Suppressive Oral Antibiotics in Orthopaedic Prosthetic Joint Infections

John E. Allison
West Virginia School of Osteopathic Medicine

Allison M. Lastinger, MD
West Virginia University, Department of Medicine, Section of Infectious Diseases

John A. Guilfoose, MD
West Virginia University, Department of Medicine, Section of Infectious Diseases

Matthew J. Dietz, MD
West Virginia University, Department of Orthopaedics

Corresponding Author: Matthew J. Dietz, MD, West Virginia University, Department of Orthopaedics, PO Box 9196, Morgantown, WV 26506-9196. Email: mdietz@hsc.wvu.edu

Funding: No internal or external funding was received in support of this study.
No regulatory approval was required for this study.

Abstract
In orthopaedics, the use of oral suppressive antibiotics for the treatment of implant related infection was a treatment regimen that had been reserved only for patients who were unable to tolerate surgery. Recent literature has begun to demonstrate the benefits of utilizing suppressive antibiotics as an adjuvant treatment in addition to surgical debridement. The use of oral suppressive antibiotics carries with it inherent hurdles regarding dosing, tolerance, side effects, and cost that need to be considered. The purpose of this review is to act as a guide for orthopaedic surgeons and medical providers to allow them to safely utilize oral suppressive antibiotic regimens as part of their treatment algorithm.

Introduction
Though the risk of joint arthroplasty infection is low (approximately 1%), those who become infected generally have poor prognoses, with the five-year prosthetic survival rates ranging from 38% to 65%.1 Patients who become infected have several treatment options. Some infections can be treated with irrigation and debridement and retention of the components. For more severe infections, single- or two-stage revision may be performed.2 Fusion or amputation of the limb are also options in severe cases. Both irrigation and debridement as well as revisions are usually followed by two to six weeks of intravenous antibiotics.3 A change in the paradigm has been the addition of oral suppressive antibiotics for a period of time (months – years) after surgical debridement and cessation of the parenteral antibiotic treatment. Though many studies agree that chronic oral antibiotics help to prevent further infections, the best treatment guidelines for the use of these antibiotics differs in the literature. Some have concluded that the duration of antibiotic treatment plays a role in treatment effectiveness,4 while others believe that only the choice of antibiotic is a major factor.5 In addition, though many infectious disease clinicians would recommend suppression, most vary widely as to how long they suggest treatment be prescribed.6 In a survey of the Emerging Infections Network, 23% of physicians would treat for months, 35% for years, and 41% for life.6

The purpose of this review is to examine literature surrounding the use of chronic oral antibiotics for the suppression of joint replacement infections and to act as a guide for the treating healthcare team, including orthopaedic surgeons, infectious disease specialists, and internal medicine physicians. The indications for treatment with chronic oral antibiotics are discussed, as well as the relevant organisms responsible for prosthetic infections. Antibiotics commonly used in the treatment of prosthesis infection are included, along with their indications for use, side effects, lab monitoring guidelines, and contraindications.

Indications for Chronic Suppression
Many studies have suggested that chronic oral antibiotics be utilized when a surgical treatment is not feasible.3,4,6-8 The Infectious Diseases Society of America (IDSA) recommends that suppressive antibiotic therapy be used in situations where the patient refuses further surgical revision or in cases where surgical revision would cause significant risk to the patient’s limb or life.3 It has also been suggested that patients who are older and have a limited life expectancy can be placed on chronic oral antibiotics.4 Another factor that may warrant the use of chronic antibiotics is a high risk of infection relapse, such as patients with a history of multiple joint infections, immunosuppression, comorbidities that predispose to periprosthetic joint infection, and infection with a virulent pathogen.1

