

Addressing Antimicrobial Resistance by Changing Our Relationships with Microbes:

Lessons from Japan

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Abstract

Antimicrobial resistance (AMR) is a global health problem, but it is only the 'tip of the iceberg' of microbial disruption caused by antibiotics. Under the surface, cultural factors such as understandings of and attitudes toward microbes may play a significant role influencing relationships between humans and microbes. Western strategies to address pathogenic microbes and AMR often overlook the symbiotic relationship humans share with beneficial microbes (our microbiota), viewing humans as separate from nature and focusing on control. Given the increasing prevalence of novel pathogens, antimicrobial resistance, and chronic illnesses associated with disturbed microbiota (dysbiosis), alternative approaches are needed. Cross-cultural studies may provide ways forward. An exploration of Japanese perspectives on microbes through the lens of food and health reveals practices where microbes are often regarded as partners and friends rather than foes.

This commentary draws on semi-structured interviews conducted with over 50 scientists, health professionals, policy makers, owners of food-related businesses utilizing microbes, and lay people in Japan to explore views on: microbes and the microbiome; germaphobia and over-sanitizing; antibiotics; marketing and beliefs about fermented foods, probiotics, and prebiotics for health; concerns about food production, waste, and environmental pollution; and other factors that affect AMR and contribute to One Health and related approaches. This commentary discusses how the predominant Western view of 'microbes as foes' contributes to AMR, and how viewing 'microbes as friends' may lead to an appreciation of the roles of the microbiome and a more nuanced approach to AMR. Traditional Japanese perspectives and philosophies highlighted in *Shindo Fuji* (body and soil are not separate), *Ishoku Dogen* (Food as Medicine),

and ‘guidance from nature’ offer lessons the West should consider for addressing AMR and public health microbiome challenges more broadly.

‘Microbes as Foes’ Leading to Antimicrobial Resistance (AMR)

The discovery of penicillin nearly a century ago ushered in the age of industrial production of antibiotics. At first, doctors thought this new class of drugs was a panacea that would end all disease. However, within a few years of penicillin’s discovery, antibiotic-resistant microbes began to appear, foreshadowing the growing realization that therapies meant to be targeted at single pathogens affect bacterial evolution far more broadly than originally assumed.¹ Antibiotic use selects for resistant microbes when microbes vulnerable to antibiotics are killed and leave open niches for the resistant microbes to reproduce and thrive. Antibiotic consumption around the world has risen dramatically over the past decades, and microorganisms are becoming increasingly resistant to drugs. The spread of antimicrobial resistance (AMR) poses a major threat to the health of humans and other animals in countries around the world.^{2,3}

AMR is defined by the World Health Organization as the ability of microorganisms to survive in the presence of agents previously able to kill them or inhibit their replication.⁴ Referred to as a silent pandemic,⁵ AMR is an urgent global health challenge. As standard treatments are rendered ineffective, infections persist and morbidity and mortality increase. Antibiotic misuse and overuse in humans and in the agricultural industry are widely assumed to be the primary drivers of AMR,⁴ and research and intervention measures have accordingly focused on antibiotic stewardship. But this dominant viewpoint obscures upstream factors and complexities.

Antibiotic overuse and misuse are behaviors that are driven by more upstream philosophical orientations toward ‘microbes as foes’ (or antimicrobial thinking) that result in over/misuse. Such views impact many interactions with microbes and nature more generally. In this way, *AMR is simply the ‘tip of the iceberg’ of issues related to human-microbe interactions.* If we look below the surface, we see that the view of ‘microbes as foes’ has led to antibiotic use that impacts many microbes besides pathogens, with significant impacts on health. Particularly as we move towards what some have called a “post-antibiotic era”⁶ we may need to explore other ways of thinking about microbes.

