



Antibiotic Prophylaxis with Penicillins

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INTRODUCTION

During the past decade significant differences in both the types of organisms and antibiotic sensitivity patterns

in isolates from various infective diseases have been seen. Studies have revealed a clear increase in antibiotic

resistance to various organisms. There are fears that extensive use of prophylactic antibiotics may

enhance the emergence of resistant bacteria. Benefit of prophylactic antibiotics is limited when there is

high prevalence of antibiotic-resistant organisms in the community. Thus clinicians must maintain a balance

between beneficial effects of prophylactic antibiotic usage and the emergence of antibiotic resistance. Role of

Penicillin as prophylactic antibiotic has been proved beyond doubt over the past century.

Prophylaxis can be directed as :

1. Specific pathogen prophylaxis
2. Protection of infection prone sites
3. Protection of vulnerable host

SPECIFIC PATHOGEN PROPHYLAXIS

The role of prophylaxis can be seen in both medical and surgical cases as :

- a. Short term courses of therapy for few days (e.g., prophylaxis against *Neisseria meningitidis* in family contacts)
- b. Several months (e.g., antitubercular medication for infants contacts)
- c. Long term prophylaxis (against group A *Streptococcus* among individuals with Rheumatic Heart Disease)
- d. Life long treatment (e.g., *Pneumocystis* prophylaxis for symptomatic individuals infected with HIV)

Protection of Infection Prone Sites

Requirement for the prophylaxis to infection prone sites depends upon :

- vulnerability to the infection is brief

- limited number of potential infecting organisms is present
- the antibiotic susceptibilities of the organism are known and stable
- antibiotics can penetrate the affected body site in effective concentrations

Protection of the Vulnerable Host

It is appropriate to protect a vulnerable host in only a few circumstances. As it is impossible to eliminate all bacteria from a human host; often, attempts to do so result in life threatening infection with antibiotic resistant organisms or fungi. Children with congenital asplenia require antibiotics for upto five years of age and for children during the first five years after splenectomy. Trimethoprim/Sulphamethoxazole (TMP/SMX) prophylaxis for children upto six years, while older children should receive either oral penicillin V or amoxicillin for *Pneumocystis carinii* during chemotherapy for hematological malignancies¹.

Penicillin prophylaxis has been recommended for a wide spectrum of medical diseases and surgical procedures.

Role of prophylaxis against medical illness such as bacterial endocarditis, prosthetic valve (biograft and homograft), previous bacterial endocarditis, congenital cardiac anomalies, rheumatic and acquired valve dysfunction, hypertrophic cardiomyopathy and MVP are well known. Chemoprophylaxis for high risk pregnancies which may transmit Grp B Streptococci infection to neonate, Sickle cell anaemia patients alongwith their vaccination, bacterial infections in neutropenic patients and breast feeding mothers alongwith their children for prophylaxis against anhrax are the new entities recognized for prophylaxis in medical diseases. Surgical procedures requiring prophylactic penicillin to avoid post-procedure infections are not to be forgotten as physicians get more involved in multidisciplinary approach in patient management. Procedures like amputation for vascular disease, open fractures with or without faecal contamination, abdominal trauma, biliary surgery ERCP and neurosurgery especially anterior fossa repair have been recommended. In an era of replacements a Total Hip Replacement with potential of increased risk of haematogeneous spread from a dental procedure also requires aggressive penicillin prophylaxis.

Table 1 : Prophylaxis for Bacterial Endocarditis

For DENTAL, ORAL OR UPPER RESPIRATORY PROCEDURES

CONDITION	DRUG	ADULT DOSE (Time Before Procedure)
Standard Regimen	Amoxicillin	2 g po 1h
Amoxicillin /penicillin allergic	Clindamycin or Cephalexin or Cephadroxil	600 mg po 1h 2 g po 1h
	Azithromycin or Clarithromycin	500mg 1h
Unable to take oral	Ampicillin	2 g IV/ IM 30min
Unable to take oral and allergic to Ampicillin / Amoxi / Penicillin	Clindamycin or Cefazolin	600 mg I/V 30 min 1 g 30 min

For GENITOURINARY / GASTROINTESTINAL (excluding esophageal)