Infectious Agents
The proper chronic oral antibiotic treatment for prosthetic joint infection (PJI) is dependent upon the causative infectious agent. Tornero et al. identified proper antibiotic treatment of the responsible infectious agent as the biggest indicator of treatment success.5 Culturing the infected area is critical to determining a proper antibiotic regimen. The majority of pathogens responsible for arthroplasty infections are Gram-positive bacteria, with multiple studies illustrating that Staphylococcal species alone make up the majority of these infections.1,4,5,7,9 Infections caused by Staphylococcus aureus (S. aureus) are generally
more severe than infections caused by other organisms. In most studies, joint arthroplasty infections where the causative agent is a *Staphylococcal* species make up over half of the cases seen. Several studies have indicated that infections caused by *S. aureus* carry a poor prognosis. In addition, patients with *S. aureus* infections have been shown to benefit the most from chronic suppressive antibiotics. In one study, the infection-free survival rate in patients with *S. aureus* infections improved from 40% to 57% with the use of chronic suppressive antibiotics. For medications suitable for the long-term treatment of methicillin-sensitive *Staphylococcus*, the IDSA recommends cephalexin, dicloxacillin, clindamycin, or amoxicillin-clavulanate. Medications suitable for the long-term treatment of methicillin-resistant *Staphylococcus* include doxycycline, minocycline, or trimethoprim/sulfamethoxazole. Rifampin can also be added to the treatment regimen, but it is not generally recommended for use in isolation due to the risk of resistance or rarely used in the setting of chronic suppression due to its numerous side effects.

Non-*Staphylococcal* Gram-positive infections of prostheses are caused by species such as β-hemolytic streptococci, *viridans streptococci*, *Enterococcus* species, and *Propionibacterium* species. The preferred treatment for these pathogens is either penicillin V or amoxicillin, unless resistance to these medications is present. The usefulness of long-term suppressive antibiotics to treat non-*S. aureus* Gram-positive arthroplasty infections is uncertain. Siqueira et al. reported that patients treated with chronic antibiotics for non-*S. aureus* arthroplasty infections had no change in five-year infection free survival rate compared to those who did not receive chronic antibiotic treatment.

Gram-negative bacteria that commonly cause arthroplasty infections include *Pseudomonas aeruginosa*, *Escherichia coli*, *Proteus* species, and *Enterobacter species*. Many times, fluoroquinolones are used empirically to treat Gram-negative infections but, if an organism is known to be resistant to fluoroquinolones, their use is not recommended. The IDSA notes that the use of fluoroquinolones for the long-term suppression of Gram-negative prosthesis infections is not unanimously recommended.

### Antibiotic Treatments

The choice of antibiotic agent for the chronic suppression of joint arthroplasty infections is of the utmost importance. In vitro susceptibilities, allergies, side effect profiles, contraindications, and intolerances must all be taken into account. In addition, the growing threat of antibiotic resistance means that care must be taken when deciding whether chronic antibiotic treatment would be of sufficient benefit to the patient. Many antibiotics also require dose adjustments based on renal function and require periodic lab monitoring to assess liver, kidney, and complete blood counts. The following is a review of the most common antibiotics used in chronic infection suppression for joint arthroplasties. A list of the IDSA-preferred treatments for certain species of bacteria is summarized in Table 1. For the dosing, side effects, lab monitoring requirements, indications for use, and contraindications for these antibiotics, refer to Table 2.

#### Table 1. Summary of IDSA-preferred treatments for common infectious agents in long-term joint infection suppression.

<table>
<thead>
<tr>
<th>Infectious Agent</th>
<th>Preferred Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSSA</td>
<td>Cephalexin</td>
</tr>
<tr>
<td>MRSA</td>
<td>TMP/SMX, doxycycline, or minocycline</td>
</tr>
<tr>
<td>β-hemolytic Strep. spp, <em>Enterococcus</em> spp (penicillin susceptible), <em>Propionibacterium</em> spp</td>
<td>Penicillin or amoxicillin</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>Ciprofloxacin</td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td>TMP/SMX</td>
</tr>
</tbody>
</table>

**Table 1.** Summary of IDSA-preferred treatments for common infectious agents in long-term joint infection suppression.

**Amoxicillin or Amoxicillin-clavulanate (e.g., Augmentin)**

Amoxicillin is the preferred treatment for non-*Staphylococcal* Gram-positive infections such as *streptococci*, *Enterococcus* species, and *Propionibacterium* species. Amoxicillin has no effect on methicillin-resistant *Staphylococci* and should not be given for methicillin-sensitive *Staphylococci* without the addition of clavulanate. As rifampin has not been shown to decrease plasma levels of amoxicillin, amoxicillin has been suggested as a possible combination therapy with rifampin in the treatment of Gram-positive infections.

