Current International Evidence and Recommendations for Antibiotic Prophylaxis in Gynecological Procedures

Review of the Cesarean Section Antibiotic Prophylaxis Program in Jordan and Workshop on Rational Medicine Use and Infection Control

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Organized by Ministry of Health, Royal Medical Services, and Jordan Food and Drug Administration in collaboration with SPS and SIAPS

USAID FROM THE AMERICAN PEOPLE

Strengthening Pharmaceutical Systems

Outline

- Overview of surgical antibiotic prophylaxis
- Overview of surgical site infections (SSI)
- Recommendations for surgical antibiotic prophylaxis in gynecologic procedures
- Other proven procedures to reduce SSI
- Summary and conclusions

Gynecologic Surgical Prophylaxis

- Ministry of Health (MOH), in collaboration with the USAID-supported Strengthening Pharmaceutical Systems (SPS) and its follow-on, Systems for Improved Access to Pharmaceuticals and Services (SIAPS), has worked extensively at 3 Jordanian hospitals to develop protocols and continuous quality improvement (CQI) activities to improve the use of antibiotics in cesarean section surgical prophylaxis
- Royal Medicine Services (RMS) has also initiated a similar program at one hospital
- This presentation reviews surgical antibiotic prophylaxis for other gynecological procedures, including hysterectomy

Prophylactic Antibiotics Widely Used, Often Inappropriately

- Antimicrobials can account for up to 30% of hospital medicine expenses
- 30%–50% of antibiotic use in hospitals is for surgical prophylaxis
- 30%– 90% of this prophylaxis is inappropriate
- Most common problems
  - Given at wrong time
  - Continued for too long

Consequences of inappropriate prophylactic antibiotic use

- Poor outcome
- Increased adverse events
- Increased cost
- Increased drug resistance

Ruttimann et al. 2004. Long-term antibiotic cost savings from a comprehensive intervention program in a medical department of a university-affiliated teaching hospital. *Clin Infect Dis* 38:348-356.
Munckhof, W. 2005. Antibiotics for surgical prophylaxis. *Aust Prescr* 28:38–40.
Gagliardi et al. 2009. Factors influencing antibiotic prophylaxis for surgical site infection prevention in general surgery: a review of the literature. *Can J Surg* 52(6):481-489.

Opportunities Exist to Improve Surgical Antibiotic Prophylaxis

- Studies have shown poor adherence to appropriate antibiotic prophylaxis in surgery
- A large scope of opportunities exists for improvement, especially with high-level evidence and clearly established guidelines

Van Kasteren et al. Adherence to local hospital guidelines for surgical antimicrobial prophylaxis: a multicentre audit in Dutch hospitals. *J Antimicrob Chemother* 2003;51:1389–1396.
Fonseca et al. 2008. Successful control program to implement the appropriate antibiotic prophylaxis for Cesarean section*Rev. Inst. Med. Trop. Sao Paulo* 50(2):79-82
Harbarth. Presentation made at ICIUM 2004.
Tourmousoglou et al. 2007. Adherence to guidelines for antibiotic prophylaxis in general surgery: a critical appraisal. *J Antimicrob Chemother* 10.1093.
Festinet al. 2009. Caesarean section in four South East Asian countries: reasons for, rates, associated care practices and health outcomes. *BMC Pregnancy Childbirth* 9:17.
Gagliardi 2009.

Surgical Site Infections—Common and Preventable (1)

- Most common surgical complication
- Occurs in up to 5% of patients undergoing operative procedures
- Second commonest cause of all nosocomial infections (accounting for 14%–16%)
- Commonest nosocomial infections among surgical patients (40% of all such infections)

Failure mode and effects analysis – SSI: antibiotic prophylaxis. Partnership for Patient Care, 2006

Bratzler, D. W., et al. 2004. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project *Clin Infect Dis* 2004; 38:1706–15.

Manniën, J., et al. 2006. Effect of optimized antibiotic prophylaxis on the incidence of surgical site infection**.** *Infect Control Hosp Epidemiol* 27:1340-1346

Mangram et al. 1999*.* Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol* 20(4):247-278.

Reed, R. L. 2010. SSI new solutions (PPT). Loyola University Medical Center, Maywood, IL.

