Orthognathic Surgery and Peri Operative Antibiotic Use

by

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TABLE OF CONTENTS

LIST OF TABLES……..… v

LIST OF FIGURES……..….. vii

ABSTRACT……...viii

LIST OF ABBREVIATIONS USED……...…… ix

ACKNOWLEDGEMENTS……..……..…… x

CHAPTER 1 INTRODUCTION……..……..... 1

1.1 Preamble……..... 1

1.2 Background……....……2

1.2.1 Orthognathic Surgery……...……2

1.2.1.1 Maxillary Surgery……....…….4

1.2.1.2 Mandibular Surgery……..……5

1.2.1.3 Post Surgical Care……..……. 7

1.2.1.4 Complications……..…….8

1.2.2 Surgical Site Infection……..……9

1.2.2.1 Diagnosis and Definition……..……9

1.2.2.2 Surgical Scrub and Site Preparation..……12

1.2.2.3 Prophylactic Antibiotics……..……..13

1.2.2.4 Corticosteroid Administration…..…….15

1.2.2.5 Patient Modifying Factors……..……...16

1.2.2.6 Smoking…….....17

1.2.2.7 Implanted Hardware……..……....17

1.2.3 SSI Microbial Pathogens ...…….……17

1.2.3.1 Oral and Maxillofacial Pathogens. ….…..18

1.2.3.2 Orthognathic Surgery Pathogens ……....20

1.2.3.3 Local Microbial Costs……..…… 22

CHAPTER 2 CANADIAN SURVEY……..…….. 25
2.1 Purpose……..…… 25
2.2 Methods……..…… 25
2.3 Results……..…….. 25
2.4 Discussion……..……29
CHAPTER 3 RETROSPECTIVE ANALYSIS……..……31
3.1 Purpose……..…… 31
3.2 Materials and Methods……..…… 31
3.2.1 Patients and Data Collection……..…….. 31
3.2.2 Antibiotic Protocol and Surgery……..…… 32
3.2.3 Diagnosis and Management of SSI…..……33
3.2.4 Statistical Analysis……..……34
3.3 Results…….35
3.3.1 Patient Demographics……..…… 35
3.3.2 Chart Screening and SSI Analysis…..……. 37
3.3.3 SSI Symptoms and Contributing Factors…..……...39
CHAPTER 4 PROSPECTIVE RANDOMIZED TRIAL……... 42
4.1 Purpose……..…… 42
4.2 Ethics……..…… 42
4.3 Materials and Methods……..…… 42
4.3.1 Patient Selection……..…….42
4.3.2 Consent……..…….. 43
4.3.3 Patient Randomization……..……... 43
4.3.4 Patient Examination, History and Physical..……43
4.3.5 Antibiotic Protocol……..…….44
4.3.6 Surgical Protocol……..……44
4.3.7 Post Operative Protocol and Complications..……. 45

4.3.8 Statistical Analysis……..…….47
4.4 Results……..…….. 48
4.4.1 Patient Demographics……..…… 48
4.4.2 Surgical Complications……..…….. 50
4.4.3 Effect of Antibiotic on SSI…..……..…….. 51
4.4.4 Surgical Site Infection Group……..…… 55
4.4.5 Patients with One Year Follow Up……..…… 56
CHAPTER 5 DISCUSSION……..…….. 58
CHAPTER 6 CONCLUSION……..……...66
Bibliography……..……. 67
Appendix A 1 year Questionnaire ……...……..……73

LIST OF TABLES

Table 1	Criteria for Defining Surgical Site Infection. National Center for Infectious Diseases, Mangram AJ, Horan TC, Pearson ML, et. al. Guideline for Prevention of Surgical Site Infection, 1999. Infection Control and Hospital Epidemiology, 20:4:247- 278, 1999……..	10
Table 2	Summary of Microorganisms Isolated. Oral and Maxillofacial Infections. Hohl T, Whitacre R, Hooley J, Williams B. Diagnosis and Treatement of Odontogenic Infections Seattle Wa. Stoma Press:1983 ……..……...……	19
Table 3	Microorganisms Isolated from Orthognathic SSI Chow *et. al.* Complications after orthognathic Surgery. Journal Oral Maxillofacial Surgery 2007; 65:984-992 ……..…….....	22
Table 4	Local Susceptibility Rates of Gram Positive Microbes to Common Antibiotics Antimicrobial Handbook 2012. Department of Pharmacy, Division of Infectious Diseases, Capital Health, Halifax QV85-103 Rev. 01/2012……...	23
Table 5	Local Susceptibility Rates of Gram Negative Microbes to Common Antibiotics Antimicrobial Handbook 2012. Department of Pharmacy, Division of Infectious Diseases, Capital Health, Halifax QV85-103 Rev. 01/2012……...	24
Table 6	Survey question 1 results……...	26
Table 7	Survey question 2 results……...	26
Table 8	Survey question 3 results……...	27
Table 9	Survey question 4 results……...	27
Table 10	Survey question 5 results……...	27
Table 11	Survey question 6 results……...	28
Table 12	Survey question 7 results……...	28
Table 13	Survey question 8 results……...	28
Table 14	Survey question 9 results……...	29
Table 15	Survey question 10 results…….....	29

Table 16 Medical conditions that impair immune system or affect healing….32

Table 17 Demographics of patients with associated prevalence of the total sample and of those with SSIs …….....36

Table 18 Medical conditions of patients with SSIs with associated prevalence and classification. ……..…37

Table 19 Summary of the prevalence of SSIs associated with the surgery performed. ……40

Table 20 Summary of the prevalence of SSIs associated with the antibiotic used. …….. 41

Table 21 Summary of the comparisons of prevalence of SSIs associated with the antibiotic used. …… 41

Table 22 Classification of Surgical Complications. Dindo D, Demartines N, Clavien P. A New Proposal With Evaluation in a Cohort of 6336 Patients and Results of a Survey. Annals of Surgery, Vol 240, Number 2, August 2004……..…… 46

Table 23. Demographics of patients enrolled in study, and that completed study. ……49

Table 24. List of Medical Conditions and Past Medical History Classification. ……50

Table 25. SSI in Antibiotic and Placebo groups Compared with Procedure…. 52

Table 26. Effect of Antibiotic on SSI by Surgeon…… 52

Table 27. Effect of Antibiotic on SSI by Length of Hospital Stay…… 53

Table 28. Effect of Antibiotic on SSI by Length of MMF…….54

Table 29. Effect of Antibiotic on SSI by Number of Extractions……..54

Table 30. SSI and procedure. …… 55

Table 31. Location of SSI…….. 56

Table 32. Self Awareness of Antibiotic or Placebo……...57

LIST OF FIGURES

Figure 1 LeFort I dissection A-C, osteotomy D-F, Downfracture G, and Fixation H. In: Perciaccante V, Bays R. Principles of Maxillary Orthognathic Surgery Miloro M (ed) Peterson's Principles of Oral and Maxillofacial Surgery 3rd Edition, section 7; Chapter 58 p1365-1385……..……... 5

Figure 2 Obwegeser's technique of intraoral sagittal split osteotomy. Obwegeser HL:Mandibular growth anomalies, Berlin, 2001, Springer, fig 80c,fig 85d and b.) In: Watzke I. Sagittal Split Osteotomy. Turvey T (ed) Oral Maxillofacial Surgery. Vol 3; Saunders Elsevier Inc 2009 Chapter 3 p. 88 ……6

Figure 3 Chart screening and SSI analysis. SSIs were analyzed for surgical site location, antibiotic treatment rendered, if there were recurrent infections, and the presence of side effects from the study antibiotics……...38

Figure 4 Analysis of the signs and symptoms in patients with SSIs and the amount of cases where surgeon diagnosis of infection was reported in the patients' chart ……... 39

ABSTRACT

Purpose : The purpose of this study was to determine the most effective duration of antibiotic prophylaxis following orthognathic surgery.

Methods: A survey of Canadian Oral and Maxillofacial surgeons (OMFS), a retrospective chart analysis, and a prospective randomized controlled trial was conducted. All patients received 1 day of IV antibiotics and then were randomized into an active antibiotic or placebo group for 2 additional days. The primary outcome measured was the presence of surgical site infection (SSI). The surgical procedures performed, duration of surgery, duration of MMF and hospital stay, concomitant extraction of teeth, and operating surgeon were documented and analyzed for effect on SSI.

Results: A survey of 115 OMFS in Canada showed varying regimens for post operative antibiotic use. The most common antibiotic was cefazolin for 24 hours post operatively. One week of antibiotics was prescribed by 43.7% of respondents. A retrospective analysis of 2268 patients found a statistically lower rate of SSI with cefazolin(6.2%) compared to penicillin(14.3%) and clindamycin(10.4%). The prospective trial consisted of 288 patients, of whom 171 were adherent to the study medication. The active antibiotic group SSI rate was 7.0% compared to the placebo group SSI rate of 17.6% ($p=0.04$). Patients that were followed for 1 year also showed statistically significant difference in rate of SSI, (active group 4%, placebo group 25%, $p<0.05$). When SSI occurred, the mandible was involved 71% of the time.

Conclusion: Cefzolin is the most effective antibiotic to use following orthognathic surgery. Extending antibiotic coverage for a total of 3 days decreases the risk of SSI. The greatest effect is in patients undergoing bilateral sagittal split osteotomies.

LIST OF ABBREVIATIONS USED

SSI	Surgical site infection
BSSO	Bilateral sagittal split osteotomy
MMF	Maxillo-mandibular fixation
CDC	Center for disease control
MRSA	Methicillin-resistant *Staphylococcus aureus*
CAD	Canadian dollars
CAOMS	Canadian Association of Oral and Maxillofacial Surgeons
FG	Functional Genioplasty
DM	Diabetes Mellitus
SLE	Systemic lupus erythematous
JIA	Juvenile idiopathic arthritis
QID	Four times per day
BID	Twice per day
REB	Research ethics board
BMI	Body mass index
WBC	White blood cell count
Hgb	Hemoglobin
PLT	Platelet count
Cr	Creatinine level
ICU	Intensive care unit
NNT	Number needed to treat
CI	confidence interval

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CHAPTER 1
INTRODUCTION

1.1 Preamble

Surgical site infection (SSI) is a problem that is encountered in any surgical procedure. Surgical procedures done through the oral cavity are at a higher risk for SSI due to the multitude of bacterial pathogens present. Lefort 1 osteotomies, bilateral sagittal split osteotomies, and functional genioplasty procedures involve incising through oral mucosa and creating osteotomies in underlying bony structures. The most common complication that can arise from this surgery is SSI. SSI is a serious concern and can effect the surgical outcomes, healing time of the patient following surgery and increase cost to the health care system. The literature is quite clear on the benefits of presurgical prophylactic antibiotics in reducing the rate of post operative surgical site infections.[1] Currently, there is conflicting literature as to the recommended length patients should receive antibiotics during their postoperative course, with the majority of studies having small sample sizes.[2,3]

Orthognathic surgery is considered a clean-contaminated surgery and thus has a reported infection rate of 10-15%.[2] In 1999 Bentley *et. al* conducted a randomized control trial comparing 1-day vs. 5-day regimen of antibiotics following orthognathic surgery.[4] The trial was stopped due to the drastic difference in the infection rate seen between the two groups, 6.7% in the 5-day group compared with 60% in the 1-day group.[4] This data varies greatly from the rates of infection that are seen at the department of Oral and Maxillofacial Surgery in Halifax, Nova Scotia. In 2007 Chow *et al.* carried

out a retrospective chart review of complications seen in orthognathic surgery. They found the rate of infection was reduced significantly by continuing antibiotics in the post operative period when compared to a single prophylactic dose.[5] They found a SSI rate of 17.3% with a single preoperative IV dose, 5.1% with a preoperative dose followed by 2-days of postoperative antibiotics, and 7.7% with a preoperative dose followed by 3 days of postoperative antibiotics.[5] They also observed that there was no significant difference in infection rates between 2 days and up to 14 days of post operative antibiotics.[5] A meta-analysis by Danda et al. in 2011 also suggested that a regimen consisting of preoperative antibiotics followed by an extended postoperative course is the most effective in decreasing surgical site infections. The incidence was decreased by 3.2 times, with the greatest effect noted with administration of post operative antibiotics for 2 days.[2] The studies included in this meta analysis had small sample sizes. Of the 8 studies included the average number of patients was 8 with a total of 532 patients.[2] This shows the need for larger randomized controlled studies in order to determine the best antimicrobial regimen for these patients.

