Applying antibiotics lessons to antivirals

READING THE PERSPECTIVE “Combating emerging viral threats” by E. Bekerman and S. Einav (17 April, p. 282), I was struck by the call for broad-spectrum antiviral drugs, given the recognition of the problems caused by broad-spectrum antibacterial drugs (1) and the recent clarion calls for precision medicine (2). “One drug, one bug” antibiotics, along with appropriate point-of-intervention diagnostics, would mitigate the spread of drug resistance. The same is likely to be true for antivirals.

Furthermore, “one drug, multiple bugs” (broad-spectrum) antibiotics damage the highly diverse populations of bacteria in and on our body. These microbiota are becoming increasingly appreciated as critical for health. Damage to the gut microbiota, particularly during early development, has lasting negative consequences for maturation and function of the immune and central nervous systems (3). The gut microbiota similarly harbor viral components important for health (4). Broad-spectrum antivirals are likely to damage these viral components of our gut microbiota.

Today’s slow and expensive drug development process presses industry to seek one drug for multiple bugs. However, efforts to manage viral infections, as for bacterial infections, should not focus on broad-spectrum agents but on technology platforms that allow the discovery, development, manufacturing, and regulatory approval of multiple precision antiviral agents, each targeting only one bug. Such drugs could be developed, produced, and approved expeditiously and cost-effectively, as the world has managed to achieve effectively for annual influenza vaccines in most years.

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Response
The main arguments against broad-spectrum therapies presented by Martin are based on the pitfalls of this approach with antibiotics. However, the spread of resistance in bacteria to which Martin refers is not directly applicable to viral resistance. Bacteria can spread antibiotic resistance either vertically by passing the antibiotic resistance genes to new generations or horizontally by sharing or exchanging antibiotic resistance genes through gene transfer mechanisms between even distantly related species (1). In contrast, the evolution of drug resistance within viruses is governed by their intrinsically error-prone replication. Hence, the likelihood that a virus develops resistance to a broad-spectrum agent is comparable to that of developing resistance to a therapeutic targeting a single virus. We therefore disagree with the statement that precision medicine for antivirals would mitigate the spread of drug resistance. Broad-spectrum host-targeted approaches with higher genetic barriers to resistance offer a more feasible approach to limiting antiviral resistance than do precisely targeted antivirals.

The prior antibiotic efforts have saved millions of lives to date. They are likely a major contributor to the markedly extended life span in developed countries over the past century. Thus, while the overuse and misuse of antibiotics warrant scrutiny, the emergence of resistance is not an indication that this strategy failed.

Understanding of the virome and its role (both beneficial and detrimental) in human disease is in its infancy (2). We agree with Martin that broad-spectrum antiviral therapies may affect the human virome. Nevertheless, this potential concern needs to be offset by the tremendous cost and difficulty of developing drugs targeting individual viruses. The biggest success story in the past decade has been the development of targeted antivirals against hepatitis C virus (HCV). However, it took many billions of dollars and more than a decade to achieve this, and drug access has now become a major challenge (3). HCV is a single virus. The list of emerging and reemerging viruses that represent major threats to global health keeps increasing. More than 11,000 individuals died from the recent Ebola outbreak, and a greater number of patients die from dengue and other emerging viral infections every year. Therefore, as we wrote in our Perspective, we advocate combining specific development approaches with broad-spectrum approaches to enable global health protection and national security readiness more rapidly.

We too recognize the value of precision medicine (4). Nevertheless, the need for novel antivirals is broad and urgent. We should therefore not let precision medicine distract from lower-cost and effective population-wide interventions (5).

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China legitimizes ivory, again

IN THE PAST, the Chinese ivory industry was licensed to purchase a certain quota of ivory on the grounds of “the inheritance of
traditional ivory arts.” Rather than helping to slow the decline of elephant populations, the policy served as a permanent protective umbrella for the illegal ivory trade (1). Unfortunately, there are no plans to change the situation for the better. On 11 May 2015, the China State Forestry Administration announced that 34 enterprises were authorized to produce ivory products, and 130 enterprises were certified for ivory trading. The count is down from 37 and 145 (2), respectively, in 2013, but the decrease will not change the effect of the policy. Once again, the Chinese government has legitimized ivory trade in China. China has attempted to regulate the ivory trade through franchise and collection certificate systems for ivory products, but to no avail. As long as some ivory is legal, even artificial ivory may not help; traders can claim that illegal ivory is artificial to regulators and that artificial ivory is authentic to buyers, thereby increasing total ivory trade and hastening the extinction of African elephants (3). Classifying even a portion of authentic ivory as legitimate may result in misinformation for consumers regarding illegal ivory trading. An inquiry conducted by the International Fund for Animal Welfare indicates that more than 70% of the Chinese public is unaware that ivory is acquired at the cost of elephant slaughter (4) or that much of the revenue supports terrorist groups (4).

The European Union and the United States, both as contracting parties of the Convention on International Trade of Endangered Species, have already banned the import of commercial ivory products. We call on the Chinese government to likewise ban international and commercial trade with a firmer hand, in order to stem the excessive consumption of ivory products and protect African elephants.

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Response to Comments on “Number-space mapping in the newborn chick resembles humans’ mental number line”
Rosa Rugani, Giorgio Vallortigara, Konstantinos Priftis, Lucia Regolin
Mangalam and Karve raise concerns on whether our results demonstrate a mental number line, suggesting auxiliary experiments. Further data analyses show that their methodological concerns are not founded. Harshaw suggests that a side bias could have affected our results. We show that this concern is also unfounded. Harshaw suggests that a side bias on whether our results demonstrate a mental number line. I argue that the hypothesis testing used to support this claim unjustifiably assumes that domestic chicks are unbiased when choosing between identical stimuli presented to their left and right.

Full text at http://dx.doi.org/10.1126/science.aaa4269

Comment on “Number-space mapping in the newborn chick resembles humans’ mental number line”
Madhur Mangalam and Shraddha Madhav Karve
Rugani et al. (Reports, 30 January 2015, p. 534) tested 3-day-old domestic chicks using an innovative experimental setup and demonstrate the presence of the mental number line. We raise concerns regarding this conclusion by highlighting the possible loopholes in the experimental design and the data analysis procedures. We further suggest auxiliary experiments that can substantiate the authors’ claim.

Full text at http://dx.doi.org/10.1126/science.aaa8577

Comment on “Number-space mapping in the newborn chick resembles humans’ mental number line”
Christopher Harshaw
Rugani et al. (Reports, 30 January 2015, p. 534) presented evidence that domestic chicks employ a “mental number line.” I argue that the hypothesis testing used to support this claim unjustifiably assumes that domestic chicks are unbiased when choosing between identical stimuli presented to their left and right.

Full text at http://dx.doi.org/10.1126/science.aaa9565

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TECHNICAL COMMENT ABSTRACTS
Comment on “Global diversity and geography of soil fungi”
Christopher W. Schadt and Anna Rosling
Tedereso et al. (Research Article, 28 November 2014, p. 1078) present a compelling study regarding patterns of biodiversity of fungi, carried out at a scale unprecedented to date for fungal biogeographical studies. The study demonstrates strong global biogeographic patterns in richness and community composition of soil fungi. What concerns us with the study is what we do not see. Unfortunately, this study underestimates the fungal diversity of one key group of soil fungi due to reliance on a single primer with known flaws.

Full text at http://dx.doi.org/10.1126/science.aaa4269
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