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FORUM

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Prophylactic
Antibiotics in Hair
Transplantation Surgery:
Recommendations to
Avoid Use Except in
Limited Circumstances

IN THIS ISSUE

Life-Threatening Infection After Hair Transplantation Surgery

Innovation and Quality in Hair Restoration Surgery

Combining Medical and Scientific Innovation in Hair "Cloning"





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Hair Transplant in the Age of MRSA

TRANSPLANT FORUM INTERNATIONAL

Sara Wasserbauer, MD, FISHRS | Walnut Creek, California, USA | drwasserbauer@californiahairsurgeon.com

The biggest threat to your practice is not a disruptive new surgical technology or medical treatment, it's MRSA. We live and practice medicine in the post-antibiotic era. Our field of elective hair transplant surgery is only possible due to the discovery of penicillin in 1928 by Alexander Fleming and the subsequent expansion of our biological warfare armamentarium. Without effective strategies to control the biological threats we live with, surgical intervention of any type is an inadvisable risk.

Now, like it or not, that existence is threatened by the very weapons we created. Worldwide, rates of antibiotic-resistant bacterial infections have steadily climbed, particularly in the past decade. In 2013, the U.S. Centers for Disease Control (CDC) categorized the threats based on level of concern: "urgent," "serious," and "concerning." The urgent threats are not commonly encountered in the normal course of a hair transplant surgery. But, among the serious threats is a bacteria known as methicillin-resistant Staphylococcus aureus (MRSA), and it is a real and emerging threat in our specialty.²

HOW DID WE GET HERE? MRSA HISTORY LESSON

Staphylococcus (S.) aureus is ubiquitous on our skin and mucous membranes, and usually it does not cause any harm. It is estimated that 25%-35% of healthy humans carry S. aureus in this post-antibiotic era. It would be a mistake, however, to assume that S. aureus is benign. If you look at data from the pre-antibiotic era and into the 1940s, S. aureus bacteremia was usually fatal.³

MRSA is the term that describes strains of S. aureus that have acquired antibiotic resistance either through overuse of antibiotics for inappropriate treatment indications (like treating a viral infection with antibiotics), or through incomplete treatment leading to the selection of antibiotic-resistant strains. Excessive perioperative antibiotic use by physicians also likely played a role in initiating these strains.

MRSA was first identified in the 1960s and at that time it was an iatrogenic infection; that is, it was typically found in hospitals, nursing homes, or isolated from medical personnel. Unless it gained access inside the body, a person's skin was an excellent barrier and his or her immune system was very good at fighting it off. Plus, if MRSA infected a patient, switching to an antibiotic that the strain still WAS susceptible to usually still cleared the infection.

In the late 1990s, the situation changed. This little bug moved from a healthcare-associated illness to one

that can be acquired from one's community. Patients and medical personnel without active infection symptoms would carry the resistant strain outside of the hospitals and nursing homes. Individuals were commonly colonized in the nose and on the skin so a simple sneeze or touch of the hand could transmit the bacteria. The more the bacterial strains spread, the more the strains got the chance to develop resistance to new antibiotics, until one by one whole antibiotic classes started to fail. In 1999, we heard the first reports of children dying due to resistant MRSA infections.

Over the past 30 years, no new major antibiotics have been developed, so now we are down to our last effective treatments.⁴ In 2002, the first reported case of vancomycin-resistant S. aureus in the United States (Figure 1) was

FIGURE 1. Magnified 20,000×, this colorized scanning electron micrograph (SEM) depicts a grouping of methicillin-resistant Staphylococcus aureus (MRSA) bacteria. *Photo credit: Public Health Image Library: https://www.cdc.gov/mrsa/community/photos/photo-mrsa-13.html*





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Telephone 1-630-262-5399
U.S. Domestic Toll Free 1-800-444-2737
Fax 1-630-262-1520

President	Ken Washenik, MD, PhD, FISHRS washenik@bosley.com
Executive Director	Victoria Ceh, MPA vceh@ishrs.org
Editors	Andreas M. Finner, MD Bradley R. Wolf, MD, FISHRS forumeditors@ishrs.org
Managing Editor & Advertising Sales	Cheryl Duckler, 1-262-643-4212 cduckler@ishrs.org
Controversies	Russell G. Knudsen, MBBS, FISHRS
Cyberspace Chat	Robin Unger, MD
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President's Message

Ken Washenik, MD, PhD, FISHRS | Beverly Hills, California, USA | washenik@bosley.com

Greetings my colleagues in the treatment of hair loss:

We are closing in on our largest events of the year: our live surgery workshop in Polanica Zdrój and the World Congress in Prague. I

have enjoyed the privilege of getting to preview the wonderful programs that Drs. Devroye, Tykocinski, and Kolasinski have put together with the help of many of our respected colleagues. We are in for some exciting days in Poland and the Czech Republic.