Amoxicillin is a generally well-tolerated antibiotic. The Food and Drug Administration (FDA) has not issued any black box warnings for amoxicillin.

Amoxicillin and clavulanate are excreted through the urine. Dosing should be adjusted according to renal function. The addition of clavulanate does not allow amoxicillin to be used against methicillin-resistant *Staphylococci*, as these bacteria have a mutation which prevents β-lactam antibiotics from interacting with the bacterial cell wall.

**Cephalexin (e.g., Keflex)**

Cephalexin is the preferred treatment for infections caused by methicillin-sensitive *S. aureus* and may be used as an alternative treatment for β-hemolytic *streptococci* and *Propionibacterium* species. Cephalexin should
**Table 2. Dosing, side effects, lab monitoring requirements, indications for use, and contraindications for antibiotics.**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dosing</th>
<th>Indications for Use</th>
<th>Side effects/Complaints</th>
<th>Lab monitoring</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>500 mg PO tid*</td>
<td>β-hemolytic *Strep. spp, *Enterococcus spp (penicillin susceptible), *Propionibacterium spp</td>
<td>Nausea, diarrhea, vomiting, rash, allergic reaction, stomach cramps, <em>C. diff.</em>-related colitis, oral thrush, vaginal yeast infection</td>
<td>Liver function, kidney function, complete blood cell count</td>
<td>Penicillin allergy</td>
</tr>
<tr>
<td>Amoxicillin-clavulanate</td>
<td>500 mg PO tid*</td>
<td>MSSA, most <em>Strep. spp.</em>, some Gram negatives</td>
<td>Nausea, diarrhea, vomiting, rash, allergic reaction, gastrointestinal irritation, <em>C. diff.</em>-related colitis, oral thrush, vaginal yeast infection, trouble breathing</td>
<td>Liver function, kidney function, complete blood cell count</td>
<td>Penicillin allergy</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>500 mg PO tid or qid*</td>
<td>*MSSA, β-hemolytic <em>Strep. spp, <em>Propionibacterium spp</em></em>, some Gram negatives</td>
<td>Nausea, diarrhea, vomiting, rash, allergic reaction, stomach cramps, <em>C. diff.</em>-related colitis, oral thrush, vaginal yeast infection</td>
<td>Liver function, kidney function</td>
<td>Cephalosporin allergy</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>500 mg PO bid*</td>
<td>*Pseudomonas aeruginosa, E. coli, Proteus spp, Enterobacter spp, MSSA, some MRSA</td>
<td>Tendon damage, peripheral neuropathy (potentially irreversible), cardiac arrhythmia/QT prolongation, nausea, diarrhea, vomiting, abnormal liver function tests, dizziness, headache, trouble sleeping, GI irritation, chest pain, rash</td>
<td>Liver function, kidney function, complete blood cell count EKG prior to starting treatment</td>
<td>QT prolongation, myasthenia gravis, caution with use in elderly, quinolone allergy, pregnancy</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>300 mg PO qid*</td>
<td>MSSA, some MRSA, most <em>Strep</em> spp</td>
<td>Decreased blood platelets, decreased neutrophil count, nausea, diarrhea, vomiting, rash, <em>C. diff.</em>-related colitis, allergic reaction, stomach cramps, oral thrush, vaginal yeast infection</td>
<td>Liver function, kidney function, complete blood cell count</td>
<td>Clindamycin allergy</td>
</tr>
<tr>
<td>Dicloxacillin</td>
<td>500 mg PO tid or qid*</td>
<td>MSSA, MS CoNS, Group-B <em>Strep. spp</em></td>
<td>Nausea, diarrhea, vomiting, rash, allergic reaction, stomach cramps, itching, <em>C. diff.</em>-related colitis</td>
<td>Liver function, kidney function, complete blood cell count</td>
<td>Penicillin allergy</td>
</tr>
<tr>
<td>Doxycycline or Minocycline</td>
<td>100 mg PO bid**</td>
<td>MSSA, MRSA, MS CoNS, MR CoNS, Diphtheroid-like bacilli, <em>Propionibacterium spp</em></td>
<td>Tooth discoloration, sun-sensitive skin, pill esophagitis, high blood pressure, head pain, loss of appetite, <em>C. diff.</em>-related colitis, nausea, diarrhea, vomiting, throat irritation, allergic reaction, oral thrush, vaginal yeast infection</td>
<td>Liver function, kidney function, complete blood cell count</td>
<td>Tetracycline allergy, myasthenia gravis, pregnancy</td>
</tr>
</tbody>
</table>