1.2 Background

1.2.1 Orthognathic Surgery

Orthognathic surgery is utilized to correct dentofacial deformities. The name originates from Greek *orthos* meaning straight, and *gnathic* meaning jaws. There are two main types of surgery, which are used alone or in combination. Maxillary osteotomies include Lefort I, II or III, as well as segmental osteotomies. Mandibular osteotomies include the bilateral sagittal split osteotomy, intraoral vertical ramus osteotomy and

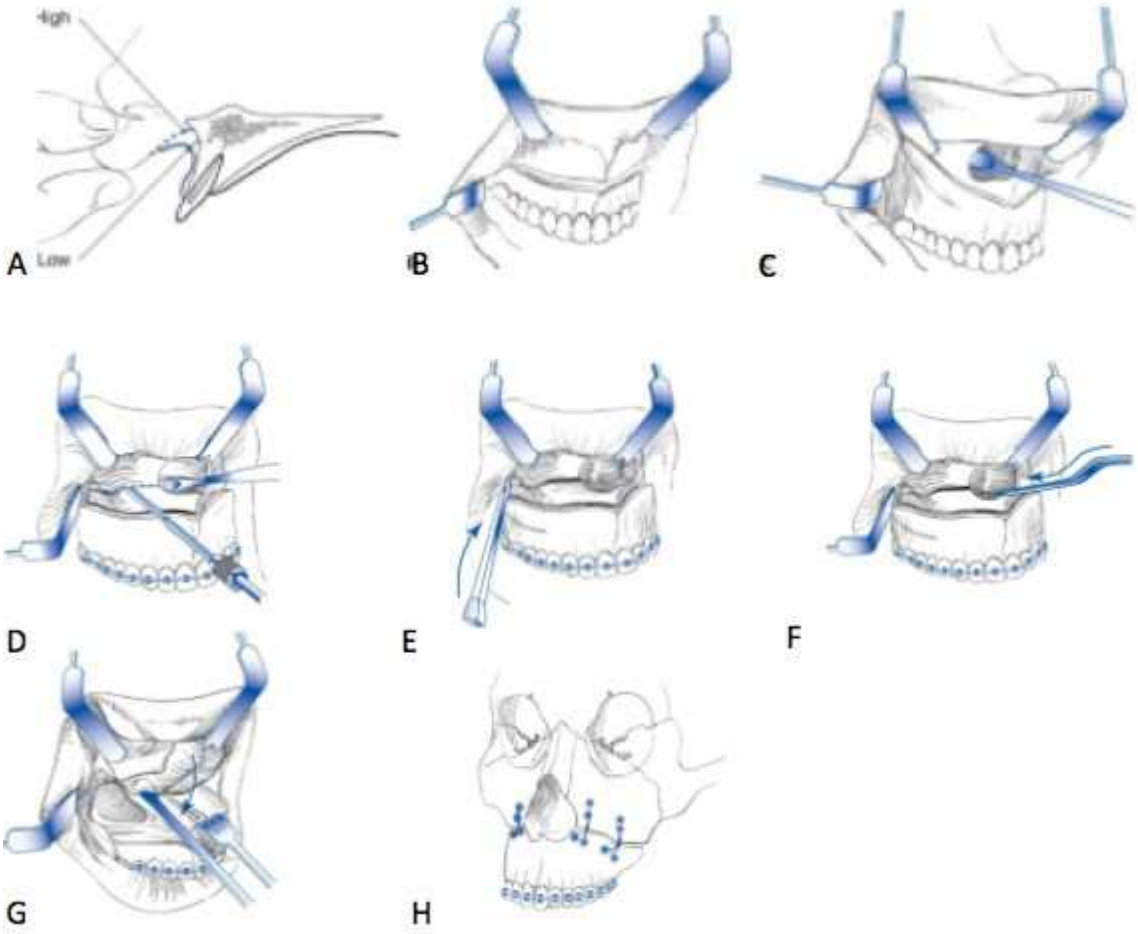
functional genioplasty osteotomy. These procedures are used individually or in combination to treat multiple dentofacial deformities. Maxillary surgery may be indicated for transverse deficiencies, asymmetries, vertical maxillary excess or deficiency, or maxillary anterior-posterior deficiency. Mandibular osteotomies are used for anterior-posterior excess or deficiency, asymmetry, and macro or microgenia. A combination of maxillary and mandibular osteotomies is regarded as bimaxillary surgery. This may be required for more complex dentofacial deformities or where correction of a cant is involved.

Patients require a period of presurgical orthodontics to facilitate outcomes. The goals of presurgical orthodontics include: alignment and positioning the teeth over basal bone, avoiding excessive intrusion or extrusion of teeth, decompensation of teeth, avoiding unstable expansion of arches, and avoiding class II and class III mechanics when possible.[6] This is normally a period ranging from 6-24 months. Following this, surgical treatment planning is preformed and assessment of the ideal occlusion is analyzed using models and cephalometric analysis. The Delaire analysis was used for interpretation of each patients dentofacial deformity and for surgical planning.[7] Patients underwent treatment plans comprised of either a Lefort I osteotomy, bilateral sagittal split osteotomy, functional genioplasty or if required a combination of these procedures. If third molars interfered with occlusion or were impacted they were removed during the surgery.

1.2.1.1 Maxillary Surgery

Orthognathic surgery involving the maxilla was described by von Langenbeck in 1859.[8] In 1901 Le Fort described the natural planes of maxillary fractures. It was from this where the osteotomy designs originate.[9] In 1927 Wassmund was the first to use the Lefort I osteotomy for treatment of midface deformities.[10] Multiple modifications occurred and complete mobilization and removal of interferences were recommended by Obwegeser in 1965.[11] The procedure is described in Peterson's Oral Maxillofacial Surgery.[12] A brief description of the surgical procedure is given and images are outlined in Figure 1. The approach to the maxilla involves a trans-vestibular incision through mucosa in the maxillary vestibule.[12] This is followed by a subperiosteal dissection which is carried out to the zygomatic buttress and along the nasal floor.[12] A LeFort I level osteotomy is then done on both sides with a reciprocating saw.[12] The nasal septum is then separated from the maxilla with a nasal septal osteotome.[12] The maxilla is then down fractured, separated from the pterygoid plates and mobilized. All interferences are removed, and the greater palatine artery may be freed or clipped if required.[12] The maxilla may then be segmentalized if required and is placed into the desired position and stabilized with rigid fixation.[12] Diagrams of the Surgical procedure is outlined in Figure1.

Figure 1. LeFort I dissection A-C, osteotomy D-F, Downfracture G, and Fixation H.



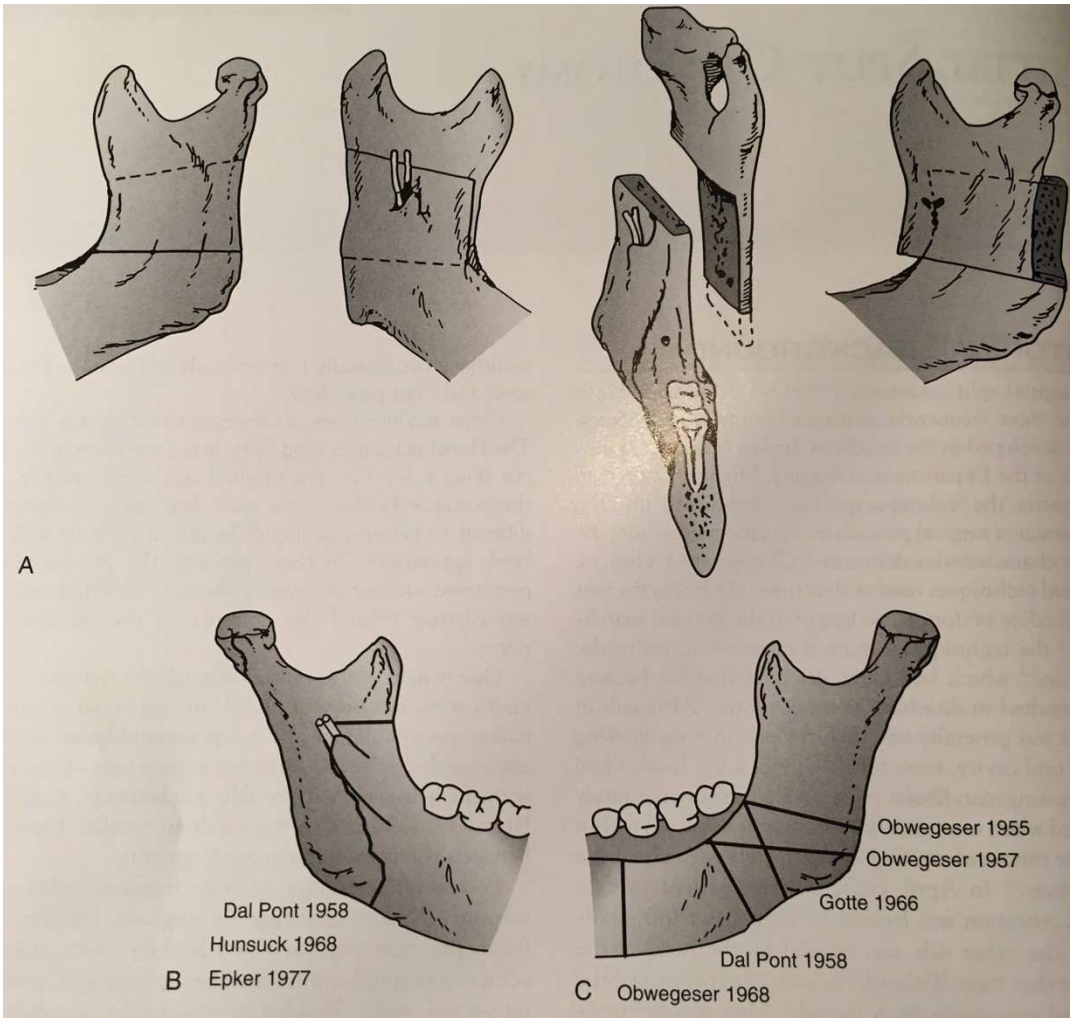
Perciaccante V, Bays R. Principles of Maxillary Orthognathic Surgery. Miloro M (ed) Peterson's Principles of Oral and Maxillofacial Surgery 3rd Edition, section 7; Chapter 58 p1365-1385.

1.2.1.2 Mandibular Surgery

There have been many styles of mandibular osteotomies described for the correction of dentofacial deformities involving the mandible. Hullihen in 1849 was the first to describe a mandibular osteotomy, which was a subapical anterior osteotomy.[13] In this study the two mandibular osteotomies preformed were the bilateral sagittal split osteotomy (BSSO) and functional genioplasty. Mandibular anterior posterior deformities and asymmetries were treated with the BSSO, and micro or macrogenia and chin

asymmetries were treated with functional genioplasty. The BSSO technique was famously first described by Obwegeser in 1955, with modifications by Dal Pont 1958, Obwegeser 1961, and Epker 1977.[14-16]

Figure 2. Obwegeser's Technique of Intraoral Sagittal Split Osteotomy. With Subsequent Modifications



Obwegeser HL:Mandibular growth anomalies, Berlin, 2001, springer, fig 80c,fig 85d and b.) In: Watzke I. Sagittal Split Osteotomy. Turvey T (ed) Oral Maxillofacial Surgery. Vol 3; Saunders Elsevier Inc 2009 Chapter 3 p. 88.

The BSSO procedure involves a vestibular incision and sub periosteal dissection with a horizontal osteotomy on the medial aspect of the ramus extending posterior to the area of the lingula, as seen in Figure 2.[14-16] Another osteotomy is made around the

external oblique ridge. These two osteotomies are then connected and the osteotomy is completed with osteotomes and spreaders.[14-16] Following mobilization of the distal and proximal segments, all patients were fixated with miniplate fixation with 4-6 monocortical screws.

The Delaire analysis was used to determine patients that would benefit from genioplasty as a part of their orthognathic surgery.[7] Dr. David S Precious, described treatment planning and osteotomy designs for a functional genioplasty. These included genioplasty advancement, setback, and superior repositioning .[17] This procedure involves a vestibular incision along the anterior chin, followed by subperiosteal dissection and stripping of the mentalis muscle. For advancement or setback sliding osteotomies a single horizontal osteotomy is made using a reciprocating saw.[17] The anterior segment of the mandible is then repositioned into the desired position and fixated.[17] For superior repositioning a mortise and tenon osteotomy may be done with removal of lateral wedges.[17] Fixation of the chin segment may be done using either 4 double twisted wire loops, or 2 wires and chin miniplate or screws.[17]

1.2.1.3 Post Surgical Care

Following surgery all patients were placed in tight maxillomandibular fixation (MMF) for a minimum period of 2 weeks, this is followed by 2-6 weeks of light guiding elastics, which the patient removes 5 times daily, for range of motion exercises, eating and maintaining oral hygiene. Patients normally stayed in the hospital for a period of 1-4 days with most going home post-operative day 2 or 3. A maxillary acrylic splint was used

in cases with transverse expansion of the maxilla, or in cases with unstable occlusion. This is usually left in place for 4 weeks, and after removal, the orthodontist promptly replaces the maxillary arch wire. All patients having orthognathic surgery have detailed post operative instructions which involve; medications, oral hygiene regimens, diet, activity restrictions, lip exercises and jaw exercises, elastics and removal in emergency situations, and how to manage nasal congestion. All patients were sent home with liquid pain medication, which includes acetaminophen 650mg po q4-6h prn, ibuprofen 600mg q6h prn, and hydromorphone 2-4mg po q4h prn. For nausea, gravol 25-50mg po liquid or per rectum is used. A dietitian in hospital met with patients to review dietary restrictions with MMF and maintaining proper nutrition. Instructions on oral hygiene care are reviewed in detail including brushing appropriately, rinsing with saline following meals, and the use of chlorhexidine 0.12% oral rinse twice daily. The operating surgeon sees most patients at 2 weeks, 4 weeks, 2 months, and once braces are removed. Some patients are seen more frequently or less often depending on the situation. Emergency support is available to all patients 24 hours per day.

