Hernia Infections

Pathophysiology • Diagnosis • Treatment • Prevention

edited by

Maximo Deysine

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Mineola, New York, U.S.A.

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Vosotros los que amais los imposibles
Los que vivis la vida de la idea
Los que sabeis the ignotas muchedumbres
Que los espacios infinitos pueblan . . .

All of you who love impossible things
All of you who live the life of ideas
All of you who know of unknown multitudes
That inhabit the realms of endless space . . .

From *Tabaré*, by Juan Zorrilla de San Martin, Montevideo, Uruguay, 1888. (Translated by Jonathan Cohen, M.F.A., Ph.D., writer-in-residence, Department of Surgery, SUNY at Stony Brook, Stony Brook, New York.)

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Foreword

To see a surgeon repair a hernia is to have a full and accurate measure of his skill. Hernias present us with the unusual paradox that a cure exists, but this cure can be fickle and elusive. Good results are never due to serendipity but require the surgeon to call upon and to apply his mastery of the necessary disciplines, in concert and on many fronts. To that end, the evolution of prosthetic materials as had been hoped by Theodore Billroth has become a reality, but it is also a mitigated blessing. Prosthetics are not meant to supplant knowledge and skill but to complement them. Their utilization calls for judgment, discernment, and relevance to that specific hernia in that particular patient. The present attitude of the surgical community leaves no doubt that prosthetics in hernia surgery have become an essential part of today's arsenal in the treatment of this most vexing surgical problem.

The early use of prosthetics in hernia surgery (e.g., nylon by Don Aquaviva of Marseilles, France, in 1944) was marred by the frequent formation of abscesses and sinuses. The discovery of olefins and the subsequent manufacture of ethylene and polypropylene (1938, 1953) by chemist and Nobel Laureate G. Natta of Italy ushered in a new era. Francis Usher (US) appreciated the potential of these materials and introduced ethylene and then polypropylene in tension-free repairs as early as 1953.

The universal bane, however, associated with foreign materials implanted in the human body, has been bacterial contamination and subsequent infection. More than any other factor this fear has delayed

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the summary acceptance of prosthetics in surgery, which the experience in orthopedics and cardiac and vascular surgeries did much to perpetuate.

The appearance of a textbook dealing with infections as they pertain to hernia surgery, and by extension all surgery that uses foreign material, is long overdue and underlines the importance of the problem. The explosion and rapid diffusion of information makes it a near impossibility for an individual to search it effectively and I am indebted to Dr. Deysine to have attempted this timely and most relevant publication. The participation of an eminent faculty leaves no doubt as to the scholarly and scientific quality of the project. I am honored to know most of the contributors and it has been my privilege to share with them many memorable publications and conferences. Every opportunity for an exchange or communication with them has left me a little richer. This time around I consider myself most fortunate.

The table of contents promises an exciting and richly informative journey, a journey that provides memorable discoveries to be recorded in that wonderful surgical attic that occasionally makes our life, during some future difficulty, a little easier and more rewarding. What surgeon has never known the misfortune of an infection complicating an otherwise perfectly executed hernia operation, with its attendant morbidity, cost, recurrence, and a most disappointed patient. My late friend and respected colleague Georges Wantz is known to have said and to have written "I would rather have a recurrence than an infected mesh." I concur and I dedicate this Foreword to him. He was a generous and selfless teacher who was our conscience in such matters as mesh and its complications for those of us who were fortunate enough to have walked with him. He would, I know, recommend this publication and I would support him as I have before, on many occasions.

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Preface

The purpose of this book is to persuade surgeons of the need for a change in surgical attitude that will allow the performance of mesh hernia surgery with virtually no infections. There is evidence in the literature that such a goal is attainable through awareness and judicious utilization of newer ideas and techniques.

The necessity to address a surgical complication is directly proportional to its impact on human health. Approximately 700,000 inguinal and 50,000 ventral herniorrhaphies are performed yearly in the United States and about 85% of these procedures utilize a prothesis. The reported infection rate is between 1 to 3% for inguinal hernias and from 4 to 6% for ventral hernias; therefore, approximately 16,000 individuals per year require further surgical treatment because of infection. The infection rate for herniorrhaphy has not changed significantly in the last three decades, but what has increased is the number of meshes inserted. In terms of human suffering and cost, the impact of wound infection in the presence of mesh is significant. The core of this problem is that prosthetic materials, bathed in nutritious body fluids, become fertile grounds for bacterial colonization, accentuating the need for stricter infection control measures.

The field of hernia repair has changed drastically in the last 20 years with the creation of European and American Hernia Societies and their joint journal: *HERNIA*. Simultaneously, international, national, and regional conferences have been held on techniques for mesh hernia repair. Such technology changes the wound biology by exponentially increasing

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the amount of foreign material left in the wound. The presence of infected mesh converts a simple ambulatory surgical procedure into a protracted and complex clinical situation requiring further surgery and may be associated with long-term disability.

Curiously, our attitude confronting postoperative infections has remained similar for hundreds of years. During the pre-antiseptic era, wound infections occurred in over 99% of all clean surgical operations; they were not only expected but considered a normal outcome. Surgeon's attitudes, based on limited knowledge, did not permit the conceptualization that infections could be curtailed. Semmelweiss, Pasteur, Lister, and others elucidated the role of bacteria, identifying the operating room environment and the surgical team as their vector, which brought about changes in attitude. This eventually led to the institution of measures to diminish the wound bacterial load, lowering the infection rate to approximately 10%. The discovery and introduction of antibiotics further reduced these figures to their present 2 to 3% level, but these drugs created a false sense of security that led to the relaxation of operating room antiseptic routines. *During the last 20 years no significant drop in the incidence of wound infection has been reported.*

Orthopedics surgeons faced a similar problem when in the 1960s, Charnley inserted a large metallic prothesis that if infected became anathema to both patient and surgeon. It was then recognized that the wounds had been exposed to bacteria emanating from the operating room air and the surgical team. Diminishing the bacterial wound load by introducing laminar air flow, improved hooded gowns, local and systemic antibiotic regimes, and antibiotic-releasing polymers significantly lowered the incidence of orthopedic infections.

The various chapters of this book give strong evidence that mesh hernia repair should be performed using the same precautions as for a total joint replacement, because the dissected wound surface for a large ventral herniorrhaphy is greater than the one produced during a total joint replacement. Most importantly, the total surface of a 15×15 cm polypropylene or ePTFE prothesis is larger than any orthopedic prothesis. Plugs utilized for inguinal repairs also exhibit large surfaces. Nevertheless, surgeons continue to perform mesh hernia surgery in ordinary operating theaters often following clean-contaminated or even infected cases.

During the last 20 years the bacterial load introduced into clean wounds has been reduced by the introduction of new antibacterial technology at every level of the surgical procedure. Bactericidal soaps

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and skin antiseptics, barrier drapes, hooded and ventilated head gear, less injurious electrocoagulation devices, systems for instrument sterilization, and new prosthetic materials incorporating antibacterial agents are all additive factors that should facilitate infection prevention. At the same time, improved conceptualization of the ultramicroscopic relationship between bacteria and host has emerged, enlightening the operating surgeon about the need to reduce the wound bacterial load. New diagnostic imaging permitting early detection plus fast and efficient bacteria identification by laboratories are all factors that will contribute to prevention improvement and better treatment of existing infections.

The authors hope that this book will help surgeons to fully avail themselves of the knowledge and armamentarium that will allow them to radically reduce postherniorrhaphy wound infections. The implementation of such measures will require additional perioperative and operating room costs, but this will be offset by the reduction in expenditures incurred for the treatment of over 16,000 yearly infections.

The contributors to this textbook are surgeons, engineers, and biologists widely acclaimed for their intellectual accomplishments. They are also practicing healers with great hands-on expertise in their particular fields. Their advice emanates from years of accumulated practice and wisdom. Their goal, to help change the attitude of all surgeons about the realities of surgical infections, will be fully met, I am sure, if a single life is saved, if a single infection has been stemmed.

Maximo Deysine

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Treatment of Postoperative Infections in Hernia Surgery: Guidelines for Antibiotic Therapy—Microbes, Antibiotic Specificity, and Dosages

Reisa F. Ullman

Antimicrobial choices in the treatment of the infected postoperative patient should be guided by a knowledge of the operative procedure, any underlying medical problems the patient may have, the hospital or facility's usual nosocomial pathogens (including resistant organisms), and subsequently by culture and sensitivity reports. Thorough evaluation of the patient should be undertaken prior to commencing antibiotic therapy. This should include obtaining a wound culture for Gram stain and culture and sensitivity testing. Further work-up may be required in patients with systemic symptoms and signs of infection, especially those who are immunocompromised. Other sources of infection (whether primary or secondary) may need to be considered as well in the postoperative patient (i.e., urinary tract infections, respiratory tract infections, percutaneous intravascular device-related infections, and bloodstream infections).

The following is a guide to assist in treatment choices in the infected postoperative patient. It is important to remember that many antibiotics require dosage adjustments for patients with renal impairment, and

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consultation with an infectious disease specialist may be helpful in the care of these patients, as well as in complicated situations, especially those involving resistant organisms (i.e., methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and resistant gram-negative organisms). Specific antibiotic choices may vary depending upon your hospital's antibiotic formulary, as well as any allergies the patient may have, and/or potential drug interactions with any concurrent medications the patient may be receiving.

Polymicrobic infections including anaerobes may also be seen in the postoperative setting and may present as a crepitant cellulitis, suppurative myositis, or clostridial myonecrosis. Pathogens such as *B. fragilis* group, *Peptostreptococcus* sp., *Clostridium* sp., *Fusobacterium* sp., and *Prevotella* sp. may be the causative organisms in these situations. A high index of suspicion should be maintained for the predisposing conditions to mixed anaerobic infections, which include diabetes mellitus, neutropenia, underlying malignancy, immunosuppression, corticosteroid use, vascular insufficiency, tissue destruction, gastrointestinal tract or pelvic disease, or trauma to these areas.

Infection control programs exist in most facilities and the infection control practitioner/hospital epidemiologist may be a useful resource for the surgeon. Most programs have a system to detect and analyze surgical wound infections and help track any trends in the commonly identified pathogens along with their respective antibiograms.

Table 1 Suggested Treatment Regimens for the Major Aerobic Pathogens in Surgical Wound Infections

Organism	Primary	Alternatives
Staph. aureus	Oxacillin	Cefazolin
Methicillin-sensitive	Nafcillin	Vancomycin Clindamycin Betalactam-betalactamase inhibitor (i.e., Augmentin, Unasyn, Timentin, Zosyn)
Methicillin-resistant (MRSA)	Vancomycin ± rifampin or gentamicin	Linezolid (Zyvox) Quinupristin-dalfopristin (Synercid)

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Organism	Primary	Alternatives
Staph. epidermidis (coagulase-negative) Methicillin-sensitive	Oxacillin Nafcillin Cefazolin	Betalactam-betalactamase inhibitor (i.e., Augmentin, Unasyn, Timentin, Zosyn) Fluoroquinolone Vancomycin
Methicillin-resistant	Vancomycin	Quinupristin-dalfopristin (Synercid) Linezolid (Zyvox)
Streptococcus sp.	Penicillin G Cefazolin	Ceftriaxone Cefuroxime Clindamycin Vancomycin
Enterococcus (E. faecalis + E. faecium)	Ampicillin ± gentamicin	Vancomycin ± gentamicin Imipenem (*E. faecalis*)
Enterococcus fascium Vancomycin-resistant (VRE)	Quinupristin-dalfopristin (Synercid) Linezolid (Zyvox)	Some strains sensitive to chloramphenicol, tetracycline, or fluoroquinolone
Escherichia coli	Ampicillin Cephalosporins (e.g., cefazolin) 1st, 2nd, 3rd generation based on sensitivity Betalactam-betalactamase inhibitors (Unasyn, Timondin, Zosyn)	Aztreonam Fluoroquinolone Sulfa-trimothoprim Aminoglycosides
Pseudomonas aeruginosa	Antipseudomonal penicillin (Ticarcillin-clavulanate-Timentin) (Piperacillin-tazobactam-Zosyn) (Mezlocillin) Cetazidime ± aminoglycoside	Aztreonam Ciprofloxacin Imipenem/meropenem ± aminoglycosides

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Organism	Primary	Alternatives
Enterobacter sp.	Antipseudomonal penicillin 3rd-generation cephalosporin (Ceftazidime) (Ceftriaxone) (Cefoperazone)	Fluoroquinolone Aztreonam Imipenem/meropenem Aminoglycoside Sulfa-trimothoprim
Proteus mirabilis	Ampicillin Cephalosporin (1st, 2nd, 3rd generation)	Betalactam-betalactamase inhibitor Aztreonam Fluoroquinolone
Klebsiella sp.	Cephalosporin (Ceftriaxone) (Ceftazidime) (Cefoperazone) Betalactam-betalactamase inhibitor Tetracycline	Aztreonam Imipenem/meropenem Fluoroquinolone Sulfa-trimethoprim Aminoglycoside
Citrobacter sp.	3rd-generation cephalosporin (Ceftriaxone) (Ceftazidime) (Cefoparazone) Fluoroquinolone	Imipenem/meropenen Tetracycline
Serratia marcescens	Antipseudomonal penicillin 3rd-generation cephalosporin (Ceftriaxone) (Ceftazidime) (Cefoperazone)	Fluoroquinolone Imipenem Aztreonam Sulfa-trimothoprim
Candida sp.	Fluconazole Amphotericin B	Caspofungin

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Table 2 Suggested Treatment Regimens for Anaerobic Pathogens in Surgical Wound Infections

Organism	Primary	Alternatives
B. fragilis group	Metronidazole Clindamycin Betalactam-betalactamase inhibitor (i.e., Augmentin-amoxicillin + clavulanate Unasyn-ampicillin + sulbactam Timentin-ticarcillin and clavulanate Zosyn-piperacillin and tazobactam)	Cefoxitin Cefotetan Chloramphenicol Imipenem
Peptostreptococcus sp.	Penicillin G	Metronidazole
	Ampicillin/amoxicillin Clindamycin	Chloramphenicol Vancomycin Imipenem/meropenem
Clostridium sp.	Penicillin G ± clindamycin	Chloramphenicol Metronidazole Clindamycin Ampicillin Imipenem/meropenem
Fusobacterium sp.	Penicillin G Metronidazole Clindamycin	Cefoxitin Chloramphenicol Imipenem/meropenem
Prevoltella sp.	Metronidazole Clindamycin Cefoxitin Cefotetan	Chloramphenicol Betalactam-betalactamase inhibitor Imipenem/meropenem

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Table 3 Usual Adult Dosages of Selected Antimicrobial Agents

Nafcillin:	1–2 g IV q 4 h.
Oxacillin:	1–2 g IV q 4 h.
*Ampicillin:	1–2 g IV q 4 h.
*Cefazolin:	1 g IV q 8 h.
*Cefoxitin:	1–2 g IV q 8 h.
*Cefotetan:	1–2 g IV q 12 h.
*Cefuroxime:	1 g IV q 8 h.
Ceftriaxone:	1–2 g IV q 24 h.
*Ceftazidime:	1 g IV q 8 h.
Cefoperazone:	2 g IV q 12 h.
*Unasyn:	3 g IV q 6 h.
*Timentin:	3.1 g IV q 6 h.
*Zosyn:	3.375 g IV q 6 h.
*Aztreonam:	1–2 g IV q 6–8 h.
Clindamycin:	900 mg IV q 8 h.
Metronidazole:	500 mg IV/PO q 6 h.
Chloramphenicol:	500 mg IV q 6 h.
*Ciprofloxacin:	200–400 mg IV q 12 h or 500mg PO q 12 h.
*Levofloxacin:	500 mg IV/PO q 24 h.
Linezolid (Zyvox):	600 mg IV/PO q 24 h.
Quinupristine + dalfopristin (Synercid):	7.5 mg/kg IV q 8 h.
*Fluconazole (Diflucan):	100–200 mg IV/PO q 24 h.
*Amphotericin B:	0.3–0.7 mg/kg IV q 24 h.
Caspofungin (Cancidas):	70 mg IV on day 1, then 50 mg IV q 24 h. down to 35 mg IV q 24 h. with moderate hepatic insufficiency
*Vancomycin:	1 g IV q 12 h
*Imipenem:	500 mg IV q 6 h
*Meropenem:	500 mg–1 g IV q 8 h.

*Dosage adjustment required for renal dysfunction/renal failure.

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1

Historical Evolution of Asepsis and Antisepsis

The Role of the Inventors, the Disseminators, and the Perennial Detractors

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As shown by Dr. Sanchez Montes in her chapter on statistics and incidence, the reported infection rate approximates 4% for elective inguinal and 10% for ventral herniorrhaphy; thus the goal of infection-free surgery remains elusive. Furthermore, as the number of operations performed around the world increases, the significance of small changes in wound infection rates grows notably larger. In essence, the question of how to prevent environmental bacteria from entering and proliferating in wounds remains as pertinent now as it did in the early 1800s.

I. THE STATE OF SURGERY CIRCA 1800 AND WHAT IT TAKES TO CARRY AN INVENTION INTO SURGICAL PRACTICE

Before the discovery of anesthesia, surgery consisted of a rapid struggle that uniformly produced an unimaginably high 60% mortality for

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amputations, herniorrhaphies, and other procedures, mostly as a result of wound infections.

As in the case of other discoveries or inventions, the expansion of the concepts of asepsis and antisepsis required three essential elements:

1. *The "Inventor,"* who conceives the idea but seldom has the ability to convince his peers of its significance (the spark must fall upon flammable material in order to start a fire). The inventor is seldom equipped for this.
2. Therefore the "disseminator," who perceives the significance of the discovery is needed. By forecasting its usefulness, the disseminator facilitates its widespread utilization, allowing the conflagration to occur. Both individuals are equally important, as many brilliant thoughts have remained obscure for decades for lack of adequate diffusion. The mentality of both the creator and the disseminator are different, and so are their goals.
3. The third human element, the "disclaimer or denier," appears to complete the equation and, by negating what seems obvious, becomes responsible for moderation, forcing clarification of the original concept. This individual decelerates the utilization of the method, producing a counterreaction from the inventor who, under pressure to prove the new idea makes it more intelligible and thus facilitates its comprehension.

All this was present in the development of asepsis and antisepsis (Fig. 1).

II. ON HOW WHAT IS NOT SEEN DOES NOT "EXIST" AND WHY AIR WAS BLAMED FOR PUTREFACTION

In the early 1800s, little was known about the pathogenesis, treatment, and prevention of surgical infections. About 4 to 5 days postoperatively, surgical wounds would suppurate, and the patient's fate would be decided by the progression of the infection. Some well-drained wounds healed, but the majority of patients went on to suffer sepsis, shock, and death.

Except in matters of religion, humans are brought up to believe what they see and the naked eye cannot perceive anything smaller than 30 μm; thus, at a time when no one could see bacteria, no one could

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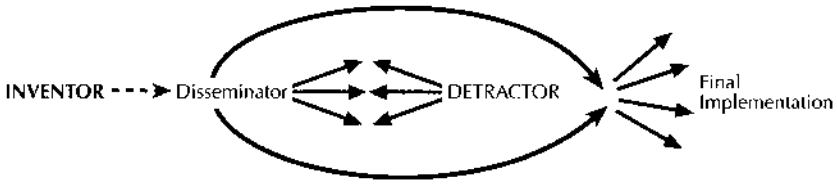

Figure 1 Diagrammatic interpretation of the path followed by the development and implementation of new ideas. Perennial detractors play an obnoxious, but perhaps necessary, role.

imagine their role in infection. A 60% mortality due to sepsis was considered *the normal evolution of surgical procedures*, just as naturally as we accept our present wound infection rates. The thought process needed to improve those conditions followed the sequential uncovering of a biological environment suspected by only a few. What follows is an attempt to narrate this process chronologically, recognizing with humility that many sparks flew in different regions of the world, but few developed into real fires.

In 1200, Roger Bacon discovered optics, and with that background, Anton van Leeuwenhoek in 1667 invented the microscope, which was improved a year later by Robert Hooke. This opened a new biological dimension, and in 1749, while looking through a microscope, John Needham observed the presence of microscopic corpuscles, the role of which was still unknown [1]. Meanwhile, the nature of meat putrefaction, a very significant event curtailing food preservation, had puzzled many; air and oxygen were blamed for its occurrence. At about that time, however, Spallazini observed that boiling prevented the decomposition of meat. Working on the same problem, Francesco Redi in 1687 forestalled maggot infestation by covering with gauze a jar containing meat. These findings gave sustenance to the idea of "contagium," hinting at the then far-fetched possibility that maggots did not emerge spontaneously but were implanted in the meat by a carrier responsible for their presence. In answer to this, flies kept a low profile. By 1794, John Hunter had established the principles of experimental methodology, creating a new discipline that would thenceforth govern scientific research [2].

During the eighteenth century, chemists had serendipitously discovered substances that would later be used as antiseptics: chlorine by von Scheele in 1774; iodine by Bernard Courtois in 1811; and creosote, distilled from beechwood tar, by Karl Reichenbach in 1833. In 1835, Friedlieb F. Runge discovered carbolic acid, which in 1860 was used in

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wounds by Jules Lemaire—who, by the way, did not comprehend the role of bacteria in wound infection and probably used it to eliminate unpleasing odors. Apparently, Robert Collins, in 1829 had already attempted to prevent puerperal fever by washing his instruments in chlorine [3].

III. WHEREUPON BACTERIA REAR THEIR UGLY HEADS TOO BOLDLY AND ARE BEFITTINGLY BLAMED FOR WHAT THEY DO

As in any other field of medicine, the question of the *possibility of improvement* must be considered if changes are to occur. In the field of surgical wound infection, it is difficult to single out an individual responsible for all the progress that has been made. Those who, in the early 1800s, realized that hospital infections and the resultant mortality were unacceptable and should be reduced or eliminated were the leaders in the struggle that followed.

The early 1800s brought forth a multidisciplinary conflagration of ideas, which came to light sequentially in several European hospitals and laboratories. These thoughts were about the presence, biological functions, and role in human infections of microscopic corpuscles latter called *bacteria*. In 1836, Franz Shulze reported that air bubbled through acid did not carry those particles; by the same time, Tyndall discovered that air dust contained germs. The next year, Theodore Schwann, observing that the boiling of meat prevented its putrefaction, blamed putrefaction on organic particles that could be rendered harmless by heating. Thus the concept that those particles could be killed or eliminated by physical means began to evolve. Also at that time, John Hunter injected pus from a patient with gonorrhea into his skin, producing a boil in his forearm; unexpectedly contracting syphilis in the process. This experiment was crucial to the idea that an infection could be transmitted by pus or an agent present in it [2]. In 1840, Oliver Wendell Holmes suggested that germs were transmitted from patient to patient, further stating in 1842 that puerperal fever could be propagated in such fashion [1].

This observations became possible because the investigative powers of physicians matured as their education became broader and deeper. Most importantly, medical and scientific societies met, subjects were

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debated, questions were asked, and scientists communicated with each other, cross-fertilizing ideas that led into otherwise unexplored regions.

IV. THAT THE CONCEPT THAT THE STATUS QUO IS UNACCEPTABLE IS THE ENGINE FOR CHANGE AND HOW SOME TOOK THAT BUMPY ROAD

Broadcasting the impact that wound infections had on surgical outcomes, J. Malgaine reported in 1842 that between 1836 and 1840 the mortality for amputations at nine Paris hospitals was 52% [4]. Similarly, in 1859, J.Y. Simpson reported in the *Medical Times & Gazette* that between 1842 and 1843, of 43 patients who underwent amputations, 21 died, for a 48.8% mortality rate. It is not known whether these figures were considered a surgical triumph; they were accepted by most, but some may have considered them inappropriate and susceptible to change [5].

Ignaz Philipp Semmelweis graduated as a medical doctor in 1844 and entered the field of gynecology and obstetrics, whereupon he made an observation that carries the same weight today as it did then. The core of his thinking was that puerperal fever, which occurred in 60% of in-hospital deliveries and was associated with a 90% mortality, should be considered unacceptable. He must have had that in mind when he attempted to change the status quo. Around 1847, Semmelweis made two outstanding observations related to the contagious nature of puerperal fever. First, he noted that women who delivered outside of the hospital fared better than those who were admitted and treated by obstetricians, who commonly transited from performing autopsies to the delivery room without washing their hands. Second, his friend and colleague Kolletscka died of septicemia after receiving a knife wound during an autopsy—a common outcome until the advent of penicillin, around 1940. Semmelweis correlated both events, perceiving that something present in the cadavers could be transmitted to the parturient, producing an infection. Linking both events, he began washing his hands in chlorinated lime before attending a delivery. Between 1847 and 1848, Ferdinand Hebra, aware of Semmelweis's ideas, wrote two editorials supporting them and comparing him with Jenner.

Meanwhile, Semmelweis's initial speculations incriminating the obstetricians as vectors of deadly infections produced a violent opposite reaction from his supervisors, and he was not reappointed as Assistant. This action prevented him from continuing his clinical and research

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career. Carl Braun, who succeeded him as Assistant, becoming eventually Chief, turned into the classic denier of Semmelweis's theories, stating that it was simply a materialistic interpretation of the old "miasma" concept. Braun supported others who, apprehensive of identifying the physicians as disease carriers, stated that puerperal fever was spread through the air and not by contaminated hands. Their claim was supported by the discovery of bacteria in women's genitalia, excluding the tainted hands as the only culprits [6].

Carl Mayrhofer—who studied medicine at the University of Vienna and worked with Ferdinand Hebra, a close friend and supporter of Semmelweis—graduated in 1860 and was encouraged by Carl Braun to study parturient fever. Mayrhofer, knowledgeable about experimental methodology, was able to reproduce the disease by injecting decomposed matter into the uteri of rabbits, giving strong support to Semmelweis's thesis. At this stage it is important to understand that the sequence of events producing postpartum fever was being successfully elucidated by these protagonists: (1) the victim was the patient, (2) the port of entry was the uterus, (3) the causative agent was a bacterium, (4) the carrier was decomposing matter, and (5) the vector was the obstetrician's hands. The equation had been resolved with all its components.

Semmelweis seems to have understood that his position was the exact opposite to that of his deniers, and the growing opposition to his ideas became overwhelming until Mayrhofer demonstrated the pathogenesis of childbed fever by his rabbit experiments [6]. Around 1848, that information traveled to other countries either by word of mouth or via journals, and corrective measures were taken in many European hospitals. Semmelweis's simple routine of handwashing before a delivery rapidly lowered the incidence of postpartum infection, giving credibility to his concept. In England, C.H.F. Routh adhered to the concept, reporting his experience in the *Lancet*. In 1849, Johann Klein rebutted the work of Semmelweis, but during the same year this new approach was carried across the Atlantic, and the *American Journal of Medical Sciences* published Semmelweis's work and explained his accomplishments [7]. The concept of transporting culprit material from cadaver to patient was accepted, but no one was sure of precisely which agent was responsible for the infection.

Touching on another aspect of the doctor–patient relationship, were some who disliked skin contact with questionable human matter and, in 1758, a surgeon called Walbaum used sheep's cecum to protect his hands. Later on, in 1834, S. Cooke developed a hard vegetable sap called caioutchiouc, which Goodyear in 1835 transformed into a flexible elastic

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product by vulcanizing it with sulfur. In 1847, W. Catell recommended the use of recently developed rubber gloves for protection against smells and particles during autopsies, and so did Actor. Later on, William Halstead followed that trend, incorporating rubber gloves into his surgical routine [8].

V. ON HOW THE UGLY BACTERIAL HEAD WAS FINALLY DECAPITATED BY BRILLIANT AND TENACIOUS SCIENTISTS

In 1850, a lively debate was being conducted all over Europe about Louis Pasteur's recent refutation of the theory of spontaneous generation (Fig. 2). This view, which suggested that a living organism could be created from nothing, was firmly supported by educated people who, unable to see bacteria, did not believe in their existence. In 1854, Schroeder and von Dusch noted that air filtered by cotton did not

Figure 2 Louis Pasteur (1881). (Courtesy of the Institut Pasteur, Paris, France.)

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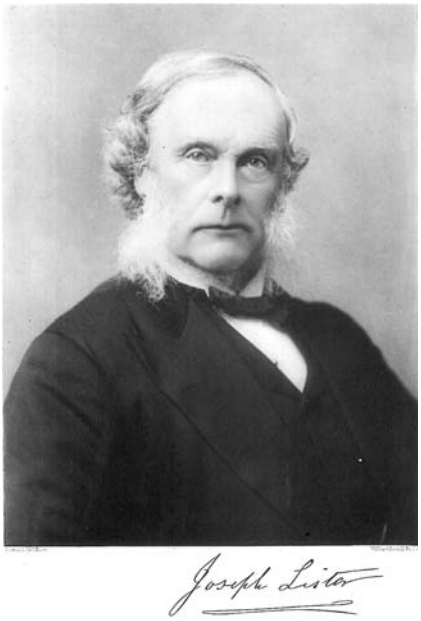

Figure 3 Sir Joseph Lister.

produce putrefaction in meat. Finally, around 1864, in a brilliant sequence of experiments, Pasteur established that elements not seen by the naked eye were responsible for fermentation. F.W. Scanzoni refuted those findings, but Pasteur's ability to convey his ideas to a group of skeptical scientists, poignantly utilizing a routine of self-denial, finally triumphed [9–11].

In 1851, F.H. von Ameth, a firm believer on Semmelweis's ideas, traveled to Scotland and France, converting skeptical colleagues. In 1852, while Semmelweis's recommendations spread through the field of obstetrics and gynecology, Joseph Lister—born in 1827 at Upton in Essex and the son of Joseph Jackson Lister, a London merchant—became a doctor (Fig. 3).

In 1858, Semmelweis published a series of papers pointing to contaminated hands, hair, and linen as sources of infection, thus widening the concept that infections were produced by particles that could reside in many articles that came in contact with patients [7]. In 1859, and while Lister served as a professor of surgery at Glasgow, it became increasingly clear that there was a direct correlation between bacteria and infections. Lister recognized the unacceptability of the

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existing rates of wound infection, and in the early 1860s his friends suggested that he read about Pasteur's work. In 1861, Semmelweis published a textbook describing his results. At the same time Virchow, a renowned medical figure, refuted his work.