*continued on next page*
**Antibiotic** | **Dosing** | **Indications for Use** | **Side effects/ Complaints** | **Lab monitoring** | **Contraindications**
--- | --- | --- | --- | --- | ---
Levofloxacin | 500 mg PO qd* | VGS, MSSA, MS CoNS, *E. coli*, *Proteus* spp, *Pseudomonas* spp | Tendon damage, cardiac arrhythmia/QT prolongation, nausea, diarrhea, vomiting, head pain, chronic trouble sleeping, allergic reaction, oral thrush, vaginal yeast infection, stomach cramps, taste problems, trouble breathing | Liver function, kidney function, complete blood cell count, EKG prior to starting treatment | QT prolongation, myasthenia gravis, caution with use in elderly, quinolone allergy, pregnancy

Linezolid | 600 mg PO bid | Gram-positive infections | Vision changes, cytopenias, anemia, lactic acidosis, neuropathy, nausea, diarrhea, vomiting, head pain, abnormal liver function tests, decreased blood platelets, rash, allergic reaction, taste problems | Liver function, complete blood cell count, eye examination | Linezolid allergy, concurrent use with MAOI inhibitor (including SSRIs)

Rifampin**** | 300-450 mg PO bid* | Organisms which produce a biofilm (e.g. *Staphylococcal* infections) | Liver disease, diarrhea, abnormal stool color, abnormal urine color, stomach cramps, discolored saliva, discolored tears, discolored sweat, abnormal liver function tests, flu-like symptoms, allergic reaction, oral thrush | Liver function, kidney function, complete blood cell count | Concurrent alcohol use, elevated liver enzymes

Trimethoprim/ Sulfamethoxazole | 1 DS tab PO bid* | MSSA, MSSA, MS CoNS, MR CoNS, VGS, *Enterobacteriaceae* | Sun-sensitive skin, GI disorders, head pain, loss of appetite, sluggishness, hepatitis, Stevens-Johnson Syndrome, toxic epidermal necrolysis, worsening renal function and hyperkalemia, cytopenias, nausea, diarrhea, vomiting, rash, allergic reaction, fever upon administration | Liver function, kidney function, complete blood cell count, urinalysis | Chronic kidney disease, sulfa allergy

*Spp – species; *C. diff.* – *Clostridium difficile; Strep.* – *Streptococcus; MAOI – monoamine oxidase inhibitors; MSSA – methicillin-sensitive *Staphylococcus aureus*; MRSA – methicillin-resistant *Staphylococcus aureus*; MS CoNS – methicillin-sensitive coagulase-negative *staphylococci; MR CoNS - methicillin-resistant coagulase-negative staphylococci; E. coli – *Escherichia coli; SSRIs –selective serotonin reuptake inhibitors; VGS – viridans group streptococci

*Requires dose adjustment for renal function.
**Counsel on timing of medication as it interacts with calcium.
***Requires dose adjustment for dialysis patients.
****Must be given in combination with another antibiotic to prevent resistance.
not be given for methicillin-resistant Staphylococci. Cephalexin is a generally well-tolerated antibiotic. The FDA has not issued any black box warnings for cephalexin.

