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Combating Antibiotic Resistance: Ineffective Drugs Push Scientists To Explore Alternative Medications

抗“耐抗生素”的战争：无效的药物促使科学家探索替换治疗

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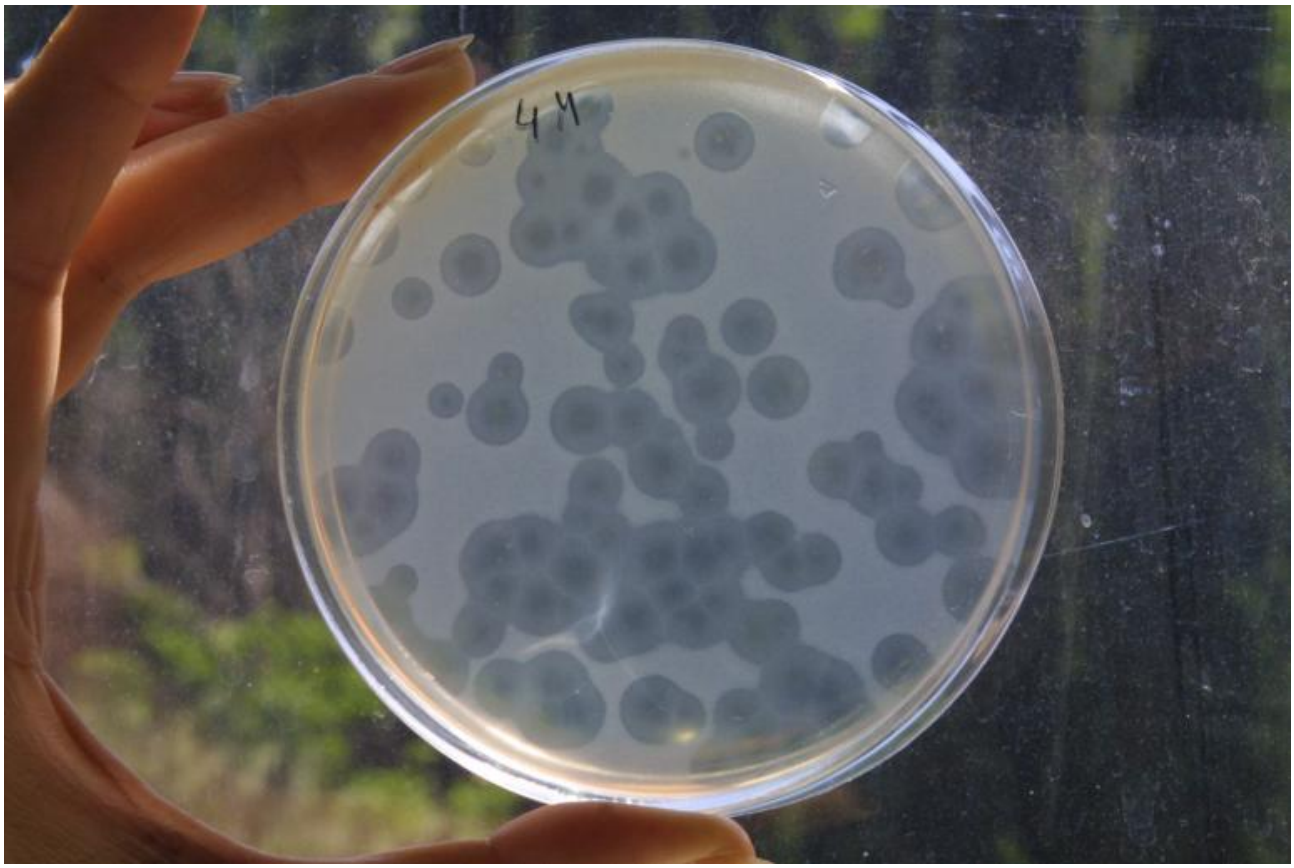

As antibiotic resistance becomes a growing threat around the world, scientists are searching for new ways to kill, but they say alternatives to antibiotics won't be ready for use for years. Above, a Georgian doctor held the bacterium staphylococcus at the laboratory of the Eliava Institute of Bacteriophage, Microbiology and Virology in Tbilisi, Georgia, in 2005. Vano Shlamov/AFP/Getty Images. 耐抗生素已在形成全世界的激增威胁，科学家正在研究能杀死病原体的新途径，但他们说抗生素的替代还需要很多年才能就绪。上图：乔治亚第比利斯的埃利阿瓦噬菌体、 微生物学和分子病毒学研究所，一位乔治亚医生手上的葡萄球菌（2005 年）。

They were once the darlings of modern medicine. With them, surgery could be clean and safe, and infections of all kinds treated quickly and relatively cheaply. But as two deaths at a University of California, Los Angeles hospital linked this week to a highly resistant infection show, antibiotics are no longer as effective as they used to be. While the California cases and similar ones elsewhere renew public interest in antibiotic resistance, scientists are trying to create ways to prepare for the day when antibiotics no longer work. 它们曾经是现代医学的宠儿。有了它们，手术可以进行得干净和安全，各种感染都相对低成本地被迅速医治。但是本周在加州大学洛杉矶分校医院的两例死亡所显示的高度耐药感染，是抗生素不再像它们以前那样有效了。而这两个加州案例