CONDITION	DRUG	ADULT DOSE (Time Before Procedure)
Standard Regimen	Ampicillin and Gentamycin	2 g IV / IM 30 min 1.5 mg/ kg IV / IM (max 80 mg) 30 min
	PLUS	
	Amoxicillin or Ampicillin	1 g po 6hr after or 1 g IV/ IM 6hr after
Ampicillin/Amoxi/Penicillin Allergic	Vancomycin and Gentamycin	1 g IV over 1-2 h 30 min 1.5 mg / kg IV / IM within 30 min of procedure
Alternate regimen for low risk patients	Amoxicillin or Ampicillin	2 g po 1h or 2g IM / IV 30 min before

Bacterial Endocarditis

Transient bacteremia may result in bacterial seedling of a previously abnormal endovascular surface such as heart valve, resulting in formation of vegetation. Although most cases of endocarditis are not attributable

to medical procedures, antibiotic prophylaxis for endocarditis has focused on the risks associated with

transient bacteremias during dental, respiratory, gastrointestinal or genitourinary procedures².

Major changes in the updated recommendations include the following:

1. The recommendation emphasizes that most cases of endocarditis do not stem from invasive procedures.
2. Risk categories are established for varying cardiac conditions as high, moderate and negligible risk for the potential outcome, if endocarditis develops.

3. Procedure which can cause bacteremia and for which prophylaxis is recommended are more clearly delineated.
4. Mitral valve Prolapse has been set into algorithm to define when such patients are to be prophylaxed.
5. The initial dose of amoxicillin is reduced to 2 grams. The follow up dose is no longer recommended for oral or dental procedures. Clindamycin and other alternatives are to be used in penicillin sensitive patients. Additionally the use of erythromycin has been discontinued.

A. High risk

Prosthetic valves (biograft and homograft)

Previous Endocarditis

Complex Cyanotic Heart disease : Single ventricle states

Transposition of Great Arteries

Tetralogy Of Fallot

Table 2 : Schedules for Children

Amoxicillin / Ampicillin	50 mg
Azithromycin	15 mg
Cephalexin	50 mg
Cefadroxil	50 mg
Cefazolin	25 mg
Clindamycin	20 mg
Clarithromycin	15 mg
Gentamycin	1.5 mg
Vancomycin	20 mg

Surgically constructed systemic pulmonary shunt or conduits

B. Moderate risk

Acquired valvular dysfunction
Hypertrophic cardiomyopathy
MVP with valvular regurgitation and/or thickened leaflets
Congenital malformations other than mentioned above and below

C. Negligible risk

Isolated Secundum ASD
Previous coronary artery bypass graft surgery
Mitral valve prolapse without valvular regurgitation
Previous Kawasaki disease without valvular dysfunction
Previous Rheumatic fever without valvular dysfunction
Cardiac pacemakers (intravascular and epicardial) and implanted defibrillator

Endocarditis prophylaxis is not routinely recommended for incisions of surgically scrubbed skin, cardiac catheterization and angioplasty, coronary stents, endotracheal intubation, bronchoscopy, endoscopy, transeosophageal echocardiography, vaginal delivery or caesarian section among other conditions, although the guidelines leave open the option for prophylaxis in high risk patients with some of these conditions.

AHA Prophylaxis Guidelines for Prevention of Bacterial Endocarditis³

Schedules followed for children are same except for the dosages, which are based on per kg wt of the child (Table 2).

Rheumatic Fever

Rheumatic fever associated with Group A streptococcal infection requires secondary prophylaxis with Penicillins has been proved beyond doubt. Intramuscular injection of 1.2 MU of benzathine penicillin G every four weeks has been accepted technique. However studies in developing countries with a high incidence of rheumatic fever have indicated that this regimen may be inadequate. In 1998, WHO & American Heart Association recommended that penicillin be given every three weeks in special circumstances or in high risk patients. Various studies have proved that rate of group A streptococcal infections and of penicillin prophylaxis failure rates were lower in patients receiving injection every three weeks than in patients receiving injections every four weeks.

Neonatal Group B Streptococcal Infection

Group B streptococci (including *Strepto. agalactiae*) are the leading bacterial causes of neonatal illness and death, causing invasive disease in 1.8 infants per 1,000 live births. These bacteria asymptotically colonize the vaginal or rectal areas of 10 to 30 percent of pregnant women, which may cause preterm labor or membrane rupture, UTI, chorioamnionitis, postpartum endometriositis, postpartum wound sepsis, pelvic thrombophlebitis, endocarditis and sepsis. Clinically diagnosed maternal intrapartum infection is strongly associated with five minute Apgar score below 6, neonatal seizures and unexplained spastic cerebral palsy in infants of normal birth weight. Upto 2 percent of maternal carriers deliver infants with invasive group B streptococcal disease, most of which is caused by in utero infection.

