Egyptian consensus for the use of antimicrobial therapy in Preoperative prophylaxis, surgical site infections and diabetic foot infections

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Received: 9 September 2019
Accepted: 24 September 2020
Published: 14 February 2020

The Egyptian Journal of Surgery 2020, 39:1–10

Use of antimicrobials in surgical prophylaxis

These consensuses focus on primary perioperative prophylaxis for the prevention of an initial infection, the administration of the first dose of antimicrobial beginning within 60 min before surgical incision is recommended, but administration of vancomycin and fluoroquinolones should begin within 120 min before surgical incision because of the prolonged infusion times required for these drugs. Dosing In general, it is advisable to administer prophylactic agents in a manner that will ensure adequate levels of drug in serum and tissue for the interval during which the surgical site is open, If the duration of the procedure exceeds two half-lives of the antimicrobial or there is excessive blood loss (>1500 ml), the re-dosing interval should be measured from the time of administration of the preoperative dose, not from the beginning of the procedure. The selection of certain antimicrobial in most of the surgeries is shown in Table 2, and the special dosing of antimicrobials in patients with renal impairment is shown in Table 3.

Surgical site infections "SSI"

SSIs or wound infections are the most common adverse events affecting hospitalized surgical patients. The most important therapy for an SSI is to open the incision, evacuate the infected material, and continue dressing changes until the wound heals by secondary intention. Before starting an empiric antibiotics course, culture should be done. The antibiotic choice is usually empiric but can be supported by Gram stain, culture of the wound contents, the site of surgery, and the hospital antimicrobial susceptibility test system 'Hospital Biogram'. The selection of Antibiotics for treatment of incisional surgical site infections is summarized in table 4.

Diabetic foot infections

Diabetic Foot infections typically begin in a wound, most often a neuropathic ulceration, while all wounds are colonized with microorganisms, and the presence of infection is defined by greater than or equal to 2 classic findings of inflammation or purulence. Most DFIs are polymicrobial, with aerobic gram-positive cocci, and especially Staphylococci spp., the most common causative organisms. Clinicians should consider the possibility of infection occurring in any foot wound in a patient with diabetes. Clinicians should evaluate a diabetic patient presenting with a foot wound at three levels: the patient as a whole, the affected foot or limb, and the infected wound. The clinically noninfected wounds should not be treated with antibiotic therapy. Prescription of antibiotic therapy for all infected wounds should be done, but with caution, as it is often insufficient unless combined with appropriate wound debridement. The clinicians need to select an empiric antibiotic regimen on the basis of the severity of the infection and the likely etiologic agent(s) (shown in Table 6).

Egyptian J Surgery 39:1–10

1110-1121

The recommendations mentioned in this consensus about antibiotic prophylaxis in surgery were taken from the American Society of Health-System Pharmacists, the Infectious Diseases Society of America (IDSA), the Surgical Infection Society (SIS), and the Society for Healthcare Epidemiology of America clinical practice guidelines for antibiotic prophylaxis in surgery in 2013.

The recommendations mentioned in this consensus about surgical site infections (SSIs) were taken from 2014 IDSA guidelines for the management of SSTIs, and the recommendations mentioned in this consensus about antibiotic use in diabetic foot infection (DFI) were taken from IDSA Guidelines 2012 for the management of DFI.

Use of antimicrobials in surgical prophylaxis [1]

These consensuses focus on primary perioperative prophylaxis for the prevention of an initial infection.

Timing of initial dose

The antimicrobial agent should be administered at a time to provide serum and tissue concentrations exceeding the minimum inhibitory concentration for the probable organisms associated with the procedure, at the time of incision, and for the duration of the procedure, so administration of the first dose of antimicrobial beginning within 60 min before surgical incision is recommended, but administration of vancomycin and fluoroquinolones should begin within 120 min before surgical incision because of the prolonged infusion times required for these drugs.

Dosing

In general, it is advisable to administer prophylactic agents in a manner that will ensure adequate levels of drug in serum and tissue for the interval during which the surgical site is open.

Weight-based dosing

The dosing of most antimicrobials in pediatric patients is based on body weight, but the dosing of many antimicrobials in adults is not based on body weight, because it is safe, effective, and convenient to use standardized doses for most of the adult patient population.

Such standardized doses avoid the need for calculations and reduce the risk for medication errors; however, in obese patients, especially those who are morbidly obese, serum and tissue concentrations of some drugs may differ from those in normal-weight patients because of pharmacokinetic alterations that depend on the lipophilicity of the drug and other factors.

If weight-based dosing is warranted for obese patients, it has not been determined whether the patient's ideal body weight or total (i.e. actual) body weight should be used, for dosing a lipophilic drug (e.g. vancomycin) could result in subtherapeutic concentrations in serum and tissue, and the use of actual body weight for dosing a hydrophilic drug (e.g. an aminoglycoside) could result in excessive concentrations in serum and tissue.

Doubling the normal dose of cephalosporins or making fewer adjustments based on renal dysfunction may produce concentrations in obese patients similar to those achieved with standard doses in normal-weight patients.

Re-dosing

Generally intraoperative re-dosing is needed to ensure adequate serum and tissue concentrations of the antimicrobial.

If the duration of the procedure exceeds two half-lives of the antimicrobial or there is excessive blood loss (>1500 ml), the re-dosing interval should be measured from the time of administration of the preoperative dose, not from the beginning of the procedure.

