Infectious Diseases, Antimicrobial Stewardship and the Annual Influenza Vaccine

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Dr. Andrew Morris

This article shares the transcript of a recent interview with Dr. Andrew Morris, Director of the Mount Sinai Hospital-University Health Network Antimicrobial Stewardship program. Dr. Morris is also Chair of the Specialty Committee of Infectious Diseases with the Royal College of Physicians and Surgeons of Canada, and a member of the Council for the Association of Medical Microbiology and Infectious Diseases Canada. In addition to his academic appointments, Dr. Morris has a strong interest in medical education, and serves as faculty advisor for Students for Antimicrobial Stewardship Society (SASS) at the University of Toronto.

UTMJ: So from my understanding, infectious diseases is a subspecialty of internal medicine. What drew you to selecting a career in infectious diseases?

AM: I went into medical school to be a psychiatrist. In fact, I even started a psychiatry training program initially before switching. For me there were two factors in wanting to become an infectious diseases specialist. One was the puzzle. Infectious disease physicians really are detectives. We probably do the most detective work out of the many sub-specialties of internal medicine and I found this quite appealing. The other factor was mentorship. I had a mentor and role model who was not only a local legend but also a national teaching legend and I guess at some point I wanted to be like him.

…Personally what gives me the most satisfaction is seeing patients with complex problems that people may or may not be treating successfully but often do not exactly understand but that my training allows me to rationally approach and oftentimes cure them. I often tell trainees that we are the surgeons of internal medicine because I like to think most surgeons like what they do because they get to cure patients. This is in contrast to internists who do not typically get the chance to cure patients, minus a small subset, but rather help patients manage their conditions. In infectious diseases most of the time we get to cure patients and that is what I also find very appealing.

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UTMJ: How did you become first interested in antimicrobial stewardship?

AM: It really came to head when I was working at McMaster University, at Hamilton General Hospital, and I had a patient who died of an infection and I had nothing to offer him. He wasn't the first patient to have a very drug-resistant infection but he was the first that was under my care to die because of it. At the time I recognized that something needed to be done despite not having a large cohort of infectious disease experts there in Hamilton, like we do now in Toronto. So that was really my foray into antimicrobial stewardship. This incident inspired me to develop a program there without knowing too much about quality improvement. The program, while informal, was actually very successful but it really was my first effort. One of my main reasons to come back to Toronto was a promise by leadership at Mount Sinai Hospital and University Health Network to help me establish an antimicrobial stewardship program.

UTMJ: Could you briefly describe what is meant by antimicrobial stewardship? Why is it important?

AM: Antimicrobial stewardship is an approach to using antimicrobials – or what most people know as antibiotics – wisely. So it is making sure that the right antibiotic is given to the right patient at the right time. Also it involves making sure that only patients that require antibiotics receive them. It is important because antibiotics are lifesaving treatments. They have been used clinically since as early as the 1940s, in the form of penicillin. However we are running out of them. We are running out of them because of the development of resistance and because our antimicrobial production pipeline has been drying up. This combination has resulted in a relative shortage of antimicrobials.

UTMJ: What is the main objective of your Antimicrobial Stewardship program and what strategies do you employ? Should such programs be set up within all intensive care units? If so, why?

AM: Our Antimicrobial Stewardship program – which is shared between Mount Sinai Hospital and University Health Network – is the largest of its kind in Canada and certainly one of the largest in the world. It involves physicians, pharmacists, nurses, and other health pro-

fessionals. It is designed to help prescribers make sure that patients get the right antibiotics and that the ones who do not need them do not get them. We are really trying to steward antibiotics in the hospital as a whole and not just in the ICU. Nevertheless, the most complicated patients and the ones most frequently on antibiotics are in the ICU but it is not always that way so we try to get involved in many other areas, including for example the neonatal intensive care unit and the emergency department. There are many different strategies to try to improve prescribing. Sometimes it's just providing education and/or reassurance. Many of my team members, especially the pharmacists, spend a lot of their time working closely with the clinical teams just to give them support to help them feel comfortable with the decision to provide antimicrobial therapy.