和各地的类似病案重新引起了公众对耐抗生素的关注。科学家们在试图创造出新的出路，为了准备有一天抗生素将失去其作用。

Scientists say there are promising options on the horizon to treat infections that are immune to standard antibiotics. A handful of new antibiotics are under development, as are other methods of combating infections that target bacteria differently from the way antibiotics do. But that horizon is distant, and many harmful bacteria already have outsmarted current methods to kill them. 科学家说，确有免疫于通常抗生素、治疗感染的方法，前途就在地平线上。好几个新的抗生素正在被研发，同时又有战胜感染的方式，其式靶向特定细菌的方式已完全不同于抗生素的。但那地平线上的目标尚远，而很多病菌的智力却已经超过了当今杀死它们的方法。

"We are way behind the curve on this," Dr. Peg Riley, who runs and researches microbial evolution at the Riley Lab at the University of Massachusetts Amherst, said of medical developments to deal with antibiotic resistance. "That's because [the government] stopped funding antibiotic development, and pharmaceutical companies stopped funding it because they thought they had the battle won." 在马萨诸塞大学阿姆赫司特分校主持莱利实验室的莱利博士说："我们大大落后于事情发展的激增曲线。因为（政府）停止了抗生药物的研发经费，而医药公司也停止了经费、以为它们已经打赢了针对细菌感染的战争。

Certain infections, like ones caused by carbapenem-resistant Enterobacteriaceae, or CRE, which was found at UCLA, are more of a threat to sick individuals in hospitals and other facilities than to the general population. But other more easily communicable infections are becoming increasingly dangerous as the bacteria that cause them develop immunity. The U.S. Centers for Disease Control and Prevention (CDC) estimates that every year more than 2 million people in the U.S. are infected with resistant bacteria and that at least 23,000 die as a result. 当然，对碳青霉烯耐药肠杆菌科（CRE）这类病源的感染，更多的是发生住在医院或医疗设施中的病人，而不是流行于公众场合。但是，由于细菌自身发展了免疫力，其他更容易传播的感染正在变得更危险。美国疾病控制和预防中心（CDC）测算每年有 2 百万以上的美国病人感染了耐药细菌，至少有 2.3 万死于耐药细菌感染。

Riley is one of the world's foremost experts on bacteriocins, toxic proteins produced by bacteria to fight off other similar bacteria. She works with Pheromonicin Biotech Ltd., a company in Beijing, to experiment with and cultivate ways to use these proteins to target and kill specific pathogens, unlike traditional antibiotics, which kill bacteria, good and bad, rather indiscriminately. Good bacteria are essential for staying healthy, and Riley called bacteriocin-based drugs "a more intelligent approach to dealing with those relatively few pathogens that actually cause us trouble." 莱利博士是世界著名的专家，专注细菌素，即由细菌产生的蛋白菌素排斥类似细菌的功效。她和信息菌素生物科技有限公司（一个北京公司）的合作，实验和创造出了用这种蛋白靶向杀伤特定病原体的途径，而不再是像传统抗生素无靶向地同等杀死益生菌和病菌。益生菌是动物保持健康的基础。莱利博士称其为基于细菌素的药剂，是更为智能的途径，因为它能针对少数实际造成疾病的病原体。

The Chinese government is investing $400 million annually in this research, according to Riley, but pharmaceutical companies aren't that interested in them. "They're very powerful," she said of bacteriocins, "but they've not been in the mainstream in drug development." She couldn't say when some of the drugs that she and her Chinese counterparts are engineering might become available. None have even entered human trials yet, but she said that of all the research into medicines that could treat resistant pathogens, drugs using bacteriocins might be available the soonest. 据莱利博士说，中国政府正进入每年 4 亿美元的投资来进行这个研究，但是医药公司对此不感兴趣。"它们很有效力，"她解细菌素说，"但是它们还没有进入主流的医药研发。"她不能透露什么时候她和她的中国合作伙伴所从事的工程技术过程能够达到就绪可用。尚没有其中任何

一种进入了人体实验。但她说，在所有可能形成药物来医治耐药病原体的研究中，细菌素离成功最近。

Another possibility to treat resistant pathogens is the use of bacteriophages, which are viruses that infect and kill bacteria. Like bacteriocines, they target specific bacteria instead of killing all bacteria they come into contact with, the way antibiotics do. Countries in the former Soviet Union have long used bacteriophage therapy to kill pathogens, while Western countries were focused on using antibiotics. But now that antibiotic resistance is growing, other countries have started to take a greater interest in the possibilities of bacteriophage therapy. 另一个对抗耐药病原体的可能是使用噬菌体，它是能感染和杀死细菌的病毒。类似于细菌素，它们靶向特定的病菌，而不是像抗生素那样去杀伤所遇到的所有细菌。前苏联的几个加盟共和国曾长期使用噬菌体治疗来杀伤病原体，而西方国家则专注于使用抗生素。但是当前耐抗生素正在增长，其他国家都已开始更加关注用噬菌体治疗的可能性。