1.2.1.4 Complications

Orthognathic surgery complications can be divided into intraoperative or postoperative complications. Intraoperative complications include: hemorrhage, either acute bleeding or hematoma formation, unfavorable osteotomies, damage to adjacent teeth and nerve damage.[18] Anesthesia related complications include: airway issues, and cardiovascular issues. Postoperative complications include: nausea, vomiting, infection, nonunion or malunion, TMJ problems, condylar resorption, hardware failure,

malocclusion, relapse, which can be immediate (hardware failure) or delayed, limited opening, and unfavorable nasal changes.[18] Post operative SSI incidence is one of the more common post operative complications encountered in orthognathic surgery patients.[5]

1.2.2 Surgical Site Infection

1.2.2.1 Diagnosis and Definition

The identification of SSI can be difficult and rates reported can vary depending on the definitions used to diagnose SSI. Often times the diagnosis may not be clear and this can affect SSI rates, thus it is important to use objective criteria in defining and diagnosing SSI. The Center for Disease Control (CDC) has developed standardized surveillance criteria for defining SSI (Table 1).[1]

Table 1. Criteria for Defining Surgical Site Infection.

Superficial Incisional SSI
- Infection occurs within 30 days after the operation and infection involves only skin or subcutaneous tissue of the incision - And at least one of the following: 1. Purulent drainage with or without laboratory confirmation, from the superficial incision 2. Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision 3. At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat and superficial incision is deliberately opened by surgeon, unless incision is culture-negative 4. Diagnosis of superficial incisional SSI by the surgeon or attending physician - Do not report the following conditions as SSI: 1. Stitch abscess (minimal inflammation and discharge confined to points of suture penetration.) 2. Infection of an episiotomy or newborn circumcision site 3. Infected burn wound 4. Incisional SSI that extends into the fascial and muscle layers (deep incisional SSI
Deep Incisional SSI
- Infection occurs within 30 days after the operation if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operations and infection involves deep soft tissues (eg. fascial and muscle layers) of the incision and at least one of the following 1. Purulent drainage from the deep incision but not from the organ/space component of the surgical site. 2. A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (>38ºC), localized pain, or tenderness, unless site is culture-negative 3. An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination. 4. Diagnosis of a deep incisional SSI by a surgeon or attending physician.
Organ/Space SSI
- Infection occurs within 30 days after the operation if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operation and infection involves any part of the anatomy (organs or spaces), other than the incision, which was opened or manipulated during an operation and at least one of the following: 1. Purulent drainage from a drain that is placed through a stab wound into the organ/space 2. Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space 3. An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation or by histopathologic or radiologic examination 4. Diagnosis of an organ/space SSI by a surgeon or attending physician.

National Center for Infectious Diseases, Mangram AJ, Horan TC, Pearson ML, et. al. Guideline for Prevention of Surgical Site Infection, 1999. Infection Control and Hospital Epidemiology, 20:4:247- 278, 1999)

As outlined in the CDC document, SSI is divided into 3 main categories, superficial incisional SSI, deep incisional SSI, and organ or space SSI.[1] Superficial incisional SSI occurs within 30 days and involves at least 1 of the following 4 criteria: [1]

1. Purulent drainage, with or without laboratory confirmation, from the superficial incision.

2. Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.

3. At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness or heat and superficial incision is deliberately opened by surgeon, unless incision is culture-negative.

4. Diagnosis of superficial incisional SSI by the surgeon or attending physician.[1]

When an implant is used and a deep incisional and organ/space SSI occurs within 1 year of the surgery, it is considered a SSI.[1]

Surgical wound classification is divided into 4 classes:

- Class I/Clean: where no inflammation is encountered and the respiratory, alimentary, genital or uninfected urinary tract is not entered.[1,19,20]
- Class II/Clean-Contaminated: operation where respiratory, alimentary, genital or urinary tracts are entered under controlled conditions and without unusual contaminantion.[1,19,20] The oral cavity and oropharynx is included in this category.[1]

- Class III/Contaminated: Open, fresh wounds or major breaks in sterile technique, such as, gastrointestinal tract spillage, acute non-purulent inflammation.[1,19,20]
- Class IV/Dirty-Infected: old traumatic wounds, clinical infection, organisms causing a post operative infection were present in the operative field before operation.[1,19,20]

From a clinical perspective, there is concern as to the reliability of the definition for diagnosing infection as well as for the classification of surgical wounds. As such comparison between studies and SSI rates is difficult, as evidenced by a large study comparing the CDC criteria and the nosocomial infection national surveillance scheme in the United Kingdom.[21] Wilson *et. al.* showed the small variations between definitions of SSI can lead to large variations in the reported rate of SSI.[21] Using a single definition consistently at one center can demonstrate reliably differences in SSI, but comparison between centers is unreliable.[21] To control for bias or diagnostic errors it is important to use a single treatment center, uniform system for diagnosis of SSI, and blinding of both the surgeon and the patient.

1.2.2.2 Surgical Scrub and Site Preparation

The cost of SSI to the health care system can be unacceptably high.[22] Many guidelines and protocols exist for effective sterilization and techniques for minimizing contamination in the operating room environment. These include surgical attire, drapes, aseptic techniques and high efficiency particulate air filters.[1,22] Skin decontamination is

also vital in preventing SSI. Proper hand scrubbing prior to gowning using 75% aqueous alcoholic solution, 4% povidine iodine or 4% chlorhexidine gluconate is important.[22,23] Extensive reviews in preoperative skin preparation for surgeons have been conducted. The consensus overall is that alcohol rubs are as effective as aqueous scrubs, chlorhexidine gluconate is more effective than povidone-iodine scrubs, and that a 2-3 minute scrub is more effective than subsequent 30 second scrubs.[22-24] A randomized controlled trial investigating 2% Chlorhexidine gluconate with 70% isopropyl alcohol to 10% povidione-iodine in patients undergoing clean-contaminated surgery (colorectal, thoracic, gynecologic, urologic procedures) found that there was statistically lower rate of infection in the 2% chlorhexidine gluconate and 70% isopropyl alcohol group(9.5% to 16.1% p = 0.004, 95% CI).[25]

1.2.2.3 Prophylactic Antibiotics

There is clear benefit in the literature for the use of systemic prophylactic antibiotics. Studies have shown significant reductions in SSI for both clean and clean-contaminated surgeries.[1,22,26] Trans-oral procedures are considered clean-contaminated procedures with an expected rate of infection of 10-15%.[26] The benefit of prophylactic antibiotics has also been shown in orthognathic surgery patients.[27] Zijderveld found a SSI rate of 11% and 17% with amoxicillin/clavulanic acid and cefuroxime respectively, which was significantly lower than a placebo (52.6%).[27] The time of antibiotic administration determines the effectiveness in preventing SSI.[22] Studies in other surgical specialties vary, with some recommending 1 hour before incision, while another large orthopedic study showed 1 to 30 min prior is effective in total hip arthroplasty.[22,28]

The duration of antibiotics for prophylaxis has also been investigated across multiple specialties. Most studies suggest there is no benefit from an extended course.[22] Other studies have shown higher rates of infection with single dose groups vs. 24 hour regimen, with some advocating ineffective antibiotic concentration at time of closure.[22,29] Antibiotic prophylaxis for the treatment of facial fractures has also been investigated. The majority of these studies have found no difference between groups with only preoperative and intraoperative antibiotics compared to those with postoperative administration.[30,31] Data relating to whether the fractures were compound was missing. This is important, as it may substantially increase the rate of SSI. The data from these studies conflicts with the literature from infectious disease journals. Patzakis *et. al.* found 65% of open fractures have wound contamination with microorganisms. They recommend antibiotics as treatment for wound contamination and thus is not considered prophylactic in these patients.[32] Orthopedic literature also varies between 1-day and 3-day administration of antibiotics for open fractures. Most recommend no longer than 3-days to prevent selection of resistant organisms.[32] There is still conflict in the maxillofacial literature as to the ideal length of antibiotic coverage following orthognathic surgery.[2-5] A comparison of 1-day versus 3-days will be investigated in this study.

The literature is not clear as to which antibiotic provides the best coverage for SSI in patients undergoing surgical procedures involving the oral cavity. Recommendations in the head and neck surgical literature, include cefazolin alone, cefazolin with metronidazole, amoxicillin/clavulinic acid, and clindamycin.[33-36] A prospective randomized trial of 176 patients investigated regimens of cefazolin, clindamycin plus

gentamycin, and amoxicillin-clavulanate in head and neck surgery patients.[37] The overall rate of SSI was 23%. There was no statistical significance between the three groups (cefazolin [26%] clindamycin with gentamycin [21.2%] and amoxicillin-clavulanate [22.8%]).[37] In the orthognathic surgery literature there is currently no consensus with regards to the most effective prophylactic antibiotic regimen in preventing SSI. The most common antibiotic used for prophylaxis in orthognathic studies is penicillin, and the most common duration is for 1 day.[38-40] Amoxicillin or ampicillin has also been suggested by several authors.[41-43] Other studies have suggested amoxicillin/clavulanate, cefuroxime, cefpiramide or clindamycin.[44-46]

1.2.2.4 Corticosteroid Administration

Orthognathic surgery patients experience significant facial swelling in the immediate post-operative period. Corticosteroids are often administered prior to surgery and in the immediate post-operative period to aid in reducing post-operative edema, improve patient comfort and to prevent upper airway compromise.[47] Common steroids used are methylprednisolone, prednisone, dexamethasone and betamethasone. Dan *et al.* found that administration of corticosteroids in orthognathic surgery decreased pain and edema significantly with minimal effects on SSI and wound healing post operatively.[48] Precious *et al.* found no relationship between high dose short-term administration of the corticosteroid methylprednisolone and avascular necrosis of the femoral head.[47] Steroids act by interfering with capillary vasodilation, leukocyte migration, phagocytosis, cytokine production and prostaglandin inhibition.[49] Even though the mechanism of action by

which steroids work is understood, multiple trials show no decreased healing, and no increased infection rate.[48]

1.2.2.5 Patient Modifying Factors

The CDC Update on SSI 2011 identifies modifying factors that can affect the concentration of antibiotics in the surgical wound. They include: renal function, body weight, half life of antibiotic, cardiopulmonary bypass, blood transfusions, aggressive fluid therapy, patient age and nutritional status.[1,22] Renal function affects the efficiency of many antibiotics. Cefazolin and cephalexin are renally excreted and thus dosing is adjusted in renal failure.[50] Clindamycin is not affected by renal function.[50] During orthognathic surgery controlled hypotension is usually requested by the surgeon, which effects renal function. As a result, antibiotics excreted by the kidneys will have an increased half-life.[22] Obese patients require higher dosing of antibiotics and mg/kg dosing may be beneficial for morbidly obese patients.[22] Some recommendations suggest 3g of cefazolin for patients over 120kg.[33]

The host defense system is also important in limiting the rate of SSI. Studies have shown that hyperglycemia is a risk factor for SSI, and suggest diabetics are at an increased risk for developing complications.[22] Immunosuppressed patients with leukopenia or neutropenia will have impaired function and are at higher risk of infection. Other factors can also affect the functionality of neutrophils, such as hypothermia and oxygen levels.[22]

1.2.2.6 Smoking

The effect of smoking on SSI has been well studied. Smoking causes vascular vasoconstriction leading to decreased tissue oxygen saturation at the wound.[22] the literature suggests smoking cessation for 4 weeks before surgery may provide benefit in decreasing the risk of SSI.[22] Kuhlefelt *et al.* found a significant difference in SSI rates between smokers and non-smokers following Lefort or BSSO surgery.[51] The rate of SSI in non smokers was 7.0% and in smokers was 14.4.[51]

1.2.2.7 Implanted Hardware

Miniplates are often used for stabilization of bony segments following orthognathic surgery. Implantable hardware may become infected. The CDC defines a SSI as any infection that occurs up to 1 year following surgery when hardware is present.[1] Cases with persistent SSI, plate mobility or dehiscence may require hardware removal. Alpha *et al.* found a disturbance of healing incidence of 26% in patients undergoing a BSSO, and reported hardware removal in 6.5% of patients.[52] Interestingly there was a statistically significantly lower rate of disturbance or SSI in patients that received bimaxillary surgery.[52] These patients received 24 hours of IV antibiotics rather than only single prophylactic dose.[52] Falter *et al.* found 13.7% required plate removal for SSI, with the average time of removal at 9.9 months post operatively.[53]