Adding to the excitement surrounding the World Congress is the growing anticipation around the celebration of the ISHRS's Silver Jubilee. We have an historic event planned that is both a celebration of today and tomorrow as well as a nostalgic tribute to the ISHRS members who have been so instrumental in advancing our field in our look back over our society's first 25 years.

Many pioneers have contributed to the field of surgical hair restoration through their advances and refinements in surgical technique, as well as volunteer teaching, in their efforts to help patients and advance the high level of skill and expertise in the field as a whole. As I think back over this time and the many accomplishments that the ISHRS has provided an educational podium to, I am also struck by the nonsurgical milestones that have contributed to our ability to care for patients with hair loss.

All the way back in 1993, at the inaugural meeting of the ISHRS, the biggest thing in the nonsurgical treatment of male and female pattern hair loss was the prescription anti-hypertensive drug, minoxidil. It had been found to slow down and, in some cases, reverse the follicular miniaturization that leads to the clinical thinning that haunts our patients with male and female pattern hair loss. At that point, minoxidil had already been approved for 5 years and there was a growing excitement around the discovery of androgen modulators that could be used in men.

5-alpha reductase inhibitors had been discovered by studying a group of men who genetically lacked one of the isoenzymes that convert testosterone to dihydrotestosterone. This research led to the approval of only the second medication ever approved to treat male pattern hair loss. The drug finasteride was approved in the U.S. in 1997. Unfortunately, approximately three decades after the approval of minoxidil and two decades after the approval of finasteride, the drug development process has disappointed when it comes to crossing the finish line with novel pharmacologic classes. Interestingly, the founding of the ISHRS occurred squarely half way between these two important hair therapy milestones.

Despite virtually countless provocative and promising discoveries of hair growth promoters in mice, we haven't been as fortunate in humans. However, things haven't been completely bleak for miniaturizing hair follicles. While we have struggled to make anagen inducers, autologous and allogeneic cells, and exogenous growth factors work, we have enjoyed advances in the use of light energy and the endogenous growth factors found in our patients' own platelets.

Critically important novel mechanistic insights have also led to very important advances in the treatment of the inflammatory cicatricial alopecias (e.g., the immunomodulatory biologics and peroxisome proliferator-activated receptor gamma agonists [PPAR- γ]) and the autoimmune disease, alopecia areata (e.g., the Janus Associated Kinase [JAK] inhibitors). These promise to be among the most important discoveries in the treatment of hair loss since the birth of the ISHRS.

We can all be proud that ISHRS members have participated prominently in the research into these nonsurgical advances, as well as the communication of their relevance to our patients and society members, over the past 25 years. While we wait for bigger and better breakthroughs, rest assured they will be front and center in the *Forum* or at one of our future meetings.

I look forward to seeing you at the ISHRS educational events and celebrations in October. ■



Co-editors' Messages

Andreas M. Finner, MD Berlin, Germany forumeditors@ishrs.org

Dear colleagues:

In front of my office, people enjoy another summer day sitting in cafés and on the lawn. Berlin is full of tourists, while many locals left the city for sunbathing in southern Europe, at the Baltic sea and on the lakes. Only

a few of them wear hats. Let's not forget to warn our balding patients of the increased risk of skin cancer from excessive sun. Another good argument for hair transplantation.

While hair protects the scalp from UV radiation, it may also be influenced by sunlight. This refers to seasonal shedding, hair shaft weathering, and even hair follicle aging.

Is it possible to find a follicular fountain of youth? As Bessam Farjo describes, the age of follicle cryopreservation seems to have arrived. Further research will show whether those young follicular tissue cells are a valuable source for hair rejuvenation.

Sara Wasserbauer's article emphasizes the importance of hygiene in hair transplantation. Regular staff screening for MRSA is advised. The use of antibiotics should be minimized, as explained in Scott Boden's article.

Our next congress will take place in Prague, a city that has preserved its heritage while being progressive and innovative, just like our society has been over the last 25 years. More great memories can be found in this issue.

