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Deepak Govil

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Co-Author: Ahmad Jan

Video 4: **Sleeve Gastrectomy for Morbid Obesity**
Author: Mahendra Narwaria
Co-Author: Ahmad Jan

Video 5: **Laparoscopic Whipple's Pancreato-duodenectomy (WPD)**
Pradeep Jain
Co-Authors: Pankaj Sharma, Vivek Goel

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Author: Shailesh V Shrikhande
Co-Authors: Manish Suresh Bhandare, Vikram Chaudhary

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Sundeep Singh Saluja

(Videos have no voice over)

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VOLUME 1

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Foreword

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Editorial Board

Foreword

Thirty years ago, general surgeons did almost all abdominal operations including those for hernia, hydrocele, as well as for diseases of the stomach and intestines. At this time, medical gastroenterology was making rapid strides by using diagnostic and therapeutic techniques driven by the advent of fiberoptic endoscopy and advances in imaging modalities. This opened up whole new challenges such as the management of massive variceal bleeding and obstructive jaundice, but there was no complementary specialty of surgical gastroenterology. This meant that the more complex procedures like portosystemic shunts and liver and pancreatic resections received little attention because they were done infrequently, demanded a lot of extra time and effort and, unfortunately, were consequently accompanied by high morbidity and mortality rates. In the late 1980s, after a rather hesitant and uncertain beginning, a few stalwarts set up separate departments of surgical gastroenterology in Trivandrum, Chennai, Lucknow and Delhi, which confined themselves to dealing with complex gastrointestinal problems, which were neglected by general surgeons, and these have since spawned over thirty others all over the country. With the advent of liver transplantation, this specialty has now acquired a certain glamour as well as extensive coverage in the media. Consequently, in 2015, surgical gastroenterology has now become the most sought after subspecialty for doctors who have just completed their Master of Surgery qualification and is, fortunately, attracting the brightest and best.

Unfortunately, there are very few textbooks which can guide the neophyte trainees in this field. Professor PK Mishra, who is a member of one of the elite and pioneering departments in the specialty, and who, incidentally, did a good PhD at All India Institute of Medical Sciences (AIIMS) under my guidance, has gathered together nearly all of India's luminaries in this comparatively new specialty and succeeded in producing a reference book which will be a sine qua non for all who venture into this exciting field.

There are introductory chapters on the approach to patients, imaging and chemoradiotherapy, followed by detailed descriptions of the management of disorders of different organs from the esophagus to the anal canal, and a section on liver transplantation. I particularly enjoyed the last 'Miscellaneous' section which deals with upper GI bleeding, robotics, tumor markers and finally ethics in surgery.

The choice of topics has been imaginative and the writing simple, informative and helpful.

I have little doubt that the book will be a success and go into many subsequent editions.

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Preface

I feel so relieved to be writing this preface, now that this massive project is near completion. Serendipity is sometimes more important than the noble motivation later ascribed to an act. The origin of the book had a bit of both. When I was approached by M/s Jaypee Brothers Medical Publishers (P) Ltd, for this book, I was in a frame of mind to strive to return to the profession a bit of what I gained from it. Fortunately or otherwise, I had no idea as to what it actually involved.

Surgical gastroenterology is relatively a new superspecialization which has established itself in the last three decades. Most of the work in surgical gastroenterology was done by general surgeons with various other responsibilities. Evolution in gastroenterology pushed the requirement of specialized care for this group of patients. Resection of liver, surgery for portal hypertension, surgery of pancreas and esophagus, for example, required specialized training and dedicated care. The challenge was taken up by a few stalwarts like Professors Samiran Nundy, Aranya, Kaushik, Wig and Chatterjee in the North and Professors Rangabashyam, Khanduri and Anantkrishnan in the South. Thanks to their efforts, surgical gastroenterology has not only become an established specialty but also, it is the most wanted one for the residents completing their MS (General Surgery). I was fortunate to train under Professor Nundy, All India Institute of Medical Sciences (AIIMS), and have been at Govind Ballabh Pant Postgraduate Institute of Medical Education and Research for last many years. GB Pant is an established pioneering superspecialty academic institute for training MCh and DM residents.

In the last many years, enormous experience has been gathered in various institutes working in this field in India. However, we are still dependent mainly on textbooks from the West. The available textbooks in surgical gastroenterology are not comprehensive, do not adequately discuss some of the diseases which are specifically relevant in the Asian context and do not have Indian protocols for therapy and follow-up even for diseases which are commonly seen by us. I, therefore, worked to compile a book, which could serve as a textbook for the students of surgical gastroenterology and could also be of help to the practicing surgeons and the gastroenterologists.

With this in mind, I got together a team of editors. We chose the authors and chapters to be covered with lots of deliberation. Most authors of the chapters are surgeons with vast experience and are well known in their field of expertise. Eminent gastroenterologists have also written some chapters, as required. All the chapters have been reviewed to add some balance in the coverage. We have also included several chapters with clinical approach which are not usually covered in other textbooks. A chapter on statistics was especially included as this knowledge is now essential for interpreting or publishing research articles. We also incorporated some chapters on robotics and telemedicine to acquaint our readers with critical knowledge in these important areas. An entire section on liver transplantation was envisaged which has now become an important and established specialization by itself. Knowledge about radiology and antibiotics relevant to our practice has been included. The last chapter in the book had to be on ethics. While teaching ethics may not by itself be a remedy for all ills, it certainly promotes responsibility, integrity and accountability in medical practice. I wish that the students undertake medical learning and research guided by ethical principles. Ethics is the essence of being human and I believe that every human effort is wasted, if it is ethically incorrect.

The idea of the book was to be a comprehensive textbook of surgical gastroenterology. When we had started, I wished to bring together a complete volume that had all the essential knowledge for a person being initiated into surgical gastroenterology. I did not realize initially that it was such a colossal project. With the full load of clinical and teaching duties, editing such a volume was really a tough task. Time delays took such a toll that at times I felt like shelving the project. We had to reject or redo many chapters. Many other chapters had to be left out. It was the effort of the editorial team, residents, and colleagues and of several authors of the book that kept me on course. I sincerely trust that the book would be a single point reference book, to the residents, gastroenterologists and surgeons.

No textbook in the present day can have all the information a person seeks. In the fast-changing medical world, readers should treat this compilation as a starter pack. Authors have worked hard on these chapters and the chapters have also been reviewed by peers. Still, there may be many shortcomings and there may be many aspects that are not up to the desirable level of discussion. I fully realize that some of the pronouncements in the ensuing chapters may already be getting modified or even outdated. A textbook takes almost two years to come to the print. I offer this to you with no apologies. I request all the readers to mail me their opinions so that the shortcomings may be corrected in the subsequent editions. It is my sincere hope that with your help the work will raise its level even further in the subsequent editions. Thank you readers for choosing the book.

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Acknowledgments

It is a privilege to thank all those who helped me complete this work. First of all, I thank my publishers M/s Jaypee Brothers Medical Publishers (P) Ltd, New Delhi, India, for choosing me to do this work. On behalf of Jaypee, Shri Jitendar P Vij (Group Chairman), Mr Ankit Vij (Group President), Mr Tarun Duneja (Director-Publishing), Mr KK Raman (Production Manager), Mr Subrata Adhikary (Commissioning Editor) and Mr Mohit Bhargava (Production Coordinator) kept goading me to get this textbook into shape. They were liaising with designers, language editors, designers, artists, management and all other people who worked hard to put the book in your hand. I thank all the members of the Jaypee team for their effort. I wish that we continue to collaborate in the same spirit in future as well.

I wish to thank all the members of the editorial board Dr Baskaran, Dr Sujoy, Dr Rajnish, Dr Shivendra, Dr Uday Somashekhar, Dr Sundeep Singh Saluja and Dr Nayeem for reviewing and editing various chapters and sections of the book. The book was impossible without their efforts and constant support. Being at Govind Ballabh Pant and always available, Dr Saluja was a sounding board for all my decisions. He deserves my special thank.

I wish to thank all the authors who have contributed their chapters in this book. Two DVD-ROMs set with videos of the procedures to accompany the book, was a last-minute decision. I especially thank all the contributors who provided the videos of the various procedures at the very last moment. This book is shaped by the immense experience put forth in these chapters by the authors. The book actually belongs to them. On their behalf, as well as mine, I wish to also thank all our patients who gave us this experience. I wish to thank all my teachers under whom I learned to treat these patients. I was privileged to have Dr Samiran Nundy, a pioneer surgeon in the field of surgical gastroenterology, as my teacher and guide at All India Institute of Medical Sciences (AIIMS). He is one of the most admired doctors in the country today and a guiding star for all of us in this field. I profusely thank him for all he has done for me and also for writing the foreword of the book.

Being in an MCh, teaching institutes gave me the opportunity to interact with some of the sharpest minds in the profession. Our residents come through a grueling selection process and are extremely hard-working. Some of our fellows have become consultants in prestigious hospitals and have also contributed in the chapters of the book. They have helped me in several ways from the intellectual inputs to proofreading. I wish to immensely thank our present and past residents for all their help. I need to especially mention, Drs Vaibhav, Kunal and Vaageesh amongst the present ones, and Drs Rajesh, Kalay, Asit, Nilesh, John, Neeraj, Dinesh, Satyajit and Harsh amongst the earlier ones.