1.2.3 SSI Microbial Pathogens

At birth the oral cavity is essentially sterile. Within a few days, species of *Streptococcus, Staphylococcus*, *Veillonella* and *Neisseria* appear.[54] In adults it is

estimated that 300 microbial species colonizing the oral cavity. The oral cavity is a mixed environment of gram positive, gram negative, and both aerobic and anaerobic bacteria. As such, SSI from clean-contaminated head and neck procedures are usually polymicrobial, with mixed aerobic/anaerobic bacteria.[33,54,55]

Whenever an incision is made through a mucous membrane, there will be a risk of SSI from endogenous flora.[1] Quantitatively, if the surgical site is contaminated with $>10^5$ microorganisms per gram of tissue there will be a markedly increased rate of SSI.[1] As such any oral surgical procedure involving breach of the mucosa will have a higher risk of SSI. Immunocompetent individuals are at low risk for SSI from fungi. Staph aureus is the most common pathogen isolated from SSI (22.5%).[33] Trends in cultured organisms from SSI change over time. From 2003-2007 there was an increased incidence of Staph aureus (30%), with increasing incidence of MRSA (16.1%-20%).[33] Bacteria in head and neck surgery patients with purulent discharge, gram positive aerobes were most frequently encountered (54%), followed by gram negative aerobes (38%) and anaerobes (8%).[37] Gram negative aerobes were more frequently seen in patients receiving cefazolin.[37]

1.2.3.1 Oral and Maxillofacial Pathogens

Predominant oropharyngeal organisms include aerobic and anaerobic *Streptococci*, *Bacteroides* species, *Peptostreptococcus* species, *Prevotella* species, *Fusobacterium* species, *Veillonella* species, *Enterobacteriaceae*, and *Staphylococci*.[33] Nasal flora includes predominately *Staphylococcus* species, *Streptococcus* species, *Haemophilus influenza, Moraxella cattarhalis*.[33] Nasal colonization by *Staphylococcus*

aureus, can occur in 20-30% of healthy patients.[1] Table 2 outlines common organisms found in odontogenic infections.[55]

Table 2. Summary of Microorganisms Isolated from Oral and Maxillofacial Infections

Gram + Cocci	**Gram + Rods**
Aerobes	Aerobes
Streptococcus mitior	*Lactobaccilus species*
Streptococcus salivarius	Anaerobes
Streptococcus mutans	*Bifidobacterium species*
Streptococcus pneumonia	*Lactobacillus species*
Streptococcus pyogenes	*Enbacterium species*
Streptococcus faecalis	*Actinomyces species*
Streptococcus sanguis	*Actinomyces Israelli*
Streptococcus intermedius	
Streptococcus epidermidis	**Gram – Rods**
Streptococcus aureus	Aerobes
Anaerobic species	*Klebsiella species*
Peptostreptococcus species	*Enterobacter species*
Peptostreptococcus anaerobis	*Escherichia coli*
Peptostreptococcus micros	Anaerobes
Peptococcus species	*Eikenella corrodens*
	Bacteroides species
Gram – Cocci	*Bacteroides fragilis*
Aerobes	*Bacteroides melanogenicus*
Neisseria species	*Bacteroides oralis*
Moraxella cattarhalis	*Fusobacterium species*
Anaerobes	*Fusobacterium nucleatum*
Veillonella paruvia	*Leptotrichia buccalis*

Hohl T, Whitacre R, hooley J, Williams B. Diagnosis and Treatment of Odontogenic Infections. Seattle Wa. Stoma Press:1983

The most common bacteria present in the oral cavity is *Streptococci,* with *S. salivarius* and *S. mutans*, being the most prevelant.[54] *Actinomyces, Bacteroides, Fusobacterium* and *Leptotrichia* are also frequently found in the oral cavity.[54] Bacteria found predominately in the gingival crevice include: *Fusobacterium nucleatum, Bacteroides melaninogenicus, Treponema macrodentium,* and *Camplybacter sputorum*.[54] Bacteria predominately found on the tongue include: facultative *Streptococci (sanguis*

and mitior), Veillonella species and *Diphtheroids*.[54] Dental plaque species include *Streptococci, Diphtheroids, Actinomyces, Veillonella, Peptostreptococci, Neisseria, Fusobacterium, Bacteroides,Vibrio.*[54] Fungi found in the oral cavity include *Candida species,* most frequently *Candida albicans*.[54] Viruses found in the oral region include herpes simplex virus 1 and 2, pox viruses, adenoviruses, papoviruses, coxsackie, aphthovirus, and paramyxoviruses.[54] Fungi and viral infections often are not primary pathogens present in SSI unless patients are immunosuppressed.

1.2.3.2 Orthognathic Surgery Pathogens

There is great difficulty in obtaining cultures for minor infections in the maxillofacial region. When a large abscess is present and requires extra-oral incision and drainage adequate cultures can be obtained. With small SSI they are often drained through an intra oral approach. This can lead to contamination from pathogens normally present in the oral cavity, thus making the sample unreliable. Few orthognathic SSI require extra-oral aspiration or incision and drainage. As a result the majority of studies investigating SSI and orthognathic surgery do not discuss culture results.

Patients with poor oral hygiene will have a larger amount of bacteria present, and will be at an increased risk of SSI following orthognathic surgery. Often, patients are placed into maxillomandibular fixation (MMF) following surgery for a period of 2-4 weeks. Some patients will also have an acrylic splint wired into the maxilla to maintain transverse expansions and post-operative occlusion. Splints also make home oral hygiene

care difficult. Subsequently, patients may have higher bacterial loads than normal in the immediate post-operative period.

Koole and Egyedi found the presence of saliva present in mandibular osteotomies up to 3 days following mandibular surgery.[56] This was determined by measuring salivary amylase present in drains placed following surgery.[56] Chow *et al.* included microbiological data in their large retrospective analysis (see table 3).[5] Most SSI were found to be polymicrobial in nature composed of endogenous oral bacteria.[5] The most common pathogens isolated were pigmented *Bacteroides*, α-hemolytic *Streptococcus*, *Enterobacter cloacae* and *Pseudomonas aeruginosa*.[5] Given the incidence of *Pseudomonas* present, nosocomial infections should be considered in patients staying in hospital

Table 3. Microorganisms Isolated from Orthognathic SSI

Microorganisms	*Number of Patients*
Gram-positive cocci	
Streptococcus viridans	19
Streptococcus miller (anginosus)	6
Staphylococcus aureus	5
Peptostreptococcus species	4
Enterococcus species	1
Gram-positive rods/bacilli	
Diphtheroid bacilli	5
Actinomyces	2
Gram-negative cocci	
Neisseria species	4
Moraxella species	1
Gram-negative rods/baccili	
Bacteroides Pigmented	29
Enterobacter cloacae	13
Pseudomonas aeruginosa	14
Klebsiella pneumoniae	9
Bacteroides species	8
Flavobacterium meningosepticum	2
Eikenella corrodens	2
Citrobacter diversus	1
Aeromonas hydrophilia	1
Acinetobacter baumanii	1
Fungus/ Yeast	
Candida albicans	1

Chow *et. al.* Complications after orthognathic Surgery. Journal Oral Maxillofacial Surgery 2007; 65:984-992.

1.2.3.3 Local Microbial Costs

It is important to consider local resistance and microbial factors when interpreting SSI. The Nova Scotia health authority provides a regular update of common pathogens and their susceptibility to common antibiotics used.[57] The cost of each antibiotic in Nova Scotia is as follows; cefazolin is $7.17 Canadian dollars (CAD) daily, cephalexin is $0.64 CAD daily, clindamycin IV is $12.81 CAD, and PO is $1.24 CAD daily.[57] Other commonly used antibiotics for orthognathic include penicillin G $15.84 CAD daily, and

penicillin VK $0.08 CAD daily, ampicillin IV $7.60 CAD and PO $0.24 CAD daily, and amoxicillin/clavulanate PO $1.22 CAD, Metronidazole IV $3.14 CAD, and PO $0.12 CAD[48]. Tables 4 and 5 include local resistance rates to common microbes seen across all specialties.[57] *Streptococcus* species are not included in this analysis. Flynn *et al.* found that oral *Streptococcus* species may have as high as 17% resistance to clindamycin which is a commonly used second line antibiotic in penicillin allergic patients.[58] *Eikenella corrodens* is also inherently resistant to clindamycin and must be considered in infections not responding to treatment with clindamycin.[59]

Table 4. Local Susceptibility Rates of Gram Positive Microbes to Common Antibiotics

	Ampicillin	Cefazolin	Cephalexin	Cloxacillin	Clindaymcin	Vancomycin
Staphlococcus aureus	NT	81	81	81	64	100
Coagulase negative *staphlyococci*	NT	38	38	38	38	100

NT – Not tested
Methicillin resistant *S. Aureus* strains are resistant to all penicillins, cephalosporins, and carbapenems

Antimicrobial Handbook 2012. Department of Pharmacy, Division of Infectious Diseases, Capital Health, Halifax QV85-103 Rev. 01/2012

Table 5. Local Susceptibility Rates of Gram Negative Microbes to Common Antibiotics

	Amoxicillin/ clavulnate	Ampicillin	Cefazolin	Cephalexin	Ceftriaxone	Piperacillin/ tazobactam	TMP-SMZ
Escherichia Coli	81	68	93	84	97	96	85
Klebsiella pneumoniae	92	IR	93	87	96	94	91
Proteus mirabilis	93	82	94	91	100	98	87
Enterobacter cloacae	IR	IR	IR	IR	IR	IR	IR
Citrobacter freundii	IR	IR	IR	3	11	IR	81
Klebsiella oxytoca	96	IR	51	49	100	96	98
Morganella morganii	IR	IR	IR	IR	IR	97	78

IR – Usually not active either because of intrinsic or acquired resistance

Antimicrobial Handbook 2012. Department of Pharmacy, Division of Infectious Diseases, Capital Health, Halifax QV85-103 Rev. 01/2012

CHAPTER 2
CANADIAN SURVEY

2.1 Purpose

In November 2013 a survey of Canadian Oral and Maxillofacial surgeons was conducted. The purpose the survey was to investigate current practices related to antibiotic use in orthognathic patients. The short survey consisted of 10 questions focused on SSI and orthognathic surgery. The primary outcome of this survey was to determine which antibiotic(s) are commonly used and the duration of their use following orthognathic surgery. Secondary outcomes measured included which presurgical preparation was used and treatment of SSI in orthognathic patients.

2.2 Methods

A short questionnaire consisting of 10 questions was created using Google forms. A link was sent to all members of CAOMS Canadian Association of Oral and Maxillofacial Surgeons (CAOMS), along with a description of the survey. Only one entry was allowed. Some questions allowed for multiple answers. The survey was open from November 1st, 2013 until December 30th, 2013.

2.3 Results

A total of 115 surgeons responded to the survey.

Question 1. Which of the following is/are your prophylactic antibiotic(s) of choice in patients with no allergies undergoing orthognathic surgery? Check all that apply

Table 6. Question 1 results

Antibiotic	Responses	Percentage
Penicillin	28	24.3%
Ampicillin/Amoxicillin	33	28.7%
Kefzol/Keflex	49	42.6%
Clindamycin	13	11.3%
Flagyl	1	0.9%
Amoxicillin/Clavulinic Acid	4	3.5%
Other	12	10.4%

Question 2. Which of the following is/are your prophylactic antibiotics(s) of choice for patients with mild reactions to penicillin (mild rash, no hives) undergoing orthognathic surgery? Check all that apply

Table 7. Question 2 results

Antibiotic	Responses	Percentage
Penicillin	0	0
Ampicillin/Amoxicillin	0	0
Kefzol/Keflex	24	21.1%
Clindamycin	95	83.3%
Flagyl	1	0.9%
Amoxicillin/Clavulinic Acid	0	0
Other	5	4.4%

Question 3. Which of the following is/are your prophylactic antibiotics(s) of choice for patients with a severe reaction/anaphylaxis to penicillin undergoing orthognathic surgery? Check all that apply:

Table 8. Question 3 results

Antibiotic	Responses	Percentage
Kefzol/Keflex	0	0
Clindamycin	112	97.4%
Clarithromycin or Azithromycin	3	2.6%
Levofloxacin or Moxifloxacin	3	2.6%
Flagyl	1	0.9%
Other	2	1.7%

Question 4. How long do you continue prophylactic intravenous antibiotics post-operatively?

Table 9 Question 4 results

Length	Responses	Percentage
Pre-operative only	21	18.4%
24 hours	84	73.7%
3 days	9	7.9%
5 days	0	0
1 week	0	0
> 1 week	0	0

Question 5. How long do you continue prophylactic oral antibiotics post-operatively?

Table 10. Question 5 results

Length	Responses	Percentage
None	32	28.1%
24 hours	0	0
3 days	2	1.8%
5 days	21	18.4%
1 week	50	43.9%
> 1 week	9	7.9%

Question 6. For orthognathic surgery patients who developed a postoperative infection, which is/are your antibiotic(s) of choice in patients with no allergies? Check all that apply:

Table 11. Question 6 results

Antibiotic	Responses	Percentage
Penicillin	22	19.1%
Ampicillin/Amoxicillin	34	29.6%
Kefzol/Keflex	11	9.6%
Clindamycin	40	34.8%
Flagyl	28	24.3%
Amoxicillin/Clavulinic Acid	34	29.6%
Other	6	5.2%

Question 7. Which presurgical preparation solution do you use?