Brad has prepared a great Visitor's Guide for us. Bring comfortable shoes to explore the old town and also some less touristy areas. Cross the Vlatva river to Malá Strana and the castle with its viewpoint. Used to counting thousands of grafts, it will be easy for you to check if the city actually has 100 towers. In the evening, some of us may want to try an absinthe or beer, but make sure not to miss the morning workshops.

See you soon. Uvidíme se brzy! ■



Bradley R. Wolf, MD, FISHRS Cincinnati, Ohio, USA forumeditors@ishrs.org

The themes of the upcoming World Congress in Prague are Innovation and Quality. Spending hours over the years performing long surgeries, while in a meditative phase, I'm sure we have all imagined ways to make the hair transplantation process faster

and/or better. I am envious of those who can take their idea and see it through to the development of a new device or technique. True innovation is a rare and special talent that all do not possess. Bob Bernstein addresses recent innovation as it relates to FUE. Bessam Farjo gives us an update on cloning, for us, the holy grail of innovation. "New paradigm" is an oft overused phrase but it appropriately describes the shift in thinking associated with HairClone®'s new model "to rejuvenate and regenerate hair."

Certainly, innovation can improve quality when appropriately applied. But quality is altogether different than innovation in that quality is available to anyone who is willing to do the demanding work necessary to attain it. In appropriate candidates, transplanting only intact follicles at the correct depth, to avoid visible scalp damage, and to approach 100% yield, reduces the number of grafts needed and preserves precious donor follicles for future use. Experience, skill, and an innate desire for perfection are also helpful in creating the best quality results possible.

But the best laid plans and perfectly placed grafts can be ruined by a MRSA infection. Sara Wasserbauer gives us an excellent review of this formidable enemy. Scott Boden follows with important guidelines on the use of prophylactic antibiotics, and Bob Leonard gives us a case report. Thanks to Sara for conceiving and organizing this section on MRSA. In Cyberspace Chat, Robin Unger outlines, with our colleagues' help, there is more than one way to correct a poor result, more than one solution to a problem.

We are fortunate that the pioneers and legends in our specialty join us at meetings and continue to contribute to our society. A special thanks to Carlos Uebel for his recollections of the Dallas meeting in 1993 and beyond. His "Punctiform Technique" was a significant step in the evolution of follicular unit transplantation. The Last Men Standing are those who have attended all 24 ISHRS meetings. Thanks to the Last Men and those who sent in their recollections of 24 years of meeting memories. I appreciate the time ISHRS members take out of their busy schedules to contribute to the *Forum*.

The meetings in Poland and Prague are just around the corner. I first visited Prague in 1996 and have returned twice. This explains my fascination with the city. I do recommend you learn a few words in Czech; it can make for a richer experience. Safe travels to all, see you in Prague.



Notes from the Editor Emeritus, 2011–13

Nilofer Farjo, MBChB, FISHRS | Manchester, UK | dr.nilofer@farjo.com

Who's Winning the Battle 25 Years On: Surgery or Science?

A Silver Jubilee year is a very special anniversary to be celebrating anything. As an ISHRS member who only missed the very first meeting, it is especially nostalgic as it is also the beginning of our 25th year in practice. I never imagined that I would have the honour as past editor of writing the Emeritus column for this issue of the *Forum*.

Many of us were asked to think back about past meetings and come up with some memorable moments. Well there have been so many, but to me, the one that sticks out was my first ISHRS meeting in Toronto, the place where I grew up. I was so overwhelmed not only by the number of people from around the world, but also by how much everyone seemed to know. That's when I realised that there seemed so much more to this field of hair transplantation and I knew so little about it. The other thing I couldn't understand was why was everyone so friendly? I'd been to medical meetings before but no one seemed to talk to each other.

The other momentous occasion was not a surgery meeting but an Institute of Trichology meeting in London where I met scientist Desmond Tobin, who had been invited to speak. Again, meeting a very friendly person willing to share his knowledge was very humbling. In fact, that is when my foray into the hair biology world began. Professor Tobin asked if we would be interested in collaborating in hair research—he didn't need to ask twice!

Over the past 24 years, I have been fortunate to see many advances in both surgical techniques and hair biology. So I asked myself the question: Which one is winning the battle to treat androgenetic alopecia? In an attempt to answer that, I will describe some of those key moments, but of course, it will be impossible to list them all.

