TAKE-HOME POINTS FROM LECTURES BY CLEVELAND CLINIC AND VISITING FACULTY

Common infections in clinical practice: Dealing with the daily uncertainties

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ABSTRACT

Common infections we see every day in the office—urinary tract infections, vaginitis, upper respiratory tract infections, and soft-tissue infections—present a number of diagnostic and treatment uncertainties. In this age of growing antibiotic resistance, these include if and when to start antibiotic therapy, and which agents to use.

KEY POINTS

Beta-lactams are not suitable for empiric oral therapy of urinary tract infections.

There are serious doubts about the accuracy of self-diagnosis of vaginal candidiasis, creating concern about the abuse of over-the-counter agents.

About half of those diagnosed with colds and about two thirds of those diagnosed with acute bronchitis are given antibiotics, which are clearly of no benefit in these situations.

In patients with cellulitis, suspect a deep soft-tissue infection if pain and swelling extend outside the area of erythema and, more importantly, if there is loss of sensation.

"If a man will begin with certainties, he shall end in doubts; but if he will be content to begin with doubts he shall end in certainties."
—Francis Bacon (1561–1626)

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BECAUSE urinary tract infections, vaginitis, upper respiratory infections, and soft-tissue infections are so common, there is often uncertainty about how to best manage them.

This paper provides an overview and update of these problems, examines the national guidelines, and emphasizes that antibiotics are still being overused for infections encountered in the ambulatory setting.

URINARY TRACT INFECTIONS

Case: A young woman with dysuria

A 22-year-old woman presents with dysuria and foul-smelling urine, which began 24 hours previously. She is sexually active and occasionally uses a diaphragm and spermicide. Her symptoms resolve after treatment with oral trimethoprim-sulfamethoxazole for 3 days.

One week later, however, her symptoms recur along with fever, left flank pain, and persistent nausea and vomiting. A urine culture grows *Escherichia coli* (> 10^5 colony-forming units/mL), which is susceptible to trimethoprim-sulfamethoxazole, and blood cultures grow the same organism.

She is hospitalized and treated with intravenous ampicillin and gentamicin. However, fever and left flank pain persist for more than 72 hours. Computed tomography (CT) shows left pyelonephritis and an intrarenal abscess (FIGURE 1).

Cystitis and pyelonephritis

The young woman in this case started with simple cystitis; fever is uncommon in simple cystitis and suprapubic tenderness is rare, present in 10% of cases or less. Sexual activity and

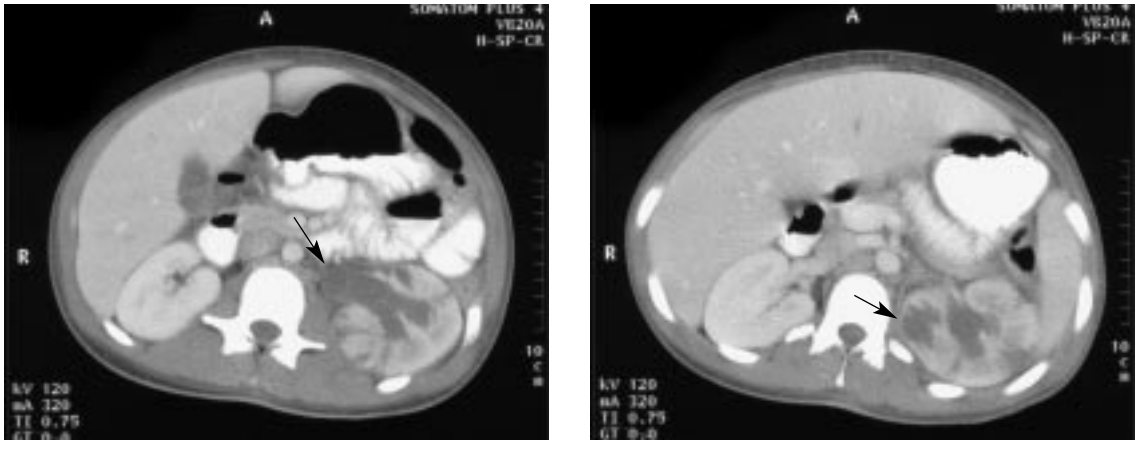

FIGURE 1. Computed tomographic scan showing left pyelonephritis and an intrarenal abscess (arrows).

use of a diaphragm clearly increase the risk of urinary tract infection.

