clinical AR prevalence in Europe, this study compared the influent and final effluent of 12 UWTPs located in seven countries (Portugal, Spain, Ireland, Cyprus, Germany, Finland, and Norway). Using highly parallel quantitative polymerase chain reaction, we analyzed 229 resistance genes and 25 mobile genetic elements. This first trans-Europe surveillance showed that UWTP AR profiles mirror the AR gradient observed in clinics. Antibiotic use, environmental temperature, and UWTP size were important factors related with resistance persistence and spread in the environment. These results highlight the need to implement regular surveillance and control measures, which may need to be appropriate for the geographic regions.

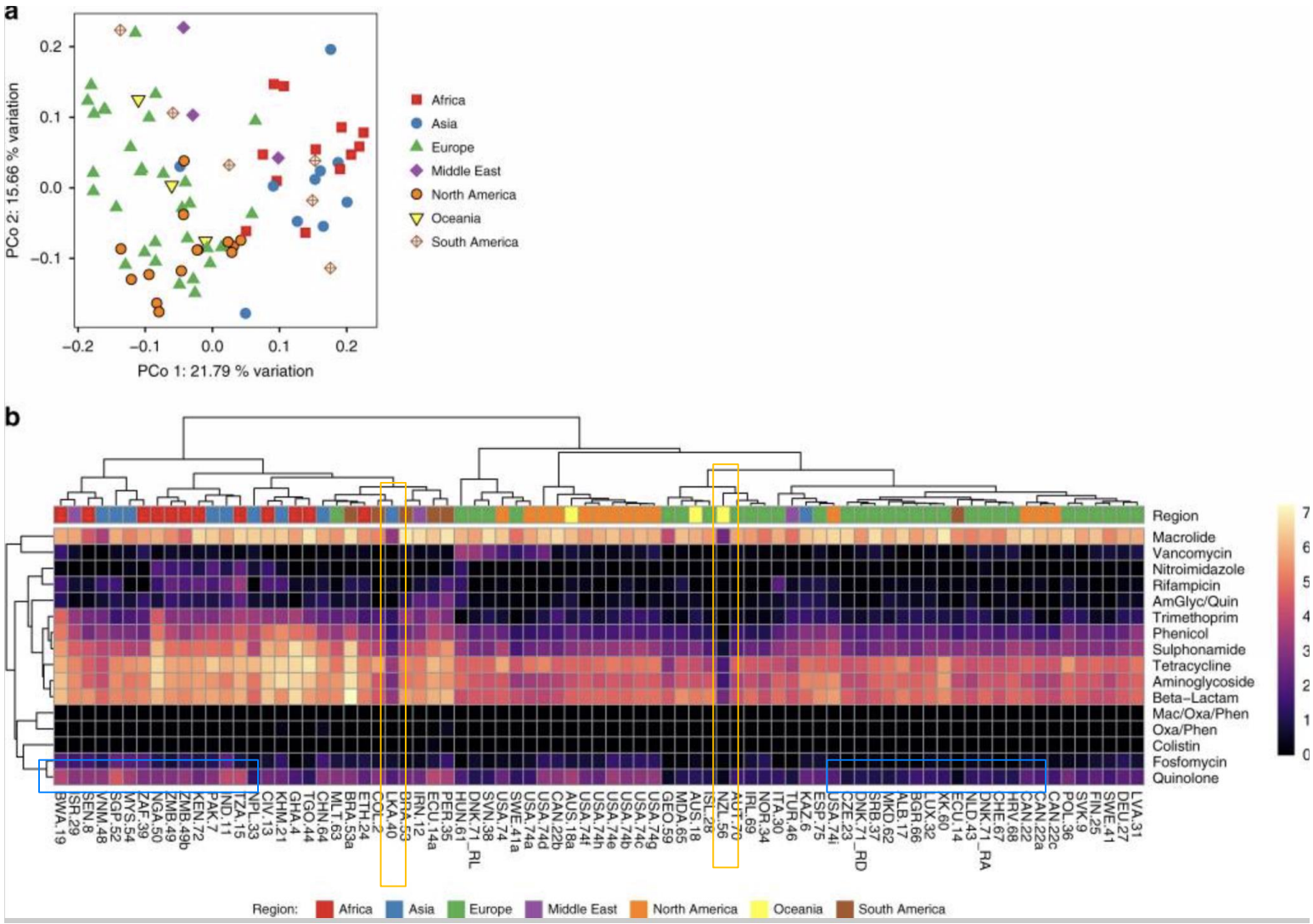
Agua entrante en plantas de tratamiento como marcador epidemiológico para la analizar la resistencia de una población.