Anderson et al. 2008. Strategies to prevent surgical site infections in acute care hospitals. *Infect Control Hosp Epidemiol* 29 (Suppl 1): S51-S61

ACOG. 2009. Guidelines Issued on Antibiotic Prophylaxis for Gynecological Procedures*. Obstet Gynecol* 113:1180-1189

Surgical Site Infections—Common and Preventable (2)

- Compared with cases without SSIs, cases with SSI involve an increase in:
  - Hospital stay (approx. 7–10 additional post-op hospital days)
  - Risk of mortality (2–11 times higher risk)
  - Cost (estimates ranging from $3,000 to $29,000)
- Estimated 40%– 60% preventable

Health Care Improvement Foundation. 2006. Failure Mode and Effects Analysis Surgical Site Infections: Antibiotic Prophylaxis. Plymouth Meeting, PA: ECRI Institute.
Bratzler 2004.
Mannien 2006
Mangram 1999
Reed, L.E. 2010
Anderson 2008.
ACOG 2009.

Antibiotic Prophylaxis Helps Prevent Post-Hysterectomy Infections

- High-level evidence (randomized controlled trials [RCTs]) show high efficacy to prevent SSI in patients undergoing hysterectomy
- Gynecologic surgical procedures are treated as most other clean, contaminated procedures—a single antibiotic in a single dose before procedure (30-60 minutes before incision)

Scottish Intercollegiate Guidelines Network (SIGN). 2008. Guideline 104. Antibiotic prophylaxis in surgery. Edinburgh, Scotland: SIGN. http://www.sign.ac.uk/pdf/sign104.pdf

General Principles of Prophylaxis

- Aim is to augment host defenses by reducing intraoperative bacterial contamination
- Should be directed against the most likely pathogens
- No need to cover all possible organisms
- Avoid antibiotics used for therapy
- Give narrow-spectrum agent for short-term use

Characteristics of a good prophylactic agent—

- Safe
- Inexpensive
- Bactericidal
- Good tissue penetration
- IV route possible

Do not depend on antibiotic prophylaxis to overcome poor surgical technique

Treatment Guidelines. 2009. Antibiotic prophylaxis for surgery. *The Medical Letter* 7(82)
Health Care Improvement Foundation. 2006.
Munchkof 2005.

General Principles of Prophylaxis—Timing of Administration

Classen study shows value of giving prophylaxis just before surgery

Prophylaxis in 2,847 patients undergoing surgery*

Antibiotic prophylaxis timing	Rate of infection
Early (2-24 hr before surgery)	3.8%
Pre-operative (0-2 hr before surgery)	0.6%
Peri-operative (0-3 hr after surgery)	1.4%
Post-operative (3-24 hr after surgery)	3.3%

*Classen et al. 1992. The Timing of Prophylactic Administration of Antibiotics and the Risk of Surgical-Wound Infection. *NEJM* 326(5):282-28.6

Surgical Antibiotic Prophylaxis—Indicators as Quality Measures

The US National Surgical Infection Prevention Project uses the following performance measures for national surveillance and quality improvement

Proportion of patients who receive parenteral antibiotic prophylaxis within 1 hour before surgical incision	Proportion of patients who receive prophylactic antibiotic consistent with current recommendations	Proportion of patients whose prophylactic antibiotics are discontinued within 24 hours after the end of surgery