In 1863, Florence Nightingale reported that wound sepsis accounted for 40% of overall postoperative mortality and started a very animated campaign to clean up the otherwise filthy hospital wards [12].

During the same period, Italians also attempted to curtail infections. In 1863, Enrico Bottini from Novara started using a 5% solution of carbolic acid dissolved in water as a surgical wound antiseptic and published his results (the effectivness of this attempt is questionable, because phenol does not dissolve well in water). Later on, realizing that carbolic acid at that concentration was caustic, he switched to zinc sulfonate [13]. Equally commendable were the efforts of Bemardino Larghi, an orthopedic surgeon, who in 1862 treated wounds with silver nitrate, and Federico Tosi, an army surgeon, who washed his instruments in a 3% sublimate of mercury solution [13].

In 1864, Lister was impressed by the account of the utilization of carbolic acid, in the form of creosote, to improve the pestilent sewage at the town of Carlisle. The bacterium responsible for the spoilage was *Torula*. Lister made a mental connection between bacteria and the "wound decomposition" that took place after compound fractures. At that time, air was blamed for wound suppuration and gangrene; he, however, rationalized that not all wounds exposed to air become infected, as in the case of pneumothorax associated with rib fractures. In that scenario, the internal wound was exposed to ambient air from which bacteria had been filtered by the nasal and bronchial passages, so that the wound did not become infected. Making the necessary connections, Lister sensed that the culprit was not the air but the bacteria it carried, and he envisioned carbolic acid as a killing agent. That concept was new, and so was its practical application. In 1865, Lister recognized that elective surgery at his hospital produced a 40% mortality rate secondary to wound sepsis and, aware of Pasteur's findings, he began to correlate infection with particles carried into the wound [14–16]. In that same year, Alexander Ogston, of later fame, graduated from medical school [17].

In March 1865, aware that compound fractures had to be routinely treated by amputation to avoid lethal gas gangrene, Lister dressed a fresh compound fracture wound with lint soaked in carbolic acid solution. Infection and amputation nevertheless ensued. But with remarkable tenacity and foresight, Lister tried it again in two other patients, this time

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avoiding sepsis. He reported his results to the *Lancet* in 1866 [14]. Parenthetically, in 1832, Karl Reichenbach had used topical creosote in superficial wounds with success. Starting the unavoidable debate, Lister's report in the *Bulletin Général de Therapeutique* was rapidly rebutted by the *London Medical Gazette*, which stated "we must of course be prepared to hear this new remedy cried out in all quarters until it is displaced by something new" [18].

Lister's findings rapidly influenced those receptive to change, and the idea was disseminated with remarkable speed. That issue of the *Lancet* arrived in America, and in 1867 the *Medical Record* referred to Lister's work, spreading the idea in the New World. The breakthrough was also published in the *American Journal of Medical Sciences* and the *Chicago Medical Examiner*, substantiating the fact that surgical infections were also a catastrophic, unsolved problem in America. In 1868, the anxiety of the American surgeons confronting the feared septic complications was exemplified by the fact that some ventured a then fearsome and dangerous ocean crossing to visit Glasgow and get first-hand information about Lister's work. In 1869, the *American Journal of Medical Science* printed guidelines for the preparation and utilization of carbolic acid while John Ashurst expressed his doubts about its efficacy [20].

Later on, trying to establish and maintain better physical contact between carbolic acid and the wounds, Lister coated them with a paste composed of calcium carbonate and carbolic acid. He also made the important observation that dead bone present in a wound would not allow granulations to heal completely—a fundamental concept in the understanding of wound healing. Semmelweis died that year, and around the same time Lister gave credit to Pasteur for demonstrating that bacteria are present in the air. On September 21, 1867, George Derby of Boston successfully treated compound fractures with carbolic acid, a policy followed by Samuel Cabot at the Massachusetts General Hospital. Edmund Andrews at the Chicago Medical College reported similar events in 1869 in the *Chicago Medical Examiner* [20].

On March 1, 1869, Faneuil D. Weisse, who visited Lister in 1868, addressed the New York County Medical Society on Lister's antiseptic treatment in surgery. At that session, Edward R. Squibb and Abraham Jacobi rose to oppose the method. Henry J. Bigelow also attacked the concept, initiating a controversy that was perhaps beneficial, because it led to the necessity of proof [19,20].

Meanwhile, the news reached Australia, where George Hogarth Pringle reported, in a letter to the *Sydney Morning Herald* on January 30,

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1868, that he had utilized a solution of carbolic acid in glycerin to successfully treat a shotgun wound. He also raised a complaint about stray goats in Marrickville, a suburb of Sydney [21].

In 1868, D.S.E. Bain, an army surgeon from Quebec, described the use of Lister's methods in surgery. This was followed by another report by William Anderson from Newfoundland in 1869. However, in the rest of Canada, the dissemination of Lister's ideas was slow and controversial [22].

In 1870 Lister solidified his principles by reporting that at his hospital, the 60% mortality rate for amputations had dropped to 15% after the utilization of carbolic acid [16].

In Spain, Lister's ideas were introduced in 1873 by Juan Creus y Manso and immediately rebutted in impeccable academic fashion by Adolfo Moreno Poso from Madrid and Nicolas de la Fuente Arrimadas from Valladolid [23].

In London, the concept of antisepsis finally took hold by 1875, when Sidney Jones utilized it in an amputation at St. Thomas hospital, while T. Smith, working at St. Bartholomew Hospital, visited London and became acquainted at first hand with Lister's methods [24]. Meanwhile, Lister's fame grew, and in 1876 he traveled to America to address Congress on his advances in the management of antisepsis, substantiating the fact that hospital sepsis was a worldwide problem recognized by surgeons, politicians, and the public alike.

In America, there was evidence that some scientists and doctors had begun to relate other specific infections to bacterial elements and, in 1861, Francis Peyre Porcher of Charleston blamed a specific "ferment" for scarlet fever [20].

In 1876, Robert Koch's work about the role of bacteria in infections gave theoretical foundation to Lister's ideas. Koch left for London in 1877. That same year, Ferdinand Cohn observed that spores were not killed by boiling, opening a new chapter on the vitality of microbes and their resistance to different agents [25].

Lister's concepts were widely disseminated and, in 1877, Mexican-born Jesus San Martin (who had graduated from the Medical School of Paris with his thesis "Plaies de sereuses traitées par le pensement de Lister") introduced those principles in Durango, Mexico, from whence they spread throughout the country [23,26].

In a similar vein, in Buenos Aires, Argentina, Dr. Augusto Montes de Oca, a young surgeon attempted to introduce Lister's principles circa 1876 but failed because of popular rejection. By that time, Dr. Ignacio Pirovano who just returned from a European Hospital tour where he met

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William Ferguson—an eminent London surgeon—and Joseph Lister, decided to reintroduce his principles and in 1877 succeeded by demonstrating tenacity and faith.

Meanwhile, advances in asepsis continued and in 1878 De Posset [26] remarked that Gailland Thomas from New York uses rubber gloves during his operations. That same year, H.H. Clutton reported on 18 cases of strangulated hernias operated at St. Thomas Hospital in London, with a mortality of 3 [16%], and 12 infections [88%] [27].

In 1879, Alexander Ogston acquired a Zeiss microscope and a year later discovered and described *Staphylococcus aureus* in the pus collected from an abscess. This led to a heated debate at the American Surgical Association, demonstrating the rapidity with which ideas diffuse [19].

By 1880, the work of Pasteur and Lister was accepted by most scientific societies, while at the same time Ogston, a staunch supporter of Lister, published his results, demonstrating that pus from "hot" abscesses contained bacteria, while that of "cold" ones did not. By that time the relationship between bacterial particles and infection seems to have been well established; the question remained how two destroy these bacteria.

In 1880 Tucker reported that Papin from St. Louis was using carbolic acid to prevent infection. In the same year, Robert Koch changed the field of infectious diseases forever by writing his postulates, which not only link bacteria to infections but also create the concept of specificity, proving that each microorganism produces a different kind of infection [25]. Counterpointing these concepts and ingeniously wrong, Watson Cheyne stated—"that pus is just a good culture media for bacteria," turning around in classic controversial fashion an otherwise very clear concept. This reiterates the fact that the birth of new ideas faces the synchronous birth of denials, which seem to grow at the same rate and in opposite direction [19,20].

By 1881, Lister was attempting to kill environmental bacteria by spraying carbolic acid into the operating room air; a complicated and cumbersome system that was soon abandoned. By this time, the delivery of carbolic acid into wounds had become controversial and somewhat confusing.

In 1881, Ogston confronted the problem that immersion of the hands in a carbolic acid solution only kills superficial skin bacteria and may not eliminate those located within the sweat glands—a problem that has yet to be solved [17]. In that same year, Koch discovered that mercuric chloride is also bactericidal, adding another compound to the now growing list of

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agents used for antisepsis. He further recommended that objects potentially contaminated by bacteria could be sterilized by heat [25].

The concept that bacteria are present everywhere in an operating theater raises the question of how to eliminate them from everything that comes in contact with the patient. This gave birth to the idea of creating barriers in the form of gowns, gloves, shoe covers, and caps. That thought—in other words, *asepsis*—was introduced in 1880 by William Harrison Cripps at St. Bartholomew Hospital an idea that had probably been brewing in the minds of many surgeons. But not everybody was happy about those changes. In 1881, therefore, at the same hospital, Sir William Savory, Morrant Baker, and Alfred Williett vigorously combated the idea of asepsis, stating that a clean operating theater might be sufficient [24]. In 1882, Bultin introduced mercury compounds for antisepsis, and in 1883, John Duncan reported that 40% of wounds washed with carbolic acid still contained bacteria, adding depth to the problem of bacterial survival and resiliency.

In 1883, Rosenbach described *Streptococcus*, adding an additional element to the new newly discovered family of bacteria; the world of bacteriology was widening, and so was the gravity of its challenge. Contemporarily, Ogston, a rabid follower of Lister, utilized five assistants to spray carbolic acid in an operating theater, demonstrating that one can carry a concept too far [17].

Between 1883 and 1884, B.A. Watson and Henry Orlando Marcy (who resolutely supported Lister in America) firmly accepted Koch's theory of bacterial specificity, cementing in America the modern understanding of the pathogenesis of infections [20]. Finally, in 1884, Neuber from Berlin consolidated the field of asepsis by using gowns, caps, and shoe covers in the operating rooms, all sterilized in his recently invented autoclave, which was based on the use of pressurized overheated steam [26]. The routine of dressing the surgical team in aseptic regalia was further developed by Ernest Von Bergman and C. Schimmelbush; their measures were eventually adopted by all of the world's major hospitals [28].

In 1885, *JAMA* printed an article disclosing the overall approval of this concept, while in New York, William Halstead decided to conduct surgery in a tent set in Bellevue Hospital's backyard, stating that the hospital could not match his needs for a cleaner environment [26]. His revolt probably marked the first conflict between doctors and hospital administrators, the results of which are still pending. Back in England, Lister continued to develop his ideas, abandoned the spray as unnecessary and probably ineffectual, but started sterilizing sutures and

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ligatures soaked in carbolic acid, adding another sterile element to items in contact with the wound. In 1888, H. Davidshon solved the problem of instrument rusting secondary to boiling by adding an alkaline to the water. Thus the number of sterile components present in the operating field was again increased [24].

In 1889 and closer to the problem at hand, H.B. Robinson from St. Thomas hospital in London reported on 57 nonstrangulated inguinal hernias operated on, with a wound infection rate of 25% and a 6% mortality, all from septic complications [29].

In 1890 Von Bergman presented to the 10th International Congress of Surgeons in Berlin his concept of utilizing sterile gowns, pants, caps, and shoe covers, while in that same year the *Lancet* called all this effort wasteful and useless, stating that cleaner hospitals would be the answer to wound infection [16]. The next year, Marcy reported that asepsis, with all its rigors and regalia, was now accepted in America. From then on, even the water utilized in the operating room was filtered, and in 1894 surgical wounds were covered with sterile dressings, replacing antiseptic ones [19].

In 1897 Flugge discovered that cough droplets contained bacteria and Mikulicz, a prestigious surgeon, decided to use a face mask, spreading the concept of asepsis. But this was not fully accepted, and many surgeons continued to operate without them well into the 1900s [26].

In 1898, William Harrison Cripps began the bacteriological sampling of wounds, leading to the isolation of the various flora present within them. In 1900, Joseph C. Bloodgood introduced the use of rubber gloves in the United States [20].

VI. WHEREUPON EACH MUSICIAN INTERPRETS MUSIC IN HIS OR HER OWN WAY

It is interesting to note that aseptic and antiseptic principles were interpreted differently by different surgeons: Monahan, in the 1905 edition of his textbook, insisted that surgeons utilize complete sterile regalia, including rubber gloves [30], while Theodore Kocher, from Bern (later awarded the Nobel Prize for Medicine), in his 1911 textbook, firmly advised that surgeons wash their faces, heads, hair, and teeth(!!) with a 0.5% carbolic acid solution before operating. He also recommended that their hands be washed with 70% ethanol and rinsed often during the

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operative procedure. Strangely enough, he also advocated the use of gloves "in between operations . . . to be removed just before surgery." The surgical procedure was then to be performed with bare hands [31]. The acceptance of all this methodology depended on its interpretation by a variety of leading individuals. The train of thought was directed toward understanding that bacteria were transported from the environment into an otherwise sterile wound. Later on, William Halstead, a determined and most powerful architect of American surgery, indoctrinated dozens of brilliant young surgeons on the necessity for careful, delicate, and germ-free surgery, principles adhered to by all today [32]. However, the problem remains that bacteria continue to enter wounds from controllable sources, producing still unacceptably high rates of wound infection. Although this problem is not totally dismissed, it tends to be politely ignored.

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2

Incidence and Epidemiology of Infection After External Abdominal Wall Herniorrhaphy

State-of-the-Art Overview, Obstacles, and Recommendations

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I. INTRODUCTION

Every surgical procedure can be considered an exercise in infection control, and surgeons have curtailed wound infections by adopting aseptic and antiseptic methodology. However, in spite of their efforts, the infection rate of so-called clean wounds has remained between 2 and 3% for the last 40 years [1]. Elective inguinal herniorrhaphy has an estimated infection rate ranging from 2–4%, generating over 25,000 infected

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wounds per year in the U.S.A. Nonetheless, these figures may not be accurate, because the reported range is from 0.6–14%. These statistical discrepancy may be due to the fact that elective inguinal herniorrhaphy should be considered "clean surgery," and as such its infection rate should match the rate of that category.

In order to establish the real impact of postinguinal herniorrhaphy infection we needed accurate figures about its incidence. But as we approached this subject, we realized that the available data were sparse and inaccurate due to several factors. The most significant shortcoming was the lack of a valid classification for post–inguinal herniorrhaphy infections; thus most of the published information was based on the subjective interpretation of clinical facts. In attempting to elucidate the real infection rate of external abdominal wall herniorrhaphy, we discovered—as in other research endeavors—unexpected complexities, misconceptions, and sparse guidelines. Our study led us to the conclusion that surgeons tend to underestimate their own infection rates by inadequately evaluating their patients' wound status and failing to share their findings with epidemiologists who, on the other hand, seldom share their findings with the surgeons. In between both elements is the nurse epidemiologist who, following the patient at close range, should relay such information to both surgeon and epidemiologist. However, this trilogy of qualified professionals seldom meet to exchange their findings, seriously complicating any proper interpretations. To obscure matters yet more, this group lacks a reliable and reproducible classification of wound infections on the basis of which to categorize their clinical findings. For these reasons, we feel that new methodology is needed to established a true postherniorrhaphy wound infection rate.

This chapter, first, details our review of the past and present literature dealing with "clean" wound infection rates. Second, it attempts to estimate the postherniorrhaphy infection rate. Finally, it reviews our personal evaluation of the problem, adding suggestions regarding methodology that may be utilized by surgeons, epidemiologists, and nurse epidemiologists.

II. NOSOCOMIAL INFECTIONS

Nosocomial infections are considered to be the consequence of hospitalization. It is estimated that anywhere from 3–5% of all discharged patients have acquired such an infection [1], and the incidence changes

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depending on the surgeon, hospital, and even patient population [2]. Surgical infections belong in the category of nosocomial infections, and they are considered indicators of the quality of medical care [3]. Approximately 45 million surgical procedures were performed in the United States in 1999, each involving the insertion of biomaterials in the form of sutures, meshes, and temporary or permanent implants [4,5].

In the United States, the Institute of Medicine estimates that 2.1 million nosocomial infections occurred yearly, for an estimated cost of $17–$29 billion per year, and that each infection costs between $583 and $4886 [6].

Approximately 325,000 surgical site infections (SSIs) occur yearly in the United States, costing over $1 billion. Furthermore, these operations are the second more frequent cause of nosocomial infections, with an incidence of 25% and they are responsible for approximately 140,000 deaths per year [7,8]. Wound infections can be considered emergent diseases, and their relevance is magnified if they involve a biochemical prosthetic device [5].

The prevalence of inguinal hernia in the U.S. male population is estimated to be 4% [9], and its repair is the most commonly performed elective surgery worldwide, accounting for approximately 750,000 operations yearly in the United States, 105,000 in Germany, 26,000 in Holland, 16,000 in Denmark, 18,000 in Sweden, 8000 in Switzerland, and 75,000 in Mexico, for a total of over 1 million hernia repairs per year [9–11]. If the infection rate were 3%, that would generate a staggering 22,500 yearly infections in the United States alone.

III. QUESTION

What is the worldwide incidence of infection after external abdominal wall herniorrhaphy?

A. Methodology

In 2002, in order to answer our fundamental question, we conducted a PubMed search utilizing the following key words: *inguinal hernia, incisional hernia, umbilical hernia, adults, infection, mesh*, and *randomization*, obtaining the results shown in Table 1.

Of the articles listed in Table 1, note that 35% included the word *infections*, 11% *mesh*, and 5% *randomization*.

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Table 1 Pub Med Search of Publications Dealing with Abdominal Wall Herniorrhaphy[a]

Key words	Number of articles	Date
Inguinal hernia		
adults	3277	1965–2002
adults, infection	246	1967–2002
adults, infection, mesh	76	1979–2002
adults, infection, mesh, randomized	25	1980–2002
Incisional hernia		
adults	386	1966–2002
adults, infection	135	1980–2002
adults, infection, mesh	43	1980–2002
adults, infection, mesh, randomized	20	1980–2002
Umbilical hernia		
adults	533	1965–2002
adults, infection	26	1968–2002
adults, infection, mesh	4	1964–2002
adults, infection, mesh, randomized	1	2002

[a] This table summarizes articles dealing with inguinal herniorrhaphy published in the last 36 years, demonstrating the difficulties encountered during our review: only 7.5% of these publications included the word *infection*; this figure dropped to 2.3% if *infection* was added and to less than 1% after *mesh* or *randomization*.

Of articles dealing with adult umbilical herniorrhaphy, only 5% included the word *infection*, 0.75% *mesh*, and 0.18% *randomization*.

These figures demonstrate the lack of uniformity and completeness in the available publications. Most importantly, the vast majority of articles dealing with external abdominal herniorrhaphy failed to mention any form of wound infection classification that would help categorize those complications.

During the review and because we could not ascertain the infections' anatomical location, their severity or the responsible bacteria, we decided to arbitrarily divide them into two categories:

1. Superficial infections: those including subcutaneous cellulitis, abscess or purulent exudate, all located above the external oblique aponeurosis and requiring incision and drainage plus systemic antibiotics and wound care.
2. Deep infections: those extending beneath the external oblique aponeurosis requiring incision and drainage. They may be associated with sinus tracts and may require prosthesis removal.

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B. Inguinal Herniorrhaphy

We performed a Pub Med literature review of 73 articles published on inguinal herniorrhaphy between 1965 and 2002. This included a 95% confidence limit, a frequency of 7%, and a design effect of 0.05. The randomized sample size was 73. In the presence of continuing variables, we determined the median and standard deviations. We calculated associated measures.

Of the 73 articles analyzed, 77% (56) were prospective, 18% (13) retrospective, and 6% (4) not specified. A total of 6.8% (5) of the studies were audited; 59% involved one hospital, 22% (16) one author, 14% were multicentric, 5.5% were national, and 23% (17) were randomized. The countries with more publications, were the United States, with 24; England, with 11; Germany and Italy, with 5 each; and France, with 3. The majority of the publications were from the last 12 years (Table 2).

These 73 reviewed articles yielded a total of 123,028 operations performed on 116,342 patients. Of the total, 42% of the articles mentioned the patient's gender (38,155 males vs. 2890 females). The median age was 57.01 ± 6.75. Of the herniorrhaphies, 96% were inguinal 16% femoral, 96% were not incarcerated, 14% were incarcerated, and 5.5% were strangulated.

Although 51 articles mentioned the utilization of a prosthesis, only 45% were specific about its composition: 53% (39) utilized polypropylene, 7% (5) ePTFE, and 1.4% (1) polyester. Twenty authors (27.4%) reported antibiotic utilization, 6 (8.2%) did not, and 47 (64%) did not specifiy either way. Four (5.5%) authors utilized a placebo. As far as the route of administration was concerned 13 (18%) authors used the intravenous route: Cefalosporin in 8 cases (11%) and gentamicin in 1 (1.4%) (Table 3).

Table 2 Articles Dealing with Inguinal Herniorrhaphy That Mention Prostheses and Infection

Date	Infection rate	Percent (%)
1960–1969	1	1.4
1970–1979	1	1.4
1980–1989	3	4.1
1990–1999	43	58.9
2000–2002	25	34.2
Total	73	100

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Table 3 Infection Rates Related to Prosthesis Utilization[a]

Infection	Number of cases	Range/percent (%)
With mesh	194	0.10–10
Without mesh	203	0.28–9
Not mentioned	314	0.10–14.04
Total	711	

[a] Note that these rates range from 0.68–14.4% and cannot be correlated with prosthesis utilization.

A total of 58% of the reported infections were diagnosed as superficial and 21% as deep. However, the need for mesh removal was not mentioned in either type, further complicating the evaluation of results (Table 4). Three articles dealing with laparoscopic surgery reported three infections, with an incidence of 0.03%.

Only 10 (14%) of the articles mentioned that a bacterial culture was obtained. The most frequently encountered bacterium was *Staphylococcus aureus*, sometimes combined with anaerobes, coliforms, or *Escherichia coli*.

A total of 43.8% of the patients were managed on an ambulatory basis; 48% needed hospitalization for more than 1 day.

It is important to stress that in our Pub Med search, only 7.5% of the articles dealing with inguinal herniorrhaphy contained the keyword *infection*, 2.3% mentioned the presence of mesh, and less than 1% mentioned randomization. This sparseness of data occurred because the presence of wound infection was omitted from the majority of articles dealing with herniorrhaphy.

Table 4 Number of Articles Describing Infection Location[a]

Type infection	Number of articles	Percent (%)
Superficial	42	57.6
Deep	15	20.5
Type not specified	16	21.9
Total	73	100.00

[a] Note that superficial infections were reported more frequently than deep ones.

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Therefore, in accord with the published data, postinguinal herniorrhaphy infection rates range from an improbable 0.1% to a staggering 14%, leading us to believe that both figures are statistically inaccurate and not acceptable. We then hypothesized that the real worldwide infection rate after inguinal herniorrhaphy is hidden by reporting deficiencies emanating from surgeons and epidemiologists. In order to gather a more precise evaluation of this problem, we analyzed it from two different prospective views: that of the surgeon and that of the epidemiologist.

C. Why Are Infections Not Being Routinely Reported?

Several reasons for improper infection reporting have been studied. First, the proper definition of a surgical wound infection may be a matter of personal interpretation. One surgeon may consider a subcutaneous collection trivial while another may label it a real wound infection. The presence of pus or any other form of exudate emanating from a given wound may be perceived differently by different surgeons, by different geographical communities, or even by different countries. Such idiosyncracies may also change according to teachings, philosophies, or historical backgrounds, revealing an urgent need for adequate definitions that will permit satisfactory statistical evaluations of outcome.

Some investigators have attempted to clarify these issues. Polk [86] in 1975 and Condon [87] in 1983, respectively, suggested the following reasons for underreporting:

> (1) A human honesty factor leading to underreporting of either suspected or documented infections. (2) Some surgeons' tendency to hide adverse results because of apprehension of unfavorable peer reviews or loss of referrals. (3) The great majority of postinguinal herniorrhaphy patients are discharged without adequate follow-up; thus infections are not detected. (4) Follow-up extension and methodology are extremely important to establish truthful infection rates [82].

Moreover, epidemiologists and surgeons work over the same subject at different intellectual and methodological levels, complicating matters further. The former systematize clinical results at a national level, while the latter limit themselves to their hospital experience. Our discussion focuses first on the epidemiological level and later from the surgeon's point of view.

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IV. EPIDEMIOLOGICAL EVALUATIONS

A. Community Surveillance Studies

Epidemiology is the science concerned with the occurrence, distribution, and determinants of health conditions and disease in human groups and populations. Epidemiological studies have three principal goals: (1) to provide the required information about specific disease groups in a given community; (2) to study the etiology and natural history of a disease, its growth and development from a general point of view and within specific locations; and (3) to contribute to public health care evaluation in specific locations and extrapolate them to general situations.

Community studies answer five cardinal questions:

1. What is the community's state of health?
2. What are the factors responsible for that state of health?
3. What is being done about it by the health care system and by the community itself?
4. What more can be done, what is proposed, and what is the expected outcome?
5. What measures are needed to continue the community health surveillance and to evaluate the effects of what has been done [88]?

Community surveillance should include the following elements:

1. Each operated patient should be evaluated as an individual at risk of infection and included in a protocol.
2. Postoperative patients should be seen daily and the wound classified utilizing specific criteria.
3. The final wound evaluation should be performed 4 weeks after surgery.
4. The clinical surveillance starts in the hospital and ends at home [89].

B. Studies on Community Surveillance of the Surgical Wound

Surgical site infections may be minimal or lethal, and they have serious social, economic, psychological, and legal consequences for both patient and surgeon [90].

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Epidemiological studies involving community surveillance (CS) of the outcome of clean wounds are carried out in the United States by the Centers for Disease Control in various programs, such as: Hospital Infections Program, Center for Infectious Diseases of the CDC, National Nosocomial Infections Surveillance (NNIS), Study on the Efficacy of Nosocomial Infection Control (SENIC). Hospital Infection Control Practices and its Advisory Committee (HICPAC). In the United Kingdom these functions are carried by the Second National Prevalence Survey of Hospital-Acquired Infections (SNPSHAI).

Community surveillance studies have determined that although approximately 50% of surgical site infections present themselves in the first postoperatively week, 90% of them were diagnosed within the first 2 weeks postoperatively; therefore a very important percentage of surgical site infections occurred after the patient had left the hospital. These late manifestations of infection hamper a true assessment of the real infection rate if such a rate is recorded before hospital discharge. Therefore, those findings have important public health implications because, without proper feedback, the adequate learning process for infection prevention and control may not occur [91].

In 1964, recognizing that a reporting problem existed in the United States, the National Research Council and the Committee on Trauma of the United States, led by W.A. Altemeier, divided surgical wounds into clean, clean contaminated, contaminated, and dirty [92]. Following this, several investigators reported their experience with surgical wound infections. In 1980, Canada's Foothills Hospital studied the outcome of 62,939 surgical wounds, stating that 1.5% of their infections occurred in clean wounds, 7.7% in clean contaminated wounds, 15.2% in contaminated wounds, and 40% in dirty wounds [93].

In 1992, The Program for Hospital Infections of the Centers of Disease Control, the Society for Hospital Epidemiology, the American Medical Association for Infection Control, and the Surgical Infections Society changed the nomenclature from surgical wound infection to surgical site infection (SSI), dividing them into superficial incisional, deep incisional, and organ/space, further defining the diagnostic criteria of SSI according to the pathological anatomy [92,94].

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C. Definition of Superficial Incisional SSI

These are infections occurring within 30 days after the operation and involving only the skin or subcutaneous tissue of the incision and at least one of the following:

1. Purulent drainage from the superficial incision with or without bacteriological laboratory confirmation.
2. Organisms isolated from an aseptically obtained culture of fluid or tissue from a superficial incision.
3. At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness or heat, plus a superficial incision deliberately opened by a surgeon unless the exudate culture is negative.
4. Diagnosis of superficial incisional surgical site infection by the surgeon or attending physician.

The following conditions should not be reported as SSI:

1. Stitch abscess (minimal inflammation and discharge confined to the point 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 (see ''deep incisional SSI,'' below).

Note: Specific criteria are used for identifying infected episiotomy, circumcision sites, and burn wounds

D. Deep Incisional SSI

These are infections occurring within 30 days postoperatively if no implant is left in place or within 1 year if an implant is in place. The infection should be related to the operation involving deep soft tissues (e.g., fascial and muscle layers) in 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. Spontaneous dehiscence of a deep incision or an incision deliberately opened by a surgeon when the patient has at least

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one of the following signs or symptoms: fever (>38°C), localized pain, or tenderness unless the site is culture-negative.
3. An abscess or other evidence of infection involving a deep incision found on direct examination or reoperation or by histopathological or radiological examination.
4. Diagnosis of deep incisional SSI by the surgeon or attending physician.

Recommendations:

1. Report infections involving both superficial and deep incision sites as deep incisional SSI.
2. Report and organ/space SSI that drains through the incision as a deep incisional SSI.

E. Organ/Space SSI

The Infection should occur within 30 days after the operation if no implant is left in place or within 1 year if an implant is in place. The infection should appear to be related to the operation and may involve any part of the anatomy (e.g., organs or spaces) other than the incision that was opened or manipulated during an operation plus at least one of the following:

1. Purulent drainage from a drain 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 on direct examination, during reoperation, or by histopathological or radiological examination.
4. Diagnosis of an organ/space surgical site infection by the surgeon or attending physician.

F. United Kingdom Studies

In 1996, The United Kingdom's National Health Service (NHS), through the Public Health Laboratory Service (PHLS) established the Nosocomial Infection Surveillance Unit (NISU) in response to the department's commissioning of a project to develop a national surveillance scheme for hospital-acquired infection. This project is known as the Nosocomial

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Infection National Surveillance Scheme (NINSS) and is managed jointly by the Department of Health and the Public Health Laboratory Service. The aims of NINSS are as follows [95]:

1. To provide national statistics on hospital-acquired infection for comparison with local data.
2. To improve patient care by helping hospitals to change their clinical practice and reduce rates and risk of hospital acquired infection.