I think the clinical teams often know what to do but sometimes feel apprehensive because of fears of undertreatment or mistreatment with more conservative antimicrobial interventions. The program also helps develop guidelines and implement them. While it is not hard to develop a guideline, to develop and implement an effective guideline requires an interprofessional approach which is difficult as you have to not only get everyone to agree on things but also to act on what has been agreed upon. That's most of what we work on these days.

UTMJ: How big is the threat of antibiotic resistance in Canada? Is Canada heading towards a post-antibiotic era?

AM: That is a hard question to answer. Those of us who treat complicated infections have all had the experience of having a patient in front of us that we cannot offer anything to. It is a very real situation and an important one. That being said, Canada is doing relatively well in the battle against antimicrobial resistance. Our resistance situation is much milder than our neighbours to the south for example. We see much fewer cases of methicillin-resistant *Staphylococcus aureus* (MRSA) and other forms of antimicrobial drug resistance.

UTMJ: How often do you encounter patients with antibiotic resistant strains of infections?

AM: I would say as an infectious diseases physician, it is pretty much a daily occurrence in a tertiary care institution. If you look in Ontario, about 1/5 patients have MRSA strain infections. Similar numbers are seen for drug-resistant *E. coli*. Now if we are talking about extremely difficult to treat superbugs, then that is much less frequent in most institutions with the exception of tertiary care centers.

UTMJ: What is done for these patients?

AM: Treating complex infections is complicated. Hence why there is an entire specialty dedicated to infectious diseases. That usually requires a combination of medical therapy in the form of antimicrobials and what we term "source control", which refers to surgical drainage or interventional radiology drainage of infections as an adjunctive therapy.

UTMJ: What are some challenges you have faced with respect to implementing this program?

AM: Because at its most basic elements the program is a quality improvement and basic safety program, we are challenged by issues such as having enough resources and gaining the support of clinical teams.

This is challenging because we are trying to change well-established behaviours that may not be in a patient's best interest. So those things are really our main barriers.

UTMJ: What has been the impact of the Antimicrobial Stewardship program since it was established 6 years ago?

AM: At the local level, we have totally changed how antimicrobials are prescribed. We see shorter durations of therapy than we used to, we see narrower spectrum antibiotics being used, and when they are being used it is more appropriate than it used to be. Also I think the overall discussion and approach around good antimicrobial practice has really changed and I think all of that has been a positive. On top of that we have been able to establish really good relationships with clinical and non-clinical teams as well as the microbiology lab. That kind of synergy of groups working together to improve practice has really made a difference. I think our program has also made a huge impact on a provincial level, as we have been involved in setting standards of care. Pretty well every teaching hospital with an antimicrobial stewardship program in the province follows our model of antimicrobial stewardship in the intensive care unit. On the national level I believe we have made a significant impact – whether it is on the education around antimicrobial stewardship as well as the accreditation of such programs. We have also made big contributions to the scientific literature on this topic.

UTMJ: Do you believe the newly discovered antibiotic, Teixobactin is a game changer?

AM: It is hard know if it is a game changer. I think what is most important is the methods that were used to isolate it, which were novel as it allowed scientists to culture previously unculturable bacteria. Whether it is really going to change the game is hard to predict.

I think one of our challenges in infectious disease is that we are continuing to use the same technology for most infectious diseases that we were using 70 years ago. That is, we are using antimicrobial agents that are primarily obtained from fungi to fight infections. I think if we are going to be successful down the road we are going to have to think of a new paradigm in terms of how to fight infections. Whether that is bet-

ter vaccines, or altering the immune system or phage therapy. Those I believe would be more game changers. Teixobactin, I believe, is more of a game shifter.

UTMJ: Will we always be racing against drug resistance?

