Published in final edited form as:

Arch Intern Med. 2011 June 27; 171(12): 1080–1081. doi:10.1001/archinternmed.2011.26.

The Antibiotic Crisis:

Can We Reverse 65 Years of Failed Stewardship?

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Society is in the midst of 2 converging public health crises: skyrocketing antibiotic resistance and plummeting new antibiotic development.^{1–3} While most physicians have become familiar with the crisis of antibiotic resistance, few may be aware of the severity of the collapse in antibiotic development (Figure).

A recent workshop, cosponsored by the National Institute of Allergy and Infectious Diseases, the US Food and Drug Administration, and the Infectious Diseases Society of America, focused on the causes of and potential solutions to the antibiotic resistance crisis.⁴ As emphasized at the workshop, calls to enhance desperately needed new antibiotic development⁵ must be matched with more effective stewardship efforts to prolong the useful lives of available antibiotics. Unfortunately, it's easy to say we need to promote judicious use of antibiotics, but it's hard to do. Warnings not to abuse antibiotics date back to Sir Alexander Fleming (discoverer of penicillin) himself, as early as 1945.⁶ If we want current antibiotic stewardship efforts to be more effective than the previous 65 years of failed discourse, more is needed than just nagging by key opinion leaders. Through active investigation, we must identify and develop new ways to promote effective antibiotic stewardship, for example, by use of rapid molecular diagnostics⁵ or quality-based clinical pathways.

Enter Jenkins et al. Their article in the current issue of the *Archives* is a follow-up to a previous observational study in which they found an alarming frequency of prolonged, inappropriately broad antibiotic therapy in hospitalized patients with skin and soft-tissue infections (SSTIs).⁷ They subsequently assembled a multidisciplinary group to create a clinical guideline for the management of SSTIs. The guideline's recommended empirical therapy was vancomycin; antibiotics with activity against gram-negative bacilli (GNB) or anaerobes, which very rarely cause SSTIs, were specifically discouraged. A total of 7 days of antibiotic therapy was recommended, with conversion to generic, oral, step-down therapy when the patient was clinically improved. Substantial efforts were made to disseminate the treatment guideline throughout their medical center, and quarterly auditing/feedback was provided to clinicians to reinforce implementation of the guideline.

Of greatest significance is that comparing the treatment of SSTIs during the 1-year periods before vs after implementation, the investigators found substantial reductions in the use of antibiotic therapy with broad GNB activity (66% vs 36%), anaerobic activity (76% vs 49%), and antipseudomonal activity (28% vs 18%). Furthermore, the median duration of antibiotic

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Financial Disclosure: None reported.

therapy for SSTIs decreased from 13 to 10 days, and there was a substantial increase in the fraction of patients treated for fewer than 10 days (14% vs 38%). There was no increase in treatment failure rates despite the use of narrower spectrum agents for a shorter duration of therapy. The investigators also found a decrease in use of expensive, advanced imaging studies (CT and MRI). All of this is good news and indicates that a comprehensive, well-advertised clinical guideline can positively affect antibiotic prescribing behavior for a common infection at a major medical center.

There is also bad news. Even after the intervention, more than a third of patients continued to receive therapy with agents with broad GNB activity. Nearly 20% of patients received therapy with an antipseudomonal agent. Our goal should be to have these numbers approach zero. Furthermore, more than half of patients continued to receive treatment for more than 10 days, when data indicate that cellulitis can be effectively treated in 5 days.⁸ Given the antibiotic crisis with which we are confronted, it is inexcusable to prescribe prolonged courses of therapy with antibiotics that have broad GNB activity when treating SSTIs caused by streptococci and *S aureus*. Hence, while Jenkins et al contribute a very important primary research study indicating that new ways of approaching antibiotic stewardship can be effective, they also underscore how much further there is to go to protect antibiotics.