‘Microbes as Friends’ Leading to Appreciating the Microbiome

Most microorganisms live in communities called *microbiota*, whose collective genomes are referred to as *microbiomes*. These unseen communities carry out essential functions for ecosystems and organisms, including keeping our planet and bodies functioning.^{7,8} Microbes are required for development and health, and scientists have linked their disruption to many chronic health conditions, ranging from asthma⁹ and obesity,¹⁰ to neurodegenerative diseases such as Parkinson’s.¹¹ In this sense, most microbes are not foes, but friends, or rather symbiotic bacteria cohabiting in and on us that are critical (or at least neutral) for our health.

But ‘friendly’ microbiota are impacted by the same behaviors that drive AMR, including antibiotic overuse in hospitals, and agriculture. Antibiotics are used heavily in the livestock industry to increase animals’ growth rates, with unintended consequences on AMR. As antibiotics increasingly find their way into our food, bodies, and environment, their presence is simultaneously associated with disruption and loss of diversity of the human microbiome (called

dysbiosis). Just as with complex ecosystems like tropical rainforests, loss of diversity in the human microbiome appears to lead to many vulnerabilities that compromise health.

Views on, and behaviors towards, microbes vary cross-culturally. Cross-cultural comparisons can help illuminate these critical human-microbe interactions that may provide not only solutions for problems such as AMR, but also for broader health problems. Most approaches to AMR focus on large-scale government and industry-related policies and behavior, but few have examined how people view and approach their relationships with microbes more generally. Contrasting Western models with Japanese models may provide important insights.

Why ‘One Health’ Approaches may be Inadequate

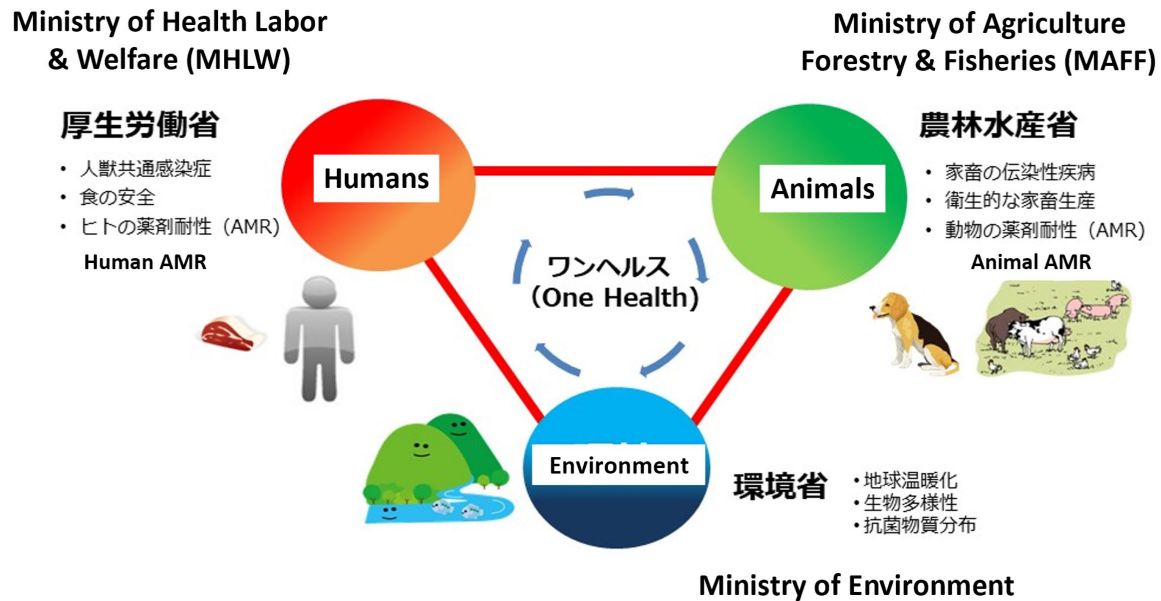
“One Health”¹² – a framework for sustainably balancing the health of people, animals, and environment by bringing together diverse stakeholders – is one solution proposed for addressing the problem of AMR. AMR has been referred to as “the quintessential One Health issue,”¹³ and stakeholders in human and veterinary medicine have so far led the application of this approach. One Health initiatives are often focused on zoonotic diseases, antibiotics in animal feed, and risks of disease and AMR for human populations. Despite depicting a triangle of human-animal-environment interactions, most One Health models clearly prioritize one point of the triangle (i.e., humans), as the problems are often approached from a very human-centered perspective.