In the UK, when I started out there wasn't a very good impression of hair transplants due to the bad publicity surrounding 4mm plug grafts and poor planning for future hair loss (Figure

1). However, when I was training, the value of smaller grafts by

FIGURE 1. 4mm plug grafts exposed following further hair loss.

quartering large plug grafts was coming into vogue, as was the idea of harvesting the plugs in a row with no gaps between and suturing the edges together. It was only a small step from here to the strip and mini-/micrograft techniques that dominated the next decade. The key to the dissemination of knowledge and the ongoing developments in surgery has been those inspired people who set up the ISHRS and founded this journal.

At the same time as the "beautiful people" (Figure 2) were enjoying the limelight in the Forum, a scientist was also featured and his work is still quoted and used experimentally today (Figure 3). Jung Chul Kim's groundbreaking experiments with himself as the guinea pig involved transplanting scalp hairs on different parts of his body with varying amounts of transection in order to understand hair follicle behaviour. In fact, after 25 years, he still has these scalp hairs on his leg growing long like a ponytail, which he shows off after a few rounds of whiskey. Amongst the hair biologists, seminal work by Mike Philpott was published in which he developed an in vitro culturing method to study hair growth in the lab. The Philpott Method for organ culture is still in popular use today by scientists around the world to assess how hair follicles and their cells behave. At about the same time, Colin Jahoda and colleagues were experimenting with hair inductive capacity of both human and murine hairs in mouse models.²⁻⁴

FIGURE 2. *Hair Transplant Forum Int'l*. 1993(Mar-May); Vol. 3, No. 3, p. 10. Original caption: Beautiful people



FIGURE 3. Hair Transplant Forum Int'l. 1993(Mar-May); Vol. 3, No. 3, pp. 14-15 (Kim article)

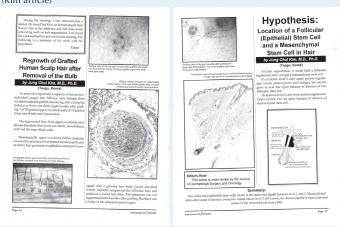


FIGURE 4. Follicular units under magnification.

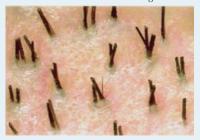
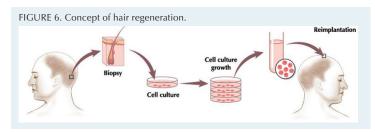


FIGURE 5. Q: Which side is transplanted and which is native hair? A: Left is transplanted.



In surgery, the next big advancement occurred with the use of stereoscopic microscopes to dissect hair follicles (Figure 4). It wasn't until higher-powered magnification was used that the realization of the follicular unit groupings became apparent to the hair transplant surgeon.4 Bobby Limmer and others advocated the use of these natural groupings and modern follicular unit transplantation was born. Unlike plug grafts and mini-/micrografts, in skilled hands, transplantation now became indistinguishable from native hair (Figure 5).

In science, great leaps in understanding were also being made. In 2003, Elaine Fuchs and her group showed that the hair follicle stem cells were located in the bulge and the migration of progenitor cells occurred into the outer root sheath and bulb. Experiments were also being performed with different cell types to understand the trichogenicity (hair follicle forming capacity) of the different cell types and structures within the hair follicle. With the understanding of the trichogenic potential of different cell types came the attempts at hair regeneration (Figure 6).



In surgery, focus moved from the recipient area to making the donor scar as aesthetically pleasing as possible. This included techniques such as trichophytic closure and eventually follicular unit extraction (FUE) to avoid linear scars. This technique is preferable in certain patients depending on their age, skin type, hair characteristics, and hairstyle. There are many devices now on the market with improvements being made all the time by innovators. Unfortunately, however, FUE surgery has been marketed by some as noninvasive and scarless, thereby diminishing the importance of the need for a well-trained hair transplant surgeon. This has led to the use of non-physicians performing the surgery and currently there is a lot of controversy surrounding this subject.

Finally, in science, a better understanding of the failures in attempts to "clone" hairs has come about in part by the work of Angela Christiano's group who showed that the genetics of cultured dermal papilla cells changes in culture with successive passages. They found that maintaining

cultured cells in a three-dimensional environment was best suited to keeping genetic integrity.⁷

So in 2017, who is the winner? In my opinion, properly done hair transplantation comes out on top. However, it remains to be seen what the damage will be to the profession by unlicensed and untrained people. For the future though, it is undoubtedly the sciences that will succeed in the ability to produce more hairs than are available in the non-balding scalp so we may see that our technicians move from dissecting in the operating room to dissecting in the lab (Figure 7).