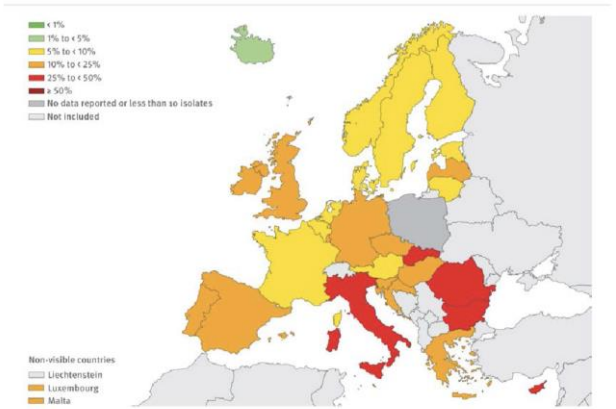
Nat Commun. 2019; 10: 1124.

Agua entrante en plantas de tratamiento como marcador epidemiológico para la analizar la resistencia de una población: ¿que antibióticos debemos usar?



Nat Commun. 2019; 10: 1124.

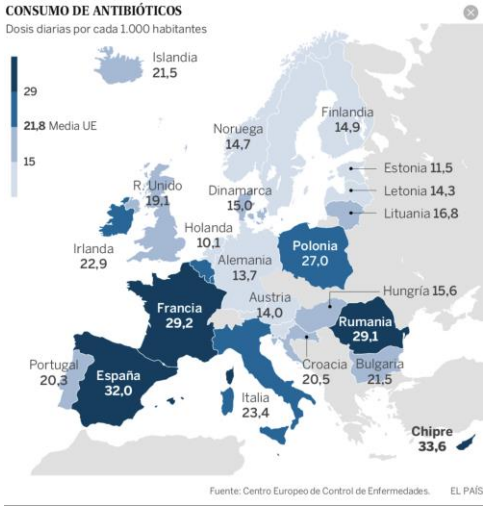
Uso de antibióticos y la prevalencia de los genes de resistencia



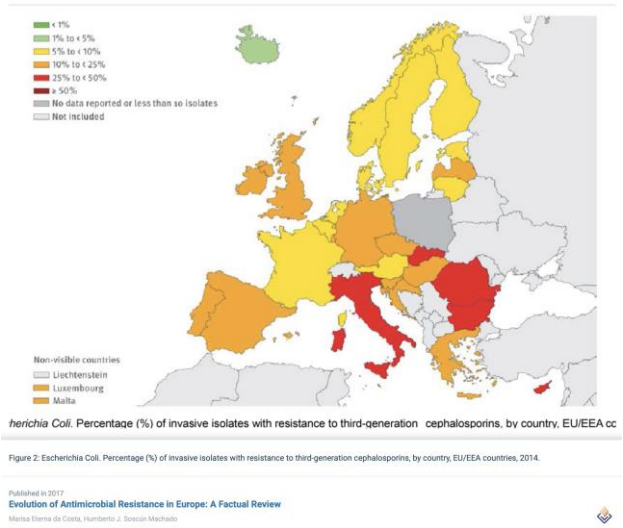
herichia Coli. Percentage (%) of invasive isolates with resistance to third-generation cephalosporins, by country, EU/EEA cc

Figure 2: Escherichia Coli. Percentage (%) of invasive isolates with resistance to third-generation cephalosporins, by country, EU/EEA countries, 2014.

Published in 2017
Evolution of Antimicrobial Resistance in Europe: A Factual Review
Marisa Elena da Costa, Humberto J. Soscún Machado



El uso de antibióticos no justifica por si solo la prevalencia de los genes de resistencia



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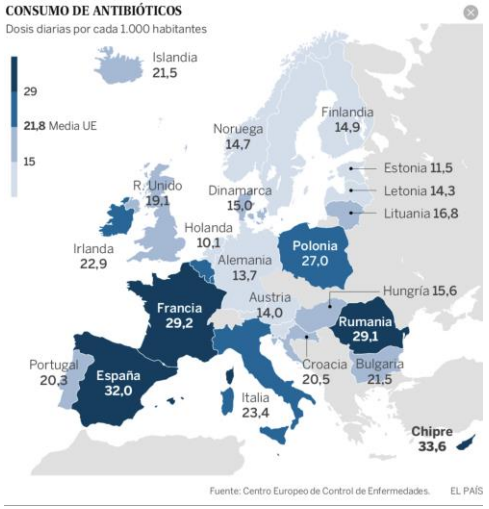