Cephalexin is excreted through the urine within eight hours. Dosing should be adjusted according to renal function. Cephalexin cannot be used against methicillin-resistant Staphylococci, as these bacteria have a mutation which prevents β-lactam antibiotics from interacting with the bacterial cell wall.

Clindamycin

The IDSA suggests clindamycin as an alternative treatment for methicillin-sensitive S. aureus, though it can also be used for infections caused by streptococcal species and, in some cases, methicillin-resistant S. aureus. Clindamycin is commonly used when the patient is allergic to β-lactam antibiotics, such as amoxicillin or cephalexin. As it has been suggested that rifampin can lower plasma levels of clindamycin, clindamycin is not suggested to be given with rifampin as a combination therapy.

The FDA has given clindamycin a black box warning for its risk in causing Clostridium difficile-associated diarrhea. Patients should report persistent diarrhea, stomach pain, and blood or mucus in their stool. They should also be educated not to use any antidiarrheal medications should these side effects occur.

Clindamycin is excreted in the urine and feces, however, dosing does not need to be adjusted for renal function.

Dicloxacillin

Dicloxacillin is an alternative medication for the treatment of streptococcal and methicillin-sensitive Staphylococcal infections. Dicloxacillin should not be given for methicillin-resistant Staphylococcal species.

Dicloxacillin is a generally well-tolerated antibiotic. The FDA has not issued any black box warnings for dicloxacillin.

Dicloxacillin is excreted in the urine and feces as an unchanged drug. Dosing should be adjusted according to renal function. Dicloxacillin cannot be used against methicillin-resistant Staphylococci, as these bacteria have a mutation which prevents β-lactam antibiotics from interacting with the bacterial cell wall.

Doxycline or Minocycline

Doxycline and minocycline are used as treatment for methicillin-resistant Staphylococcal species. They can also be used as an alternative for methicillin-sensitive Staphylococcal species and Propionibacterium species when the patient is allergic to β-lactam antibiotics, such as amoxicillin or cephalexin.

Patients taking tetracyclines should be informed about the risk of tooth discoloration, sun-sensitive skin, and pill esophagitis in less than 1% of patients. Tetracyclines should not be given to patients with myasthenia gravis or patients who are pregnant.

Doxycline and minocycline excretion both occur in the urine and the feces. As both doxycline and minocycline absorption are decreased by calcium, patients should be instructed to avoid calcium-containing substances for one hour before or two hours after taking the antibiotic.

Tetracyclines are bacteriostatic antibiotics and have an antagonistic effect on penicillins; thus, the two should not be used in combination.

Fluoroquinolones (e.g., Cipro, Levaquin)

The IDSA recommends that a fluoroquinolone be given as a companion drug for rifampin in treating Staphylococcal prosthetic joint infections, as long as in vitro sensitivities and patient allergies allow. In a study by Tornero et al., only four out of 53 patients with Gram-positive infections treated with a combination of rifampin and levofloxacin experienced treatment failure. In addition, Rodríguez-Pardo et al. call ciprofloxacin the cornerstone of Gram-negative prosthesis infection treatment, citing its oral bioavailability, good bone diffusion, and activity against biofilm.

The FDA has given fluoroquinolones a black box warning for the risk of causing tendonitis or tendon rupture in less than 1% of patients. This complication is more prevalent in those over the age of sixty, those on steroids, and transplant recipients. Patients who develop tendon pain should rest and seek medical help. In addition, the FDA warns that fluoroquinolones can cause potentially irreversible peripheral nerve damage, and patients who exhibit symptoms of pain, numbness, tingling, or weakness in their arms, hands, legs, or feet should stop taking fluoroquinolones and call their doctor. This complication occurs in less than 1% of patients. Fluoroquinolones also have the potential to cause QT prolongation in less than 1% of patients and should not be given to those with an already existing QT prolongation.