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FIGURE 7. Top: Traditional setup for FUT surgery. Middle: Technicians training in dermal papillae isolation in Claire Higgins lab, Imperial College London. Bottom: Close-up of dermal papillae isolation; flamed-shaped structure is the DP.





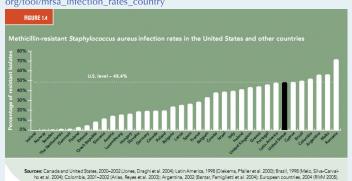


established. Since vancomycin was one of the last antibiotics we had to treat infections of this kind, the isolation of this strain of bacteria served as a wake-up call that we are headed toward a post-antibiotic era in which elective surgeries like hair transplantation may give you an untreatable infection.⁵

A problem for all hair surgeons worldwide

Worldwide rates of MRSA can be tracked to antibiotic overuse and misuse. As such, excellent and robust health care systems with an abundance of resources are just as vulnerable to MRSA spread as those in less developed countries where less clean facilities and fewer trained staff exist. In fact, MRSA rates are just as high in industrialized "First World" countries as they are in less economically fortunate ones, although the various strains may be different. 6 (See Figure 2.)

FIGURE 2. MRSA infection rates by country. Graph obtained from http://www.cddep.org/tool/mrsa_infection_rates_country



No matter which strain you are dealing with, MRSA can cause a range of infections, including in skin and surgical wounds. This is why out of the list of infectious agents considered "serious" by the U.S. Centers for Disease Control, MRSA is the one that will most affect hair surgeons. MRSA has the potential to cause problems with hair transplant patients even more so than with other forms of elective surgery because the areas with hair can never be completely sterilized. Additionally, there is the problem of asymptomatic carriers. Staff and patients alike may be colonized with MRSA without knowing it, and may easily spread it to each other due to the close proximity during a hair transplant surgery.

Medical tourism to obtain low-cost hair transplantation (or other surgeries) is an additional risk for new MRSA infections and fosters the spread of individual strains along the most heavily traveled air routes. Epidemiological experts can track certain strains or resistant bacteria to specific regions worldwide, and often the new host (the medical tourism patient) is less able to fight off the novel infection than is the native population where the surgery was performed. The native staff also may be unaware of the problems that they cause, since they never see their patients again in most cases. Additionally, appropriate treatment may not be as promptly administered and follow-up care is interrupted, worsening the plight of the patient.

Studies show that about 1 in 3 people carry staph in their nose, usually without any illness. Two in 100 people carry MRSA. No data shows the total number of people who get MRSA skin infections in the community, and data that breaks out MRSA rates with scalp surgeries likewise does not exist at this time.⁸ Given the proximity of the nose (the

most commonly colonized area in asymptomatic carriers) to the scalp, hair surgeries in general are at higher risk. Compounding the danger is that hair surgery is often performed as an outpatient procedure, with minimally trained or licensed personnel who may not adhere to sterile techniques as rigorously as more highly trained individuals.

MRSA carriers

Carriers of MRSA are asymptomatic (Figure 3). Clues to having a carrier would be repeated infections in your patients! The best way to find those carriers is to screen yourself and your staff (including those with minimal patient contact) via culture of nasal passage since the nose is the most commonly colonized mucous membrane area.

Factors that facilitate transmission between both asympwith swab of nasal passage.

FIGURE 3. MRSA infection in an

asymptomatic carrier patient verified

tomatic carriers and infected patients include the following:

- Crowding or close proximity of individuals
- Antimicrobial use
- Contaminated surfaces and shared items
- Compromised skin
- Frequent contact

It goes without saying that most or all of these are factors in hair transplant surgery, and all of them can be controlled with proper vigilance.

MRSA infection presentation and treatment

MRSA will present in several different ways, including infections of the blood, lungs, joints, eyes, and urine. Admittedly, infections in these systems are less common and not as relevant to our field, but they bear mentioning for completeness sake. In hair surgery patient populations, infections usually present in otherwise healthy individuals as a skin infection (Figure 4). In hair surgery patients, look for the following:

- Clusters of sores (that resemble "spider bites")
- Impetigo (pus-filled blisters)
- Any incision that is erythematous, swollen, or has pus
- Erythematous painful boils or abscesses in donor or recipient areas⁹

Infections that recur after one or more courses of antibiotics should immediately raise a red flag. Similarly, a cluster of patient infections without a clear source may



indicate a staff source. The best course of action is to swab the infected area BEFORE BEGINNING TREATMENT WITH

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FIRST-LINE ANTIBIOTICS and send for culture and sensitivities.