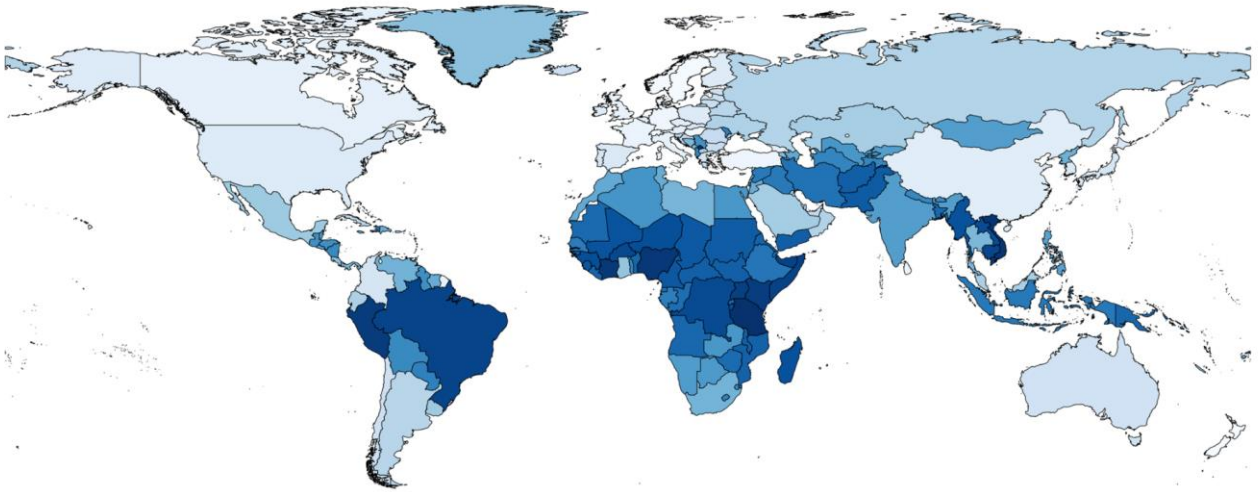

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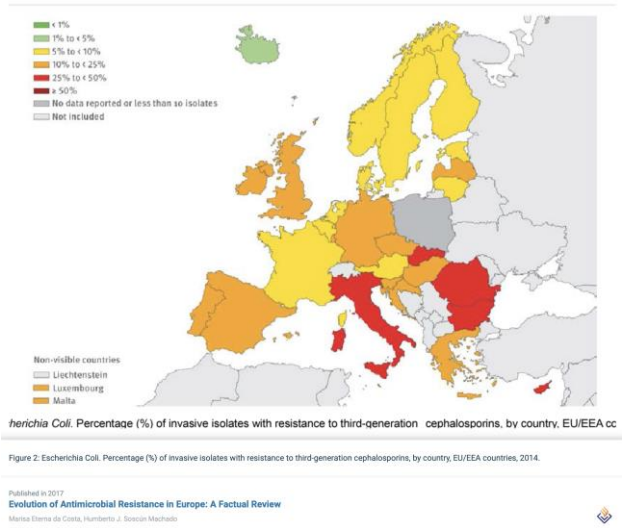