G. U.K. Definition of a hospital-Aquired Infection and a Surgical Site Infection

A Hospital-acquired infection (HAI) is an infection found to be active or under active treatment (at the time of the survey) which was not present or incubating at the time of admission to hospital. Further,

1. A patient readmitted with an established infection which has resulted from an earlier admission is recorded as suffering from HAI.
2. When doubt exists, infections appearing at or after 48 h are classified as HAI.
3. Some community-acquired infections (CAIs)—e.g., typhoid—have incubation periods greater than 48 h.

As to diagnostic criteria for the presence of an infection (HAI or CAI), there should be clinical evidence of infection. Colonization is to be excluded other than by methicillin-resistant *S. aureus* (MRSA) and aminoglycoside-resistant enterobacteria [96].

H. Wound Infection

A wound is defined as a break in an epithelial surface, which may be surgical or accidental. A wound infection should exhibit a purulent discharge exuding from the wound or a painful spreading erythema indicative of cellulitis. Infection should be considered to be present when there is fever ($>38^{\circ}C$) tenderness, edema, and an extending margin of erythema or the patients is still receiving active treatment for a wound that has discharged pus.

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I. Notes

1. Burns, ulceration and pressure sores have been excluded from this definition, but drain sites should be included.
2. Bruising, hematoma formation, and serous and lymph collections, are complications that may predispose to the development of wound infection and may lead to diagnostic difficulties.
3. The discharge of clear fluid from a wound does not indicate an infection unless accompanied by cellulitis.
4. The definition of wound infection should not be dependent on the results of bacteriological studies.
5. False-negative cultures can occur, and on other occasions organisms isolated from cultures may represent either secondary colonization or merely contamination.
6. Wound infection may be classified according to etiology or severity.
7. As to primary and secondary wound infections, the infection should be considered primary unless there is a predisposing complication. Secondary infection may follow a complication that results in the discharge of serum, hematoma, cerebrospinal fluid, urine, bile, pancreatic juice, or gastric or intestinal contents from the wound contaminated by bacteria from within the patient or from the environment.
8. As to severity, a wound infection should be classified as minor when there is a discharge of pus from the wound without lymphangitis or deep tissue destruction and as major when the purulent discharge is accompanied by a partial or complete dehiscence of the fascial layers of the wound, deep tissue destruction, or by spreading cellulitis and lymphangitis that require antibiotic therapy.

V. PROBLEMS FOUND IN PUBLICATIONS EMANATING FROM EPIDEMIOLOGISTS

Data collected by surgeons have revealed deficiencies producing unreliable incidence rates, which become apparent when nurse epidemiologists perform community surveillance. Utilizing the above-mentioned classifications, clean wounds community surveillance studies were

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performed in various countries at different periods; results are shown in Table 5.

In the United States, L.L. Rosendorf [91], in 1983 reported a 5% clean wound infection rate. R.E. Condon [87] in the same year reported that surveillance lowered the initial 3% clean wound infection rate to 1%. He attributed this decline to two factors: (1) regular reporting by the surgical staff and (2) the ''sentinel effect'' generated by surveillance programs. Eight years later, R.A. Garibaldi [104] reported an incidence of 2.6%.

D.J.W. Law [101] from the United Kingdom reported in 1990 that the clean wound infection rate in 790 patients was 5.3%; however, in only 1.3% of those was the infection discovered in the hospital, and the incidence grew to 4.1% after discharge.

I. Noel [107] reported in 1997 a 9% frequency, while J. Really [89] recorded an initial 14% rate which dropped to 8% in a later report.

In Germany, Spain, Holland, and Italy, the reported infection rate for clean wounds was between 2.1 and 3.7% [106,108,110,111].

VI. COMMUNITY SURVEILLANCE OF CLEAN SURGICAL WOUNDS AND ITS RELATIONSHIP TO POSTHERNIORRHAPHY INFECTIONS

Several studies have analyzed the infection rate of different surgical procedures considered clean by the CDC, and all of those studies revealed a SSI incidence higher than that reported for inguinal herniorrhaphy (Table 6).

A. Studies on Postinguinal Herniorrhaphy Community Surveillance

Because the great majority of inguinal herniorrhaphies are performed on an ambulatory basis, the role of community surveillance should be fundamental for the evaluation of infection rates. Unfortunately, only an estimated two-thirds of the patients are followed at a clinic, and the rest are not seen by the surgical team after discharge. Furthermore, 40% of patients harboring an infection report them to their general practitioner, thus disturbing the flow of information to the surgeon and the epidemiologist [115].

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Table 5 Results of the Community Surveillance of Clean Wounds in Different Countries[a]

Author	Year	Country	Patients	Number of infections	Percent of infections	Percent before	Percent after	Data
Cruse [97]	1975	Canada	30,989	555	1.8			
Rosendof [91]	1983	USA	493	25	5			3 months
Condon [87]	1983	USA	8,227			3 (1976)	1 (1981)	5 years
Olson [98]	1984	USA	12,503			2.2 (1977)	0.8 (1981)	5 years
Reimer [99]	1987		385	18	4.7			
Brown [100]	1987	USA	688	36	5.2	2.6 (18) H[c]	2.6 (18) C[d]	3 months
Law [101]	1990	UK	797	42	5.3	1.3 (10) H	4 (32)C	
Olson [102]	1990	USA	25,919	373		2.3 (1977)	1.5 (1986)	10 years
Culver [103]	1991	USA	49,333		2.1			4 years
Garibaldi [104]	1991	USA	788	21	2.6			
Moro [105]	1996	Italy	2,262	83	3.7			
Kampf [106]	1996	Germany	3,383		2.1			
Noel [107]	1997	UK		155	9			
Lizan-Garcia [108]	1997	Spain	2,237[b]	60	2.7			
Santos [109]	1997	Brazil	146	19	13			6 months
Mintjes-de Groot [110]	1998	Holland	32,869	25	2.2			
Really [89]	1999	UK	1,851			14	8	2 years

[a] 28- to 30-day follow-up.
[b] Use prophylactic antibiotic.
[c] H = hospital.
[d] C = community.

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Table 6 Other Surgical Procedures Classified as Clean by Community Surveillance Studies

Author	Country	Year	Surgery	Percent of infection without antibiotics	Percent of infection with antibiotics
Platt [112]	USA	1990	Breast	12.2	6.6
Gupta [113]	UK	2000	Breast	18.8	17.7
Hall [114]	USA	2000	Cardiac surgery (sternum)	10	
			Arterial surgery	14	
			Abdominal surgery	5.5	

Some community surveillance studies have documented the incidence of postinguinal herniorrhaphy infection for different countries and periods. (Table 7). Canada, in 1975, reported the lowest infection rate of 0.5% in 1875 patients [97]. In 1960, a multicentric UK [116] study of 21 participating hospitals reported a 7% infection rate, while a 1992 report showed an incidence of 9%, which fell to 3% after a surveillance program was instituted [79]. Equally so, in Italy the infection rate dropped from 14.2 to 7.3% after community surveillance was implemented [118]. Other European countries, such as France, Italy, Germany, and Spain, reported infections rates varying from 2.9 to 6% [83,105–117].

The reported infection rate in the United States ranged from 1 to 4% [102,112]. In one study, antibiotic administration lowered it from 4.2 to 2.3% [112], while in Brazil a community surveillance study reported an infection rate of 14% [85].

This example depicts the accepted reporting methodology when the community surveillance criteria of SSI established by the CDC.

In Brazil, Santos et al. [85] studied postinguinal herniorrhaphy infections, finding a rate of 14.04%. Of these, 87% were discovered after the patient was discharged; only 21.4% of patients responded their mail questionnaires and only one-third of their infections were diagnosed in the first postop week (Table 8).

It seems that the reported incidence of infection depends on the definition criteria or classification used. In 1983, Condon discovered a

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Table 7 Results of the Community Surveillance in Inguinal Hernia in Different Countries[a]

Author	Year	Country	Number of patients	Number of infections	Percent of infections	Percent of infections before	Percent of infections after	Data (years)
PHLS [116]	1960	UK	480	34	7			2
Cruse [97]	1975	Canada	1,875	9	0.5			
Ehrenkarnz [117]	1981	USA	1,637	22	1.3			5
Olson [98]	1984	USA	1,222	14	1.2			5
Platt [112]	1990	USA	20		4.2%[d]	2.3%[c]	2.5	
Olson [102]	1990	USA	2,764	28	1			10
Simchem [81]	1990	Israel	1,487	68	4.6			2
Lazorthes [83][b]	1992	France	162	7	4			
Moro [105]	1996	Italy	527	32	6			
Kampf [106]	1996	Germany			2.9			
Moro [118]	1997	Italy	799			14.2	7.3	2
Santos [85]	1997	Brazil	114	16	14.0			6 months
LizanGarcia [108][b]	1997	Spain	273[c]	9	3.4			
NNI Report [119]	2001	USA	9,292		0.77			9

[a] 28- to 30-day follow-up.
[b] Epidemiologists and surgeon worked together.
[c] Use of prophylactic antibiotic.
[d] Without antibiotic.

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Table 8 Characteristics of Hospital and Outpatient Wound Infection After Hernia Surgery

	Number of cases	Percent
Overall wound infection rate	16/114	14.04
Incisional site infection	13/16	81.25
Organ/space infection	03/16	18.75
Inpatient infection rate	02/16	12.50
Outpatient infection rate	14/16	87.5
Outpatient clinic assessment	11/14	78.57
Postal questionnaire	03/14	21.42
Detection time		
3–7 days	05/16	31.25
8–14 days	09/16	56.25
Over 14 days	02/16	12.50

minor increase in clean infection rates and added that surveillance was difficult because of problems with honesty, denial, or direct coverup [87]. However, there was consensus that home surveillance is effective and can be fulfilled utilizing a variety of available methodologies. Nonetheless, the efficacy and validity of these techniques has defied critical evaluation.

B. Problems with Community Surveillance

Platt et al. [120] in 2001 analyzed the described methodology for CS studies. The majority of the described methods utilized a questionnaire filled by surgeons—a method found to have poor sensitivity (15%) and a positive predictive value of only 28%. Moreover, a surveillance system based on a questionnaire requires a large budget and resources. Patient response to a questionnaire has also shown a poor sensitivity (28%) because many fail to mail back the forms. Telephone surveillance can be effective but is also expensive, as it requires personnel trained with a solid understanding of the natural history of wound infections.

C. Proposed Methodology

There are three modes for data acquisition: (1) in-hospital surveillance, (2) post-patient-discharge surveillance, and (3) a combination of both. To

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achieve these objectives, the survey can be based in the now growing body of epidemiological information routinely collected by health systems, organizations, hospitals, doctors' offices, and insurance companies during the delivery of care. Many of these systems are available, including patient information, surgical procedure, postoperative course, etc.

Accordingly, Platt proposed automated methodology to augment the yield, improve quality, and reduce cost of surveillance methods for surgical site infection [120]. This may permit a solution of the problem of surveillance and feedback to surgeons.

D. Other Classifications Not Considered Official

Wilson in 1984 [121] devised the ASEPSIS method of surgical wound classification, which has been modified and validated. This is based on a given percentage describing the extension of the signs of infection, such as erythema, serous or purulent exudate, and deep tissue separation. Purulent exudate and wound separation are given double points, as they are the most frequent signs of infection (range is 0–10, Table 9). Other parameters included are antibiotic treatment, wound drainage, antibiotic utilization, local or general anesthesia, identified bacteria, and hospital length of stay (Table 10).

Wound evaluation is performed within the first 5 days of the first postoperative week. A score higher than 20 determines the presence of infection (Table 10) [122,123].

The Southampton Wound Assessment Scale (Table 12) is a calificative community and hospital surveillance system created by Bailey in 1985 to study postherniorrhaphy infections. Wounds were qualified in degree 10–14 days postop by a home care nurse epidemiologist.

Table 9 Daily Assessment of Wound Infection: Scale of Points

Wound characteristic	Proportion of wound affected (%)					
	0	<20	20–39	40–59	60–79	>80
Serous exudates	0	1	2	3	4	5
Erythema	0	1	2	3	4	5
Purulent exudates	0	2	4	6	8	10
Separation of deep tissues	0	2	4	6	8	10

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Table 10 The Wound Score—ASEPSIS

Characteristic	ASEPSIS score
Daily scores	
Serous exudates	0–5 by extent for 1 week
Erythema	0–5 by extent for 1 week
Purulent exudates	0–10 by extent for 1 week
Separation of deep tissues	0–10 by extent for 1 week
Score within 2 months	
Antibiotics	10
Drainage of pus under local anesthesia	5
Debridement of wound under general anesthesia	10
Isolation of bacteria	10
Stay prolonged >14 days	5

Microbiological studies were excluded because wound cultures were not routinely obtained [79].

This classification can also be utilized to assess postherniorrhaphy infections.

Two systems have been validated, to obtain objectivity and reproducibility in wound status evaluation: one is called ASEPSIS and the other is The Southampton Wound Assessment Scale, initiated by Wilson, who classified infected wounds utilizing different parameters [121,123].

In 1998, Wilson [123] compared the CDC, NPS, ASEPSIS, and Southampton surgical wound infections definitions and classifications, concluding that ASEPSIS had a sensitivity of $p < 0.0001$, that CDC did

Table 11 Classification of Infection Grade

Classes	Score
Normal healing	0–10
Disturbance of health	11–20
Minor wound infection	21–30
Moderate wound infection	31–40
Severe wound infection	>40

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Table 12 The Southampton Wound Assessment Scale

Grade		Appearance
0		Normal healing
I	Normal healing with bruising or erythema	
a		Some bruising
b		Considerable bruising
c		Mild erythema
II	Erythema plus other signs of Inflammation	
a		At one point
b		Around sutures
c		Along wound
d		Around wound
III	Clear or hemoserous discharge	
a		At one point only ($\leqslant 2$ cm)
b		Along wound (>2 cm)
c		Large volume
d		Prolonged (>3 days)
	Major complications	
IV	Pus	
a		At one point only ($\leqslant 2$ cm)
b		Along wound (>2 cm)
V	Deep or severe wound infection with or without tissue breakdown; hematoma requiring aspiration	

not register 24% of the infections, and that NPS had a 19% failure of infection identification.

VII. AUDITING STUDIES

In the United Kingdom, a clinical audit is defined as an initiative that permits improvements in quality of care through a structured peer review, where the clinicians analyze their practice and results, comparing them with agreed-upon standards and then modifying their practice accordingly and when indicated [10].

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Reid in New Zealand published in 2002 the results of an 18-month prospective audit of 1934 patients with a clean wound infection rate of 12.6%. Hernias had an 8% incidence of infection, vascular surgery 18.3%, and breast surgery 16% [124].

In 1991 the postherniorrhaphy infection rate in Australia was found to be 3% [125]. Parenthetically, in Denmark and Sweden, a study of 34,206 Lichtenstein inguinal herniorrhaphies failed to mention infection as a complication or a risk factor. This demonstrates that some investigators have overlooked these complications [84].

In 1998 O'Riordan published the results of a U.K. audit and also summarized audits in other European countries, but he did not consider infection a complication of inguinal herniorrhaphy [10]. (Table 13).

Emphasizing the role of proper protocol design is a the fact that when surgeons received feedback information about the frequency of infection, a reduction in the infection rate is observed (Fig. 1).

In order to fulfill the requirements of clinical audits, surgeons should be more rigorous with their design.

VIII. ECONOMIC IMPACT OF WOUND INFECTION

These values vary wildely, depending on the institution, the region, and the country involved [126].

In 1980, Brachman et al. found that, in the United States, different hospitals reported different infection rates, with municipal institutions having the highest (7%), followed by university hospitals (5.6%), federal hospitals (5.6%), and community hospitals (4.3%) [127].

IX. COSTS OF INFECTION

Really [89] states that the cost the infection can be divided into three categories: hospital level, community level, and patient level (Fig. 2).

Haley et al. [128] reviewed 16 published protocols between 1933 and 1975, finding that a nosocomial surgical infection resulted in 1.3–26.3 extra hospitalization days, with adittional cost ranging from $670 to $2400. In 1980, Brachman et al. [127] concluded that an infection required 7.4 additional hospital days at a cost of $1100.

The cost of treating an infection was estimated in 1970s to be $5000 to $7000 per patient [98]. However, in 1991, Zoutman [129] studied this

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Table 13 Summary of European Audits of Inguinal Hernia

Country	Holland		Germany		Switzerland		Sweden		U.K.	
Period of audit		1989		1992		1986–1995	1992	1996	1996 (4 months)	
No. of operations per year		26,000		105,228		8,000	20,000		5,038	
Audit of groin hernias							12,542			
Hospitals participating						134	7	21	131	
Percent response of hospitals					74	55%			118	90%
Surgeons	774	94%							368	
Percent response of surgeons									276	72%
Prophylactic antibiotics									2749	61.6%
Surgical technique anatomic	24,960	96.6%	76,500	72.7%	More often Bassini		66%	18%		1,416
Tension-free	260	1%	Rest				7%	51%		3,359
Laparoscopic	260	1%	Rest					21%		493
Type of hospitalization										
Inpatient	15,600	60%								2,914
Outpatient	10,400	40%				33%	52%		4,725	
Complications										
First recurrence hernia	10%					7 to 23				
Second or later recurrence		20%		14.7%				16%		
SSI[a]										

[a] SSI: not reported.
Source: Ref. 10.

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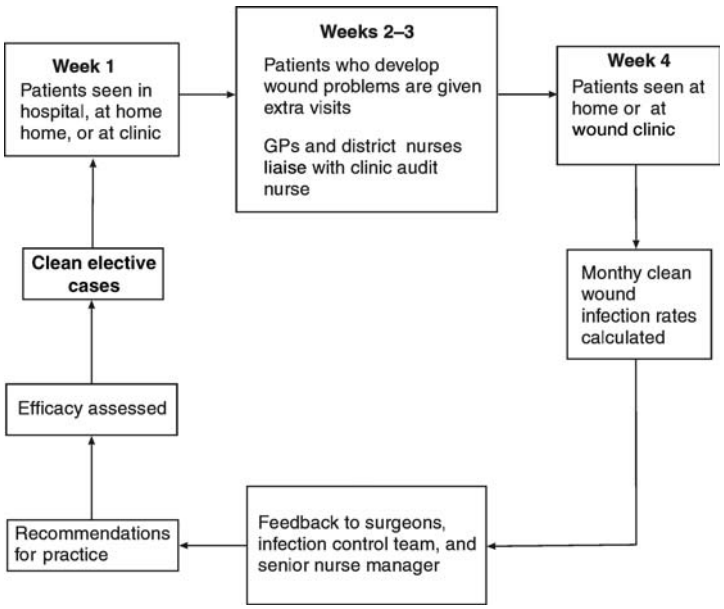

Figure 1 A summary of the methodology of a surgical audit cycle. (From Ref. 89.)

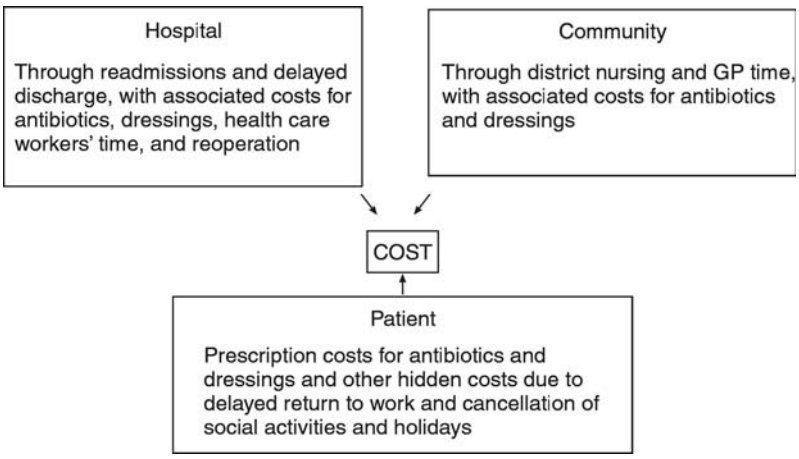

Figure 2 Three elements involved in the cost of postherniorrhaphy infection.

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economic factor in clean and clean contaminated wounds at a Canadian teaching hospital and the total cost was estimated to be $4000 per infection.

In France, Lazorthes published a 1992 comparative study on the results of inguinal herniorrhaphy with and without prophylactic antibiotics. The infection rate in the group that did not receive antibiotics was 4.5%. The calculated cost of antibiotics on a home care basis was $517.22 (162 patients at $3.19 per dose), while the cost of the infected patients was $4975.27—a 10-fold difference, including labor costs and hospitalization expenses. This did not include the revenue lost for unemployment and a possible recurrence [83]. The cost of SSI in the United States has been estimated to be around $5038, taking into account that a complication adds an average of 12 extra hospital days [130].

Postlethwait in his 1985 study of inguinal hernia recurrence did not mention infection as a risk factor after anatomical repairs [131]. Lowham in 1997 did not mention infection as a mechanism of recurrence postpreperitoneal and laparoscopic repair [132]. Bendavid from the Shouldice Clinic reported an infection rate of 0.06% after mesh repair; however, this group utilized a local antibiotic powder. He did not elaborate on the location of the infection [133].

Surgeons dedicated to herniorrhaphy may have a lower infection rate than those who perform this operations as part of a general surgical practice. In 1991, Deysine et al. were able to lower an institutional infection rate from 5.6 to 0.45% ($p < 0.005$) by instituting a surgical protocol [134].

Table 14 Herniorrhaphists Reporting an Infection Rate Lower Than 1%

Author	Year	Infection Rate (%)
Lichtentein [44]	1987	0.20
Deysine [37]	1990	0.30
Berliner [71]	1993	0.29
Rutkow [39]	1993	0.39
Gilbert [31]	1993	0.84
Wantz [80]	1996	0.07
Bendavid [133]	1998	0.06

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X. INFECTIONS FOLLOWING VENTRAL HERNIORRHAPHY

A. Introduction

Approximately 90,000 ventral hernias are operated on yearly in the United States. The majority of these hernias emanate from infected exploratory laparotomies. If postinguinal herniorrhaphy infections are usually circumscribed to the groin, postventral herniorrhaphy infections constitute a major surgical complication that poses a serious challenge to both the surgeon and the patient and may end in the patient's death. In some reports, the infection rate of these hernias is 12% [135–139].

In addition, the direct contact between the bowel and polypropylene or polyester prostheses can lead to life-threatening bowel perforations, fistula formation, and peritonitis; all these complications are considered infections [140]. Finally, the surgical correction of a ventral hernia is a technically demanding task, vastly augmenting the significance of an infection [138].

What is the infection rate after ventral herniorrhaphy?

In order to reach credible figures, we performed a Pub Med search (Table 15) utilizing the following, key words: *incisional hernia, adults, infection, prostheses*, and *randomization*. A total of 386 articles were published during the last 36 years dealing with ventral herniorrhaphy; however, only 20, or 5%, of those include the five key words. This study includes randomized reports about the outcome of postlaparotomy abdominal wall closures utilizing different techniques. Unfortunately, these studies do not include randomized papers on ventral herniorrhaphy. We reviewed 32 articles that incorporated the key words *adult*, *infection*, and *mesh*.

The majority of the publications were from the last 12 years.

Similarly, as in the case of inguinal herniorrhaphies, the authors of articles on ventral herniorrhaphy (Table 16) did not define or classify the infections encountered; therefore, we utilized the definitions previously used for inguinal herniorrhaphy. Furthermore, these authors did not include in their descriptions the size of the repaired hernia.

B. Results

Of these studies, 43.8% were prospective and 34.4% retrospective. However, in 22% of these publications, those variables were not specified.

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Table 15 Pub Med Search on Publications Dealing with Incisional Hernia

Key words	Number of articles	Dates
Incisional hernia		
& adults	386	1966–2002
& adults & infection	135 (35%)	1980–2002
& adults & infection & mesh	43 (11%)	1980–2002
& adults & infection & mesh & randomization	20 (5%)	1980–2002

Neither were surveillance or auditing. Only one study was randomized (Table 17).

The 32 reviewed articles yielded 3454 patients who underwent 3462 operations, with similar numbers according to sex. Gender was mentioned in 22 of these articles totaling 1314 males and 1198 females. The average age was 55 years. Of the total, 2111 were primary hernias, 32 were incarcerated, and 22 were strangulated. Table 17 depicts the techniques utilized.

XI. ANTIBIOTIC UTILIZATION

In 56.3% of the operations, a prophylactic antibiotic was utilized; the rest of the publications did not mention antibiotic utilization. Half of the authors who used antibiotics used them systemically and 12.5% utilized

Table 16 Articles Dealing with Incisional Hernia That Mention Prostheses and Infection

Date	Number of publications	Percent (%)
1985–1990	03	9.3
1991–1995	07	21.8
1996–2000	19	59.3
2001–2002	03	9.3
Total	32	100

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Table 17 Publications Dealing with Different Ventral Herniorrhaphy Surgical Techniques

Surgical technique	Number of articles	Number of patients
Anatomic	6	419
Tension-free	19	2723
Laparoscopic	7	812

them locally. The presence or absence of drainage was mentioned in 37.5% of the operations; in 28.1% of those, it involved a closed system.

210 patients (6.06%) experienced an infection. Infections were considered superficial in 85 patients; 2 corresponded to laparoscopy ports and the rest were deep infections requiring prosthesis removal. Only 12.5% of the articles mentioned the utilization of a wound bacteriological culture, and in such cases the most common bacterium found was *S. aureus* (12.5%). In 3.1% of the patients, *E. coli* was isolated, suggesting bowel injury. All these patients were treated in the hospital where they remained over 48 h.

In the late 1980s, Sitzmann reviewed 16 articles dealing with the repair of massive ventral hernias with polyproplylene meshes. He found that the reported infection rate was 5%; however, in his literature review, the infection rate ranged from 0–25% [25].

A. Remarks

This study suggests that the process of reporting postventral hernia infections is far more deficient than that for inguinal hernias. There were no reports on surveillance utilization and there was a definite lack of attempts to classify these complications. Furthermore, the incidence spread was found to range between 1.2 and 30%, meaning that out of 90,000 repairs performed in the United States, between 1080 and 27,000 infections may have occurred. This profound disparity exemplifies a serious problem that invalidates the accuracy of reporting this severe complication.

We can make the same recommendations for these operations that we did for inguinal hernia, reinforcing the concept that infected ventral herniorrhaphies may be far more common than reported.

There are no studies dealing with cost analysis.

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XII. REALITIES OF INFECTION CONTROL

The incidence of SSI has continued to decline since Pasteur and Lister. However, it has not disappeared. Cruse and Olson, working between 1960 and 1980, estimated a 1.5% clean wound infection rate. Nevertheless, their figures may not be accurate, because later breast and herniorrhaphy reports disclosed figures up to 18 and 14%, respectively.

The authors believe that any attempt at obtaining creditable figures on the rate of inguinal herniorrhaphy infections should follow the guidelines described by Peto and Platt. Accordingly, to ascertain an infection rate of 2%, one would have to analyze the outcome of at least 2600 patients. It is then apparent that multicentric studies would be ideal in order to study a very large number of patients. This would allow the harvesting of significant and reliable data [135,136].

XIII. SHORTCOMINGS OF THE PRESENT SYSTEM

1. The epidemiologists working with the nurse epidemiologists perform CS and recommend measures to lower the infection rates. This is a long process and thus may become obsolete before it is completed. It also expensive and time-consuming. Furthermore and more important, it does not include the surgeon.
2. Internal hospital audits effectively lower the SSI rate by their sentinel effect. This improvement may be reversed if the study is discontinued because it eliminates the surveillance effect.
3. For the surgeon, infection control is one of the many daily activities, and it may become diluted by other duties. Under those circumstances, quantifying and reporting becomes a secondary priority.
4. The lack of specific definitions and classifications further complicates and impedes proper disclosure, adding unwanted subjectivity to the issue.
5. There is reported evidence that specialization in the field of herniorrhaphy reduces wound infection rate by allowing the surgeon to focus on a specific subject, a sentinel effect.

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XIV. RECOMMENDATIONS

In order to reach realistic SSI postherniorrhaphy rates, surgeons should work in conjunction with a nurse epidemiologist and an epidemiologist to define, validate, and apply SSI classifications.

A. Data Processing

1. Data should be collected by the nurse epidemiologist and fed into an automated data collection processing system.
2. Information should be conveyed from the nurse epidemiologist to the surgeon and to the epidemiologist at a constant rate of flow in order to allow the necessary procedure modification.
3. The working process should be expedient to reduce human suffering and expenses.
4. Data should be automatically shared with other surgical or epidemiological centers for comparison and eventual procedural modification.

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3

Classification of Mesh Infections After Abdominal Herniorrhaphy

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The appearance of a wound infection after repair of an abdominal wall hernia with mesh is a serious event. It is not an isolated event but rather a complex one, wherein multiple factors describing the patient, the bacteria, and the operation must be defined or classified. Several classifications have been created to describe (1) the wound, (2) the bacterial agents, (3) the patient (ASA score), (4) the risk of infection (SENIC and NNIS), (5) the surgical site infection, and (6) the mesh.

In the 1960s, one of the earliest classifications stratified surgical wounds as class I, clean; II, clean contaminated; III, contaminated; and IV, dirty-infected [1]. This system provides a first approximation of the risk of a postoperative wound infection, now renamed surgical site infection (SSI). This classification has stood the test of time. It is still used today, as clinical experience continues to show that the higher the class, the higher the rate of wound infection or SSI. However, these classes do not provide a precise rate of infection but rather a range of rates. In general, class I clean wounds—typically almost all herniorrhaphies except for those done for emergency indications—are believed to have an infection rate of about 1%. However, some studies show this rate may be as high as 4%.

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The definitions within this classification system are quite straightforward; they are summarized in Table 1.

Although the cleanliness or contamination of surgical wounds is easy to classify, universally accepted criteria for a wound infection were not codified until about 1990. At that time a consensus [2] was obtained for the definitions of an SSI—the term that has now replaced the phrase *postoperative wound infection*. The terms *incisional* (*superficial* or *deep*) and *organ/space infection* are now widely used by infection surveillance programs. As these programs are usually hospital-based, the collection of data on infection rates after herniorrhaphy has been minimal, as most hernia patients are operated on in an ambulatory setting and have the majority of their follow-up in the surgeon's office. Additionally, the office-based surgeon may or may not inform the hospital-based surveillance team of an SSI. These data are lost and, as a result, the rate of SSIs after hernia repair is generally understated.