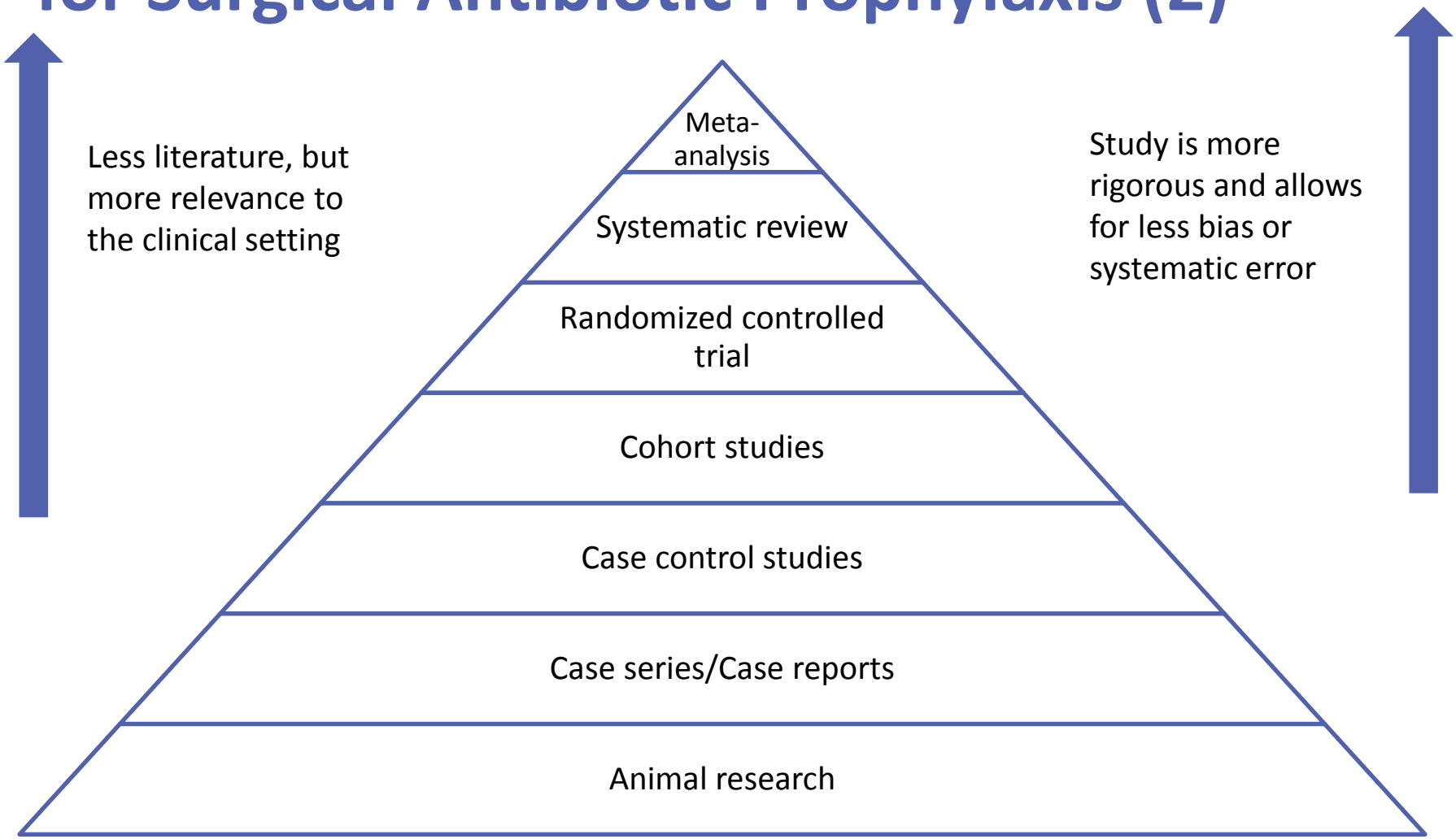
Bratzler 2004.

Evidence Used to Make Recommendations for Surgical Antibiotic Prophylaxis (1)

Recommendation grades	Level of evidence	Study characteristics to determine efficacy
A	1a	Systematic review (SR) (with homogeneity) of RCTs
	1b	Individual RCT (with narrow confidence interval)
	1c	All or none study
B	2a	SR (with homogeneity) of cohort studies
	2b	Individual cohort studies (including low quality RCT)
	2c	Outcomes research, ecological studies
	3a	SR (with homogeneity) of case-controlled studies
	3b	Individual case-controlled studies
C	4	Case series (and poor quality cohort and case-controlled studies)
D	5	Expert opinion without explicit critical appraisal

Centre for Evidence Based Medicine – University of Oxford, March 2009

Evidence Used to Make Recommendations for Surgical Antibiotic Prophylaxis (2)



American College of Obstetrics and Gynecology Recommendations for Surgical Prophylaxis (1)

Level A recommendations (based on good and consistent scientific evidence)

Antibiotic prophylaxis ***strongly recommended***

- Hysterectomy
- Elective suction curettage abortion

Antibiotic prophylaxis ***not recommended***

- Intrauterine device insertion
- Diagnostic laparoscopy

ACOG 2009.

ACOG Recommendations for Prophylaxis (2)

Level B recommendations (based limited or inconsistent scientific evidence)

- Hysterosalpinography can be performed without prophylactic antibiotics
  - Prophylaxis recommended however for history of dilated fallopian tubes
- Before undergoing hysterectomy, patients with preoperative bacterial vaginosis should be treated

ACOG 2009.