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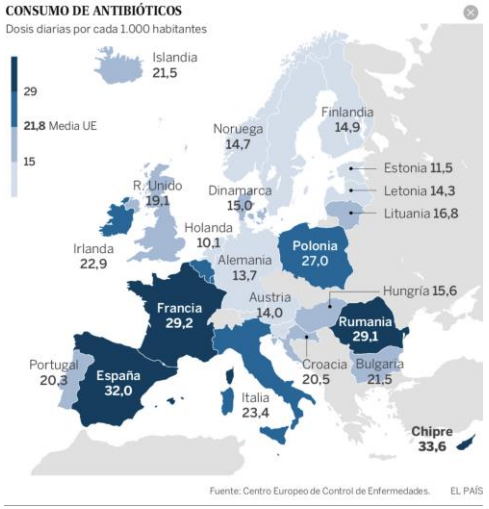
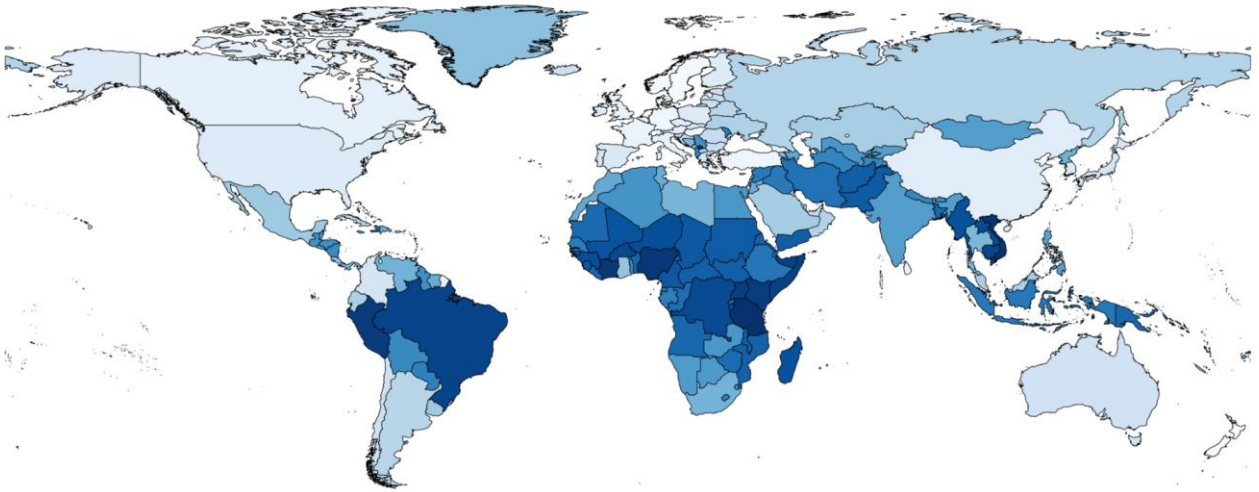
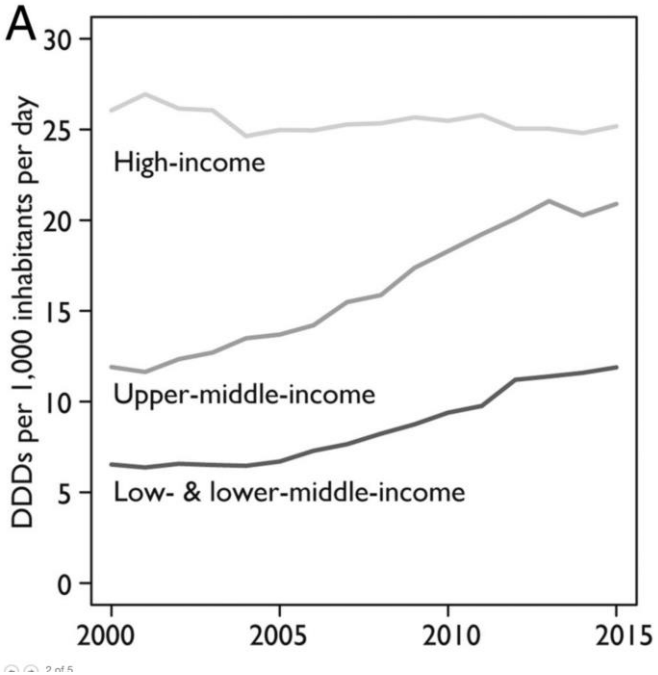
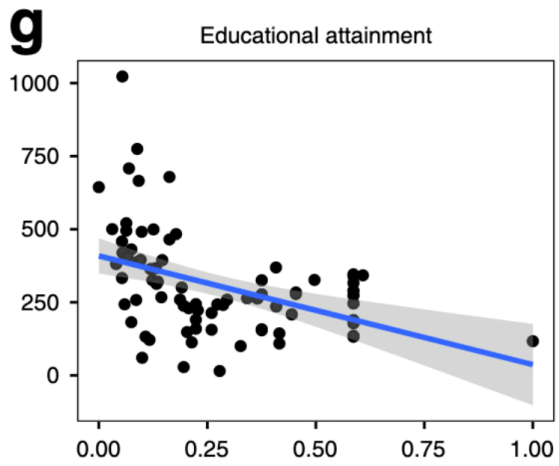
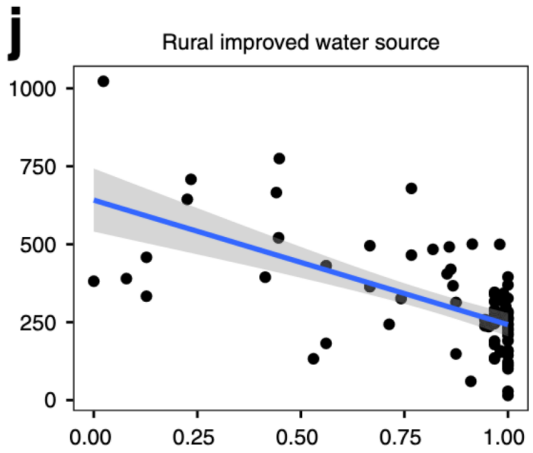


