Name a domesticated animal

When poll is active, respond at **PollEv.com/johnblynch547**

Text **JOHNBLYNCH547** to **22333** once to join

UW TASP tele-antimicrobial stewardship program | echo

May 22, 2018

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Paul Pottinger MD
Erica Stohs MD, MPH
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Agenda

- John Lynch: *Abx and Animals*
- Case Discussions

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Antibiotics and Animals

John Lynch, MD, MPH
UW Medicine | Harborview Medical Center
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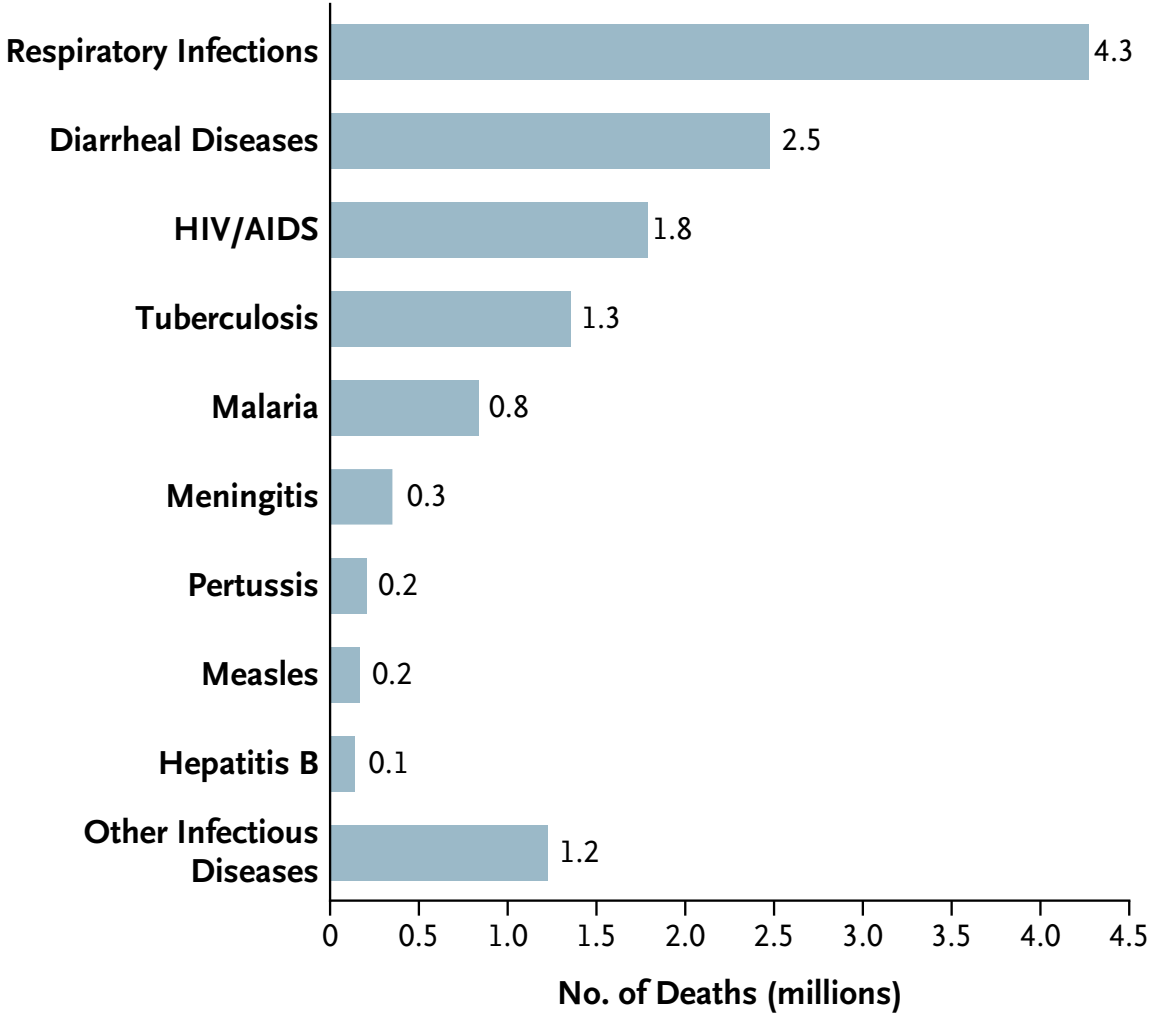
May 22, 2018

This presentation is intended for educational use only, and does not in any way constitute medical consultation or advice related to any specific patient.

The Perpetual Challenge of Infectious Diseases



What is different about infectious diseases?

Potential for unpredictable and explosive global impact

Frequent acquisition by host of durable immunity against reinfection after recovery

Reliance of disease on a single agent without requirement for multiple cofactors

Transmissibility

Potential for becoming preventable

Potential for eradication

Evolutionary advantage over human host because of replicative and mutational capacities of pathogens that render them highly adaptable

