EDITORIAL

PROPHYLACTIC ANTIMICROBIAL AGENTS

R V Scoy

SINGAPORE MED J 1993; Vol 34: 289-291

This article is based on a paper presented at the 1993 MoH-Mayo Clinic Update held on 20 and 21 February 1993 in Singapore.

The use of prophylactic antimicrobial agents in medicine is widespread, often helpful, and sometimes controversial. In certain instances, efficacy has been documented. In other cases, prophylaxis is accepted, but not carefully documented to be beneficial. An extensive review of the use of prophylactic antimicrobial agents is beyond the scope of this editorial. However, the following discussion is meant to be an overview of this author's opinion of a variety of uses in adults in the USA. Indications in other populations may vary considerably.

Tuberculosis Prophylaxis[1*]

Tuberculosis prophylaxis is really treating suspected subclinical infection by the tubercle bacillus. There are three categories of such patients according to the suspected sensitivities of the organism the patient harbours.

- Isoniazid (INH) sensitive
- INH (only) resistance
- Multiple drug resistance

INH sensitivity suspected cases without evidence of active disease that would qualify for prophylaxis would include:

- Recent (less than 2 years) conversion of purified protein derivative(PPD) at any age
- Household or other similar close contact
- Positive 5 test units PPD

and

No active disease

and

Not previously adequately treated

and

No contraindication to treatment

and either

Under the age of 35

or

Underlying predisposing disorder

or

High risk population group

The prophylaxis treatment for this group would be INH 300mg per day, Vitamin B_6 10 to 25 mg per day, avoidance of daily alcohol and monthly follow-up for liver and other toxicities for nine to twelve months.

When exposure to INH resistance is suspected and the patient meets the above criteria, rifampin 600mg per day with monthly follow-up for appropriate compliance and toxicity monitoring is indicated. This prophylaxis has not been proven, but the highly effective nature of rifampin against the tubercle bacillus strongly suggests it would be effective.

The menacing problem of multiple drug resistant tuberculosis (MDR TB) has become a major problem, particularly in AIDS patients in the United States. Prophylaxis in those significantly exposed to such patients is of unknown value. Furthermore, which agent or agents to use is obscure. If sensitivity data of the organism to which the patient had significant exposure are known, it may be indicated to treat the patient prophylactically with one or more agents to which the organism is sensitive. There is hope, but no documentation, that the quinolones will be of benefit.

The definition of a positive PPD in the USA has been changed. The old definition was greater than or equal to 10 mm of induration at 48 hours to a 5 test unit PPD. The new definition depends on the status of the host:

Greater or equal to 5 mm induration at 48 hours if:
- Recent close contact
- Fibrotic lesion on chest X-ray
- HIV infection

Greater or equal to 10 mm induration at 48 hours if:
- People who do not meet the 5 mm criteria and
- Medical factors that increase risk of TB disease
- High prevalence area past or present
- Under-served population
- Residents of long term care facilities
- IV drug users

Greater or equal to 15 mm induration at 48 hours:
- All others who do not meet 5 mm or 10 mm criteria

Medical conditions that increase the risk of tuberculosis include:

- HIV infection
- Silicosis
- Fibrotic lesion on chest X-ray
- Diabetes mellitus
- Prolonged corticosteroid therapy
- Immunosuppressive therapy
- Hematologic and reticuloendothelial diseases
- End stage renal disease
- Intestinal bypass
- Post gastrectomy
- Chronic malabsorption syndromes
- Carcinomas of the oropharynx and upper GI tract
- 10% or more below ideal body weight

Rheumatic fever prophylaxis is not new. However, there may be an increase in rheumatic fever in the USA.

Benzathine penicillin is best for compliance reasons.
- 1.2 million units I.M if more than 25 kg weight
- 600,000 units I.M if less than 25 kg weight

or

Penicillin V
- 250 mg bid if more than 25 kg weight
- 125 mg bid if less than 25 kg weight

Mayo Clinic
Rochester, Minnesota 55905
U.S.A

R V Scoy, MD
Consultant, Infectious Diseases & Internal Medicine

If the patient is allergic to penicillin, several antimicrobials may be effective:

Sulfonamide
Erythromycin
Clindamycin
Cephalexin, cephradine or cefadroxil

There is a syndrome of recurrent cellulitis and lymphangitis in patients who have lymphedema for a variety of reasons including:

Modified radical mastectomy
Prominent trauma to an extremity
Irradiation therapy
Pelvic lymphadenectomy - exenteration surgery

The syndrome includes sudden onset of fever, often with rigors, pain, swelling, redness and increased warmth in the affected extremity. It responds to treatment with penicillin G or cefazolin, but is frequently recurrent. The recurrences should be prevented because each recurrence may produce further impairment of the lymphatic drainage. No carefully controlled studies have been performed, but the rheumatic fever regimes may well be effective. Another regimen that seems to work in most instances is penicillin

500 mg bid daily for 2 weeks, then
500 mg bid daily every other week, for 3 months, then
500 mg bid daily first week of each month for life

Adjust dosage to what works.