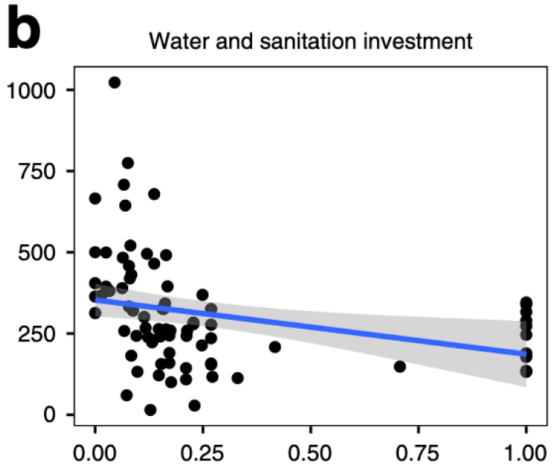


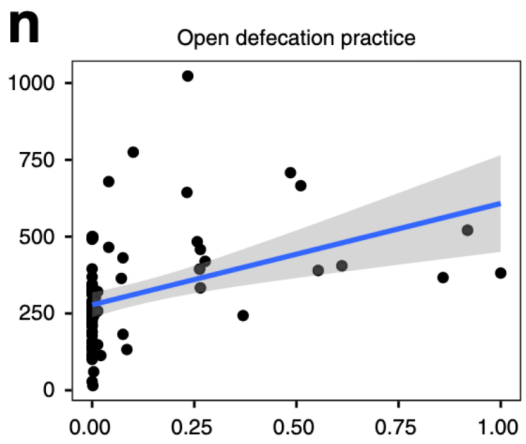


Condiciones socieconómicas que favorecen la resistencia





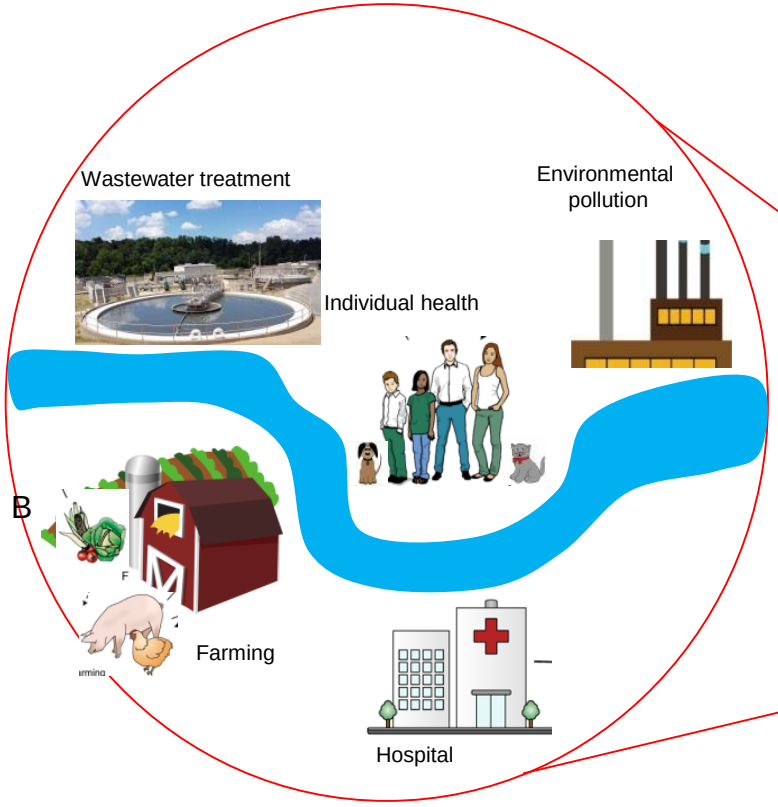




El uso de los antibióticos favorece la selección de resistencia.
La falta de tratamiento de aguas favorece la diseminación

Nat Commun. 2019; 10: 1124.

El efecto mariposa y la resistencia a los antibióticos



One Health(s)