One Health also encompasses socio-ecological relationships, and social scientists have proposed agendas for research on microbes and the microbiome.¹⁴ Any solution aimed at addressing AMR will require an understanding of how people think about microbes – whether as foes or friends or somewhere in between – since such views influence how people behave on individual and societal levels. Elucidating people’s understandings, feelings and behaviors toward microbes may aid in shaping interventions to the ever-growing threat posed by AMR¹⁵ and microbiome disruption (*dysbiosis*) more generally.

Scholars investigating Western notions of public health have criticized One Health and related concepts for focusing disproportionately on the Western industrialized world, and not paying sufficient attention to other sources of knowledge on the role of ecosystems in contributing to human health.¹⁶ Thus, there is a need for more diverse stakeholders and perspectives, such as the Japanese, to come to the proverbial table. Japanese may introduce distinct notions of health, environment, body, and disease, as well as views on microbes as seen through their traditional approaches to food culture.

The Japanese government One Health model¹⁷ (figure 1) features humans and animals at the top of an inverted triangle and environment at the base, but we discovered that in Japan very few people were familiar with the government-produced education materials or had even heard of ‘One Health.’ While the One Health model explicitly links humans-animals-environment, it still separates spheres of humans and animals and environment, instead of seeing humans as one among many species of animals in a relational environment, interconnected by microbes through various mechanisms. One participant explained that microbes are not inherently ‘good’ or ‘bad’ but need to be understood in their ecological context, and that microbes only cause problems for humans when humans disrupt the ‘natural order’ of things. This observation begs the question of what is the ‘natural order?’

Figure 1. Japanese One Health Model¹⁷ with English Translations



Japanese Alternatives: Microbes as ‘Partners in Health’

While Japan has embraced use of broad-spectrum antibiotics, *probiotic*¹⁸ (i.e., using or supporting microbes) traditions have existed there for millennia,¹⁹ and might hold clues to alternative ways of interacting with microbes that can be harnessed to counter the trends driving AMR and microbiome disruption. Japanese food culture includes traditional fermented foods made from soybeans (e.g., *miso* and *natto*), to more recent so-called Food for Specialized Health Uses (FOSHU) such as the popular probiotic drink Yakult, consumed by many children and adults throughout Japan. The country thus represents an important case study for examining attitudes towards microbes generally, and AMR and One Health specifically.

Drawing on the methods and instrument developed for exploring public understandings of the microbiome,²⁰ we interviewed over 50 scientists, health professionals, policy makers, owners of businesses utilizing microbes (e.g., miso and sake production, food waste processing) and lay people in Japan from fall 2023 to spring 2024. We explored views on the following topics: microbes and the microbiome; germaphobia and over-sanitizing; antibiotics; marketing and beliefs about fermented foods, probiotics, and prebiotics for health; concerns about food production, waste, and environmental pollution; and other factors that affect AMR and contribute to One Health and related approaches. The University of Delaware IRB determined this project to be exempt (category 2ii) on 25 September 2023. The interviews led to our discovery of several philosophical models of human-nature and health that have potential implications for how humans relate to microbes, and for AMR in particular.