Concerning the role of bacteria in wound infections, three variables have traditionally been used to evaluate the risk of infection: (1) host resistance, (2) bacterial virulence, and (3) the amount of wound contamination. A simplified formula used to visualize this relationship is the dose of bacteria times the virulence of bacteria divided by host

Table 1 Traditional Classification of Surgical Wounds

Class I — Clean
A surgical wound/incision is created through prepared skin where no inflammation is present. No organ system (respiratory, gastrointestinal, biliary, or genitourinary) is entered.
Class II—Clean Contaminated
During surgery, the respiratory, gastrointestinal, biliary, or genitourinary tract is entered under controlled conditions. There is a limited amount of contamination.
Class III—Contaminated
This class includes operations on open fresh wounds or acute traumatic wounds as well as operations with a major break in sterile technique or with gross spillage from the gastrointestinal tract. Also included are incisions in which the surgeon encounters acute nonpurulent infection.
Class IV—Dirty-Infected
These are old, traumatic wounds with devitalized tissue or wounds with an existing clinical infection or perforated viscus.

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resistance, which equals the risk of SSI [1]:

$$\frac{\text{Dose of bacteria} \times \text{virulence of bacteria}}{\text{Host resistance}} = \text{risk of SSI}$$

Accordingly, infections following abdominal wall herniorrhaphy might be classified according to the causative bacterial organism as described by surgical investigators [3–5]. Explosive infections occurring within the first 24–36 h are typically streptococcal, clostridial, or synergistic aerobic/anaerobic combinations of bacteria, all of which demand urgent evaluation and treatment. The common superficial SSI is found about 4 to 7 days after surgery, and most are caused by staphylococci. Opening of the incision and active dressing changes successfully treat these infections. Antibiotics may or may not be required. Deeper SSIs may occur from enteric organisms if an organ system has been entered (e.g., enterotomy) or an unrecognized injury to an organ system has occurred, with subsequent perforation and contamination of either the hernial incision or prosthetic material (mesh) that is nearby. Finally, the inflammatory reactions associated with some mesh prostheses or their mechanical characteristics may result in late erosion into an organ (usually the gastrointestinal tract) with the delayed appearance of a chronic organ/space infection. This is why the Centers for Disease Control and Prevention (CDC) guidelines extend the postoperative surveillance interval from 30 days to 1 year when an implant such as mesh is left at the operative site.

Evaluation of the host or patient risk factors has been well documented. Factors include age, diabetes mellitus, concurrent active infection upon or within the patient, malnutrition, obesity, altered immune responsiveness, the use of tobacco or steroids, and the duration of hospitalization prior to surgery. Several perioperative factors, mostly under the control of the surgeon, have also been shown to affect the patient's risk for an SSI [6]. These include the preoperative use of blood products or prophylactic antibiotics, the operative site skin preparation and hair removal techniques, the maintenance of aseptic operative technique, the technical expertise of the surgeon as measured by the amount of tissue injury (mass ligatures, excessive electrocautery destruction, etc.), and the duration of the operation. Although all of these factors have been recognized by clinicians and most are supported in literature studies, the first major investigation into evaluating intrinsic patient risk was the 1985 Study on the Efficacy of Nosocomial Infection

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Control (SENIC), where 10 patient risk factors were studied using statistical techniques [7]. A model was developed in which four risk factors were identified: (1) an operation upon the abdomen, (2) an operation over 2 h in duration, (3) an operation classified as class III (contaminated) or class IV (dirty-infected), and (4) an operative patient with three or more coded diagnoses at the time of hospital discharge. This SENIC index proved to be better at estimating the risk of SSI than did the traditional classification of wounds, as this index added a factor that evaluated intrinsic patient risk—namely, the number of diagnoses at the time of discharge.

Searching to improve upon the SENIC index, the National Nosocomial Infections Surveillance (NNIS) system was published in 1991 [8,9]. This CDC group effort utilized the information from 44 hospital databases over the years 1987–1990. Three risk factors were identified: (1) an American Society of Anesthesiologists (ASA) score of 3 or greater, (2) an operation classified as class III (contaminated) or class IV (dirty-infected), and (3) an operation whose duration was greater than the 75th percentile for that procedure. The resulting NNIS risk for an SSI was 1.5% for a score of 0, 2.9% for 1, 6.8% for 2, and 13% for 3. These investigators believe that this new index is a significantly better predictor of SSI than the traditional wound classification system using classes I through IV.

From examination of the CDC definitions of SSI, it is apparent that the placement of mesh during a herniorrhaphy alters the amount of follow-up required. The period at risk for infection now extends from the traditional 30 days to 1 year. This is appropriate, as mesh infections may be slow to become apparent, especially as the mesh prosthesis is usually placed deep within the abdominal wall or within the abdominal cavity during a hernia repair. The mesh may have been contaminated at the time of placement, with bacteria surviving either within the mesh substance [expanded polytetrafluoroethylene (PTFE)] or in crevasses created within woven sutures or excessively large suture knots. This concept is discussed by Amid, who has examined the interaction of infection and mesh biomaterials according to the mesh's porosity or pore size in ranges from submicronic to macroporous [10]. Additionally, a mesh prosthesis may create an inflammatory reaction that serves as a site for bacterial implantation during the transient bacteremias that humans experience every day.

In choosing a classification system for SSIs following abdominal wall herniorrhaphy with mesh in place, the most rational one to use is

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Table 2 Criteria for Surgical Site Infection

I. Superficial Incisional

The infection occurs within 30 days, involves only the skin or subcutaneous tissues, and has at least one of the following:

1. Purulent drainage from the incision.
2. A positive bacterial culture of fluid or tissue from the superficial incision.
3. At least one of following symptoms or signs of infection: pain, tenderness, localized swelling, redness, warmth. The superficial incision is reopened by the surgeon unless the incision is culture-negative.
4. A superficial site infection diagnosed by the surgeon or a physician.

This definition does not include stitch abscesses that contain a small localized inflammation or discharge at the point of suture penetration of the skin.

II. Deep Incisional

The infection occurs within 30 days of surgery or within 1 year if an implant (mesh) is in place and the infection appears to be related to the operation. Additionally, the infection involves the deep soft tissues (that is, the fascial and muscle layers) and at least one of the following:

1. Purulent drainage from the deep incision but not from the organ/space.
2. A deep incision that either spontaneously dehisces or is opened by the surgeon in a patient who has at least one of the following symptoms or signs: fever ($> 38^{\circ}C$) and localized pain or tenderness unless the site is culture-negative.
3. An abscess or overt infection is found to involve the deep incision upon direct examination by the surgeon during reoperation or by histopathological or radiological examination.
4. A deep incisional surgical site infection is diagnosed by the surgeon or a physician.

Note: The CDC defines an infection that involves both superficial and deep incisional sites as a deep incisional SSI.

III. Organ/Space

This infection occurs within 30 days after surgery or within 1 year if an implant (mesh) is in place and the infection appears related to the operation. The infection involves an organ or space 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 placed into the organ
2. A positive culture of the organ/space that is obtained aseptically.
3. An abscess or other evidence of infection involving the organ/space that is found by the surgeon during reoperation or by histopathological or radiological examination.
4. An organ/space infection diagnosed by the surgeon or a physician.

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that published by Horan [11] and summarized in 1999 in Mangram's "Guidelines for Prevention of Surgical Site Infection." [6]. These CDC investigators have classified SSI as (1) superficial incisional, (2) deep incisional, or (3) organ/space in location. These criteria are summarized in Table 2.

In summary, there are many different ways to classify SSIs that occur after abdominal wall herniorrhaphy with or without the placement of mesh. These involve characterizing (1) the patient and his or her risk factors; (2) the bacteria as well as the dose and virulence; and (3) the operative and perioperative events. From a practical perspective, the practicing surgeon should catalog the following:

- Significant patient risk factors (age, diabetes, impaired immune response, etc.)
- The class of the operative wound (I, clean, through IV, dirty-infected)
- The preoperative ASA class and duration of the operation
- The type of mesh and suture used

Finally, surgeons should use the CDC definitions for classifying SSIs, namely (1) superficial incisional, (2) deep incisional, and (3) organ/space. Such record keeping will be most consistent with and complement the procedure used by hospital-based infection control committees or surveillance programs. This system will also allow the surgeon to compare his or her results with other series or norms from national data sources in a meaningful manner.

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4

Pathology of Infected Mesh

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I. PATHOPHYSIOLOGY OF MESH INFECTION

Modern hernia surgery is no longer imaginable without the application of surgical meshes. Today approximately 1 million meshes are implanted worldwide per year. The net-like alloplastic mesh is used to close the hernial gap and, with extended overlap, to reinforce the abdominal wall [1].

Infections of meshes used in hernia surgery have been reported to occur in up to 6% of implanted specimens and rank third in the list of mesh-associated complications [2–16]. However, the true rates of mesh-associated infection may be even higher than those reported in the literature [17]. Physicians who care for patients with surgically implanted meshes may rely on cultures with relatively low yield. The failure of currently used microbiological techniques to consistently culture organisms located in bacterial biofilms may thus result in an underestimation of the true rate of infections. Furthermore, antibiotics are often administered before the appropriate diagnostic cultures are obtained, thereby possibly yielding false-negative results [17–23].

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Mesh-related infections result from a multifaceted interaction of bacterial, device, and host (immune) factors [24]. This has been well demonstrated in detail for two bacterial species that are of particular interest for hernia surgeons—i.e. *Staphylococcus epidermidis* and *Staphylococcus aureus*. Adherence of *S. epidermidis* to the surface of polymers is not a one-time phenomenon but rather an evolving process. Initially, there is a rapid attachment of bacteria to the surface of the device that is mediated either by nonspecific factors such as surface tension, hydrophobicity, and electrostatic forces or by specific adhesins such as proteinaceous autolysins or capsular polysaccharide intercellular adhesins (PSA) [25]. This initial phase of *S. epidermidis* adherence is followed by an accumulative phase, during which bacteria proliferate, adhere to each other, and form a complex biofilm—a process that is again mediated by polysaccharide intercellular adhesions [26] (Fig. 1). Unlike *S. epidermidis* organisms, which use well-defined adhesins on the bacterial surface to adhere to one another and to the device, adherence of *S. aureus* appears to be more dependent on the presence of host-tissue ligands, including fibronectin, fibrinogen, and collagen. *S. aureus* adheres to such host-tissue ligands via genetically defined microbial surface proteins, commonly referred to as ''microbial surface components recognizing adhesive matrix molecules'' (MSCRAMM) [27–29].

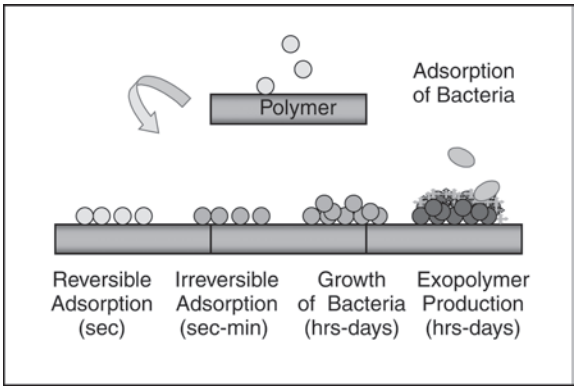

Figure 1 Adsorption of *Staphylococcus epidermidis* to an implanted polymer. Several steps lead to the development of a biofilm composed of bacteria, bacterial polysaccharides, and host-cell glycoproteins. The biofilm provides a protective niche for the bacteria.

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Device-related factors that may favor bacterial adherence are (1) an irregular surface of the device, (2) polymeric tubing, and, in particular, (3) hydrophobic physicochemical properties of the polymers. Immune-mediated phenomena that are induced by the implant may promote bacterial persistence and lead to the exacerbation of infections. This is illustrated by, for example, the reduced complement-mediated opsonic activity and the decreased bactericidal activity of phagocytic white blood cells in tissues surrounding medical implants [30]. Furthermore, it has been proposed that the generation of microthromboemboli within devices may result in blockade of the reticuloendothelial system and so impair the patient's ability to clear micro-organisms from the circulation [31].

Early morphological analyses of devices have established the role of biofilms in the contamination of medical implants. Electron microscopy studies of implants revealed various bacteria residing in biofilms on these abiotic surfaces, and this has recently also been demonstrated in meshes used for hernia surgery [24,32–35]. Originally, these bacteria were thought to be saprophytic, their sole pathogenic mechanism being the ability to persist in spite of host defenses and antibiotic chemotherapy. However, direct studies of infected tissues have demonstrated that these bacteria, embedded in copious amounts of exopolysaccharide matrix material, may become foci of chronic infections and, under certain circumstances (impaired host defense), the source of severe life-threatening systemic infections [24,36,37]. While a biofilm infection can give rise to an acute, clinically evident infection at any time, the biofilm infection itself in many cases seems not to be notably aggressive. However, it may adversely affect the function of the indwelling device. For example, capsular contracture, the most common reason for the removal of mammary implants, is etiologically related to bacterial colonization of the implant, usually by coagulase-negative staphylococci, without clinical evidence of infection [38]. Similarly, loosening of joint prostheses may also be caused by bacterial colonization of the prosthesis [17]; it may also be possible that the shrinking of surgical meshes is caused by similar pathomechanisms [13,39,40].

The specific pathomorphological host responses to the mesh infection are most likely the result of the distinct pathophysiological characteristics of a bacterial biofilm and the changing phenotypes of the causative bacteria. Biofilms are programmed to regularly release bacterial cells into the circulation or surrounding tissues, and the total number of the detached bacteria that challenge the body's defenses depends on the

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size of the colonized area. The bacteria detached from the biofilm may show a completely different phenotype. For example, several studies have shown that sessile bacteria are up to 1000 times as resistant to antibiotics as their circulating "planktonic" counterparts [41]. Furthermore, the adherent population, by virtue of their different phenotype and their position in a protective matrix, may also withstand the vigorous attack of the body's immune system [42].

The acquisition of a biofilm on surgical meshes may be the result of bacterial contamination during surgery or subsequent hematogenous spread [3,17,24,41]. Consequently the microbiological risks posed by implanted surgical meshes are likely to diminish as the surgery used in their implantation is improved and refined and as hematogenous sources (dental procedures) are controlled [3].

Analytical tools to elucidate mesh infections should comprise culture techniques as well as detailed histopathological studies of tissue specimens. Microbiological scraping and plating techniques for the recovery of sessile bacteria from biofilms and solid surfaces are notoriously difficult and unreliable [24]. Detailed histopathological analyses—including special techniques like histochemistry, scanning electron microscopy or confocal scanning laser microscopy (CSLM)—are thus of particular importance to reliably detect mesh infections.

II. TISSUE RESPONSE TO IMPLANTED MESHES

To appreciate the specific morphological events occurring in mesh infection, it is important to understand the pathology of the host response occurring over time. The implantation of meshes is carried out using a surgical procedure. This initiates a response to injury by the body, and mechanisms are activated to maintain homeostasis. The mechanisms can be divided into blood-material and tissue-material interactions (Table 1). These cell-cell and cell-biomaterial interactions are extremely complex and involve a myriad of mediators, including chemotactic substances and growth factors that mediate cell function, such as activation, proliferation, and protein production [43,44]. The most important mediators of inflammation are summarized in Table 2.

Our knowledge of the tissue response to implanted meshes in humans and their long-term biocompatibility is still poor. Nearly all the data concerning the biological behavior of these implants are obtained from

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Table 1 Local Host Reactions

A. Blood-material interactions	
	1. Protein adsorption
	2. Complement activation
	3. Coagulation
	4. Fibrinolysis
	5. Platelet activation
	6. Leuckocyte adhesion
B. Tissue-material interactions	
	1. Granulation tissue formation
	2. Tissue adhesion
	3. Tissue ingrowth
	4. Fibrosis

Table 2 Mediators of Inflammation

Chemical mediators	Examples
A. Vasoactive amines	Histamines and serotonin
B. Plasma proteases	
1. Kinin system	Bradykinin, kallikrein
2. Complement system	C3a, C5a, C3b, C5b-C9
3. Coagulation/fibrinolytic system	Fibrin degradation factors; activated Hageman factor (XIIa)
C. Arachidonic acid metabolites	
1. Prostaglandins	PGI_2, TxA_2
2. Leukotrienes	HETE, leukotriene B_4
D. Lysosomal proteases	Collagenase, elastase
E. Oxygen-derived free radicals	H_2O_2, superoxide anion
F. Platelet activating factors	Cell membrane lipids
G. Cytokines	Interleukin1 (IL-1), tumor necrosis factor α (TNF-α)
H. Growth factors	Platelet-derived growth factor (PGDF), fibroblast growth factor (FGF), transforming growth factor (TGF-α or TGF-β)

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animal experiments. Biocompatibilty is defined in terms of the ability of a material to perform with an appropriate ''host response'' in a specific application. A completely biocompatible material would not (1) irritate the surrounding structures, (2) provoke an inflammatory response, (3) incite allergic reactions, or (4) cause cancer [45]. Main polymers for the production of surgical meshes are polypropylene (PP), polyester (polyethylene-terephthalat; PET) and expanded polytetrafluoroethylene (ePTFE), all nonabsorbable [46–50]. Some newer mesh modifications are combined with absorbable polymers such as polyglactin PG910 (Vicryl) to improve the handling characteristics for implantation [49,51,52]. Basically, surgical meshes are regarded as physically and chemically inert and stable, nonimmunogenic, and nontoxic. However, these materials are not biologically inert. In fact, all experimental and clinical studies have revealed a typical foreign-body reaction in the interface of all mesh modifications on the market today [34]. In contradiction to their physical and chemical stability, the meshes trigger a wide variety of adverse responses in vivo, including inflammation, fibrosis, calcification, thrombosis, and infection. The quality of the inflammatory reaction on foreign bodies of different nature is surprisingly constant and characterized by a rapid accumulation of huge numbers of phagocytic cells, in particuliar blood monocytes and tissue-derived macrophages and the formation of a granulomatous cellular reaction, including characteristic multinucleated foreign-body giant cells [34]. The aim of this process is to isolate the foreign body from the host tissues forming an artificial ''outside world'' at the place of implantation. The same principles are thought to be responsible for the formation of the prototypic granulomas in tuberculosis. Here, again, the host is not able to remove the inflammatory agent—namely, *Mycobacterium tuberculosis* [53].

However, why inert and nonimmunogenic materials like meshes induce this particular type of inflammatory tissue reaction is still poorly understood. An important hypothesis is that this reaction is triggered by the adsorption of host proteins, which subsequently undergo conformational changes leading to persistent tissue injury. The protein adsorption from biofluids onto polymeric surfaces obviously plays a mediating role not only in the development of the foreign-body reaction but also in the process of regeneration and ingrowth of connective tissue and is, therefore, also crucial for the long-term performance of medical devices. Protein adsorption is now widely acccepted in biomaterials research as one of the most important pathomechanisms leading to the very typical tissue responses to implants [54–58].

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The adsorption of plasma proteins to implanted polymers takes place within milliseconds to seconds, long before an initial cellular response on the biomaterial can be observed, and is affected by the electrosurface properties of the various polymers [58]. Examples comprise the binding of kininogen to negatively charged surfaces and the heparin-like activity of negatively charged macromolecules. Interestingly, the binding of the proteins does not lead to a stable polymer-protein interaction. It is a dynamic process that is obviously subject to a distinct hierarchy described by Vroman and coworkers (''Vroman effect'') [59,60]. Initially there is binding of low-molecular-weight proteins in particular albumins, which are gradually replaced over time by proteins of higher molecular weight, like fibrinogen and immunoglobulins. Finally, the latter proteins are replaced by even larger molecules, like kininogen and extracellular matrix molecules (Fig. 2) [59,60].

Secondary to their adsorption to the biomaterial surface, the proteins may undergo conformational changes, triggering a plethora of local host reactions that drive the evolution of the inflammatory tissue response [55]. The most important host reactions are summarized in Table 1. Changes in the conformation of polymer-bound proteins may, on the one hand, render them susceptible to the action of proteases and thus lead to continuous protein degradation. On the other hand, the

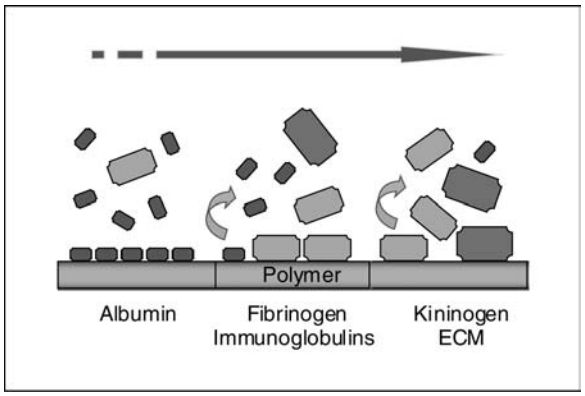

Figure 2 Vroman effect. Adsorption of proteins from biofluids is a dynamic process starting with small proteins such as albumins which are, with time, replaced by larger proteins. Large proteins such as extracellular matrix proteins are important for the ingrowth of granulation tissue and fibrous connective tissue.

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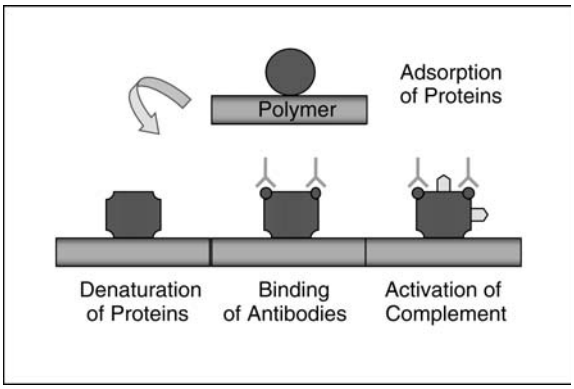

Figure 3 Binding of proteins leads to conformational changes. The proteins become immunogenic, resulting in antibody formation and binding and activation of the complement system via the classic pathway.

proteins may become immunogenic, leading to antibody formation and binding of IgG or IgM immunoglobulins [54]. These antigen-antibody complexes can than lead to an antibody-mediated activation of the complement system by either the classic or the alternative pathway (Fig. 3). The complement system consists of at least 13 serum proteins that are activated by enzymatic cleavages and aggregations to produce components with biological activity that trigger multiple pathomechanisms resulting in leukocyte adhesion and activation [61]. Chemotactic complement activation products (i.e., C5a) may contribute to the accumulation of phagocytic cells at the implant site. C5a is also found to enhance leukocyte adhesion and aggregation. C3a activates macrophages to synthesize and secrete interleukin-1 (IL-1). Bound active C3b fragments mediate the attachment of macrophages and polymorphonuclear granulocytes (PMNs, or neutrophils) to the polymer surface. This adhesion leads to degranulation and release of lysosomal enzymes and other cytoplasmic components from the adherent macrophages. The adherent C3b then initiates the amplification and completion of the alternative pathway and liberates the active fragment C5a. Finally, C5a induces activation and release of highly reactive oxygen metabolites, lysosomal enzymes, and IL-1 from PMNs or monocytes/macrophages [62].

Binding of proteins to the polymers is furthermore responsible for the activation of the blood clotting and fibrinolysis system. The

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activation of blood coagulation by polymers is apparently triggered at the level of the kinin system (also called the contact system) of the blood plasma. The initial phase of this activation is thought to require negatively charged sites on the mesh polymers. Important proteins of the clotting cascade which bind to polymeric surfaces are factor XII (Hageman factor), factor XI, prekallikrein (PK) and high-molecular-weight kininogen (HMWK) (Fig. 4). It has been assumed that negative charges at the surface of the material serve the induction of a conformational change in factor XII that renders it highly susceptible for proteolytic activation, the promotion of interaction between the active factor XIIa, HMWK, and prekallikrein, favoring proteolytic activation and the promotion of HMWK-dependent activation of factor XI by factor XIIa [45,55,62].

All the events mentioned above thus form the basis for understanding tissue responses when meshes are implanted. Following the surgical procedure and implantation of a surgical mesh, the events that occur are (1) the acute inflammatory response, (2) the chronic inflammatory response (3) the foreign-body reaction with the development of granulation tissue (macrophages, fibroblasts, and capillary formation) and foreign-body giant cells, and (4) fibrosis. Alterations in the magnitude or duration of these responses or alterations induced by infection may significantly modify the morphological characteristics of the tissue response and also lead to a compromise in the functional capacity or permanent bioacceptance of the implanted mesh [45,55,62].

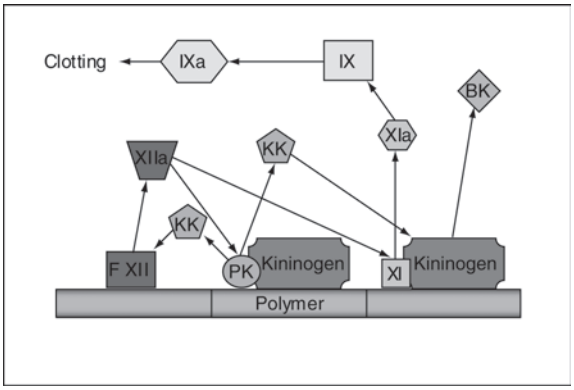

Figure 4 Activation of the blood clotting cascade by binding of the factors XII, XI, prekallikrein, and high-molecular-weight kininogen to the implant polymer.

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Immediately following the injury, there are changes in vascular flow, caliber, and permeability. Fluid, proteins, and blood cells escape from the vascular system into the injured tissue by a process called exudation. The invasion of neutrophils and monocytes is controlled and directed by the chemotatic or chemokinetic factors inherent in the inflammatory response, which include complement factors, lymphokines, fibronectin, platelet factors, and leukotrienes; in the case of infection, they also include bacterial fragments (Table 2) [43,63].

The predominant cell type in the inflammatory response varies with the age of the injury. In general, neutrophils predominate during the first several days following injury; they are then gradually and finally almost completely replaced by monocytes. These monocytes migrate from the vasculature and then differentiate into macrophages that have a life span of several months. Macrophages are suggested to follow the mode of responding to the same mediators as neutrophils when interacting with biomaterials and it has been shown that they adhere to implanted polymers already within 24 h [62,64]. In the chronic inflammatory phase the major mechanism of tissue damage at the implant site is phagocytosis and activation of macrophages in coordination with the major histocompatibilty complex (MHC) of the body. The acitivity of macrophages involves adhesion to the polymer, activation and secretion within the implant site. Macrophage activation via phagocytosis or endocytosis leads to secretion of a large number of substances ranging in a molecular mass of 32 (superoxide anion) to 440,000 (fibronectin) and includes about 100 substances [43,65,66]! The macrophage is thus considered to be the pivotal cell in the determination of the biocompatibility of implanted materials. It is involved not only in the clotting, fibrinolytic, and complement cascades but also in the production of mediators (FGF, PDGF) that can induce the proliferation and protein synthesis of other cell types constituting the granulation tissue (i.e., endothelial cells and fibroblasts). Furthermore, the macrophage interacts with T lymphocytes to activate them, allowing the secretion of lymphokines. Recent evidence has shown that macrophages secrete tumor necrosis factor alpha (TNF-α) and prostaglandins in concert with interleukin-6 (IL-6) when exposed to polyethylene [67], and there is evidence indicating that the surface charge on the biomaterials plays a crucial role in the activation of macrophages and the mechanisms of release of TNF-α [58].

Cellular adhesion studies have shown that monocytes, macrophages, and foreign-body giant cells were the only cells adhering to the

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surfaces of biomaterials [68]. Macrophages are, in fact, a constant finding in the evaluation of retrieved meshes and are typically present at or on the surfaces of the mesh structures [34,40,69]. (Fig. 5). Due to their active state, they frequently undergo morphological and cytoplasmic changes resembling the characteristics of epithelial cells and are termed epithelioid macrophages. In most cases they are accompanied by foreign-body giant cells. These cells are the prototypical cell type characterizing the development of the typical foreign-body granulation tissue response. The detailed pathomechanisms of the formation of foreign-body giant cells are still not completely clear, but it is likely that these cells develop

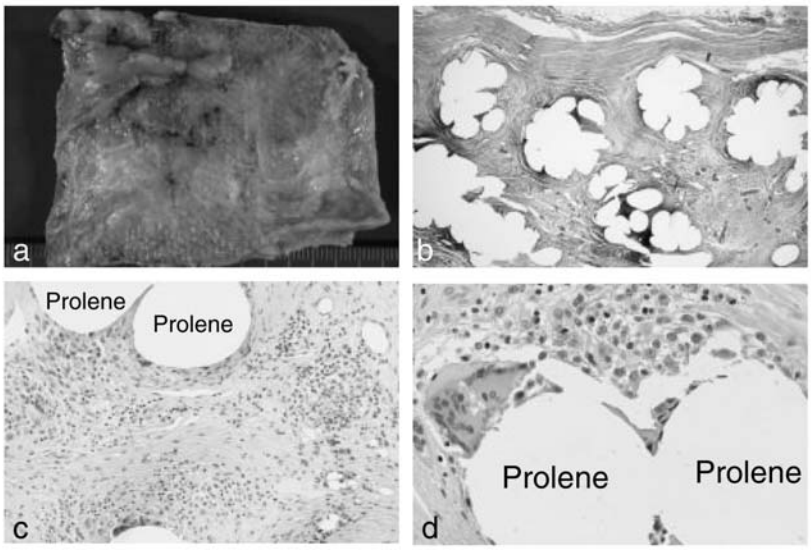

Figure 5 Morphology of a sterile prolene mesh retrieved because of chronic pain 1 year after implantation. (a) The mesh is covered by connective tissue. (b) Histopathology reveals characteristic empty spaces, which indicate the place of the polymer structures within the tissue. The polymer is largely destroyed during tissue processing and cutting of the histological slides, leaving empty spaces. (H&E, × 40.) (c) There is fibrous tissue betweeen the polymer structures and a chronic inflammatory infiltrate located preferentially in direct contact to the polymer structures. (H&E, × 200.) (d) Epithelioid (activated) macrophages are in direct contact with the polymer and intermingled with classic multinucleated foreign-body giant cells. There are a few eosinophils and lymphocytes but no PMNs. There is no evidence of infection. (H&E, × 400.)