Global Health

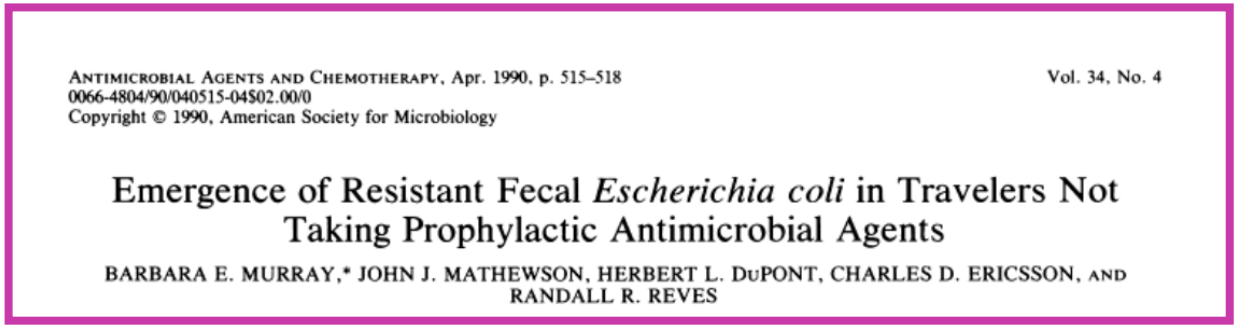
Hernando-Amado, S. Coque, T. M., Baquero. F., Martínez, J. L. Defining and combating antibiotic resistance from One-Health and Global-Health perspectives. Nature Microbiology 2019 Sep;4(9):1432-1442

Transmisión internacional de la resistencia

Reference(s)	Resistant organism	Antibiotic resistance	Route of importation	Likely mode of importation
[57]	*Escherichia coli*	β-Lactams, mediated by plasmid-borne SHV-5 β-lactamase gene	Indian subcontinent to United Kingdom	Human travel
[58, 59]	*Salmonella typhi*	Multiple antibiotics	Developing countries (mainly South Asia) to United States and Canada	Human travel
[31]	MRSA	Multiple antibiotics	Great Britain to The Netherlands	Human travel (health workers)
[60]	MRSA	Multiple antibiotics	Brazil to Portugal	Unknown
[45]	*Shigella sonnei*	Ampicillin, TMP-SMX, streptomycin	Mexico to United States	Imported food (parsley)
[4]	*Campylobacter jejuni*	Quinolones	Europe and Asia to United States	Human travel
[61]	*Streptococcus pneumoniae* 6B	Multiple antibiotics	Spain to Iceland	Unknown

NOTE. MRSA, methicillin-resistant *Staphylococcus aureus;* SHV-5, sulphydryl variable-5; TMP-SMX, trimethoprim-sulfamethoxazole.

Clinical Infectious Diseases, Volume 33, Issue 3, 1 August 2001, Pages 364–369, https://doi.org/10.1086/321877



ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 1990, p. 515–518
0066-4804/90/040515-04$02.00/0

Vol. 34, No. 4

Emergence of Resistant Fecal *Escherichia coli* in Travelers Not Taking Prophylactic Antimicrobial Agents

BARBARA E. MURRAY,* JOHN J. MATHEWSON, HERBERT L. DuPONT, CHARLES D. ERICSSON, AND RANDALL R. REVES

La ruta de transmisión de países de alta incidencia a países de baja incidencia: ¿Que hacer?

Tuberculosis in migrants moving from high-incidence to low-incidence countries: a population-based cohort study of 519 955 migrants screened before entry to England, Wales, and Northern Ireland

Robert W Aldridge, Dominik Zenner, Peter J White, Elizabeth J Williamson, Morris C Muzyamba, Poonam Dhavan, Davide Mosca, H Lucy Thomas, Maeve K Lalor, Ibrahim Abubakar, Andrew C Hayward**

Interpretation Migrants from countries with a high incidence of tuberculosis screened before being granted entry to low-incidence countries pose a negligible risk of onward transmission but are at increased risk of tuberculosis, which could potentially be prevented through identification and treatment of latent infection in close collaboration with a pre-entry screening programme.