ACOG Recommendations for Prophylaxis (3)

Level C recommendations (based primarily on consensus and expert opinion)

- Exploratory laparotomy – antibiotic prophylaxis is **not recommended**
- Patients with a history of pelvic inflammatory disease or tubal damage, **prophylaxis may be considered** for transcervical procedures such as hysterosalpingography, chromotubation, and hysteroscopy
- Urodynamic testing – **antibiotic treatment** should be given if pretest screening show UTI

ACOG 2009.

ACOG Recommendations for Prophylaxis (4)

Recommended Antibiotics for Hysterectomy

- Cefazolin preoperatively (cefuroxime is an acceptable alternatives)
  - Based on broad antimicrobial spectrum, efficacy, safety, pharmacokinetics, and low cost
  - 1 gm, single dose, preoperatively
- For those women who have allergy to penicillin
  - *Immunoglobulin E mediated* (immediate hypersensitivity)
    - Metronidazole and clindamycin
- *For non-immune mediated hypersensitivity*
  - Cephalosporin prophylaxis is acceptable

Alexander et al. 2011. Updated recommendations for control of SSI. *Ann Surg*;253:1082-1093 Lewis et al. Gynecologic Surgical Site Infections: Simple Strategies for Prevention. *The Female Patient* 2011; 36: 14-22.
ACOG 2009.

ACOG Recommendations for Prophylaxis (5)

Recommended antibiotics for urogynecology procedures, including those involving mesh

Preferred regimen—Single dose

- Clindamycin 600 mg IV ***PLUS***
- Gentamicin 1.5 mg/kg IV ***OR***
- Quinolone 400 mg IV ***OR***
- Aztreonam 1 gm IV

Acceptable quinolones include ciprofloxacin, levofloxacin, moxifloxacin

ACOG 2009.
Lewis 2011.

ACOG Recommendations for Prophylaxis (6)

Recommended antibiotics for hysterosalpingogram or chromotubation (prophylaxis is needed ONLY if patient has history of pelvic inflammatory disease or procedures demonstrated dilated fallopian tubes)

Preferred regimen

- Doxycycline 100 mg orally, twice daily for 5 days

ACOG 2009
Lewis 2011.

Other International Recommendations for Gynecologic Surgical Prophylaxis

SIGN Guidelines

- Single antibiotic dose preoperatively (IV)
- Antibiotic—choose based on local microbial flora

Medical Letter Guidelines

- Single antibiotic dose preoperatively (IV)
- Antibiotic—cefoxitin, cefotetan, or cefazolin (1-2 gm) OR ampicillin/sulbactam (3 gm)

SIGN 2008.

Other Proven Procedures to Reduce SSI (1)

Skin Decontamination, Patient

- Studies have shown that both povidone-iodine and chlorhexidine/alcohol lower bacteria counts and SSI
- A randomized controlled trial showed a 40% reduction in total surgical site infections among patients undergoing clean-contaminated surgery who received a single chlorhexidine/ alcohol scrub as compared to povidone-iodine scrub

Skin Decontamination, Surgeon

- Chlorhexidine is more effective than povidone-iodine and chlorhexidine plus alcohol was even more effective in reducing bacteria on the hands

Alexander 2011.

Other Proven Procedures to Reduce SSI (2)

Hair Removal

- Shaving has been shown to increase SSI
- No hair removal has the lowest incidence of SSI
- Where hair removal is deemed necessary by the surgeon, use of clippers is the best choice and is preferable to the use of razor and has decreased infection rate

Alexander 2011.

Other Proven Procedures to Reduce SSI (3)

Surgical Gloves

***A recent study of 4,147* surgical patients** found there was a higher incidence of SSI in procedures in which gloves were perforated compared with procedures where they were not perforated (odds ration, OR=2.0)

The risk of infection with glove perforation was significantly greater in those procedures in which no antibiotic prophylaxis was given

***In an analysis of 655 surgical procedures*,** perforations were found to occur in 31% of operations

Double-indicator gloves made the intraoperative detection of perforations much easier

Using double gloving techniques, perforation of the outer glove was associated with less perforation of the inner glove (OR=0.10)

Alexander 2011.

Other Proven Procedures to Reduce SSI (4)

Preoperative Bathing and Antiseptic Agents

- Preoperative showering with chlorhexidine has been shown to reduce the number of organisms at the incision site better than using povidone-iodine or soap and water
- Using a shower the evening before *and* the morning of the procedure is more effective in colony reduction than a single shower either the night before or the morning of the procedure
- Additional use of chlorhexidine impregnated cloth is more effective than a single simple showering

Alexander 2011.