Table 12. Question 7 results

Preparation	Responses	Percentage
Betadine 10%	49	43%
Chlorhexidine 4%	22	19.3%
Chlorhexidine 2%	35	30.7%
Other	8	7%

Question 8. Which oral rinse do you recommend following orthognathic surgery? Check all that apply:

Table 13. Question 8 results

Rinse	Responses	Percentage
Saline	46	40%
Chlorhexidine	89	77.4%
Ethanol Based	2	1.7%
None	7	6.1%
Other	3	2.6%

Question 9. How long do you prescribe the rinse for following orthognathic surgery?

Table 14. Question 9 results

Length	Responses	Percentage
< 1 week	5	4.6%
1 week	35	32.1%
2 weeks	54	49.5%
1 month	11	10.1%
> 1 month	4	3.7%

Question 10. How many orthognathic surgery cases do you perform per year?

Table 15. Question 10 results.

Number of Procedures	Responses	Percentage
<10	26	22.8%
10-30	36	31.6%
30-50	19	16.7%
50-70	13	11.4%
70-100	9	7.9%
> 100	11	9.6%

2.4 Discussion

Results of the survey found that for orthognathic patients there is no consensus for antibiotic prophylaxis in the peri and post operative period. Cefazolin was the most common prophylactic IV antibiotic with 42.6%, followed by ampicillin at 28.7% and penicillin at 24.3%. Clindamycin was the most common antibiotic used in penicillin allergic patients. The most common length of IV antibiotic use following surgery was 24 hours at 73.7%. There was large variance in use of oral antibiotics following IV administration with 43.9% continuing them for one week followed by no oral antibiotics at 28.1% and then for five days at 18.4%. There was an equal distribution in use of

antibiotics for treatment of SSI with clindamycin, amoxicillin and amoxicillin/clavulanic acid being the most frequently prescribed.

A survey was done in 1991 of Oral and Maxillofacial surgery residency programs in the United States on antibiotic use following orthognathic surgery.[60] At that time, penicillin was the most commonly used antibiotic (76%), followed by cephalosporins(24%).[60] Tremendous variation was found in the length of use for antibiotics (ranging from preoperative only to 2 weeks).[60] For IV antibiotic administration, 10% used an intraoperative dose only, 15% continued IV antibiotics for 24 hours, 15% continued for 48 hours, and 13% continued for 72 hours.[60] For oral antibiotic administration following IV antibiotics, 27% recommended penicillin PO for 7-10 days, 6 % penicillin PO for 5 days, and 9% recommended cephalosporin PO for 5-7 days.[60] Many programs did not have a regular regimen. Clinical practice did not correlate with the literature recommendations.[60] The American survey and our Canadian surveys show no consensus among OMF surgeons as to the ideal regimen for antibiotic prophylaxis in orthognathic surgery. More high quality randomized controlled trials are required.

CHAPTER 3

RETROSPECTIVE ANALYSIS

3.1 Purpose

The primary purpose of this retrospective study was to determine the prevalence of acute SSI following orthognathic surgery, and to compare kefzol, penicillin and clindamycin as prophylactic antibiotics in preventing SSI.

3.2 Materials and Methods

3.2.1 Patients and Data Collection

A retrospective cohort analysis was conducted of consecutive patients undergoing orthognathic surgery between October 2005 and April 2013 at the department of Oral and Maxillofacial Surgery in Halifax, Nova Scotia, Canada. Ethical approval for chart review was obtained from the Capital Health Research Ethics Board of Nova Scotia. Patient information from the hospital electronic database and paper charts were reviewed. Inclusion criteria were all patients over the age of 16 with dentofacial deformities or obstructive sleep apnea that underwent either a LeFort osteotomy, BSSO, FG, or any combination of these. Exclusion criteria were patients that did not return for follow up or had insufficient information in the chart.

The charts of 2268 patients were reviewed in detail. Information extracted from the charts included patient demographics such as age, gender, and medical and smoking statuses; the antibiotic used for prophylaxis (cefazolin, clindamycin, or penicillin); details of the surgical procedure (type, duration, if third molars were extracted); and if the

patient had a SSI following surgery. The medical statuses were organized into three categories: (Class 1) the patient is healthy; (Class 2) the patient has a medical condition that does not increase risk of infection; or (Class 3) the patient has a medical condition that increases the risk of infection (Table 16). A patient was considered a smoker if they either were an active smoker at the time of surgery or had quit less than 3 months before their surgery. A positive smoking status (cigarettes and/or marijuana) and drinking more than 2 servings of alcohol per day also categorized the patient as having a class 3 medical status.

Table 16. Medical conditions that impair immune system or affect healing

Medical Condition	
Diabetes mellitus (DM)	Juvenile idiopathic arthritis (JIA)
Hodgkin's lymphoma	Juvenile psoriatic arthritis
Breast cancer	Juvenile idiopathic arthritis
Systemic lupus erythematosus (SLE)	>2 servings of alcohol/day
Hepatitis	Ulcerative colitis
Immunosuppressant medications	Kidney cancer
Smoking (tobacco & marijuana)	Rheumatoid arthritis
Crohn's disease	HIV/AIDS

3.2.2 Antibiotic Protocol and Surgery

Patients were given a prophylactic dose of an antibiotic prior to and after surgery. The choice of antibiotic was dependent on the operating surgeon and any antibiotic allergy status disclosed preoperatively. The three antibiotic courses used were cefazolin, clindamycin or penicillin G. Patients treated with cefazolin received either one or two grams of cefazolin, which was administered 30 minutes prior to surgery, followed by three post-operative doses, every 8 hours. For patients with a penicillin allergy, 600 mg of clindamycin were given 30 minutes prior to surgery, followed by three post-operative doses, every 8 hours. Patients treated with penicillin G received 2 million units of

penicillin G 30 minutes prior to surgery, followed by four doses every 6 hours following surgery.

A staff oral and maxillofacial surgeon and their resident preformed all surgical procedures. The surgical site was prepared with a 10% betadine solution prior to surgery. LeFort osteotomies were performed using a reciprocating saw and the maxilla was segmented if required. Fixation of the maxilla was obtained with wires and/or titanium miniplates. BSSO fixation was obtained using titanium miniplates. FG fixation was obtained with wires, titanium miniplates, or bicortical screws. Third molars were removed at time of surgery if indicated by the patients' treatment plan. All patients remained in maxillomandibular fixation (MMF) following surgery for a minimum of 2 weeks. All patients were in the hospital following surgery for a minimum of 1 day with the exception of some patients that only received a FG, who were discharged on the same day. Patients, once discharged, were given oral hygiene instructions and a two-week supply of 0.12% chlorhexidine rinse to be used twice daily.

Patients were seen by their surgeon at 2 and 4 weeks following surgery to assess their recovery status. Patients that developed a SSI were prescribed antibiotics, where the surgeon determined the type and regimen of the antibiotic. Patients were followed closely until the resolution of the infection.

3.2.3 Diagnosis and Management of SSI

The diagnosis of a SSI followed the criteria of the CDC, which is outlined in section 1.2.2.1.[1] The prevalence of SSIs was then determined for each of the individual

groups used for statistical analysis (see "statistical analysis" section). For patients that developed a SSI, charts were retrieved and assessed for the following information: days after the surgery at which the SSI was identified, the antibiotic(s) prescribed for the treatment of the SSI, the location of the infection, the signs and symptoms of the infection, if any recurrent infections occurred, and if hardware removal was required. Chart analysis of these patients was performed at a minimum of 6 months from the date of their surgery.

3.2.4 Statistical Analysis

All raw data was entered into Microsoft Excel (2010). For statistical analysis, patients were divided into groups according to the antibiotic that they received for prophylaxis, gender, medical status, and smoking status, the duration of surgery, third molar extractions, bimaxillary surgery, and the type of surgery (LeFort only, BSSO only, FG only, LeFort & BSSO, LeFort & BSSO & FG, LeFort & FG, or BSSO & FG). A Chi square analysis with a two-tailed p-value, 1 degree of freedom, and Yates correction compared these categorical variables against the prevalence of infection to determine significant relationships. Age and duration of surgery, being continuous variables, were compared against the prevalence of infection using binary logistic regression analyses in order to determine any significant associations. All statistical tests considered a p-value of less than 0.05 to be significant. SPSS statistics software (SPSS Inc., Chicago IL) was used for calculations. A statistician at the Nova Scotia Health Authority reviewed the statistics.

3.3 Results

3.3.1 Patient Demographics

Patient demographics were not associated with an increased risk of infection

2268 orthognathic cases were performed between October 2005 and April 2013 (mean age ± SD: 26.9 ± 11.7 years). A total of 182 (8%) of SSIs were documented. Age was not significantly associated with an increased prevalence of SSI (odds ratio, 0.9987; 95% CI, 0.9857-1.0119; p=0.846). There was a higher prevalence of females than males in both the overall sample (+/- SSI) and the group of patients with SSIs (Table 17). Gender did not pose an increased risk for SSI (p=0.05). The following trend in prevalence of medical history classifications was evident in both the overall sample (+/- SSI) and only those patients with SSIs: class 1>class 2>class 3. Many of the class 3 conditions noted were autoimmune and cancerous diseases, and smoking (Table 16). Of the few health conditions noted in the group of patients with SSIs, only 2.8% were co-morbidities that directly affected infection, including Crohn's disease, diabetes mellitus type 2, and breast cancer (Table 18). There was no significant correlation with infection in class 1, 2, or 3 patients (p=0.15, 0.34, and 0.41, respectively). The prevalence of non-smokers was greater than smokers in both the overall sample (+/- SSI) and only those patients with SSIs. Smoking status did not significantly affect the prevalence of SSIs (p=0.30).

Table 17 Demographics of patients with associated prevalence of the total sample and of those with SSIs.

Demographic	Total Patients	Prevalence of all patients (%)[b]	p-value[c]	Prevalence of SSI Patients (%)[d]
Gender (overall)	--	--	--	--
- Male	**796**	**35**	--	--
- Female	**1471**	**65**	--	--
Gender (SSI)	--	--	--	--
- Male	**82**	**3.6**	--	**45**
- Female	**100**	**4.4**	**0.05**	**55**
Medical History[a]	--	--	--	--
- No SSI	--	--	--	--
- Class 1	**1330**	**59**	--	--
- Class 2	**424**	**19**	--	--
- Class 3	**333**	**15**	--	--
- SSI	--	--	--	--
- Class 1	**105**	**4.6**	**0.15**	**58**
- Class 2	**42**	**1.9**	**0.34**	**23**
- Class 3	**33**	**1.5**	**0.41**	**18**
Smoking	--	--	--	--
- No SSI	--	--	--	--
- Non-smokers	**1808**	**80**	--	--
- Smokers	**279**	**12**	--	--
- SSI	--	--	--	--
- Non-smokers	**151**	**6.7**	--	**83**
- Smokers	**29**	**1.3**	**0.30**	**16**

[a] Class 1: healthy; Class 2: condition that does not increase the risk of infection; Class 3: condition that does increase the risk of infection.
[b] Percent of the total sample (2268).
[c] χ^2 compared the relationship between the given demographic and mean SSI prevalence (8.0%).
[d] Percent of the total number of patients with SSIs (182).

Table 18. Medical conditions of patients with SSIs with associated prevalence and classification.