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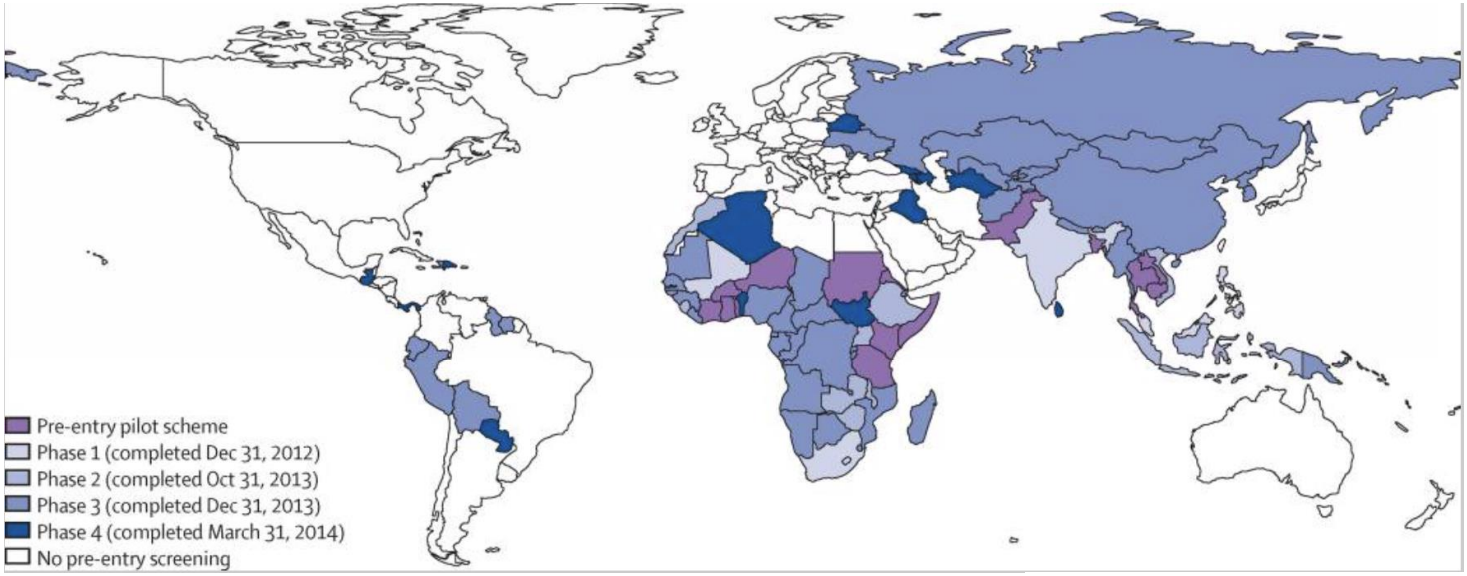

Diferentes niveles para contrarrestar la resistencia a los antibióticos

Salud individual: Acciones terapéuticas directas

Salud Unica: Acciones directas y regulatorias que requieren su aprobación por autoridades locales/nacionales.

Salud Global: Esencialmente recomendaciones por instituciones transnacionales como ONU u OMS. Regulaciones globales, que tienen implicaciones éticas, políticas y económicas más complejas.

The Spanish Royal Philanthropic Expedition to Bring Smallpox Vaccination to the New World and Asia in the 19th Century

Carlos Franco-Paredes,[1,2] Lorena Lammoglia,[1] and José Ignacio Santos-Preciado[1]

[1]Hospital Infantil de México, Federico Gómez, México City, Mexico; and [2]Division of Infectious Diseases, Emory University School of Medicine, Atlanta, Georgia

Clinical Infectious Diseases 2005; 41:1285–9

1058-4838/2005/4109-0012$15.00

Globalización: en busca de un equilibrio

Being conscious of AR is of huge heuristic value for illustrating principles and generating hypotheses that guide human activity. The global spread of resistant organisms caused by our actions (antibiotic and general pollution) and inactions (lack of proper sanitation) shows how a defined and measurable biological risk, influencing both our health and the health of the planet, can alter our biosphere. As such, AR should be treated as a Global-Health problem that requires - as do many other problems - a sense of "selfish equality" on the part of developed nations. Anything that improves global equality - increasing the wealth and dignity of "the others", where AR is emerging due to shortage of resources, will benefit everyone with respect to AR.

Hernando-Amado, S. Coque, T. M., Baquero. F., Martínez, J. L. Nature Microbiology 2019 Sep;4(9):1432-1442

Servicios de salud universales

El foco del debate es en los aspectos políticos, económicos y éticos.
Debemos pensar en términos técnicos

Cáncer es una enfermedad individual. Si alguien sufre un cáncer, no afecta al resto de la población.
Infección es una enfermedad social: lo que ocurra en un paciente puede afectarnos a todos y cada uno de nosotros.

PLANT PATHOLOGY

The economic cost of an epidemic

Andrew M. Sugden

+ See all authors and affiliations

Science 14 Jun 2019:
Vol. 364, Issue 6445, pp. 1044-1045
DOI: 10.1126/science.364.6445.1044-b

Native tree populations in many parts of the world are threatened by alien pathogens, which are often imported inadvertently via the trade in living plants. Hill *et al.* estimate the likely economic cost of the current epidemic affecting ash (*Fraxinus excelsior*) in Britain. They find that ash dieback, caused by the fungal pathogen *Hymenoscyphus fraxineus* imported from continental Europe in ash saplings, may cost £14.8 billion over the next 100 years, with half of that amount accrued over the coming decade. Most of the cost is in lost economic services such as recreation, avoided runoff, and carbon sequestration, although there are also substantial costs incurred by felling dead trees and replanting. The authors point out that these potential costs dwarf the value of the plant trade.

Curr. Biol. **29**, R315 (2019).