Over the last two years, I have had extra-long hours and my contribution at home in my absence was borne by my family. I wish to thank my wife Yuthika and daughters Pragya and Bhavya for their constant support and encouragement. Above all, they make this effort worthwhile.

In the end, the book represents desire of my parents for my learning and higher education. My late mother with her simplicity and affection nurtured me. My father has always strived for excellence and discipline. His generosity and deep love for all of us is exceeded only by his desire for us to be useful to the society. My gratitude for them is more than I can ever express. I dedicate this book to them and seek their blessing for me, my patients and for all my future endeavors.

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CHAPTER 3

Infections and Antibiotics in Gastrointestinal Surgery

Archana Thakur

INTRODUCTION

Postoperative infections increase mortality, morbidity and prolong hospitalization leading to increase in cost of treatment. Many of these infections are believed to result from contamination of the operative site during the surgical procedure. Such contamination is unavoidable when the procedure involves a nonsterile area, such as the gastrointestinal tract (GIT), hence postoperative infections are common in gastrointestinal (GI) surgery. Incidence is higher in emergency surgery (16%) than in elective surgery (6%).[1,2] The operations which are complicated and of longer duration like colorectal and small intestine procedure, are more strongly associated with complications as compared to smaller operations. The incidence of infection is higher in lower gastrointestinal surgeries than in upper gastrointestinal surgeries as the bacterial load is higher in lower GIT.

COMMON INFECTIONS ENCOUNTERED IN GI SURGERY[1,3,4]

- Postoperative wound and tissue complications
  - Surgical-site infections: Which can be superficial or deep wound infection, wound abscess
  - Intra-abdominal infection: Abdominal abscess or peritonitis
  - Disruption of tissue, e.g. wound, fascia or leakage from anastomosis site
- Pulmonary complications and infections: Hypoxemia, collapse of alveoli (atelectasis), respiratory failure leading to endotracheal intubation and mechanical ventilation, ventilator-associated pneumonia, aspiration pneumonia, etc.
- Urinary tract infection
- Septicemia.

Wound and Tissue Infections

Wound and tissue infections after surgery occur in 2–30% cases depending upon risk factors[5] which are:

- Degree/density of bacterial contamination at the surgical site
- Duration of the operation
- Host susceptibility.

Density of Bacterial Contamination

Number and type of organisms present at the surgical site is the major factor influencing the risk of postoperative infection. This was recognized several decades ago in the wound classification system that divides all wounds into the four categories.[5-7]

Class I: Clean

Elective procedure, clean nontraumatic, not infected/inflamed wound, no break in technique, respiratory, gastrointestinal and genitourinary tracts not entered. Examples: elective inguinal hernia repair, splenectomy, exploratory laparotomy (no bowel involvement), *Staphylococcus aureus* is the most common pathogen and infection rate is 2% or less, depending on presence of other risk factors.

Class II: Clean contaminated

Emergency case, nontraumatic, clean wound, no unusual contamination, minor break in technique, controlled opening of gastrointestinal, respiratory or genitourinary tract with no or minor spillage. Examples: elective intestinal resection and other gastrointestinal procedures (including laparoscopy, colonoscopy, gastroscopy, vagotomy and pyloroplasty).

Contaminants are endogenous bacteria. For example, *Escherichia coli* and *Bacteroides fragilis* are common pathogens

encountered in sigmoid colectomy wounds. Infection rate varies from of 4% to 10%.

Class III: Contaminated

Emergency procedures. Wound Created without normal antisepsis and sterile technique, operative wound contaminated, gross spillage from the GIT, nonpurulent inflammation.

Examples: Elective intestinal procedures with gross contamination of surgical site, intestinal spillage during laparotomy for penetrating injury, acute nonperforated, nongangrenous appendicitis.

Large spillage of intestinal bacteria in surgical field increases infection rate, which can be greater than 10–20% even with preventive antibiotics. Contaminants are the intestinal bacteria introduced by gross spillage in the surgical field.

Class IV: Dirty infected

Operative wound dirty and contaminated, acute bacterial inflammation of operative wound, traumatic wound from dirty source, presence of foreign body or devitalized tissue, fecal contamination, operative wound where clean tissue is transected to gain access to a collection of pus. Examples: abdominal exploration for acute peritonitis and intra-abdominal abscess, perforated appendicitis with abscess, wound debridement.

Unusual pathogens are often encountered and infection rate can be up to 30–40%.

Duration of the Operation

For duration of the operation, based on national nosocomial infections surveillance (NNIS) database, a standard T point was determined, which is the length of time in hours that represents the 75th percentile of procedures reported in the NNIS survey. It is different for different type of surgery. Longer the duration, higher the risk of infection. Depending on the duration of surgery risk category 0, 1, 2 or 3 is identified.[5,7-11]

Host Susceptibility

American Society of Anesthesiologists (ASA) has defined preoperative assessment score of 3, 4 or 5:[5,7]

- Class I: A patient in normal health
- Class II: A patient with mild systemic disease resulting in no functional limitations
- Class III: A patient with severe systemic disease that limits activity, but is not incapacitating
- Class IV: A patient with severe systemic disease that is a constant threat to life
- Class V: A moribund patient not likely to survive 24 hours.

Considering above variables a risk index has been developed. This has a range from 0 to 3 points. A point is added to the patient's risk index for each of the following three variables:[5,9,11]

- 1 point: The patient has a contaminated or dirty operation.
- 1 point: The duration of the operation exceeds the 75th percentile
- 1 point: The patient has an ASA preoperative assessment score of 3, 4 or 5.

The risk of postoperative wound infections increases with increase in risk index. The infection rate with risk point 0, 1, 2 or 3 being 1.5%, 2.9%, 6.8% and 13%, respectively. This risk can be used to decide preoperative prophylactic antibiotics administration.[5,6,9,11]

Other variables associated with increased risk of tissue and wound complications are smoking, comorbidity like diabetes, cardiovascular disease, lung disease, malnutrition, obesity, etc., perioperative blood loss and, type and site of surgery following elective operations.

Following emergency operations, gender (males more at risk), peritonitis (with localized or generalized pus more at risk), type of operation, (gastroduodenal, small bowel and colorectal surgery more risk) and if multiple operations are done, are some of the variables associated with wound infections.[1,3,7]

Diagnosis of Wound Infections

Diagnosis of postoperative wound is obvious when the wound opens and discharges pus. It is evident only after the fourth or fifth postoperative day except infections caused by beta-hemolytic Streptococci and by Clostridium species, which are evident within 24 hours. The classic signs of infection include localized erythema, localized pain, localized heat, cellulitis, edema, abscess, discharge, discoloration of tissues, friable and bleeding granulation tissue, abnormal smell, etc. Because most of the patients have some fever in the first several days after major operative procedure, fever is not a specific sign of postoperative infection.[5] Microbiological diagnosis can be made after culture of sample from local site. Common organisms causing infection will depend on the type of bacteria contaminating surgical site and that would be the flora of the viscera entered during surgical procedure. GIT is colonized by large number of aerobic and anaerobic bacteria. The number and type of organisms are different at different levels of GIT. The number of microorganisms varies from 10^4 organisms/g to 10^{11} organisms/g, increases at the distal portions of the GIT. Streptococci, Lactobacillus, Diphtheroids and few Peptostreptococcus usually colonize the stomach. Jejunum harbors Streptococci, Enterococci, aerobic Gram-negative bacteria and Bacteroides, whereas colon has predominantly *E. coli* and *B. fragilis*, concentration of anaerobes being many thousands times greater than aerobes.[12] Hence, the predominant bacteria causing infection are *E. coli,* Klebsiella spp., *Enterococcus faecalis*, Enterobacter spp. and anaerobic bacteria, like *B. fragilis*, Prevotella, Peptostreptococcus and Clostridium spp.

Hospital acquired abdominal infections, especially in the intensive care unit (ICU), are more likely to be caused by Pseudomonas species, Enterococcus species, *S. aureus* and fungi.[6,7,13]

Treatment of Wound Infections

In the event of infection, bacteriological identification and sensitivity of pathogen may not be available for more than 48–72 hours. Hence, empirical therapy by antibiotics has to be started as soon as possible along with other recommended procedures. Empirical therapy should be based on likely pathogen to be encountered and the local antibiogram of the hospital.

Mixed infections, aerobic and anaerobic are expected in gastrointestinal surgeries, so antimicrobials effective against both aerobic and anaerobic infection should be administered. Infection by *Pseudomonas aeruginosa* and Enterococcal species may also be considered when starting the treatment in patients in ICUs.

Single-agent or combination regimens can be considered.

Antimicrobials used as single agents are second generation cephalosporins (cefoxitin and cefotetan), carbapenems or combination of ticarcillin/clavulanic acid, piperacillin/tazobactam or ampicillin/sulbactam.[5,13]

The advantage of single-agent therapy is that aminoglycosides which are used in combination therapy and cause ototoxicity and nephrotoxicity are avoided. Single-agent therapy may also be less expensive. But single agent may not always be effective in hospital-acquired wound infection because they are mostly caused by multidrug resistant (MDR) bacteria.

If *S. aureus* is suspected, antistaphylococcal antimicrobials should be used. If methicillin-resistant *Staphylococcus aureus* (MRSA) is present or suspected, cefazolin, sulfamethoxazole/trimethroprim or vancomycin should be given.[5,13]

Combination regimens generally include two agents, one with activity against aerobic Gram-negative bacilli and the other against anaerobic bacteria.

Antimicrobials effective against the Enterobacteriaceae but not Bacteroides group are aminoglycosides (gentamicin, tobramycin, amikacin and netilmicin), third generation cephalosporins (cefotaxime, ceftriaxone, ceftazidime, cephoperazone and ceftizoxime), fourth generation cephalosporins (cefepime and cefpirome), quinolones and aztreonam. Antibiotics effective against *B. fragilis* group are metronidazole, cefoxitin, a combination of penicillin and beta-lactamase inhibitor (ticarcillin/clavulanic acid, piperacillin/tazobactam), newer quinolones (moxifloxacin) and carbapenems.[13-17]

Ampicillin/sulbactam combination is not effective in cases of infection with Pseudomonas species, hence it should be avoided for hospital-acquired infections (HAIs).

To cover infection with Enterococcus spp., ampicillin may be added as third agent.

Along with antibiotics, other recommended supportive treatment, e.g. opening of wound, surgical drainage, etc. should also be carried out for better outcome.

Perioperative Antimicrobial Prophylaxis

Perioperative antimicrobial prophylaxis is widely used to reduce the risk of postoperative wound infection. It can decrease morbidity, shorten hospital stay and contribute to reduce the overall cost of treatment. There is wide consensus and statements by various societies on specific procedures that warrant antimicrobial prophylaxis[5] and which do not need administration of prophylactic antibiotic. Recommendations are based on studies on animal models, randomized clinical trials and observational clinical data[6] and the principals of antimicrobial prophylaxis are well-defined.

Definition of Antimicrobial Prophylaxis

Prophylactic antibiotics are those antibiotics, which are given to the patients before contamination, or infection has occurred. They are recommended when the risk of postoperative infection is high or the expected consequence of infection is extreme morbidity or death.

Guidelines for Antimicrobial Prophylaxis in Surgery

The principles of antimicrobial prophylaxis in surgery involve the following considerations:[12]

- Surgical procedures for which prophylactic antimicrobials is to be used
- Selection of antimicrobial agent
- Timing of antimicrobial administration
- Route of antimicrobial administration
- Duration for which antimicrobial is to be given

Surgical procedures: Antimicrobial prophylaxis is beneficial in surgical procedures associated with a high risk of infection (clean contaminated, contaminated or dirty procedures), procedure in which the postoperative infection, however unlikely, may be severe or fatal, surgical procedures that enter the GIT (colorectal operations and high risk gastro duodenal and biliary-tract operations) and pose the risk of bacterial contamination or if the patient is immunocompromised (e.g. receiving immunosuppressive agents or neutropenic).

The number of organism is low in the stomach, duodenum and proximal small bowel, reducing the risk of infection associated with procedure entering these sites. For these procedures routine prophylaxis is not mandatory. However, number of bacteria increase with decrease in gastric acidity. So, the use of agents like antacids, histamine blocker or proton pump inhibitors or conditions, such as upper gastrointestinal bleeding or gastrointestinal stasis which reduce gastric acidity, increase the risk of wound infection.[18] Prophylactic antibiotics are indicated in such cases. Colorectal procedures have a high risk of infection, prophylaxis is strongly recommended for these procedures. Antibiotic prophylaxis for biliary tract procedure is recommended, if risk factors, like elderly patient (60 years or above), presence of jaundice, biliary obstruction, disease of the common duct, cholecystitis, etc. are associated.

Timing of antimicrobial administration: The timing of antimicrobial administration is important as antimicrobials given at inappropriate times can be ineffective for surgical prophylaxis. To be most effective in preventing postoperative infections an antimicrobial must be present in the contaminated tissues before bacteria enter the site (i.e. before the surgical incision) and must persist in tissues throughout the period of potential contamination.[19,20]

When antimicrobials are given after bacterial contamination, their ability to prevent infection is reduced. All the guidelines recommend that prophylaxis should be given, at induction of anesthesia or 30–60 minutes before incision.[21]

If an operation is expected to last more than 6–8 hours, an antimicrobial with a longer half-life and duration of action should be used. If short-acting agents are used, they should be readministered at intervals of twice the half-life of the agent. Increasing the dose of an agent provides less benefit than shortening the dosing interval because of drug clearance.[19,20]

Duration of antimicrobial prophylaxis: The shortest duration of antimicrobial administration that is effective in preventing postoperative operation is not known; however, recent studies document that postoperative antimicrobial administration is not necessary for many operations.[21,22]

Route of antimicrobial administration: Antimicrobials used for surgical prophylaxis may be administrated intravenously, intramuscularly, orally, rectally and topically (into the surgical wound). Most often intravenous and intramuscular routes are

used. Oral antimicrobials are often used for gut decontamination in elective colorectal operations.[12]

Selection of antimicrobial agents: The antibiotic selected should be based on the site-specific flora, its spectrum of activity, its toxicity and pharmacokinetic properties. The agent selected should have antibacterial activity against the expected most common wound pathogens. In clean operations, Gram-positive cocci like staphylococci predominate, penicillinase-resistant penicillins (oxacillin and nafcillin) are suitable antibiotic. If methicillin-resistant staphylococci are suspected vancomycin or cephalosporins may be required.

For clean contaminated operations, the expected pathogen is bacteria found in the GIT. For these, first generation cephalosporin, such as cephazolin is the agent of choice due to its low cost, long duration of action and because it is effective against most of the pathogens commonly associated with clean and clean contaminated operations. The use of other first generation cephalosporins, such as cephalothin which although have a shorter duration of action, are more resistant to staphylococcal beta-lactamases, should be evaluated. First generation cephalosporins are as effective as second or third generation agents and a single preoperative dose is as effective as multiple dose.[12,23]

Pharmacological Considerations

Dosages of antimicrobial should be adjusted according to the minimum inhibitory concentration (MIC) against bacteria causing infection. Tissue concentrations at the operative site should be maintained higher than the MIC. Antimicrobial with short half-life have to be repeated if procedure is long.[7,21]

Antimicrobial should have bactericidal effect. Bactericidal effect of some antibiotics such as beta-lactams is not dose-dependent, rather it increases with contact time. Whereas bactericidal effect of aminoglycosides and quinolones depends on the concentration used rather than the contact time. They are called dose-dependent antibiotics.

Inoculum Effect

The MIC increases with the density of bacterial inoculums.[21]

Postantibiotic Effect

Some antibiotics show a persistent inhibitory effect on bacterial growth after elimination from tissue. Aminoglycosides have a postantibiotic effect (PAE) on Gram-negative bacteria and beta-lactam antibiotics on Gram-positive bacteria that persist for several hours. Fluroquinolones have PAE on both.[21]

Specific Recommendations for the Selection of Prophylactic Antimicrobials for Various Surgical Procedures (American Society of Health-System Pharmacists)

Biliary-Tract Surgery

Explorations of the common bile duct and choledochoenterostomies are among the most commonly performed abdominal procedures on biliary tract. In the majority of patients, the biliary tract is sterile and the risk of infection is no higher than that of other clean operation. If bacterial count increases in the biliary tract, the rate of infection may reach as high as 36%. Elderly patients above 70 years of age, patients of acute cholecystitis or with obstruction in biliary tract are at a higher risk of acquiring infection. The organisms most likely to be associated with wound infection are *E. coli*, Klebsiella and Enterococci.[5,23-25]

Recommendations: Antimicrobial prophylaxis is recommended for patients undergoing cholecystectomy. Single 1 g cefazolin should be given intravenously before or within 30 minutes of the start of the operation.

Gastroduodenal Surgery

Gastric operation for which antimicrobial prophylaxis is considered are resection with or without vagotomy for gastric or duodenal ulcers, resection for gastric carcinoma, and gastroplasty or gastric bypass for morbid obesity.[26] The risk of postoperative infection after gastroduodenal surgery varies markedly, depending on the type of operation performed and the patient's clinical condition. The wound infection rate was 4% after operation for duodenal ulcer, 29% for gastric ulcer and 33% for gastric resection for cancer. With gastric bypass operation a wound infection rate of 21% has been reported.[27-29] Other important factors associated with infection risk are the use of histamine H2 receptor blocker or the presence of achlorhydria, gastric obstruction or bleeding. They can increase bacterial concentration in stomach and may increase the risk of postoperative infection.[30,31] Wound infections after gastroduodenal surgery are polymicrobial and involve *E. coli* and Enterococci.

Recommendations: Prophylactic antimicrobials are not needed when the lumen of the intestinal tract is not entered. They should be used when the stomach or duodenum is entered surgically. Although some authors believe that antimicrobial are not necessary for patient undergoing gastric resection for non-obstructing ulcer, the widespread use of H2 receptor blockers make it likely that these patient will have high intraluminal bacterial concentration making antimicrobial prophylaxis advisable.

Cefazolin is preferred as a single preoperative dose.[12]

Colorectal Surgery

Surgical-site infection is the most common complication following colorectal surgery. It was believed to be because of large numbers of aerobic and anaerobic organisms are present in colon which causes bacterial contamination of surgical wound. Most frequently isolated organisms are *E. coli* and *B. fragilis*.

To reduce the risk of contamination of the surgical wound, it was considered necessary that resident bacterial concentration is reduced at site. It can be achieved by use of mechanical bowel preparation which decreases the total number of bacteria. Recently single day (12 hours or less) orthograde lavage techniques using an iso-osmotic nonabsorbable electrolyte solution or mannitol solution have been used.[32-34] Two liters of a polyethylene glycol-electrolyte lavage solution is given over 3 hours starting the morning of the day before surgery. It is used in conjunction with three doses of 1 g neomycin sulphate and 1 g erythromycin given orally at 19, 18 and 9 hours before surgery.

Antimicrobial agents combined with mechanical cleansing of the colonic lumen in some studies have significantly reduced

postoperative wound infection rates from 30–60% to less than 10% in clean contaminated procedures.[35,36] However, level I evidence has now accumulated to omit mechanical preparation from the preoperative regimens. Several systematic reviews and meta-analysis have indicated that mechanical bowel preparation does not improve outcomes in terms of anastomotic leaks or surgical-site infections.

Recommendations:
Mechanical bowel preparation: Mechanical bowel preparation for surgery remains controversial, although frequently practiced. Bowel preparation is required for colonoscopy and can be omitted for bowel surgery.

A single intravenous dose of a 2 g cephalosporin that is effective against both aerobic and anaerobic bacteria and has a half-life of 60 minutes or longer (cefotetan, cefmetazole, cefotaxime or ceftizoxime) should be administered at induction of anesthesia.

If a cephalosporin with a half-life of 60 minutes or less is used (cefoxitin), and surgery lasts longer than 3 hours, a second dose of the intravenous antimicrobial should be given.

If the patient is to undergo a colostomy closure or rectal procedure, a combination of oral and intravenous agents should be given.[12]

Appendectomy

The incidence of infections depends on the condition of the appendix at the time of surgery. In uncomplicated appendectomy, the postoperative infection rate is reported to be between 0% and 30%.[37-39] However, if the appendix is gangrenous, perforated or abscessed (complicated appendicitis), wound infection rates approach 80% without antimicrobial prophylaxis.[40] Appropriate antimicrobial prophylaxis has reduced surgical wound infection rates to as low as 1% in both uncomplicated and certain complicated appendectomies. The majority of studies have shown that even when appropriate antimicrobials are used, infections will occur in 10–25% of patients with a gangrenous or perforated appendix.[40-42]

Microorganisms commonly isolated from wound infections after appendectomy are *E. coli* and *B. fragilis*. Streptococci, *S. aureus* and Enterococcus species have also been isolated frequently. Pseudomonas species has also been reported.[43,44]

Recommendations:
Uncomplicated appendicitis: Cephalosporin effective against both aerobic and anaerobic bacteria, i.e. cefoxitin, cefotetan, cefmetazole, cefotaxime or ceftizoxime. Dosage is 1–2 g intravenous at induction of anesthesia, to be repeated if surgery lasts longer than 3 hours.

Complicated appendicitis: Same regimen but to be continued for 3 to 5 days.

Alternatives are aminoglycosides or aztreonam plus metronidazole.[12]

Common Errors in Antibiotic Prophylaxis

Common errors in antibiotic prophylaxis include choosing the wrong antimicrobial, administering the prophylactic dose too early, omitting second dose in long operations or continuing the prophylactic antibiotic longer than required. The worst error is inappropriate use of valuable therapeutic agents with expanded spectrum and excessively long-term administration. Indiscriminate antibiotic use is costly and exposes the patients to adverse effects, and promotes resistance to the drugs.

Although prophylactic antimicrobials reduce the incidence of postoperative wound infections, but number of other factors, such as any underlying comorbid medical condition in the patient, break in sterile technique at any stage during operation, environment of operating-room, duration of procedure and the expertise of the surgeon also have a strong impact on wound infection rates. The drug-resistant organisms are selected as a result of inappropriate and indiscriminate use of prophylactic antibiotic and necessitate more expensive infection control measures and antibiotics. Along with antibiotic prophylaxis good infection control practices, good technique and good patient care is essential in reducing postoperative infections.[6]

Pulmonary Complications

Postoperative pulmonary complications can be atelectasis, endotracheal intubation and ventilation, aspiration pneumonia, ventilator-associated pneumonia (VAP), pleural effusion, respiratory failure, bronchospasm and exacerbation of chronic obstructive pulmonary disease.[45]

Pulmonary complications remain an important cause of mortality and morbidity in spite of many advances in anesthetic and surgical techniques.[46-48]

Most important risk factor of postoperative pulmonary complications is the site of incision; thoracic or upper abdominal procedure (e.g. cholecystectomy), in which the incision has to be near the diaphragm, carry higher risk than the procedures on lower abdomen or gynecology surgeries.[49-52] Other factors associated with higher probability of postoperative pulmonary complications include chronic respiratory disease, increasing age, obesity, history of smoking, malnutrition, long lasting anesthesia and a longer stay in hospital before operation. Men have two to three times higher incidences than women.[46]

Ventilator-Associated Pneumonia

Ventilator-associated pneumonia (VAP) is the pneumonia that develops 48 hours after mechanical ventilation by means of an endotracheal tube or tracheostomy is given. During intubation, the integrity of the oropharynx and trachea is compromised and microorganisms enter the lower respiratory tract and lung parenchyma leading to infection. Eight to twenty-eight percent of patients receiving mechanical ventilation develop ventilator-associated pneumonia. The mortality rate for VAP is very high varying from 24% to 50% and if the infection is caused by high-risk pathogens like *P. aeruginosa* and Acinetobacter, it can go up to 76%.[53-55]

Diagnosis of VAP

Ventilator-associated pneumonia is identified by using a combination of clinical, radiological and bacteriological criteria.

Clinically: Signs and symptoms of fever, purulent sputum, cough, dyspnea and raised total lung capacity (TLC) count or worsening gas exchange.

Radiologically: Persistent infiltration, consolidation and cavitation.

Bacteriologically: Positive culture growth in blood/pleural fluid/quantitative culture of bronchoalveolar lavage (BAL).

By using a combination of presence of positive radiological findings and two of the clinical signs 69% cases of VAP can be diagnosed with specificity of 75%.[56]

Bacteriological Diagnosis

Appropriate antimicrobial treatment of patients with VAP significantly improves outcome, the goal should be rapid identification and accurate selection of antimicrobial agents.

Variety of samples and techniques has been used for culture to diagnose bacterial pneumonia.

For clinical diagnosis of VAP, nonquantitative or semiquantitative cultures of airway samples, e.g. endotracheal aspirate (ETA) can be done but it has less sensitivity and specificity (sensitivity of 82% but a specificity of only 27%)[57] as compared to quantitative cultures of airway specimens, such as quantitative endotracheal aspirate (QEA), blind bronchial sampling (BBS), bronchoscopic protected specimen brush (PSB) and BAL culture, etc. Specificity of this technique is more but it needs technical expertise and advance equipment.

Frequent method followed in labs is nonquantitative or semiquantitative cultures of endotracheal aspirate and BAL.[56]

Blood and Pleural Fluid Cultures

Although infection to the blood or pleural space spreads in less than 10% cases of VAP, it is recommended that two sets of blood cultures and a pleural fluid, if effusions is present should be part of investigation.[58] Blood culture is positive in less than 25% patients of VAP and in most of these positive cultures the organisms may originate from an extrapulmonary site of infection.[59,64]

Etiological Agents

The etiological agents responsible for infection differ according to the prevalent infections present in an ICU, prior antibiotic therapy and length of stay in the hospital. Prior antimicrobial therapy in the preceding 90 days, hospitalization of more than 5 days, prevalence of resistance in the community or local hospital, and immunosuppressive disease and/or therapy increases the risk of infection by MDR organisms.

Common causative organisms are *S. aureus*, *P. aeruginosa*, Acinetobacter spp. and Enterobacteriaceae group (Klebsiella, *E. coli*, proteus, Enterobacter, Citrobacter). *Streptococcus pneumoniae*, Haemophilus spp. and *Stenotrophomonas maltophilia* are also isolated from few patients. Candida spp. rarely causes invasive pulmonary disease. But if isolated in culture it indicates *P. aeruginosa* may be the cause of VAP in that patient.[48]

The prognosis of VAP is worse in patients having infection with aerobic Gram-negative bacilli as compared to infection with Gram-positive pathogens. Death rates are maximum in infections caused by *P. aeruginosa*, ranging from 70% to more than 80% in several studies[60,61] compared with 55% for pneumonias due to other organisms.[60]

Treatment of VAP

Selection of antibiotics: Patients with early-onset VAP and not likely to have infection with MDR organism, empirical therapy may be started with one of the following antibiotics:[56]

- Fluoroquinolones
- Ceftrioxone
- Ampicillin and sulbactum or
- Ertapenem.

In patients of VAP with late-onset or likely to have infection with MDR pathogens, initial single agents effective against Pseudomonas like:

- Cephalosporins (cefepime and ceftazidime)
- Carbapenems (imipenem and meropenem).

or

- Combination of beta-lactam/beta-lactamase inhibitors (piperacillin/tazobactam) and an antipseudomonal fluoroquinolone (ciprofloxacin and levofloxacin).

or

- Aminoglycoside (amikacin, gentamycin and tobramycin) and vancomycin or linezolid (if MRSA are suspected) may be considered for empirical treatment
- Telavancin is indicated in infections caused by methicillin-susceptible and resistant isolates, if the alternative treatments are not suitable.[56,62]

Probability of infection with MDR organisms increases if stay of the patient is prolonged (more than 5 days), patient is immunocompromised on immunosuppressive therapy, or had received antibiotics in last 90 days. The risk of infection with MDR organisms further increases if the incidence of resistant organism is more in the hospital or community.[56,63]

Development of resistance can be prevented by prescribing combination therapy. Combination therapy provides synergy and sufficient coverage also if the pathogen is resistant to the agent chosen as a single therapy, leading to improved outcome.[20]

Antibiotics should be changed on the basis of culture results.

Factors which Influence the Outcome of VAP

Early administration of antibiotics, choosing antibiotics based on the patient's risk for having MDR pathogens and local antibiogram, using combination therapy, using antibiotic of different class than received in the recent past and shortening the duration of antibiotic therapy if initial antibiotic was appropriate can influence the outcome of VAP.

Prevention

To reduce the incidence of postoperative pulmonary complications, supportive treatment for preoperative and postoperative chronic respiratory disease, such as breathing exercises, postural drainage, physiotherapy with or without intermittent positive-pressure breathing and incentive spirometry has been recommended.

Intra-abdominal Infections

Intra-abdominal infections (IAIs) include a variety of pathological conditions and can be categorized as being either uncomplicated or complicated.[63]

In uncomplicated case of IAI, the infection involves only a single organ and does not extend to the peritoneum.

In complicated IAI, the infectious process extends beyond the organ, causing either localized or diffuse peritonitis.

Many regimens have been recommended to treat IAI, e.g. guidelines by Surgical Infection Society and Infectious Diseases Society of America. The World Society of Emergency Surgery in consensus with surgeons, infectious disease specialists, pharmacologists, radiologists and intensivists defined following recommendations for early treatment of IAIs.[63]

Recommendations by the World Society of Emergency Surgery (WSES) for Management of Intra-Abdominal Infections (Table 1)

Community-acquired Extra-Biliary Intra-abdominal Infections (Table 2)

Empirical antibiotic treatment of community-acquired IAIs should be according to the most frequently isolated bacteria and the local trends of antibiotic resistance. The major pathogens involved in community-acquired IAIs are enterobacteriaceae, streptococci and anaerobes.

Treatment may be with either single or multiple antimicrobial regimens depending on the patient's condition as well as the specific microorganisms and resistance patterns.

For stable, non-critical patients presenting with no extended-spectrum β-lactamase (ESBL)-associated risk factors, amoxicillin/clavulanate and ciprofloxacin plus metronidazole regimens are recommended. For critically ill patients presenting with no ESBL-associated risk factors, treatments of piperacillin/tazobactam are recommended.

For stable, non-critical patients presenting with ESBL-associated risk factors, ertapenem or tigecycline are recommended. For critically ill patients presenting with ESBL-associated risk factors, meropenem or imipenem plus fluconazole regimens (the latter in the event of risk factors for *Candida*) are recommended.

Biliary Intra-abdominal Infections

The microorganisms, most often isolated in biliary infections are the Gram-negative aerobes; *E. coli* and *K. pneumoniae* and several anaerobes, especially *B. fragilis*.

The antimicrobial drug selection in biliary infections depends on antimicrobial activity against causative bacteria, the clinical condition of the patient, and the biliary levels of the antimicrobial agents and the manner in which it is secreted into the bile.

For stable, non-critical patients presenting with no ESBL-associated risk factors, amoxicillin/clavulanate or ciprofloxacin plus metronidazole is recommended.

For stable, non-critical patients presenting with ESBL-associated risk factors, tigecycline is recommended.

For critically ill patients presenting with no ESBL-associated risk factors, piperacillin/tazobactam is recommended.

For critically ill patients presenting with ESBL-associated risk factors, tigecycline plus piperacillin (plus fluconazole in the event of risk factors for *Candida*) is the recommended drug regimen.

Antimicrobial Regimens Recommended by WSES for Hospital-Acquired IAIs (Table 3)

The incidence of HAIs caused by resistant microorganisms has risen significantly because of higher levels of antibiotic exposure. The other factors, such as advanced age, comorbidity, degree of organ dysfunction, low albumin level, poor nutritional status, severity of illness and the presence of malignancy also contribute to acquiring HAIs due to resistant organisms. Common pathogens are MRSA, vancomycin-resistant *Enterococcus* species, carbapenem-resistant *P. aeruginosa*, ESBL producing *E. coli* and *Klebsiella* species and MDR *Acinetobacter* species. These infections have higher risks of complication and mortality than community-acquired disease. Hence, for these infections, complex multi-drug regimens are usually recommended.

For stable, non-critical patients presenting with risk factors for MDR pathogens, fluconazole and tigecycline plus piperacillin are recommended.

Table 1: Antimicrobial regime recommended by the World Society of Emergency Surgery (WSES) for treating community-acquired extrabiliary intra-abdominal infections

Condition of patient		*Antimicrobial agents*	*Dosage*
Stable patients	With no ESBL-associated risk factor	Amoxicillin/clavulanate Ciprofloxacin plus Metronidazole	2.2 g every 6 hours 400 mg every 8 hours 500 mg every 6 hours
	With ESBL-associated risk factor	Ertapenem or Tigecycline	1 g every 24 hours 100 mg LD than 50 mg 12 hours
Critically ill patients	With no ESBL-associated risk factor	Piperacillin/tazobactam	9 g LD then 18 g per day (continuous infusion) or 4.5 g every 6 hours
	With ESBL-associated risk factor	Meropenem or Imipenem plus Fluconazole	500 mg every 6 hours 500 mg every 6 hours 600 mg LD then 400 mg every 24 hours

Abbreviations: ESBL, extended-spectrum β-lactamase; LD, loading dose.

Table 2: Antimicrobial regime recommended by WSES for treating community-acquired biliary intra-abdominal infections

Condition of patient		*Antimicrobial agents*	*Dosage*
Stable patients	With no ESBL-associated risk factor	Amoxicillin/clavulanate Ciprofloxacin plus Metronidazole	2.2 g every 6 hours 400 mg every 8 hours 500 mg every 6 hours
	With ESBL-associated risk factor	Tigecycline	100 mg LD than 50 mg every 12 hours
Critically ill patients	With no ESBL-associated risk factor	Piperacillin/tazobactam	9 g LD then 18 g per day (continuous infusion) or 4.5 g every 6 hours
	With ESBL-associated risk factor	Piperacillin Plus Tigecycline plus/minus Fluconazole	9 g LD then 18 g per day (continuous infusion) or 4.5 g every 6 hours 100 mg LD than 50 mg every 12 hours 600 mg LD then 400 mg every 24 hours

Abbreviations: ESBL, extended-spectrum β-lactamase; LD, loading dose.

Table 3: Antimicrobial regimens recommended by WSES for hospital-acquired IAIs

Condition of patient	*Antimicrobial agents*	*Dosage*
Stable patients	Piperacillin plus Tigecycline plus Fluconazole	8 g LD then 16 g per day (continuous infusion) or 4 g every 6 hours 100 mg LD than 50 mg every 12 hours 600 mg LD then 400 mg every 24 hours
Critically ill patients	Piperacillin plus Tigecycline plus Echinocandin (capsofungin and micafungin) or Meropenem or Imipenem or Doripenem plus Teicoplanin Plus Echinocandin	8 g LD then 16 g per day (continuous infusion or 4 g every 6 hours 100 mg LD than 50 mg every 12 hours 500 mg every 6 hours 500 mg every 6 hours 500 mg every 8 hours 1.6 g via continuous infusion or 400 mg 6 hours

Abbreviation: LD, loading dose.

In critically ill patients presenting with risk factors for MDR pathogens, meropenem, imipenem/cilastatin and doripenem (plus an echinocandin and teicoplanin) or tigecycline (plus an echinocandin and piperacillin) are recommended.

Prevalence and Antimicrobial Profile of Pathogens Isolated from Patients having Postoperative Infections in GI Surgery in Govind Ballabh Pant Institute of Post Graduate Medical Education and Research

In our facility, which is a super specialty hospital, large number of gastrointestinal surgeries is done, and being a government organization, patients with various risk factors associated with infections are encountered.

Over a period of one year, 6517 culture positive samples, received from patients undergone gastrointestinal surgery, were evaluated in regards to type of organism isolated and antimicrobial sensitivity of these organisms. Only aerobic culture was done.

Type of samples received were wound swab, pus, discharge from surgical site, bile and drain fluids from various sites.

From 42.8% samples (2789), more than one type of organisms were isolated. Gram-negative bacteria (*Klebsiella pneumoniae*, *E. coli*, *Acinetobacter* and *Pseudomonas*) were predominant pathogens as shown in the Table 4.

Table 4: Predominant pathogens isolated

Organisms	*Number (%)*
Klebsiella pneumoniae	792 (12.15%)
Escherichia coli	739 (11.3%)
Acinetobacter spp.	505 (7.7%)
Pseudomonas spp.	399 (6.1%)
Enterococcus spp.	280 (4.2%)
Staphylococcus aureus	172 (2.6%)
Proteus mirabilis	162 (2.4%)
Enterobacter spp.	48 (0.7%)
Citrobacter spp.	37 (0.56%)
Providencia stuartii	34 (0.52%)

Other organisms isolated were *Burkholderia cepacia*, coagulase negative staphylococcus and *Morganella morganii*.

Antibiotics Susceptibility (Tables 5 and 6)

- For the Enterobacteriaceae group, tigecycline was the most effective antibiotic followed by amikacin, imipenem, ertapenem and piperacillin/tazobactam.

Table 5: Antibiotic (%) susceptibility pattern for Gram-negative bacteria

Antibiotics	*Klebsiella species*	*E. coli*	*Acinetobacter species*	*Pseudomonas species*	*Proteus*	*Enterobacter spp.*
Ampicillin	0	0	0	0	0	20
Ampicillin-sulbactam	22.2	12.2	4.7	-	100	20
Piperacilli-tazobactum	59.6	43.3	28.5	62.5	100	40
Cefazolin	18.5	10.3	0	-	0	20
Ceftriaxone	22.2	16	19	36.8	0	20
Cefotaxime	0	20	0	-		
Cefepime	22.2	18.8	19	52	0	40
Aztreonam	18.5	9.4	0	14.5	0	20
Imipenem	62.9	34.5	57.1	58.4	100	60
Meropenem	54.9	33.5	57.1	33.5	100	60
Etrapenem	60.5	75	56.4	67.6	100	60
Amikacin	77.7	74.5	52.3	78.8	100	60
Gentamicin	44.4	30.1	23.8	36.2	0	60
Tobramycin	33.3	17.9	33.3	48	0	40
Ciprofloxacin	22.2	16	19	18.4	0	20
Ofloxcin	15	8.0	0	0		
Netilmicin	28.7	10.5	14	50.0		
Levofloxacin	37.2	43.7	17.6	53.7		
Moxifloxacin	22.2	13	14.2	-	0	20
Cotrimoxazole	18.5	9.4	4.7	-	0	20
Tigecycline	100	95.2	95.2	-	0	100
Ticarcillin-clavulanic acid	28.5	33.7	23.5	46.8		

- Isolates of *Pseudomonas spp.* were most sensitive to amikacin followed by ertapenem, imipenem, pipercillin/tazobactam, cefepime and netilmycin.
- Isolates of *Acinetobacter* spp. were most sensitive to tigecycline followed by carbapenems and amikacin.
- Linezolid was the most effective antibiotic for *S. aureus* and *Enterococcus* spp. followed by teicoplanin, cefuroxime, cefadroxyl and amoxy-clav.

Table 6: Antibiotic (%) susceptibility pattern for Gram-positive bacteria

Antibiotics	*Enterococcus spp.*	*S. aureus*
Amoxy-clav	33.3	25.6
Ofloxacin	27.7	15.1
Netilmicin	14.8	63.6
Gantamicin	46.5	0
Amikacin	24.6	58
Roxithromycin	38.2	22.2
Teicoplanin	94.4	86.5
Linezolid	100	100
Cefuroxime	52.5	48.6
Cefadroxyl	42.8	55.3

Commonly used Antibiotics in Clinical Practice (Table 7)

Five functional groups cover most antibiotics are:

- Inhibitors of cell wall synthesis
- Inhibitors of protein synthesis
- Inhibitors of membrane function
- Inhibitors of nucleic acid synthesis
- Antimetabolites

Table 7: Commonly used antibiotics[65-71]

Class	*Drugs*	*Indications*	*Side effects*
Inhibitors of cell wall synthesis			
Penicillins (Bactericidal)			
Natural penicillins	Penicillin G Aqueous penicillin G Procaine penicillin G Benzathine penicillin G Penicillin V	• Drug of choice for infections due to: *S. pneumoniae* and other Streptococci, pharyngitis, bacteremia, endocarditis • *Neisseria meningitidis*-meningitis, meningococcemia • *Treponema pallidum*-syphilis • Actinomycosis other uses • Endocarditis prophylaxis in patients with valvular heart disease undergoing dental procedures at high risk for bacteremia. Prevention of rheumatic fever • Very little activity against *Staphylococcus* spp. due to penicillinase production • Anaerobes: good activity against Gram-positive mouth anaerobes such as *Peptococcus* spp., *Peptostreptococcus, Clostridium* spp. except *Clostridium difficile*	• Hypersensitivity reaction with serious anaphylactic reaction. Cross-allergenicity is observed among penicillins • Irritability, jerking, confusion, generalized seizures • Leukopenia, neutropenia or thrombocytopenia • Gastrointestinal upset and diarrhea • Brain and kidney damage (rare)
Penicillinase-resistant penicillins	Methicillin Nafcillin Oxacillin Cloxacillin Dicloxacillin	• Infections due to MSSA such as skin and soft tissue infections, septic arthritis, osteomyelitis, bacteremia, endocarditis, etc. • Not active against MRSA • No activity against Enterococcus spp. or *S. pneumoniae* • Gram-negative: No activity • Anaerobes: Limited	Above + transient increases in liver enzymes Interstitial nephritis
Aminopenicillins	Ampicillin Amoxicillin	• Because of activity against respiratory tract pathogens, useful for the treatment of mild to moderate pharyngitis, sinusitis, bronchitis and otitis media • Useful for uncomplicated urinary tract infections, Enterococcal infections and *Listeria monocytogenes* meningitis • Endocarditis prophylaxis in patients with valvular heart disease. Treatment of *Salmonella* (amoxicillin) and *Shigella* (ampicillin) • Ineffective against *S. aureus* • Gram-negative: Better activity than natural penicillins • Anaerobes: Activity similar to penicillin G	As natural penicillin
Carboxypenicillins	Carbenicillin Ticarcillin	• Due to enhanced activity against Gram-negative bacteria, including *P. aeruginosa*, useful for the treatment of serious infections such as bacteremia, pneumonia, complicated urinary tract infection, peritonitis, intra-abdominal infections, skin and soft tissue infections, bone and joint infections, and meningitis caused by Gram-negative bacteria (hospital-acquired infections) • May be used as empiric therapy in immunocompromised patients • Not active against *Klebsiella* spp. or *Serratia* • Not active against Enterococcus or *Staphylococcus* spp.	• As above + • Hypokalemia + • Sodium overload and fluid retention

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Class	*Drugs*	*Indications*	*Side effects*
Ureidopenicillins	Piperacillin	• Same as above + active against *Klebsiella* spp. and *Serratia marcescens* • Piperacillin is the most active penicillin for infections due to *P. aeruginosa* • Anaerobes: Activity similar to penicillin G against *Clostridium* and *Peptostreptococcus* Some activity against *B. fragilis*	As above
Amidinopenicillins	Mecillinam	• Restricted use to urinary infection with *E. coli* • Active against penicillinase and low-level cephalosporinase producing organism	Gastrointestinal upset and diarrhea Hypersensitivity reaction
Combination-β-lactams and β-lactamase inhibitor			
With clavulanic acid	Amoxicillin-clavulanate	• Due to expanded activity against Gram-positive and Gram-negative bacteria (including anaerobes), often used in the treatment of polymicrobial infections, such as intra-abdominal infections, gynecological infections, diabetic foot infections, etc. • Useful for the treatment of otitis media, sinusitis, bronchitis, lower respiratory tract infections and human or animal bites	• Hypersensitivity reaction • Hemolytic anemia
	Ticarcillin/clavulanic acid	• Indicated for septicemia, lower respiratory infections, skin and skin structure infections and bone and joint infections, for UTIs, peritonitis caused by beta-lactamase-producing isolates of *S. aureus*, *Haemophilus influenzae*, *Klebsiella* spp., *E. coli*, *P. aeruginosa* and other Gram-negatives.	• Rash • Nausea • Diarrhea • Phlebitis at injection site • Increased eosinophils • Increased AST • Increased ALT
With sulbactam	Ampicillin-sulbactam	• Same activity of the parent penicillin against non β-lactamase producing organisms, and will have enhanced activity against beta-lactamase producing bacteria, e.g. *E. coli*, Proteus spp., Klebsiella spp., *H. influenza*, etc. • Not very active against beta-lactamase enzymes produced by *Serratia marcescens*, *P. aeruginosa*, *Proteus* spp., *Citrobacter* spp. and *Enterobacter* spp. • Useful for the treatment of mixed aerobic/anaerobic infections by susceptible bacteria	• Gastrointestinal upset and diarrhea, stomach pain, blood in stool • Hypersensitivity reaction • Painful urination • Vaginal yeast infection • Chest pain, dizziness
With tazobactam	Piperacillin/tazobactam	• Useful for the treatment of polymicrobial infections or other infections involving Gram-negative bacteria including hospital-acquired pneumonia, bacteremia, complicated urinary tract infections, complicated skin and soft tissue infections, intra-abdominal infections • And empiric therapy for febrile neutropenia	• Gastrointestinal upset and diarrhea • Hypersensitivity reaction
Cephalosporins (Bactericidal)			
First generation cephalosporins	Cefazolin Cephalothin Cephradine Cephapirin Cephalexin Cefadroxil	• Excellent activity against Gram-positive aerobes • Used for the treatment of mild to moderate infections of skin and soft tissue, septic arthritis, osteomyelitis and endocarditis due to MSSA and streptococci • Treatment of uncomplicated urinary tract infections. • Cefazolin is the drug of choice for surgical prophylaxis against surgical-site infection. • Also have activity against a limited number of Gram-negative aerobes • *P. mirabilis*, *E. coli, K. pneumoniae*	• Hypersensitivity reactions in patients with a history of penicillin allergy • Stevens-Johnson syndrome • Erythema multiforme • Exfoliative dermatitis • Gastrointestinal upset, diarrhea, nausea (if alcohol taken concurrently)

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Class	*Drugs*	*Indications*	*Side effects*
Second generation cephalosporins	Cefamandole Cefonicid Cefaclor Cefprozil Cefuroxime Loracarbef Cefoxitin Cefotetan Cefmetazole	• Slightly less active than first generation agents against Gram-positive aerobes, such as Staphylococci and Streptococci, cefprozil and cefuroxime have the best Gram-positive coverage; cefoxitin and cefotetan have the worst but More active against Gram-negative aerobes and anaerobes • Cefuroxime is useful for the treatment of pharyngitis, tonsillitis, sinusitis, otitis media, bronchitis and mild to moderate community-acquired pneumonia. • Treatment of mild to moderate skin and soft tissue infections, and uncomplicated urinary tract infections due to susceptible bacteria. • Cefoxitin, cefotetan and cefmetazole have activity against Gram-negative aerobes and anaerobes, including *B. fragilis* • So they are useful for prophylaxis in abdominal surgical procedures and • For the treatment of polymicrobial infections such as intra-abdominal infections (diverticulitis, appendicitis, bowel perforation), pelvic infections (pelvic inflammatory disease), and skin and soft tissue infections in patients with diabetes	• Above + • Hypoprothrombinemia • Allergic reactions • Ethanol disulfiram reaction • Pseudomembranous colitis • Phlebitis • Drug fever • Interstitial nephritis (rare);
Third generation cephalosporins	Cefotaxime Ceftriaxone Ceftazidime Cefoperazone Ceftizoxime Moxalactam Cefixime Cefpodoxime Ceftibuten Cefdinir	• More activity than the second generation agents against Gram-negative aerobes (even beta-lactamase producing strains) • Are used for the treatment of bacteremia, pneumonia, complicated urinary tract infection, peritonitis, intra-abdominal infections, skin and soft tissue infections, bone and joint infections, and meningitis caused by Gram-negative bacteria (nosocomial infections) • If *P. aeruginosa* is known or suspected, ceftazidime or cefoperazone should be used • If anaerobes are known or suspected, metronidazole or clindamycin should be added • Ceftriaxone is used as a single intramuscular (dose for uncomplicated gonorrhea) • Cefotaxime and ceftriaxone have good activity against Gram-positive aerobes, and may be used for the treatment of infections due to PRSP (meningitis and pneumonia) • Ceftriaxone can be used for the treatment of endocarditis caused by *Streptococcus viridans*	• As above + • Biliary sludging (ceftazidime)
Fourth generation cephalosporins	Cefepime Cefpirome	• Cefepime is used for the treatment of community-and hospital-acquired pneumonia, bacteremia, uncomplicated and complicated urinary tract infections, skin and soft tissue infections, intra-abdominal infections • Empiric therapy for febrile neutropenia • Cefepime also has anti pseudomonal activity • If anaerobes are known or suspected, metronidazole or clindamycin should be added	Nonconvulsive status epilepticus (cefepime)
Fifth generation	Ceftraoline fosamil	• Broad spectrum, active against Gram-positive drug resistant bacteria (*S. pneumoniae*, MRSA, VRSA) • Also effective against *H. influenzae*, *M. catarrhalis* and some common Gram-negative bacteria	Gastrointestinal upset and diarrhea Allergic reaction *C. difficile*-associated diarrhea Direct Coombs test seroconversion

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Class	*Drugs*	*Indications*	*Side effects*
Sixth generation	Ceftobiprole	• Broad spectrum, active against MRSA, methicillin-resistant *Staphylococcus epidermidis*, *E. faecalis* • Common Gram-negative bacteria *E. coli* and also *Pseudomonas*	• Nausea, diarrhea, vomiting • Infusion-site reaction • Headache • Dysgeusia (caramel-like taste)
Carbapenems	Imipenem (+ Cilastatin) Meropenem Doripenem Ertapenem	• Currently the most broad-spectrum antibiotics, with good activity against many Gram-positive and Gram-negative aerobes and anaerobes • Used for polymicrobial infections such as intra-abdominal infections or skin and skin structure infections in diabetic patients • Empiric therapy for nosocomial infections, such as serious lower respiratory tract infections, septicemia and complicated urinary tract infections, while waiting for the results susceptibility data • Ertapenem does not have activity against *P. aeruginosa* • Febrile neutropenia: imipenem or meropenem • Meningitis (children): meropenem • Carbapenems do not have activity against MRSA	• Hypersensitivity reactions in patients with a history of penicillin allergy. (5–15%) • Gastrointestinal upset, diarrhea, nausea • Insomnia, agitation, confusion, dizziness, hallucinations, and depression • Seizure • Antibiotic-associated pseudomembranous colitis (*C. difficile*)
Monobactams	Aztreonam	• Same as carbapenems + • Used for the treatment of infections caused by Gram-negative aerobes such as complicated and uncomplicated urinary tract infections, lower respiratory tract infections, meningitis, bacteremia, skin and skin structure infections, intra-abdominal infections and gynecologic infections caused by susceptible Gram-negative aerobes • Combination therapy is recommended to ensure coverage of Gram-positive and anaerobic bacteria • Aztreonam is especially useful for the treatment of Gram-negative infections in patients with a history of a severe penicillin allergy • If anaerobes are known or suspected, metronidazole or clindamycin should be added	• Hypersensitivity rash, pruritus, urticaria, angioedema, anaphylaxis (rare) • Negligible cross-reactivity with penicillin • Diarrhea, nausea, vomiting • Neutropenia, thrombocytopenia, eosinophilia, • Transient LFT increases • Phlebitis • Drug fever
Glycopeptides	Vancomycin Teicoplanin	• Infections due to methicillin-resistant staphylococci including bacteremia, pneumonia, empyema, endocarditis, peritonitis, osteomyelitis and skin and soft tissue infections • Intraventricular vancomycin is used for the treatment of meningitis • Serious Gram-positive infections in patients allergic to beta-lactam antibiotics • Infections caused by multidrug resistant Gram-positive organisms, such as *Corynebacterium*, *S. pneumoniae* • Perioperative prophylaxis to reduce the risk of infection in patients undergoing cardiac, neurosurgical, orthopedic, or vascular surgical procedures where the incidence of MRSA is high • Oral vancomycin. for the treatment of choice for moderate to severe *C. difficile* colitis • Vancomycin is not active against Gram-negative aerobes or anaerobes	Red-man syndrome characterized by flushing, pruritus, and a maculopapular or erythematous rash on the face, neck, chest, and upper extremities, may also be accompanied by hypotension. Resolves spontaneously after the discontinuation of the infusion Nephrotoxicity and Ototoxicity Neutropenia, thrombocytopenia

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Class	*Drugs*	*Indications*	*Side effects*
Inhibitors of membrane function (Bactericidal)			
Lipopeptides (previously polypeptides)	Polymyxin B Polymyxin E Bacitracin Colistin	• Gram-negative MDR infections • Polymyxin can be used in combination against very resistant *Pseudomonas* • Used in Gram-negative infection of eye and ear usually applied directly to the eye • Bacitracin for topical Gram-positive infections • The use of polymyxin and colistin is experiencing a resurgence due to the emergence of multidrug resistant *Acinetobacter*, *Pseudomonas* and *Klebsiella* infections • Colistin is ineffective for *Proteus* and *Burkholderia* • Polymixin not effective against Gram-positives and anaerobes	• Kidney and nerve damage • Pruritis, rash
	Daptomycin	• Gram-positive organisms: Excellent activity • Reserved for the management of serious or complicated infections caused by resistant Gram-positive organisms where vancomycin and/or linezolid cannot be used • Daptomycin should not be used for the treatment of pneumonia since the compound is inactivated by pulmonary surfactant	• Nausea, diarrhea, headache • Injection site reactions • Rash • Myopathy and • CPK elevation
Inhibitors of protein synthesis			
Aminoglycosides (Bactericidal)	Gentamicin Neomycin Kanamycin Amikacin Tobramycin Netilmicin Streptomycin Paromomycin Spectinomycin	• Aminoglycosides are rarely used alone • Amikacin, gentamicin and tobramycin are used for the treatment of serious infections due to Gram-negative bacteria such as septicemia, bone and joint infections, skin and soft tissue infections, respiratory tract infections, intra-abdominal infections, and complicated urinary tract infections • Gentamicin or streptomycin may be used (with ampicillin, vancomycin, etc.) for the treatment of serious infections (endocarditis) due to enterococci, viridans streptococci or staphylococci • Streptomycin or amikacin is used in conjunction with other antituberculous medications in the treatment of non tuberculous infections • Anaerobes-aminoglycosides are inactive	• Nephrotoxicity • Ototoxicity auditory and vestibular • Vertigo • Kidney damage • Neuromuscular blockade (neomycin), • Hypersensitivity • Sterile abscess formation at intramuscular site
Tetracyclines Bacteriostatic	Tetracycline Doxycycline Minocycline Demeclocycline Oxytetracycline	• Tetracyclines display activity against Gram-positive and Gram-negative aerobic bacteria, as well as unusual bacteria • The emergence of bacterial resistance and the availability of more potent and useful antibiotics have limited the therapeutic usefulness of the tetracyclines • Can be used in community-acquired pneumonia due to penicillin susceptible *S. pneumoniae*, *Mycoplasma* spp. • Treatment of rickettsial infections • Chlamydial infections • Nongonococcal urethritis • Brucellosis, bartonellosis • Acne (minocycline)	• Gastrointestinal upset, nausea • Sensitivity to sunlight • Potential toxicity to mother and fetus during pregnancy • Impaired growth • Enamel hypoplasia • Permanent tooth discoloration • Transient depression of bone growth • Hepatotoxicity • Avoid in children less than 8 years of age • Rash, pruritus, urticaria, angioedema, anaphylaxis, serum sickness, • Stevens-Johnson syndrome • Lightheadedness, dizziness, vertigo, ataxia, headache