Body and Soil are not Two (Shindo Fuji)

Although awareness of ‘One Health’ was minimal, participants reported several Japanese concepts that take more explicit ecological approaches to human-animal-environment interconnections and may explain why One Health has not ‘caught on’ in Japan. For example, one participant (a cram school and taichi teacher) said such human-animal-environment

interconnections were ‘*atarimae*’ (obvious). She went on to suggest that the phrase ‘*Shindo Fuji*’ (literally body and soil are not two separate things), an explicit Meiji-era response to western Cartesian human-nature dualism, might better represent Japanese understandings. This view has implications for the optimal built environment for health human-microbiome interactions.²¹ The concept of *Shindo Fuji* is particularly interesting given recent scientific interest in human-soil microbe interactions.²² One registered dietitian reported that she intentionally exposed her children to environmental microbes to build microbiome resilience specifically to prepare for disasters such as earthquakes, which can disrupt access to basic services such as clean water. This suggests ecological thinking, in that she was promoting microbial diversity and resilience in her children’s microbiome so that they might be less susceptible to harmful infections following an earthquake. Following earthquakes, human attempts to separate the body from the soil (nature) may be thwarted and preparing for such disasters by facilitating human-microbe interaction at a young age is a more ecological strategy, compared to ensuring one has plenty of antimicrobials and water purification on hand for a disaster.

Food as Medicine (Ishoku Dogen)

The concept of *Ishoku Dogen* - Food as Medicine - is particularly relevant here and was mentioned by several participants. Everyone we interviewed was aware of fermented foods, including traditional foods made from fermented soybeans such as *miso* and *natto*, and ‘medicinal foods’ such as the Yakult probiotic drink. Interviews with people involved in producing and selling fermented foods showcased how they were viewed as good for *chonai saikin* (intestinal microflora), and by extension for health. While some people we interviewed thought that antibiotics were essential to treat conditions such as sinus infections, others spoke of alternatives such as *Kampo* (Japanese herbal medicine) and *funazushi* (fermented fish) which people traditionally used instead of antibiotics to treat respiratory tract infections during pregnancy and in people with vulnerable conditions. Japanese appreciation of seasons, seasonality, and the concept of enjoying food at its peak freshness (*shun*) may serve to enhance human-microbe-environmental interconnections and microbial diversity and resilience, which in turn may support health.

Guidance from Nature

Several interviews led to discussions about traditional Japanese philosophies that suggest that approaches to AMR and One Health might be more effective if focused upstream on minimizing disruption to our own gut microbiota (with antibiotics) and the ecological balance (including microbes) of the larger environment. As Seiichi Kondo, retired foreign ministry diplomat, shared in his interview and described in his 2013 Ted Talk, Japanese traditionally look to nature for guidance,²³ whether that be for producing fermented foods, garden design, or human health as in *Kampo*. An important *Kampo* principle is ‘know your body,’ which Dr. Kenji Watanabe, a renowned *Kampo* physician, extends to ‘know your society.’ Could this also be extended to ‘know your food’ and the greater environmental context including microbes, particularly in the use of antibiotics in agriculture and health?

Implications and Future Directions

When examined through the lens of food production and health, traditional Japanese attitudes and practices toward microbes are seen to differ from those commonly observed in the West. The

One Health model has not caught on in Japan, perhaps because it does not capture traditional Japanese concepts of *Shindo Fuji*, *Ishoku Dogen*, and ‘guidance from nature’ for supporting health. Instead, these traditional concepts not only influence human-nature interactions but also Japanese behavior toward and impact on relationships with microbes. These alternative models might be more effective in addressing not only the growing problem of AMR but also microbiome-related disease and dysbiosis, in Japan and beyond.

Cross-cultural studies suggest alternative ways of being in relation with microbes and may provide different approaches and solutions. Traditional Japanese views challenge the oft-assumed separation of “the environment” as a thing needing protection and “microbes” as things requiring control. Militaristic thinking (e.g., aiming to kill all pathogenic microbes) is part of what created the AMR crisis. More ecological and probiotic thinking¹⁸ such as exists in traditional Japanese approaches to food and health, as highlighted in *Shindo Fuji* (Body and soil are not separate), *Ishoku Dogen* (Food as Medicine), and ‘guidance from nature’ (using nature as inspiration) may provide a way out of the crises of AMR, microbiome disruption and dysbiosis, for Japan and beyond.

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