Urine culture is not indicated in simple cystitis because the microbiology is predictable; empiric treatment is the standard of care. In a recent study in young women with uncomplicated urinary tract infections,[1] patient-initiated treatment resulted in clinical cure in 92% of cases and microbiologic cure in 96%. However, McIsaac et al[2] found that testing for pyuria in women with classic symptoms of cystitis would decrease unnecessary antibiotic use by 26%.

Urine culture is not needed in simple cystitis

When this patient relapsed, she developed symptoms of acute pyelonephritis. Remember that renal calculi and infarction can present with similar symptoms.

Urine cultures and blood cultures are indicated in patients hospitalized for pyelonephritis and are positive in 15% to 20% of cases. However, 20% of patients with pyelonephritis have fewer than 10^5 colony-forming units/mL on urine culture.

The indication for hospitalization and treatment with intravenous antibiotics in our patient was the expected dehydration due to persistent nausea and vomiting.

Improvement is expected in 48 to 72 hours after starting intravenous antibiotic therapy. Symptoms that persist beyond this time mandate an imaging study, such as ultrasonography or CT, looking for anatomical defects, stones, or a localized abscess. Some patients may not respond to appropriate antimicrobial therapy due to impaired host defenses or virulence factors of the organism. If no correctable anatomic defect is found, a "test of cure" culture is indicated 1 to 2 weeks after therapy is completed.

Microbiology of urinary tract infections

E coli accounts for about 80% of cases of acute uncomplicated cystitis and 90% of cases of acute uncomplicated pyelonephritis, but it accounts for a lesser percent of cases of complicated urinary tract infection, ie, those in men, renal transplant recipients, and patients with recent genitourinary surgery, obstruction, pregnancy, or diabetes mellitus (**TABLE 1**).[3,4]

Organisms are gaining resistance to antimicrobial agents. Two recent epidemiologic studies[5,6] found that resistance to trimethoprim-sulfamethoxazole in *E coli* has doubled over 5 years, from 9% to 18%.[5] *E coli* resistance to nitrofurantoin, quinolones, and aminoglycosides has remained about the same, at 0 to 2%.[5] Resistance in *Proteus mirabilis* is at 12.1%, *Klebsiella pneumoniae* 7.8%, and *Staphylococcus saprophyticus* 3%.[6] Organisms are resistant to beta-lactams in 20% of cases.[5] There is wide geographic variation in resistance patterns, however.[6]

Risk factors for resistance in urinary tract infections, as identified by Gupta et al,[7] are:

- A local rate of resistance to trimethoprim-sulfamethoxazole greater than 20%
- Recent use of trimethoprim-sulfamethoxazole
- Current use of any antimicrobial agent

- Recent hospitalization
- Recurrent urinary tract infections in the past
- Estrogen exposure (oral contraceptives or hormone replacement therapy).

Diabetes mellitus was a possible risk factor, although when patients who were recently hospitalized were excluded, it was no longer an independent risk factor for resistance.

Treatment of acute bacterial cystitis

In general, single-dose treatment is more likely to fail than 3-day treatment. High-risk or complicated cases require longer courses, eg, 7 to 10 days in men, patients with renal transplants, pregnancy, use of a diaphragm, age greater than 65 years, symptoms lasting longer than 7 days, known antimicrobial resistance, or *Pseudomonas* or *Enterococcus* infection.[8]

First-choice agents are trimethoprim-sulfamethoxazole, trimethoprim alone, and ofloxacin—but not beta-lactams. Second-choice agents are other quinolones (ciprofloxacin, norfloxacin). Alternatives are nitrofurantoin and fosfomycin.[8]

First-generation penicillins and cephalosporins and sulfonamides are no longer effective because of a high frequency of resistance. Fluoroquinolones are very effective but not recommended as initial empiric therapy because they are much more expensive, and using them unnecessarily promotes emergence of resistant organisms.[8]

Treatment of acute pyelonephritis

Acute uncomplicated pyelonephritis is treated with a 7-day course in mild or moderate cases, and 14 days in severe cases. There is usually no benefit of treatment beyond 2 weeks, even if blood cultures were positive.