Gracias

Examples of actions for reducing AR burden

	Individual Health	One Health	Global Health
Reduction of antimicrobial selective pressure	• Evidence-based prescription of ABs. • Personalized prescription based on rapid identification of ARBs and ARGs. • Awareness of local resistance burden to orientate prescription. • Reduction of the time of AB selective exposure. Moving from general to personalized PK/PD. • Use of species-specific antibiotics versus wide-spectrum. • Use of delivery systems to target an antibiotic to the point of infection. • Use of AB adsorbents or compounds able to degrade ABs for decreasing ABs concentration at the gut. • Vaccines against bacterial pathogens, including preventive and therapeutic vaccines.	• Surveillance of AB consumption in hospitals, the community, and agriculture. • Control and supervision of the sale of ABs for human health and animal production. • Local guidelines for prescription considering AR burden. • Local control and regulation of AB release in the environment. • Removal of antibiotics and ARBs from environment. • Improve decontamination of metals and biocides. • Continued local surveillance of known and emergent AR traits in humans and animals. • Surveillance of AB pollution in water and food. • Development of fastly degradable antibiotics. • Novel systems in animal production focusing in the reduction of antibiotic use. • Use of non-antibiotic compounds for prophylaxis and metaphylaxis • Vaccines against animal pathogens.	• Worldwide surveillance of AB production and consumption. • Worldwide guidelines for ABs utilization based on evidence-based studies. • Global regulation of pharma-chemical industry concerning release of ABs in the environment. • Global regulation of hazardous industrial wastes, particularly in dumping grounds countries. • Global regulation of AB contamination in food, animals, and in general in goods.

Hernando-Amado, S., Coque, T.M., Baquero, F., Martínez, J. L. Nature Microbiology. In the press

Examples of actions for reducing AR burden

	Individual Health	One Health	Global Health
Reduction of transmission of ARBs and ARGs	• Surveillance of commensals that can be carriers of ARGs • Antibacterial vaccination to prevent colonization and transmission of AR clones. • Isolation of patients with high risk ARBs or ARGs • Intestinal decontamination of resistant bacteria.	• Development of anti-conjugation drugs. • Prevention of cross-colonization and infection among different ecosystems.. • Increase local hygiene and sanitation within the local agro-food chain management systems. • Increase local hygiene, sanitation in LMICs, including safe collection, treatment and disposal of waste, and safe food storage. • Implementation of surveillance networks to analyze the risks in hubs of the food chain • Implement risk assessment of food management systems at local level. • Control of AR in local animal and food trade. • Prevention of environmental mixing of wastes from hospitals, farms, and AB-contaminating industries, including pharma. • One-Health surveillance systems, integrated analysis of surveillance data.	• Surveillance of global ecological disturbances attributable to the exposure of AB (e.g., as in primary producers). • Global surveillance of AR pollution in the Earth (air currents, oceans, migratory animals). • Monitoring of climate changes to predict infectious diseases and spread of ARBs. • Early identification and medical control of travelers from countries with high AR incidence. • International surveillance of the emergence and spread of high-risk ARGs and ARBs. • Surveillance and control of transnational movement of humans, goods, animals and food polluted with ARBs. • Global centralized electronic reporting of national One-Health surveillance systems, global analysis of surveillance data. • Educational policy, integrating human, animal, and ecosystems health.

Hernando-Amado, S., Coque, T.M., Baquero, F., Martínez, J. L. Nature Microbiology. In the press

Examples of actions for reducing AR burden

	Individual Health	One Health	Global Health
Restoration of populations of antibiotic susceptible bacteria	• Preservation of autologous microbiota before clinical interventions for potential microbiome transplantation. • "Selection for susceptibility": antibody-drug conjugates, enhancers of fitness costs, pairs of ABs with reciprocal collateral susceptible profile, drugs activated by mechanisms of resistance. • Genetic engineering to disrupt AR; CRISPR-based editing and metagenomic engineering. • Heterologous microbiota/probiotic transplantation for displacing ARBs • Vaccines against ARBs. • Drugs targeting the metabolism of resistant organisms.	• Microbiota-transplantation procedures for ecological displacement of ARBs. • Genetic engineering to disrupt AR; CRISPR-based editing and metagenomic engineering. • Phage cocktails against ARBs • Vaccines against animal AR pathogens	• Regulation of biobanks of susceptible human, animal, and environmental microbiotas. • Regulation of genetic engineering to disrupt AR; CRISPR-based editing and metagenomic engineering.

Hernando-Amado, S., Coque, T.M., Baquero, F., Martínez, J. L. Nature Microbiology. In the press