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similarly to the giant cells of Langhans in tuberculosis—i.e., by fusion of macrophages [70]. Factors that may induce the fusion of monocytes and macrophages are direct physical contact with the polymer combined with the action of various cytokines like TNF-α, IL-4 or interferon gamma (IFN-γ) [34,53,55,71]. Like epithelioid macrophages, the foreign-body giant cells are seeded directly at the interface of the mesh and the recipient host tissue. Due to the action of macrophages and a multitude of potent inflammatory mediators, other cell types—including T cells, B cells, eosinophilic granulocytes, plasma cells, fibroblasts, and endothelial cells—are attracted to the implant site. Within a few days, this cell cocktail forms the early granulation tissue. This tissue is not a static type of chronic inflammation but represents a chronic wound with an increased cell turnover even years after implantation. Monocytes and tissue-derived macrophages of the interface and in contact with the polymer undergo apoptotic cell death and are continuously replaced by other cells [34]. With time, the propagation of fibroblasts to the implant site and the formation of collagen and mucopolysaccharides from fibroblasts leads to a change of the histopathological features. There is a decline in the number of inflammatory cells and capillaries and a relative increase in fibrous tissue, finally leading to fibrosis. At these later stages of the host response, there is a clear zonation of this tissue, with most of the inflammatory cells found in direct contact with the polymer structures (Fig. 5). In contrast to solid biomaterials in meshes, the process of fibrosis is not associated with the formation of a capsule but with a progressive ingrowth of fibrous tissue into the polymer. This is actually a desired tissue response. Good tissue ingrowth is dependent on the mechanical stability of the implant and little micromotion between the implant and the surrounding tissue. The velocity of this tissue ingrowth is also dependent on pore size and increases from 50-μm pores to reach a peak at about 400–500 μm. A prerequisite of the tissue integration of the mesh is adhesion and cellular binding to proteins adsorbed to the implant surface, for example, fibronectin and other extracelluar matrix molecules [59,60]. In some patients, progressive fibrosis may result in the shrinkage of the mesh after implantation [39,40].

III. TISSUE RESPONSE TO MESH INFECTION

Infection is the third major complication after mesh implantation [2–4]. Pathogenic factors that favor infection of biomaterials include-necrosis,

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poor vascularity, formation of abundant reparative fibrous and granulation tissue, immunosuppression of the host, and the inhibitory effect of implant biomaterials on the host inflammatory response [13,30,31,72,73]. These conditions favor the attachment of bacteria to the implant surface and their growth in a glycocalyx biofilm composed of bacteria, bacterial polysaccharides, and host-cell glycoproteins. Bacteria may reach the tissue-implant interface by direct inoculation or by hematogenous spread. The most common infecting organisms are *S. epidermidis* and *S. aureus* [2–6, 9–14, 74]. Aerobic streptococci, gram-negative bacilli, and a variety of anaerobic bacteria are also significant pathogens. Fungal infections are exceedingly rare [23,75].

Mesh infections may be classified on the basis of the time at which they present after surgery. Early (acute) infections occur within days to a few months of surgery and are most often due to direct inoculation of organisms, most often staphylococci, at the time of surgery. Delayed (subacute) infections occur between 3 months and 2 years after surgery and are usually due to direct inoculation of a causative organism of low virulence, most commonly *S. epidermidis*. Late infections, occurring more than 2 years after mesh implantation, are more likely to be due to hematogenous spread from a distant focus of infection (e.g., skin, dental, urinary tract) [76,77].

The diagnosis of infection may be extremely difficult when one is relying solely on microbiological techniques [17]. Pathogenic organisms are frequently present in low numbers and are not readily cultured following aspiration biopsies. Particularly in delayed or late infections. Even microbiological cultures of periprosthetic tissues removed at the time of revision surgery do not always provide clear evidence of infection. If cultures are positive, *S. epidermidis* is the most common pathogen. However, as this organism is a skin commensal, it may be difficult to determine whether micobiological culture of *S. epidermidis* represents isolation of a pathogen or growth of a skin contaminant [26].

Histopathological analyses, by contrast provide a reliable guide as to whether a mesh infection has occurred. The morphological hallmark of infection is the presence in the periprosthetic tissue of a large number of neutrophil polymorphs. In most cases of infection more than five neutrophils per high-power field can be found, on average. However, to obtain representative information, at least 10 microscopic high power fields should be evaluated. Fewer PMNs (generally more than one per high-power field on average) may be found in low-grade infections. In highly active infections abscesses with or without bacteria can be detected

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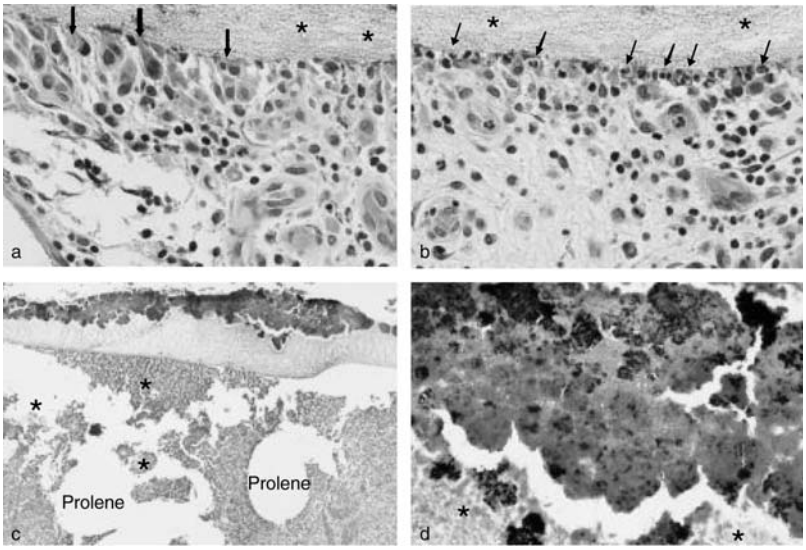

Figure 6 Morphology of an infected composite mesh harboring an abscess. (a) Large portions of the mesh are ''unremarkable'' and show a characteristic chronic inflammatory infiltration. Epithelioid macrophages (arrows) are in close contact with the mesh (asterisks). (H&E, × 400.) (b) However, in other areas, there is a significant accumulation of PMNs (arrows) directly at the tissue-implant interface, a feature indicative of infection. (H&E, × 400.) (c) In another area there is dense infiltration of PMNs with dissolution of the tissue and formation of an abscess. The polymer fibers seem to ''float'' in a sea of PMNs (asterisks) (Gram stain, × 100.) (d) High-power magnification reveals gram-positive cocci consistent with staphylococci. (Gram stain, × 400).

(Fig. 6). In a given case, it is particularly important that adequate sampling of the retrieved implant be undertaken, as the polymorphonuclear granulocytes are not always diffusely distributed within periprosthetic tissues. Organisms may be identified using special stains; Gram's stain as well as periodic acid–Schiff (PAS) and Grocott stains should be performed routinely. However, these stains are frequently negative even in cases of proven infection. The histopathological diagnosis is thus usually based on the identification of a heavy neutrophilic polymorphic infiltrate within inflamed periprosthetic tissues.

In the meanwhile, we have more than 400 explants of meshes on record and have already analyzed more than 300 specimens in detail. The

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Table 3 Results of Retrieval of Surgical Meshes: Complications

Mesh	Polymer	Features	Fibers	No.	Months	Rec.	CP	Inf.	Fist.
Mersilene	PET	LW/SP	multi	31	28	65%	13%	26%	4%
Marlex	PP	HW/SP	mono	90	26	57%	34%	22%	8%
Prolene	PP	HW/SP	mono	90	26	57%	40%	22%	6%
Atrium	PP	HW/SP	mono	64	20	67%	33%	17%	9%
Surgipro	PP	HW/SP	multi	17	24	70%	35%	17%	9%
Vypro	PP/PG	LW/LP	multi	34	15	82%	6%	12%	0%
Gore-Tex	ePTFE	HW/SP	-	21	33	57%	19%	24%	0%
Total	-	-	-	347	24.4	63%	30%	21%	7%

Key: LW, low weight; HW, heavy weight; SP, smell pores; LP, large pores; Rec., recurrence; CP, chronic pain; Inf., infection; Fist., fistulation.

results of the retrieval study indicate that all mesh modifications seem to have similar infection rates of 12–26%. Table 3 depicts the frequencies of complications demonstrated in our retrieval material. Infections thus rank third after recurrence and chronic pain.

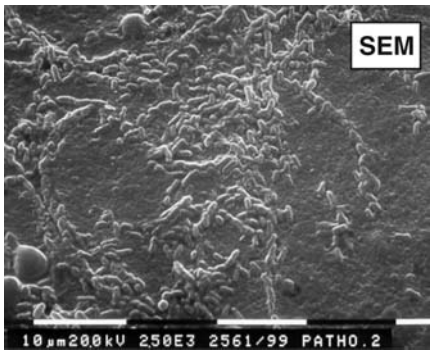

Figure 7 Scanning electron micrograph of a bacterial biofilm consistent with *Staphylococcus epidermidis* on the fibers of a retrieved polyproylene mesh. The mesh was removed because of chronic pain. Clinically there was no clear evidence of infection. Microbiological cultures from representative periprosthetic tissue specimens failed to demonstrate an infection. (SEM; bar = 10 µm.)

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A striking finding of the postretrieval studies is the high rate of histomorphologically evident infections without evidence of clinical signs of infection. The rate of "silent" and persistent infections is in the range of 50% of all infected meshes on record. Therefore mesh infection must be separated in clinically evident and clinically nonevident entities. The intensity of the infiltration by PMNs was generally less pronounced in clinically nonevident infections.

Scanning electron microscopy (SEM) studies confirmed the results obtained by light microscopy. In more than 80% of the meshes that were interpreted as being infected by light microscopy we were able to detect persisting germs on the surface of the meshes by SEM (Fig. 7) [34].

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5

Prosthetic Materials and Their Interactions with Host Tissue

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I. INTRODUCTION

Prosthetic biomaterials have become standard and accepted in the surgical repair of all types of abdominal wall hernias. While this addition to current surgical practice has reduced recurrence rates and improved the outcomes of complex hernia repairs, it has created some new problems related to the presence of the prosthetic material in the parahernial tissues. Infection remains the Achilles' heel of prosthetic repair of hernias and is the result of complex interactions at the cellular level involving a dynamic between healing, inflammatory reactions to foreign material, and bacterial contamination and activity.

The goal of this chapter is to review the pathophysiology of the host response to mesh. The characteristics of different types of mesh are differentiated based on their reactivity to the host and to bacterial infection. The induction of inflammatory changes and changes that occur to the mesh in response to the host are evaluated. The choice of prosthetic material for hernia repair can then be individualized to the patient to hopefully optimize the repair.

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II. IDEAL MESH CHARACTERISTICS FOR HERNIA REPAIR

Hamer-Hodges and Scott [1] determined the criteria for the ideal prosthetic biomaterial—based on Cumberland [2] and Scales [3] and expanded by DeBord [4]:

> The ideal material should not be physically modified by tissue fluids; it should be chemically inert; it should not excite an inflammatory or foreign body reaction; it should be non-carcinogenic; it should not produce a state of allergy or hypersensitivity; it should be capable of resisting mechanical strains; it should be capable of being fabricated in the form required; it should be capable of being sterilized; it should be resistant to infection; it should provide a barrier to adhesions on the visceral side; and it should respond in vivo more like autologous tissue (long-lasting repair without scarring and encapsulation).

Today's biomaterials fulfill almost all of the characteristics required of the ideal material. Nonabsorbable synthetic meshes are not modified by the host, they maintain their integrity and strength after implantation, are fabricated with consistent characteristics, and can be sterilized. The shortfalls of synthetic meshes include induction of chronic inflammation with incomplete tissue incorporation and resultant scarring and encapsulation; they cannot routinely be placed adjacent to the abdominal viscera because they fail to provide a barrier to adhesions; additionally and most importantly, they are not completely resistant to infection. Despite these shortfalls, polypropylene, polyester, and expanded polytetrafluoroethylene (ePTFE) have found use in all types of reconstruction of the body wall. The newer biomaterials, specifically those based on porcine or human cadaveric collagen, show promise in inducing less inflammation and having greater resistance to infection [5]. Thus, the evolution of the ideal biomaterial continues.

III. MECHANICAL AND STRUCTURAL PROPERTIES OF PROSTHETICS

All synthetic mesh starts with an extruded filament. The mesh is either woven or knitted in order to offer the maximum mechanical integrity [6,7]. Mesh characteristics of interest are weight, proportion of pores (interstices) or pore size, and textile surface per square centimeter.

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Mechanical characteristics include bending stiffness, maximum tearing force, suture tear-out force, tensile strength, and elongation at 16 N/cm, which is the maximum tensile strength of the human abdominal wall based on maximal intra-abdominal pressure and human body diameter. Tauber and Seidel found the same maximum on postmortem examinations of human fascia. Thus, the tensile strength of mesh does not have to exceed 16 N/cm [8]. All the nonabsorbable meshes currently used exceed this tensile strength. Suture tear-out force (kilograms per square centimeter) is thus more important, because mesh failure tends to occur at the muscle fascia–mesh interface [6], where suture tends to pull through the fascia and not the prosthetic mesh.

The primary concern of the surgeon is not to introduce a substantial amount of foreign body that can harbor or perpetuate infection. The ability to minimize infection is due to the size of the pore or interstices. The key number is 10 μm. When interstices or pores are less than 10 μm in size in any of their dimensions, bacteria averaging 1 μm cannot be eliminated by macrophages and neutrophilic granulocytes, which are too large to enter a 10-μm pore. Larger pore sizes also allow rapid fibroplasia and angiogenesis and can reduce seroma formation. Since the prosthetic mesh will serve as a framework for the ingrowth of connective tissue, pore size is of paramount importance [6]. The porous area of the mesh serves as a scaffold for the subsequent ingrowth of a dense infiltrate of fibrous tissue. Optimal pore size for the strongest attachment is greater than 50 μm. This is the size of the fibroblast. Amid classifies the different types of mesh based on pore size [9,10] as follows:

> Type I: Totally macroporous meshes include Atrium (Atrium Medical Corp., Cambridge, MA), Marlex (C.R. Bard, Inc., Bellerica, MA), Prolene (Ethicon, Inc., Somerville, NJ), Surgipro monofilament (U.S. Surgical Corp., Norwalk, CT), Trelex (Meadox Boston Scientific Corp., Oakland, NJ), and Composix (Davol, Inc. Cranston, RI). These meshes have pore sizes larger than 75 microns, which is the required pore size for admission of macrophages, fibroblasts, blood vessels, and collagen fibers into the pores. Polypropylene monofilament mesh is the most common of this type of mesh.
>
> Type II: totally microporous prostheses with multifilament or microporous components, such as expanded PTFE or Gore-Tex Soft Tissue Patch and Gore-Tex DualMesh (W.L. Gore and Assoc., Flagstaff, AZ). These prostheses contain pores that are less than 10 microns in at least one of their two surface dimensions.

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Type III: macroporous prostheses with multifilament or microporous components, such as nonexpanded PTFE mesh or Teflon mesh (C.R. Bard, Inc., Billerica, MA), braided polyester mesh or Mersilene (Ethicon, Inc., Somerville, NJ), braided polypropylene mesh or Surgipro (comes as monofilament as well), and perforated expanded PTFE patch or Gore-Tex MycroMesh.

Type IV: biomaterials with submicronic pore size, such as Silastic, polypropylene films. These are not suitable prostheses for hernia repair; however, in combination with type I biomaterials; they can be used as a physical barrier between mesh and viscera in the form of adhesion-free composites such as Composix mesh (Davol, Inc., Cranston, RI).

Other important properties of mesh include thickness and rigidity. These properties have a direct impact on mesh handling, performance, and conformability. Conformability determines the distance between the mesh-tissue interface and therefore the deposition of collagen. Poor conformability can result in seroma formation. Smooth conformability results in a more rapid deposition of collagen [6].

IV. MESH IN VIVO

Within hours of creation of the wound, the prosthetic-tissue interface is heavily populated with inflammatory cells and bioactive mediators (platelet-derived growth factor, fibroblast growth factor, transforming growth factor beta, Insulin-like growth factor, and epidermal growth factor). As polymorphonuclear leukocytes adhere and become activated at the mesh interface, they release a variety of products capable of causing tissue injury. These agents allow cleansing and debridement of wounded or dead tissue and/or organisms. The presence of prosthetic material may prolong or enhance this process and induce enhanced tissue destruction. Also, prosthetic material may sequester slime-producing pathogenic organisms or necrotic debris, thereby preventing the cellular and metabolic defense mechanisms from accomplishing their goal of removing microbes and debris.

The cellular population at the prosthetic-tissue interface 5–7 days after creation of the wound is largely composed of mononuclear phagocytes that differentiate into resident macrophages. Macrophages attempting to phagocytose the prosthetic eventually coalesce into foreign-body giant cells in the presence of indigestible prosthetic material.

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Connective tissue synthesis is the final stage of wound healing. Collagen is initially secreted from fibroblasts and smooth muscle cells as a monomer. The collagen monomers polymerize into a thick helical arrangement of insoluble fibers in the extracellular space. Collagen synthesis remains elevated for months in the wound area although net collagen loss becomes greater than that deposited by day 21 as the collagen matures. Collagen remodeling begins after day 21. At this time collagen is reoriented and remodeled into an interlocking network of fibers that are more compact, thick, and parallel to one another (i.e., mature collagen). Because of the remodeling, bursting strength increases for up to 6 months after this period. However, healed tissue regains only 80% of its normal strength. The presence of permanent prosthetics supplements wound strength, whereas absorbable meshes are lysed at this time and add no further synergy to the repair [11].

Surface properties of different meshes determine the nature of the inflammatory response. Meshes with irregular surface characteristics allow migration of inflammatory tissues and ingrowth of connective tissues. Surface tension is defined as the ability of a material to induce interaction with the biological phase, including promotion of cell spreading and attachment. The higher the surface tension, the more intense the response. Alternatively, low surface tension reduces the ability of inflammatory cells to migrate onto the mesh, thus leading to the inability to resist infection (as in the case of Teflon mesh). The nature of the surfaces from which the biomaterials are fabricated determines the type of interaction those surfaces are likely to have with the protein-rich aqueous environment after implantation. Thus, if we attempt to classify meshes based on their surface tensions Teflon (PTFE) has the lowest and Nylon would have the highest. This is borne out on studies of explanted materials used in vascular procedures. Teflon had a minimal response, with a thin inner and outer layer of fibrin, while Nylon had a thick fibrin lining on the inner surface and thrombus occluding the lumen [12]. Unfortunately, studies of surface tension comparisons between the newer prosthetic materials have not been done. However, it would follow that ePTFE has lower surface tension than polypropylene, which, in turn, has lower or equivalent surface tension to polyester.

The interactions at the mesh-tissue interface involving surface protein shape change may lead to the initiation of any of the four major pathophysiological phenomena (inflammation, thrombosis, infection, and neoplasia). The sequelae of initiation of these pathophysiological

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phenomena range from clinical insignificance to major medical complications and device failure [13].

Inflammation is marked by an acute phase involving dilation of blood vessels as well as the accumulation of fluid and plasma components in the affected tissue. Platelets and polymorphonuclear leukocytes mediate the vascular and tissue elements. Chronic inflammation occurs when the acute phase is unable to eliminate the injurious agent or restore injured tissue to its normal physiological state. Macrophages are the most prominent cells in this state. The immune response is a complex defense reaction involving antibodies and a variety of cells. Finally, wound healing follows any of the first three responses chronologically and is marked by the replacement of damaged tissue with extracellular components needed for scar. Physiological wound contraction increases with the extent of inflammation [13]. Amid reported shrinkage of implanted polypropylene mesh is $\sim$20% of length and 30–40% of mesh area. Shrinkage appears to be a consequence of the thickness of the fibrous capsule rather than from the chemical properties of the implanted material [9,10].

Thrombosis has minimal relevance in mesh usage, as mesh is generally placed extravascularly. However, mesh clearly can activate platelets and induce thrombosis. Different meshes have different abilities of activating platelets and thrombosis based on their surface tension. However, data are not available on all biomaterials as not all are used in vascular surgery [12,13].

Infection as it pertains to the surface interaction is discussed further on in this chapter. Neoplasia has not been demonstrated as yet in human studies. Rodent studies have demonstrated the occurrence of sarcomas, although the mechanisms for induction of the tumors are unclear [13].

V. PROSTHETICS AND INFECTION

Infection in a surgical wound results from the inoculation of bacteria within the wound, the virulence of the bacterial contaminant, the presence of adjuvant variables in the wound, and the integrity of the host inflammatory/immune response [14].

In clean hernia wounds, factors that act as adjuvants for wound infection include the presence of hematoma, necrotic tissue (perhaps from cautery use), and foreign bodies. Elek and Conen demonstrated that silk

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sutures in a wound reduced by 100-fold the number of bacteria needed to cause an infection [15]. The mechanism of infection appears to be related to the small interstices that can hide micro-organisms from polymorphonuclear leukocytes and macrophages.

Infections from the body of the mesh are rare. Most infections appear to arise at the periphery from the knots applied to sutures securing the mesh. Additionally, bunched mesh at the edges may create dead space, which may lead to infection [14].

Accumulation of pus around the foreign body results in inflammation on the surface of the closed wound. Digestion of soft tissues and fascia from the edges of the mesh results in failure of the hernia repair as the mesh separates from tissue [14].

The utility of mesh in an infected wound is discussed further on. In a field with a high inoculum of bacteria and frank infection, placement of nonabsorbable mesh is unwise. The use of absorbable mesh to temporize the repair has been advocated in the literature. This will do little to repair the hernia but will allow later repair after the infection has been resolved. The development of collagen tissue grafts, whether porcine or human, has revolutionized plastic surgery. The use of these allo- and xenografts in hernia surgery is presently being evaluated. The advantage offered is rapid incorporation of the tissue, with development of vascular channels and ingrowth of tissue and migration of phagocytes. Whether these grafts can be used in contaminated fields remains to be seen.

VI. PROSTHETIC MATERIALS

Many different types of meshes have been utilized in the history of hernia repair [5]. These have included silver filigrees, tantalum gauze, stainless steel, fortisan fabric, polyvinyl sponge, nylon, Silastic, and Teflon. Development of the ideal mesh for repair has not yet been achieved. At present, the most commonly used meshes in hernia repair include polypropylene, polyester, and ePTFE. Over recent years these meshes have been manipulated to include changes in pore sizes, textures, and additives. Additives include impregnated antimicrobials and elements of absorbable mesh or non-adhesion-forming substances in hybrid meshes.

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VII. NONABSORBABLE MESHES

A. Polypropylene Mesh (Marlex, Proline, Surgipro, Trelex)

Usher introduced a new polyethylene plastic mesh called Marlex-50 in 1958–59 (15–17). Usher and Wallace placed various plastics into the peritoneal cavities of dogs and found that Teflon and Marlex caused the least foreign-body reactions of the meshes tested. Marlex was found to possess a high tensile strength (50,000–150,000 psi) and pliability; it was also impervious to water and resistant to most chemicals, with a softening temperature of 260°F, so sterilization by boiling was not a problem; and, as an implant, it became infiltrated by connective tissue [18].

By 1962, a survey of American surgeons by Adler reported that 20% were using Marlex mesh for complicated hernia repairs [19]. Usher introduced a new version of Marlex in 1963 constructed of a knitted mesh of polypropylene monofilament fiber [20,21]. In 1965, Jacobs and colleagues found knitted mesh to be useful in the repair of difficult incisional hernias [22]. In the February 1989 issue of the *American Journal of Surgery*, Lichtenstein and associates reported on 1000 consecutive patients with primary repair of inguinal hernia using a tension-free repair and employing a Marlex mesh prosthesis to bridge the direct floor of the groin without approximation of the tissue defect [23]. Marlex is a monofilament mesh. Each filament has a diameter of 0.017 cm. The mesh is 0.065 cm thick and has a density of $0.23\,g/cm^3$. Bursting strength is $68.9 +/- 1.9$ kg and $4.5 +/- 0.12\,kg/cm^2$. Pores vary from 68–23 μm × 23 μm. Tensile strength is 2.66 kg 10 weeks after implantation. Strength increases 50% over weeks 2–10 [13].

The pores of Marlex enable penetration of fibrous tissue. Greca and associates evaluated polypropylene meshes of different pore sizes and reported their results in canine models. They found that larger pore size did not decrease tensile strength in the mesh 30 days after implantation. The larger-pore-size mesh (T-mesh) also had more mature collagen, with better fiber orientation [24].

Wound seromas and sinuses have been reported to occur with polypropylene mesh. It may cause fistula formation (whether due to the inflammatory reaction or inherent stiffness and roughness of the mesh). Law and Ellis found that Marlex induced a dense fibroblastic response [25]. Mesothelial cell ingrowth was also irregular as compared with ePTFE [11]. According to Amid, the roughness of the mesh is a positive

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aspect that increases fibroblastic reactions and host tissue incorporation [10]. Most authors and experts report that this particular property of Marlex makes placement intraperitoneally less desirable in the repair of incisional hernias [10].

Marlex has a reputation for being resistant to infection. Jones and Jurkovich [26] in 1989 reviewed their experience of using polypropylene mesh in the closure of infected abdominal wounds. Complications directly related to the mesh placement occurred in four patients; small bowel fistula developed in all of them; and wound dehiscence also occurred in one. All the meshes had to be removed. In 2000, Mandala and associates [27] evaluated the use of nonabsorbable mesh in different categories of wounds. They found that nonabsorbable mesh could be utilized in clean contaminated cases with a low risk of infection; however, use in contaminated and dirty cases is contraindicated in most cases. Marlex implanted in infected fields can become chronically infected and then may extrude. If infection occurs after implantation, it can generally be resolved with local care and antibiotics [28].

B. Dacron Mesh (Mersilene)

A polyester polymer from ethylene glycol and terephthalic acid was developed in 1939 and introduced to the United States in 1946. By the late 1950s, this material, known as Dacron, was machine-knitted into a fabric mesh and marketed as Mersilene by Ethicon. Polyethylene terephthalate is the most widely used polymer in the fabrication of textile components for medical devices [5].

Mersilene is a multifilament mesh, each filament of which is 0.0014 cm in diameter. The mesh is 0.023 cm thick and has a density of $0.19\,g/cm^3$. Bursting strength is $19.9 +/- 0.3\,kg$ and $1.3 +/- 0.02\,kg/cm^2$. Pores measure $120 \times 85\,\mu m$ [13].

Wolstenholme [29], in 1956, utilized a commercial Dacron fabric in the repair of 15 inguinal and 4 ventral hernias because of reluctance to implant the stiff metal prostheses then available. His results were encouraging, all patients healed without complications, but no long-term follow-up was reported. Durden and Pemberton [30], in 1974, emphasized that successful hernia repair with Dacron mesh requires careful and meticulous surgical technique. They repaired 96 large direct inguinal hernias with Mersilene mesh with one seroma, one recurrence, and no infections. In a group of 13 patients undergoing ventral herniorrhaphy with Dacron mesh as a bridge across the defect, complications included

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five seromas, no recurrences, and one patient with infection. The follow-up period was 2–5 years. No patient with Dacron mesh had difficulty with fragmentation of the implant, extrusion of the mesh, or pain from the presence of the prosthesis.

Abul-Husn in 1974 published his results on the repair of 23 hernias [31]. He noted that the mesh was fine and light yet strong and pliable, durable, and moderately elastic, also that it could be autoclaved and, because of its interlocking polyester fibers, could be cut with scissors to any shape desired by the surgeon without producing frayed edges.

In 1985, Von Damme [32] reported a series of 100 consecutive patients who underwent prosthetic repair of inguinal hernia through a preperitoneal approach. In 49%, the hernia was recurrent. Using a technique similar to Stoppa's, which is currently described as a "giant prosthetic reinforcement of the visceral sac" (GPRVS), he used mostly Dacron mesh to achieve a 100% success rate with one chronic draining sinus tract, one hematoma, and two hydroceles as complications. Von Damme emphasized that if there were no technical errors with this technique, there was no recurrence. In classical herniorrhaphy, however, even after a perfect operation, recurrence is always possible, even many years later, because the result depends not only upon the surgeon but also to a large extent on the tissues and the strain to which they are subjected.

In 1989, Wantz [33] reviewed his results using the procedure of GPRVS with 237 hernias of the groin in patients at high risk for recurrence. He used primarily Mersilene prostheses. His data emphasized that Dacron is the mesh of choice for GPRVS because it does not become rolled up or folded upon itself in the preperitoneal space. There were nine recurrences, most of which were noted within 6 months of surgery. Four of these recurrences were in the patients who had Mersilene placed. These were due to inadequate positioning of the mesh by the surgeon. Wantz stated, "Herniation after GPRVS is inconceivable, providing the mesh suitably adheres, does not disintegrate, and is correctly sized, shaped, and placed."

In vivo studies of polyester suture material show little to 10–20% loss of fiber strength after implantation. Studies of Dacron vascular grafts recovered from humans in the late 1970s showed evidence of in vivo degradation. Mersilene has been found to degrade after a sufficiently long period of time (20–30 years after implantation). Dacron has complement-activating properties. The material also has the propensity to swell and trap small molecules, which may result in the transfer of industrial processing solutions into the final anatomical site, where they

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may induce injury. The swelling (5% over 30 years) has been postulated to result from either absorption of water and blood proteins or due to chain scission (breaks in the molecular structure) and molecular weight loss associated with the introduction of hydroxy and carboxy groups into the surface layers of the fibers. In fiber form, the material evokes an aggressive macrophage-mediated inflammatory response coupled with a significant infiltrate of fibroblasts and neovascular tissues. Dacron also has a propensity to cause fistulization [13].