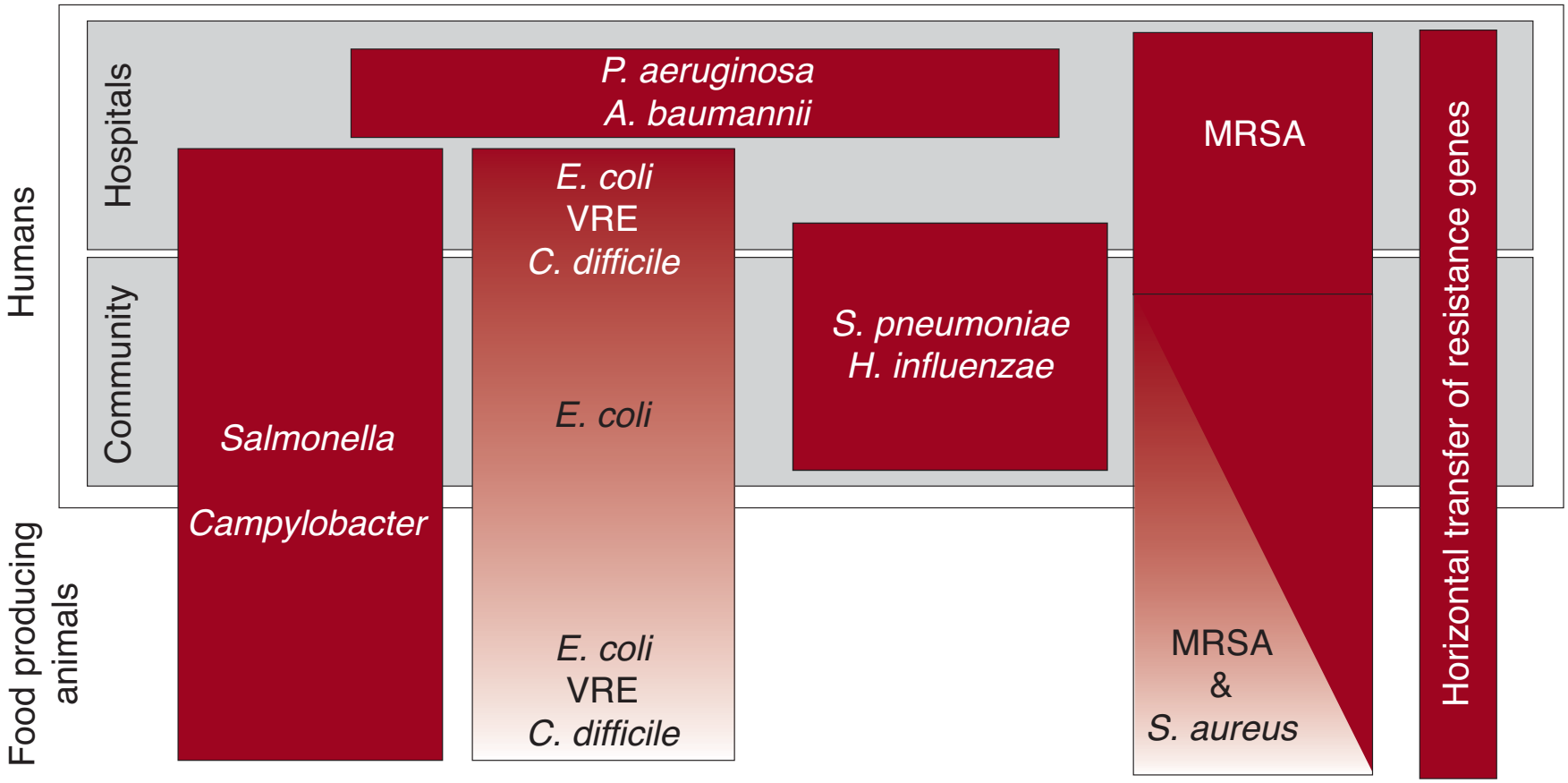
Close dependence on the nature and complexity of human behavior

Frequent derivation from or coevolution in other animal species

Possibility of treatment for having multiplying effects on preventing infection in contacts and the community and on microbial and animal ecosystems

Fauci and Morens NEJM 2012

Reservoirs of Drug Resistant Bacteria



Source: The Evolving Threat of Antimicrobial Resistance, WHO (2012)

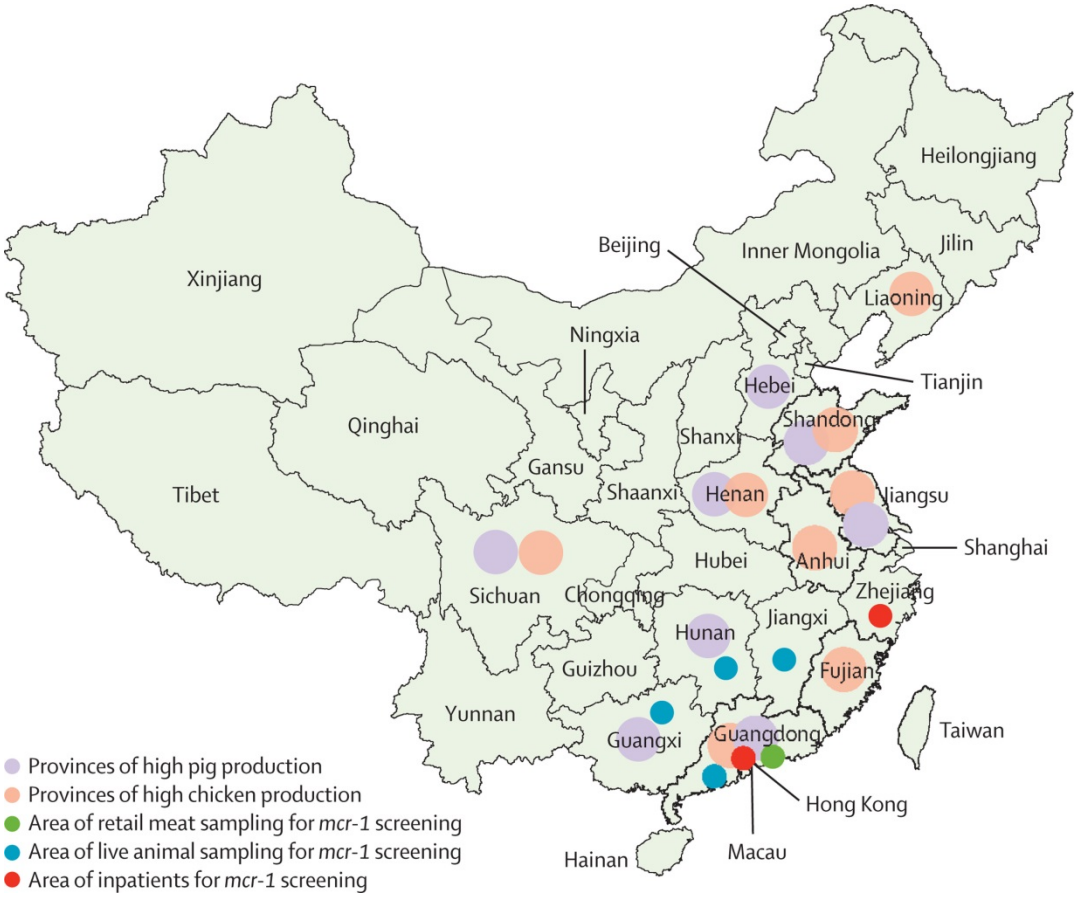
Community reservoirs of antimicrobial-resistant bacteria

Table 1 | **Community reservoirs of antimicrobial-resistant bacteria**

Bacterial species	Common types of antimicrobial resistance	Types of infection	Community reservoirs
Streptococcus pneumoniae	Penicillin, macrolides, cephalosporins, tetracyclines	Otitis media, pneumonia, sinusitis, meningitis	Childcare facilities[41,42], paediatric populations[121]
Streptococcus pyogenes	Macrolides, tetracyclines	Pharyngitis, impetigo, cellulitis	Childcare facilities[122,123], paediatric populations[124,125], schools[126]
Staphylococcus aureus			
Community-associated	Meticillin, cephalosporins, macrolides	Skin, soft tissue, pneumonia, sepsis	Native Americans[127], homeless people[128], soldiers[109], prisoners[105], childcare facilities[129], injection-drug users[130]
Healthcare-associated	Meticillin, cephalosporins, quinolones, aminoglycosides, macrolides	Endocarditis, pneumonia, sepsis	People exposed to healthcare facilities such as nursing homes[131], dialysis[83], recent surgery or hospitalization
Enterococcus spp.	Ampicillin, vancomycin, aminoglycosides	Sepsis, urinary tract	People exposed to hospital care (in the United States)[132], food animals (exposure to avoparcin in Europe)[133]
Neisseria gonorrhoeae	Penicillin, cephalosporins, quinolones	Urethritis, pelvic inflammatory disease	Commercial sex workers[134]
Salmonella spp. (non typhoidal)	Cephalosporins, quinolones, tetracyclines	Diarrhoea	Food animals (poultry, cows)[66,67]
Escherichia coli	Trimethoprim, sulphonamides, quinolones	Urinary tract, diarrhoea	Childcare facilities[135]
Campylobacter jejuni	Erythromycin, quinolones	Gastroenteritis	Food animals (poultry)[136]

Furuya EY and Lowy F, NAt Rev Micro (2006)

The Apocalypse Pig….