Oral options are trimethoprim-sulfamethoxazole, fluoroquinolones, or amoxicillin with or without clavulanic acid (the latter for gram-positive cocci).

Initial parenteral therapy is indicated in cases with nausea and vomiting and can later be changed to oral therapy. Parenteral options include intravenous fluoroquinolones, aminoglycosides with or without ampicillin, extended-spectrum cephalosporins with or without an aminoglycoside, and ampicillin-sulbactam with or without an aminoglycoside (the latter for gram-positive cocci).[8]

TABLE 1

Agents of urinary tract infections

TYPE OF INFECTION AND ORGANISM	PREVALENCE
Acute uncomplicated cystitis	
Escherichia coli	80%
Staphylococcus saprophyticus	10%
Other gram-negative bacilli	5%
Other organisms	5%
Acute uncomplicated pyelonephritis	
E coli	90%
Other gram-negative bacilli	10%
Complicated urinary tract infection	
E coli	30%
Pseudomonas aeruginosa	20%
Enterococcus species	20%
Staphylococcus epidermidis	15%
Other organisms	5%
Catheter-related urinary tract infections	
E coli	25%
Yeast	30%
Pseudomonas aeruginosa	10%
Other gram-negative bacilli	15%
Enterococcus species	10%
Other organisms	10%

DATA FROM STAMM WE, HOOTON TM. MANAGEMENT OF URINARY TRACT INFECTIONS IN ADULTS. N ENGL J MED 1993; 329:1328–1334; AND FALGAS ME, GORBACH SL. PRACTICE GUIDELINES: URINARY TRACT INFECTIONS. NFECT DIS CLIN PRACT 1995; 4:241–257.

VAGINITIS

Case: A young woman with candidiasis

A 24-year-old, sexually active, diabetic woman presents with dyspareunia, vaginal pruritis, and a curd-like discharge. This is her fifth episode this year, and these usually occur just before menstruation. She is taking prednisone for rheumatoid arthritis and has just finished a course of oral amoxicillin for sinusitis.

She usually treats herself for vaginitis with topical agents such as clotrimazole, but her symptoms have persisted now for more than 7 days.

A potassium hydroxide (KOH) preparation test (fungal smear) shows fungal hyphae. Fungal culture grows *Candida glabrata*, sensi-

TABLE 2

Vaginitis: Clinical presentation, diagnosis, and treatment

	CANDIDA	BACTERIAL VAGINOSIS	*TRICHOMONAS*	ATROPHIC
Main symptom	Pruritis	Bad odor	Copious discharge	Dryness
Signs	Erythema White discharge	Adherent discharge	Purulent discharge	Thin mucosa
pH	4.0–4.5	> 4.5	5.0–6.0	> 6.0
Whiff test	Negative	Positive	Positive	Negative
Wet mount	Hyphae	Clue cells	Many PMNs Protozoa	PMNs
KOH prep	Hyphae	Negative	Negative	Negative
Culture	Positive	N/A	Positive	N/A
Topical treatment	Clotrimazole Miconazole Terconazole	Metronidazole Clindamycin	—	Estrogen
Oral treatment	Fluconazole Itraconazole	Metronidazole Clindamycin	Metronidazole Tinidazole	Hormone replacement

PMNs = polymorphonuclear leukocytes, N/A = not applicable

ADAPTED FROM SOBEL JD. VAGINITIS. N ENGL J MED 337:1896–1903.

tive to fluconazole. She finally improves after 10 days of therapy with oral fluconazole.

Candida is common, recurrent candidiasis is not

This patient has several risk factors for recurrent vulvovaginal candidiasis: diabetes and use of steroids and antimicrobials.

Candida is part of the normal vaginal flora and is not traditionally considered a sexually transmitted disease. Nevertheless, sexual transmission can occur, and the frequency of vaginal candidiasis increases when women begin regular sexual activity. Episodes occur most often just before menstruation and during pregnancy, because of elevated progesterone levels.

Seventy-five percent of all women have at least one episode of candidiasis during their lifetime, but recurrent episodes are very rare in healthy women.

