"Theirs be the music, the colour, the glory, the gold;
Mine be a handful of ashes, a mouthful of mould."

John Masefield.

* * * * * *

PENICILLIN THERAPY

1. Special

a. It is anticipated that the supply of penicillin available in this theater will be sufficient to allow for its widespread use in the treatment of all battle wounds. Directions for the use of penicillin are incorporated in the circular letter entitled "Principles of Surgical Management in the Care of Battle Casualties" (Circular Letter No. 71, Office of the Chief Surgeon, 15 May 1944).

b. Special attention is directed to paragraph b, stating that the words "Penicillin treated" will be entered on the E.T or Field Medical Record, after the diagnosis, in every case which is so treated. Additional data, including dosage in units, method of administration (parenteral or local) and time and date of administration, will be entered on the back of the EMT or on the Clinical Record form in cases where a Field Medical Record has been initiated.

c. Only by the conscientious addition of the words "Penicillin treated" to the diaghosis list will it be possible to separate these cases. This will permit the collection and study of a large group of cases in which this drug has been used, to determine its efficiency in the treatment of battle casualties.

2. General

a. Penicillin is a potent antibacterial agent. Its action is not inhibited by the presence of para-aminobenzoic acid, pus, blood, serum, or by the products of tissue destruction. It is, however, destroyed by heat, acids and alkalis, oxidising agents, certain enzymes, alcohol, and various antiseptic agents.

b. Pencillin can be given intravenously, intramuscularly, or locally. It is not effective when given by the mouth. It is rapidly excreted in the urine; therefore, to obtain adequate levels in blood or tissue it must be

given at frequent intervals, and fluids should be moderately restricted unless other considerations preclude this measure.

c. A period of inadequate penicillin therapy may render a sensitive organism penicillin-resistant. This fact should be borne in mind in determining penicillin dosage.

d. Penicillin must be kept refrigerated. Stored at 4 degrees C., or cooler, and in sealed ampoules, penicillin maintains its potency for long periods of time. Although an expiration date appears on each ampoule, use of it later than the date shown is countenanced. In such instances a note will be made indicating manufacturer, lot number, expiration date, date used, and the result of therapy. In solution penicillin deteriorates somewhat rapidly but maintains full potency for at least one week when refrigerated.

e. Penicillin is relatively non-toxic. Among the reported toxic reactions, all probably due to impurities, are fever, chills, urticaria, thrombophlebitis at the site of intravenous injection, burning pain at the site of intramuscular injection, headache, and flushing of the face. The presence of any of these reactions does not constitute an indication for discontinuance of penicillin therapy.

f. Organisms sensitive to the action of penicillin are the gonococcus, meningococcus, staphylococcus, hemolytic streptococcus, pneumococcus, streptococcus viridans, B. anthracis, and certain of the clostridia.

g. Organisms resistant to the action of penicillin are the tubercle bacillus, C. diphtheriae, Friedlander's bacillus, Ps. pyocyaneus, the colondysentery group, the typhoid-paratyphoid group, and the anaerobic streptococcus.

3. Methods of preparing penicillin for administration

a. Intravenous injection: For intravenous injection the dry powder will be dissolved in sterile physiological saline solution in concentrations of 1,000 units per cubic centimeter.

b. Intramuscular injection: For intramuscular injection the dry powder will be dissolved in sterile physiological saline solution in concentrations of 10,000 units per cubic centimeter.

c. Local application : For use in the dry state

the powdered salt may be mixed, under sterile conditions, with sulfanilamide, using 5,000 to 20,000 units of penicillin per gram of sulfanilamide (one teaspoonful of crystalline sulfanilamide equals 3 grams). For use in solution the dry powder will be mixed with physiological saline solution in amounts from 250 to 1,000 units per cubic centimeter.

4. Therapy

a. Commanding officers will be responsible for selecting patients for penicillin therapy.

b. Conditions for which penicillin may be given:

(1) Septicemia due to staphylococcus; and (2) meningitis, empyema thoracis, bacterial endocarditis, and osteomyelitis.

(3) Infections of serious nature which have failed to respond to sulfonamide therapy and which are due to organisms in the penicillin-sensitive group.

(4) Less serious infections in personnel the importance of whose duties makes it desirable that they return to duty in the shortest time possible.

(5) Superficial wound infections due to organisms in the penicillin-sensitive group in which wound revision, secondary closure, or skin grafting are contemplated.

(6) Gas gangrene.

(7) Battle casualties and non-battle injuries.

(8) Sulfonamide-resistant gonorrhea.

5. Dosage: The objective in penicillin therapy is the maintenance of a concentration of penicillin at the site of infection sufficient to inhibit the growth of the infecting organism. The dosage as well as the duration of treatment will vary in individual cases. It can be determined only by the response of the patient, plus aid from the laboratory. The following schedules as to dosage are given as guides and may be altered at the discretion of the responsible medical officer.

a. For serious systemic infections an initial

intravenous dose of 20,000 units will be given. This will be followed by intramuscular doses of 10,000 to 20,000 units every 2 hours until the infection is under control, or proven to be resistant to penicillin therapy.

b. For less serious infections the initial intravenous dose will be omitted, and 10,000 units may be given intramuscularly every 2 hours.

c. In treating meningitis it must be remembered that penicillin given intramuscularly or intravenously does not reach the cerebrospinal fluid in appreciable amounts. Meningitis will be treated by intrathecal administration of 15,000 units every 8 to 12 hours, in addition to intramuscular doses as outlined above. Penicillin is prepared for intrathecal administration in the same proportions as for intravenous therapy.

d. Empyema and similar localized abscesses may be treated by the local application of penicillin in saline solution without parenteral administration. Depending upon the size of the cavity and the response to therapy, 20,000 to 50,000 units of penicillin will be instilled locally once or twice daily.

e. For superficial wound surfaces penicillin in dehydrated plasma (1 teaspoonful plasma equals ½ gram), or mixed with sulfanilamide, or as an ointment, will be used. The dosage will depend upon the size of the wound and the susceptibility of the organism; however, 10,000 to 50,000 units, once or twice daily, probably will be required. Wounds in which early surgery cannot be done will receive a similar application of penicillin which will be repeated every 8 to 12 hours. Penicillin will not be used routinely as a prophylaxis for infection in wounds where early surgery is possible.

f. Gas gangrene will be treated with penicillin as outlined for serious systemic infections. Local penicillin will also be used as described above. In addition to penicillin therapy, early radical excision of the involved tissue must be done and antitoxin administered.

6. Penicillin therapy in the treatment of gonorrhea

a. Penicillin may be used as the initial treatment of gonorrhea in patients whose duties will be interfered with by sulfonamide therapy.

b. Gonorrhea will be considered sulfonamide-resistant if a definitely favorable therapeutic response to adequate sulfonamide therapy is not produced in 10 days.

c. Dosage: 20,000 units of penicillin dissolved in 3 cc. of pyrogen-free water to be given intramuscularly every 3 hours until a total of 100,000 units have been administered. Patients who fail to respond to this dosage will be re-treated with 10,000 units intramuscularly every hour for a total of ten doses. Further treatment will be determined by the course of the disease. Patients failing to be cured by this regime will be transferred to a general hospital for observation.

7. Laboratory tests for patients receiving penicillin therapy

a. Test for sensitivity:

(1) The determination of sensitivity of an organism to penicillin is done by the trench-plate technique. A blood agar plate is used. A trench 1 cm. wide is removed from the middle of the plate. This is then filled with a mixture of agar and penicillin, containing 1 unit of penicillin per cc. of the mixture. (Precaution: cool agar to below 50 degrees C. before adding the penicillin.) The plate is then streaked across with the standard strain and with the organism to be tested. Inhibition of the standard strain averages about 8 to 10 mm. Very insensitive strains occasionally grow across the penicillin-filled trench. Freshly prepared plates must be used for each test, otherwise the penicillin diffuses throughout the plate.

(2) When facilities are available, this test must be carried out on the organism causing infection in each case (excepting cases of gonorrhea).

b. Test for bacteriostatic power, patient's serum:

(1) Some means of attempting to determine whether or not the patient is receiving enough penicillin is desirable. This is done by testing for a bacteriostatic level in the serum. The patient's blood is removed and the serum separated, using sterile technique. Four test tubes are set up containing the following: (a) undiluted serum; (b) serum diluted 1:2 with broth; (c) serum diluted 1:4

with broth; (d) broth without serum (control). If facilities permit, more accurate estimations of the amount of penicillin in the blood serum can be obtained by making dilutions up to 1:32, or 1:64. Each tube is now inoculated with a loopful of a diluted (1:1,000 or 1:10,000) 12-hour broth culture of either the patient's organism or the Florey staphylococcus. After 12 hours' incubation the result may be determined either by inspection, or subculture on agar plate. The latter is more desirable. If the serum is bacteriostatic, the first tube should show no growth; frequently inhibition is noted in the second and third tubes as well. Repeating this procedure on samples drawn at hourly intervals between two successive doses gives an indication as to whether the patient is receiving enough penicillin to produce bacteriostasis in the first place, and secondly, whether the bacteriostasis persists through the interval between doses.

(2) When facilities are available this test must be carried out in every case (excepting cases of gonorrhea) receiving penicillin parenterally. Should the period of penicillin administration be protracted, test every 48 hours at hourly intervals between two successive doses.

c. Bacteriological studies: Make aerobic and anaerobic cultures where facilities are available by inoculating washings from debrided tissue. For aerobic cultures inoculations should be made on blood agar and enriched broth. For anaerobic, washings should be inoculated into cooked meat media and iron milk, each of which has been boiled and rapidly cooled. Seal with vaseline and incubate. Preliminary bacteriological report in 18 to 24 hours. Make anaerobic sub-cultures from cooked meat media on blood agar plate for species identification.

8. Records

The words "Penicillin treated" must follow the diagnosis list in all such cases in order that records may be collected for further study and appraisal of the value of this agent. It is essential that accurate data be kept on all cases receiving penicillin, for these records will periodically be reviewed in order that we may determine the benefits which accrue from this agent and modify dosage and methods of therapy. Records should contain the following data:

a. Concise, but comprehensive history and physical findings.

b. Laboratory data, particularly results of penicillin sensitivity and bacteriostasis tests.

c. Details of penicillin therapy, including dosage, route of administration, interval between dosage, dates of administration, and toxic reactions, if any.

d. Summary of previous chemotherapy.

e. Necropsy findings for cases with fatal termination.

2. Supply

All hospitals, including field hospitals, evacuation hospitals, station hospitals and general hospitals, are authorized to keep a supply of penicillin on hand.

* * * * * * *

"Oh wonderful, wonderful, and most wonderful, wonderful! and yet again wonderful, and after that out of all hoping." - Shakespeare: As You Like It.