One limitation is that this was a single-center study, and further investigation is needed to determine generalizability of the intervention across different medical venues. Also, more than half of the identified cases were excluded from the analysis, primarily because of complicating factors that altered the possible microbiologic characteristics of the infections, or because the patients were too young. It is not clear if the recommended guideline is safe and effective for sicker patients or those with infections with other possible microbiologic characteristics, or for children. Conversely, for less severe infection, it is not at all clear that vancomycin, or any parenteral therapy, is required to treat cellulitis and skin abscesses. Generic, orally bioavailable agents, such as clindamycin, seem adequate to treat such infections.⁹ Furthermore, some have suggested that no antibiotic therapy may be needed in addition to incision and drainage for treating uncomplicated skin abscesses—unfortunately, no adequately powered studies have yet settled this ongoing debate.¹⁰

Antibiotics fundamentally revolutionized the practice of medicine by arming physicians, for the first time, with broadly active medical therapy to affect patient outcomes.^{11–13} In 1981, Walsh McDermott, MD, wrote¹⁴(p303):

It is not too much to state that the introduction of [antibiotics] has represented a force for change in the 20th century of the same general kind as James Watt's modification of the steam engine did in the 18th. The crossing of the historic watershed could be felt at the time. One day we could not save lives, or hardly any lives; on the very next day we could do so across a wide spectrum of diseases. This was an awesome acquisition of power.

If we are to maintain that “awesome” power, physicians must embrace new ways of preserving the precious, limited resource that is effective antibiotics, even as we try to renew the wellspring of antibiotic development that is drying up. Jenkins et al present to us an encouraging sign that we can do better while also showing us how much more work there is to do.

References

1. [Accessed January 13, 2011.] Bad bugs no drugs: as antibiotic discovery stagnates, a public health crisis brews. <http://www.idsociety.org/10x20.htm>

2. Spellberg B, Guidos R, Gilbert D, et al. Infectious Diseases Society of America. The epidemic of antibiotic-resistant infections: a call to action for the medical community from the Infectious Diseases Society of America. *Clin Infect Dis*. 2008; 46(2):155–164. [PubMed: 18171244]
3. [Accessed 2009.] The bacterial challenge: time to react: call to narrow the gap between multidrug-resistant bacteria in the EU and the development of new antibacterial agents. www.ema.europa.eu/pdfs/human/antimicrobial_resistance/53394009en.pdf
4. [Accessed 2009] FDA/NIAID/IDSA Public Workshop: antibacterial resistance and diagnostic device and drug development research for bacterial diseases. <http://www.idsociety.org/arworkshop.html>
5. Gilbert DN, Guidos RJ, Boucher HW, et al. Infectious Diseases Society of America. The 10 × '20 Initiative: pursuing a global commitment to develop 10 new antibacterial drugs by 2020. *Clin Infect Dis*. 2010; 50(8):1081–1083. [PubMed: 20214473]
6. Penicillin's finder assays its future. *New York Times*. June 26, 1945 :21.
7. Jenkins TC, Sabel AL, Sarcone EE, Price CS, Mehler PS, Burman WJ. Skin and soft-tissue infections requiring hospitalization at an academic medical center: opportunities for antimicrobial stewardship. *Clin Infect Dis*. 2010; 51(8):895–903. [PubMed: 20839951]
8. Hepburn MJ, Dooley DP, Skidmore PJ, Ellis MW, Starnes WF, Hasewinkle WC. Comparison of short-course (5 days) and standard (10 days) treatment for uncomplicated cellulitis. *Arch Intern Med*. 2004; 164(15):1669–1674. [PubMed: 15302637]
9. Frei CR, Miller ML, Lewis JS II, Lawson KA, Peddaiahgari R, Talbert RL. Retrospective cohort study of hospitalized adults treated with vancomycin or clindamycin for methicillin-resistant *Staphylococcus aureus* skin infections. *Clin Ther*. 2010; 32(12):2024–2029. [PubMed: 21118737]
10. Spellberg S, Boucher HW, Bradley J, Das A, Talbot G. To treat or not to treat: adjunctive antibiotics for uncomplicated abscesses. *Ann Emerg Med*. 2011; 57(2):183–185. [PubMed: 21251530]
11. Thomas, L. *The Youngest Science: Notes of a Medicine-Watcher*. New York, NY: Viking Press; 1983.
12. Spellberg, B. *Rising Plague: The Global Threat From Deadly Bacteria and Our Dwindling Arsenal to Fight Them*. Amherst, NY: Prometheus Books; 2009.
13. McDermott W, Deuschle K, Adair J, Fulmer H, Loughlin B. Introducing modern medicine in a Navajo community. *Science*. 1960; 131(3395):197–205. [PubMed: 17732683]
14. McDermott W, Rogers DE. Social ramifications of control of microbial disease. *Johns Hopkins Med J*. 1982; 151(6):302–312. [PubMed: 6757513]

Figure.
Number of new systemic antibacterial agents approved by the US Food and Drug Administration per 5-year period. New molecular entities are considered. Data are accurate through February 2011.