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Class	*Drugs*	*Indications*	*Side effects*
		• Useful as either primary or alternative therapy for the treatment of plague,tularemia, chancroid, pertussis, Clostridial infections, anthrax, listeria, syphilis, Lyme disease, *Helicobacter pylori*, Cholera • Prevention of malaria (doxycycline) • Chronic SIADH (demeclocycline)	
Glycylcyclines	Tigecycline	• Active against a broad range of Gram-positive and Gram-negative aerobic and anaerobic bacteria • Tigecycline is approved for the treatment of polymicrobial infections • Complicated skin and skin structure infections • Complicated intra-abdominal infections • Tigecycline is not active against *Proteus mirabilis* or *P. aeruginosa*	Same as above
Macrolides Bacteriostatic	Erythromycin Azithromycin Clarithromycin Roxithromycin	• Useful alternative in penicillin-allergic patients • Respiratory tract infections, pharyngitis, tonsillitis, otitis media, sinusitis, acute exacerbations of chronic bronchitis • Azithromycin and clarithromycin are best if *H. influenzae* is suspected • Community-acquired pneumonia especially for atypical coverage, pertussis, *C. diphtheria* • Uncomplicated skin and soft tissue Infections. • Sexually-transmitted diseases: Azithromycin is effective for the treatment of nongonococcal urethritis or cervicitis due to *Chlamydia trachomatis* • Prophylaxis of bacterial endocarditis syphilis and gonorrhea. • *Mycobacterium avium* complex infections • *Campylobacter jejuni* infections, *H. pylori*	• Epigastric distress, abdominal pain, nausea, vomiting, diarrhea • Cholestatic hepatitis seen in adult patients • Allergic reactions • QT prolongation • Visual disturbance • Liver toxicity
Ketollides	Telithromycin Spiramycin	• The spectrum of activity of telithromycin is similar to that of azithro and clarithro with additional activity against macrolide-resistant *S. pneumoniae* • Currently approved only for the treatment of mild-moderate community-acquired pneumonia due to adverse effect. (risk outweighs benefit in treatment of sinusitis or bronchitis) • Acute bacterial sinusitis • Acute exacerbations of chronic bronchitis	• Diarrhea, nausea, vomiting, • Hepatotoxicity QT interval prolongation • Decreased visual acuity and blurred vision
Chloramphenicol Bacteriostatic		• Active against Gram-positives and Gram-negatives but not indicated as first line therapy for treatment of infections • Due to the low cost of this continues to be used for bacterial meningitis, pneumonia and typhoid fever • Not active against *P. aeruginosa*	• Aplastic anemia • Gray Baby Syndrome • Optic neuritis • Hypersensitivity reactions, anaphylaxis (rare) • Herxheimer-like responses • Nausea, vomiting diarrhea • Stomatitis • Acute attacks of porphyria • Interference during development of immunity and should not be given during active immunization

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Class	*Drugs*	*Indications*	*Side effects*
Lincosamides Bacteriostatic	Clindamycin Lincomycin	• Primarily useful for infections due to anaerobes (including *B. fragilis*), pulmonary infections, pelvic infections, diabetic foot infections, decubitus ulcers • Alternative to penicillin in the treatment of infections due to *C. perfringens* • Treatment of skin and soft tissue infections due to *Staphylococcus* and Streptococci including MRSA • Alternative agent for the treatment of infections due to Gram-positive aerobes in patients allergic to penicillin (cellulitis, septic arthritis, osteomyelitis) • Alternative for the treatment of encephalitis due to *Toxoplasmosis gondii* in AIDS patients • Alternative for the treatment of *Pneumocystis carinii* pneumonia in AIDS patients allergic to sulfonamides • Treatment of bacterial vaginosis (vaginal cream)	• Nausea, vomiting, diarrhea • Pseudomembranous colitis • Antibiotic-associated diarrhea (*C. difficile*) • Hepatotoxicity Hypersensitivity
Oxazolinidinones	Linezolid	• Reserved for management of serious or complicated infections caused by resistant organisms, especially for infections where vancomycin cannot be used • Treatment of infections (bacteremia) due to vancomycin-resistant *Enterococcus* spp. • Complicated skin infections caused by MSSA or *S. pyogenes* • Community-acquired pneumonia due to PSSP, penicillinase producing Streptococci (MSSA) • Nosocomial pneumonia due to MSSA, MRSA and PSSP • Serious infections due to MRSA or VRE including endocarditis, meningitis and osteomyelitis	• Gastrointestinal nausea, diarrhea lactic acidosis • Headache • Peripheralneuropathy • Thrombocytopenia and anemia
Streptogramins	Quinupristin: Dalfopristin	• Dalfopristin is used for the treatment of vancomycin-resistant *Enterococcus faecium* bacteremia • Complicated skin and skin structure infections caused by MSSA or *S. pyogenes*; catheter-related bacteremia • Infections due to MRSA and community-acquired pneumonia (when vancomycin, linezolid and daptomycin cannot be used)	• Venous site irritation • Nausea, vomiting diarrhea • Myalgias • Arthralgias • Rash
DNA synthesis inhibitors (Quinolone/fluoroquinolones)			
First generation	Nalidixic acid	Only for Gram-negatives, used to treat urinary tract infections	• Stomach upset • Loss of appetite • Headache • Dizziness
Second generation	Ciprofloxacin Norfloxacin Enoxacin Ofloxacin Levofloxacin	• Gram-negative and Gram-positive coverage including anaerobes • More widespread tissue distribution • Used in UTI, bacterial prostatitis, osteomyelitis, community-acquired pneumonia, bacterial diarrhea, mycoplasma infections and gonorrhea • Effective against *Pseudomonas* also	• As above + • Phototoxicity • Tendinosis • Achilles tendon rupture • Impaired fracture healing • CNS damage

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Class	*Drugs*	*Indications*	*Side effects*
Third generation	Gatifloxacin Sparfloxacin	• As above + expanded activity against Gram-positive organisms, particularly penicillin-sensitive and PRSP, and atypical pathogens such as *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* • Acute sinus infections, skin infections, pneumonia, complications of chronic bronchitis, kidney and urinary tract infections, and gonorrhea • Less active than ciprofloxacin against Pseudomonas species • Used in ophthalmic infections	• Diarrhea, nausea stomach pain, vomiting • Dizziness, headache • Heart palpitations, high blood pressure • Labored breathing • Vaginal inflammation
Fourth generation	Moxifloxacin Gemifloxacin	• As above + anaerobes • Acute exacerbations of chronic bronchitis • Acute bacterial sinusitis • Community-acquired pneumonia • Uncomplicated skin and skin structure infections community-acquired pneumonia caused by multidrug resistant *S. pneumoniae* • Complicated skin and skin structure infections • Complicated intra-abdominal infections • In ophthalmology in conjuctival infections	• Diarrhea, nausea stomach pain, vomiting dizziness, headache • Reversible peripheral neuropathy • Spontaneous tendon rupture tendonitis • Acute liver failure or serious liver injury • QT prolongation, • *C. difficile* associated colitis
Other DNA inhibitors			
Metronidazole	Metronidazole (Flagyl®)	• Gram-positive and Gram-negative anaerobic bacterial • Protozoal infections	• Nausea, loss of appetite, headache, seizures • Cerebellar dysfunction • Ethanol disulfram reaction
Antimetabolites **Folic acid synthesis inhibitors**			
Sulfonamides	Trimethoprim/ sulfamethoxazole Sulfisoxazole Sulfadiazine	• Acute, chronic or recurrent infections of the urinary tract • Acute or chronic bacterial prostatitis • Acute bacterial exacerbations of chronic bronchitis • *P. carinii* pneumonia: The drug of choice for both treatment and prophylaxis • Skin and soft tissue infections due to MRSA • Acute otitis media, sinusitis • Nocardia infections • *Stenotrophomonas maltophilia* infections • Listeria meningitis if patient is allergic to penicillins • Toxoplasmosis • Not active against *P. aeruginosa*	• Thrombocytopenia Avoid in third trimester of pregnancy • Nausea, vomiting, diarrhea, anorexia, glossitis, abdominal pain • Hypersensitivity reactions, Stevens Johnson syndrome, exfoliative dermatitis, headache, insomnia, depression

Abbreviations: MSSA, methicillin-susceptible *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*; AST, aspartate aminotransferase; ALT, alanine transaminase; VRSA, vancomycin-resistant *Staphylococcus aureus*; QT, Q wave and T wave; LFT, liver function test; PSSP, penicillin-susceptible *Streptococcus pneumoniae*; PRSP, penicillin-resistant *Streptococcus pneumoniae*; MDR, multidrug resistant; CPK, creatine phosphokinase; VRE, vancomycin-resistant enterococci; UTI, urinary tract infection; CNS, central nervous system; SIADH, syndrome of inappropriate antidiuretic hormone secretion.

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