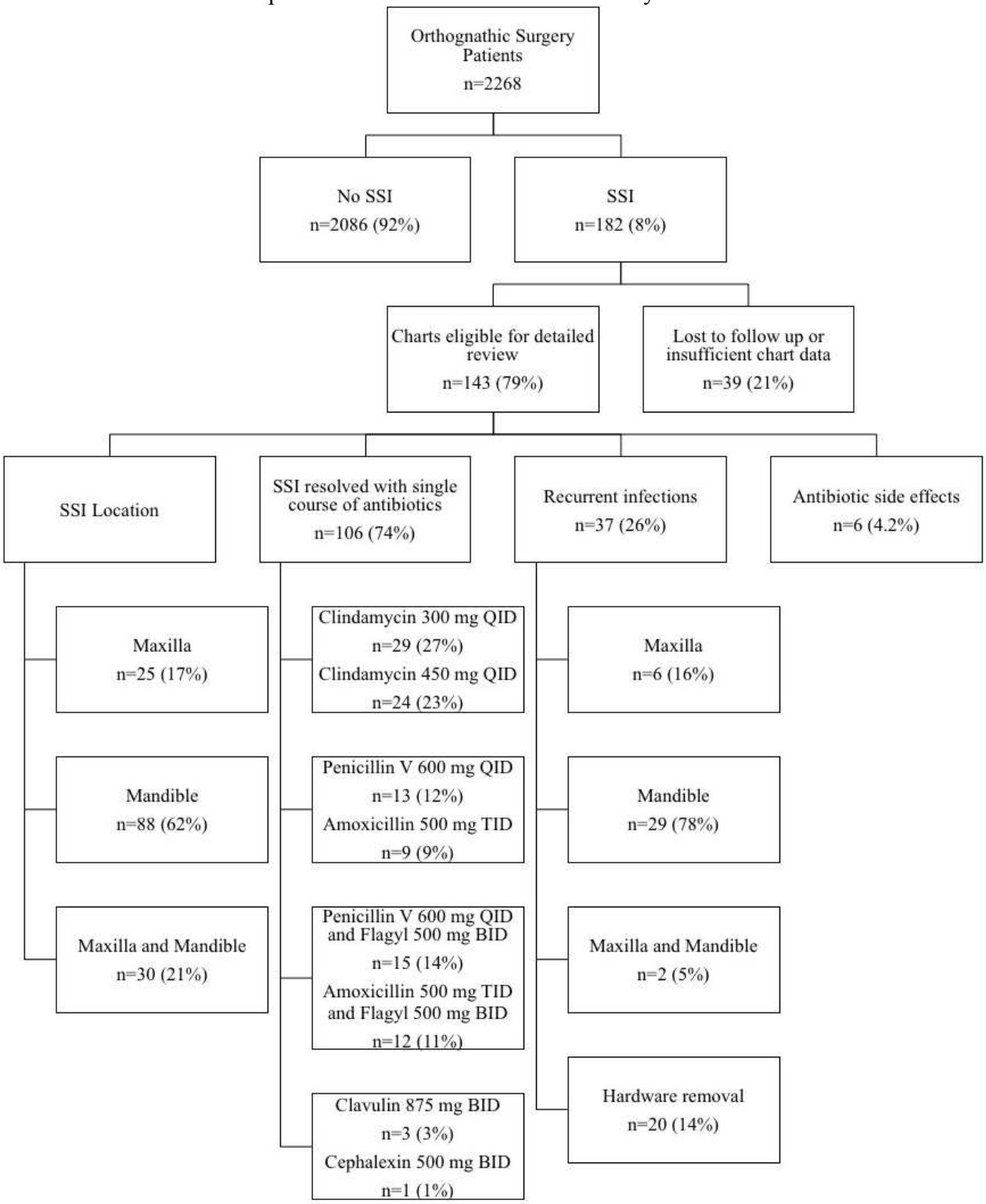
Medical Condition	Total Patients (%)[a]	Medical History Classification[b]
Asthma	**10**	**2**
Anxiety	**4.4**	**2**
Obstructive sleep apnea	**4.4**	**2**
Gastrointestinal (GI) reflux	**3.9**	**2**
Hypertension	**2.2**	**2**
Depression	**2.2**	**2**
Neurofibromatosis	**0.6**	**2**
Hypothyroidism	**0.6**	**2**
von Willebrand disease	**0.6**	**2**
Epilepsy	**0.6**	**2**
Fibromyalgia	**0.6**	**2**
Aspergers	**0.6**	**2**
Hemochromatosis	**0.6**	**2**
Crohn's disease	**1.7**	**3**
Breast cancer	**0.6**	**3**
Diabetes mellitus type II	**0.6**	**3**

[a] Percentage of total patients with a SSI (182 patients).
[b] Class 1: healthy; class 2: condition that does not increase the risk of infection; class 3: condition that does increase the risk of infection.

3.3.2 Chart Screening and SSI Analysis

The charts of 79% of patients with SSIs met the criteria for detailed review, where 21% were lost to follow up or had insufficient data (Figure 3). The majority of infections occurred in the mandible (62%), and this was also the site of the most recurrent infections (78%). The most common antibiotic prescribed for SSIs was clindamycin, either 300 mg 4 times per day (QID), or 450 mg QID; followed by penicillin 600 mg QID with or without metronidazole 500 mg twice per day (BID). Twenty six percent of patients who developed SSIs had recurrent infections following antibiotic treatment, and 14% of patients with SSIs required hardware removal from the surgical site. Negative side effects from antibiotics were reported in 4.2% of patients, which included nausea, vomiting, and rash. No cases of *Clostridium difficile* infection were reported.

Figure 3 Chart screening and SSI analysis. SSIs were analyzed for surgical site location, antibiotic treatment rendered, if there were recurrent infections, and the presence of side effects from the study antibiotics.

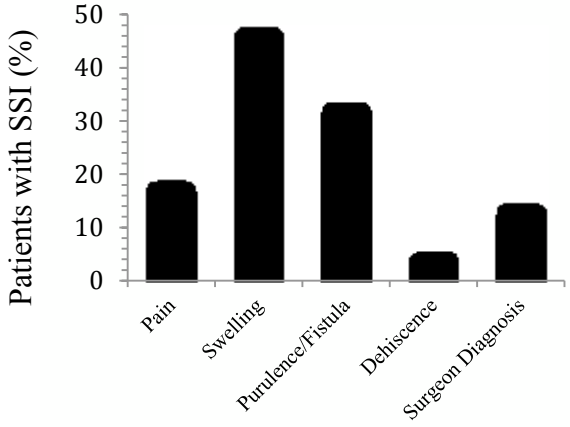


3.3.3 SSI Symptoms and Contributing Factors

Swelling was the most common diagnostic sign or symptom of a SSI

The diagnosis of SSIs most commonly occurred 11-15 days following surgery (36% of cases). The signs and symptoms of infection as described by patients and health care practitioners were categorized into five groups (Figure 4), multiple signs and symptoms were reported in some cases. Swelling was the most common sign and/or symptom described (46% of cases). Others included pain (18%), purulence and/or fistula (32.9%), and dehiscence (4.9%). Surgeon diagnosis without reporting of signs or symptoms occurred in 14% of cases.

Figure 4 Analysis of the signs and symptoms in patients with SSIs and the amount of cases where surgeon diagnosis of infection was reported in the patients' chart.



Surgery length, third molar extractions, and bimaxillary surgery increased SSI rate

The average length of surgery for all 2268 cases was 151 minutes, compared to an average of 157 minutes for the patients who had a SSI, and this difference was significant

(odds ratio, 1.0051; 95% CI, 1.0026-1.0076; p=<0.001). Third molars were extracted in 49.6% of patients and extractions were associated with a borderline significant higher prevalence of infection (p=0.048). The mean SSI prevalence for bimaxillary surgery (9.2%) was significantly greater than that of single surgical procedures (5.3%, p=0.0013).

Patients that underwent LeFort only surgery had a significantly lower prevalence of SSI

The prevalence of infection ranged from 3.5% in patients receiving only LeFort surgeries to 11.5% in patients receiving the BSSO/FG combination of surgeries (Table 19). The patients receiving only a LeFort surgery had a significantly lower prevalence of infection when compared to the overall prevalence (p=0.02). There was no significant difference between the prevalence of infection in one-piece and segmental LeFort osteotomies (p=0.98). The prevalence of infection in all of the other types of surgeries was not significantly different than the overall prevalence of infection.

Table 19 Summary of the prevalence of SSIs associated with the surgery performed.

Procedure	Total Patients	Infection (%)	p-value[a]
BSSO	422	7.0	0.70
Lefort	254	3.9	0.02[b]
- 1 Piece Lefort	115	3.5	0.11[c]
- Segmental Lefort	139	4.3	0.16[c]
FG	33	6.1	0.93
BSSO/FG	157	11.5	0.17
LeFort/FG	66	4.6	0.42
BSSO/LeFort	898	8.2	0.90
BSSO/LeFort/FG	418	10.5	0.11
Total	2268	8.0	--

[a] Compares prevalence of infection for each type of surgery to mean prevalence (8.0%).
[b] χ^2 test significantly different than mean (8.0%).
[c] χ^2 test p= 0.98 comparing 1 piece versus segmental LeFort surgeries.

Patients taking cefazolin had the lowest prevalence of infection

Patients that received cefazolin for antibiotic prophylaxis had a significantly lower prevalence of SSI compared to the overall prevalence ($p=0.03$, Table 20) and to patients that received penicillin and clindamycin ($p<0.0001$ and $p<0.02$, respectively, Table 21). Patients that received penicillin had a significantly higher prevalence than the mean ($p<0.0001$). Patients that received clindamycin did not have a significant difference in SSI prevalence compared to the mean ($p=0.16$). There was no statistical difference in SSI prevalence between the penicillin and clindamycin groups ($p=0.24$, Table 21).

Table 20. Summary of the prevalence of SSIs associated with the antibiotic used.

Antibiotic	Total Patients	Infection (%)	p-value[a]
Cefazolin	1627	6.2	0.03[b]
Penicillin	371	14.3	<0.0001[b]
Clindamycin	270	10.4	0.16
Total	2268	8.0	--

[a] Compares prevalence of infection for each type of antibiotic to the mean prevalence.
[b] χ^2 test significantly different than mean (8.0%).

Table 21. Summary of the comparisons of prevalence of SSIs associated with the antibiotic used.

Antibiotic 1	Antibiotic 2	Infection 1 (%)[a]	Infection 2 (%)[b]	p-value[c]
Cefazolin	Penicillin	6.2	14.3	<0.0001[d]
Cefazolin	Clindamycin	6.2	10.4	<0.02[d]
Penicillin	Clindamycin	14.3	10.4	0.24

[a] Refers to the prevalence of infection in the total sample (2268) for antibiotic 1.
[b] Refers to the prevalence of infection in the total sample (2268) for antibiotic 2.
[c] Compares the prevalence of infection between the two listed antibiotics in each row.
[d] χ^2 test significantly different.

CHAPTER 4

PROSPECTIVE RANDOMIZED TRIAL

4.1 Purpose

The primary purpose of this study is to determine the effect of a 1-day antibiotic regimen compared to an extended 3-day regimen of antibiotics on SSI in patients undergoing orthognathic surgery. The primary outcome is the development of SSI. Secondary outcomes include: compliance with antibiotic use, side effects of antibiotics, complications following surgery and demographics of SSI.

4.2 Ethics

Ethics application was submitted to the Capital Health Research Ethics Board (REB) for clinical trial approval. REB was approved July 12, 2013, file number CDHA-RS/2013-297, and registered on clinicaltrials.gov.

4.3 Materials and Methods

4.3.1 Patients Selection

Study enrollment began on July 20, 2013. All patients over 14 years old, undergoing orthognathic surgery at the QEII VG hospital were asked to participate in the study. Patients undergoing either isolated Lefort I osteotomy, bilateral sagittal split osteotomies, functional genioplasties, or any combination, with or without the extraction of teeth were included. Exclusion criteria included, use of antibiotics in the preceding 2 weeks, the presence of systemic, oral or odontogenic infections.

4.3.2 Consent

Study protocol as well as risks was explained in detail to all patients eligible for participation. This was done by either a resident or nurse working in the department. If the patient agreed to participate they would sign the consent form.

4.3.3 Patient Randomization

Patients were then separated into two groups. Three hundred envelopes were created. One hundred and fifty of them contained a piece of paper labeled A and another 150 labeled B. If a patient was allergic to penicillin this would be written on the envelope. Patients were then instructed to provide the envelope to the hospital pharmacist. The pharmacist documented if the patient was allocated to group A or B, and if they did not pick up the medication. The pharmacist then dispensed a patient labeled brown opaque bottle containing either the active antibiotic or the placebo. The nurse, surgeon, anesthetist, and patient were all blinded as to which group the patient was in.

4.3.4 Patient Examination, History and Physical

Prior to surgery, each patient required a history and physical examination, orthognathic evaluation, radiographic evaluation, and blood work including: CBC, INR/PTT, and electrolytes. Consent for orthognathic surgery, presurgical planning and model surgery proceeded in the same manner as patients not included in study. Demographic information was obtained including: age, sex, body mass index (BMI), past medical history (PMHx), medications, allergies, smoking status, preoperative white blood cell count (WBC), hemoglobin (HgB), platelet count (PLT) and creatinine level (Cr). The

medical status of each patient was organized into three categories: Class 1 healthy; Class 2 medical condition(s) that do not increase risk of infection; or Class 3 medical condition(s) that increases the risk of infection (Table 16). A patient was considered a smoker if was an active smoker at the time of surgery or had quit less than 3 months before their surgery.

4.3.5 Antibiotic Protocol

Standard preoperative IV prophylactic antibiotic was given to all patients. Two grams of cefazolin was given prior to incision, and in allergic patients 600 mg of clindamycin was administered. All patients received 3 IV doses postoperatively of one gram cefazolin q8h or 600mg clindamycin q8h if allergic. Following the completion of the IV antibiotics, patients would continue with study medication four times a day for 2 days. Group A received oral liquid cephalexin 500 mg or clindamycin 300 mg four times per day for 2 days, and group B received a flavored liquid placebo four times per day for 2 days.