All that itches is not yeast

There are serious doubts about the accuracy of self-diagnosis of candidiasis, creating concern about the abuse of over-the-counter agents.

When symptoms persist despite what should be appropriate therapy, one should think about other infectious and noninfectious causes of vaginitis, and also consider antimicrobial resistance. The non-albicans *Candida* species are less susceptible to topical imidazoles, requiring treatment for 10 to 14 days with other agents, such as the triazoles.

The four most common causes of vaginitis (several others exist) are:

- *Candida* (by far the most common)
- Bacterial vaginosis
- *Trichomonas*
- Atrophic vaginosis.

About 15% of adolescent girls and young women in the United States practice vaginal douching. It should be discouraged, at least in this age group, because it is associated with increased risk for pelvic inflammatory disease, bacterial vaginosis, and ectopic pregnancy.[9]

Identifying the cause of vaginitis

Certain clinical features may help identify the cause of vaginitis (TABLE 2).[10,11]

Symptoms. Dyspareunia is a common symptom in all these causes except in bacterial vaginosis. I urge you not to make a "telephone diagnosis" based on symptoms alone, since this has been shown to be inaccurate.

Examination. *Candida* causes an adherent curd-like discharge and vulvar erythema. Trichomoniasis has frothy purulent and malodorous discharge. Bacterial vaginosis has thick adherent discharge. Overlapping features may be seen.

Vaginal pH. The normal vaginal pH is 4.0 to 4.5; a low pH excludes bacterial vaginosis and trichomoniasis.

The whiff test is performed by adding a drop of 10% KOH to vaginal secretion on a slide; a positive whiff test is an amine or fishy odor. This can be found in bacterial vaginosis and trichomoniasis.

Microscopy. A wet mount (adding a drop of saline to the secretions on a slide) will show mycelia and pseudohyphae in most cases of symptomatic candidiasis. Gram staining is a bit more sensitive.

Clue cells—granulated or stippled epithelial cells with overlying organisms such as *Gardnerella vaginalis*—are seen in bacterial vaginosis. If you see many polymorphonuclear neutrophils, think about trichomoniasis rather than bacterial vaginosis. Look for trichomonal flagellates in an area away from neutrophils; they are highly motile in fresh specimens.

Culture for *Trichomonas* requires special media and may take several days. Culture and sensitivity for *Candida* are indicated only if antimicrobial resistance is suspected.

Vaginitis treatment

The FDA approved the first over-the-counter imidazole for candidal vaginitis in 1990. Despite the wide use of these products, there has been little study of the outcome of the switch from prescription to over-the-counter agents. Over-the-counter agents clearly increase patient autonomy. However, whether harm is increased due to misdiagnosis, resulting in inappropriate use and delay in treatment of other conditions, remains unclear.[12]

One should usually start with a topical agent if the patient agrees except for cases of trichomoniasis, in which oral therapy is preferred. Oral and intravaginal agents are equally effective in the treatment of uncomplicated candidiasis. Data are insufficient with regard to side effects and cost-effectiveness.

If candidiasis recurs or persists, try the triazole terconazole, in case it is due to a non-albicans *Candida* species.

A single 2-g dose of metronidazole is less effective than 7 days of fractionated oral metronidazole therapy for bacterial vaginosis, but it is the recommended treatment for trichomoniasis.[13]

The sexual partner should always be treated in trichomoniasis.

Bacterial vaginosis is independently associated with preterm delivery of low-birthweight infants,[14] but it is not predictive of early miscarriage.[15] Treatment of bacterial vaginosis with oral metronidazole during the second and third trimesters of pregnancy does not reduce the occurrence of preterm delivery,[16] but oral clindamycin does.[17] The use of intravaginal clindamycin late in pregnancy may increase the risk of neonatal infections.[18]

There is limited evidence that *Lactobacillus acidophilus* can prevent candidal vaginitis with very few adverse effects.[19] Anecdotally, I know of several women who increased their oral intake of yogurt while taking long courses of intravenous antibiotics with some success in preventing vaginal candidiasis.

I urge you not to make a telephone diagnosis of vaginitis

UPPER RESPIRATORY TRACT INFECTIONS

Upper respiratory tract infections are among the most common problems seen in an internal medicine practice. Below are a few common presentations. What is your diagnosis?