Having an electrocardiogram (EKG) prior to treatment initiation can help determine this risk factor. Fluoroquinolones should not be given to patients with myasthenia gravis or patients who are pregnant.
Levofloxacin and ciprofloxacin are both excreted through the urine and feces. Dosing should be adjusted according to renal function.

**Linezolid (e.g., Zyvox)**

Linezolid is effective against many Gram-positive infections, including methicillin-resistant *Staphylococci* or vancomycin-resistant enterococci. For this reason, it should be reserved for pathogens which are not susceptible to other antibiotics. The efficacy of linezolid has been shown by Rao et al., who treated 53 Gram-positive orthopaedic infections with linezolid with only one treatment failure. However, only one patient was treated with linezolid for chronic infection suppression due to the fact that they were allergic to many other antibiotics. This patient had to discontinue treatment with linezolid after 24 months due to the development of mild blurry vision, tingling, and numbness. The treatment was ultimately switched to minocycline for chronic suppression. Therefore, the ability to use linezolid as a long-term infection suppressor is still in question. Tornero et al. found that a combination therapy of linezolid and rifampin led to more treatment failures than with just linezolid alone; thus, they do not suggest that the two be used together.

As linezolid has the ability to cause cytopenias and anemias, Rao et al. suggest hematologic monitoring on a weekly basis. A decrease in hemoglobin is seen in 1% to 16% of patients, thrombocytopenia is seen in less than 1% to 16% of patients, and leukopenia is seen in less than 1% to 2% of patients. Vision changes are also a possibility in less than 1% of patients, so ophthalmologic monitoring is suggested if treatment lasts for over two months. Linezolid is a weak monoamine oxidase inhibitor (MAOI), and consequently should not be used with MAOI inhibitors, including selective serotonin reuptake inhibitors (SSRIs) due to an increased risk of serotonin syndrome. Linezolid is excreted in the urine and feces. Dosing should be adjusted according to renal function.

All Gram-negative bacteria are effectively resistant to linezolid, as they are able to pump the linezolid molecules out of cells faster than it can get in.

**Rifampin**

Rifampin has been shown to have good bioavailability and is active against *Staphylococci* which are able to adhere to surfaces such as arthroplasties. The IDSA suggests the use of rifampin following *Staphylococcal* prosthetic joint infection for three months following total hip arthroplasty and six months following total knee arthroplasty. Rifampin must be used in combination with other antibiotics to prevent resistance. Levofloxacin and ciprofloxacin are suggested as companion drugs, with trimethoprim/sulfamethoxazole, minocycline or doxycycline, cephalaxin, or dicloxacillin being alternatives if allergies or in vitro susceptibilities suggest them. However, Tornero et al. found that combining rifampin with ciprofloxacin, levofloxacin, or amoxicillin leads to better treatment outcomes than combining rifampin with linezolid, clindamycin, or trimethoprim/sulfamethoxazole. The use of rifampin for indefinite oral antimicrobial suppression is not generally recommended by the IDSA.

Patients should be informed that rifampin may cause liver dysfunction. If given to patients with liver disease, liver function should be monitored closely before treatment begins and every two to four weeks during treatment. Patients should also be aware that rifampin may cause a harmless discoloration of their stool, urine, saliva, tears, or sweat. This discoloration may permanently stain contact lenses. The frequency of this discoloration has not been defined.

**Rifampin is excreted in the urine and feces. Dosing should be adjusted according to renal function.**

**Trimethoprim/Sulfamethoxazole (TMP/SMX) (e.g., Bactrim)**

TMP/SMX is used as a treatment for methicillin-resistant *Staphylococci* and Enterobacteriaceae species. Tornero et al. found that a combination therapy of TMP/SMX and rifampin led to more treatment failures than with just TMP/SMX alone and thus do not suggest that the two be used together.

Patients with chronic kidney disease should not be treated with TMP/SMX. TMP/SMX may cause worsening renal function, as well as anemias and cytopenias. Therefore, renal function and complete blood counts should be taken at frequent intervals.