4.3.6 Surgical Protocol

One of 6 staff Oral and Maxillofacial surgeons and a resident performed all surgical procedures. All surgical sites were prepared with a 10% betadine solution prior to surgery. LeFort osteotomies were performed using a reciprocating saw and the maxilla was segmented if required. Fixation of the maxilla was obtained with wires and/or titanium miniplates. BSSO fixation was obtained using titanium miniplates. FG fixation was obtained with wires, titanium miniplates, or bicortical screws. Third molars were

removed at time of surgery if indicated by the patients' treatment plan. If autogenous or allogenic bone grafting occurred this was documented. All patients remained in MMF following surgery for a minimum of 2 weeks. All patients were admitted to the hospital following surgery for at least 1 day.

Surgical procedures preformed, duration of surgery, length of hospital stay and presence of third molars were documented and recorded. Each staff Oral Maxillofacial surgeon was allocated a number 1 through 6. Duration of surgery was recorded in minutes, and duration of stay in hospital prior to discharge was recorded in days.

4.3.7 Post Operative Protocol and Complications

Post operative care and patient instructions followed section 1.2.1.3. Length of MMF was recorded in weeks. Any complications that occurred was documented and then classified according to Clavien-Dindo classification of surgical complications (Table 22)[61].

Table 22. Classification of Surgical Complications

Grade	Definition
Grade 1	Any deviation from the normal postoperative course without the need for pharmacological treatment of surgical, endoscopic, and radiological interventions Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
Grade II	Requiring pharmacological treatment with drugs other than such allowed from grade I complications, blood transfusions and total parenteral nutrition are also included
Grade III	Requiring surgical, endoscopic or radiological intervention
Grade IIIa	Intervention not under general anesthesia
Grade IIIb	Intervention under general anesthesia
Grade IV	Life-threatening complication (including CNS complications) requiring ICU management
Grade IVa	Single organ dysfunction (including dialysis)
Grade IVb	Multiorgan dysfunction
Grade V	Death of patient

Dindo D *et. al.* Classification of Surgical Complications A New Proposal With Evaluation in a Cohort of 6336 Patients and Results of a Survey. Annals of Surgery, Vol 240, Number 2, August 2004

Antibiotic type, the duration of treatment, surgical drainage and plate removal was recorded. Most patients returned for follow up at 2 weeks, 4 weeks, and after orthodontic treatment was completed. If a complication occurred, patients were asked to return for assessment.

The diagnosis of a SSI followed the criteria of the CDC, see section 1.2.2.1.[1] Patients were monitored for signs and symptoms of SSI or complications while in hospital. For patients that developed SSI further information was obtained including: date following surgery, location of SSI (quadrant), mechanism of SSI diagnosis, and how SSI

was treated. To ensure a SSI was not missed, all patients that completed the study were called 1 year following surgery and asked the following 5 questions.

1. What was date of last visit to Orthodontist?
2. Since surgery have you developed any infections?
3. Were you placed on antibiotics for this infection?
4. If so what antibiotic and how long?
5. Do you think you received placebo or antibiotic in study?

Any comments regarding the surgery or study received at this time were also documented (Appendix A).

4.3.8 Statistical Analysis

Raw data for all patients was entered into Microsoft Excel (2010). Patients that did not complete the study were removed. Demographic analysis was done for gender, medical status, smoking status, duration of surgery, number of extractions and the type of surgery (LeFort only, BSSO only, FG only, LeFort & BSSO, LeFort & BSSO & FG, LeFort & FG, or BSSO & FG). A Chi square analysis with a two-tailed p-value, 1 degree of freedom, and Yates correction compared these categorical variables against the prevalence of infection to determine statistical significance. Age and duration of surgery, being continuous variables, were compared against the prevalence of infection using logistic regression analyses in order to determine any significant associations. All statistical tests considered a p-value of less than 0.05 to be significant. SPSS statistics software (SPSS Inc., Chicago IL) was used for calculations. A statistician at the Nova Scotia Health Authority reviewed the statistics.

4.4 Results

4.4.1 Patient Demographics

A total of 288 patients were enrolled in the study, including 190 female and 98 male patients. The medical status class 1 group had 209 patients, class 2 had 66 patients, and class 3 had 3 patients (Table 23). Only 22 patients were smokers and 266 were non-smokers. Age range was 14 to 60 years old, with an average age of 25 years old. The average BMI was 25.4. Surgical times were between 46 minutes and 273 minutes, with an average of 145 minutes. Cefazolin/cephalexin was used in 156 patients, and 15 received clindamycin due to penicillin or cephalosporin allergy. There was no surgical site infection seen in the clindamycin group. Of the 288 patients enrolled, 109 patients did not complete the study. 76 did not pick up the study medication from the pharmacy, 17 did not finish the study medication or take it as prescribed, 8 withdrew themselves from study, 6 were removed from the study by the surgeon and placed on antibiotics, and for 2 patients the nurse did not give the study medication because of an error in the medical orders. In total 179 patients completed the study. Demographics are listed in Table 23 and separated into total patients (288), and completed patients (179).

Table 23. Demographics of patients enrolled in study, and that completed study.

Demographic	Patients	Prevalence of all patients (%)[b]
Gender (overall)	--	
- Female	**190**	**66**
- Male	**98**	**34**
Gender(Completed)	--	--
- Female	**126**	**74**
- Male	**53**	**26**
Medical History[a]	--	--
- Overall	--	--
- Class 1	**209**	**73**
- Class 2	**66**	**23**
- Class 3	**13**	**4**
- Completed	--	--
- Class 1	**132**	**73**
- Class 2	**39**	**22**
- Class 3	**8**	**5**
Smoking	--	--
- Overall	--	--
- Non-smokers	**266**	**92**
- Smokers	**22**	**8**
- Completed	--	--
- Non-smokers	**168**	**94**
- Smokers	**11**	**6**

The most frequently seen medical conditions were asthma (8%) and anxiety (7%). The most frequent Class III medical condition affecting infection was juvenile idiopathic arthritis (JIA), of which 3 patients (1%) were included in the study (Table 24).

Table 24. List of Medical Conditions and Past Medical History Classification.

Medical Condition	Total Patients (%)[a]	Medical History Classification[b]
Cleft Lip and Palate	**6 (2%)**	**1**
Asthma	**24 (8%)**	**2**
Anxiety	**19**	**2**
Obstructive sleep apnea	**6**	**2**
Hypertension	**6**	**2**
Depression	**8**	**2**
Hypothyroidism	**2**	**2**
von Willebrand disease	**1**	**2**
Epilepsy	**1**	**2**
Hodgkins Lymphoma	**1**	**2**
IBS/Crohn's disease/Colitis	**4**	**2**
Osteogenises imperfecta	**1**	**3**
Diabetes mellitus type II	**2**	**3**
Juvenile idiopathic arthritis	**3**	**3**
Sarcoidosis	**1**	**3**
Graves Disease	**1**	**3**
Addison's Disease	**1**	**3**

4.4.2 Surgical Complications

Surgical complications were classified using the Dindo classification outlined in Table 22. There were 54 complications recorded. A total of 15 patients had a Grade I complication. The most common complication was nausea. Other complications included, pain, swelling, and headaches. Grade II complications were seen in 29 patients. This group included SSI that required antibiotic prescription, other Grade II complications included trauma to the mandible post op and angular chelitis. Grade III complications were seen in 9 patients, which required surgical or radiographic intervention. These included patients requiring plate removal, buccal plate fracture, hardware failure, and TMJ MRI investigation. One Grade IV complication occurred. This was an anaphylactic shock to cefazolin and rocuronium in patient number 16. This

occurred prior to the beginning of surgery, the patient was stabilized in the operating room and transferred to the intensive care unit.

4.4.3 Effects of Antibiotic on SSI

A total of 179 patients completed the study appropriately. Eight patients had comorbidities associated with infection (Class 3) and were removed from statistical analysis. Final analysis was done on the 171 patients that completed the study correctly and were Class 1 or 2 past medical history.

Extended Antibiotics statistically reduced SSI

Eighty-six patients received the antibiotic (group A) and 85 received a placebo (group B), 117 patients were female and 54 male. SSI was seen in 21 patients (12%). In Group A, SSI occurred in 6 patients (7.0%), and in group B, SSI was seen in 15 patients (17.6%). This was statistically significant p=0.04. The number needed to treat (NNT) was 9.37 to prevent 1 SSI.

Effect of Extended Antibiotics on SSI by Procedure

Logistical regression was done to compare SSI between each surgical procedure group; results are outlined in Table 25. There was no statistical significance between each of the procedure groups. For patients that received BSSO only there were no SSI seen in the antibiotic group, versus 22% was seen in the placebo group. This was not significant, although by a close margin p=0.08, NNT was 5 (95% CI 2.6-20.5).

Table 25. SSI in Antibiotic and Placebo groups Compared with Procedure

Procedure	Group A		Group B		p value
	n	SSI	n	SSI	
BSSO	14	0	23	5	**0.08**
Lefort	12	1	5	1	**0.59**
BSSO/FG	7	1	6	2	**0.51**
LeFort/FG	3	1	4	0	**0.43**
BSSO/LeFort	40	2	36	5	**0.21**
BSSO/LeFort/FG	10	1	11	2	**0.66**
Total	**86**	**6**	**85**	**15**	**0.04**

Group A – Antibiotic, Group B – Placebo

Effect of antibiotic on SSI by operating surgeon was not significant

A total of 6 surgeons from the QE II were the primary operators included in our study; the operating resident with the surgeon was not evaluated. There was no statistical significance in SSI between the active antibiotic group, and the placebo group when analyzed by operating surgeon (Table 26.)

Table 26. Effect of Antibiotic on SSI by Surgeon

Surgeon	Group A		Group B		p value
	n	SSI	n	SSI	
1	14	1	10	2	**0.43**
2	2	0	9	1	**0.82**
3	27	2	21	2	**0.81**
4	14	0	12	2	**0.20**
5	21	3	25	8	**0.18**
6	8	0	8	0	**-**
Total	**86**	**6**	**85**	**15**	**0.04**

Effect of antibiotic on SSI by length of hospital stay was statistically significant

Patients were discharged home between post operative days 1 to post operative day number 4. Most patients stayed 2 days in hospital (66%). Patients who were discharged home on day number 2 were found to be statistically significant p=0.03 (Table 27). This may be due to the majority of patients being discharged home on post operative day number 2.

Table 27. Effect of Antibiotic on SSI by Length of Hospital Stay

Days Post op	Group A n	Group A SSI	Group B n	Group B SSI	p value
1	11	0	14	3	**0.16**
2	58	3	54	10	**0.03**
3	17	3	16	2	**0.72**
4	0	0	1	0	**-**
Total	**86**	**6**	**85**	**15**	**0.04**

Effect of antibiotic on SSI by length of MMF was not significant

Patients were in MMF for a period of 1 to 5 weeks following surgery. There was no significant increase in SSI between each of the groups comparing 1-5 weeks (Table 28).

Table 28. Effect of Antibiotic on SSI by Length of MMF

Weeks MMF	Group A		Group B		p value
	n	SSI	n	SSI	
1	2	0	-	-	**-**
2	57	4	62	10	**0.14**
3	13	2	14	3	**0.72**
4	12	0	9	2	**0.17**
5	2	0	-	-	**-**
Total	**86**	**6**	**85**	**15**	**0.04**

Effect of antibiotic on SSI by number of extractions was not significant

The number of teeth extracted during surgery was between 0 and 6. There was no statistical significance between each of the groups (Table 29.)

Table 29. Effect of Antibiotic on SSI by Number of Extractions

Extractions	Group A		Group B		p value
	n	SSI	n	SSI	
0	40	4	76	9	**0.79**
1	3	0	8	2	**0.51**
2	11	1	19	3	**0.67**
3	3	0	8	1	**0.73**
4	28	1	58	5	**0.45**
5	0	0	1	0	**-**
6	1	0	1	0	**-**
Total	**86**	**6**	**85**	**15**	**0.04**

4.4.4 Surgical Site Infection Group

There were 21 patients that developed SSI in the completed study group. The overall rate of SSI was 12%. Table 30 outlines the surgical procedure and rate of SSI. The time of diagnosis ranged from 8 days to 165 days with a mean of 28 days.

Table 30. SSI and procedure

Procedure	Total Patients	Infection (%)
BSSO	37	5 (14%)
Lefort	17	2(12%)
BSSO/FG	13	3(23%)
LeFort/FG	7	1(14%)
BSSO/LeFort	76	7(10%)
BSSO/LeFort/FG	21	3(14%)
Total	171	21(12%)

SSI occurred more frequently in the mandible

The location of SSI was documented. SSI frequently occurred at the BSSO incision (71%), followed by the Lefort incision (19%), and the FG incision(5%). Table 31 outlines the location and percentage of SSI. The maxillary and mandibular incisions were divided by quandrant. Quadrant 1 was right maxilla (Q1), quadrant 2 was left maxilla (Q2), quadrant 3 was left mandible (Q3), and quadrant 4 was right mandible (Q4). SSI was most frequent in Q3. Plate removal was done in two patients and occurred both in the mandible and on postoperative day 147, and 175.