- ❑ A 20-year-old college student presents with fever, sore throat, myalgia, splenomegaly, and generalized swollen lymph nodes
- ❑ A 29-year-old teacher has nasal discharge, sneezing, and headaches for 24 hours
- ❑ A 30-year-old man with human immunodeficiency virus (HIV) infection has persistent nasal discharge and maxillary toothache 2 weeks after a cold

- A 55-year-old diabetic nurse presents with sudden onset of fever, headache, cough, and myalgia during winter
- A 34-year-old mother presents with sudden onset of sore throat, odynophagia, and swollen anterior cervical lymph nodes

Infectious mononucleosis: Therapy is symptomatic

Our college student has mononucleosis, a very common illness in this age group.

Diagnosis. Even though Epstein-Barr virus is by far the most common cause of a mononucleosis-type illness, one must remember HIV in the correct clinical setting, and HIV testing should be considered.[20] The differential diagnosis also includes cytomegalovirus, toxoplasmosis, and human herpesvirus 6.

The diagnosis is usually clinical, but the findings of atypical reactive lymphocytes, a positive Monospot test, and Epstein-Barr virus immunoglobulin G (IgG) and IgM can aid in confirming the diagnosis. Splenomegaly and abnormal liver function tests are more common in adults than in adolescents with mononucleosis.[21]

Therapy is symptomatic. The course of illness is self-limited; it may last for 3 weeks. Patients with mononucleosis who are prescribed ampicillin or amoxicillin for presumed streptococcal pharyngitis characteristically develop a rash. Acyclovir is of no clinical value.[22]

A recent epidemiologic study suggested that the Epstein-Barr virus plays a role in the development of multiple sclerosis.[23] Further studies are awaited.

In bacterial vaginosis, a single dose of metronidazole 2 g is less effective than 7 days of therapy

Common cold: Vitamin C, zinc are controversial

The teacher has a common cold, which she probably caught from one of her students.

The common cold, or nonspecific upper respiratory infection, is a mild, self-limited illness affecting about 5% of the population at any given time. Most cases are viral, but the etiology remains unknown in almost one third of cases. One common, confusing entity is allergic rhinitis, characterized by nasal and eye itching and excessive lacrimation.

Symptomatic treatment includes alpha adrenergic agonists, anticholinergics, antihistamines, and nonsteroidal anti-inflammatory drugs. The role of vitamin C and zinc supplements remain controversial.

Several antiviral agents have been studied, including nonspecific agents such as interferon and, more recently, specific agents such as tremacamra and pleconaril, none of which has been approved by the US Food and Drug Administration.

Antibiotics are misused for the common cold

"A desire to take medications is, perhaps, the greatest feature which distinguishes man from other animals."
—Sir William Osler, 1891.

Antibiotics have never been shown to be of value in shortening the duration or decreasing the symptoms of the common cold, nor in preventing complications such as sinusitis.

Yet, antibiotic prescriptions for upper respiratory infections account for 30% of all antibiotic prescriptions in adults.[24] About half of those diagnosed with colds and about two thirds of those diagnosed with acute bronchitis are given antibiotics, which are clearly of no benefit in this situation. Only about one fifth of those getting antibiotics for sore throat will benefit from them.

Physicians are more likely to prescribe antibiotics if the patient has a cough productive of yellow sputum, a sore throat, fever, or colored nasal discharge, even though there is little evidence to suggest that therapy for a bacterial infection is indicated in patients with these symptoms.[25]

Recent data have shown that between 1991 and 1999, antibiotics were used less frequently to treat acute respiratory tract infections.[26] However, the use of broad-spectrum antibiotics has increased, especially by internists in the Northeast and South United States.[26,27] Community-wide campaigns can result in more appropriate use of antibiotics.[28] Most patients will listen when their doctors address their concerns, show personal interest, and explain the treatment options other than antibiotics.[29]

Acute sinusitis

The HIV-positive man has typical symptoms of acute maxillary sinusitis.

Typical organisms in acute sinusitis are *Streptococcus pneumoniae*, *H influenzae*, *M catarrhalis*, *Staphylococcus aureus*, and group A beta-hemolytic streptococcus (GABHS),[30] although some patients have acute sinusitis caused purely by viruses. Anatomic abnormalities that can lead to blockage of the sinus ostium include deviated nasal septum, concha bullosum, and ciliary dysfunction seen with cystic fibrosis. Allergies, immunodeficiency states such as hypogammaglobulinemia and AIDS, and viral infections can all predispose to sinusitis.[31] Other less common predisposing factors include diving and cocaine abuse.

Symptoms highly suggestive of acute sinusitis are maxillary toothache, unilateral facial pain, purulent nasal discharge, lack of response to decongestants, and decreased transillumination, but these rarely occur simultaneously.[32]

Diagnostic studies. CT is more informative than plain radiography and costs about the same in most hospitals. CT is usually indicated to define the anatomy before an anticipated surgery.[32] Nasal endoscopy or aspiration by sinus puncture are not indicated in acute cases, except if resistant or unusual organisms are expected such as in patients with recurrent episode and in immunosuppressed individuals.[31]

Treatment. Most mild cases of sinusitis respond to topical and oral decongestants alone. Antibiotics should be reserved for moderate and severe cases. Amoxicillin, doxycycline, or trimethoprim-sulfamethoxazole are first-line agents.[32] The usual duration of therapy is 10 to 14 days, but some studies have shown equal efficacy with 3 or 10 days of therapy.[33]

Second-line, more expensive agents should be considered if there is lack of response to first-line agents, multiple prior antibiotic courses, or a high prevalence of beta-lactamase–producing organisms in the community. Examples are broader-spectrum penicillins, cephalosporins, macrolides, and quinolones.[34]

In a recent study, the addition of intranasal fluticasone to cefuroxime and an intranasal decongestant improved the clinical success rate in acute sinusitis.[35]

Influenza

The nurse has influenza. She had at least three reasons to be vaccinated: she is older than 50 years, is a health care provider, and has diabetes.

Diagnosis. Typical symptoms are the sudden onset of fever, headache, cough and myalgia. Clinical diagnosis is 80% accurate during epidemics.[36] The sensitivity and specificity of the rapid office diagnostic tests vary according to the type of sample (nasal wash is better than throat swab). They all cost $15 to $20, and most take about 30 minutes.

Treatment. The M2 ion channel blocker amantadine has been available for about 30 years, and the less-toxic rimantadine for about 10 years. Introduction of the neuraminidase inhibitors, zanamivir and oseltamivir, has increased interest in treating influenza. These agents have fewer side effects, are active against both influenza A and B, and pose little risk of promoting resistance. They all should be started within 1 or 2 days of the onset of symptoms. Mild and nonfebrile influenza-like illnesses should not be treated with antiviral agents.

Even though all these drugs have been approved as prophylactic agents for certain groups of patients, the influenza vaccine remains the most effective and cost-saving measure to prevent influenza and its complications.[37] The intranasal vaccine will be more appealing because it obviates the need for injection. Whether it would be more immunogenic in immunocompromised people remains to be seen.

Most mild cases of sinusitis respond to topical and oral decongestants alone

Streptococcal pharyngitis

The mother has streptococcal pharyngitis ("strep throat"), probably contracted from one of her children.

About 7 million adults in the United States have sore throat each year, and about three fourths of those who visit their health care providers are prescribed antibiotics.

The differential diagnosis of a sore throat includes pharyngitis, epiglottitis, Ludwig angina, thyroiditis, and gastroesophageal reflux disease.[38] However, the most important question in someone presenting with sore throat is whether he or she has GABHS infection,

which accounts for 5% to 10% of adult cases of pharyngitis and is readily treatable.

A sudden onset, as in this patient, is typical for GABHS compared with viral causes. Viruses account for about 30% to 40% of cases of pharyngitis. Other organisms that can cause sore throat are group G and C streptococci, diphtheria, *Arcanobacterium haemolyticum*, gonococci, and *Mycoplasma pneumoniae*.[38] Unfortunately, the clinical manifestations of GABHS and other microbial etiologies of pharyngitis overlap quite broadly.

The Centor criteria (fever, tonsillar exudate, tender anterior lymphadenopathy, absence of cough, and exposure to GABHS within 2 weeks of onset of illness) and other algorithms have a positive predictive value of about 60% for the presence of GABHS on culture, but they are actually more helpful in identifying low-risk patients.[39]

Results of a highly sensitive rapid antigen detection test may be used as a basis for diagnosis and treatment in adults, without confirmatory culture. Unfortunately, a positive culture does not differentiate acute infection from chronic streptococcal colonization. It is not 100% sensitive or specific.[40,41] Culture may be needed to investigate an outbreak, however, or if other pathogens are clinically suspected.

A sudden onset is typical for group A beta-hemolytic streptococcal pharyngitis

Treatment. Penicillin remains universally effective.[41] Antimicrobial therapy for GABHS pharyngitis prevents suppurative sequelae and acute rheumatic fever, limits spread to contacts, and shortens illness by 1 to 2 days when started early.

If a patient has suggestive clinical and epidemiologic features, the Infectious Disease Society of America[42] suggests a throat culture or rapid antigen detection test, symptomatic therapy, and empiric antimicrobials (penicillin V or amoxicillin; intramuscular benzathine penicillin G, erythromycin, or a first-generation cephalosporin). If either test is positive the antimicrobial is continued for 10 days; if negative, the antimicrobial is stopped. If features suggestive of strep pharyngitis are absent, only symptomatic therapy is indicated.

Acute rheumatic fever is extremely rare in adults in the developed world. If therapy is not started until several days after the onset of symptoms, it may not shorten the acute illness but it would still be effective in preventing rheumatic fever.

Amoxicillin dosage is 750 mg in a single daily dose. Intramuscular benzathine penicillin should be used for patients with expected noncompliance, and is the only agent proven to prevent acute rheumatic fever. Erythromycin and a first-generation cephalosporin should be considered for patients who are allergic to penicillin.

Shorter courses of newer agents, such as azithromycin, are effective in eradicating GABHS from the pharynx, but cannot be endorsed at this time. Sulfonamides and tetracyclines are not recommended because of high rates of resistance.

Recurrent episodes of pharyngitis in patients with positive cultures or rapid antigen detection tests are more likely to be due to persistent carriage in the face of intercurrent viral infection. In the small percentage of patients who have multiple episodes of streptococcal pharyngitis over the course of months, higher eradication rates may be achieved with agents such as clindamycin, amoxicillin-clavulanate, or intramuscular benzathine penicillin.

Follow-up cultures of asymptomatic patients after adequate therapy are indicated only if there is a history of rheumatic fever, or if pharyngitis develops during an outbreak of rheumatic fever or poststreptococcal glomerulonephritis.

The antistreptolysin-O (ASO) titer is valuable in patients suspected of having acute rheumatic fever or poststreptococcal glomerulonephritis.

Routine testing or treatment of asymptomatic household contacts with group A streptococcal pharyngitis is not recommended. Streptococcal carriers pose very little risk to their contacts. They are also at very low risk for developing any suppurative or nonsuppurative complications.

SOFT-TISSUE INFECTIONS

Soft-tissue infections are also frequently encountered in the outpatient setting. What is your diagnosis and what treatment would you recommend for these three cases?

- A 46-year-old diabetic man with varicose veins has pain and an ill-defined redness on the medial aspect of the right lower leg.
- A 79-year-old man with chronic lymphocytic leukemia has an area of well-demarcated redness and tenderness over his nasal bridge, which later spreads to his cheeks.
- A 65-year-old right-handed woman presents with swelling and pain of the right index finger after being bitten by a cat. She is febrile and hypotensive.

Cellulitis

The man with diabetes in the first case has cellulitis. Antimicrobial coverage for staphylococci and streptococci is indicated, with either a penicillinase-resistant penicillin, such as dicloxacillin, or a first-generation cephalosporin, such as cephalexin. Diabetic patients who have an open wound on their lower extremity are at risk for infection with other organisms, including aerobic gram-negative bacilli and anaerobes. These patients should be treated with broader-spectrum agents, such as amoxicillin-clavulanate.

The patient's predisposing factors include diabetes and possibly the varicose veins impairing the skin over his leg. Differentiation between staphylococcal and streptococcal cellulitis is not possible on clinical grounds alone. Thus, antimicrobial coverage for both is indicated. An ASO titer is usually not positive at the time of presentation. The yield of blood cultures in patients with uncomplicated cellulitis is very low, and has marginal impact on clinical management.[43]

If someone with cellulitis has marked systemic toxicity out of proportion to the local findings, pain and swelling outside the area of erythema, crepitus, or loss of sensation in the involved area, one should suspect necrotizing fasciitis and obtain a consult with a surgeon. Eagle described the inoculum effect in the 1950s. It simply means that in cases of deep soft-tissue infections, streptococci reach a stationary phase of growth, which makes penicillin less effective. Clindamycin, which acts by inhibiting protein and bacterial toxin synthesis, works best in conjunction with penicillin in these cases.[44,45]

A rapidly progressive cellulitis with hemorrhagic bullae in an immunocompromised patient, particularly if cirrhotic, exposed to sea water, or who has eaten raw oysters should raise the question of *Vibrio vulnificus*. Bacteremic cases are fatal in 30% to 50% of cases. Thorough cooking of seafood remains the only effective means of prevention. Treatment is with a tetracycline.

Cellulitis due to *Aeromonas hydrophila* is seen with fresh water exposure, particularly in patients with cirrhosis or cancer. Other manifestations include gastroenteritis and spontaneous bacterial peritonitis. Optimal antibiotic therapy is unclear, but agents that inhibit protein synthesis, such as tetracycline, clindamycin, and erythromycin, should be considered.

Erysipeloid, caused by *Erysipelothrix rhusiopathiae*, usually occurs in healthy people after occupational exposure, such as in fishermen and butchers. The violaceous lesion develops 1 week after exposure, and spreads peripherally with a raised border and central clearing. Ulceration does not develop. It is usually a localized infection as compared to that caused by the prior two organisms. Treatment is with penicillin.

For suspected streptococcal pharyngitis, obtain a culture or antigen test and start penicillin at the same time

Erysipelas

The man in the second case has classic erysipelas. He had the habit of frequently cleaning his nose with saline squirts, which may have precipitated this infection.

While cellulitis involves the deeper subcutaneous tissues, erysipelas is a more superficial infection, resulting in a well demarcated area of erythema and induration. Most of the literature classically describes facial involvement, but the lower extremities have been recently more commonly affected.

Attempts at surface cultures are rarely useful, and blood cultures are also rarely positive.

Postmastectomy lymphedema and chronic venous insufficiency after deep venous thrombosis or vein stripping are commonly associated with recurrent erysipelas.

The classic cases are almost always due to GABHS, so penicillin remains the drug of choice. In some cases one may not be

able to differentiate cellulitis from erysipelas clinically. In these cases, empiric treatment with a penicillinase-resistant penicillin or a first-generation cephalosporin is indicated.[44]

Bites

Almost half of all Americans will be bitten at some point by an animal or by another person. The third case suggests joint or bone involvement, which is not uncommon with the thin, penetrating teeth of cats, with ensuing sepsis. Prompt surgical intervention is imperative for any deep hand or face infection resulting from a bite.

Although dog bites are much more common that human bites, the latter are associated with more complications, because they are usually clearly intended and possibly premeditated.

Certain infectious organisms are seen more frequently with certain animals[46]: *Pasteurella multocida* (cats more than dogs), alpha hemolytic streptococcus (dogs more than cats), and *Eikenella corrodens* (humans, clenched-fist bites). Anaerobic organisms and *Staphylococcus aureus* may be cultured from one third of all cases of bite infections.

It is not necessary to culture bite wounds that are less than 8 hours old. Plain films should be done if you suspect a bone was fractured in the case of large animal bites, if the bite occurred over a joint, or in cases where a tooth fragment from an animal that has long thin teeth may be impacted and form a nidus for infection.

Most bite wounds should be left open with delayed closure. Irrigation, debridement, elevation, and immobilization are the main principles for managing a bite wound.[47]

Prophylactic antibiotics in clinically uninfected bites should only be considered for severe wounds, those involving joints or bones, near prosthetic joints, or in immunocompromised patients.

Remember the tetanus booster, particularly in the elderly, where the vaccination status may have lapsed. In the United States, persons bitten by dogs do not require rabies prophylaxis, but it should be considered with wild animal bites and rodents, particularly raccoons.

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