If the patient is allergic to penicillin, try erythromycin or cephalexin. Adjunctive therapy is important and includes:

Decompression of the lymphedematous extremity
Elastic sleeve or hose
Life long treatment of dermatophytosis
Dry well between toes after shower
Antifungal topical agent
eg clotrimazole, ketoconazole etc
Cotton stockings (to absorb moisture)

The patient frequently does not remember such instructions from the first instruction session so it should be repeated in the presence of the spouse or nearest relative until learnt.

Meningococcal infections, including meningitis and particularly meningococcal bacteremia with disseminted coagulation and fibrinolysis are severe, life-threatening events. Prophylaxis is indicated for those with household contacts, same room day care centre contacts or other such close contacts. The doses are:

Adults: 600mg bid for 2 days
1-48 months: 5 mg/kg twice daily for 2 days
less than 1 month: 2.5 mg/kg twice daily for 2 days.

This regimen has been shown to be approximately 85% effective. Minocycline is also effective, but causes vestibular reaction and should not be given to young children or pregnant women.

Similarly, rifampin should be given to all household members if:

- Any household member is less than 48 months of age
- Even if they have received immunisation for hemophilus
- Perhaps to day care centre children in the same room.

Human and animal bite wounds are prone to become infected. The common organisms include anaerobic organisms of the mouth, certain aerobic organisms eg *Pasteurella multocida* in animal bites and *Staphylococcus aureus* in human bites. The recommended prophylaxis in such cases is:

Amoxicillin/clavulanate 250 to 500 mg bid for 3-5 days.
Doxycycline as alternative
Avoid erythromycin, dicloxacillin, cephalexin
(*P. multocida* frequently resistant)

Staphylococcus aureus is perhaps the major hospital acquired pathogen. It may be present in the innocuous carrier state or be the cause of infection. Some *S. aureus* are resistant to all of the beta lactam antimicrobial agents, and usually multiple other antimicrobials as well. These are referred to as MRSA which formerly represented methicilllin resistant *Staphylococcus aureus*, but probably now should stand for multiply resistant *Staphylococcus aureus* because the resistance usually extends beyond the beta lactam antibiotics. Presently, it is not feasible to eliminate all such organisms from the hospital environment although great efforts are made. In some areas attempts at eradicating the carrier state include: [2,3]

Rifampin 600 mg/day for 10 to 14 days, plus
Mupirocin intranasally bid x 5 days
pHisoHex or other antiseptic soap bathing

It may be advisable to employ the latter two measures for a few days before adding the rifampin in order to decrease colony counts and hopefully diminish the chance of rifampin resistance developing. In areas where tuberculosis is quite common, such use of rifampin may not be wise due to possible induction of rifampin resistant tuberculosis. Again, consultation with local infectious disease experts is valuable.

Recurrent cystitis[4] in women is a common and annoying problem for the patient. Trimethoprim/sulfamethoxazole 40/200mg or trimethoprim 100mg h.s. or three times per week or after intercourse, but no more than once per day is very effective prophylaxis. Some women do not like to take medicines regularly. In those patients a prescription for the above medications may be given to take at the onset of symptoms for three days.

Ophthalmia neonatorum[5] may be prevented in most newborns with topical silver nitrate 1%, erythromycin ointment 0.5% or tetracycline ointment 1%. Consult your local infectious disease specialist for the prophylaxis of choice in your area.

Intravenous gammaglobulin (IVIG) is not an antibiotic, but it is an important prophylactic antimicrobial agent. Patients with hypogammaglobulinemia have monotonously, recurrent sino-otic-pulmonary infections due to *Streptococcus pneumoniae* and *Hemophilus influenzae*. Occasionally, bacteremia or meningitis is also present. Giardia lamblia infection is fairly frequent. Rare infections include Enterovirus, particularly ECHO virus, encephalitis, dermatomyositis or polymyositis and Mycoplasma species multifocal destructive arthritis or osteomyelitis. It is important to prevent the recurrent sinopulmonary infections with IVIG to prevent the development of bronchiectasis. This latter mechanical complication also predisposes to pulmonary infections which are then not prevented by IVIG. The author's usual dose regimen is:

IVIG 200 mg/kg/4 weeks
May give bigger doses if clinically indicated
Goal is to prevent infections and bronchiectasis
IVIG is better than intramuscular IG (IMIG) because bigger doses can be given
Several preparations available but which is the best?
Expensive, but worth it.