Summary: Benefits of Prophylaxis

- Surgical prophylaxis is highly beneficial in many gynecological procedures in reducing post-surgical febrile morbidities and surgical site infections
- A single dose of a single antibiotic is sufficient and is highly recommended (for hysterectomy)
  - High-level evidence (from meta-analysis or RCT)

Smaill, F. M., and G. M. L. Gyte. 2010. Antibiotic prophylaxis versus no prophylaxis for preventing infection after cesarean section (Review). *Cochrane Database of Systematic Reviews* 1. Art. CD007482
van Schalkwyk et al. 2010. Antibiotic prophylaxis in obstetric procedures. *J Obstet Gynaecol Can.* 32(9):878-92.
SIGN Guideline 104 (antibiotic prophylaxis in surgery), July 2008.
Alexander 2011.

Summary: Choice and Dose

- First generation cephalosporin—most commonly recommended is cefazolin 1-2 gram IV (cefuroxime is considered to be interchangeable with cefazolin).
  - High-level evidence (from meta-analysis or RCT)

Alexander 2011. ACOG 2009. Lewis 2011. van Schalkwyk 2010. raft therapeutic guideline on antimicrobial prophylaxis in surgery. American Journal HP Medical Letter.2009. ACOG. 2003. ACOG practice bulletin number 47, October 2003: Prophylactic Antibiotics in Labor and Delivery. *Obstet Gynecol* 102:875-82 Tita et al. 2009. Emerging concepts in antibiotic prophylaxis for cesarean delivery: a systematic review. *Obstet Gynecol* 2009;113:675-82

Summary: Alternative in Cases of Beta Lactam Allergy

- In women allergic to beta lactams, a reasonable alternative is clindamycin with gentamicin
  - Clindamycin—600 to 900 mg IV

    AND
  - Gentamicin—1.5 mg/kg IV
- ACOG recommends using metronidazole 500 mg IV in place of gentamicin

van Schalkwyk 2010.

ASHP. 2010. Draft therapeutic guideline on antimicrobial prophylaxis in surgery. www.ashp.org/DocLibrary/Policy/PracticeResources/Orthopedics-ForPublicComment.aspx

Medical Letter 2009.

Tita 2009.

ACOG 2009.

Bratzler 2004.

Summary: Timing of Administration

- Guidelines all recommend perioperative administration -30-60 minutes prior to skin incision.

Costantine et al. Timing of perioperative antibiotics for cesarean delivery: a metaanalysis. *Am J Obstet Gynecol* 2008;199:301.e1-6
Tita 2009.
van Schalkwyk 2010.
ASHP. 2010.
Medical Letter 2009.

Summary: Duration of Prophylaxis

- A single dose is recommended. No added benefit obtained from multiple doses.
  - High-level evidence (from meta-analysis or RCT)
- An additional dose recommended 3 to 4 hours after the first dose if the procedure is extended beyond 3 hours or blood loss is >1,500 mL

van Schalkwyk 2010.

SIGN Guideline 104 (antibiotic prophylaxis in surgery), July 2008

Medical Letter 2009.

Fonseca et al. 2006. Implementing 1-dose antibiotic prophylaxis for prevention of surgical site infection. *Arch Surg* 141:1109-1113

Hopkins, L., and F. M. Smaill. 1999. Antibiotic prophylaxis regimens and drugs for cesarean section. *Cochrane Database of Systematic Reviews* 2. Art. No.: CD001136. DOI: 10.1002/14651858.CD001136.

Summary: Other Infection Control Practices that Reduce SSI—Use of Chlorhexidine

- Chlorhexidine/alcohol combinations for skin decontamination in patients and for surgical staff have been shown to be effective in decreasing bacteria on the skin and decreasing surgical site infections
- Preoperative showering with chlorhexidine has been shown to reduce the number of organisms at the incision site
- Additional use of chlorhexidine impregnated cloth is more effective than a single simple showering

Alexander 2011.

Conclusion: Antibiotic Prophylaxis in Gynecological Procedures

- Well-established international recommendations exist backed by high-grade evidence
- Using or adapting these recommendations in local settings have potential to significantly improve outcomes, save costs, reduce adverse events, and contain drug resistance