C. Expanded Polytetrafluoroethylene (ePTFE; Soft Tissue Patch)

PTFE is a fully fluorinated polymer with the chemical formula (CF2-CF2)n. RJ Plunkett of DuPont and Company discovered it accidentally in 1938 [34]. Its unique chemical and physical properties are well documented [35]. In 1963, Shisaburo Oshige discovered a process for expanding PTFE to produce a highly uniform, continuous fibrous, and porous structure that, after sintering, retained its microstructure with vastly improved mechanical strength [36]. The technique for expansion was refined by Gore [37] and initially applied clinically to the development of a functional vascular prosthesis introduced in 1975. The ePTFE was made into a sheet material and first used clinically for hernia repair in 1983. The ePTFE sheet appears smooth and is very pliable. The patch is composed of pillar-shaped nodes of PTFE that are connected by fine fibrils of PTFE with a multidirectional arrangement of the fibrils in the surface view, which imparts balanced strength properties to the patch in all directions. An internodal distance of 22 μm is noted, with 80% void volume for potential cellular penetration and collagen deposition. This material allows very low mesenchymal ingrowth and prevents adhesion formation [5].

ePTFE initiates a minimal inflammatory reaction. There is less dense scarring than with polypropylene, but the orderly deposition of collagen leads to better overall strength after implantation. Tensile strength is 1.565 kg after 10 weeks, which increases to 2.67 kg/cm at 15–20 weeks after implantation. ePTFE has been further engineered in two forms. Gore-Tex DualMesh, which is like the soft tissue patch but is multilaminar, has a relatively nonporous 3-μm surface that prevents adhesion formation. Gore-Tex MycroMesh contains macroperforations

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that allow collagen bridging to occur; it is used primarily in inguinal hernia repair [11].

The repair of large primary and recurrent ventral incisional hernias is the most demanding of all hernia repairs and is accompanied by high recurrence rates if a prosthetic biomaterial is not used [38]. Laparoscopic techniques for the repair of these difficult hernias are now well described [39–41]. ePTFE prostheses and transabdominal fixation sutures are standard for the repairs. No long-term data are presently available; however, 10- to 22-month data of laparoscopic ventral hernia repairs show a significantly lower recurrence rate [42].

Gillion in 1997 reviewed his experience with incisional and ventral hernia repairs with ePTFE [43]. Their infection and recurrence rates were each 4%. Follow-up was 37 months. Balen reported similar results in 1998 [44]. Gonzalez in 1999 had a 1- to 3-year follow-up, showing an infection rate of only 1.7% and a recurrence rate of 2.4% [45]. Bauer in 1999 had a recurrence rate of 19%, but nine of these cases were due to removal of infected mesh [46]. None of these series demonstrated bowel complications related to intraperitoneal placement of the mesh. To date, no bowel-related complications have been reported in the literature.

The most difficult problem with the ePTFE patch is the development of infection. Infection of the mesh can lead to poor tissue incorporation, as described in the 1991 study of Law and Ellis [47]. However, Brown, et al. [48] reported reduced bacterial adherence to the mesh as well and felt that the mesh might be utilized safely in a clean contaminated procedure. When the mesh does become infected, it is relatively easily removed. Gore-Tex impregnated with silver and chlorhexidene has been shown by DeBord et al. [49] in preliminary evaluations to be acceptable for implantation without adverse systemic or clinical effects. Dent and colleagues [50] presented experimental data using a Gore-Tex soft tissue patch impregnated with silver and chlorhexidene in a contaminated rat model. Adherence of bacteria to the prosthetic material is the initial step in the pathogenesis of prosthesis colonization. Impregnation of broad-spectrum antimicrobial agents has been shown to reduce bacterial colonization. In this study, 100% of the control patches were colonized vs. 30% in the antimicrobial impregnated patches. Additionally, control patches had more than 10^5 colony-forming units (CFUs) versus 10–200 CFUs in the silver-chlorhexidene patches. The antimicrobial was also retained in this model for more than 3 weeks. Systemic antibiotics often fail to prevent patch infections clinically

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because the drugs cannot penetrate the bacterial biofilm. The infectious risk should be theoretically lessened with the use of this mesh [5].

VIII. ABSORBABLE MESHES

Polyglycolic acid and polyglactin 910 meshes have been developed as outgrowths of the successful utilization of these slowly absorbable synthetic fibers as suture materials [5].

The use of Dexon (Davis & Geck, Inc., Danbury, CT) mesh to repair contaminated abdominal wall defects in patients was reported by Dayton and colleagues [51] in 1986. As an alternative to placing polypropylene mesh in a contaminated field, they used polyglycolic acid mesh to repair infected abdominal wall defects in 8 patients. In follow-up studies up to 18 months, 6 of the 8 patients developed hernias at the site of the absorbable mesh repair. Dayton et al. concluded that post-operative hernia development was probable in patients whose defects were repaired with absorbable mesh. However, this complication must be balanced against the serious complications of sepsis, fistula, bleeding, skin erosion, and drainage, which require removal of nonabsorbable meshes in a large percentage of cases when the latter are used in contaminated areas. The authors felt that placement of absorbable mesh for temporary abdominal wall support until wound contamination resolved might enhance the likelihood of subsequent successful placement of a permanent prosthesis [5].

Dexon mesh is a wide-weave version of polyglycolic acid braided fibers; it produces a soft, pliable, stretchable prosthetic netting that is biodegradable and gradually reabsorbed within 90–180 days. Tensile strength decreased approximately 50% from weeks 2–10 of implantation [13,52]. This mesh does cause adhesions, though evidence suggests that they fade as the mesh absorbs. It cannot be used for the definitive repair of hernias.

Vicryl (Ethicon, Inc. Somerville, NJ) mesh is a tightly woven cloth that is flexible although not elastic and shares physical and biodegradable properties with Dexon mesh [53]. Polyglactin 910 appears to be completely absorbed within 90 days. There is a variable rate of degradation. Tensile strength increases from weeks 2–10. Granulation and fibrosis can occur at the mesh interface. However, Vicryl promotes less collagen ingrowth than Dexon [13].

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In 1983, Lamb and colleagues [54] repaired clean rabbit abdominal wall defects using Vicryl mesh and found, at 3 weeks, that there was no weakness when compared with results from nonabsorbable meshes. However, at 12 weeks, the bursting strength of the Vicryl repair was significantly less than that of nonabsorbable meshes. In addition, 40% of the animals repaired with Vicryl mesh developed hernias due to inadequate fibrous tissue incorporation in to the mesh before hydrolysis of the prosthesis occurred. Lamb et al. concluded that Vicryl mesh was not a suitable biomaterial for the permanent repair of abdominal wall defects.

IX. NEW HORIZONS IN PROSTHETICS

A. Vypro (Ethicon, Inc., Norderstedt, Germany)

Klinge et al. [55] suggested that polypropylene was overengineered. The maximal tensile strength required of the abdominal wall is 16 N/cm, corresponding to the maximal intra-abdominal pressure that can be generated, about 20 kPa. For Prolene mesh, an intraabdominal pressure of more than 130 kPa would have to be generated to cause bursting. Additionally, Amid suggests that mesh structure is important to the clinical outcome due to both the amount of material and the pore size. The greater the total amount of foreign body, the greater the reaction by the host tissue. The greater density of Prolene mesh also makes it more rigid and difficult to handle.

Therefore Klinge et al., along with Ethicon, pioneered the development of a low-density mesh with a mechanical strength of 16 N/cm. The mesh is composed of polypropylene with large pores (5 mm) and is supplemented with absorbable polyglactin to improve its handling characteristics. In animal studies, the mesh had a high level of elasticity and evoked a low inflammatory response.

In December 1997, a prospective randomized trial was begun with Vypro. The infection rate for Vypro was 3.3% and recurrence rate was 2.8% (1 of 71 cases). Patients with the low-density mesh had improved functional outcomes. Histological analysis demonstrated a lower inflammatory response in low-density mesh in comparison to the higher-density Prolene and Marlex meshes. The lightweight mesh appears to incorporate with collagen fibers, which form a moderate capsule around the mesh structures and encircle single mesh filaments, whereas the periphery shows a thin scar plate oriented parallel to the mesh.

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Shrinkage of the mesh, which can be as high as 50% with heavyweight meshes, was found to be lower in dog studies with the low-density meshes, probably due to the low inflammatory response generated. The authors concluded that although long-term data are not yet available, the short-term data suggest improved tissue reaction and reduced functional restriction with use of this lightweight composite mesh.

B. Composix

Composix consists of an ePTFE surface placed intraperitoneally, with polypropylene mesh used to provide better incorporation of the mesh to the abdominal wall and to ensure a low potential for adhesion formation and chronic inflammation. There is not a large body of literature for this mesh currently. Amid has described its use in animals, where it shows promise in preventing intraperitoneal adhesions [10]. Bendavid describes his use of the two biomaterials (ePTFE and polypropylene) separately for the repair of incisional hernia, with good success in a few patients [56]. Millikan et al., in August 2002, described their experiences with Composix in ventral hernia repairs. They found no recurrences and no obstructions or fistulaes at a mean follow-up of 28 months [57].

C. Seprafilm

Seprafilm (Genzyme Corp., Cambridge, MA) is a bioabsorbable translucent membrane composed of carboxymethylcellulose and hyaluronic acid that has been shown to prevent postsurgical intra-abdominal adhesions. Several recent animal studies have assessed the use of Seprafilm in intraperitoneal mesh repairs. Rodent and pig models of incisional hernias have been repaired with polypropylene after insertion of Seprafilm to the viscera [58–61]. Short follow-up of 4–6 weeks has demonstrated no adhesion formation with good incorporation of the mesh. However, since polypropylene reactivity appears to be chronic and therefore the risk of adhesion formation and fistula formation persists, long-term studies of the utility of this approach will have to be assessed in animals and humans.

D. Collagen Grafts

Several biomaterials composed of cross-linked collagen are currently in use for the treatment of burns, diabetic ulcers, soft tissue defects, and

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gynecological and urological reconstructions. They—such as AlloDerm (Lifecell Corp. Branchburg, NJ)—are derived from human cadaveric dermis as well as porcine or ovine dermis; e.g., Surgisis (Cook Biotech, Inc., West Lafayette, IN), PeriGuard (LAmed, Oberhading bei Munchen), Permacol (Tissue Science Laboratories, Covington, GA, and Fortaflex Organogenesis, Inc., Canton, MA). These biomaterials have already been approved for use in humans for varying conditions, as noted above. Only recently are they being actively pursued for the repair of complex abdominal wall defects.

The dermis contains about 40% of the total collagen content of the body. The dermis combines optimal flexibility with high tensile strength in all directions due to its three-dimensional fibrous structure [62]. The use of dermis to repair abdominal wall defects would seem to fit the requirements of Hamer-Hodges criteria for the ideal prosthetic. The advantages of xenograft or allograft collagen over synthetic meshes include ease of handling, flexibility, permanence, and incorporation into the host tissue without chronic inflammation. The advantage over autologous flaps and grafts is reduced morbidity to the patient from the harvesting of these tissues.

All of these collagen matrices require some form of cross-linking of the collagen to prevent degradation by host collagenases and bacterial collagenases. The cross-linking process appears to be proprietary to each company. Initial use of the meshes had shown that particular processes for cross-linking led to calcification of the graft in vivo [62]. The new processes are purported to avoid this phenomenon.

All of the companies selling these matrices state that the advantages over synthetics include less tissue inflammation due to rapid incorporation in the host. All have histological data demonstrating vascularization through the implant. These characteristics may also improve the utility of these matrices in contaminated fields, where phagocytic activity is desirable. The grafts allow granulation to occur over their surfaces. All companies also state that these matrices can be directly apposed to bowel with minimal adhesion formation [63,64]. Studies are presently ongoing on the use of these grafts for abdominal wall repair [65–68]. Additionally, studies are ongoing on the risk of transmission of viral vectors, although the matrices are designed to be acellular.

Van Wachem and van Gulik report that the initial studies with dermal sheep collagen demonstrated weakening of the fibers over time, with some degree of degradation at 20 weeks despite improvement in the techniques for cross linking [62].

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X. CONCLUSION

Repair of abdominal wall defects continues to be an evolving science. The "ideal" mesh remains to be found. Host interactions with mesh are based on both the chemical and physical structure of the mesh as well as the character of the host tissue and the presence of bacteria. Clearly synthetic meshes lead to a wide variety of chronic inflammatory states and, ultimately, this leads to problems with recurrences, infections, fistulas, and abscesses.

The wide range of current biomaterials does allow the surgeon to pick and choose a particular prosthetic based on strength, resistance to infection, conformability, host factors, and invariably cost. Synthetic meshes offer a long history of successful use in human abdominal wall repairs. Will the new dermal collagen matrices prove to be the final word on hernia repair? Only future studies will answer that question. Ultimately, each patient must be approached individually in regard to the choices made for a surgical technique and the best prosthetic.

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6

Processes Governing Bacterial Colonization of Biomaterials

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I. THE PROBLEM: BACTERIAL COLONIZATION OF BIOMEDICAL DEVICES

Patients faced with death or disability are now routinely restored to health because of artificial organs, organ supplements, ventricular assist devices, wound-healing biosorbable hydrogels, lyposome drug delivery particles, and assorted endoprostheses. The production of biomedical devices and tissue engineering–related materials in the United States is a $600-million-per-year industry and expanding rapidly. It is estimated that over 5 million artificial or prosthetic parts are implanted per annum in the United States alone [1]. However, over half of hospital-acquired infections are associated with implants or indwelling medical devices, with the case-to-fatality ratio of these infections ranging between 5 and 60% [1,2]. Bacterial infections by adherent bacteria have been observed [1] on prosthetic heart valves (valve endocarditis), orthopedic implants, intravascular catheters, cardiac pacemakers, vascular prostheses, cerebrospinal fluid shunts, urinary catheters, ocular prostheses and contact lenses, and intrauterine contraceptive devices (Fig. 1).

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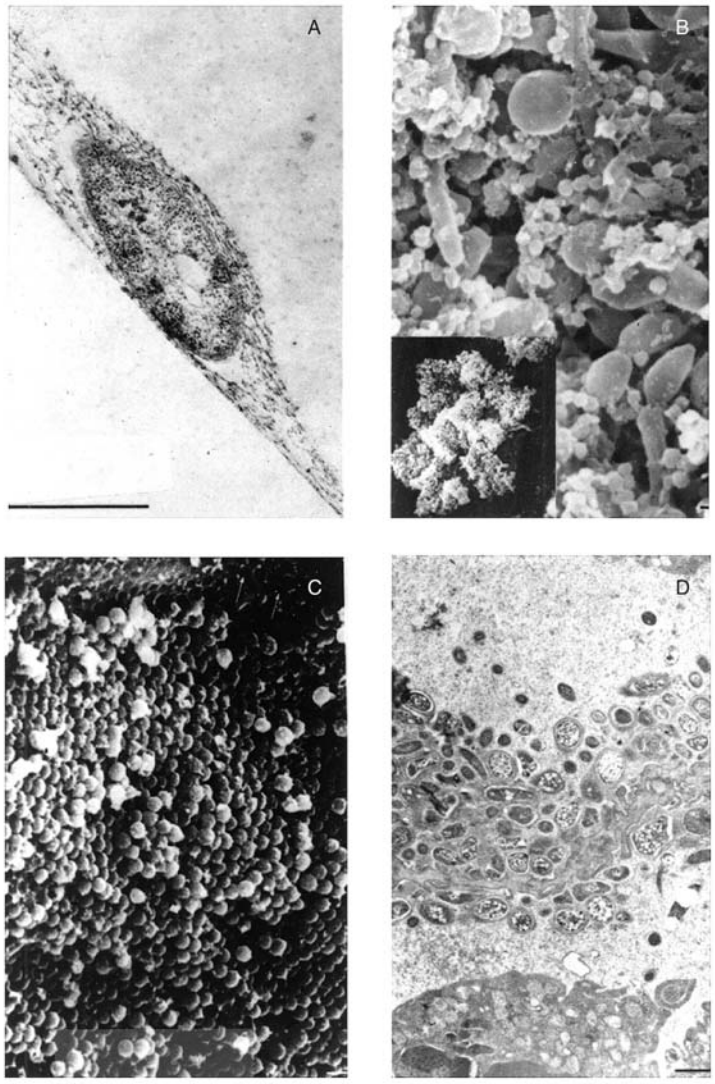

Figure 1 A. *Pseudomonas aeruginosa* attached to plastic cup portion of prosthetic hip replacement. B. *Staphylococcus epidermidis* biofilm occluding a Hickman catheter. C. *S. epidermidis* colonization of cardiac pacemaker. D. Microbial flora found on intrauterine contraceptive device. (From Ref. 139.)

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The body reacts to prosthetic implants by coating them with a film comprising various proteins (e.g., fibronectin, laminin, fibrin, collagen, and immunoglobulins), some or all of which can serve as binding ligands to the receptors of colonizing bacteria. Bacteria, transported to the substratum by either molecular diffusion or convective transport, can adhere by either a nonspecific adhesion mechanism (governed by electrostatic forces acting between the cell and surface) or a specific adhesion binding reaction. Certain cell surface molecules, termed *receptors* can bind to specific molecules, termed *ligands*, found on the substratum. Once attached to the substratum, bacteria can produce copious amounts of extracellular mucopolysaccharides [3,4] that bind divalent cations, forming a tenacious three-dimensional matrix of extracellular polymers [5]. These bacterial polymers can mix with those of other species, products of host cells, or blood platelets to form a mixed-cell line biofilm that is highly resistant to rigorous antibiotic challenges [6–8]. Dankert et al. [1] and Jacques et al. [9] provide excellent albeit dated reviews of bacterial infections associated with a myriad of indwelling biomedical devices.

This chapter focuses on recent research on processes that govern biofilm colonization of biomedical implants. Only a cursory overview of bacterial cell transport, nonspecific bacterial adhesion, and cellular growth is given here; for greater detail the reader may consult reviews by Bryers (2000) [10], O'Toole et al. (2000) [11], and Bisno and Waldvogel (1994) [12]. Rather, emphasis here is placed on recent advances in the areas of substratum control of bacterial adhesion, bacterial-specific adhesion processes, and cell:cell communication control of bacterial adhesion processes.

II. PROCESSES GOVERNING BIOFILM FORMATION AND PERFORMANCE

Figure 2 illustrates, for an arbitrary analytical measure, the typical accumulation of biofilm at a surface as a function of time. Initially, the substratum is conditioned and cells attach reversibly, then irreversibly. Next, attached cells grow, reproduce, and secrete insoluble extracellular polysaccharide material. As the biofilm matures, biofilm detachment and growth processes come into balance, such that the total amount of biomass on the surface remains approximately constant in time.

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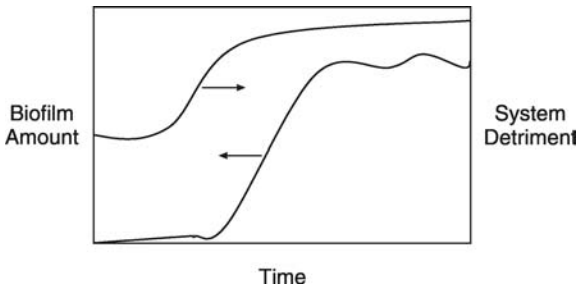

Figure 2 Net accumulation of biofilm and concomitant symptoms of biofilm formation.

Processes governing biofilm formation and persistence (Fig. 3) include the following:

1. Biasing or preconditioning of the substratum by macromolecules present in the bulk liquid
2. Transport of planktonic cells from the bulk liquid to the substrate.
3. Adsorption of cells at the substrate for a finite time followed by desorption (release) of reversibly adsorbed cells.
4. Irreversible adsorption of bacterial cells at a surface.
5. Transport of substrates to and within the biofilm.
6. Substrate metabolism by the biofilm-bound cells and transport of products out of the biofilm. These processes are accompanied by cellular growth, replication, and extracellular polymer production.
7. Biofilm removal (detachment or sloughing).

Research in the past 10 years has expanded our understanding of the molecular and genetic parameters that control many of these macroscopic processes. Biofilms are no longer considered uniform biological structures in time or space, and processes that control this heterogeneity have been characterized and are being mathematically described.

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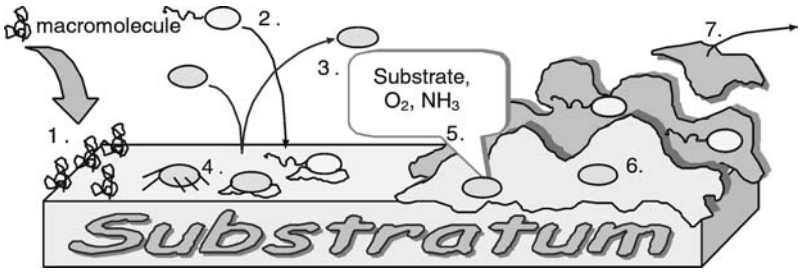

Figure 3 Processes governing biofilm formation. See text for definition of numbered processes.

III. TRANSPORT OF MICROBIAL CELLS TO THE SUBSTRATUM

When a clean surface is immersed in natural water containing dispersed microorganisms, nutrients, and organic macromolecules, transport of these components to the substrate can control the initial rate of cell adhesion or biofilm accumulation. In very dilute dispersions of microbial cells and nutrients, transport of microbial cells to the substrate may be the rate-controlling step in biofilm accumulation.

Mass transport processes are influenced strongly by the mixing in the bulk fluid, which is generally related to the fluid flow regime. Laminar and turbulent flow are the two distinct fluid flow regimes that influence mass transport. Transport of molecules and small particles ($<10\,\mu m$) in quiescent or laminar flow is controlled by sedimentation, motility, or molecular diffusion. In turbulent flow, both convective and diffusive transport prevail.

A. Quiescent Conditions

Under quiescent conditions, transport of bacteria from a bulk fluid phase to a surface is by either gravitational forces (i.e., sedimentation), Brownian diffusion, or motility for those organisms capable of motility. Sedimentation rates are small for bacteria because of their size and specific gravity (approximately 1.05–1.10). Microorganisms of a size 1–$4\,\mu m^3$ are limited in Brownian motion and hence have a small Brownian diffusivity (see below). Therefore, motility may be a more important

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transport process in quiescent systems. Many microbes are capable of motility through their own internal energy, independent of fluid forces. Motility is frequently related to some form of taxis (i.e., cell motility induced by external stimuli) in response to a concentration gradient.

In an unbounded fluid medium, flagellated, motile bacteria move in a manner resembling a three-dimensional random walk. That is, they swim in nearly a straight line for about a second (running), tumble in place, and then begin a run in another direction [13]. If there is not chemical or external stimulus (chemotaxis), the angle of deviation between one run and the subsequent run is totally random. Angles are influenced in the case of positive chemotaxis so that, on the average, cells move toward the source of the chemical attractant; the opposite is true for negative chemotaxis.

B. Laminar Flow

For laminar flow, the mechanism for mass transport of cells in the liquid phase is molecular diffusion, as described by Fick's first law of diffusion, Eq. (1):

$$N_{Ax} = -\mathfrak{D}_{AB}\, dC_A/dx \tag{1}$$

Fick's law states that diffusive flux of solute A in solvent B in the x direction is proportional to the concentration gradient in that direction. Fick's law is used not only to describe diffusion of soluble components but can also be applied for large molecules or small particles, such as microbial cells, diffusing in water. In the case of particles, the Brownian (or non-Brownian) diffusion coefficient is used in Fick's law. If the cells are motile, their transport rate is increased significantly and can be estimated as per Jang and Yen (1985) [14].

C. Turbulent Flow

Within a turbulent flow regime, larger particles suspended within the fluid are transported to the solid surface primarily by fluid dynamic forces. Particle flux to the surface increases with increasing particle concentration. However, particle flux is also strongly dependent on the physical properties of the particle (e.g., size, shape, density) and is influenced by many other forces near the attachment surface.

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Larger particles develop a ''sluggishness'' with respect to the surrounding fluid. As the particle approaches the wetted surface, eddy transport diminishes and the viscous sublayer exerts a greater influence. For soluble matter and small particles, diffusion can adequately describe transport in the viscous layer [15]. For larger particles, other mechanisms must be considered to explain experimental observations. Transport of microbial cells (0.5–1.0 μm effective diameter) can be transported from the bulk fluid to the wetted surface can be influenced by several mechanisms, including the following: diffusion (Brownian and non-Brownian), gravity, thermophoresis, fluid dynamic forces, inertia, lift [16], drag [17,18], drainage [19], and turbulent bursts [20,21]. Thermophoresis is only relevant when particles are being transported in a temperature gradient [19]. If the surface is hot and the bulk fluid is cold (e.g., a power plant condenser), the thermophoretic force will repel the particle from the surface.

D. Surface Topography Effects

One factor contributing to transport and potentially to physicochemical effects on attachment is the influence of surface topographical features. Historically, it is assumed that bacteria preferentially stick to rougher surfaces for three reasons: (1) a higher surface area available for attachment, (2) protection from shear forces, and (3) chemical changes that cause preferential physicochemical interactions. For example, work with bacterial suspensions has shown that a rough metallic surface had 1.4 times more microorganisms attached than an electropolished, smooth surface [22]. Adhesion rate constants of *Pseudomonas aeruginosa* to electropolished 316-L stainless steel plates were 100 times lower than those to 120-grit hand-polished surfaces [23]. Other work with stainless steel has shown that bacteria were preferentially associated with the grain [24], although, one should realize that grain boundaries exhibit not only a change in topography but also a change in chemistry [25]. Perturbances in fluid flow create zones of negative pressure and thus eddy currents immediately downstream of the outcropping. Unfortunately, prior to 1999, most studies investigating the effects of surface topography on bacterial cell adhesion were unable to independently vary topography without also changing surface chemistry.

In a benchmark paper, the effect of substratum topography on bacterial surface colonization was studied by Scheuerman et al. (1999) [26] using a chemically homogeneous silicon coupon as substratum. Their

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experiments used two motile bacterial species, one nonmotile strain of one species, and an inert colloidal particle. "Grooves" 10 μm deep and 10, 20, 30, and 40 μm wide were etched on the coupon perpendicular to the direction of flow. Flow (Re = 5.5) of a bacterial suspension (10^8 cells per milliliter) was directed through a parallel-plate flow chamber inverted on a confocal microscope. Quantitative image analysis was used to document adsorption patterns and calculate rates of adhesion.

Motile bacteria attached at a higher rate than *P. fluorescens* mot- mutants. For all bacteria, the rate of adhesion was independent of groove size and was greatest on the downstream edges of the grooves. There was a significant effect of the presence of the grooves on the rates of attachment of the cells, with preferential attachment seen on the downstream edges. The rates of attachment followed the general trend of being highest on the downstream edge and lowest at the flat, control sections of the coupon. While the presence of grooves had a pronounced effect on bacterial attachment, there was no significant difference in attachment due to groove widths. This is somewhat surprising, since hydrodynamic models predicted no disruption of the streamlines in the vicinity of a 10-μm-wide groove; but for the 40-μm-groove, there is expected marked perturbation of flow, including corner eddies. In the Sheuerman experiments, only motile bacteria could be found regularly in bottoms of the grooves at numbers comparable to those on the control surfaces. Nonmotile organisms and colloidal beads could not be found in the grooves, suggesting that the presence of organisms in these troughs is a nonselective function of motility. This finding was somewhat surprising, as hydrodynamic models suggest that there would be eddies in the corners of the larger grooves that should have resulted in localized hydrodynamic entrainment of the cells and particles.

IV. MOLECULAR ASPECTS OF BACTERIAL ADHESION

Nonspecific adhesion interactions are defined as interactions between a cell and surface or a cell and another cell that do not involve molecular structures on the cell surface—i.e., receptors—binding in a lock-and key fashion, to a complementary *ligand* molecule on an surface. Nonspecific interactions are thus not biochemically specific, but they do act to increase or decrease the overall strength of the interaction. The three relevant types of nonspecific forces for cell-cell and cell-surface adhesion (Fig. 4) are electrostatic forces, steric stabilization, and van der Waals

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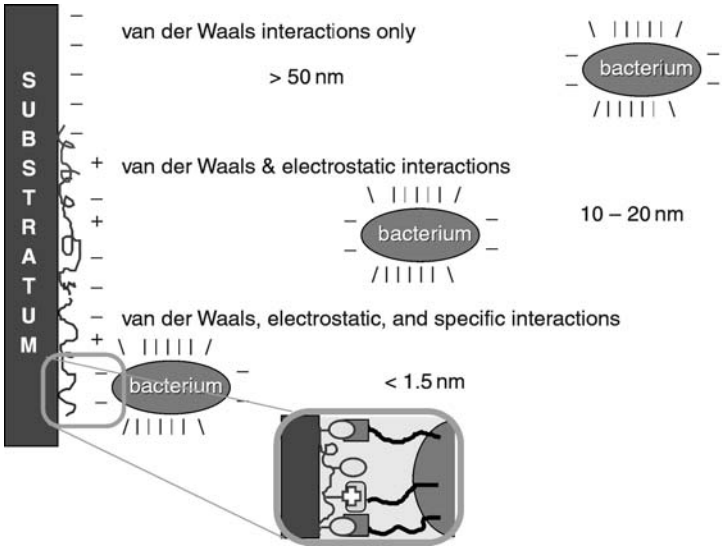

Figure 4 Nonspecific forces contributing to bacterial adhesion at an inert interface. Inset: Specific adhesion.

forces. These are discussed thoroughly in a number of recent review articles [27,28].

Specific adhesion refers to the involvement of receptor:ligand bonds in cell adhesion (Fig. 5). In many cases, it is believed that permanent adhesion would not occur without these interactions, and thus the expression of receptors on a cell and/or the modulation of receptor affinity or receptor number with time serves to control the types of surfaces with which a cell will interact.

A. Substrate Preconditioning

1. Intentional Surface Pretreatments

Studies of protein adsorption to various substrates indicate that protein adsorption is a complex phenomena influenced by surface chemistry, surface charge, solvent effects, and protein composition [29]. Investigation of fibrinogen adsorption to tertrafluoroethylene glow-discharge–

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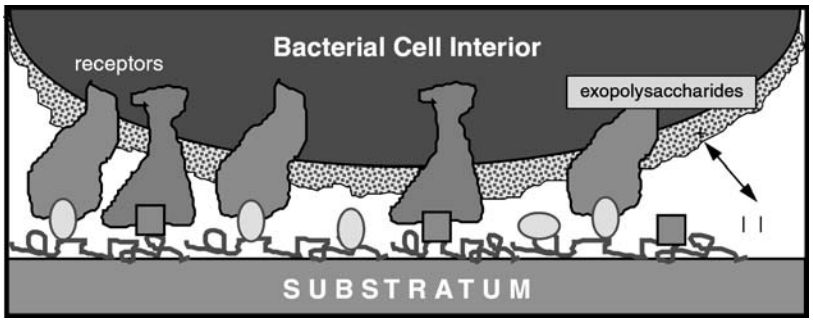

Figure 5 Schematic of receptor:ligand–mediated specific bacterial adhesion.

treated polymers indicated surface-dependent changes in ''tightness'' of binding as well as conformational changes that affected the exposure of several platelet binding regions [30]. Adsorbed proteins thus may influence subsequent cellular interactions with an implanted material surface by altering interfacial free energy, conformational changes that expose/hide cell binding regions, dynamic turnover, and replacement with other adsorbed protein species, and protein mobility on the surface [29].