AM: Yes, if you believe in evolution. As long as there are antimicrobials out there that are exerting very selective forces on rapidly multiplying bacteria, we are always going to be playing catch up. We can't really anticipate when the next resistant strain will emerge. All it takes is one mutation in a bacterium that has the right selective advantage for it to take hold in the population and then spread out. We are already starting to see that.

UTMJ: Now shifting focus a bit to flu shots. What are your views on the seasonal flu shot? Why was this year's not as effective?

AM: I am a huge fan of the flu shots. I am fan because the flu is not only an infectious disease problem, but also a public health problem and a problem for someone interested in antimicrobial stewardship. We know that patients who get flu vaccines are less likely to receive antibiotics relative to those who do not receive the shot. It is not that we have a problem with the flu shot, but rather we have a challenge in matching the strains. Because flu vaccine production requires a time lag and we have to start producing the flu vaccine months in advance of when the flu season arrives, we have to predict what the strains are going to be based on what is going on in the southern hemisphere and that isn't always well predictive of what's going to happen in Canada. Last year, that is exactly what happened: it wasn't well protective and thus we didn't have a good match. For this reason, the flu vaccine was woefully inadequate. However this doesn't mean that flu vaccination isn't a public health good.

If I were to give a parallel, it is similar to saying that if we have a very cold winter, that global warming is not happening and we should not take action on climate change. There are long-term trends and within that that there are peaks and valleys. Over the long-term patients and general members of the public are better off getting the flu shot than not.

UTMJ: Now as you mentioned, flu shots remain the best self-defense available to protect against influenza. However, do you think flu shots should be mandatory among healthcare professionals?

AM: This is a tricky question. I work at two institutions –one that makes it mandatory, and the other that does not. As a public health intervention we have said that there are some things that people shouldn't necessarily opt out of. The best example I can give is seat belts. Seat belts are not 100% effective. You will not prevent death 100% of the time there is an accident by wearing a seat belt. Sometimes, seat belts can cause damage. Nevertheless in the grand scheme seat belts are beneficial. At most seat belts are 50% effective yet no-one questions whether they should be mandatory.

I think the same thing goes for flu shots. I do not think anyone questions whether flu shots are beneficial. What I think people do disagree about is the extent of benefit. Most estimates are in the order of 50%. Sure there will be years where it will be considerably less than that but overall, over time the effectiveness approaches 50%. That said, if we think that seat belts should be enforced with a 50% success rate, why should we not enforce flu shots with the same success rate?

UTMJ: How is success being measured?

AM: I think there are different measures that have been looked at. This is certainly one of our problems as a healthcare community. We have endorsed influenza vaccination and yet our data is not perfect. We should by now, at least in Ontario, know very well how effective the vaccine is to at least prevent people from feeling sick. This shouldn't be hard given the money invested in this program.

UTMJ: There was a recent issue in the CMAJ discussing that repeated flu shots may blunt effectiveness of the vaccine. What are your thoughts regarding this?

AM: I am familiar with the study and I believe it is based on relatively weak data. I do not think we know the whole picture. Our understanding of how, when, and to what degree the vaccine is effective is still quite poor. We understand the immunogenicity of the vaccine in healthy people. But the whole concept that, over time, repeated antigenic stimulation reduces flu effectiveness doesn't make sense to me pathophysiologically. This does not mean that it could not be true but I believe more work needs to be done to explore the mechanisms driving these findings.

UTMJ: A universal flu vaccine that could eliminate the need for yearly flu shots has been under development for several years. Can you comment on its current status, the challenges of creating this vaccine, and what the implications would be?

AM: It remains a huge challenge. In order to have a universal vaccine for influenza you need to have an antibody response to antigens on the virus that are persistent across all seasons and all strains of influenza. And on top of that, being able to trigger an immune response. This has been the challenge so far. There are a few candidates in the horizon but most of those are still relatively early in their testing.

UTMJ: That concludes the interview questions. Thank you Dr. Morris.

AM: My pleasure.