But using bacteriophages to kill pathogens is far from full-fledged therapy. “It’s quite basic research at the moment,” said Dr. Rob Meijers, who studies bacteriophages at the European Molecular Biology Laboratory in Hamburg, Germany. Although such therapies were used in the Soviet Union, “it was sort of a haphazard approach, because sometimes it worked and sometimes it didn’t.” 然而，用噬菌体杀死病原体距离完全的治疗还很远。“当前它还是个非常基础性的研究”。在德国汉堡的欧洲生物分析实验室研究噬菌体的迈.罗伯博士说。

What Meijers and his fellow researchers are trying to figure out is how bacteriophages that kill one particular strain of bacteria, Clostridium difficile, actually work. Bacteriophages will kill bacteria, Meijers explained, but it won’t them entirely, because otherwise the phages themselves cannot survive. “It won’t immediately start killing everything. We are trying to find out how this is regulated,” he said. Still, he emphasized, “This [research] is, at the moment, at the stage where we are just trying to understand how this works.” 迈.罗伯博士和他的同事在试图找出噬菌体能杀死一种特定“艰难梭菌株”的实际效应。噬菌体能杀死细菌，迈.罗伯博士解说，但它不能把细菌完全消灭，因为如此噬菌体自身也就不能幸免。他说：“它不肯即时开始杀伤。我们正在寻找它的规律。”诚然，他强调说，“这个（研究）在当今，还是在发现原理的阶段。

Although bacteriophages seem promising in the distant future, after their mechanisms are better understood and can be controlled, commercializing drugs that make use of them also has many obstacles. Because phage therapy has been used for the past century, patenting it is difficult. It’s also expensive, especially when compared with antibiotics, Meijers said. “This is not something that will suddenly now cure the problem of antibiotic-resistant bacteria,” he said. “I don’t think it will replace antibiotics, but using both in combination could be very powerful.” 虽然噬菌体似乎有个相当远的前途，在它们的结构被更好地了解而且可以受控之后，在商业化药品中使用它们仍会有很多障碍。因为噬菌体治疗在过去的世纪曾被使用，很难建立专利。迈.罗伯博士说，它的应用尤其比抗生素更为昂贵，“这可不是忽然在今日就能够医治耐抗生素细菌的。”

The so-called drug pipeline also has some new antibiotics aimed at fighting resistant bacteria. According to a brief from the Pew Charitable Trusts, as of last September, 38 new antibiotics aimed at superbugs were in clinical trials or had submitted applications to the Food and Drug Administration for approval. The number might seem high, but the brief was quick to point out that only 20 percent of drugs tested in humans are ultimately approved by FDA. 在所谓的制药“管线”上，尚有一些标的抗耐抗生素的抗生素在研发中。据 PEW 慈善组织的报告，有 38 种新高端抗生素在临床实验或申请批准的过程中。这个数字可能看上去相当高，但报告很快即指出：只有 20%的这些药物取得了 FDA 批准的最终人体实验。

One reason the number of new antibiotics is so limited is that pharmaceutical companies have little financial incentive to invest in them. Drugs that treat chronic diseases are far more profitable than

antibiotics, which are taken for a limited time. As UMass' Riley noted, "How can you argue to your investors to invest $1 billion in a drug that you hopefully won't have to use very often?" Most of the companies trying to develop the drugs noted in the Pew brief were small, with just four of the 29 companies coming from the top 50 pharmaceutical companies in sales. 新抗生素的数量之少，其一个原因是医药公司觉得投资研发新抗生素是无利可图。治疗慢性病的药物比抗生素的利润要搞得多、而费时却很有限。正如马萨诸塞大学的莱利教授所注意到的，“怎能说服你的投资人需要 10 亿美元去研发一种（希望它见效、而）不会用得频繁的药物呢？” 在 PEW 报告中能看到，大部分试图研发抗生素的是小公司，在 50 个销售量最大的医药公司中，在 29 家被统计公司中只有 4 家参与了新抗生素的研发。

Last month, scientists discovered an antibiotic found to be effective against several highly resistant pathogens. They called it teixobactin, and its discovery unleashed a spate of media coverage and praise as a sort of miracle antibiotic. But Dr. Kim Lewis, lead researcher of the team that discovered the antibiotic, has estimated it would be at least another two years before the drug hits human trials and another five before it could be used in a medical setting. 上个月，科学家发现了一种抗生素能有效对抗若干高度耐药的细菌。他们称它为 teixobactin，这个发现引起了媒体接二连三的报道并赞美为一个抗生素奇迹。但是领军发现该抗生素的金.路易斯博士推测说，这种药进入人体实验至少还得两年，再加上五年才能有医疗应用。