Re-dosing may also be warranted if there are factors that shorten the half-life of the antimicrobial agent (e.g. extensive burns).

Re-dosing may not be warranted in patients in whom the half-life of the antimicrobial agent is prolonged (e.g. patients with renal insufficiency or renal failure) (see Table 1 for antimicrobial specific re-dosing recommendations).

Duration

The shortest effective duration of antimicrobial administration for preventing SSI is not known; however, evidence is mounting that postoperative antimicrobial administration is not necessary for most procedure.

The duration of antimicrobial prophylaxis should be less than 24 h for most procedures.

Duration of prophylaxis

The recommendations for a shortened postoperative course of antimicrobials involving a single dose or continuation for less than 24 h are provided.

Selection of antimicrobial(s) in preoperative prophylaxis

Antimicrobial prophylaxis may be beneficial in surgical procedures associated with a high rate of infection (i.e. clean–contaminated or contaminated procedures) and in certain clean procedures where there are severe consequences of infection (e.g. prosthetic implants), even if infection is unlikely.

Prophylactic antimicrobials are not indicated for clean surgical procedures, except for the patients at high risk of infections like diabetic patients, smokers, patients receiving immunosuppressant therapy, and immunocompromised patients and patients who have received an implant as in cardiac and vascular surgeries.

The selection of certain antimicrobial in most of the surgeries is shown in Table 2, and the special dosing of antimicrobials in patients with renal impairment is shown in Table 3 [2].

Table 1 Recommended doses and redosing intervals for commonly used antimicrobials for surgical prophylaxis

Recommended dose			Half-life in adults with normal renal function, hr	Recommended re-dosing interval (from initiation of preoperative dose; hr)[c]
Antimicrobial	Adults[a]	Pediatrics[b]		
Ampicillin–sulbactam 3 g	3 g (ampicillin 2 g Sulbactam 1 g)	50 mg/kg of the ampicillin component	0.8–1.3	2
Ampicillin	2 g	50 mg/kg	1–1.9	2
Cefazolin	2 g, 3 g for patients weighing ≥120 kg	30 mg/kg	1.2–2.2	4
Cefuroxime	1.5 g	50 mg/kg	1–2	4
Cefotaxime	1 g[d]	50 mg/kg	0.9–1.7	3
Cefoxitin	2 g	40 mg/kg	0.7–1.1	2
Ceftriaxone	2 g[e]	50–75 mg/kg	5.4–10.9	NA
Ciprofloxacin[f]	400 mg	10 mg/kg	3–7	NA
Clindamycin	900 mg	10 mg/kg	2–4	6
Fluconazole	400 mg	6 mg/kg	20	NA
Gentamicin	5 mg/kg based on dosing weight (single dose)	2.5 mg/kg based on dosing weight	2–3	NA
Levofloxacin	500 mg	10 mg/kg	6–8	NA
Metronidazole	500 mg	15 mg/kg Neonates weighing <1200 g should receive a single 7.5 mg/kg dose	6–8	NA
Moxifloxacin	400 mg	10 mg/kg	8–15	NA
Piperacillin–tazobactam	3.375 g	Infants 2–9 months: 80 mg/kg of the piperacillin component Children >9 months and ≤40kg: 100 mg/kg of the piperacillin component	0.7–1.2	2
Vancomycin	15 mg/kg	15 mg/kg	4–8	NA
Oral antibiotics for colorectal surgery prophylaxis (used in conjunction with a mechanical bowel preparation)				
Erythromycin base	1 g	20 mg/kg	0.8–3	NA
Metronidazole	1 g	15 mg/kg	6–10	NA
Neomycin	1 g	15 mg/kg	2–3 (3% absorbed under normal gastrointestinal conditions)	NA

[a]Adult doses are obtained from the studies cited in each section. When doses differed between studies, expert opinion was used, with the most-often recommended dose. [b]The maximum pediatric dose should not exceed the usual adult dose. [c]For antimicrobials with a short half-life (e.g. cefazolin, cefoxitin) used before long procedures, redosing in the operating room is recommended at an interval of ~two times the half-life of the agent in patients with normal renal function. Recommended redosing intervals marked as 'not applicable' are based on typical case length; for unusually long procedures, redosing may be needed. [d]Although FDA-approved package insert labeling indicates 1 g, 14 experts recommend 2 g for obese patients. [e]When used as a single dose in combination with metronidazole for colorectal procedures. [f]While fluoroquinolones have been associated with an increased risk of tendinitis/tendon rupture in all ages, use of these agents for single-dose prophylaxis is generally safe. [g]In general, gentamicin for surgical antibiotic prophylaxis should be limited to a single dose given preoperatively. Dosing is based on the patient's actual body weight. If the patient's actual weight is more than 20% above ideal body weight (IBW), the dosing weight (DW) can be determined as follows: DW=IBW+0.4(actual weight–IBW).

Surgical site infections

SSIs or wound infections are the most common adverse events affecting hospitalized surgical patients (Brennan, 1991) [3,4].

SSIs classification

SSIs are divided into the categories of superficial incisional SSI, deep incisional SSI, and organ/space SSI. Superficial incisional SSIs involve only the subcutaneous space (as shown in Fig. 1 of skin layers), occur within 30 days of the surgery, and are documented with at least one of the following:

(1) Purulent incisional drainage.
(2) Positive culture of aseptically obtained fluid or tissue from the superficial wound.
(3) Local signs and symptoms of pain or tenderness, swelling, and erythema after the incision is opened by the surgeon (unless culture negative), or
(4) Diagnosis of SSI by the attending surgeon or physician based on their experience and expert opinion.

Table 2 Recommendations for surgical antimicrobial prophylaxis

Type of procedure	Recommended agents[a,b]	Alternative agents in patients with β-lactam allergy	Strength of evidence[c]
Biliary tract			
Open procedure	Cefazolin, cefoxitin, cefotetan, ceftriaxone[k] ampicillin–sulbactam[h]	Clindamycin or vancomycin +aminoglycoside[g] or fluoroquinoloneh[j] Metronidazole+aminoglycoside[g] or fluoroquinoloneh[j]	A
Colorectal[m]	Cefazolin+metronidazole, cefoxitin, ampicillin–sulbactam[h] ceftriaxone +metronidazole[n]	Clindamycin+aminoglycoside[g] or fluoroquinolone[h,j] metronidazole +aminoglycoside[g] or fluoroquinolone[h,j]	A
Laparoscopic procedure			
Elective, low risk[l]	None	None	
Elective, high risk[l]	Cefazolin, cefoxitin, ceftriaxone[k] Ampicillin–sulbactam[h]	Clindamycin or vancomycin +aminoglycoside[g] or fluoroquinolone[h],j Metronidazole+aminoglycoside[g] or fluoroquinolone[h,j]	
Gastroduodenal			
Procedures involving entry into lumen of gastrointestinal tract (bariatric, pancreaticoduodenectomy[f])	Cefazolin	Clindamycin or vancomycin +aminoglycoside[g] or fluoroquinolone[h,j]	A
Procedures without entry into gastrointestinal tract (antireflux, highly selective vagotomy) for high-risk patients	Cefazolin	Clindamycin or vancomycin +aminoglycoside[g] or fluoroquinolone[h,j]	A
Small intestine			
Nonobstructed	Cefazolin	Clindamycin+aminoglycoside[g] or fluoroquinolone[h]	C
Obstructed	Cefazolin+metronidazole, cefoxitin	Metronidazole+aminoglycoside[g] or fluoroquinolone[h,j]	C
Hernia repair (hernioplasty and herniorrhaphy)	Cefazolin	Clindamycin, vancomycin	A
Appendectomy for uncomplicated appendicitis	Cefoxitin, cefazolin+metronidazole	Clindamycin+aminoglycoside[g] or fluoroquinoloneh[j] Metronidazole +aminoglycoside[g] or fluoroquinolone[h,j]	A
Head and neck			
Clean	None	None	B
Clean with placement of prosthesis (excludes tympanostomy tubes)	Cefazolin, cefuroxime	Clindamycin[d]	C
Clean contaminated cancer surgery	Cefazolin+metronidazole, cefuroxime +metronidazole, ampicillin–sulbactam	Clindamycin[d]	A
Other clean-contaminated procedures with the exception of tonsillectomy and functional endoscopic sinus procedures	Cefazolin+metronidazole, cefuroxime +metronidazole, ampicillin–sulbactam	Clindamycin[d]	B
Neurosurgery			
Elective craniotomy and cerebrospinal fluid-shunting procedures	Cefazolin	Clindamycin[d] vancomycin[d]	A
Implantation of intrathecal pumps	Cefazolin	Clindamycin[d] vancomycin[d]	C
Urologic			
Lower tract instrumentation with risk factors for infection (includes transrectal prostate biopsy)	Fluoroquinolone[h,j] trimethoprim–sulfamethoxazole, cefazolin	Aminoglycoside[g] with or without clindamycin	A
Clean without entry into urinary tract	Cefazolin [the addition of a single dose of an aminoglycoside may be recommended for placement of prosthetic material (e.g. penile prosthesis)]	Clindamycin[d] vancomycin[d]	A
Involving implanted prosthesis	Cefazolin±aminoglycoside, ampicillin–sulbactam	Clindamycin±aminoglycoside Vancomycin±aminoglycoside	A
Clean with entry into urinary tract	Cefazolin [the addition of a single dose of an aminoglycoside may be recommended for placement of prosthetic material (e.g. penile prosthesis)]	Fluoroquinolone[h,j] aminoglycoside[g] with or without clindamycin	A
Vascular	Cefazolin (add vancomycin if graft used)	Clindamycin[d] vancomycin[d]	C

[a]All procedures should be less than 24 h. If an agent with a short half-life is used (e.g. cefazolin, cefoxitin), it should be readministered if the procedure duration exceeds the recommended redosing interval (from the time of initiation of the preoperative dose; see Table 1). Readministration may also be warranted if prolonged or excessive bleeding occurs or if there are other factors that may shorten the half-life of the prophylactic agent (e.g. extensive burns). Readministration may not be warranted in patients in whom the half-life of the agent may be prolonged (e.g. patients with renal insufficiency or failure). [b]For patients known to be colonized with methicillin-resistant *Staphylococcus aureus*, it is reasonable to add a single preoperative dose of vancomycin to the recommended agent(s). [c]Strength of evidence that supports the use or nonuse of prophylaxis is classified as A (levels I–III), B (levels IV–VI), or C (level VII). Level I evidence is from large, well-conducted, randomized controlled clinical trials. Level II evidence is from small, well-conducted, randomized controlled clinical trials. Level III evidence is from well-conducted cohort studies. Level IV evidence is from well-conducted case–control studies. Level V evidence is from uncontrolled studies that were not well conducted. Level VI evidence is conflicting evidence that tends to favor the recommendation. Level VII evidence is expert opinion. [d]For procedures in which pathogens other than *Staphylococci* spp. and *Streptococci* spp. are likely, an additional agent with activity against those pathogens could be considered. For example, if there are surveillance data showing that Gram-negative organisms are a cause of surgical-site infections (SSIs) for the procedure, practitioners may consider combining clindamycin or vancomycin with another agent (cefazolin if the patient is not β-lactam allergic; aztreonam, gentamicin, or single-dose fluoroquinolone if the patient is β-lactam allergic). [e]Prophylaxis should be considered for patients at highest risk for postoperative gastroduodenal infections, such as those with increased gastric pH (e.g. those receiving histamine H2-receptor antagonists or protonpump inhibitors), gastroduodenal perforation, decreased gastric motility, gastric outlet obstruction, gastric bleeding, morbid obesity, or cancer. Antimicrobial prophylaxis may not be needed when the lumen of the intestinal tract is not entered. [f]Consider additional antimicrobial coverage with infected biliary tract. See the biliary tract procedures section of this article. [g]Gentamicin or tobramycin. [h]Due to increasing resistance of *Escherichia coli* to fluoroquinolones and ampicillin–sulbactam, local population susceptibility profiles should be reviewed prior to use. [i]Ciprofloxacin or levofloxacin. [j]Fluoroquinolones are associated with an increased risk of tendonitis and tendon rupture in all ages. However, this risk would be expected to be quite small with single-dose antibiotic prophylaxis. Although the use of fluoroquinolones may be necessary for surgical antibiotic prophylaxis in some children, they are not drugs of first choice in the pediatric population due to an increased incidence of adverse events as compared with controls in some clinical trials. [k]Ceftriaxone use should be limited to patients requiring antimicrobial treatment for acute cholecystitis or acute biliary tract infections which may not be determined prior to incision, not patients undergoing cholecystectomy for noninfected biliary conditions, including biliary colic or dyskinesia without infection. [l]Factors that indicate a high risk of infectious complications in laparoscopic cholecystectomy include emergency procedures, diabetes, long procedure duration, intraoperative gallbladder rupture, age of more than 70 years, conversion from laparoscopic to open cholecystectomy, American Society of Anesthesiologists classification of 3 or greater, episode of colic within 30 days before the procedure, reintervention in less than 1 month for noninfectious complication, acute cholecystitis, bile spillage, jaundice, pregnancy, nonfunctioning gallbladder, immunosuppression, and insertion of prosthetic device. Because a number of these risk factors are not possible to determine before surgical intervention, it may be reasonable to give a single dose of antimicrobial prophylaxis to all patients undergoing laparoscopic cholecystectomy. [m]For most patients, a mechanical bowel preparation combined with oral neomycin sulfate plus oral erythromycin base or with oral neomycin sulfate plus oral metronidazole should be given in addition to intravenous prophylaxis. [n]Where there is increasing resistance to first-generation and second-generation cephalosporins among Gram-negative isolates from SSIs, a single dose of ceftriaxone plus metronidazole may be preferred over the routine use of carbapenems. [o]The necessity of continuing topical antimicrobials postoperatively has not been established. [p]Prophylaxis is not routinely indicated for brachiocephalic procedures. Although there are no data in support, patients undergoing brachiocephalic procedures involving vascular prostheses or patch implantation. (e.g. carotid endarterectomy) may benefit from prophylaxis.

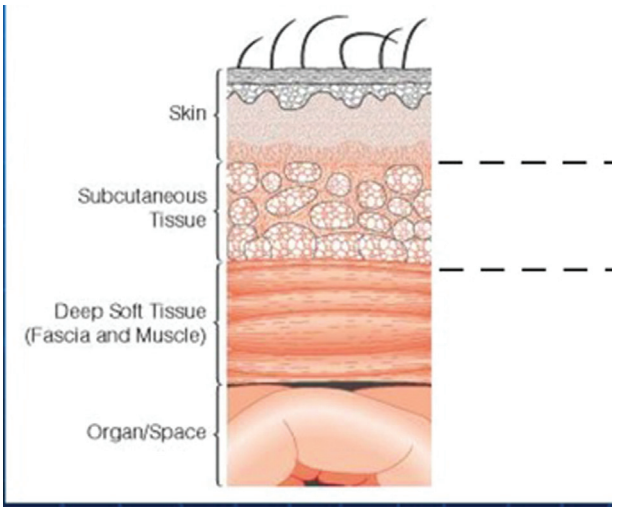
Table 3 Dosing of antibiotics in renal-impairment patients

Renal dosage adjustment antimicrobial	Dosing regimen with normal renal function	Dosing regimen with CrCl less than 50 ml/min	Dosing regimen with CrCl less than 10 ml/min
Ampicillin/Sulbactam	3 g i.v. q6h	3 g i.v. q8h (CrCl 30–50) 3 g i.v. q12h (CrCl <30)	Only administer preop dose 3 g
Cefazolin			
<120 kg	2 g i.v. q8h	2 g i.v. q12h	Only administer preop dose 2 g
≥120 kg	3 g i.v. q8h	3 g i.v. q12h	Only administer preop dose 3 g
Cefoxitin	2 g i.v. q6h	2 g i.v. q12h (CrCl <30)	Only administer preop dose 2 g
Clindamycin	900 mg i.v. 8 h	900 mg i.v. 8 h	900 mg i.v. 8 h
Gentamicin			
Use actual bodyweight (ABW) unlessthe patient is >20%over their ideal bodyweight (IBW), then usedosing body weight(DBW=IBW +[0.4(ABW–IBW)]	Only administer preop dose 5 mg/kg i.v. once	Only administer preop dose 5 mg/kg i.v. once	Only administer preop dose 3 mg/kg i.v. once
Levofloxacin	500 mg i.v. q24h	Only administer preop dose	Only administer preop dose
Metronidazole	500 mg i.v. q8h	500 mg i.v. q8h	500 mg i.v. q8h
Trimethoprim/Sulfamethoxazole	Trimethoprim component 160 mg i.v. q12h	Only administer preop dose Trimethoprim 160 mg	Only administer preop dose Trimethoprim 160 mg
Vancomycin	15 mg/kg i.v. q12h	Only administer preop dose (15 mg/kg×1)	Only administer preop dose (15 mg/kg×1)

A deep incisional infection involves the deeper soft tissue (e.g. fascia and muscle) and occurs within 30 days of the operation or within 90 days if a prosthesis was inserted and has the same findings as described for a superficial incisional SSI.

An organ/space SSI has the same time constraints and evidence for infection as a deep incisional SSI, and it may involve any part of the anatomy (organs or spaces) other than the original surgical incision.

Figure 1



Layers of the skin.

Table 4 Antibiotics for treatment of incisional surgical site infections

Surgery of intestinal or genitourinary tract
Ceftriaxone 1 g every 24 h+metronidazole 500 mg every 8 h i.v.
Ciprofloxacin 400 mg i.v. every 12 h or 750 mg po every 12 h +metronidazole 500 mg every 8 h i.v.
Levofloxacin 750 mg i.v. every 24 h+metronidazole 500 mg every 8 h i.v.
Ampicillin-sulbactam 3 g every 6 h+gentamicin or tobramycin 5 mg/kg every 24 h i.v.
Surgery of trunk or extremity away from axilla or perineum
Oxacillin or nafcillin 2 g every 6 h i.v.
Cefazolin 0.5–1 g every 8 h i.v.
Cephalexin 500 mg every 6 h po
SMX-TMP 160–800 mg po every 6 h
Vancomycin 15 mg/kg every 12 h i.v.
Surgery of axilla or perineuma
Metronidazole 500 mg every 8 h i.v.
PLUS
Ceftriaxone 1 g every 24 h
Ciprofloxacin 400 mg i.v. every 12 h or 750 mg po every 12 h i.v. po
Levofloxacin 750 mg every 24 h i.v. po

i.v., intravenous; po, by mouth; SMX-TMP, sulfamethoxazole-trimethoprim. [a]May also need to cover for methicillin-resistant *Staphylococcus aureus* with vancomycin 15 mg/kg every 12 h.

Diagnosis

Local signs of pain, swelling, erythema, and purulent drainage provide the most reliable information in diagnosing an SSI, whereas many patients with a SSI will develop fever. It usually does not occur immediately postoperatively.

After 48 h, SSI is a more common source of fever, and careful inspection of the wound is indicated; by 4 days after surgery, a fever is equally likely to be caused by an SSI or by another infection.

Later infections are less likely, but surveillance standards mandate 30 days of follow-up for operations without placement of prosthetic material and for 90 days for operations where a prosthesis was inserted.

Management

The most important therapy for an SSI is to open the incision, evacuate the infected material, and continue dressing changes until the wound heals by secondary intention.

If there is less than 5 cm of erythema and induration, and if the patient has minimal systemic signs of infection (temperature <38.5°C, WBC count <12 000 cells/μl, and pulse <100 beats/min), antibiotics are unnecessary.

Patients with temperature more than 38.5°C or heart rate more than 110 beats/ min or erythema extending beyond the wound margins for more than 5 cm may require a short course (e.g. 24–48 h) of antibiotics, as well as opening of the suture line.

Principles of antibiotic selection

Before starting an empiric antibiotics course, culture should be done. A brief course of systemic antimicrobial therapy is indicated in patients with SSIs following clean operations on the trunk, head and neck, or extremities that also have systemic signs of infection, whereas for infections following operations on the axilla, gastrointestinal tract, perineum, or female genital tract use, agents active against gram-negative bacteria and anaerobes, such as a cephalosporin or fluoroquinolone in combination with metronidazole, are used.

Infections developing after surgical procedures involving nonsterile areas such as colonic, vaginal, biliary, or respiratory mucosa may be caused by a combination of aerobic and anaerobic bacteria, and these infections can rapidly progress and involve deeper structures than just the skin, such as fascia, fat, or muscle.

The antibiotic choice is usually empiric but can be supported by Gram stain, culture of the wound contents, the site of surgery, and the hospital antimicrobial susceptibility test system 'Hospital Biogram' (Table 4).

Diabetic foot infections [5]

Foot infections in persons with diabetes are an increasingly common problem and are associated

Table 5 Infectious Diseases Society of America and International Working Group on the Diabetic Foot Classifications of Diabetic Foot Infection

Clinical manifestation of infection	PEDIS grade	IDSA infection severity
No symptoms or signs of infection	1	Uninfected
Infection present, as defined by the presence of at least 2 of the following items		
Local swelling or induration		
Erythema		
Local tenderness or pain		
Local warmth		
Purulent discharge (thick, opaque to white or sanguineous secretion)		
Local infection involving only the skin and the subcutaneous tissue (without involvement of deeper tissues and without systemic signs as described below). If erythema, must be >0.5 cm to ≤2 cm around the ulcer. Exclude other causes of an inflammatory response of the skin (e.g. trauma, gout, acute Charcot neuro-osteoarthropathy, fracture, thrombosis, venous stasis)	2	Mild
Local infection (as described above) with erythema > 2 cm, or involving structures deeper than skin and subcutaneous tissues (e.g. abscess, osteomyelitis, septic arthritis, fasciitis), and No systemic inflammatory response signs (as described below)	3	Moderate
Local infection (as described above) with the signs of SIRS, as manifested by	4	Severe[a]
≥2 of the following		
Temperature >38°C or <36°C		
Heart rate >90 beats/min		
Respiratory rate >20 breaths/min or PaCO2 <32 mmHg		
White blood cell count >12 000 or <4000 cells/μl or ≥10% immature (band) forms		

IDSA, Infectious Diseases Society of America; $PaCO_2$, partial pressure of arterial carbon dioxide; PEDIS, perfusion, extent/size, depth/tissue loss, infection, and sensation; SIRS, systemic inflammatory response syndrome. [a]Ischemia may increase the severity of any infection, and the presence of critical ischemia often makes the infection severe. Systemic infection may sometimes manifest with other clinical findings, such as hypotension, confusion, vomiting, or evidence of metabolic disturbances, such as acidosis, severe hyperglycemia, and new-onset azotemia.

with potentially serious sequelae. DFIs typically begin in a wound, most often a neuropathic ulceration, while all wounds are colonized with microorganisms, and the presence of infection is defined by greater than or equal to 2 classic findings of inflammation or purulence.

Classification of diabetic foot infections

Infections are then classified into mild (superficial and limited in size and depth), moderate (deeper or more extensive), or severe (accompanied by systemic signs or metabolic perturbations), as shown in Table 5.

Etiology

Most DFIs are polymicrobial, with aerobic gram-positive cocci, and especially *Staphylococci* spp., the most common causative organisms. Aerobic gram-negative bacilli are frequently copathogens in infections that are chronic or follow antibiotic treatment, and obligate anaerobes may be copathogens in ischemic or necrotic wounds.

These infections can then spread contiguously, including into deeper tissues, often reaching bone.

If the infection progresses, many patients require hospitalization and, all too often, surgical resections or an amputation, diabetic foot complications continue to be the main reason for diabetes-related hospitalization and lower extremity amputations.

Recommendations for a clinician to suspect infection

(1) Clinicians should consider the possibility of infection occurring in any foot wound in a patient with diabetes.
(2) Evidence of infection generally includes classic signs of inflammation (redness, warmth, swelling, tenderness, or pain) or purulent secretions but may also include additional or secondary signs (e.g. nonpurulent secretions, friable or discolored granulation tissue, undermining of wound edges, foul odor).
(3) Clinicians should be aware of factors that increase the risk for DFI and especially consider infection when these factors are present; these include a wound for which the probe-to-bone test is positive, an ulceration present for more than 30 days, a history of recurrent foot ulcers, a traumatic foot wound, the presence of peripheral vascular disease in the affected limb, a previous lower extremity amputation, loss of protective sensation, the presence of renal insufficiency, or a history of walking barefoot.

Table 6 Suggested empiric antibiotic regimens based on clinical severity for diabetic foot infections[a]

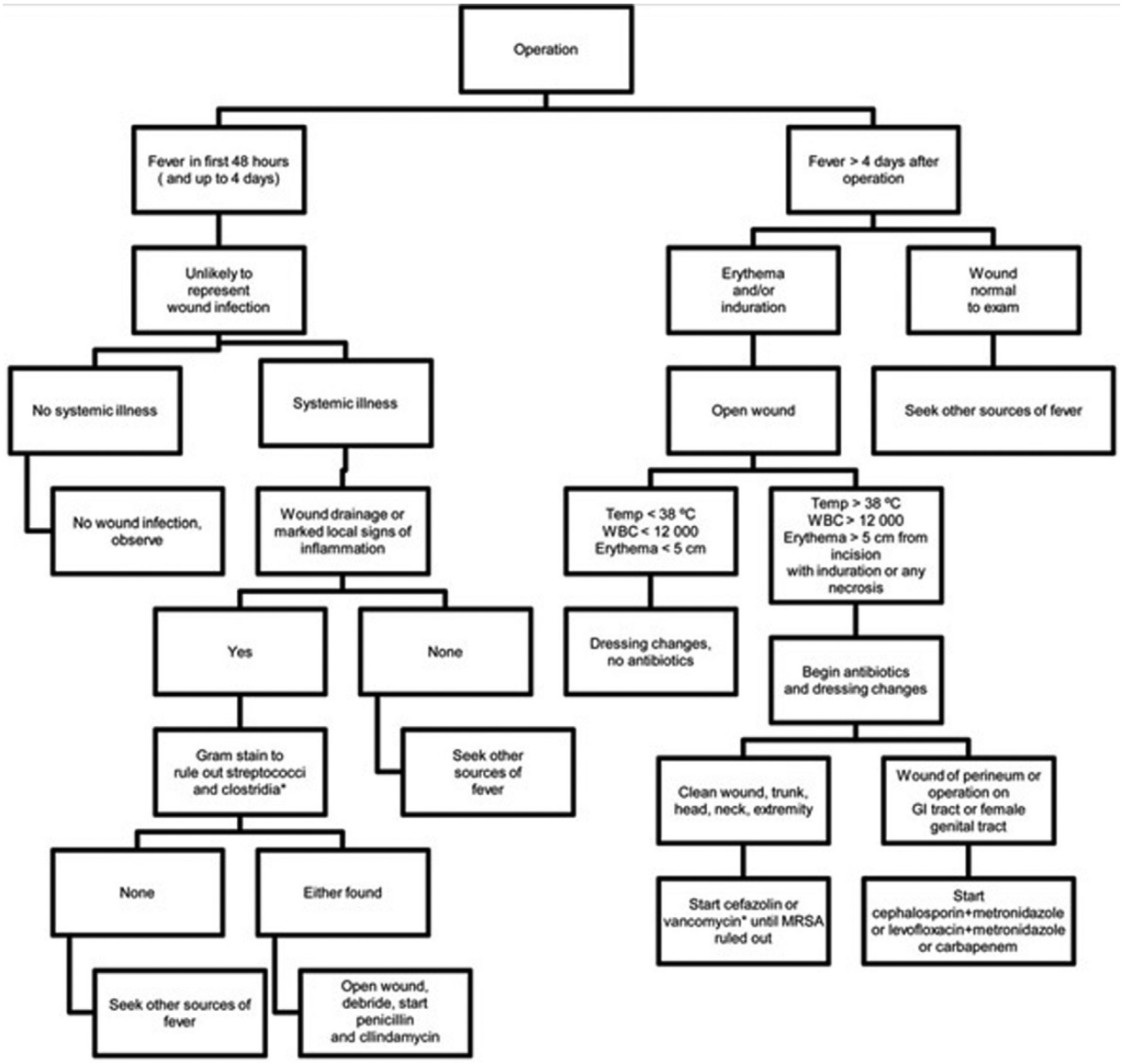
Infection severity	Probable pathogen(s)	Antibiotic agent	Comments
Mild [usually treated with oral agent(s)]	*Staphylococcus aureus* (MSSA); *Streptococcus spp.*	Dicloxacillin	Requires QID dosing; narrow spectrum
		Clindamycinb	Usually active against community-associated MRSA, but check macrolide sensitivity and consider ordering a 'D-test' before using for MRSA. Inhibits protein synthesis of some bacterial toxins
		Cephalexin[b]	Requires QID dosing
		Levofloxacin[b]	Once daily dosing; suboptimal against *S. aureus*
		Amoxicillin-clavulanate[b]	Relatively broad-spectrum oral agent that includes anaerobic coverage
	Methicillin-resistant *S. aureus* (MRSA)	Doxycycline	Active against many MRSA AND some Gram-negatives; uncertain against *Streptococcus* spp.
		Trimethoprim/sulfamethoxazole	Active against many MRSA and some Gram-negatives; uncertain activity against *Streptococci* spp.
Moderate [may be treated with oral or initial parenteral agent(s)]	MSSA, *Streptococcus* spp., *Enterobacteriaceae* spp., obligate anaerobes	Levofloxacin[b]	Once daily dosing; suboptimal against *S. aureus*
		Cefoxitin[b]	Second-generation cephalosporin with anaerobic coverage
		Ceftriaxone	Oncedaily dosing, third-generation cephalosporin
		Ampicillin-sulbactam[b]	Adequate if low suspicion of *Pseudomonas aeruginosa*
		Moxifloxacin[b]	Once daily oral dosing. Relatively broad-spectrum, including most obligate anaerobic organisms
		Ertapenem[b] (recommended only in severe infections)	Once daily dosing. Relatively broad spectrum including anaerobes, but not active against *P. aeruginosa*
		Tigecycline[b] (recommended only in severe infections)	Active against MRSA. Spectrum may be excessively broad. High rates of nausea and vomiting and increased mortality warning
		Levofloxacin[b] or ciprofloxacin[b] with clindamycin[b]	Limited evidence supporting clindamycin for severe *S. aureus* infections; PO and i.v. formulations for both drugs
		Imipenem-cilastatin[b] (recommended only in severe infections)	Very broad-spectrum (but not against MRSA); use only when this is required. Consider when ESBL-producing pathogens suspected
	MRSA	Linezolid[b]	increased risk of toxicities when used >2 weeks
		Vancomycin[b]	Vancomycin MICs for MRSA are gradually increasing
	Pseudomonas aeruginosa	Piperacillin-tazobactam[b]	TID/QID dosing. Useful for broad spectrum coverage. *P. aeruginosa* is an uncommon pathogen in diabetic foot infections except in special circumstances (2)
	MRSA, *Enterobacteriacae* spp., *Pseudomonas* spp., and obligate anaerobes	Vancomycinc plus one of the following: ceftazidime, cefepime, piperacillintazobactam[b], or a carbapenem[b]	Very broad-spectrum coverage; usually only used for empiric therapy of severe infection. Consider addition of obligate anaerobe coverage if ceftazidime or cefepime, selected