Table 31. Location of SSI

Location	Patients	(%)
FG	1	5
Q1	1	5
Q2	3	15
Q3	9	43
Q4	6	29
Not Documented	1	
Total	21	

SSI was treated with a 7-10 day course of amoxicillin 500mg TID combined with metronidazole 500mg BID in 11 cases, clindamycin 450mg QID in 5 cases, with clindamycin 300mg QID in 3, and 1 patient was treated with amoxicillin/clavulanic acid 875mg BID. No patients required readmission or treatment with IV antibiotics.

4.4.5 Patients with One Year Follow Up

There were 150 patients followed for 1 year. Ninety patients from this group completed the study appropriately (60%). The active antibiotic (group A) had 46 patients and SSI occurred in 2 patients (4%). The placebo (group B) had 44 patients and SSI occurred in 11 patients (25%). This difference was statistically significant $p<0.05$. These patients either returned for follow up 1 year following their surgery, or an attempt was made to contact them by phone in order to inquire if another health care practitioner had diagnosed the occurrence of a SSI. We were unable to contact 47 patients after 2 attempts were made. Five patients had disconnected phones. A total of 38 patients completed the questionnaire. Self-awareness was questioned with similar rates between groups A and B (Table 32).

Table 32. Self-awareness of Antibiotic or Placebo

Patients perception	Group A	Group B
Antibiotic	3	3
Placebo	1	2
Unsure	14	15

CHAPTER 5

DISCUSSION

The primary purpose of our study was to determine the best antibiotic regimen for orthognathic surgery patients. This was done conducting survey of OMF surgeons in Canada, completing a retrospective chart analysis and finally a prospective randomized controlled trial.

Currently there is no consensus in the literature as to the ideal antibiotic to use in orthognathic surgery, or how long patients should be on antibiotics following surgery. The primary outcome of our retrospective analysis was to investigate 3 different antibiotics: penicillin, cefazolin and clindamycin in orthognathic surgery. This retrospective review showed that there was a statistically significant difference in the SSI rate for cefazolin when compared to penicillin and clindamycin. Thus cefazolin was chosen as the primary antibiotic in our prospective randomized trial.

Whenever investigating SSI in any specialty certain challenges exist. These include how to classify patients according to comorbidities, and their effect on SSI. We addressed this by dividing patients into groups depending on their PMHx. Another challenge is the diagnostic criteria for SSI, which can vary greatly among centers and among practitioners. The best way to approach this is by using defined criteria, which we developed from the CDC guidelines. We also included the operating surgeon as a variable in our prospective analysis, in order to control for any differences in surgeon diagnosis. The criteria that we noted in this study included swelling, pain, purulent

drainage, dehiscence, and surgeon diagnosis. Unless cultures are obtained one cannot be certain that SSI was the absolute cause of the symptoms. Orthognathic surgery patients in particular present a significant challenge in obtaining adequate cultures, as the location of the surgery lies within the oral cavity. The oral microflora can contaminate samples retrieved from the surgical sites, and studies have shown that bacterial counts in 1mL of whole saliva can be around 10^7 aerobic microorganisms plus $5x10^8$ anaerobic.[56] This is well above the CDC number of $>10^5$ microorganisms for marked increased SSI.[1] Contamination from endogenous flora can make interpretation of cultures unreliable. This can be avoided by obtaining sterile samples from an aseptic technique, or by obtaining tissue samples. However, these approaches are impractical for orthognathic surgery patients. Cultures were not investigated in our retrospective analysis. In the prospective analysis one adequate culture was obtained, in which *Streptococci milleri* was isolated as the primary organism. With the use of implantable hardware, an infection that develops in that location is considered a result of the surgery until one year post operatively.[1] Retrospective analysis showed a SSI rate of 8%. Our prospective analysis showed a SSI rate of 12%, and for patients followed for one year a SSI rate of 14%.

It is imperative that we maintain good antibiotic stewardship in order to prevent antibiotic overuse. Although antibiotics are routinely used, there are significant side effects that can occur. This was seen in our study where one patient had a Grade IV complication, anaphylactic shock. The evidence for the use of perioperative antibiotic prophylaxis is extensively studied throughout many surgical specialties and the benefits are quite clear. Reducing the prevalence of SSI is important to achieve the best treatment

outcomes and patient satisfaction, and to reduce the overuse of antibiotics and costs to the health care system. Antibiotic side effects warrant additional caution in prescribing these drugs. The common side effects of antibiotics are nausea, vomiting, and rash. Furthermore, antibiotics, especially clindamycin, pose an increased risk of infection by *Clostridium difficile*.[62] Overall, antibiotic side effects reported in this study was low, and no cases of *Clostridium difficile* were reported.

Retrospective chart analysis found that there was no correlation between any of the patient demographics or extraction of teeth with the prevalence of SSIs. Increased surgical time and having multiple jaws operated were associated with an increased prevalence of SSIs. Lefort only surgeries had a significantly lower SSI prevalence when compared to the mean prevalence. Many studies recommend the use of penicillin as the first-line antibiotic for orthognathic surgery in preventing SSIs.[4,5,38,39] The retrospective analysis shows that patients who received cefazolin prophylaxis had a significantly lower prevalence of infection than patients who received penicillin. Penicillin may be less effective in prophylaxis for orthognathic surgeries for a variety of reasons. Firstly, in orthognathic surgeries, there may be surgical site exposure to pathogens that are not present in odontogenic infections. For example, microbes that are present on our skin, such as *Staphylococcus epidermidis* and *Staphylococcus aureus*, may contaminate surgical sites. In addition, LeFort osteotomy surgical sites may become contaminated from both the maxillary sinus and the nasal cavity, which harbour potential pathogens including *Streptococcus pneumonia, S. aureus, Haemophilus influenza*e, and *Moraxella catarrhalis*.[63] Secondly, the concentration of cefazolin and cephalexin in saliva is

significantly greater than penicillin and amoxicillin.[64] Therefore greater levels of antibiotic will be over the BSSO incision during the healing period. Lastly, the prevalence of antibiotic resistance varies between different test centers and hospitals. Comparison of local resistance rates to other centers is required to accurately compare the prevalence of SSI. We found that patients treated with cefazolin had a lower rate of SSI than those treated with clindamycin. This difference may be due to the resistance of *Streptococci spp.* to clindamycin, which can be as high as 17%.[58] The prospective study had only a small clindamycin group (15 patients). No infections were seen in this group, but the sample size was too small to be significant.

Age and gender in both the retrospective and prospective study, were not associated with an increase in SSI. This is different than Bouchard *et al.* who found that age was the only statistically significant variable for SSI in BSSO patients.[65] Our results corroborate those obtained by Chow *et al.*, who performed a 15 year retrospective study and found no connection between age and gender with SSI.[5] The medical status of the patients in our studies reflected the relatively young average age. Most of the patients were healthy, or had a condition that did not affect their immune function. Retrospective chart analysis found no difference in rate of SSI infection between PMHx Class 1, 2 or 3. This contrasted with findings of the prospective trial, Class 1 patients had a statistically significant lower rate of infection than Class 2 or 3. Although this was significant by a close margin p=0.048. To clarify this finding, more research into medical comorbidities in patients undergoing orthognathic surgery would be beneficial. Smoking did not

significantly increase the prevalence of SSIs. This was found in both studies, despite the fact smoking has a well-documented connection to an increased risk of infection.[51]

The anatomical differences between the maxilla and the mandible may create differences in the susceptibility to infection. Firstly, the mandible is less vascular than the maxilla.[66] Secondly; gravitational forces cause bacteria-rich saliva and food to collect in the mandible along the site where the surgical incision is located. This saliva and food cannot be cleared easily when a patient is in maxillo-mandibular fixation. The surgical incisions may take up to 3 days for initial healing and wound closure, during this time bacteria can easily enter the surgical site.[66] These anatomical differences may explain the results, as patients undergoing only LeFort surgeries had a significantly lower prevalence of SSI compared to the overall prevalence of SSI in the retrospective analysis. In contrast, the prevalence of SSI in all of the other types of surgeries, which included the mandible, was not significantly different than the mean prevalence of SSI. Prospective randomized trial found that the BSSO groups for placebo and active antibiotic was not significant by a slim margin p=0.08. There was no SSI seen in the BSSO antibiotic group (n=14) vs. the placebo group, which had a SSI rate of 22% (n=28). The NNT was 5 for this group, but with a wide CI from 2.6 to 20.5. Most SSI occurred in the mandible (62% retrospective, 71% prospective). Hardware removal was required in 14% of the SSI patients in the retrospective study and 10% of SSI patients in the prospective study. Therefore, surgeries involving the mandible could benefit from an extended antibiotic course for the prevention of SSIs. Dual jaw deformities that require upper and lower jaw surgeries may increase the risk of SSI. Retrospective analysis showed that dual jaw deformities were

present in 68% of patients, which is similar to the 65% reported by Chow *et al*.[5] Not surprisingly, this investigation found that the prevalence of infection was lower with single jaw surgery compared to multiple procedures. This is in contrast to those results found by Alpha *et al.*, where a lower prevalence of infection was seen for BSSOs with adjuvant procedures.[67] In that study, patients that received multiple procedures remained in the hospital and received intravenous (IV) antibiotics in the post operative course. This was in contrast to patients who underwent only a BSSO, who received oral antibiotics postoperatively, because they were discharged home the same day.[67] These differences in antibiotic duration and method of administration have may affected the prevalence of SSI seen in their patient cohort.

Duration of surgery was found to be significant in our retrospective analysis with 21 min difference between the SSI and non-SSI groups ($p<0.05$). This was not significant in our prospective trial, where the mean difference was only 6 minutes. This may be due to smaller sample size in the prospective trial. This study did not find a significant association between third molar extraction and the prevalence of SSIs. This agrees with Doucet *et al.* who found that extracting third molars during orthognathic surgery did not increase risk of complications and avoided additional surgical procedures, associated morbidities, and additional costs to the patient and the healthcare system.[68]

Length of stay in hospital was found to be significant in the prospective study with a statistically difference in the 2 day group compared to the 1,3,4 and 5 day groups.

This is most likely a sampling bias due to very small amount of patients staying 1,3,4,5 days.

Length of antibiotics statistically reduced the rate of SSI. There was statistically significant difference between 1 day and 3 day groups was found in the completed 171 patient group ($p=0.04$), and the 1 year 90 patient follow up group ($p<0.05$). The NNT was found to be 9.37. Thus for every 9 patients put on extended antibiotic regimen 1 SSI will be prevented. Of note, none of the patients with SSI required readmission, or treatment with IV antibiotics. Overall the patient comorbidity associated with a minor SSI was minimal, other than 1 week of antibiotic treatment.

It is concerning the compliance rate of prescribed antibiotics. Clear instructions of study protocol were given to all patients and any accompanying family member or friend. In addition there was no cost associated with receiving the study medication. The pharmacy is located one floor directly above the clinic. Even with this, 288 patients enrolled in the study and signed consent and only 177 patients picked up the medication and completed the study correctly. This is important to consider when we recommend treatment or medications, as patients may not always be compliant. This may also introduce selection bias for our patient cohort. The number actually treated was analyzed rather than the number intended to treat. This was done in order to more accurately assess the effect of an extended antibiotic compared to a placebo had on SSI.

Another limitation of our study was the assessment of oral hygiene. For skin incisions, proper incision wound care in the first 24-48 hours will help in decreasing SSI.[1] This is very difficult if not impossible for patients undergoing orthognathic surgery. In patients with poor oral hygiene, there are significantly greater amounts of bacteria present, and more pathogenic bacteria present. This will definitely increase their risk of SSI. In the definition of surgical wound classification, these patients may fall under Class III or even IV. The definition of dirty/infected or Class IV surgical wound include organisms causing post operative infection that are present in the operative field before the operation. This is true for orthognathic surgery patients, especially those with poor oral hygiene. This makes it difficult to correctly place any oral cavity incisions into this classification.

There may be benefit to additional antibiotics in preventing SSI. Currently no randomized controlled trials exist investigating the effect of adding metronidazole in addition to cephalosporin or penicillin for prophylaxis in orthognathic patients.

CHAPTER 6

CONCLUSION

Many different antibiotic regimens exist for prophylaxis of SSI in orthognathic patients. Currently there is no consensus in the literature or among Canadian OMFS. Our retrospective analysis found that cefazolin was the most effective prophylactic antibiotic in orthognathic surgery. Prospective randomized controlled trial found there was a lower rate of SSI with 3 days of antibiotic prophylaxis compared with 1 day. Age, gender, surgeon, number of extractions, and length of MMF did not have effect on the SSI rate. SSI frequently occurred at the mandibular BSSO incision, which is contaminated with saliva, and receives lower blood flow than the maxilla. Mandibular osteotomies may benefit from an extended antibiotic regimen to minimize SSI and complications.

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Appendix A 1 year Questionnaire

Orthognathic and Post Operative Antibiotic Use

Follow up Questionnaire

Name:

Date of Surgery: _____

Last visit to OMFS: _____

Last visit to Orthodontist: _____

Since surgery have you developed any infections?

Were you placed on antibiotics for the infection?

If so what antibiotic? How long?

Do you think you were on placebo or antibiotic?

Notes: