

# EVIDENCE – BASED CLINICAL PRACTICE GUIDELINES FOR ANTIBIOTIC PROPHYLAXIS IN ELECTIVE SURGICAL PROCEDURES

## Table of Contents

I	Introduction	
II.	Scope of the Guidelines	
III	Methodology	
IV.	General Guidelines / Recommendations	
V.	Surgical Procedures	
	Breast Surgery . . . . .	Loreto Codamos, MD Rey Melchor F. Santos, MD, FPCS
	Hernia repair. . . . .	Nelson D. Cabaluna, MD, FPCS Domingo S. Bongala, Jr, MD, FPCS
	Biliary Surgery. . . . .	Nestor E. Dela Cruz, MD, FPCS
	Gastroduodenal Surgery. . . . .	Jose D. Quebral, MD, FPCS
	Colorectal Surgery. . . . .	Edgardo R. Cortez, MD, FPCS Ramon S. Estrada, MD, FPCS
	Neurosurgery . . . . .	Loreto Codamos, MD Rene C. Encarnacion, MD, FPCS
	Cardiac Surgery . . . . .	Adrian C. Peña, MD, FPSMID
	Non-cardiac Surgery. . . . .	Domingo S. Bongala, Jr, MD, FPCS
	Orthopedic Surgery . . . . .	Emily Tanchuling, MD, FPCS
	Transurethral Resection of the Prostate (TURP). . . . .	Antonio Anastacio, MD, FPCS
V.	References	

## INTRODUCTION

Sometime in 1999 the Committee on Surgical Infections, in one of its meeting came up with an idea of developing evidence based practice guidelines on the use of prophylactic antibiotics in selected elective operations. Among the operations chosen were the following (operations for Hernia (with & without mesh), Breast surgery, Cholecystectomy, Gastroduodenal surgery, Colon surgery, TURP, Thoracovascular surgery, Neurosurgery, and Orthopedic surgery). In December that year, with the approval of the Board of Regents, the Committee on Surgical Infections spearheaded a literature search to answer several clinical questions on the use of prophylactic antibiotics on selected elective operations, the primary aim of which is to reduce the incidence of surgical site infection. Among the issues that will be answered by these guidelines are the following: the timing of administration, the optimal dose, the frequency of administration, and the most appropriate type of antibiotics.

These practice guidelines have undergone four phases during its preparation and another four phases after its production. Phase I was for the preparation of the evidence based report (EBR) by the technical working group. Phase II was for the preparation of the Interim Report. Phase III was for the preparation of the draft guidelines. Phase IV was for the preparation of the final output of the clinical practice guidelines.

Phase V will be for the dissemination of these guidelines to the end users. Phase VI will be the actual implementation and Phase VII will be the monitoring and impact assessment. The final phase will be the review and revision of these guidelines every two to three years.

By January 2000 the final draft was ready to come out until a letter from the Philippine Society for Microbiology and Infectious Diseases, Inc. was received by the committee stating their position and concerns. The committee took them point by point and decided to expand the review of literature beyond RCT's and meta-analysis. And so the whole process was repeated, from phase I to IV.

To be more acceptable to the end users, the best available evidence tempered by expert's opinion supports the recommendations of these guidelines.

## **Methodology**

These evidence based practice guidelines underwent several phases during its development.

### **Phase I preparation of evidence based report (EBR)**

A Technical Working Group (TWG) was tasked to track, retrieve and appraise current evidences and this began work on July 1999. The literature search, limited to English publications, used both electronic and manual methods. Three electronic databases were used 1) The Cochrane Library, Issue 2, 2000 2) National Library of Medicine – Medline (PubMed, no time limit), and 3) HERDIN Health Research and Development Information Network) Version 1, 1997 of DOST-PCHRD and ancestry techniques and cross-reference). The literature search covered the period 1970 to 2000. From those actually retrieved a total of 216 were used as references. The search method used utilized the word prophylactic antibiotics, surgical site infection and the specific operations (e.g. cholecystectomy, colectomy, etc.) in question. The final output of this phase was an EBR.

### **Phase II Preparation of Interim Report (IR)**

The Technical Working Group held several meetings to review and discuss the EBR. A Nominal group technique was utilized after each discussion of specific topics to reach a consensus. A consensus was reached after having attained a 70% agreement among the members of the TWG.

### **Phase III Preparation of Draft Guideline**

The Technical Working Group together with the expert panel reviewed the interim report. Each report was analyzed and participant was allowed to give his opinions and views, after which the modified Delphi Technique was utilized to settle the issues.

The first experts panel was held in Evercrest, Batulao, Nasugbu, Batangas on Septmebr 24-26, 1999. The second experts panel was held in Mimosa, Pampanga on November 17-19, 2000.

### **Phase IV Preparation of Clinical Practice Guidelines**

**The draft guidelines were then presented to the stakeholders namely the surgeons, the presidents or representatives of pharmaceutical companies, government organizations like the PMA, Philhealth, and Chairman of the Department of Surgery of the different institutions. The final output will now be known as clinical practice guidelines on selected elective surgical procedures, after taking into consideration the opinions of the stakeholders and incorporating them into these guidelines.**

The first presentation to the stakeholders were done at the PCS Multi-Purpose Hall on November 13, 1999. The second presentation to the stakeholders were done at the Edsa Shangrila Hotel on December 13,2000 during the 56<sup>th</sup> PCS Annual Congress.

# CLINICAL PRACTICE GUIDELINES IN ANTIBIOTIC PROPHYLAXIS IN ELECTIVE SURGICAL PROCEDURES

## Scope of the Guidelines:

The following questions were addressed by the guidelines:

1. Is antibiotic prophylaxis recommended in elective surgical procedures?
2. If recommended, what is the appropriate drug, dose, dosage schedule, timing, and duration of prophylaxis?

The following elective surgical procedures were included in the guidelines:

1. Breast surgery
2. Hernia repair
3. Biliary surgery
4. Gastroduodenal surgery
5. Colorectal surgery
6. Neurosurgery
7. Cardiac surgery
8. Non-cardiac thoracic surgery
9. Orthopedic surgery
10. Transurethral resection of the prostate (TURP)

## Levels of Evidence:

Evidence addressing the above questions covering the 10 procedures were classified according to a modified system adapted by the Infectious Diseases Society of America (IDSA) as follows:

**I** Evidence from at least one properly done randomized controlled trial or meta-analysis.

**II** Evidence from at least one well-designed clinical trial without proper randomization, from cohort or case-control analytic studies (preferably from more than one center), from multiple time-series studies, or from dramatic results in uncontrolled experiments.

**III** Evidence from opinions of respected authorities on the basis of clinical experience, descriptive studies, or reports of expert committees.

**Grading System for Recommendations:**

The recommendations were classified according to a system adopted by the Infectious Diseases Society of America (IDSA) as follows:

**A Good evidence to support a recommendation for use**

(based on one or more studies at Level I)

**B Moderate evidence to support a recommendation for use**

(based on one or more studies at Level II)

**C Poor evidence to support a recommendation for or against use**

(the best evidence is only Level III)

**Moderate evidence to support a recommendation against use** (based on one or more studies at Level II)

***Good evidence to support a recommendation against use***

(based on one or more studies at Level I)

## General Guidelines:

The following **general guidelines** for antibiotic prophylaxis in elective surgical procedures were derived from the principles and evidence discussed during the guideline preparation and are recommended in clinical practice:

1. The chosen antibiotic for prophylaxis should be given within two hours before the start of the surgical procedure (**Grade A Recommendation**).

## Summary of Evidence:

A cohort of 2874 patients undergoing elective clean or clean-contaminated surgical procedures at a large community hospital was divided into four groups (early – antibiotics given 2-24 hours before surgical incision; preoperative – within 2 hours before incision; peri-operative – 3 hours after incision; and postoperative – more than 3 but less than 24 hours after incision). The groups were prospectively monitored for the occurrence of surgical site infections. Ten of 1708 (0.6%) patients who received preoperative antibiotics developed postoperative infections. Four of 282 (1.4%) patients had such infections ( $p = 0.12$ ; Relative Risk (RR) as compared with the preoperative group, 2.4; 95% CI for RR = 0.9, 7.9). Sixteen of 488 (3.3%) who received antibiotics postoperatively had wound infections ( $p < 0.1$ ; Relative Risk (RR) = 5.8; 95% CI for RR = 2.6, 12.3). Fourteen of 369 (3.8%) patients given early antibiotics had surgical site infections ( $p < 0.001$ ; Relative Risk = 6.7; 95% CI for RR = 2.9, 14.7). Stepwise logistic regression analysis confirmed that the administration of the antibiotics in the preoperative period was associated with the lowest risk of surgical site infection (**Level I Evidence**).

2. In most elective surgical procedures, single dose antibiotic prophylaxis is recommended.
3. If a procedure lasts longer than the half-life of the prophylactic antibiotic given, a second dose of the antibiotic is recommended. Subsequent doses, if necessary should be given at intervals not longer than twice the half-life of the drug.
4. The choice of the antibiotic should be based on the following parameters:
  - 4.1. Efficacy
  - 4.2. Safety and adverse reactions
  - 4.3. Epidemiology of expected pathogen
  - 4.4. Local resistance pattern
  - 4.5. Cost
  - 4.6. Availability

5. The Guidelines do not address the issue of recommending other antibiotics with the presumed same spectrum of activity based on in-vitro studies. This may be an option for surgeons to choose a different antibiotic belonging to the same class of drugs.
  
6. **Antibiotic prophylaxis is not a substitute for the proper observance of aseptic and antiseptic techniques, good surgical technique and gentle handling of tissues, and good clinical judgment.**

**References:**

Classen DC, Evans RS, et al. The Timing of prophylactic administration of antibiotics and the risk of surgical wound infection. N. Engl. Med. 1992; 326:281-286.

Di Piro JT, Bowden Jr, TA, Hooks Li VH. Prophylaxis parenteral cephalosporins in surgery. Are the newer ones better ? JAMA 1984; 252:3277-3279.

## BREAST SURGERY

### 1. Is antibiotic prophylaxis recommended in elective breast surgery?

Antibiotic prophylaxis is recommended for the following elective breast surgical procedures: **(Grade A Recommendation)**

- a) Mastectomy
- b) Axillary lymph node dissection
- c) Reduction mammoplasty
- d) Excisional biopsy and lumpectomy

#### Summary of Evidence:

A meta-analysis of 3 randomized controlled trials (Codamos, 1999) that evaluated the effectiveness of antibiotic prophylaxis in 902 breast surgical procedures showed that 44% of the operations were simple or modified radical mastectomies, 36% were lumpectomies, segmental or local excisions, 16% were axillary node dissections, and 4% were reduction mammoplasties. This meta-analysis showed that patients in the control group had a significantly higher incidence of surgical site infection than in the treatment group (9.52% vs. 5.63%, respectively). The Absolute Risk Reduction (ARR) was 4% (95% CI for ARR = 0.5%, 7.5%) and the Odds Ratio (OR) was 0.57 (95% CI for OR = 0.35, 0.93;  $p < 0.05$ ). **(Level 1 Evidence)**

Another meta-analysis (Platt, 1993) evaluated 2587 breast operations, including 606 that were part of the randomized clinical trial and 1981 that were not, showed that 46% of the operations were mastectomies, 40% were lumpectomies or excisional biopsies, 10% were reduction mammoplasties and 4% were axillary node dissections. This meta-analysis concluded that: (1) there was no significant variation in efficacy of antibiotic prophylaxis according to operation type or duration; and (2) prophylaxis prevented 38% of infections after controlling for operation type, duration of surgery and participation in the randomized trial (Mantel-Haenszel Odds Ratio = 0.62, 95% CI = 0.40, 0.95,  $P = 0.03$ ) **(Level 2 Evidence)**

### 2. What is the appropriate drug, dose, dosage schedule and timing of antibiotic prophylaxis?

**Cefazolin 2 grams IV (Grade A Recommendation) single dose**

(Grade C Recommendation)

**Cefuroxime 1.5 grams IV single dose is recommended as an alternative (Grade C Recommendation)**

Summary of Evidence:

A meta-analysis of 3 randomized controlled trials (Codamos, 1999) concluded that the use of antibiotic prophylaxis in breast surgery resulted to a decrease in surgical site infections from 9.5% to 5.5%. This Absolute Risk Reduction (ARR) of 4% means that 25 patients would need to be given prophylaxis (NNT) in order to prevent 1 surgical site infection (95% CI for NNT = 14, 192 patients). The Odds Ratio (OR) was 0.57 (95% CI for OR = 0.35, 0.93,  $p < 0.05$ ). In one study included in the meta-analysis, Cefazolin was used as antibiotic prophylaxis at a dose of 25mg/kg IV given at least 30 minutes prior to surgery then every 6 hours for a total of 6 doses. (**Level 1 Evidence**)

Another meta-analysis (Platt, 1993) of 1 randomized (606 patients) and 1 large cohort (1981 patients) study showed that: (1) antibiotic prophylaxis prevented 38% of infections, after controlling for operation type, duration of surgery and participation in the randomized trial (Mantel-Haenszel Odds Ratio = 0.62, 95% CI for OR = 0.40, 0.95,  $p = 0.03$ ). In the large cohort included in the meta-analysis, Cefazolin accounted for 75% of the antibiotic prophylaxis used. (**Level 2 Evidence**)

Other studies (see Biliary & Colorectal guidelines) have shown the efficacy of single dose prophylaxis. For this reason, the Technical Working Group recommends that Cefazolin be given as a single dose. (**Grade C Recommendation**)

As an alternative to Cefazolin, the second-generation cephalosporin, Cefuroxime is preferred over the third generation cephalosporins, which should be used for serious infections. Like Cefazolin, they have better coverage than the third generation cephalosporins against *Staphylococcus aureus*, which is the most common pathogen involved in surgical site infections. (**Grade C Recommendation**)

## **REFERENCES:**

1. Platt R, Zucker JR, Zaleznik DF, Hopkins CC, Dellinger EP et al. Perioperative antibiotic prophylaxis and wound infection following breast surgery. *Journal of Antimicrobial Chemotherapy* 1993; 31; Supplement B: 43-48.
2. Codamos LJ, Catungal MM, Coronel RF. Antibiotic prophylaxis for breast surgery: a meta-analysis of randomized placebo-controlled trials. *Philippine Journal of Surgical Specialties* 2000; 55(1):30-32.
3. Platt R, Zaleznik DF, Hopkins CC, Delinger EP et al. Perioperative antibiotic prophylaxis for herniorrhaphy and breast surgery. *The New England Journal of Medicine*, 1990; 322:153-60.
4. Platt R, Zucker JR, Zaleznik DF, Hopkins CC, Dellinger EP et al. Prophylaxis against wound infection following herniorrhaphy or breast surgery. *The Journal of Infectious Diseases*, 1992; 166: 556-60

## GROIN HERNIA SURGERY

### Is antibiotic prophylaxis recommended in elective groin hernia surgery?

Antibiotic prophylaxis is NOT recommended in elective groin hernia surgery (**Grade D Recommendation**). For groin hernia repair using mesh, antibiotic prophylaxis is also NOT recommended (**Grade C Recommendation**).

#### Summary of Evidence:

*A randomized, double-blind placebo-controlled trial (Platt, 1990) evaluated the effectiveness of pre-operative Cefonicid versus placebo in preventing surgical site infections in a mixed group of breast and hernia patients. Six hundred twelve patients who underwent elective inguinal and femoral herniorrhaphy were included in the study. Seven of 301 patients (2.3%) in the Cefonicid group and 13 of 311 patients (4.2%) in the placebo group developed surgical site infections. The Absolute Risk Reduction (ARR) is 1.86% (95% CI for ARR = -0.94%, 4.66%,  $p > 0.05$ ). Since the difference is not statistically significant, a single dose of Cefonicid given before surgery is not effective in reducing the incidence of surgical site infection after groin hernia surgery (**Level II Evidence**).*

*Another study (Taylor, 1997) compared Amoxicillin-clavulanic acid with placebo in 619 patients undergoing open groin hernia repair. Of 563 evaluable patients, 283 patients received Amoxicillin-clavulanic acid while 280 patients were given placebo. Twenty-five patients (9%) in the test group and 25 patients (9%) in the placebo group developed surgical site infection. This study likewise shows that antibiotic prophylaxis does not reduce the incidence of surgical site infection (**Level II Evidence**).*

*A literature review was done (Mann, 1998) to compare the incidence of surgical site infection after mesh repair and suture repair of groin hernias. In a review of 1,834 mesh inguinal repairs, Gilbert and Felton reported 14 cases with infections (0.8%) compared with 659 suture repairs with 7 infections (1%). In a comparison of prosthetic inguinal hernia repair with the Bassini operation, Thill and Hopkins found infection rates of 0.54% and 1.2% respectively. The use of a foreign body (mesh) for primary repair of inguinal hernias does not appear to increase the incidence of surgical site infection (**Level II Evidence**).*

#### References:

1. Platt R, Zaleznic DF, Hopkins CC, et al. Perioperative antibiotic prophylaxis for herniorrhaphy and breast surgery. *New Engl J Med*, 1990 Jan; 322(3): 153-160.
2. Taylor EW, Bryne DJ, Leaper DJ, et al. Antibiotic prophylaxis and open groin hernia repair. *World J Surg*, 1997 Oct; 21(8):811-814.
3. Mann DV, Prout J, Havranek E, et al. Late-onset deep prosthetic infection following mesh repair of inguinal hernia. *Am J Surg*, 1998 Jul; 176:12-14.

## BILIARY SURGERY

### 1. Is antibiotic prophylaxis recommended in biliary surgery?

Antibiotic prophylaxis is recommended in biliary surgery (**Grade A Recommendation**)

Antibiotic prophylaxis is recommended in patients undergoing the following procedures:

- Cholecystectomy
- Sphincterotomy
- Cholecystectomy plus sphincterotomy
- Choledochoenterostomy
  - Choledochoduodenostomy
  - Choledochoduodenostomy plus sphincterotomy
  - Choledochojejunostomy
- Cystojejunostomy
- CBD exploration

#### Summary of Evidence:

*A meta-analysis (Meijer et al, 1990) of 42 randomized, controlled trials involving 4129 patients was done in which patients given antibiotics were compared with patients not given antibiotics. The wound infection rate in the control group was 15%, with a range of 3% to 47%. The infection rate in patients given antibiotics was 6% for an Absolute Risk Reduction (ARR) of 9% (95% CI of ARR = 7,11%) while the common Odds Ratio (OR) is 0.3 with  $p < 0.005$  (95% CI of OR = 0.23, 0.38). (Level I Evidence)*

### 2. What is the appropriate drug, dosage, timing and duration of antibiotic prophylaxis?

Cefazolin 1 gm IV (**Grade A Recommendation**) given as single dose (**Grade A Recommendation**)

Cefuroxime 1.5gm IV may be given as an alternative (**Grade A Recommendation**).

#### Summary of Evidence:

*The percentage differences and odds ratios for 11 trials involving 1128 patients in the meta-analysis of Meijer (1990) comparing first, second and third generation cephalosporins with one another were compared. The common percentage difference was 0.5% (range = -1.5%, 2.5%). The common Odds Ratio (OR) was 0.80 (95% CI of OR = 0.69, 2.00). This means that the infection rates in these groups of patients are not significantly different from one another (Level I Evidence).*

*Another section of the meta-analysis of Meijer covering 15 trials and 1226 patients looked into single dose versus multiple dose antibiotic prophylaxis regimens in preventing surgical site infection. The common percentage difference was 0.4% with a 95% CI of -1.1 to 1.9%. The common Odds Ratio (OR) was 0.80 (95% CI of OR = 0.41, 1.57). Both figures mean that there is no difference in the infection rates between single and multiple dose prophylaxis. (Level I Evidence)*

*A randomized controlled double-blind multi-center trial (Meijer, 1993) to assess the*

efficacy of a short acting antibiotic, Cefuroxime ( $n = 1004$  patients). The study compared a single pre-operative dose against multiple doses of the same drug. The major wound infection rates were 4.6% for the multiple dose arm 3.8% for the single dose arm for an Absolute Risk Reduction (ARR) of 0.8% (95% CI of ARR = -1.7%, 3.3%) and  $p = 0.52$ . The conclusion is that there is no advantage in giving multiple dose prophylaxis compared with single dose prophylaxis in preventing postoperative wound infections. **(Level II Evidence)**

### 3. Is antibiotic prophylaxis recommended in laparoscopic cholecystectomy?

Antibiotic prophylaxis is recommended in laparoscopic cholecystectomy **(Grade C Recommendation)**

#### Summary of Evidence:

A prospective placebo controlled randomized controlled trial (Illig, 1997) evaluated prophylactic antibiotics in patients undergoing laparoscopic cholecystectomy. In this study, the computed sample size for each treatment arm was 419 patients for an 80% chance of detecting a 4% absolute difference in the infection rate between prophylaxis and control groups. The study was terminated after 250 patients (128 test, 122 control) due to the very low incidence of surgical site infection, which was the primary endpoint. The infection rate in the placebo group was 0.8% against no infections in the prophylaxis group. Given the 0 incidence in the test group the Confidence Interval (CI) of the log Odds Ratio (OR) is not calculable. The very low overall infection rate of 0.4% precluded any analysis between the two groups. **(Level II Evidence)**

Another double blind randomized controlled trial (Higgins, 1999) (N=450) comparing placebo (N=135) with Cefazolin (N=140) and Cefotetan (N=137) showed no statistical difference in infection rates with a  $p > 0.05$ . The infection rate in the placebo group was 2.2%, while for Cefazolin group it was 2.9% and for Cefotetan group it was 2.2%. **(Level II Evidence)**

Based on the above evidence it seems logical not to recommend the use of prophylactic antibiotics in patients undergoing laparoscopic cholecystectomy. However, the Technical Working Group noted that in the prevailing local practice, disposable trocars are re-used and are at times not sterilized in the correct manner. This may increase the risk of surgical site infection and until adequate local data is available, the Technical Working Group deemed it prudent to recommend the use of prophylactic antibiotics in patients undergoing laparoscopic cholecystectomy. **(Level III Evidence)**

#### REFERENCES:

Open cholecystectomy

1. Meijer, WS, Schmitz PI. Prophylactic use of cefuroxime in biliary tract surgery: Randomized controlled trial of single vs multiple doses in high risk patients. Galant trial study group. Br J Surg., 1993 July; 80(7) 917-21.
2. Meijer WS, Schmitz PIM, Jeekel J. Metaanalysis of randomized controlled antibiotic prophylaxis in biliary tract surgery. Br.J.Surg., 1990, March; 77: 283-290.

## Laparoscopic cholecystectomy

1. Higgins A, London J. et al. Prophylactic antibiotics for elective laparoscopic cholecystectomy: Are they necessary? Arch Surg, 1999; Jun; 134(6): 611-3; discussion 614. National library of medicine. Medline.
2. Illig K.A., et al. Are prophylactic antibiotics required for elective laparoscopic cholecystectomy? J AM Coll Of Surg., 1997; 184(4): 353-6

## GASTRIC AND DUODENAL SURGERY

### 1. Is antibiotic prophylaxis recommended in gastroduodenal surgery?

Antibiotic prophylaxis is recommended in elective surgery of the stomach and duodenum (**Grade B Recommendation**). Antibiotic

prophylaxis is recommended for gastroduodenal surgery for the following indications: (a) gastric cancer, (b) chronic or bleeding gastric ulcers, and (c) bleeding or obstructing duodenal ulcers.

#### Summary of Evidence:

*A randomized, prospective double blind, placebo-controlled study (Nichols, 1982) was done on 43 patients for gastric cancer, chronic and bleeding gastric ulcers, and bleeding and obstructing duodenal ulcers. The study showed that the wound and intra-abdominal infection rate was lower in patients given antibiotics compared with the control group (5.3% versus 35%, respectively). The Absolute Risk Reduction (ARR) was 29.7% (95% CI for ARR = 2.3%, 57.1%) (Level II Evidence).*

*Another randomized, prospective, double blind trial (Stone, 1976) was done on 400 patients for elective surgery on the stomach, biliary tract or colon. 96 of these patients underwent gastric operations. Patients who were given antibiotics 1-4 hours or 8-12 hours preoperatively had a lower incidence of intraabdominal and wound infection than those patients not given antibiotics at all or whose antibiotics were started postoperatively (8.16% versus 30.43%, respectively). The Absolute Risk Reduction (ARR) was 22.3% (95% CI for ARR = 2%, 42.6%) (Level II Evidence)*

### 2. What is the appropriate drug, dose, dosage schedule, and timing of antibiotic prophylaxis?

**Cefazolin** (Grade B Recommendation) **1 Gm IV** (Grade C Recommendation) **single dose**

**Cefuroxime 1.5 gms IV may be given as an alternative**  
(Grade B Recommendation)

#### Summary of Evidence:

*A randomized, prospective, double blind trial (Stone, 1976) was done on 400 patients for elective surgery on the stomach, biliary tract or colon. 96 of these patients underwent gastric operations. Patients who were given Cefazolin 1 Gm IM the evening before surgery, 1 GM IM on call to OR and 1 Gm IM on the evening of the operation (3 doses) or 1 Gm IM on call to OR, 1 Gm IM on the evening of the operation and 1 Gm IM on the morning after surgery (3 doses) had a lower incidence of intra-abdominal and wound infection than those patients not given antibiotics at all or whose antibiotics were started postoperatively (8.16% versus 30.43%, respectively). The Absolute Risk Reduction (ARR) was 22.3% (95% CI for ARR = 2%, 42.6%) (Level II Evidence).*

*In his study, Stone used 3 doses of Cefazolin. Cefazolin and Cefuroxime are similar in terms of spectrum and half-life (1.8 versus 1.3-1.5 hours, respectively).*

*Cefuroxime is more potent against E. coli but Cefazolin is more effective against Staphylococcus aureus. Morris showed that a single dose of Cefuroxime is effective in reducing surgical site infection. Thus the Technical Working Group deems it logical to recommend Cefazolin as single dose prophylaxis (Level III Evidence)*

*A prospective, randomized controlled trial (Morris, 1984) done on 78 patients undergoing elective gastric surgery compared single dose Cefuroxime 1.5 Gm IV with Mezlocillin 2 Gm IV. The infection rate was 2.5% in the Cefuroxime group and 18% in the Mezlocillin group for an Absolute Risk Reduction (ARR) of 15.5%. In order to prevent one surgical site infection the Number Needed to Treat (NNT) is 6 (95% CI for NNT = 2, 9 patients). (Level II Evidence)*

**References:**

1. Nichols RL, Webb WR, Jones JW, et al. Efficacy of antibiotic prophylaxis in high risk gastroduodenal operations. *American Journal of Surgery*, 1982; 143: 94-98.
2. Stone HH, Hooper CA, Kolb LD, et al. Antibiotic prophylaxis in gastric, biliary and colonic surgery. *Annals of Surgery*, October 1976; 184(4): 443-452.
3. Morris DL, Young D, Burdon DW, et al. Prospective randomized trial of single dose cefuroxime against mezlocillin in elective gastric surgery. *J Hosp Infect*, 1984; 5(2): 200-204 in *The Database of Abstracts of Reviews of Effectiveness in the Cochrane Library, Issue 1, 1999, Oxford: Update Software, Updated Quarterly.*

## COLORECTAL SURGERY

### 1. Is prophylactic antibiotics recommended in elective colorectal surgery?

Antibiotic prophylaxis is recommended in the following elective colorectal procedures (**Grade A Recommendation**).

- 1) right hemicolectomy
- 2) left hemicolectomy
- 3) transverse colectomy
- 4) segmental colon resection
- 5) anterior resection
- 6) low anterior resection
- 7) Hartmann's procedure
- 8) abdominoperineal resection
- 9) total abdominal colectomy

#### Summary of Evidence:

**A meta-analysis (Song, 1998) of 147 randomized clinical trials from 1984 to 1995 was published in the British Journal of Surgery. This review identified 4 trials in 1984 that compared patients given antibiotic prophylaxis and a control without any antibiotics. The wound infection rate in the control group was 40% versus 13% in the antibiotic group with an Absolute Risk Reduction (ARR) of 27% and Odds Ratio (OR) of 4.08 (95% CI for OR = 2.33, 7.13 (Level I Evidence).**

*Another meta-analysis (Baum, 1981) utilizing 26 trials from 1965 to 1980 evaluated the use of prophylactic antibiotics in colorectal surgery. The infection rate in the control group was 36% versus 22% in the group with antibiotics for an Absolute Risk Reduction (ARR) of 14% and a Number Needed to Treat (NNT) of 7. The review further concluded that no treatment control groups for antibiotic prophylaxis in colorectal surgery should no longer be used in subsequent studies because of ethical reasons. (Level I Evidence)*

### 2. What are the appropriate drugs, dose, dosage schedule, and timing of antibiotic prophylaxis?

The following antibiotics are recommended as a single dose:

1. Amoxicillin-clavulanic acid 1.2 Gms IV
2. Cefoxitin 2 Gms IV
3. Ampicillin-sulbactam 1.5 Gms IV

Cefazolin 2 Gms IV plus Metronidazole 500 Mg IV may be given as an alternative.

#### Summary of Evidence:

*The antibiotics used in the meta-analysis by Song showed a significant decrease in surgical site infection complications in patients undergoing colorectal surgery. The antibiotics used include Amoxicillin-clavulanic acid, Cefoxitin, Cefazolin plus Metronidazole, and Ampicillin-sulbactam. A single drug is as effective as multiple drugs were but because of cost,*

*lesser potential of adverse effects and convenience of administration it is recommended to use only a single drug*

*A single dose administered preoperatively is as effective as long term or multiple dose prophylaxis continued postoperatively. The Odds Ratio (OR) was 1.17 (95% CI for OR = 0.9, 1.53). There was no convincing evidence to suggest that new generation cephalosporins are more effective than the first generation cephalosporins (OR = 1.07, 95% CI = 0.54, 2.12) (Level I Evidence).*

**Parenteral antibiotics alone versus parenteral plus oral antibiotics:**

*The meta-analysis of Song of 147 randomized controlled trials showed that the infection rate for those patients receiving parenteral prophylaxis alone was 12% versus 10% for those with additional non absorbable erythromycin base plus neomycin given orally. The Absolute Risk Reduction (ARR) was 2% with Number Needed to Treat (NNT) = 50, Odds Ratio (OR) of 1.13 (95% CI for OR = 0.6, 2.14). This means that the addition of non-absorbable oral antibiotics (erythromycin and neomycin) has no conclusive advantage over parenteral antibiotics alone. The randomized controlled trials included in the analysis were non-blinded, non-placebo controlled (Level II Evidence).*

**REFERENCES:**

1. Song F, Glenny AM. Antimicrobial prophylaxis in colorectal surgery: a systematic review of randomized control trials. Br J Surg, 1998; 85:1232-1241.
2. Baum ML, Anon DS, Chalmus TC, Sachs HS, Smith H. A survey of clinical trials of antibiotic prophylaxis in colon surgery: evidence against further use of no treatment controls. N Engl J of Med, 1981; 305(14): 795-799.

## **NEURO SURGERY**

### **1. Is antibiotic prophylaxis recommended in clean cranial surgical procedures?**

Antibiotic prophylaxis is recommended in elective clean cranial surgical procedures (**Grade A Recommendation**)

Antibiotic prophylaxis for the following clean cranial surgical procedures is recommended:

- 1.1. cerebrospinal fluid (CSF) shunts
- 1.2. tumor resection
- 1.3. neurovascular surgery; and
- 1.4. cranioplasty

#### **Summary of Evidence:**

##### **1. Cerebrospinal fluid shunts**

A meta-analysis (Langley et al 1993) of 12 randomized trials of 1359 patients demonstrates that antibiotic prophylaxis in CSF shunt placement significantly reduced the risk of subsequent infection (Mantel-Haenszel) risk ratio: 0.52; 95% CI 0.37; 0.73;  $p=0.0002$ ). **Level 1 Evidence**

##### **2. Other cranial surgical procedures**

A meta-analysis (Yu, Codamos et al 2000) of 6 randomized trials involving a total of 2007 patients showed that antibiotic prophylaxis significantly reduced the risk of surgical site infection in non-shunt, clean cranial surgical procedures (odds ratio: 0.21; 95% CI 0.13, 0.33; Absolute Risk Reduction: 6.33%; 95% CI 4.54% to 8.12%; Number Needed to Treat: 16 patients; 95% CI 12 to 20 patients) **Level 1 Evidence.**

The types of neurosurgical procedures included in the study are craniotomy, cranioplasty, trepanation, tumor resection, burrholing and vascular surgery.

**2. What are the appropriate drugs, timing, dose and dosage schedule for antibiotic prophylaxis in clean cranial surgical procedures?**

The following antibiotic prophylaxis are recommended:

1. CSF Shunts

Cloxacillin 1 gram IV is the recommended antibiotic prophylaxis  
**(Grade A Recommendation)**

Oxacillin 1 gram IV is the recommended alternative antibiotic prophylaxis **(Grade A Recommendation)**

2. Other cranial surgical procedures:

Cefuroxime 1.5 grams IV is the recommended antibiotic prophylaxis **(Grade B Recommendation)**

Cefazolin 1 gram plus Gentamicin 80 mg are the recommended alternative antibiotic prophylaxis **(Grade B Recommendation)**

**Summary of Evidence:**

Several trials have conclusively demonstrated the value of various antibiotic regimens in decreasing surgical site infection in neurosurgical procedures.

A study by Van Ek et al in 1998 showed that Cloxacillin 1 gram IV significantly reduced surgical site infection (Absolute Risk Reduction: 9.14%; Number Needed to Treat: 11; Odds Ratio: 0.31; 95% CI 0.14, 0.68) **Level I Evidence.**

In the meta-analysis by Haines et al, pooled results showed that antibiotic prophylaxis lead to approximately a 50% reduction in the infection rate in the antibiotic-treated patients (pooled odds ratio: 0.48; 95% CI 0.31, 0.73). When the results are combined, there is no evidence to suggest that the results are so disparate that the studies must have come from differing populations (chi-square for homogeneity, 9.46; 9 degrees of freedom (df).  $p=0.40$ ). One of the trials (Djindjian et al 1986) included in the meta-analysis used Oxacillin 1 gram IV as antibiotic prophylaxis . **Level II Evidence.**

In a large prospective cohort study (Holloway et al 1996) involving 595 neurosurgical patients, 0.3% infection rate was noted using Cefuroxime 1.5 grams IV as antibiotic prophylaxis . **Level II Evidence**

In the meta-analysis by Yu, Codamos et al, one of the trials included a randomized single-blind, no treatment-control study (Young et al 1987) using Cefazolin 1 gram IV plus Gentamicin 80 mg IV. A significant reduction in infection rate was noted (Peto odds ratio: 0.14; 95% CI 0.04; 0.53). **Level II Evidence.**

#### **References:**

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Holloway KL, Smith KW, Wilberger JE Jr et al. Antibiotic prophylaxis during clean neurosurgery: a large, multicenter study using cefuroxime. *Clin Ther* 1996 Jan – Feb; 18(1): 84-94.

Van EK B, Dijkmans BA, van Dulken H, van Furth R. Antibiotic prophylaxis in craniotomy: a prospective double-blind placebo-controlled study. *Scand J Infect Dis* 1988; 20(6):633-9.

## CARDIAC SURGERY

### 1. Is antibiotic prophylaxis recommended in elective cardiac surgery?

Antibiotic prophylaxis is recommended in elective cardiac surgery (**Grade A Recommendation**).

#### Summary of Evidence:

*In a meta-analysis of thirty years of clinical trials addressing the use, selection and efficacy of antibiotic prophylaxis in cardiothoracic surgery (Kreter and Woods, 1992) four placebo controlled studies evaluating a total of 405 patients that met the meta-analysis inclusion criteria showed that there was a significant reduction in wound infection rates in patients receiving antibiotic prophylaxis (summary Odds Ratio (OR) = 4.96; 95% CI, 2.06, 9.72). This corresponds to a reduction of infection rate from 20%-25% in the placebo group to 4%-5% in the antibiotic treated group (Level I Evidence).*

### 2. What is the appropriate drug and dosage, timing and duration of antibiotic prophylaxis ?

Cefazolin 1gm (**Grade A Recommendation**) given as single dose (**Grade A Recommendation**) is recommended.

#### Summary of Evidence:

##### a. Drug and Dosage

*A meta-analysis of six studies (Kreter and Woods, 1992) evaluating a total of 2630 patients comparing Cefazolin with Cefamandole and Cefuroxime showed a summary Odds Ratio (OR) of 1.58 (95% CI for OR = 1.03, 2.45). Although not significant, this suggests that despite the generally low rates of wound infection in the Cefazolin group (5%), there was still a reduction of infection rates to approximately 3% with the use of the second generation cephalosporins (Level I Evidence).*

*However, in a prospective randomized double blind trial (Kaiser, 1987) in 1030 patients showed that compared to Cefazolin, Cefamandole was able to reduce infection at both sternal (1.8% vs 0.4%,  $p < 0.05$ ) and donor (1.3% vs 0%,  $p < 0.01$ ) sites. The study also showed that Gentamicin had no role in the prophylaxis of cardiac surgery (Level I Evidence).*

*Townsend (1993), in a randomized double blind clinical trial of Cefamandole, Cefazolin and Cefuroxime involving 1641 patients undergoing cardiac operations, operative site infections occurred in 46 of 549 (8.4%) Cefamandole recipients, 46 of 547 (8.4%) Cefazolin recipients, and 49 of 545 (9%) of Cefuroxime recipients ( $p = 0.92$ ). The rates of infection were not significant among the three groups. Moreover, the sites of infections and depth of tissue involvement were not significantly different across groups (Level I Evidence).*

DiPiro (1984) reviewed three randomized double blind studies comparing Cefazolin with Cephalothin, Cefamandole with Cephalothin and Cephalothin with Ceforanide in open heart surgery. No significant differences in wound infection rate or incidence of endocarditis were found in the studies which showed that there is no evidence that second or third generation cephalosporins result in post-operative infection rates lower than the first generation cephalosporins. **(Level I Evidence).**

**b. Duration**

Maki (1992), in a randomized double blind study of Cefazolin, Cefamandole and Vancomycin monitored the blood levels of the drugs in 22 patients undergoing cardiac operations under cardiopulmonary bypass. All drugs provided therapeutic levels for the duration of the operation (Table 1) **(Level I Evidence).**

Table I Blood levels of cefazolin, cefuroxime and vancomycin in 22 patients undergoing cardiopulmonary bypass.

Mean serum concentration in ug/ml (range)		
Cefazolin 1 gm	Cefamandole 2gm	Vancomycin ~15mg/kg

**Pre-bypass**

<b>Peak (post dose)</b>	<b>89.00 (79-116)</b>	<b>68.6 (32-156)</b>	<b>35.2 (32-46)</b>
On bypass (min)			
0	65.7 (50-86)	40.9 (21-80)	23.0 (19-32)
20	59.1 (31-60)	30.8 (18-69)	17.3 (11-32)
40	51.4 (31-60)	32.2 (14.74)	15.5 (10-25)
100	42.8 (31-58)	29.0 (11-58)	8.7 (7 -22)
Completion of bypass	39.8 (21-54)	26.6 (11-58)	14.0 (10-27)
<u>Post-bypass, at wound closure</u>	<u>41.7 (20-58)</u>	<u>10.6 (10-34)</u>	<u>11.2 (10-18)</u>

In a prospective randomized double blind study by Conte (1972), a single intraoperative dose of 1 gm Cephalothin was compared to 20-1 gram doses of the same drug. Post-operative infections were 1 major and 1 minor/30 patients who received single dose and 1 major and 1 minor/34 patients for the multiple dose (p = NS). Moreover, multiple dose prophylaxis appeared to shift adversely the infecting bacteria to a more resistant group of organisms **(Level I Evidence).**

In a review of antimicrobial prophylaxis for surgical wound infections, Page (1993) recommended that for agents that are rapidly cleared, repeat dosing at an interval two times the plasma half-life of the antibiotic is appropriate. However, since cardiopulmonary bypass decreases the elimination of the drug, additional intraoperative doses may not be necessary for lengthy operations **(Level III Evidence).**

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## **NON-CARDIAC THORACIC**

### **1. Is antibiotic prophylaxis recommended for elective non-cardiac thoracic procedures?**

Antibiotic prophylaxis is recommended in elective non-cardiac thoracic procedures to prevent incisional surgical site infection. **(Grade A Recommendation).**

#### **Summary of Evidence:**

*A randomized double-blind trial was done on 127 patients undergoing thoracic surgery (Aznar, 1991) to compare the effectiveness of administering a single preoperative dose of Cefazolin versus placebo in decreasing the incidence of surgical site infection. One out of the 70 patients (1.5%) randomized to the Cefazolin group and 8 out of the 57 patients (14%) given placebo developed incisional surgical site infections. The Relative Risk (RR) of surgical site infection of the patients from the placebo group was 3.27 (95% CI for RR = 1.5, 11.5). The Absolute Risk Reduction (ARR) was 12.5%. Therefore, a single preoperative dose of Cefazolin 1 gram is effective in reducing the rate of incisional surgical site infections in non-cardiac thoracic procedures (Level I Evidence).*

### **2. What is the appropriate drug, dose, dosage schedule and timing of antibiotic prophylaxis ?**

Cefazolin 1 gram IV single dose **(Grade A Recommendation)**

#### **Summary of Evidence:**

*A randomized double-blind trial was done on 127 patients undergoing thoracic surgery (Aznar, 1991) to compare the effectiveness of administering a single preoperative dose of Cefazolin versus placebo in decreasing the incidence of surgical site infection. One patient out of the 70 patients (1.5%) randomized to the Cefazolin group and 8 cases out of the 57 patients (14%) given placebo developed incisional surgical site infections. The Relative Risk (RR) of surgical site infection of the patients from the placebo group was 3.27 (range 95% CI for RR = 1.5, 11.5). Therefore, a single preoperative dose of Cefazolin 1 gram is effective in reducing the rate of incisional surgical site infections in non-cardiac thoracic procedures. (Level I Evidence)*

*A randomized double-blind trial (Olak, 1991) involving 208 patients was done to compare the efficacy of one dose versus six doses of Cefazolin as prophylaxis in general thoracic surgery. There were no wound infections in the one-dose group and two in the six-dose group (95% CI = -0.008, 0.048). Therefore, giving six doses of Cefazolin does not confer any clinically important benefit beyond that obtained from a single dose for prophylaxis of wound infection in elective general thoracic surgery. (Level I Evidence)*

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## ORTHOPEDIC SURGERY FOR CLOSED FRACTURES

### 1. Is antibiotic prophylaxis recommended in open reduction-internal fixation/replacement arthroplasty for closed fractures?

Antibiotic prophylaxis is recommended in orthopedic surgery involving internal fixation of hip fractures or other closed long bone fractures with metallic implants or replacement arthroplasty (**Grade A Recommendation**).

Antibiotic prophylaxis is recommended in the following surgical procedures:

- a) Internal fixation for closed hip and long bone fractures using metallic devices
- b) Total/partial joint replacement

#### Summary of Evidence:

Data pooled from 10 trials in a meta-analysis (Gillispie, 1999) comparing a pre-operative dose and two or more post-operative doses of parenteral antibiotics with placebo or no treatment showed a significant reduction in the incidence of deep incisional surgical site infection (Peto Odds Ratio (OR) = 0.34, 95% CI = 0.19, 0.59) and of superficial incisional surgical site infection (Peto Odds Ratio (OR) = 0.46, 95% CI = 0.27, 0.78). The incidence of deep wound infection in control patients was 4.3%, compared with 1.4% in the treatment group for an Absolute Risk Reduction (ARR) of 2.9% (95% CI for ARR = 1.3%, 4.4%) (**Level I Evidence**).

Other data from six trials in the meta-analysis of Gillispie, including one large multi-center trial (Boxma, 1996) showed that a single pre-operative dose of parenteral antibiotic compared with placebo or no treatment reduced the incidence of deep wound infection (Peto Odds Ratio (OR) = 0.42, 95% CI = 0.26, 0.68) and superficial wound infection (Peto Odds Ratio (OR) = 0.67, 95% CI = 0.47, 0.94). The Absolute Risk Reduction (ARR) was 1.8% (95% CI for ARR = 0.8%, 2.8%) (**Level I Evidence**).

### 2. What is the appropriate drug, dose, dosage schedule, and timing of antibiotic prophylaxis?

Ceftriaxone 2 Gm IV single dose (**Grade A Recommendation**)

Cefotaxime 1 Gm IV (**Grade B Recommendation**) may be given an alternative

#### Summary of Evidence:

The Dutch Trauma Trial (Boxma, 1996) reported the efficacy of antibiotic prophylaxis in fracture surgery. The study was a prospective, randomized, double-blind, placebo-controlled trial with a 120-day follow up of 2195 patients scheduled for primary osteosynthesis or placement of a prosthetic device in the treatment of closed limb fractures. 1105 patients were allocated to receive Ceftriaxone 2 Gm IV single dose at induction of anesthesia, and 1090 patients were randomized to the placebo control. Ten days after surgery, 5 patients (0.5%) in the Ceftriaxone group and 41 patients (4.0%) in the control group developed wound infection for an Absolute Risk Reduction (ARR) of 3.5% ( $p < 0.001$ ). The Number Needed to Treat (NNT) was 29 patients (95% CI for NNT = 20, 43 patients). The Relative Risk Reduction (RRR) was 88% (95% CI for RRR = 71%, 95%)

After the 10<sup>th</sup> day, the infection rates were similar in the two groups – 31 new infections in the Ceftriaxone group and 38 in the placebo control. The over all infection rates (after 120 days) were 4% in the Ceftriaxone group and 8% in the control for an Absolute Risk Reduction (ARR) of 4% and an NNT = 22 (95% CI for NNT = 15, 39) and a RRR = 56% (95 CI for RRR = 36%, 70%). Adequate single-dose prophylaxis with a long-acting, broad-spectrum antibiotic achieving high serum levels, with high tissue penetration and a long-elimination half-life substantially reduced the incidence of wound infection immediately after surgery for closed fractures (**Level I Evidence**).