TMP/SMX is excreted in the urine as metabolites and unchanged drug. Dosing should be adjusted according to renal function.

**Discussion**

The decision to place a patient on chronic suppressive antibiotics can be based on several factors. In situations where a surgical revision is inappropriate, either because of risk to the patient or patient refusal, suppressive antibiotics are a viable option to decrease the overall bioburden in an attempt to prevent greater systemic illness. Other patient populations which may indicate chronic antibiotic use include patients who are immunocompromised and patients who have a short life expectancy. Though not as effective as surgical revision, chronic suppressive antibiotics have been shown to reduce the occurrence of clinically significant infection.

The antibiotic selected for use in chronic infection suppression should be based on multiple factors. The antibiotic must be effective against the responsible pathogen; therefore, sensitivities must be taken into account during the selection process. In addition, due to the...
length of treatment, side effects must be taken into consideration. β-lactam antibiotics are generally well-tolerated and are ideal for long-term use. However, patient allergies and intolerances must also be considered and may preclude these antibiotics from use. Whether due to in vitro sensitivities or allergies, other classes of antibiotics with more serious side effects may be needed.

Monitoring of patients on long-term antibiotics is important to ensuring continuing patient health. After beginning treatment, most antibiotics require dose adjustments to compensate for renal function. Fluoroquinolones such as ciprofloxacin and levofloxacin may also necessitate an EKG prior to treatment, in order to check for QT prolongation. Almost all antibiotics require periodic complete blood counts, as well as liver and kidney function testing. In addition, the use of linezolid for a treatment duration of longer than two months requires periodic eye examinations. Patients must also be educated on nutrition and the timing of doses to ensure that the greatest effect of the medication is attained.

Treatment failure with chronic oral antibiotics has been associated with multiple factors. Prendki et al. found that low albumin levels, the presence of a sinus tract, and infections caused by Staphylococcus aureus were all associated with treatment failure. They found that patients with an average albumin level of 22 g/L had more adverse events than those with an average level of 31 g/L, and concluded that educating the patient on proper nutrition is important in avoiding hypoalbuminemia and preventing treatment failure.6 In addition, Byren et al. has found that a treatment duration of less than six months has been associated with treatment failure, especially in the period three to four months after antibiotic discontinuation,4 though failure has been seen up to a year after treatment cessation.9 However, a recent study with a median treatment duration of 69 days found that treatment duration was not an important factor and that antibiotic selection was the most important factor. It is unclear whether the duration of therapy impacts outcome.

The risk of prosthetic infection must ultimately be assessed against the threat of antibiotic resistance, as well as the possibility of side effects. Care must be taken during antibiotic selection to ensure that the organism is susceptible to the antibiotic chosen while having as narrow a spectrum of activity as possible. Using antibiotics that are more powerful than necessary, or for a longer amount of time than they should be, can lead to an increase in antibiotic resistance. For this reason, there is a need for more information concerning the length of treatment necessary to suppress prosthetic infection. Discovering the optimal length of treatment would not only reduce the risk of side effects from the use of chronic antibiotic use, but also decrease the cost to the patient so they are not paying for unnecessary treatment. Future research should be conducted to assess treatment length. In addition, current practices performed by clinicians can be evaluated to determine the best treatment methods.

Conclusion

In conclusion, oral suppressive antibiotics may have an important role in the long-term treatment of prosthetic joint infection. The clear delineation of what this role is has yet to be fully elucidated, but many studies have shown that the use of antibiotics for the purpose of suppressing further joint infection can be effective in certain patient populations. This assertion is especially true for those patients who cannot undergo further joint operations, who are immunocompromised, or who have a short life expectancy. The use of such antibiotics should always focus on optimized care for the infecting organism and patient needs. Collaboration between orthopaedic surgeons, infectious disease specialists, and medical colleagues should always be attempted to provide the safest experience and most efficacious treatment for patients.

References