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► **To cite this version:**

Didier Raoult. Resistance to antibiotics of bacteria in tropical countries. *Lancet Planetary Health*, 2019, 3 (6), pp.e238-e239. 10.1016/S2542-5196(19)30092-0 . hal-02512546

HAL Id: hal-02512546

<https://amu.hal.science/hal-02512546>

Submitted on 25 Oct 2021

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1 **Resistance to antibiotics of bacteria in tropical countries**

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12 **Key words:** Antibiotic resistance, tropical countries, natural antibiotic compounds

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27 The identification of the source of resistance of bacteria to antibiotics is, in my opinion, too naïve and
28 too much based on the guilt of human-related activity. This perception of the world yields analyses
29 that claim to establish an exclusive link between the use of man-made antibiotics and the resistance
30 of microorganisms to antibiotics. This illusion neglects the importance of the source of natural
31 antibiotics. Most antibiotics are secreted naturally by microorganisms, bacteria, of the actinomycetes
32 phylum, or fungi(1). These antibiotics are naturally present in the environment and the antibiotic
33 resistance of microorganisms existed long before their medical use. Beta-lactamases are found in
34 genetic sequences of microorganisms from the Middle Ages, and the resistance of *Staphylococcus*
35 *aureus* in the 19th century has recently been demonstrated (2). Antibiotics are assembled in
36 microorganisms by non-ribosomal protein synthases and polyketides synthases, which are the only
37 known translation devices outside the ribosome. Their existence may have preceded that of
38 ribosomes and may be archaic translation machineries. Since biodiversity in general is much higher in
39 the humid intertropical zone, it is also likely to be the place where the most diverse microorganisms
40 are found, as evidenced by the richness of the human microbiota in rural intertropical areas
41 compared to urban or temperate areas(3). This biodiversity can be accompanied by a biodiversity of
42 molecules with antibiotic activity. Finally, the molecules secreted by non-ribosomal protein synthase
43 and polyketide synthase have multiple activities, not only antimicrobial but also antifungal. Against
44 eukaryotes, some molecules are used as anti-cancer treatments. Some human beta lactamases have
45 anticancer drug inhibitory activity as with mitomycin(4). The spectrum of activity of beta lactamases
46 far exceeds the anti-beta lactamine activity, playing a role in the digestion of nucleic acid (4).

47

48 Antibiotic resistance is a global concern and, interestingly, the source of resistance is often found in
49 the world's intertropical or hottest regions (5). This specificity has not been satisfactorily explained
50 and has just been confirmed by a very extensive study carried out in this journal(6) which shows that
51 a country's overall antibiotic consumption is not correlated with the level of bacterial resistance. On
52 the contrary, there is an inverse relationship, the lower the prescription rate, the higher the

53 resistance level. We have confirmation of this in France, where antibiotic consumption is one of the
54 highest in the world, and where the level of resistance is one of the lowest in the world, particularly
55 in Marseille(7).The same is true in the United States, where difficult-to-treat Gram-negative bacteria
56 represent a very small proportion of the bacteria isolated from the blood cultures of hospitalized
57 patients(8). The reason for these differences remains poorly explained. One of the explanations
58 proposed was the poor management of antibiotics prescribing in humans, which could explain this
59 discrepancy(5). This seems to overlook the idea that man-made antibiotics are the only source of
60 antibiotics, neglecting those produced in the environment. Antibiotics can eventually be used as
61 food by other microorganisms, which in turn develop enzymes to digest them for consumption(9). It
62 has been evaluated that most families of antibiotics can be used as growth factors for soil
63 microorganisms, and the digestion of penicillin and its use as a sole source of carbon has been
64 demonstrated in *Escherichia coli* transformed in vitro. This shows that antibiotics do not only kill
65 microorganisms, but can also serve as a nutrient, especially in areas particularly rich in environmental
66 microorganisms. In addition, it has recently been shown that some arthropods are capable of
67 secreting penicillins and cephalosporins, leading to a less simplistic view of antibiotics, of selection
68 pressure exclusively from human-made drugs, and resistance(10). Thus, beta-lactam resistance genes
69 are detected in all vertebrates, including humans, but also in archaea, which are not sensitive to
70 beta-lactams (11).The work conducted in this journal on Kenya shows that in a city where antibiotic
71 prescribing is extremely low, the level of resistance of *Escherichia coli* is particularly high, not only in
72 humans but also in wildlife. This study must put into perspective a much less anthropocentric
73 approach but integrate the fact that antibiotics are probably more than 3 billion years old, as are
74 antibiotic resistance enzymes, and that we can only understand, and therefore combat antibiotic
75 resistance, if we have a more scientific vision of this world.

76 In conclusion, public health considerations lead to a significant simplification, in particular for
77 sending simple messages that can be understandable to all, but partially false. This needs to be
78 acknowledged. Control measures should not prevent the integration of recent scientific data for fear

79 of misuse of antibiotics. Such a line of thought might end up being dangerous for humans and more
80 emphasis should be put on the complexity of the relationships between antibiotics and the enzymes
81 that, among others, digest them.

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83 **Funding**

84 No funding was received for this work.

85

86 **Competing interests**

87 There are no conflicts of interest.

88

89 **Reference List**

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