This may be a change for practices that are used to starting empiric antibiotics, but it is important for two reasons. First, and most obvious, once the pathogen is known, antibiotic courses then can be tailored to the specific strain and avoid breeding further resistant bacteria. Second, in some countries, certain dangerous bacterial strains need to be reported to infection control authorities and knowing the pathogen involved allows infection control efforts to be more effective worldwide. We are all going to need to do our part if we are going to avoid the serious consequences of our current antibiotic prescribing habits.

One last point worth mentioning is that each practice should screen its patients for random antibiotic use, or incomplete antibiotic use. We are all human, and non-compliance with treatment is common (or even self-treatment with old, leftover, and inappropriate antibiotics). Simply ask the question as a matter of routine to all of your patients, particularly those presenting with any signs of infection.

MRSA action steps

It is easier to ignore these sobering facts and soldier on with our practices without changing any routine. Commonly, physicians consider their area "safe," and that MRSA is a problem in "other places." According to the World Health Organization (WHO), this belief is inaccurate. Their first global report on antibiotic resistance demonstrated soberingly high percentages of S. aureus infections that were reported to be MRSA. That is why the first and best thing you can do to protect your practice and the future of our specialty is to educate yourself.¹⁰

WHO Region	% Staph infections reported to be MRSA
African	80%
Americas	90%
Eastern Mediterranean	>50%
European	60%
South-East Asia	>25%
Western Pacific	80%

(http://www.who.int/mediacentre/news/releases/2014/amr-report/en/)

Below are practical action steps you can take to protect your patients and staff from spreading or contracting MRSA:

- Make a history of MRSA infection a part of your preoperative history. A surprising number of patients are now aware of their MRSA history and can alert you to their infectious potential if you ask.
- Evaluate ALL members of your staff for MRSA—even those who might have minimal patient contact. This involves swabbing the noses of everyone including yourself, which may not sound enjoyable, but is preferable to dealing with an epidemic among your patients.
- 3. Avoid shaving the scalp. Various studies and meta-analyses paradoxically have shown that higher rates of infection occur with shaving than occur without.¹¹
- 4. *Discourage medical tourism*. We all love it when our expertise is sought by patients from outside our usual catchment, and yet where possible, we should be en-

- couraging local treatment options. This reduces the risk or inadequate follow-up treatment for your patient and it also protects you and your staff from novel bacterial strains. Isolationism is economically unhealthy, and in the case of medical tourism, potentially the wiser course.⁷
- 5. Avoid unnecessary perioperative antibiotic use (and emphasize that your patients should take ALL of the antibiotics that you prescribe!). The guidelines for perioperative antibiotics are based on observed rates of infection and are different than we originally were taught in medical school. Not only is it interesting to read, it is our responsibility to keep up on this information, AND it will help you prep for your ABHRS Board Exam (or recertification!). Here are three references for directing your perioperative use of antibiotics:
 - A. Bratzler, D.W., et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health-Syst Pharm.* 2013; 70:195-283. (Also available at http://www.idsociety.org/Antimicrobial_Agents/).

This is a consensus document with over 1,000 references to back up its data, analyses, and suggestions.

- B. http://ecdc.europa.eu/en/healthtopics/Healthcare-associated_infections/guidance-infection-prevention-control/Pages/guidance-perioperative-antimicrobial-prophylaxis.aspx (European Centre for Disease Prevention and Control)
- C. https://www.guideline.gov/summaries/summary/39533. This link is to the guidelines page from the National Guideline Clearinghouse. Another source with expert commentary, which is broken out into age group and surgical site for easy searchability.

The increasing frequency of bacterial infections with a MRSA strain mean that minor injuries could once again kill patients. Since we are in the business of creating minor injuries, it is our responsibility to know the facts and have a high level of suspicion for hair transplant surgery infections that could be MRSA.

References

- For your reference, these are Clostridium Difficile, or CDIFF, Carbapenem-Resistant Enterobacteriaceae, or CRE, and Neisserie Gonorrhoeaea. (From the CDC's 2013 report—see reference #2.)
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- See MRSA History Timeline: http://mrsa-research-center.bsd.uchicago.edu/timeline.html
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