Neonatal grp B streptococcal infection can be prevented by identifying and treating pregnant women who carry the streptococci or who are at highest risk of transmitting the bacteria to newborns. Such women can be identified through the use of an anogenital culture for group B streptococci obtained at 35 to 37 weeks of gestation and by presence of at least one of many risk factors associated with neonatal infection. These risk factors include preterm labor or rupture of the membranes at less than 37 weeks of gestation, previous delivery of an infant with invasive grp B streptococci disease, grp B streptococcal bacteruria during the present pregnancy, maternal intrapartum fever of 38°C (100.4° F) or rupture of the fetal membranes for 18 hrs or more⁴. The recommended agent for intrapartum Chemoprophylaxis is intravenous Penicillin G; Clindamycin is used in penicillin allergic patients⁵.

Sickle Cell Anaemia

Children with sickle cell anaemia have an increased susceptibility to bacterial infections, especially to those caused by *Streptococcus pneumoniae* and *Neisseria*. Meningococci, which are the leading cause of infection in young children. Other bacteria like *Salmonella*, *H. influenzae* may also cause sepsis. Acute Chest Syndrome caused due to *Chlamydia pneumoniae* and *Mycoplasma pneumoniae* is commonly seen⁶. Children with sickle cell anaemia should receive prophylactic therapy with oral penicillin by four months of age till 3 yrs to decrease morbidity and mortality associated with pneumococcal septicaemia. A daily dose of 125 mg Penicillin V potassium po BID was recommended to reduce the incidence of documented septicaemia due to *S. pneumoniae*⁷. 3 yrs to 5yrs of age group should receive 250 mg po BID, while it is safe to discontinue penicillin prophylaxis after the age of 5 yrs. Vaccination, penicillin prophylaxis and prompt attention to fever can prevent serious pneumococcal infections. SBE prophylaxis should be given if heart murmurs are caused by valve pathology or if hip or other prosthesis are in place⁶.

Neutropenic Patients

Bacterial sepsis remains a major cause of morbidity and mortality in patients rendered neutropenic following cytoreductive therapy for hematological malignancy. The introduction of more aggressive anti neoplastic chemotherapeutic regimens in individuals with solid organ malignancies has resulted in increasing numbers of

Table 3 : Surgical Prophylaxis

Condition	Drug
Amputation or vascular disease	Cefazolin plus metronidazole (for prevention of clostridial myonecrosis) Clindamycin if allergic to penicillin.
Open fractures	Penicillin IV for 48 hrs (metro if allergic to penicillin)
Open fracture (with fecal contamination)	Penicillin, Gentamycin and Metro
Abdominal trauma (When bowel breached)	Penicillin, Gentamycin and Metro
Biliary surgery, ERCP	Penicillin and Genta
Neurosurgery ¹⁵ (Anterior fossa repair)	Ampicillin 2 g plus Cefazolin 1 g (Ampi for streptococcal Cefazolin for staphylococcal)
CSF leaks	No prophylactic antibiotics
Bites	Penicillin, if allergic give Tetracycline Human bites need Co-amoxiclav

these patients experiencing the profound neutropenia that puts them at risk of infection⁸.

Many approaches have been developed to prevent infection by microorganisms. Many of these strategies have fallen out of favour due to poor drug compliance and lack of scientific data to support their efficacy. Of particular concern has been bacteremia with Viridans Grp streptococci (VGS). These infections have been characterized by significant morbidity including respiratory distress syndrome and endocarditis. The risk factors have been identified for VGS sepsis which include high dose cytosine chemotherapy, use of antacids, presence of mucositis, oral herpes simplex virus and co- trimoxazole prophylaxis. Combination of penicillin and ofloxacin have been used with success to cover as agents with increased anti-Gram positive activity⁹. Some populations of neutropenic patients have high prevalence of penicillin resistance VGS¹⁰ and blood culture isolates of these bacteria from neutropenic patients may be resistant to penicillin. Studies have reported an increase in infections with strains of VGS intermediately susceptible or resistant, to penicillin¹¹. Subsequent approaches have included the addition of macrolides, rifampicin, vancomycin and quinolones, with varying degree of success.

