



La menace sanitaire de l'antibiorésistance

Grands enjeux en élevage et santé humaine à l'échelle mondiale

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Antibiorésistance :
de quoi parle-t-on ?



ANTIBIOTICS

THE END OF MIRACLE DRUGS?

WARNING

**NO LONGER
EFFECTIVE
AGAINST
KILLER
BUGS**

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 4584 ST ANTHONY LN #015975
 COLUMBUS OH 43213-1926

NOTHING WORKED. FOR NINE MONTHS DR. Cynthia Gibert desperately tried one antibiotic after another on her 57-year-old kidney patient, but no matter which tablets, capsules or even IVs she gave him—from plain-vanilla ampicillin to fancy experimental teicoplanin—the man's blood was still flooded with enterococcus bacteria, which were slowly poisoning his red blood cells. "We tried six or seven different medications. Some alone. Some in combination. Some we didn't think would work. But we had nothing else to try," says Gibert, an infectious-disease specialist at the Veterans Affairs Medical Center in Washington. Sometimes her patient's blood tested clean, but within days the infection came roaring back: a few rogue bacteria, no more threatened by the antibiotics than an urban gang by a pop gun,

pneumonia, septicemia (blood poisoning), syphilis, gonorrhea and other bacterial infections that hark back to a time of high-button shoes were vanquished. Yes, people died—and still die—from these ills, but not so many, and not those who began antibiotics before the microbes wrecked some vital system. "The perception [in the 1960s] was that we had conquered almost every infectious disease," says Dr. Thomas Beam of the Buffalo, N.Y., VA Medical Center. Science was sure the real challenges would lie in the conquest of cancer, heart disease and other chronic ailments. Instead, "medicine's purported triumph over infectious disease has become an illusion," writes Dr. Sherwin Nuland in his best-selling "How We Die."

Indeed, it looks like medicine declared victory and went home too soon. Every disease-causing bacterium now has versions that resist at least one of medicine's 100-plus antibiotics. Some resist all but one (chart, page 48). Drug-resistant tuberculosis now ac-

The End of Antibiotics

SCIENCE THOUGHT IT HAD VANQUISHED INFECTIOUS DISEASES. BUT NOW THE BUGS ARE FIGHTING BACK.

BY SHARON BEGLEY

bided their time until their more vulnerable cousins had been killed. Then they multiplied by the billions. So one morning last year, Gibert gathered her courage and walked softly into the man's room. "I guess you're coming to tell me I'm dying," he said. Nothing had worked, she explained; they had run out of options. Antibiotics, the miracle drugs of the 20th century, had been bested by bacteria, the most primitive organisms on earth. Several days later the man died of a massive bacterial infection of the blood and heart.

Ever since 1928, when Alexander Fleming serendipitously discovered penicillin oozing out of mold in a laboratory dish, "man and microbe have been in a footrace," says Dr. Richard Wenzel of the University of Iowa. It's a race in which the lead keeps changing. In 1946, just five years after penicillin came into wide use with World War II, doctors discovered staphylococcus that was invulnerable to the drug. No problem: smart pharmacologists invented or discovered (often in samples of soil they collected like souvenirs whenever they visited exotic locales) new antibiotics. The drugs pounded the microbes into submission once again. But the bacteria regrouped, and mutants capable of fending off the latest drugs appeared. New drugs, newer mutants. And so it went. Overall the drugs retained a slight lead and, slowly, scourges such as tuberculosis, bacterial

counts for one in seven new cases; 5 percent of those patients are dying. Several resistant strains of pneumococcus, the microbe responsible for infected surgical wounds and some children's ear infections and meningitis, appeared in South Africa in the 1970s, spread to Europe and now are turning up in the United States. In January the federal Centers for Disease Control and Prevention (CDC) reported an epidemic of resistant pneumococcus in rural Kentucky and in Memphis. The bugs had spread through day-care centers like a chain letter, leaving toddlers with ear infections, pneumonia and, in six cases, meningitis. In 1992, 13,300 hospital patients died of bacterial infections that resisted the antibiotics doctors fired at them, says the CDC. It was not that they had infections immune to every single drug but rather that, by the time doctors found an antibiotic that worked, the rampaging bacteria had poisoned the patient's blood, seared the lungs or crippled some other vital organ.