Biomaterials with randomly coated plasma proteins present an ill-defined surface that fails to mediate ''normal'' mammalian cell behavior. Thus, a major research emphasis in the biomaterials community is directed toward developing interfaces that present specific biomolecules designed to solicit a desired cellular response. Polymer materials shown to resist nonspecific adhesion can be modified by covalent immobilization of bioactive peptides (such as the arginine-glycine-aspartic acid-serine RGDS, a tetrapeptide present in many extracellular matrix proteins identified as the cell binding region of many mammalian cells) and proteins (such as fibronectin) (see, for example, Massia and Hubbell, 1991; Kao and Hubbell, 1998) [31,32]. These materials have been shown to promote adherence and proliferation of fibroblasts and endothelial cells (see, for example, Drumheller and Hubbell, 1994; Neff, et al., 1999) [33,34]. Studies by Kao and Hubbell (1998) [32] suggest that it is possible to achieve specific monocyte/macrophage adherence by using covalently grafted peptides such as RGDS. Research with RGD-containing peptides

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suggested that ligand density, as well as ligand identity, are important in dictating specific cellular adhesion to the material [31,33,35,36].

Covalent immobilization of specific cell signals (peptides or other biological molecules) to substrates has been achieved by a variety of methods. Biomolecule immobilization techniques are widely used in such areas as enzyme-linked immunosorben assay (ELISA), biosensors, bioseparations, and biomaterials [37]. Examples of such techniques include biotin-streptavidin binding, carbodiimide chemistry, or coupling via photoreactive species (e.g., arylazides, nitrobenzyl, diazerines) (Zull, et al., 1994; Blawas and Reichert, 1998) [37,38]. These chemistries usually produce linkages between amino and carboxyl groups present in proteins or peptides to a similarly functionalized surface.

The activity of the immobilized protein is a function of its conformational stability; thus, immobilization techniques that produce site-specific attachment and orientation of a protein on a surface that minimize protein denaturation have been investigated (Zull, et al., 1994) [38]. A hydrophilic tether between the protein and surface as well as chemistries that target sulfhydryl groups in proteins (present in smaller quantities than amino or carboxyl groups) are suggested as techniques to increase protein stability and produce uniformly orientated surfaces [37–39]. An additional advantage of the use of tethering molecules is enhanced accessibility of the attached ligand to promote receptor-ligand–mediated adhesion.

However, many of these molecules selected to decorate new biomaterials to attract macrophage may unfortunately promote bacterial adhesion and colonization. In addition, passive contamination of a substratum can also bias surfaces for bacterial adhesion.

2. *Unintentional Substrata Preconditioning*

Transport of Molecules. Transport of molecules and small particles ($<$0.01–0.1 μm) in quiescent or laminar flow is described satisfactorily in terms of molecular diffusion, i.e., Fick's law. In turbulent flow, the diffusion equation must be modified to include turbulent eddy transport (an eddy is a current or bundle of fluid moving contrary to the main current). Compared to larger particles such as bacterial cells, the transport of molecules and small particles is quite rapid. Consequently, adsorption of an organic conditioning film is frequently reported to occur "instantaneously."

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Adsorption of a Conditioning Film. Adsorption of an organic film is an interfacial transfer process (i.e., the molecule is transferred from the bulk liquid compartment to the substratum compartment) and occurs within minutes of exposure causing changes in the properties of the wetted surface. Bryers (1980) observed 15 mg m^{-2} of organic material within minutes on glass in a laboratory system [40].

Adsorption of an organic conditioning film is very rapid as compared to the other biofilm processes. Investigators have shown that materials with diverse surface properties (e.g., wettability, surface tension, electrophoretic mobility) are rapidly conditioned by adsorbing organic molecules when exposed to solutions with low organic concentrations. In the case of biomedical implants, preconditioning molecules are predominantly blood plasma or extracellular matrix proteins or glycolipids. The layer is not static, as evidenced by the results of Brash and Samak (1978) [41], indicating significant turnover in molecular (proteinaceous) films on polyethylene. Protein molecules in the bulk fluid (laminar flow) were continuously exchanging with adsorbed proteins. With increasing molecular weight, polymers adsorb more strongly due to multiple binding sites and they may displace molecules of lower molecular weight [42].

The conditioning film is generally observed or presumed to be uniform in both composition and coverage. But there appears to be little conclusive evidence that the spatial distribution of the conditioning film is uniform so that a "patchy" distribution is possible. The film may be heterogeneously distributed over the substratum and may not cover the entire surface, especially when viewed at the scale of a micro-organism or compared to the size of the appendages and polymers, which first interact with the substratum.

B. Nonspecific Adhesion Processes

Adhesion is a ubiquitous aspect of microbial life in most natural and engineered systems. Bacterial adhesion is often studied from a biological viewpoint—i.e., based on the assumption that adhesion is brought about by specific molecules, appendages, or sites at the cell surface, called adhesins or receptors. Alternatively, general models for the description of adhesion can use a physicochemical viewpoint, for which literature provides two approaches. The first is based on the Gibbs energy involved in the destruction and creation of interfaces [43,44] while the second is

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based on the theory of Derjaguin, Landau, Verwey, and Overbeek (DLVO) for colloidal stability [45,46].

Based on observations, initial bacterial adhesion has been divided into two separate stages: reversible and irreversible adhesion. *Reversible adhesion* refers to that association of a bacteria to a surface where the bacterial cell continues to exhibit a two-dimensional Brownian motion and can be removed from the surface by relatively weak forces, including the bacterium's own mobility. *Irreversibly adherent* bacteria no longer exhibit Brownian motion and cannot be removed by moderate shear forces.

Treating bacterial adhesion as a physicochemical process is complicated by the nature of bacterial cells, which are not "ideal" particles. They have no simple geometry, definitive boundary, or uniform exterior molecular composition. Internal chemical reactions can lead to changes in molecular composition both in the interior and at the surface, with molecules and ions constantly crossing the bacterium/water interface. Although altered, these chemical processes also continue after adhesion. Therefore the adhered cells are rarely in complete chemical equilibrium with their environment. So while many have tried to model bacterial adhesion processes with colloidal theory, one should be aware that interpretations must be regarded with caution.

C. Receptor-Ligand–Mediated Specific Adhesion

While it may appear below that bacterial-specific adhesion is dominated by protein-protein or lectin interactions, this is only because the major source of definitive research comes from the infection-pathogenesis microbiology sector or literature on biomedical device-based infections. While bacteria in open waters or in heat exchanger tubes probably employ specific adhesion mechanisms, almost nothing is known about adhesion in such systems, since the ligands may be complex carbohydrates, humic acids, or proteins. Unfortunately, less quantitative information about these latter receptor-ligand pairs exists in comparison to that found in the infection literature.

In intact organisms, most extracellular matrices (ECM) are covered by epithelial or endothelial cells and therefore are not available for bacterial binding and colonization. However, any type of trauma (e.g., injury, surgery, biomedical implant placement) that damages the host tissue may expose the ECM and allow colonization by bacteria. Accordingly, many micro-organisms that cause opportu-

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nistic infections have been shown to express microbial surface components recognizing adhesion matrix molecules (termed MSCRAMMs by Höök and coworkers) [47,48]. A bacterium can simultaneously express several adhesion receptors that recognize a variety of matrix proteins. Furthermore, some micro-organisms, such as enteropathogenic *Yersinia* [49] and *Porphyromonas gingivalis*, appear to express an adhesin that can bind multiple host ligands [50]. Ligand-binding sites in microbial adhesion receptors appear to be defined by relatively short contiguous stretches of amino acid sequences (motifs). Because a similar motif can be found in several different species of bacteria, it appears as though these functional motifs are subjected to interspecies transfer. Unfortunately, the ligand-binding sites in only a few microbial adhesion receptors have been defined so far; therefore generalizations are risky.

First, to be classified as a microbial adhesion receptor, the molecule of interest must be bound to the microbial cell surface. Second, the microbial component must recognize a macromolecular ligand that can be found within the extracellular matrix. These ligands include components such as collagen and laminin that are found exclusively in the ECM, whereas other molecules defined as ligands (e.g., fibronectin, fibrinogen, and vitronectin) are part-time ECM molecules and also occur in soluble forms in body fluids such as blood plasma. Other potential microbial ligands, such as heparin sulfate proteoglycans, occur both in ECM forms and as intercalated cell membrane proteoglycans. Third, the microbial adhesion receptor's interaction with the extracellular matrix component should be of high affinity and exhibit a high degree of specificity; i.e., unrelated molecules should not be able to significantly interfere with the interaction between the adhesion receptor and its ECM ligand. Thus, adhesins of the lectin type that recognize carbohydrate determinants present on many different classes of molecules should not be classified as microbial adhesion receptors even though they may bind to ECM components. One could argue that adhesins recognizing glycosaminoglycans are both microbial adhesion receptors and lectins. Höök and coworkers have chosen to classify these adhesins as microbial adhesion receptors. Although numerous bacteria have been shown to bind a variety of ECM components (see Tables 1 and 2 in Patti, et al. [47]), the molecules involved in these interactions have in many cases not been identified nor characterized at a molecular level. Before a microbial component can be classified as a microbial adhesion

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receptors, its interaction with the ECM ligand should be characterized in sufficient detail to show that it fulfills the criteria above.

A single microbial adhesion receptor can bind several ECM ligands. For example, the plasmid-encoded outer membrane protein *Yad*A, which appears to be a collagen-binding microbial adhesion receptor on enteropathogenic *Yersinia* [51], can also bind laminin and an isoform of fibronectin [52]. A fibrinogen-binding microbial adhesion receptor present on *Porphyromonas gingivalis* is seems to also recognize fibronectin [53]. In addition, a microorganism can express several microbial adhesion receptors that recognize the same matrix molecule. For example, *Staphylococcus aureus* appears to express several fibrinogen-binding proteins [54,55], and *Streptococcus dysgalactiae* [56,57] and *S. aureus* [58] each have at least two genes encoding fibronectin-binding microbial adhesion receptors. This type of variation in the interactions between microbial adhesion receptors and their matrix ligands resembles the interactions between the eukaryotic integrins and matrix molecules, where one integrin can bind several different ligands.

The nonspecific adhesion forces described above provide only a weak attractive force, of the order of 10^3 dyne/cm^2 (10^{-5} dyne/μm^2) for typical cell-cell separation distances. In order to strengthen adhesive interactions as well as provide specificity, cell-surface receptors must play a role. One can examine the strength of a receptor-ligand bond from both an equilibrium and kinetic standpoint. From the equilibrium perspective, Bell (1978) [59] estimates the strength of a single receptor-ligand bond from the relation $f_c = \Delta G/r_o$, where f_c is the force required to break the bond, ΔG is the free energy of bond formation, and r_o is the range of the bond potential energy minimum. For $r_o = 10$ Å and $\Delta G = 13$ kcal/mole (corresponding to an equilibrium dissociation constant $K_D = 10^{-9}$ M), then $f_c = 9 \times 10^{-6}$ dyne/bond. A covalent bond with $\Delta G \sim 70$ kcal/mole and $r_o \sim 1$ Å, would require $f_c \sim 4 \times 10^{-4}$ dyne/bond. Noncovalent receptor:ligand bonds with $K_D < 10^{-9}$ M (i.e., higher-affinity bonds) would fall somewhere in between, with a logarithmic dependence of f_c on $(K_D)^{-1}$.

A related approach to analyzing the strength of a receptor:ligand bond is by the kinetic approach. This approach was introduced by Bell (1978) [59] and is based on the kinetic theory of isotropic materials [60]. Considering the forward and reverse rate constants, k_f and k_r, for receptor-ligand association and dissociation, Bell proposed that the dissociation rate constant is increased by a physical stress, as stated in

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Eq. (2):

$$k_r = k_{r,0} \exp\left\{\frac{\gamma f}{K_b T}\right\} \tag{2}$$

where $k_{r,o}$ is the unstressed dissociation rate constant, f is the applied force stressing a bond, and γ is a parameter loosely defined as the bond interaction range and likely of the order of r_o. T is absolute temperature and K_b is Boltzmann's constant. Bell used Eq. (3) to determine the force needed to detach a cell initially attached via multiple receptor-ligand bonds. He obtained an expression for the approximate total detachment force divided by the initial number of bonds, or the *adhesion strength per bond*, F_{bond}:

$$F_{bond} \approx 0.7\left(\frac{k_B T}{\lambda}\right) ln\{\frac{n_s}{K_D}\} \tag{3}$$

where n_s, is the surface ligand density and K_D is the surface equilibrium dissociation constant. For $\gamma = 10\,\text{Å}$, $n_s = 10^{11}\,\#\,\text{ligands/cm}^2$, and $K_D = 10^5\,\#/\text{cm}^2$ (corresponding to a solution value of $10^{-9}\,\text{M}$; using an effective volume with height of 200 Å), Eqs. (2–3) yield $F_{bond} = 4 \times 10^{-6}\,\text{dyne/bond}$. Note that the kinetic approach thus gives a similar but lower estimate for the bond strength than does the equilibrium approach, because it does not require all bonds to break simultaneously. An advantage to the kinetic approach is that it permits dynamic modeling. It is typically assumed that k_r is unaffected by stress, but some analyses have suggested how it could vary with strain (see Ref. 61).

Now compare estimates of specific bond interactions to previous estimates of nonspecific interactions. We stated earlier the estimate that a force per unit area of about 10^{-5} dyne/μm^2 is sufficient to detach a cell held by only *nonspecific* forces to form another cell. This is equivalent to a single high-affinity receptor-ligand bond per μm^2 of cell-cell contact area. Given that the cell surface receptor number density will usually be about 10–100/μm^2, receptor-ligand bonds can be expected to provide at least an order of magnitude stronger adhesive strength than nonspecific interactions.

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VI. CELL-CELL SIGNALING CONTROL OF VARIOUS BIOFILM PROCESSES

A. Gram-Negative Bacteria

Davies and Geesey (1995) [62] used reporter gene technology to observe the regulation of the alginate biosynthesis gene, *algC*, in a mucoid strain of *Pseudomonas aeruginosa* in developing and mature biofilms. The plasmid pNZ63, carrying an *algC-lacZ* transcriptional fusion, was not lost by segregation in continuous culture over a period of 25 days in the absence of selection pressure. Biofilm cells under bulk phase steady-state conditions demonstrated fluctuations in *algC* expression over a 16-day period, although no consistent trend was obvious. In vivo detection of *algC* up-expression in developing biofilms was carried out with a fluorogenic substrate for the plasmid-borne *lacZ* reporter gene product (β-galactosidase). Using microscopic image analysis, cells were tracked over time and analyzed for *algC* activity (via *lacZ* expression). During the initial stages of biofilm development, cells attached to a glass surface for at least 15 min exhibited up-expression of *algC*, detectable as the development of whole-cell fluorescence. However, initial cell attachment to the substratum appeared to be independent of *algC* promoter activity. Furthermore, cells not exhibiting *algC* up-expression were shown to be less capable of remaining at a glass surface under flowing conditions than were cells in which *algC* up-expression was detected.

Such studies [62–64] have shown that alginate synthesis is upregulated in *Pseudomonas* species when they become associated with a surface. As the alginate is synthesized, biofilm forms, resulting in the formation of cell clusters comprising cells embedded within dense alginate gel matrices with these clusters separated by open torturous channels. Recent advances in cell-cell communication in bacteria have shed light on the possible mechanism by which biofilm matrix polymer production and dissolution may be regulated. Research in gram-negative species has demonstrated that bacteria in batch cultures release specific molecules, known as homoserine lactones (HSLs). These HSL molecules pass readily through the cells membrane, where they accumulate to a threshold concentration at which they are able to induce the transcription of specific genes. Due to this mode of action, these molecules are referred to as *autoinducers*. All known, small, diffusible autoinducers in gram-negative bacteria belong to the class of *N*-acylated homoserine lactones [65]. Two chemically and genetically

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distinct autoinducer-dependent regulatory circuits are found in *P. aeruginosa*. The *lasI* gene is responsible for the production of *N*-(3-oxododecanoyl)-*L*-homoserine lactone (OdDhl) [66] and the *RHII* gene is responsible for the production of *N*-butylyl-*L*-homoserine lactone (BHL) [67,68]. In *P. aeruginosa*, quorum sensing has been shown to be involved in the regulation of a large number of exoproducts including elastase, alkaline protease, *LasA* protease, hemolysin, cyanide, pyocyanin and rhamnolipid [67–69]. Most of these exoproducts are synthesized and exported maximally as *P. aeruginosa* enters stationary phase. It is during stationary phase also, that gram-negative bacteria have been shown to develop stress response resistance that is coordinately regulated through the induction of a stationary-phase sigma factor known as *RpoS* [70]. Biofilm bacteria are generally considered to show physiological similarity to stationary phase bacteria in batch cultures. Thus, it is presumed that the synthesis and export of stationary-phase autoinducer-mediated exoproducts occurs generally within biofilms. The stationary phase behavior of biofilm bacteria may be explained by the activity of accumulated HSL within cell clusters. The mechanism causing biofilm bacteria to demonstrate stationary-phase behavior is hinted at by the recent discovery that *RpoS* is produced in response to accumulation of BHL in *P. aeruginosa* cultures [71].

The production of alginate by *P. aeruginosa* has been shown by many authors to be a stationary-phase response. Furthermore, the breakdown of alginate on solid media has been shown to occur after approximately 50 h incubation. These observations indicate that HSLs may be involved in the regulation of the production and digestion of alginate in biofilms composed of *P. aeruginosa*.

By artificially manipulating the binding of homoserine lactones to their cognate receptor molecules, it might be possible to control the formation, persistence and dispersion of microbial biofilms. Hypothetically, the addition of an analog which blocks the binding of OdDh1 to its cognate receptor (*LasR*), may prevent the production of the biofilm polymer matrix as the bacteria continue to multiply. Potentially, cell aggregates formed under these conditions could be easily dispersed by the addition of simple surfactants. Further, existing biofilms could be treated with the homoserine lactone, BHL, to induce the release of enzymes (e.g., lyase), which would digest the biofilm matrix material and disperse the biofilm into the bulk medium. Thus, nontoxic treatment regimens could be used as effective means of controlling biofilms in industrial settings and in the household.

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B. Gram-Positive Bacteria

Unlike gram-negative bacteria that employ transcription control of phenotypic expression by HSL signal molecules, in gram-positive bacteria, the diffusible molecules are small peptides that bind to membrane-bound receptors.

One process that may influence or instigate the adhesion process is autoinduction of plasmid conjugation. The main mechanism of plasmid transfer, conjugation, requires the intimate contact of two bacterial cells, a donor and recipient. In certain bacterial species, the initiation of conjugation is within the species own control. Conjugation between sexually differentiated bacterial cells requires physical and chemical interaction. *Enterococcus faecalis*, a nonmotile gram-positive species, needs cell interactions for sex plasmid transfer during conjugation. *E. faecalis* produces a family of peptide signaling molecules designated as sex pheromones [72–74]. Each pheromone triggers the conjugal transfer system of a particular plasmid such as the hemolysin plasmid pAD1, the bacteriocin plasmid pPD1, or the antibiotic tetracycline resistance plasmid pCF10 [74,75]. When the plasmid-containing donor bacteria are with close proximity to a plasmid-free recipient, the conjugal transfer system encoded on the plasmid is activated, and a copy of the plasmid is transferred to the recipient. At least 18 plasmids that encode a pheromone response have been described [76]. Several pheromones have been purified and shown to be different hydrophobic octapeptides, or in one case a heptapeptide [77]. Pheromones are typically active at concentrations below 5×10^{-11} M, and as few as two molecules per donor cell may be sufficient to induce the transcription of genes on the target plasmids [76,78]. The response to pheromone is not only very sensitive but its specificity is also high. Pheromone cAD1 is unable to induce expression (indicated by clumping by cells) from the heterologous plasmid pPDI, even at a concentration of 1 μM, which is 10^5-fold higher than that needed to induce expression from the homologous plasmid.

The pheromone-induced surface-bound adhesins specified by plasmids pAD1 and pCF10 have been purified and their structural genes have been cloned and sequenced [76,77]. These adhesins are large, closely related proteins that may form dense, hair-like structures on the cell wall of the induced bacteria [79]. The ligand for the adhesin on *E. faecalis* cells is a surface constituent present on all cells, whether or not they carry a plasmid. Available evidence strongly favors involvement of lipoteichoic acid, the major wall antigen of gram-positive cells [80,81]. These and

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other experiments imply that the adhesion system is a system binding heterophilic adhesin-lipoteichoic acid [82].

Once transferred from donor to recipient, the plasmid directs the synthesis of a plasmid-encoded inhibitor that specifically blocks the inducing action of the cognate sex pheromone [76]. The inhibitors for *cAD1* and *cPD1* have been purified and shown to be hydrophobic octapeptides that have sequences weakly related to their corresponding pheromones [77]. In one case, the inhibitor has three identical residues among seven total. The inhibitor peptide neutralizes its cognate pheromone, probably by competition, thus preventing a donor cell from responding to its own pheromone.

VI. BIOFILM DETACHMENT PROCESSES

Detachment has always been considered as an "interfacial transfer process" that transfers cells and other biofilm components from the biofilm to the bulk liquid. By the 1990s, the biofilm community considered "desorption" of microbial cells from the substratum to occur from the moment of initial cell adsorption. "Detachment" was considered material loss from the biofilm matrix as opposed to material loss from the substratum. As a consequence, detachment was assumed to occur only at the leading edge of the biofilm–bulk liquid interface. Subsequently, most hypotheses regarding mechanisms controlled detachment were based on biofilm responses to interfacial forces such as shear stress related erosion and abrasion. Evidence does indicate that increasing shear suddenly over that which prevailed during a biofilm's development will result in an increased detachment.

However, there is also evidence to indicate that should shear stress remain constant, that the detachment rate of biofilm is independent of shear stress but highly dependent on growth. Thus, advances in our understanding of biofilm detachment have occurred in the past decade that point to physiological control of biofilm detachment processes.

Most of the alginate biosynthetic genes of *P. aeruginosa* are clustered at 34 min on the chromosome [64]. Alginate lyase enzymes cleave the 4-*O*-linked glycosidic bonds between uronate residues by an eliminative mechanism to produce unsaturated sugar derivatives [83]. The *algL* gene, which codes for alginate lyase, is also located within the alginate gene cluster [63,84]. Alginate lyase (*algL*) of *P. aeruginosa* has optimal activity against nonacetylated polymannuronic acid [85–87]. The

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role of the *P. aeruginosa* alginate lyase in alginate production is intriguing. Several other microbes, including *Bacillus circulans* and two marine *Pseudomonas* species that possess such an enzyme can utilize alginate as a carbon source [87]. However, it appears that *P. aeruginosa* 8821 and 8830 are unable to do so. The *algL* gene of *P. aeruginosa* is indispensable for alginate production. Disruption of the *algL* gene results in a nonmucoid phenotype that can be changed to a mucoid phenotype solely by the presence in *trans* of the downstream gene *algA* [63]. *AlgL* could be involved in alginate modification, as it could be important for determining the molecular size of the alginate polymer produced. A decrease in polymer length could affect the properties of the alginate, including its ability to enhance attachment of the bacteria to solid surface.

Boyd and Chakrabarty [64] hypothesized that increased expression of the alginate lyase in *P. aeruginosa* would alter the size of the alginate synthesized and this would in turn affect the adherence properties of the bacteria. The stable mucoid strain *P. aeruginosa* 8930 harboring the vector pmMB22 or the *algL* plasmid pSK700 were used for their experiments. IPTG served as inducer of alginate lyase expression from the *tac* promoter of plasmid pSK700. pMMB22 served as the vector control. The level of alginate activity of *P. aeruginosa* 8830-pMMB22 grown in the presence or absence of IPTG was low. *P. aeruginosa* 8830/pSK700 grown in the absence of IPTG had a higher level of alginate lyase activity than the vector control because of the leakiness of the *tac* promoter in *P. aeruginosa*. This approximately 10-fold increase in alginate lyase specific activity was not sufficient to alter the amount of alginate produced or to affect can detachment.

However, *P. aeruginosa* 8830-pSK700 with IPTG induction exhibited a high level of alginate lyase specific activity because of increased expression of the *algL* gene from the *tac* promoter. The amount of cell detachment from a biofilm of *P. aeruginosa* 8830-pSK700 grown in the presence of IPTG was 17-fold greater than that observed for *P. aeruginosa* 8830-pMMB22. The amount of alginate produced by *P. aeruginosa* 8830-pSK700 with IPTG was similar to that produced by *P. aeruginosa* 8821. Thus, the increase in sloughing observed for *P. aeruginosa* 8830-pSK700 with IPTG can not be attributed solely to a decrease in the amount of alginate present. However, the increase in cell detachment did correlate with the degree of depolymerization of the alginate. Alginate samples of the above strains were found to be quite different from each other qualitatively

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when they were visualized on a 5% polyacrylamide gel. The alginate of *P. aeruginosa* 8830/pSK700 with IPTG was greatly degraded as seen by its polydisperse gel pattern. The alginate samples of *P. aeruginosa* 8830-pMMB with and without IPTG and *P. aeruginosa* 8830/PSK700 without IPTG each showed a high-molecular-weight monodispersed band with little or no alginate degradation.

Boyd and Chakrabarty (1994) [64] further investigated the effects of lyase induction on cell detachment at various stages of biofilm growth. Either *P. aeruginosa* 8830/pMMB22 or *P. aeruginosa* 8830/pSK700 were cultivated as biofilm on membranes separating two chambers. To induce the alginate lyase of pSK700, IPTG was added to the bottom chamber, either at the time of incubation ($t = 0$ h) or 24 h after inoculation. Biofilm were then allowed to develop for 48 hrs. Addition of IPTG caused a large increase in alginate lyase–specific activity, and extensive alginate degradation was observed for both IPTG-induced *P. aeruginosa* 8830/pSK700 samples. Induction of the alginate lyase in *P. aeruginosa* 8830/pSK700 at 0 h resulted in a threefold reduction in the overall amount of alginate produced. The number of detached cells increased 9- to 16-fold over the number produced by the vector control. A less pronounced decrease in alginate formation was seen when IPTG was added at 24 h versus when it was added at time = 0 h. Cell detachment increased fourfold to eightfold over that of the vector control, compared with a 9- to 16-fold increase when the alginate lyase was induced at time = 0 h.

VII. CONTROL OF BACTERIAL COLONIZATION

A. Past Attempts

Once a foreign device or implant develops a bacterial infection, doses of a single or a multiple antibiotic regimen are unsuccessful, even at concentrations several orders of magnitude greater than the minimum inhibitory concentrations observed for suspended cultures. The common trend in biomaterials design is to prevent bacterial infection by eliminating bacterial adhesion. Two popular approaches in colonization prevention are either: (1) to develop a nonadhesive surface by modifying the substratum's surface chemistry or (2) design a material to slowly release an agent that is lethal to the incoming bacterial cells.

In the first approach, numerous studies prior to 1997 have considered either different substrata or different substrata pre-treatments to prevent bacterial adhesion [88–92]; all indicating marginal success in

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the short-term and eventual failure to prevent biofilm formation over extended time periods. In what appears to be a first successful noncolonizing interface, Johnston [93] details the development of a simple surface coating that appears to obviate both protein and bacterial adhesion. Johnston [93] polymerized oligoglymes CH_3-(O-CH_2-CH_2)$_N$-O-CH_3 (where $N = 1$ mono-, $N = 2$ di-, $N = 3$ tri- , and $N = 4$ tetra-glyme) onto glass substrates, using a radiofrequency argon gas plasma. Oligoglyme monomers were heated to $\sim 60^{\circ}C$ to increase their vapor pressure prior to plasma deposition. After the reaction, the reactor chamber was flooded with argon for 10 min, then evacuated to evaporate any condensate.

To evaluate the protein fouling efficacy of the various modified surfaces, human fibrinogen (FGN) (sigma) was ^{125}I labeled using carrier free Na ^{125}I (Amersham) and Iodobeads (Pierce). Control substrata samples were placed at the bottom of individual wells (pretreated with BSA, then air dried) in a 96-well tissue culture plate, then protein solutions of known concentration placed in each well. Protein solutions were infinitely diluted with buffered saline prior to removing the sample, then counting the adsorbed ^{125}I labeled protein. Results for FGN adsorption to the various oligoglyme-coated substrata are shown in Figure 6.

Control and glyme-treated glass substrata were placed flush to the inner surfaces of a radial bacterial cell adhesion flow cell [93]. A radial flow cell consists of two circular discs held apart parallel to each other, forming a small gap. A cell suspension is delivered through a port in the bottom disc, where it impinges on the top plate, then flows radially outward toward a collection weir. The advantage of the radial disc geometry is that cells experience a decreasing shear stress as the fluid moves radially outward from the center. Samples of control and glyme-treated glass discs are used as one of the two circular discs. Adherent cells were determined by direct microscopic counting. Figure 7 illustrates the effect of the different glyme coatings on bacterial adhesion.