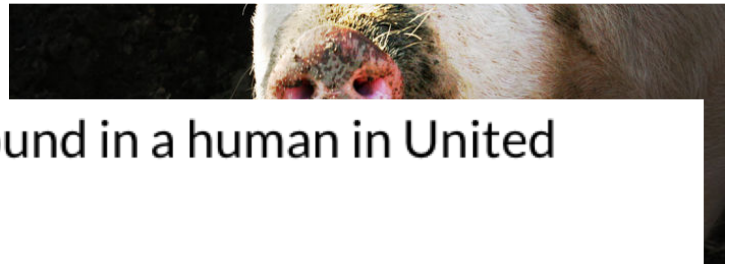
- First description of a plasmid-mediated polymixin resistance mechanism (MCR-1)
- Found on animal meat and in human infection samples
- In December, also reported in Denmark

Liu, Lancet ID, Nov 2015

HEALTH

Infection Raises Specter of Superbugs Resistant to All Antibiotics

By SABRINA TAVERNISE and DENISE GRADY MAY 26, 2016



Discovery of first mcr-1 gene in E. coli bacteria found in a human in United States

MCR-1 causes resistance to colistin, a last-resort drug for treating resistant infections

Media Statement

For Immediate Release: Tuesday, May 31, 2016

Contact: Media Relations,

(404) 639-3286

The Centers for Disease Control and Prevention is part of a coordinated public health response after the Department of Defense (DoD) announced the discovery of the first *mcr-1* gene found in bacteria in a human in the United States . CDC is working with DoD, the Pennsylvania Department of Health, local health departments, and others to identify people who have had contact with the patient and take action to prevent local spread.

Volume 23, Number 5—May 2017

Research Letter

mcr-1 Colistin Resistance in ESBL-Producing *Klebsiella pneumoniae*, France

Yvan Caspar✉, Mylène Maillet, Patricia Pavese, Gilles Francony, Jean-Paul Brion, Marie-Reine Mallaret, Richard Bonnet, Frédéric Robin, Racha Beyrouthy, and Max Maurin

Author affiliations: Centre Hospitalier Universitaire Grenoble-Alpes, Grenoble, France (Y. Caspar, M. Maillet, P. Pavese, G. Francony, J.-P. Brion, M.-R. Mallaret, M. Maurin); University Grenoble-Alpes, CNRS, Grenoble; Centre Hospitalier Universitaire Clermont-Ferrand, Clermont-Ferrand, France (R. Bonnet, F. Robin, R. Beyrouthy); Centre National de Référence de la Résistance aux Antibiotiques, Clermont-Ferrand (R. Bonnet, F. Robin, R. Beyrouthy); Université Clermont Auvergne, Clermont-Ferrand (R. Bonnet, F. Robin, R. Beyrouthy); Institut National de la Santé et de la Recherche Médicale, Clermont-Ferrand (R. Bonnet, F. Robin, R. Beyrouthy); Institut National de la Recherche Agronomique, Clermont-Ferrand (R. Bonnet, F. Robin, R. Beyrouthy)

Main Article

Table

Resistance genes identified by whole-genome sequencing of an ESBL-producing *mcr-1*–positive *Klebsiella pneumoniae* strain isolated from a 38-year-old man, France*

Resistance gene	Target antimicrobial drug
mcr-1 and inactivation of *mgrB* by *IS5* insertion	Colistin
$bla_{SHV-106}$	β-lactams
aac(3)-IId and *aad*A16-like	Aminoglycoside
aac(6')Ib-cr	Quinolone and aminoglycoside
*fos*A5	Fosfomycin
sul1 and *folP*	Sulfonamide
*dfr*A27	Trimethoprim
tetD	Tetracycline

A fatal outbreak of ST11 carbapenem-resistant hypervirulent *Klebsiella pneumoniae* in a Chinese hospital: a molecular epidemiological study

Danxia Gu, Ning Dong*, Zhiwei Zheng, Di Lin, Man Huang, Lihua Wang, Edward Wai-Chi Chan, Lingbin Shu, Jiang Yu, Rong Zhang, Sheng Chen*

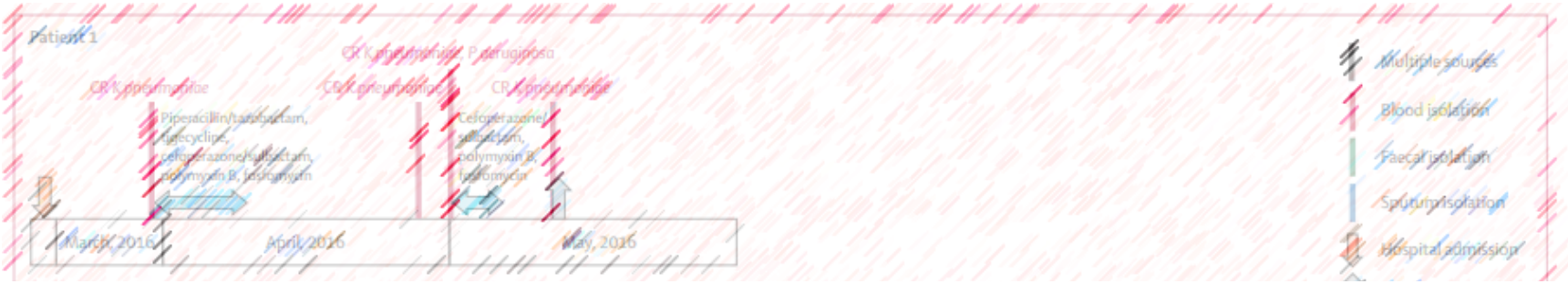
Summary

Background Hypervirulent *Klebsiella pneumoniae* strains often cause life-threatening community-acquired infections in young and healthy hosts, but are usually sensitive to antibiotics. In this study, we investigated a fatal outbreak of ventilator-associated pneumonia caused by a new emerging hypervirulent *K pneumoniae* strain.