Another study (Jones, 1987) compared a single-dose long-acting antibiotic with a multiple dose regimen. One group received Cefotaxime 1 Gm IV at the start of anesthesia with a second dose if the operation exceeded 2 hours; a second group received Cefazolin 1 Gm IV at the start of anesthesia and 8 hourly thereafter for 24 hours; and a third group received Cefoxitin 2 Gm IV at the start of anesthesia and 6 hourly thereafter for 24 hours. Jones found no difference in the incidence of wound infection among the 3 groups (Peto Odds Ratio (OR) = 0.19; 95% CI = 0.02, 2.02) (**Level II Evidence**)

#### **References:**

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## *TRANSURETHRAL RESECTION OF THE PROSTATE*

### 1. Is antibiotic prophylaxis recommended in transurethral resection of the prostate?

Antibiotic prophylaxis is recommended in transurethral resection of the prostate to prevent immediate postoperative bacteriuria. **(Grade A Recommendation)**

#### Summary of Evidence:

*In a randomized, double-blind placebo-controlled trial (Prokocimer et al, 1986) on patients with sterile urine preoperatively 34% (14/41) of patients assigned to the placebo group developed early bacteriuria compared with 4% (2/49) of patients assigned to the cefotaxime group who were given a dose of 20 mg/kg body weight 1-2 hours preoperatively and 4 hours post-operatively. This absolute risk reduction of 30% means that 3 patients would need to be treated with 2 doses of cefotaxime to prevent 1 additional early bacteriuria in this study which included preoperatively catheterized patients. **(Level I Evidence)***

*In a prospective randomized double-blind study on patients with sterile urine (Dorflinger and Madsen 1984), cefoperazone reduced urinary tract infection rate from 17% to 0% 5-7 days postoperatively. **(Level I Evidence)***

*In a study of (Scholz et al 1998) 62 patients with sterile urine were randomly assigned to receive a single dose of 1 gm ceftriaxone intravenously 1-2 hrs before TURP. Sixty five patients were randomly assigned to receive no treatment preoperatively. Twenty six percent in the no treatment group developed immediate postoperative bacteriuria (>10<sup>5</sup> cfu/ml of midstream urine on removal of catheter 1-2 days postoperatively) compared with 8.5% in the ceftriaxone group. This absolute risk reduction of 17.7% means that 6 patients would need to be treated to prevent 1 urinary tract infection in this study which excluded patients with indwelling catheter preoperatively. There was no significant difference in bacteriuria 4 weeks postoperatively between ceftriaxone group and the no treatment group. **(Level II Evidence)***

*In another study (Charton et al, 1987) 48 patients with sterile urine were randomly allocated to receive 150 mg of netilmicin sulfate intramuscularly 1 hr preoperatively. Forty seven patients were randomly allocated to receive 1.5 ml of 0.9% NaCl solution 1 hr preoperatively. Thirty four percent in the placebo group developed significant bacteriuria (>10<sup>5</sup>) compared with 2% in the netilmicin group. **(Level II Evidence)***

*In a multicenter study (Viitanen et al, 1993) 197 patients with sterile urine were randomly assigned to receive 2 gms of ceftriaxone as a single dose. Two hundred three patients were assigned to receive a single dose trimethoprim sulfamethoxazole at 160/180 mg and 199 to control group without antibiotic. Catheterized patients were excluded. The study drugs were administered intravenously during anesthesia induction beginning approximately 20 min before the start of the procedure. Twenty one percent in the control group developed*

postoperative infectious complications compared with 7.6% in the ceftriaxone group and 12.3% in the TMP-SMX group (>10<sup>5</sup> cfu/ml). Both antibiotics reduced the infectious complications without significant difference between each other. **(Level II Evidence)**

2. What is the appropriate drugs, dose, dosage schedule, and timing of antibiotic prophylaxis?

Gentamycin inj 80 mg IV within 2 hours before surgery, single dose **(Grade B Recommendation)**

Alternative: Ofloxacin tablets, 600 mg orally 4-12 hours before surgery, single dose **(Grade B Recommendation)**

Summary of Evidence:

*In a randomized study (Ramsey and Sheth, 1983) using three schedules of gentamycin administration all were effective in lowering the incidence of postoperative bacteriuria with a single dose of gentamycin 2 hrs preoperatively being the most effective. **(Level II Evidence)***

*In a clinical trial (McEntee et al , 1987) 36 patients with indwelling urethral catheters undergoing emergency transurethral resection of the prostate were evaluated after randomization 17 patients were give 80 mg of Gentamycin IV. After induction of anesthesia whereas 19 were not given antibiotics. Patients with bacteriuria were not excluded. 29 of the 36 patients had bacteriuria before surgery. A catheter specimen of urine was taken postoperatively, before catheter removal which was usually on the second postoperative day and a midstream urine specimen was obtained 24 hours after catheter removal. Prophylaxis resulted in a significant reduction in postoperative bacteriuria, pyrexia, bacteremia and septicemia. **(Level III Evidence)** Peripheral blood culture specimens were obtained from all patients within 30 minutes of completion of surgery and postoperatively when clinically indicated (B.P. less than 100 mmg Hg, pyrexia 37.5°C or higher or rigors). Significant bacteriuria was defined within 30 minutes of surgery. Postoperative septicemia was defined as the presence of clinical features (B.P. less than 100 mm Hg, pyrexia 37.5°C or greater or rigors) together with a positive-blood culture. Administration of a single dose of gentamycin in this and other studies did not appear to have any nephrotoxic or neurotoxic side effect.*

*In an open label, randomized, active controlled two-center study (Madsen et al, 1984) 55 patients undergoing transurethral surgery were randomized to receive either a single dose of ofloxacin 600 mg administered orally 4-12 hours before surgery, or a single dose of cefotaxime 1 g administered intravenously or intramuscularly 15-90 minutes before surgery. Patients with indwelling foley catheter for greater than 14 days before surgery were excluded. Of the 55 patients, 24 underwent transurethral resection of the prostate. Postoperative urine cultures taken 24 hours postoperatively, at the time of catheter removal and upon study completion (5-9 days after surgery) were negative in all ofloxacin recipients including one with positive urine culture before the surgery. In the cefotaxime group 2 patients had positive urine culture postoperatively. **(Level II Evidence)***

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