Selective bowel decontamination using non absorbable per oral or per nasogastric tube antimicrobial agents and an oral-

naso-pharyngeal paste with antimicrobial agents in intensive care patients including surgical patients has been tried in several centres. The agents used are usually an aminoglycoside, a polymyxin and an antifungal agent. The theory is to eradicate the aerobic organisms and leave the anaerobic normal flora intact.

Some studies have shown decreased antimicrobial use and decreased numbers of infections. There has been no decrease in mortality or length of hospital stay. Most of the studies have not been double blind, randomized prospective studies. Selective bowel decontamination may be effective, but it has not yet been proven.

Burn wounds[6] require topical antimicrobial agents. The two most commonly used topical agents are silver sulfadiazine = Silvadine, and methylated sulfonamide = Sulfamylon. Debridement produces bacteremia so parenteral agents are given prior to debridement.

Antibiotic prophylaxis for surgical procedures is an important, complex and somewhat controversial study. The literature is full of studies, only some of which are properly conducted. Endocarditis prophylaxis should be remembered when appropriate in addition to surgical prophylaxis regimens.

Influenza is best prevented by yearly immunisation in those most susceptible to complications of influenza. In patients with hypogammaglobulinemia or those who were not immunised prior to influenza occurring in the community, amantadine 100 mg bid has been shown to be effective for Influenza A. There are a few reports of influenza A strains resistant to amantadine. The drug has a long shelf life and may be kept for several years. The dose should be reduced appropriately for renal insufficiency or the elderly.

Herpes simplex genitalis recurrences are commonly prevented with acyclovir 200 mg p.o. tid in normal hosts. A variety of regimens are used for transplant patients as well as those with AIDS and others with impaired cellular immunity. Ganciclovir prophylaxis or suppression for cytomegalovirus as well as Herpes infections is employed in AIDS patients.

Prophylaxis for most sexually transmitted diseases is given to sexual contacts. Resistance patterns vary. Local experts should be contacted for recommendations. Such infections include:

Chancroid
Chlamydia trachomatis infection
Gonorrhea
Lymphogranuloma venereum
Non gonococcal urethritis
Pediculosis pubis (lice)
Scabies
Syphilis
Trichomonas infection

Patients with human immunodeficiency virus infection require a variety of prophylaxis or suppression treatment, the full discussion of which is beyond the scope of this editorial. Trimethoprim sulfamethoxazole combination of one double strength table three times a week is the preferred prophylaxis regimen for the very common, life threatening pneumocystis carinii infection. Prophylaxis or suppression for candida infections range from topical agents such as clotrimazole to orally absorbed azoles such as ketoconazole or fulconazole. Those with a positive PPD, a past history of a positive PPD, a past history of tuberculosis or a significant exposure to tuberculosis should be given appropriate prophylaxis. Perhaps in the future prophylactic, as well as suppressive, regimens for toxoplasmosis, Mycobacterium avium intracellulare complex and other infections will be indicated.

It is beyond the scope of this editorial to discuss or even list all the areas of antimicrobial prophylaxis known or thought to be effective. Some of the miscellaneous infections for which prophylaxis is indicated include:

Plague	Tetracycline or Streptomycin
Pertussis	Erythromcyin
Malaria	Frequently changes. Area of travel specific. Find best source of information in your area or Centers for Disease Control, Atlanta GA
Hepatitis	Various gammaglobulin preparations are recommended for hepatitis A, B, C exposure
Endocarditis	Prophylaxis has been outlined in detail by the American Heart Association. Billfold cards with instructions for patients are available via American Heart Association, National Center, 7320 Greenville Ave, Dallas, TX 75231, USA.

References

1.* New guidelines will soon be coming from the Centers for Disease Control and The American Thoracic Society and will likely be available at time of publication of this article.

2. Chow JW, Yu VL. Staphylococcus aureus nasal carriage in hemodialysis patients: Its role in infection and approaches to prophylaxis. Arch Intern Med 1989; 149:1252-8.

3. Reagan DR, Doebbeling BN, Pfaller MA, Sheetz CT, Houston AK, Hollis RJ, et al. Elimination of coincident staphylococcus aureus nasal and hand carriage with intranasal application of mupirocin calcium ointment. Ann Intern Med 1991; 114:101-6.

4. Brumfitt W, Hamilton-Miller JMT. Prophylactic antibiotics for recurrent urinary tract infections. J Antimicrob Chemother 1990; 25:505-12.

5. Hammerschlag MR, Cummings C, Roblin PM, Williams TH, Delke I. Efficacy of neonatal ocular prophylaxis for the prevention of chlamydial and gonococcal conjunctivitis. N Engl J Med 1989; 320:769-72.

6. Monafo WW, West MA. Current treatment recommendation for topical burn therapy. Drugs 1990; 40:364-73.