Methods The outbreak occurred in the integrated intensive care unit of a new branch of the Second Affiliated Hospital of Zhejiang University (Hangzhou, China). We collected 21 carbapenem-resistant *K pneumoniae* strains from five patients and characterised these strains for their antimicrobial susceptibility, multilocus sequence types, and genetic relatedness using VITEK-2 compact system, multilocus sequence typing, and whole genome sequencing. We selected one representative isolate from each patient to establish the virulence potential using a human neutrophil assay and *Galleria mellonella* model and to establish the genetic basis of their hypervirulence phenotype.

Findings All five patients had undergone surgery for multiple trauma and subsequently received mechanical ventilation. The patients were aged 53–73 years and were admitted to the intensive care unit between late February and April, 2016. They all had severe pneumonia, carbapenem-resistant *K pneumoniae* infections, and poor responses to antibiotic treatment and died due to severe lung infection, multiorgan failure, or septic shock. All five representative carbapenem-resistant *K pneumoniae* strains belonged to the ST11 type, which is the most prevalent carbapenem-resistant *K pneumoniae* type in China, and originated from the same clone. The strains were positive on the string test, had survival of about 80% after 1 h incubation in human neutrophils, and killed 100% of wax moth larvae (*G mellonella*) inoculated with 1×10^6 colony-forming units of the specimens within 24 h, suggesting that they were hypervirulent *K pneumoniae*. Genomic analyses showed that the emergence of these ST11 carbapenem-resistant hypervirulent *K pneumoniae* strains was due to the acquisition of a roughly 170 kbp pLVPK-like virulence plasmid by classic ST11 carbapenem-resistant *K pneumoniae* strains. We also detected these strains in specimens collected in other regions of China.

Interpretation The ST11 carbapenem-resistant hypervirulent *K pneumoniae* strains pose a substantial threat to human health because they are simultaneously hypervirulent, multidrug resistant, and highly transmissible. Control measures should be implemented to prevent further dissemination of such organisms in the hospital setting and the community.



Emergence of *mcr-1* and carbapenemase genes in hospital sewage water in Beijing, China

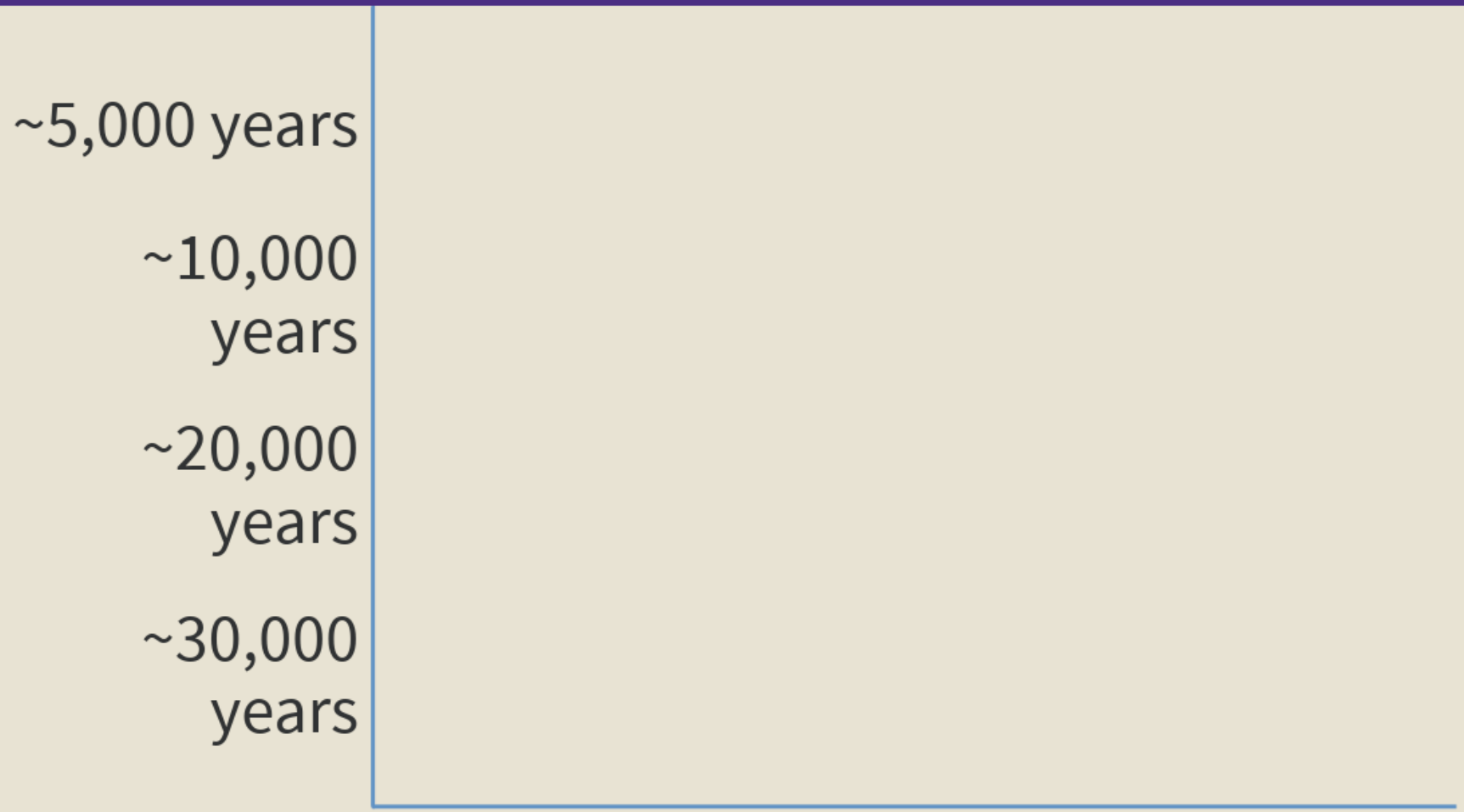
Longyang Jin, Ruobing Wang, Xiaojuan Wang, Qi Wang, Yawei Zhang, Yuyao Yin, Hui Wang ✉ Author Notes

Journal of Antimicrobial Chemotherapy, dkx355, https://doi.org/10.1093/jac/dkx355

Published: 10 October 2017 **Article history** ▾

Figure 1. Epidemiology of the *Klebsiella pneumoniae* outbreak cases

How long ago was the first domesticated animal?

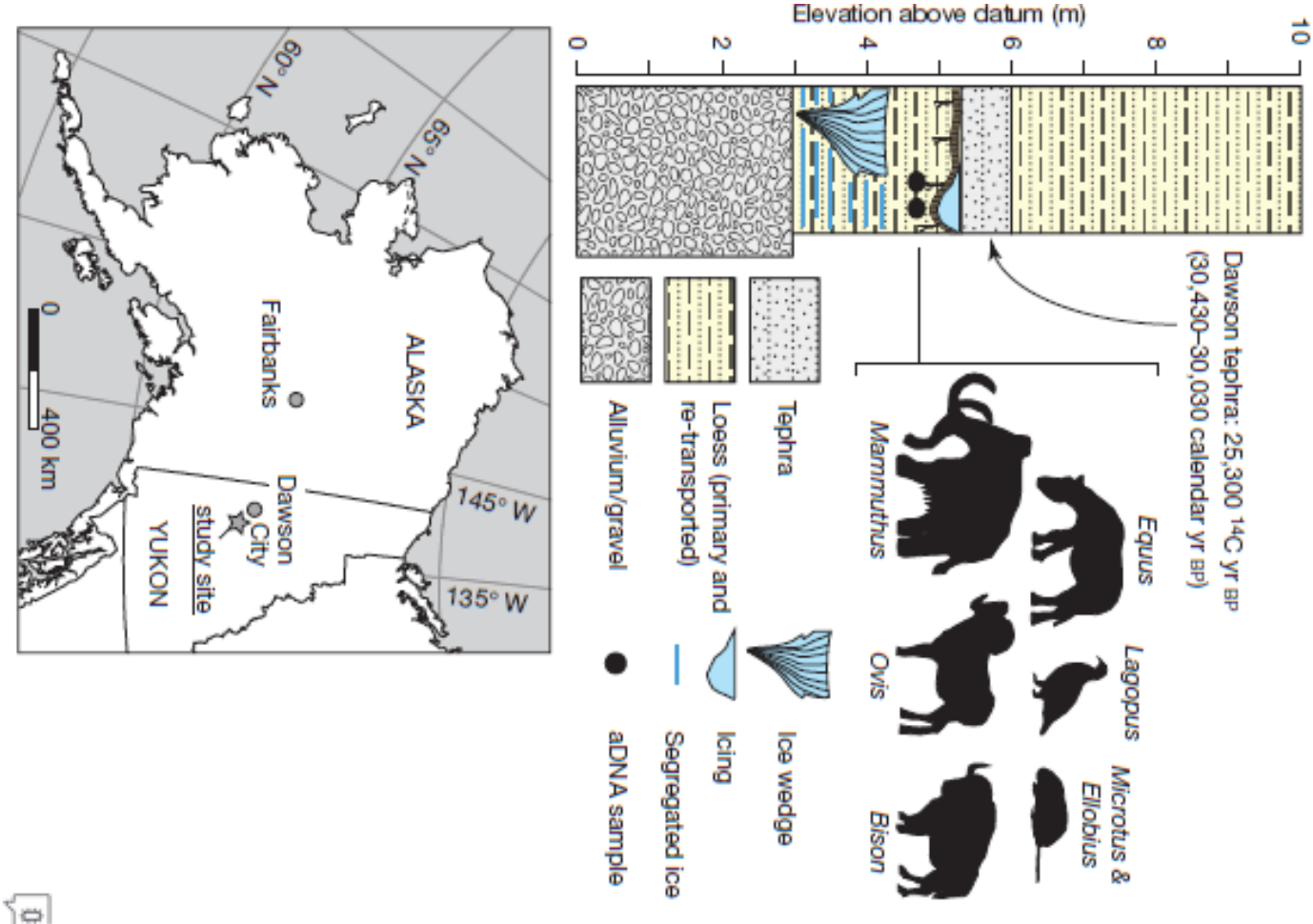


LETTER

doi:10.1038/nature10388

Antibiotic resistance is ancient

Vanessa M. D'Costa[1,2]*, Christine E. King[3,4]*, Lindsay Kalan[1,2], Mariya Morar[1,2], Wilson W. L. Sung[4], Carsten Schwarz[3], Duane Froese[5], Grant Zazula[6], Fabrice Calmels[5], Regis Debruyne[7], G. Brian Golding[4], Hendrik N. Poinar[1,3,4] & Gerard D. Wright[1,2]



KEEP THEM OUT!

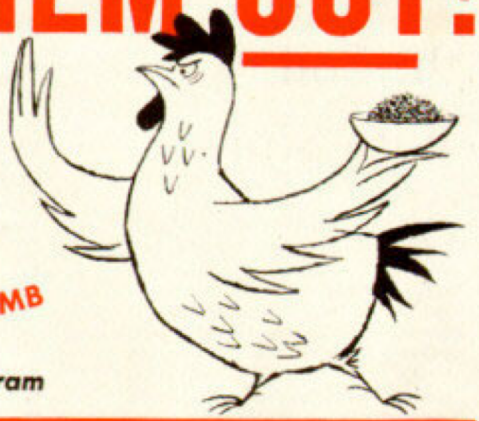
CRD

AIR SAC

SINUSITIS

NONSPECIFIC ENTERITIS

BLUE COMB



Follow this preventive program

Continuous HIGH LEVEL feeding of AUREOMYCIN*

CHLORTETRACYCLINE

"Much less disease... particularly AIR SAC and ENTERITIS... with HIGH LEVELS of AUREOMYCIN"

These are the words of a large broiler producer in the Delmarva area. The comparison figures below show the results from old flocks *before* AUREOMYCIN was fed . . . and the results from new flocks *after* AUREOMYCIN was fed *continuously* at 50 grams per ton of feed.

	Before AUREOMYCIN	*After* AUREOMYCIN
No. flocks	25	18
No. birds started	234,500	129,000
Mortality (%)	9.6	5.7
Av. Market Wt.	3.19 (lb.)	3.49 (lb.)
Feed per lb. of gain	3.24 (lb.)	3.03 (lb.)
Total market wt. per 1000 birds started	2,882 (lb.)	3,230 (lb.)
NET RETURN per 1000 birds started (figured on a 25c market)	$64	$119
EXTRA PROFIT, including cost of AUREOMYCIN, per 1000 birds started		**$55**

Why *wait* until disease has caused weight losses, poor egg production, feed waste, culls and dead birds? Feed AUREOMYCIN Chlortetracycline to chickens and turkeys *continuously at* HIGH LEVELS and prevent these losses! Give them *internal* sanitation with the antibiotic that knocks out MORE disease-producing germs!

Many poultrymen have already discovered that this new, preventive program is more profitable! They've compared feeding costs and profits of the new program with their former program . . . and seen the remarkable results obtained with continuous HIGH LEVELS of AUREOMYCIN. More birds saved! Heavier, top-quality meat birds! More eggs to sell . . . premiums for extra hatchability! Better feed conversion! And PROFITS . . . *several times higher!*

Talk to your feed dealer or feed mixer. He can advise you on the program of HIGH LEVEL AUREOMYCIN that best suits your needs.

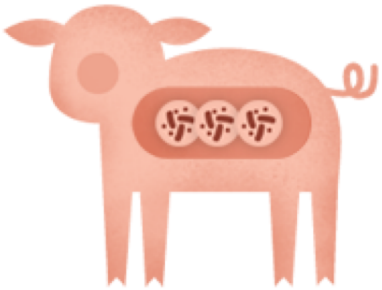
* Trade-Mark

Fine Chemicals

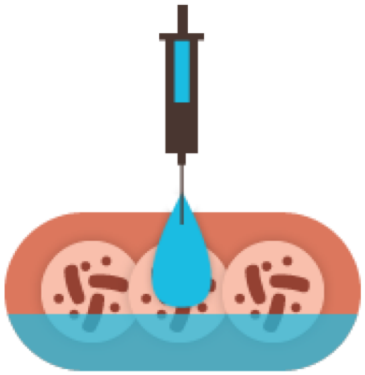
AMERICAN Cyanamid COMPANY

Fine Chemicals Division

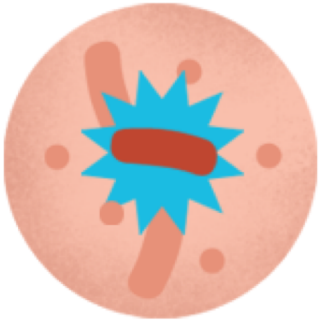
30 Rockefeller Plaza New York 20, N. Y.



Factory farms are breeding grounds for bacteria, with thousands of animals living in crowded, unsanitary conditions.



Producers use antibiotics to prevent, control and treat disease – and to fatten up their animals quickly.



The drugs kill off weak but leave the strongest bacteria, creating superbugs.

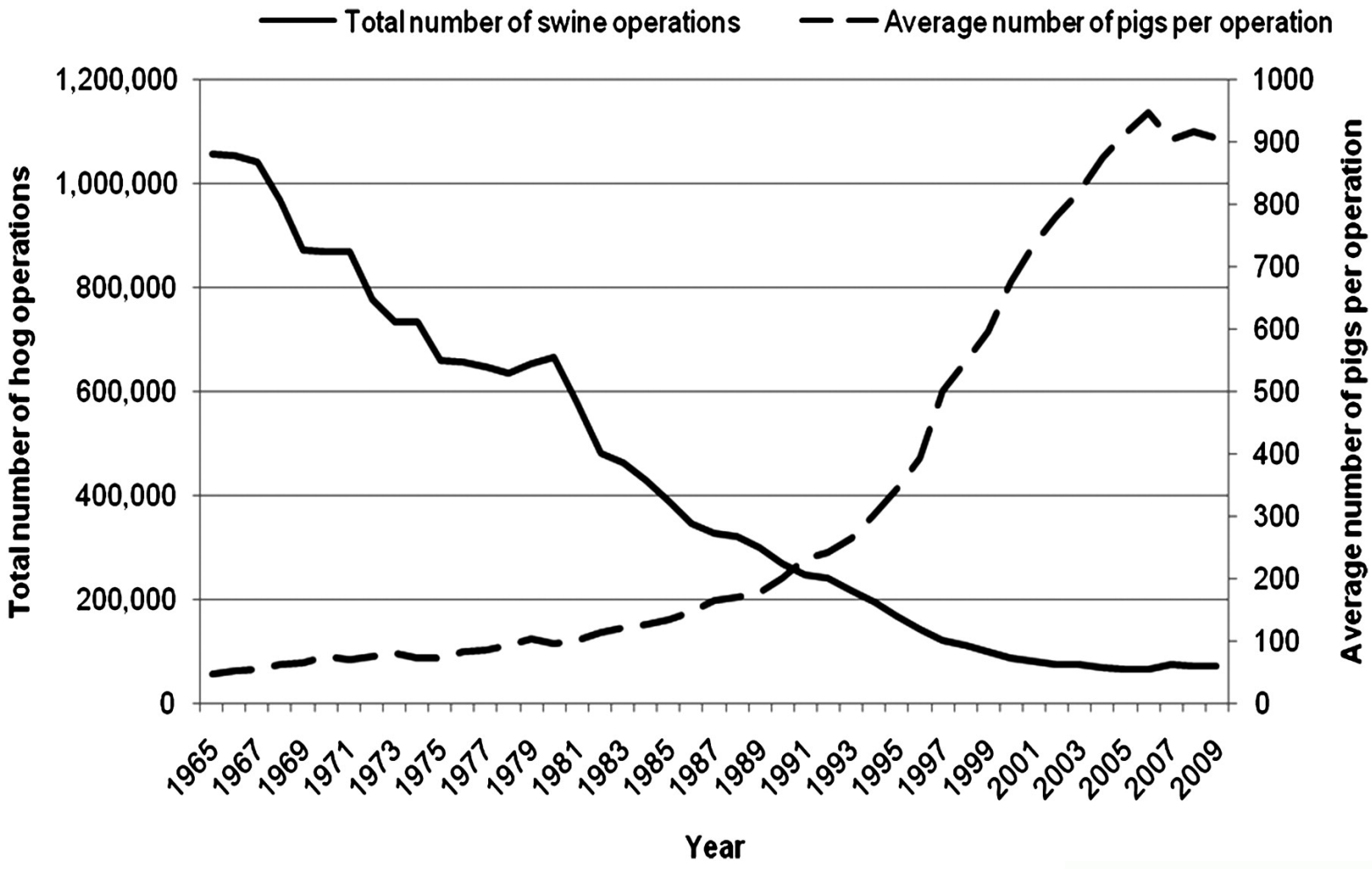
Resistant superbugs travel out via farmworkers, the animals we eat and when manure gets into the air and soil.

The result can be serious, life-threatening infections that can no longer be treated by antibiotics.

Self Magazine - June, 2012

UWTASP
tele-antimicrobial stewardship program

Trends in hog operations in the United States.



Gray G C , Baker W S Clin Infect Dis. 2011;52:19-22

Clinical Infectious Diseases

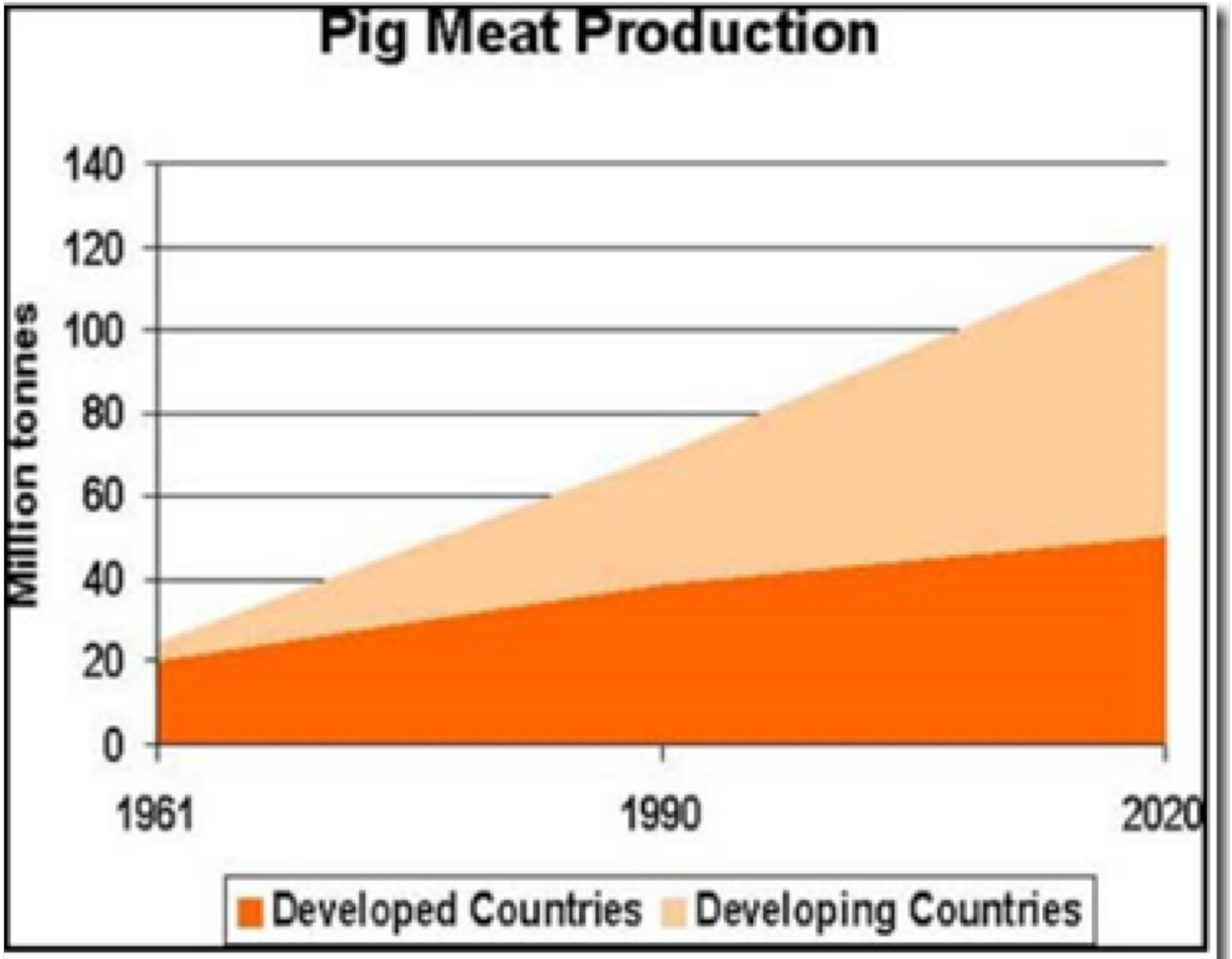
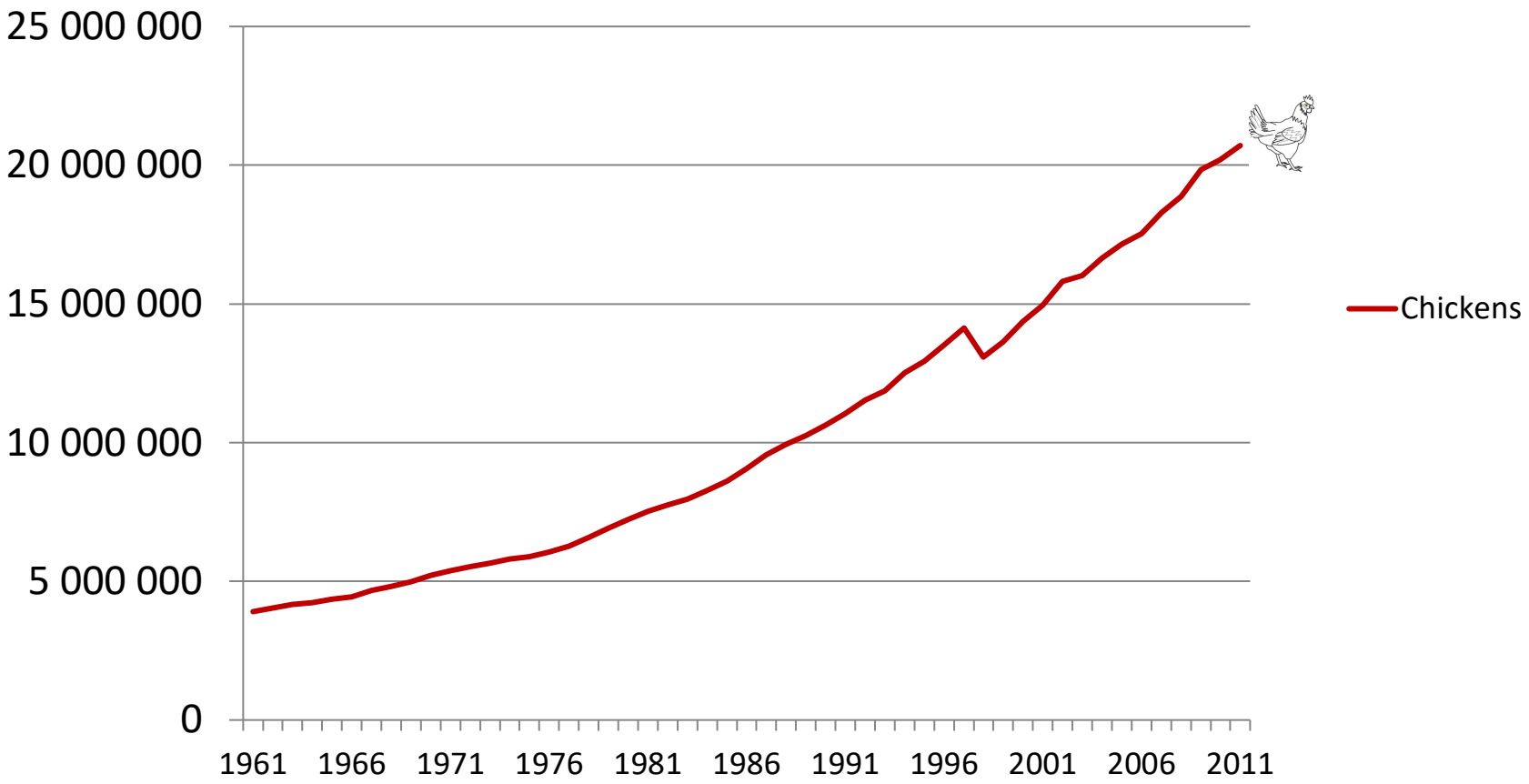


Figure 3. Historical and predicted world production of pig meat

Chicken Population (1000)

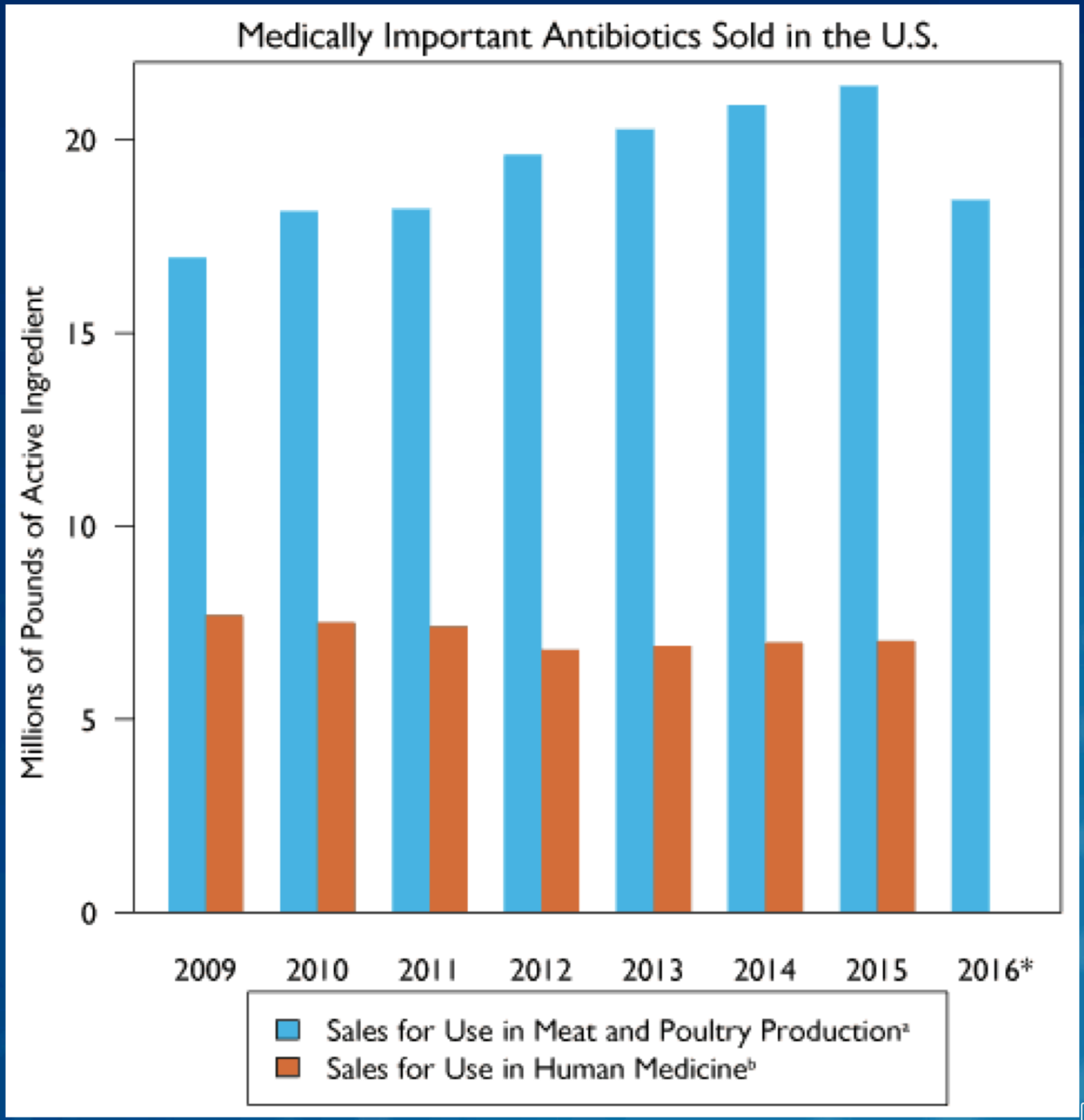


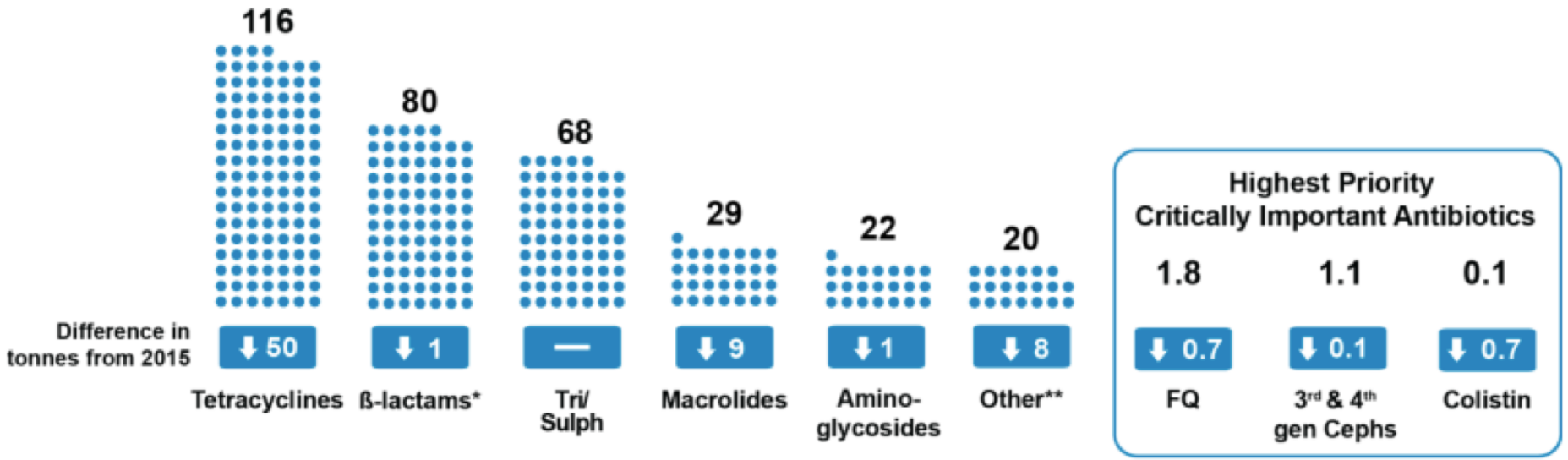
Intensification of Agriculture

Back to the Apocalypse Pig....

- First description of a plasmid-mediated polymixin resistance mechanism (MCR-1)
- Found on animal meat and in human infection samples
- In December, also reported in Denmark

Liu, Lancet ID, Nov 2015





UK VARRS 2016

Consumers Union Chain Reaction III