Narrow-spectrum agents (e.g. vancomycin, linezolid, daptomycin) should be combined with other agents (e.g. a fluoroquinolone) if a polymicrobial infection (especially moderate or severe) is suspected. Use an agent active against MRSA for patients who have a severe infection, evidence of infection or colonization with this organism elsewhere, or epidemiological risk factors for MRSA infection. Select definitive regimens after considering the results of culture and susceptibility tests from wound specimens, as well as the clinical response to the empiric regimen. Similar agents of the same drug class can probably be substituted for suggested agents. Some of these regimens do not have FDA approval for complicated skin and skin structure infections. ESBL, extended-spectrum β-lactamase; FDA, US Food and Drug Administration; IV, intravenous; MIC, minimum inhibitory concentration; MRSA, methicillin-resistant Staphylococcus aureus; MSSA, methicillin-sensitive *Staphylococcus aureus*; PO, oral; QID, four times a day; TID, three times a day. [a]Agents approved for treating skin and skin structure infections on the basis of studies that excluded patients with diabetic foot infections (e.g. ceftaroline, telavancin) are not included. [b]Agents shown to be effective in clinical trials including patients with diabetic foot infections. [c]Daptomycin or linezolid may be substituted for vancomycin.

Table 7 Suggested route, setting, and duration of antibiotic therapy by clinical syndrome

Site of infection by severity or extent	Route of administration	Setting	Duration of therapy
Soft tissue only			
Mild	Oral	Outpatient	1–2 weeks; may extend up to 4 weeks if slow to resolve
Moderate	Oral (or initial parenteral)	Outpatient/ inpatient	1–3 weeks
Severe	Initial parenteral, switch to oral when possible	Inpatient, then outpatient	2–4 weeks
Bone or joint			
No residual infected tissue (e.g. postamputation)	Parenteral or oral		2–5 days
Residual infected soft tissue (but not bone)	Parenteral or oral		1–3 weeks
Residual infected (but viable) bone	Initial parenteral, then consider oral switch		4–6 weeks
No surgery, or residual dead bone postoperatively	Initial parenteral, then consider oral switch		≥3 months

Figure 2



Algorithm for the management and treatment of surgical site infections. *For patients with type 1 (anaphylaxis or hives) allergy to β-lactam antibiotics. If Gram stain not available, open and debride if purulent drainage is present. Where the rate of infection with methicillin-resistant *Staphylococcus aureus* infection is high, consider vancomycin, daptomycin, or linezolid, pending results of culture and susceptibility tests. Adapted and modified with permission from Dellinger *et al.* GI, gastrointestinal; MRSA, methicillin-resistant *Staphylococcus aureus*; WBC, white blood cell count.

Assessment of a diabetic patient presenting with a foot infection

(1) Clinicians should evaluate a diabetic patient presenting with a foot wound at three levels: the patient as a whole, the affected foot or limb, and the infected wound.
(2) Clinicians should diagnose infection based on the presence of at least two classic symptoms or signs of inflammation (erythema, warmth, tenderness, pain, or induration) or purulent secretions and the presence of any systemic findings of infection.
(3) Assessing the affected limb and foot for arterial ischemia, venous insufficiency, presence of protective sensation, and biomechanical problems.
(4) Clinicians should debride any wound that has necrotic tissue or surrounding callus; the required procedure may range from minor to extensive.

Obtain specimen(s) for culture

(1) The recommendation is to send a specimen for culture that is from deep tissue, obtained by biopsy or curettage and after the wound has been cleansed and debrided with saline not with antiseptics.

Initiation and modification of an antibiotic regimen for a diabetic foot infection

(1) The clinically noninfected wounds should not be treated with antibiotic therapy.
(2) Prescription of antibiotic therapy for all infected wounds should be done, but with caution, as it is often insufficient unless combined with appropriate wound debridement.
(3) The clinicians need to select an empiric antibiotic regimen on the basis of the severity of the infection and the likely etiologic agent(s) (shown in Table 6):
    (a) For mild to moderate infections in patients who have not recently received antibiotic treatment, we suggest that therapy just targeting aerobic gram-positive cocci is sufficient.
    (b) For most severe infections, we recommend starting broad-spectrum empiric antibiotic therapy, pending culture results and antibiotic susceptibility data.
    (c) Empiric therapy directed at *Pseudomonas aeruginosa* is usually unnecessary except for patients with risk factors for true infection with this organism.
    (d) Consider providing empiric therapy directed against MRSA in a patient with a prior history of MRSA infection, when the local prevalence of MRSA colonization or infection is high.
    (e) A definitive therapy based on the results of an appropriately obtained culture and sensitivity testing of a wound specimen is recommended as well as the patient's clinical response to the empiric regime.
(4) Route of administration: parenteral therapy is preferred for all severe, and some moderate, DFIs, at least initially, with a switch to oral agents when the patient is systemically well and culture results are available (Table 7).
(5) Duration of antibiotic therapy:
    (a) We suggest continuing antibiotic therapy until, but not beyond, resolution of findings of infection, but not through complete healing of the wound.
    (b) We suggest an initial antibiotic course for a soft tissue infection of approximately 1–2 weeks for mild infections and 2–3 weeks for moderate to severe infections (Table 7, Fig. 2).

Financial support and sponsorship
Nil.

Conflicts of interest
None declared.

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