The financial toll is steep, too. Because the first antibiotic prescribed often fails, the patient has to try several, this adds some \$100 million to \$200 million to the nation's health-care tab. "Right now the microorganisms are winning," says Iowa's Wenzel. "They're so much older than we are... and wiser."

They are indeed wise, especially in the ways of evolution. Bacteria

La fin des antibiotiques ?

« ... le monde s'achemine vers une ère post-antibiotiques, où des infections courantes et des blessures mineures qui ont été soignées depuis des décennies pourraient à nouveau tuer. »



Dr Keiji FUKUDA, sous-directeur de l'OMS, 30 avril 2014



Pneumocoque

Pneumonie franche lobaire aiguë
« Congestion pulmonaire »

Mortalité > 80 % avant la pénicilline



Staphylocoque doré

ARCHIVES of INTERNAL MEDICINE

VOLUME 68 NOVEMBER 1941 NUMBER 5

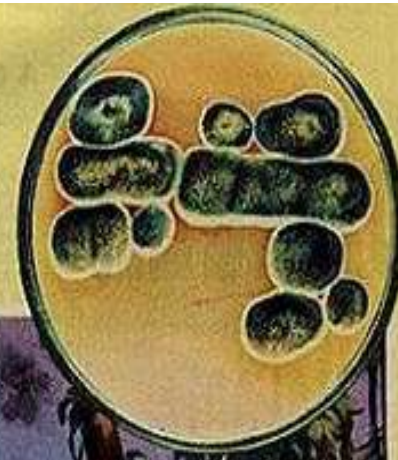
COPYRIGHT, 1941, BY THE AMERICAN MEDICAL ASSOCIATION

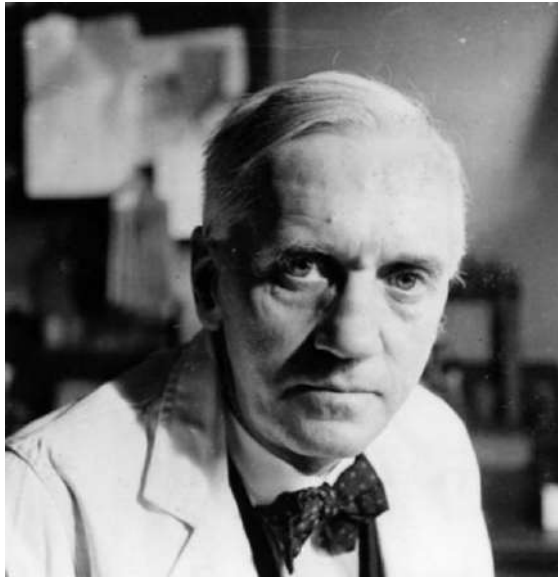
SIGNIFICANCE OF BACTEREMIA CAUSED BY
STAPHYLOCOCCUS AUREUS
A STUDY OF ONE HUNDRED AND TWENTY-TWO CASES AND A REVIEW
OF THE LITERATURE CONCERNED WITH EXPERIMENTAL
INFECTION IN ANIMALS

DAVID SKINNER, M.D.
AND
CHESTER S. KEEFER, M.D.
BOSTON

Mortalité > 80 % avant la pénicilline

Thanks to PENICILLIN
...He Will Come Home!





Self-Medication Decried

"But the public will demand a preparation which can be taken by mouth, and doubtless they will get it. Then will begin an era of self-medication with penicillin, with all its abuses. The wrong source of infection will be treated, but this does not matter so much so long as large doses are not taken. It will only mean disappointment to one individual.

"The greatest possibility of evil in self-medication is the use of too-small doses, so that, instead of clearing up the infection, the microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out which can be passed on to other individuals and perhaps from there to others until they reach someone who gets a septicemia or a pneumonia which penicillin cannot save.

"In such a case the thoughtless person playing with penicillin treatment is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted."

L'utilisation de quantités trop faibles de pénicilline lors de l'automédication peut conduire à un effet inverse car au lieu de guérir l'infection, les microbes deviennent programmés pour résister à la pénicilline et un grand nombre de germes pénicillorésistants se multiplient, ceux-ci pouvant se transmettre à d'autres individus et... atteindre un patient souffrant d'une septicémie ou pneumonie qui ne pourront plus être guéries par la pénicilline.

L'âge d'or des antibiotiques

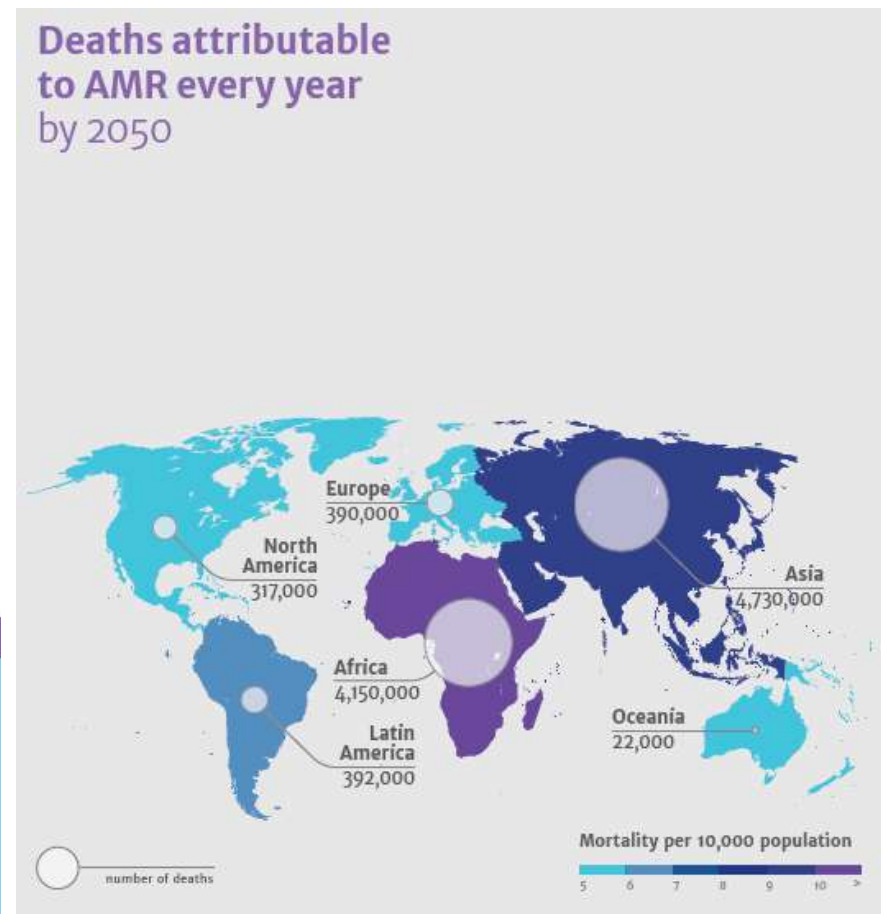
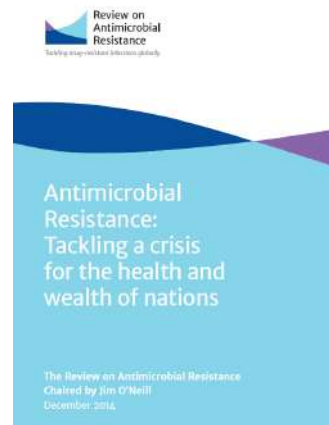
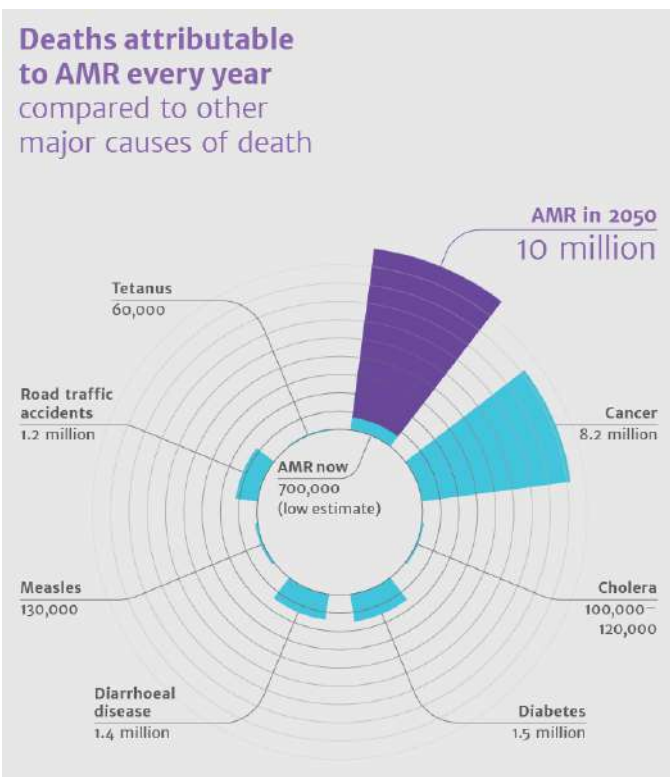
2003 lipopeptides
1999 oxazolidinones
1962 quinolones
1962 streptogramines
1958 glycopeptides
1952 macrolides
1950 aminosides
1949 tétracyclines
1940 β -lactamines
1936 sulfamides

1930 1940 1950 1960 1970 1980 1990 2000 2010



Jim O'Neill

Impact global sur la santé



25 000 morts / an
500 millions d'habitants

38 000 morts / an
70 millions d'habitants



Global trends in antimicrobial use in food animals

Thomas P. Van Boeckel^{a,1}, Charles Brower^b, Marius Gilbert^{c,d}, Bryan T. Grenfell^{a,e,f}, Simon A. Levin^{a,g,h,1}, Timothy P. Robinsonⁱ, Aude Teillant^{a,e}, and Ramanan Laxminarayan^{b,e,j,1}

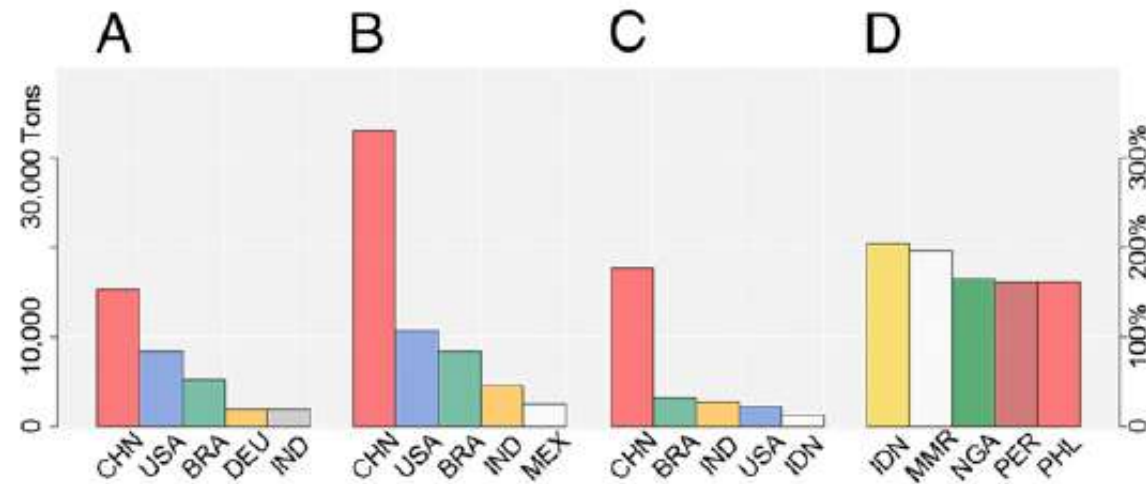
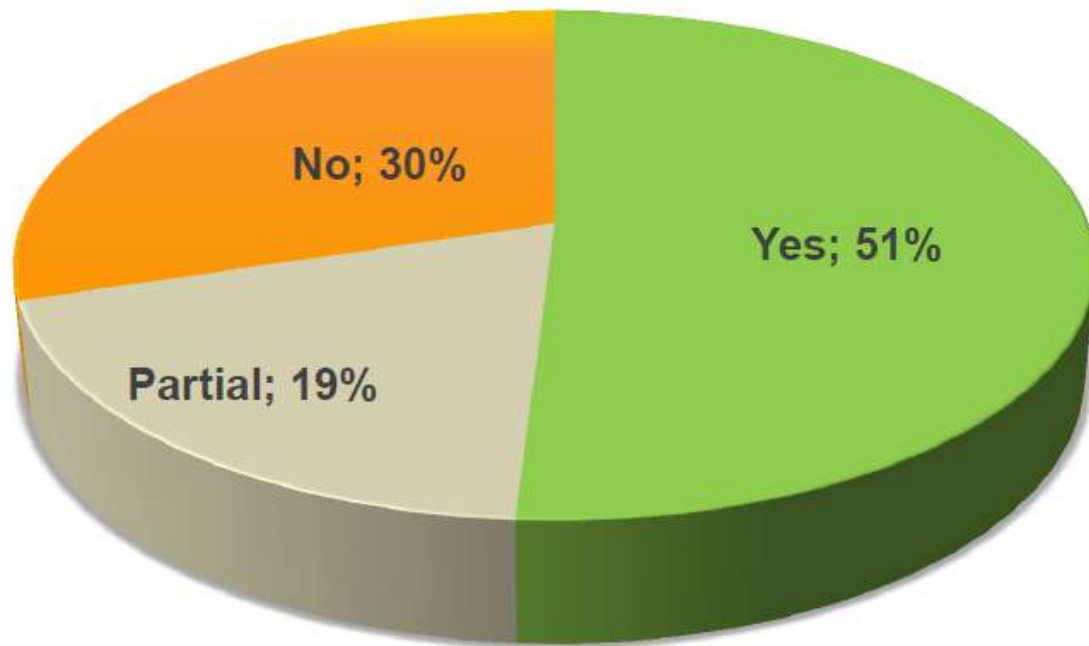


Fig. 1. (A) Largest five consumers of antimicrobials in livestock in 2010. (B) Largest five consumers of antimicrobials in livestock in 2030 (projected). (C) Largest Increase in antimicrobial consumption between 2010 and 2030. (D) Largest relative increase in antimicrobial consumption between 2010 and 2030. CHN, China; USA, United States; BRA, Brazil; DEU, Germany; IND, India; MEX, Mexico; IDN, Indonesia; MMR, Myanmar; NGA, Nigeria; PER, Peru; PHL, Philippines.

Proportion of OIE Member Countries banning the use of antimicrobial agents as growth promoters



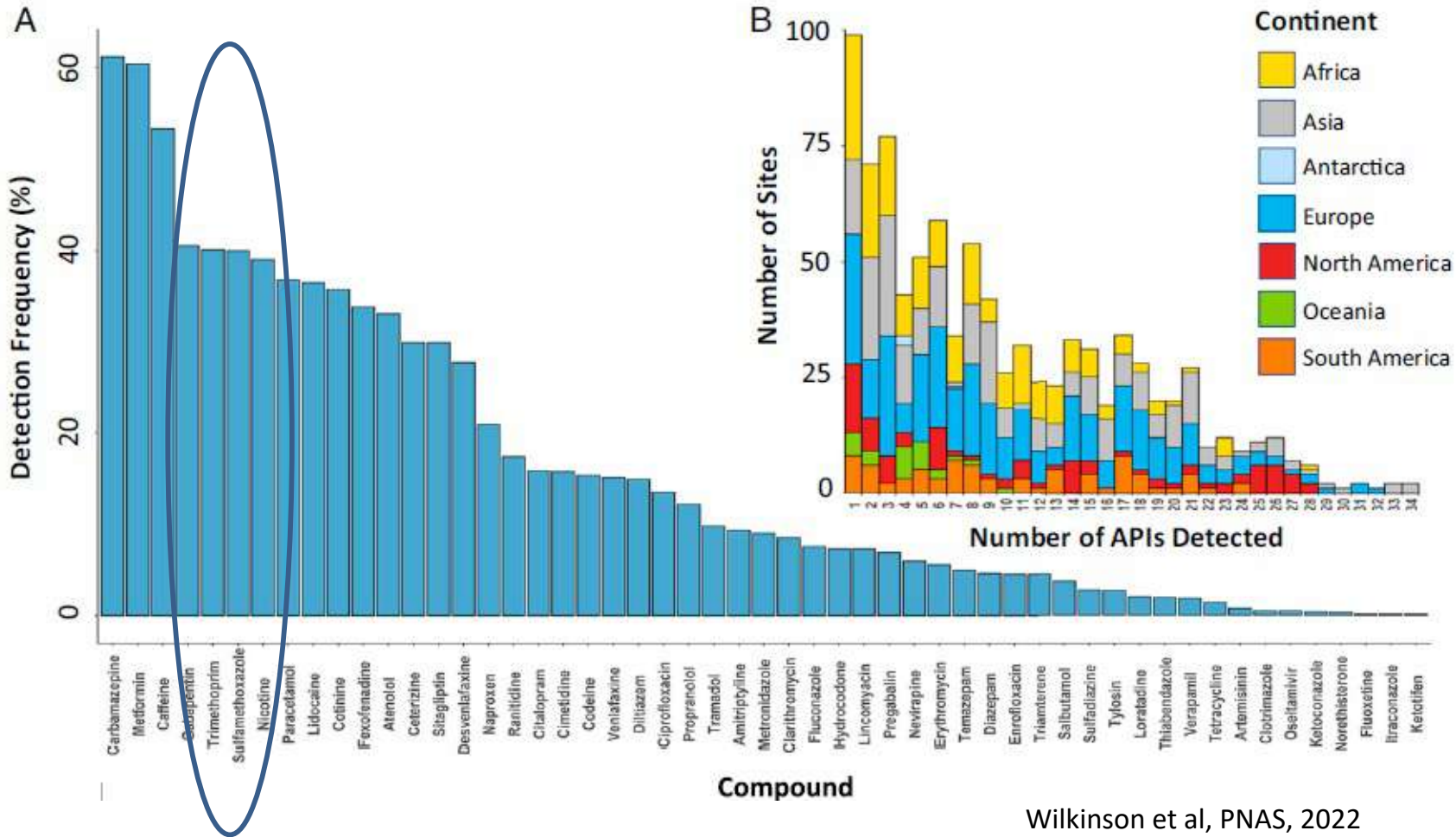
Organisation
Mondiale
de la Santé
Animale

World
Organisation
for Animal
Health

Organización
Mundial
de Sanidad
Animal

Antimicrobial use in animals:
Analysis of the OIE survey on monitoring of the quantities of antimicrobial agents used in animals

Pollution par les produits pharmaceutiques



Wilkinson et al, PNAS, 2022

Pollution par les produits pharmaceutiques



Sulfamethazine et oxytétracycline dominants en élevage et aquaculture

12 tonnes/an de sulfamides déversées du Mekong dans la mer de Chine

Shimizu et al, Sci of the Total Environment, 2013

Pollution par les produits pharmaceutiques



31 mg/L



0,5 à 3,7 mg/L



Larsson *et al.*, J Hazard Mat, 2007; 148: 751-755



Pollution par l'antibiorésistance



Hernandez PLoS One 2013



Blaak AEM 2014



Bréchet CID 2014



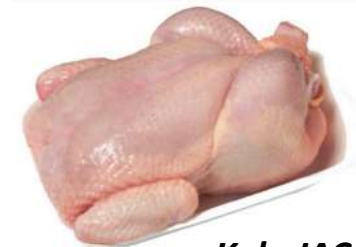
Hartmann Frontiers 2012



Mani AAC 2018



Yaici JAC 2017

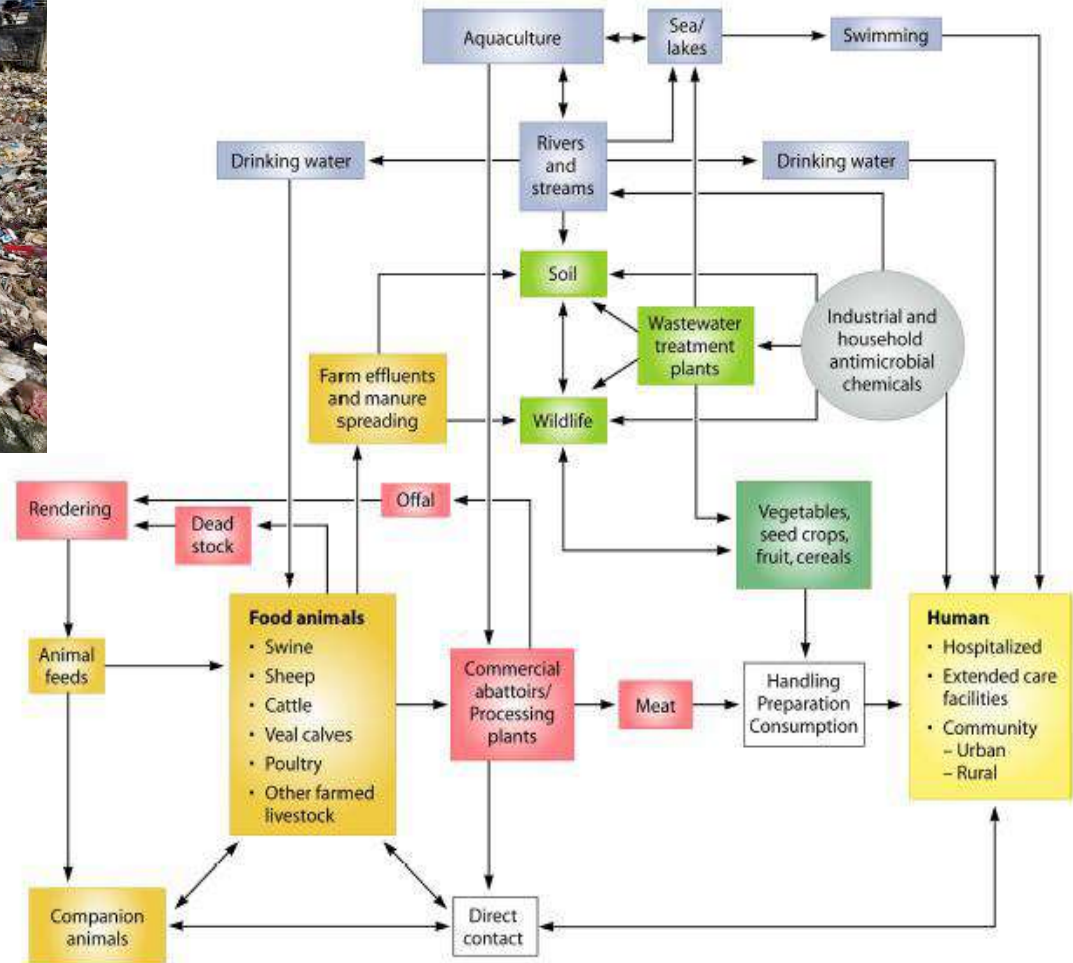


Kola JAC 2012



Van Hoek IJFM 2015

L'antibiorésistance est une problématique One Health



The complex interplay between different sectors in the spread of antimicrobial resistance
(from Davies & Davies, Microbiol Mol Biol Rev. 2010)

L'antibiorésistance se transmet

NEWSFOCUS

INFECTIOUS DISEASE

From Pigs to People: The Emergence of a New Superbug

The discovery of a novel strain of MRSA able to jump from livestock to humans has sparked a multicountry effort to see how dangerous it might be

The first infection was puzzling, almost inexplicable. In July 2004, Andreas Voss of Radboud University Nijmegen Medical Center in the Netherlands admitted a 6-month-old girl for surgery to repair a congenital heart defect.

Because an infection with the common bacterium *Staphylococcus aureus* could pose a grave risk following heart surgery, Voss and his colleagues screened the baby girl for the microbe. They found not just *S. aureus* but also a menacing drug-resistant form known as methicillin-resistant *S. aureus* (MRSA). The physicians were flummoxed. Although MRSA has reached epidemic proportions in much of the developed world, MRSA infections are rare in the Netherlands, thanks to an aggressive “search and destroy” policy the

or other livestock harbored MRSA, and no MRSA strain had ever been known to jump from livestock to humans. If the Dutch doctors' fears were correct, a novel strain had just gained stability, opening up a new route for a potentially dangerous superbug to spread among humans. “Initially, we were very much afraid that this would be a major problem that could spread to the entire population,” says Jan Kluytmans, a microbiologist at VU University Medical Center in Amsterdam whom Voss recruited early on to help investigate.

In recent months, the dangers



Index case. MRSA from pigs on Eric and Ine van den Heuvel's farm was detected in their daughter, Eveline, when she was an infant.

Dissémination de l'antibiorésistance par les échanges commerciaux

Impact of food animal trade on the spread of *mcr-1*-mediated colistin resistance, Tunisia, July 2015

R Grami ^{1,3}, W Mansour ^{2,3}, W Mehri ⁴, O Bouallègue ³, N Boujaâfar ³, J Madec ¹, M Haenni ¹



F2:A-:B- plasmid carrying the extended-spectrum β -lactamase *bla*_{CTX-M-55/57} gene in *Proteus mirabilis* isolated from a primate



Contents lists available at SciVerse ScienceDirect

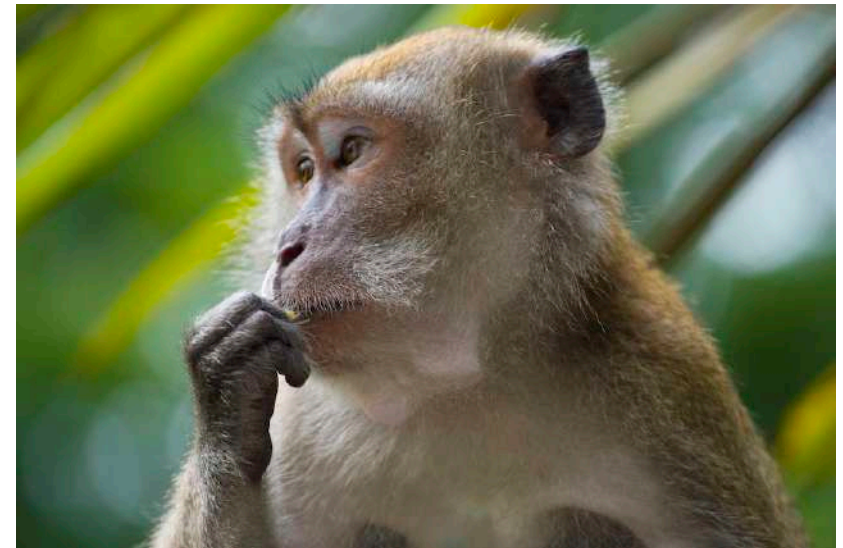
International Journal of Antimicrobial Agents

journal homepage: <http://www.elsevier.com/locate/ijantimicag>

Safia Dahmen
Jean-Yves Madec
Marisa Haenni*

Unité antibiorésistance et virulence bactériennes, ANSES site de Lyon,
31 avenue Tony Garnier, Lyon, France

- mars 2011
- femelle macaque (*Macaca fascicularis*) 5 ans
- née en captivité au Vietnam
- importée en France (Strasbourg)
- quarantaine 6 semaines
- 6 jours après son arrivée, forte diarrhée
- colistine et fluoroquinolones



Médicaments contrefaits

30 % sont des antibiotiques

General review

Update on counterfeit antibiotics worldwide; Public health risks

Falsification des antibiotiques dans le monde : état des lieux et risques de Santé Publique

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Received 23 January 2012; accepted 11 April 2012

Available online 22 May 2012

United Nations Environment Programme (UNEP)

**United Nations Environment
Programme's work on AMR**



Tackling Environmental Antimicrobial Resistance

United Nations Environment Programme (UNEP)

an authoritative advocate for the global environment



United Nations Environment Assembly (UNEA):

- World's highest-level decision-making body on the environment.

The Assembly is the governing body of the United Nations Environment Programme (UNEP).

- UNEP sets the global environmental agenda

UNEP's mission is to provide leadership and encourage partnership in caring for the environment by inspiring, informing, and enabling nations and peoples to improve their quality of life without compromising that of future generations.

Merci pour votre attention

EN INDE :