Anthrax

In an era of bioterrorism especially due to associates anthrax the role of prophylaxis in preventing the spread of an epidemic¹². Ciprofloxacin or Doxycycline is recommended for antimicrobial prophylaxis and treatment of adults and children with Bacillus anthracis infection. Amoxicillin is an option for antimicrobial prophylaxis for children and pregnant women¹³ Amoxicillin has been recommended for treatment of cutaneous disease when B. anthracis is susceptible to penicillin. Penicillins are effective for antimicrobial prophylaxis as relatively few organisms are expected to be present. Amoxicillin may be used for the 60 day antimicrobial prophylaxis in infants and children as ciprofloxacin and doxycycline may be associated with adverse effects in children and liquid formulations of these drugs are not widely available¹⁴. Because of its known safety for infants, amoxicillin can be used for prophylaxis in breast feeding mothers.

Post Splenectomy

Splenectomy performed for Hodgkin's lymphoma, post traumatic or for any other etiology in adults and children are

more susceptible to infections with *Strep. pneumoniae*, *H. influenzae* and *Capnocytophaga canimorous* (occurring after dog bite). Penicillin prophylaxis in form oral Penicillin V potassium 125 mg BD in children and 250 mg BD in adults in recently splenectomized patients has been used by some experts especially in Hodgkin's disease who have under gone antineoplastic chemotherapy or radiotherapy. Oral Ampicillin is also used as for its antimicrobial cover. But neither the optional antibiotic nor the optimal dose of antibiotic prophylaxis in splenectomized patients has been yet established.

Surgical Prophylaxis

Post-operative wound infections are a major source of morbidity. Use of perioperative antibiotics has become an essential component of the standard care in all surgical procedures and has resulted in a reduced risk of post-operative infection when sound and appropriate principles of prophylaxis are applied (Table 3).

Basic principles are :

1. Probable risk of infection
2. Contaminating flora associated with the operative wound or organ
3. Administration of drug must occur 30- 45 mins prior to incision
4. Procedures lasting more than 3 hrs require additional effective dose

Total Joint Replacements

Antibiotic prophylaxis to prevent haematogeneous prosthetic joint infections in dental patients who have undergone total joint arthroplasties is not indicated. However it is advisable to consider premedication in a small number of patients who have potential risk of haematogeneous spread as in

1. Immunocompromised
 - a. Inflammatory arthropathies: Rheumatoid arthritis, SLE
 - b. Disease or drug induced suppression
2. Others
 - a. Diabetes Mellitus Type I
 - b. First 2 yrs after joint replacement
 - c. Previous prosthetic joint infection
 - d. Malnourishment

c. Haemophilia

Not allergic to penicillin : Cephalexin, Cephadrine or Amoxicillin
2 grm PO/IV

Allergic to penicillin : Clindamycin 600 mg PO/ IV

PANDAS

Paediatric Autoimmune Neuropsychiatric Disorders Associated Streptococcal infections (PANDAS) is a known identity with presence of main elements as obsessive compulsive disorder (OCD) or tic disorder, pubertal onset, episodic course, neurologic abnormalities (i.e., choreiform movements) and streptococcal triggered symptom exacerbations. The exacerbation has been related to group A Streptococcal infection in manner similar to rheumatic fever and neurological variant Sydenham's chorea. Because penicillin prophylaxis has been effective in preventing recurrences of rheumatic fever it was postulated that it might also prevent PANDAS. No conclusion was drawn from various studies regarding the efficacy of penicillin prophylaxis in PANDAS or OCD and it was recommended that further studies should be employed.¹⁶

CONCLUSION

Antimicrobial prophylaxis can reduce the incidence of infections which might be anticipated following certain clinical procedures. All antimicrobial prophylaxis should follow these rules. Bacterial concentrations of drug should be present in the tissue of interest before bacterial inoculation occurs. Inoculum size determines the frequency of infection.

Antimicrobial prophylaxis should not be substituted for measures designed to reduce the number of bacteria that enter the tissue of interest. If it is likely that bacterial infection exists, full course of therapy appropriate for the specific infection should be initiated.

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