In the second approach, various chemical agents can affect bacterial adhesion indirectly by detrimentally affecting (or terminating) bacterial cell metabolism. The reader is directed to two articles by Schifferli and Beachey on antibiotics that inhibit bacterial adhesion by perturbing protein synthesis [94] and those antibiotics that operate on metabolic targets other than protein synthesis [95]. The idea of incorporating antibiotics into a biopolymer during fabrication is not new. Antibiotics have been incorporated in bone cement [96–98], vascular grafts [99,100],

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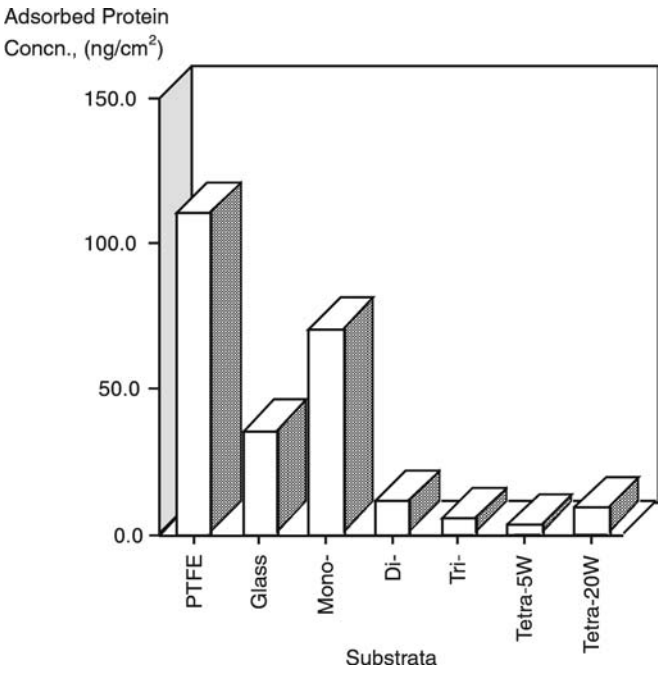

Figure 6 Fibrinogen adsorption to control and glyme-treated glass substrates. (From Ref. 93.)

hydrocephalus shunts [101], and in prosthetic heart valves [102]. Periods of release were never measured in the above cases but reduced levels of bacterial infection were observed in these applications over time periods ranging from 1 week to 2 months. Ackart et al. [103] reports on the incorporation of a variety of antimicrobial agents (sulfathiazone, sulfadiazine, hydroxyquinoline, benzalkonium) into carboxyl-containing ethylene copolymers. Viable cell numbers attached to said materials increased at a lower rate versus controls; however, trials were carried out for only 2 h. Van Noort and Bayston report on the mechanical properties of silicone rubber impregnated with gentamicin sulfate [104], where initial kill rates are high but the longevity of the drug was < 2 days. Effects of incorporation into and slow release of an antibacterial (*p*-hydroxybenzoic acid esters, or parabens) from polyurethanes on bacterial colonization have been published [105]. Control of drug release rates was modulated

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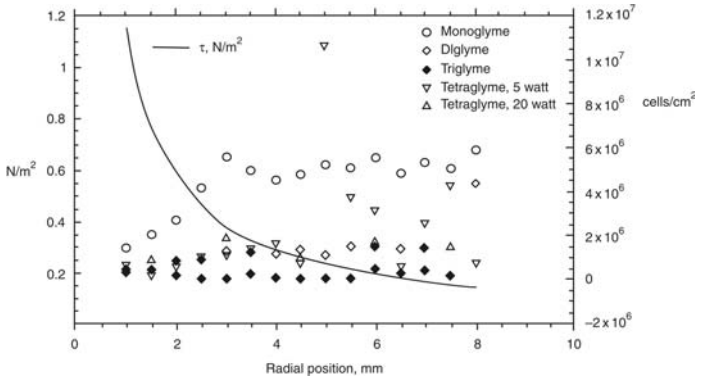

Figure 7 Adhesion assay using radial flow cell. *Pseudomonas aeruginosa* cell suspensions supplied at $1x10^{-6}$ cells per milliliter at a flow rate of 1.5 mL/min. (From Ref. 93.)

either by using different molecular weight parabens or by adhering a second layer of unloaded polyurethane over the antibacterial loaded one. Nearly complete release of the parabens occurred in less than 4 days. These materials were shown to greatly reduce the *Staphylococcus epidermidis* colony forming units of the polymer after 48-h incubation in a suspension of the bacteria. Polymers have also been impregnated with nonantibiotic materials to prevent bacterial adhesion, including silver-laden nylon [106], carboxyl-containing poly(ethylene) copolymers [107], and materials incorporating quaternary ammonium salts [108].

In collaboration with researchers at the University of Washington [109], we developed series of polyetherurethane (PEU) base materials that incorporated a known amount of the fluoroquinalone antibiotic, Ciprofloxacin™ (Bayer, AG). Poly(ethylene glycol) PEG (MW = 5500) was employed as the pore-forming agent. PEU drug loaded matrices were then glow discharge plasma deposited with a poly(butyl methacrylate) (polyBMA) barrier membrane of controlled porosity, which allowed sustained release of the therapeutic agent [110,111,113]. Results (not shown here; ref. 112, 113) illustrate that the rate of ciprofloxacin release from PEU materials in static batch studies was a function of poly (BMA) membrane plasma deposition conditions (i.e., membrane permeability). Under optimum conditions, sustained release of ciprofloxacin was maintained for a period of 8 months. Bacterial cell adhesion and biofilm

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formation (if any) on these loaded PEU materials was studied within a parallel plate flow cell of constant rectangular cross-sectional area. Our results indicate that (1) the total number of adhering cells and rate of adhesion of cells to the PEU control and the PEU-Cipro were about the same; (2) the detachment rates were significantly higher for PEU-Cipro materials than PEU controls; which (3) results in fewer numbers of cells permanently accumulating at the surface. Our results suggest that PEU-ciprofloxacin materials effected the bacterial cell physiology after adhesion, resulting in a higher detachment rate but had no effect on the cell adhesion process.

B. A Rationale for a New Approach

Bacterial infections of short- and long-term indwelling devices have always prompted one classical medical response; repeated pulse injection of one or more antibiotic challenges at high dosage in a ''reactive'' attempt to ''kill'' the infecting bacteria. Once a bacterial infection is established at an implant surface, classic antibiotic challenges prove ineffectual in almost all cases [94,95,114]; thus, necessitating surgical removal and replacement of the implant. The practice of killing bacterial cells to eliminate infection would not be desirable in long-term use because the patent is exposed to high doses of antibiotic, which may, over repeated challenges, promote resistant bacterial strains.

In our pBMA-coated ciprofloxacin-releasing PEU materials discussed above, killing of the arriving bacteria increased cell detachment, which dramatically lowered bacterial net accumulation. However, any preventative strategy based the killing arriving microbial cells as they initially attach, may not be prudent, since debris from dead bacterial cells can still stimulate an acute inflammatory response [115–117]. What is needed is a nonlethal way of preventing bacterial cell attachment while promoting a true healing process.

A number of complex biological phenomena are governed by dynamic processes that occur at interfaces including: cell-cell adhesion, cell–basement membrane adhesion, metastasis, nerve regeneration, tissue repair, complement and immune response to bacterial infection, phagocytosis, inflammation, chemotaxis, healing, and bacterial colonization and infection of mammalian cells and biomedical implants. Research has shown that procaryotic and eucaryotic biological processes can be controlled through ligand:receptor binding. Further, proper stimulus of specific cell receptors can trigger changes in cell responses, secretion of

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other molecules, and cell phenotype. For example, the process of leukocyte adhesion is a complex phenomenon involving the interactions between several ligand-receptor superfamilies orchestrated in a precise spatial and temporal sequence of events [118–120]. Consequently, many research groups are devoting significant resources to develop new biomaterials with the sole purpose of attracting mammalian to a surface, promoting their adhesion, then regulating metabolic response [118–132]. The biomaterials community believes that a device that promotes "true" healing and tissue integration would be less likely to become infected.

However, one reality that will promote excessive inflammation of a biomedical implant is bacterial colonization and infection. Unfortunately, as depicted in an early section, many of the molecules selected to decorate biomaterials to attract mammalian cells may also exacerbate bacterial adhesion.

As a consequence, our research group has also explored a number of nonlethal approaches that biologically interfere with the bacterial adhesion process. For example, we have been successful in biologically blocking *Pseudomonas aeruginosa* (*PA*)–specific adhesion. *PA* is an opportunistic pathogen that causes devastating corneal infections, particularly in users of soft extended-wear contact lenses. To initiate such an infection, *PA* must first adhere to the corneal epithelium. Gupta et al. [133] reported that a specific *PA* membrane receptor binds to asialo GM_1, a neutral glycolipid on the corneal epithelium membrane. Hazlett and coworkers were able to prevent *PA* infections of bovine and mouse corneal epithelium by preincubating *PA* with monoclonal antibodies raised against the membrane-bound asialo GM_1 receptor (Mab_{GM1}). As an alternative to the antibiotic ciprofloxacin, we have also loaded a PEU base film with Mab_{GM1} (courtesy Dr. L. Hazlett, Wayne State University) in order to biologically block *PA* specific adhesion. Bacterial cell adhesion kinetics for net *PA* cell accumulation were determined from image analysis for PEU-releasing Mab_{GM1} (surfaces preadsorbed with asialo GM_1 glycolipid), as shown in Figure 8. Results indicate the feasibility of blocking bacterial infection by biologically interrupting specific adhesion.

Expanding further with this application, we propose to prevent bacterial colonization in a number of select situations by interfering with the species-specific receptor that binds to portions of a corresponding specific ligand molecule. Table 1 enumerates a number of biomedical device based infections that could be prevented by blocking a specific adhesion mechanism.

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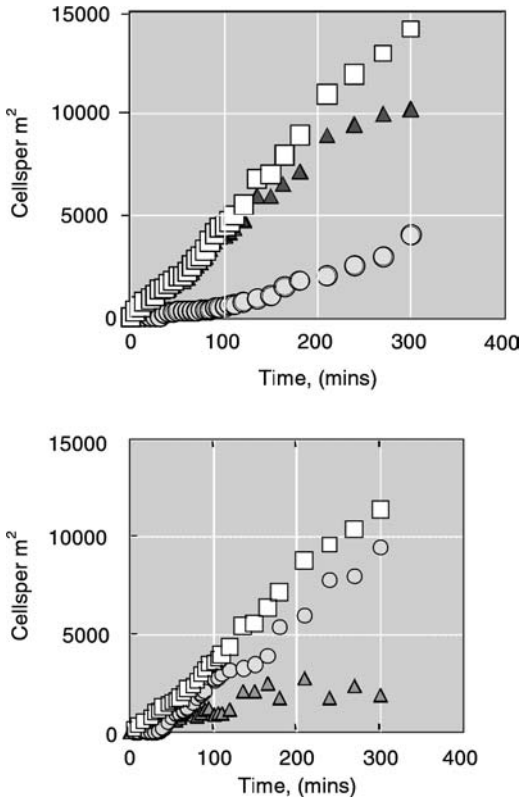

Figure 8 *Pseudomonas aeruginosa* adhesion to PEU substrates. Shear stress = 1.25 N/m^2; $X_{in} = 2 \times 10^6$ cells per milliliter. **A**. Control; no release agent. **B**. PEU releasing Mab GM1 (see text for further details). □ = adhering cells; ○ = desorbing cells; Δ = net cell accumulation.

VIII. SUMMARY

Several prokaryotic and eukaryotic intra- and intercellular processes are initiated and controlled by a communication pathway from stimulus → to cell surface receptor → to cell nucleus → to mRNA → to cytokine signaling agents and higher tissue response. We recognize that both prokaryotic and eukaryotic biological processes can be influenced through cell membrane receptor mechanisms. This chapter has focused

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Table 1 Device-Based Infections Potentially Controlled by Antiadhesion Therapy

Colonizing bacteria/ infection situation	Proposed antiadhesion, antibiofilm molecular strategy	Availability of therapeutic agent	Ref.
Staphylococcus aureus (SA) abscess, periodontal wound infections, post-surgical implant infections, extraction wounds (aerobic)	*SA* adheres to surfaces by receptor mediated binding to bound fibronectin (FN) molecules. **Proposed:** block binding of *SA* to FN using $F(ab')_2$ fragments of monoclonal antibodies (Mabs) generated against the FN-binding portion of the *SA* FN receptor.	FN binding motifs in *SE* bacterial FN receptor identified. Mabs to entire receptor and to FN-binding motifs generated; $F(ab')_2$ fragments of Mabs to binding motifs available.	134
Staphylococcus epidermidis (SE) cardiovascular device-based infections, open transdermal surgical wounds (aerobic)	140-kDa extracellular protein identified as phenotypic requirement for infecting strains of *SE* to adhere and form biofilm. 140-kDa protein suspected to be "quorum sensing" receptor on *SE* membrane. **Proposed:** block "quorum sensing" receptor on *SE*; prevent biofilm formation.	140-kDa extracellular protein identified as phenotypic requirement for infecting strains of *SE* to adhere and form biofilm. Antibody to receptor can block biofilm formation.	135

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Table 1 Continued

Colonizing bacteria/ infection situation	Proposed antiadhesion, antibiofilm molecular strategy	Availability of therapeutic agent	Ref.
Streptococcus mutans (SM) formation of dental caries, abscess, post-surgical implants infections, extraction wounds (facultative)	Cell surface protein antigen (PAc) 190-kDa cell surface antigen binds to saliva receptors on surfaces; *SM* produces biofilm extracellular glucan polymers from sucrose via glucosyltransferase enzymes GTF-I and GTF-SI. **Proposed:** create Mab to a fusion protein, PAc-Gb (fusion of Pac binding receptors and glucan binding domain of enzyme, GTF-I). Mab simultaneously blocks adhesion and polymer formation.	Mab to fusion protein of PAc-Gb generated. Mab to fusion protein can block both adhesion and polymer formation. (Mab available courtesy T. Koga, Kyushu Univ., Japan.)	136
Streptococcus gordonii (SG) periodontal diseases, abscess, implant infection, extraction wounds (facultative)	Streptococcus surface protein Ssp proteins of *SG* mediate initial binding. Ssp also believed to bind directly to a 120k-Da protein on *Porphyromonas gingivalis (PG)* surface.	**Proposed:** employ bacteriophage protein display libraries to generate peptides that block the specific binding receptors on each bacterium.	136
Porphyromonas gingivalis (PG) periodontal diseases, abscess, implant infection, extraction wounds (anaerobic)	*PG* fimbriae mediate binding to *SG* specific, yet unidentified receptors.	SG and PG receptor blocking peptides not yet available; awaiting phage display research proposed here.	137, 138

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on recent research on processes that govern biofilm colonization of biomedical implants; including substrate control of bacterial adhesion, bacterial-specific adhesion processes, and cell-cell communication control of bacterial adhesion processes.

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7

Diagnosis of Postherniorrhaphy Infections

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I. INTRODUCTION

The first step in treating a mesh infection is prevention. The infection rate for elective open hernia repairs, considered clean cases is about 1.5% [1]. Laparoscopic inguinal hernia repairs have rare infections with rates varying from 0.03 to 0.095% [2]. Early infection rates with open complicated incisional hernias can be as high as 16% with or without mesh. The incidence of late graft infections is not known [3]. The use of perioperative antibiotics is controversial. Some studies have demonstrated benefit, but others show no real advantage [4,5]. Early wound infections are usually readily identified, but late mesh infections can be indolent and difficult to diagnose. This chapter evaluates different modalities for diagnosing postherniorraphy infections, with an emphasis on the use of ultrasound and computed tomography.

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II. PHYSICAL EXAMINATION AND DIAGNOSIS

The first step in diagnosing a mesh infection is suspecting one. The diagnosis is usually obvious, and any diagnostic examination is only confirmatory. The majority of mesh infections present within the perioperative period, usually in 7–10 days, but a few present months to years later. Determining the presence of an infection can be simple or difficult. The development of laparoscopic hernia repairs adds a new level of difficulty. There is no easy route for exteriorization of an infection in a laparoscopic repair. The mesh is placed far from the skin, unlike the case with most open repairs. The consequence is a slow-growing abscess that presents in an atypical manner and outside the traditional perioperative period [6].

Fever, focal tenderness, erythema, and swelling are good indications that an inflammatory process is occurring outside the normal postsurgical changes. The presence of drainage in the area of recent surgery or history of foreign body is an infection until proven otherwise. Palpation of crepitus, indicating subcutaneous emphysema, is an ominous sign in the presence of local signs of infection. This indicates that a gas-forming bacterial infection is present. At times the diagnosis of a mesh infection can be rather difficult. There may not be the typical local changes just stated. The naturally occurring changes with surgery and wound remodeling can make the diagnosis difficult. There is natural firmness, swelling, tenderness, and slight erythema along the incision that can be mistaken for an infection. The patient's body habitus and comorbidity also make it difficult to diagnose a mesh infection. Obese patients may manifest tenderness, but significant erythema or areas of firmness may be obscured because of the pannus. Diabetics may not demonstrate significant erythema or tenderness from their underlying disease but have only purulent drainage, crepitus, or a foul odor.

Late infections are more indolent and presentations varied. Fistula formation, swelling, pain, or fever of unknown etiology may be encountered. Individual symptoms can present alone or in combination with other symptoms.

Radiological imaging confirms or aids in the diagnosis of an abscess or mesh infection, but clinical suspicion and physical examination make the diagnosis most of the time. Cultures via needle aspiration or swab add to the diagnosis and identification of the organisms for treatment. There

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are some instances where removal of the mesh is required for definitive diagnosis.

A. Ultrasound

Ultrasonography requires two components, the transducer and the computer. The transducer is a handheld attachment that generates sound waves as energy is passed through piezoelectric crystals. These same crystals subsequently receive the reflected sound waves, which are converted back to electrical energy. The computer analyzes these electrical pulses and creates images. This principle of transmitting and receiving sound waves via these crystals is known as the *piezoelectric effect*. An example is the telephone. At one end, for example, a person's voice (mechanical energy) is transformed into electrical energy through the telephone transmitter and transmitted through cable lines to its destination. The telephone receiver reconverts the electrical energy back to sound waves (mechanical energy) [7].

Sound waves travel through media of different density at different speeds, faster through more solid material, and the majority are reflected back if the medium is air. As sound waves move through a medium that is homogeneous and encounters another medium of different density, portions of the sound wave are transmitted through and portions are reflected back. This difference is known as *acoustic mismatch*. The greater the density difference, the greater the mismatch and reflection. This difference can be seen as a visual image that is constructed by the computer.

Transducers come in many different sizes and shapes and are available in different frequencies. This is important, because the amount of sound penetration and resolution is dependent on the frequency. The lower the frequency, the greater the penetration but the lower the resolution.

We use a 7.5-MHz probe to evaluate occult hernias, hernia repairs, and subcutaneous fluid collections. The higher frequency gives more detail, but the depth of penetration is less. The 3.5- to 5.0-MHz probe is typically used to evaluate intra-abdominal or retroperitoneal organs, masses, or fluid collections.

Ultrasound is an excellent tool for evaluating superficial fluid collections as well as hernia recurrences. Most meshes are seen with ultrasound, since there is a difference in density between tissue and foreign body. Most thicker polypropylene and expanded polytetrafluoroethylene (PTFE) meshes are easily seen, but thinner, lighter meshes such

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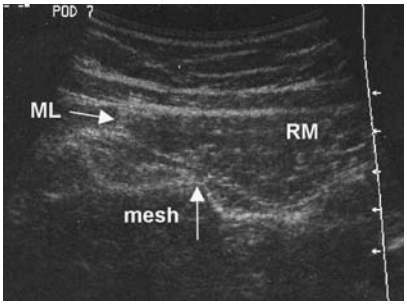

Figure 1 Prolene mesh in preperitoneal space on postoperative day 7, following laparoscopic right inguinal hernia repair. Transverse view. The mesh (arrow) is hyperechoic. ML, midline; RM, rectus muscle.

as those made of knitted polyester are difficult to see with ultrasound. The mesh appears as a hyperechoic line (Fig. 1). At times, the density is great enough that most of the sound waves are reflected back. A shadow is cast behind the mesh, which obscures structures deep to the mesh (Fig. 2). This is more evident before a mesh is completely incorporated into the tissues.

Hematomas are seen as discrete masses usually anterior to the mesh. As the hematoma liquefies, there are different densities within the mass. This appears a hypoechoic and hyperechoic complex mass with septations and swirls (Fig. 3). The more hypoechoic clear portions represent a liquefied hematoma.

Seromas are more uniformly hypoechoic with minimal or no internal septations (Fig. 4A and 4B). There is minimal internal debris. Seromas are usually a diagnosed clinically and occur soon after surgery

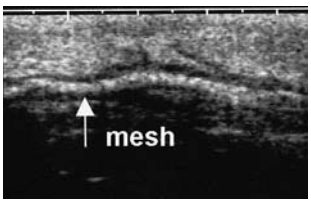

Figure 2 Prolene mesh placed in open ventral hernia repair. Note the hyperechoic mesh (arrow) with posterior shadowing due to the lack of transmitted sound waves. This is usually more evident early postoperatively, before the mesh has been completely incorporated.

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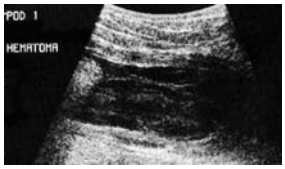
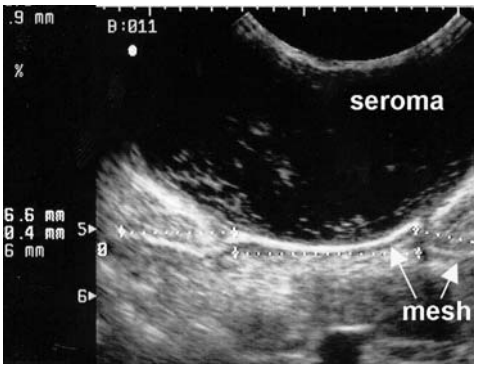


Figure 3 Large scrotal hematoma on postoperative day 1 in a patient who had a laparoscopic inguinal repair for a recurrent right inguinal hernia. Note the hypoechoic mass with internal septations.



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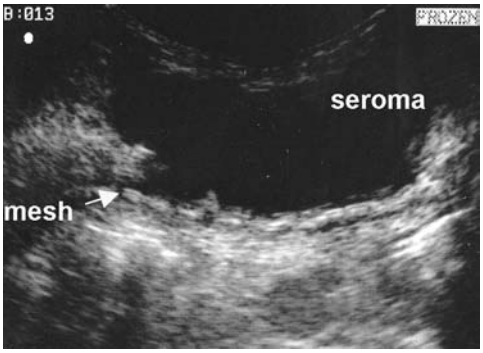

B

Figure 4 (A) Large postoperative seroma in patient 2 weeks after laparoscopic repair of an incisional hernia with Gore-Tex mesh. There was concern that this could dislodge the tacks and mesh. Note that the mesh is firmly adherent to the abdominal wall. (B) Resolving seroma 4.5 weeks after laparoscopic repair of an incisional hernia with Gore-Tex (same patient as in Fig. 4A).

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(Fig. 5). Most are resorbed in by 3 to 4 months, but some may encapsulate and persist chronically, especially if a combination of meshes is used (Fig. 6) [8].

In infections, ultrasound demonstrates soft tissue swelling. Ill-defined increased echogenic areas may indicate panniculitis or fat necrosis secondary to any of numerous possible causes of inflammation. Chronic cellulitis not only demonstrates increased echogenic areas but also a "cracked paving" pattern, indicating interstitial fibrosis. Despite this advantage, ultrasound cannot distinguish the edema of early infective tissue changes from postoperatively induced local edema. An abscess cavity is readily seen by ultrasound as a fluid collection. There may be some debris in the abscess cavity or some air (Fig. 7A). Air in the subcutaneous tissue can persist up to 4 weeks after surgery, so it is not a reliable sign of early infection early on (Fig. 8). It can be used reliably in later infections [9]. Ultrasound is also useful for identifying and following a fistula tract, which may be associated with a suture or mesh infection (Fig. 7B).

Ultrasound by itself cannot diagnose an abscess, but with clinical history and sometimes ultrasound-guided aspiration, an abscess can be confirmed (Fig. 9A–C). We as well as others have found ultrasound to be extremely useful in evaluating inguinal hernias postoperatively. Furtscheggar et al. studied 824 patients with a total 1139 inguinal

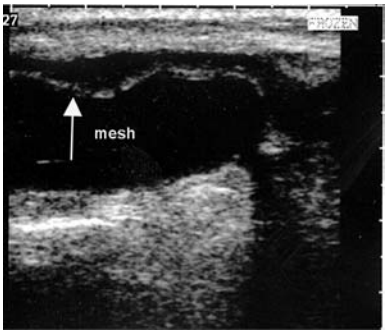

Figure 5 A large ventral hernia repaired using Gore-Tex mesh in a 75-year-old woman. One month postoperatively, a large seroma developed, which subsequently drained spontaneously. Later, cultures were positive for methicillin-resistant *S. epidermidis*. This patient had fever and an elevated white blood cell count.

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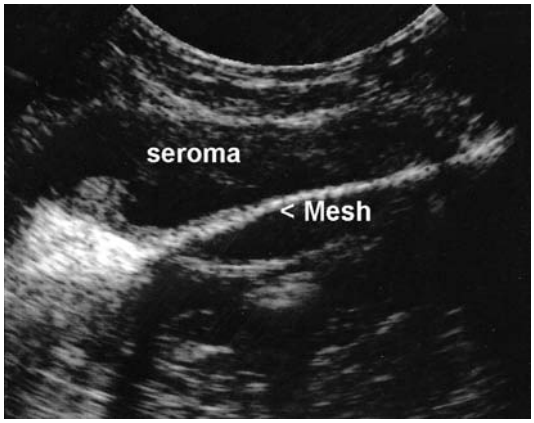

Figure 6 Colon cancer resected 1996. The male patient developed a local wound recurrence and subsequently had a full-thickness wide resection of the left rectus abdominis muscle, including fascia, with abdominal wall reconstruction in 1998. A combination of prolene and Gore-Tex mesh was used for the reconstruction. Four years later, the patient has a chronic seroma with no evidence of cancer recurrence.

hernias with ultrasound after surgery at 2, 14, and 90 days. In their cohort, 2 patients had findings consistent with infections that were confirmed with aspiration. Eventual removal of the mesh was required. In addition, there were 8 clinically suspicious recurrent hernias, but only 3 were confirmed with ultrasound [10].

When there is suspicion of an infection, ultrasound is our preferred initial examination. It is simple and convenient to perform and less costly than other modalities. It is easily performed in the office setting and does not expose the patient to ionizing radiation. Mesh and other non-opaque foreign objects that are not seen with CT, plain films, or xeroradiography can often be seen with ultrasound [11]. Ultrasound is limited by its inability to visualize deep structures, which may by obscured by overlying bowel gas.

B. Computed Tomography

Computed tomography (CT) is a valuable noninvasive tool for identifying an abscess cavity. In spite of an extensive literature search,

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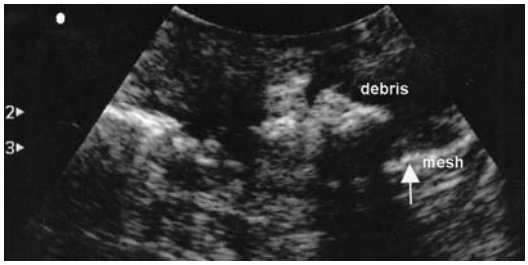

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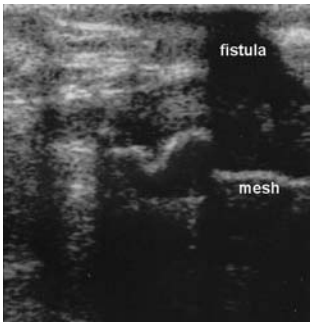

B

Figure 7 (A) A 59-year-old woman whose incisional hernia was repaired with Marlex mesh in 1998 subsequently, in 2001, developed a mesh infection. Partial excision of the mesh was performed at that time. She now has a recurrent infection with fistula formation. Debris is seen in the chronically infected mesh abscess. (B) In the same patient, a fistula tract is seen draining at skin level. Subsequent repair included resection of the small bowel, which had been eroded by the mesh, and complete removal of the mesh.

we have not found formal studies using CT for evaluating postoperative mesh infections, although it is the primary modality used by most surgeons and its use in this area has been anecdotally reported in numerous publications. There is, however, fairly extensive information on prosthetic infections in the literature on vascular and orthopedic surgery. Much of the information presented here is extrapolated from this literature and that on intra-abdominal abscesses of various etiologies. This information applies not only to CT but also to ultrasound and MRI.

Radiological changes surrounding the mesh are similar to those that occur with intra-abdominal or other prosthetic infections. There is a surrounding soft tissue edema initially indicating an inflammatory

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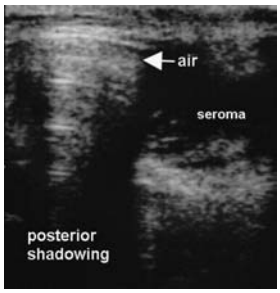

Figure 8 Day 14 after repair of an incarcerated epigastric hernia with multiple defects, using prolene mesh in the preperitoneal space. Postoperatively, a seroma developed with unresorbed air seen as hyperechoic with reverberation artifacts. Note posterior shadowing behind the air.

process from either surgery or early infection (Fig. 10). The edema becomes more distinct with the formation of a vascular wall or peal that is enhanced with IV contrast. Eventually, air-fluid levels may develop. Radiology can also be useful in identifying a small bowel fistula (Fig. 11A–C).

As with ultrasound and MRI, early postoperative changes may produce the same finding as an infection. There is the expected surrounding soft tissue edema and possible subcutaneous air. Clinical history and physical examination are essential to make the diagnosis.

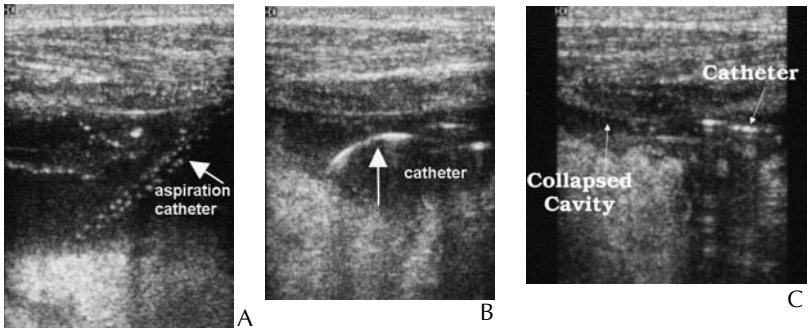

Figure 9 (A) Catheter aspiration of an abscess cavity. (B) Insertion of a drainage catheter. (C) collapse of the cavity with the drainage catheter in place.

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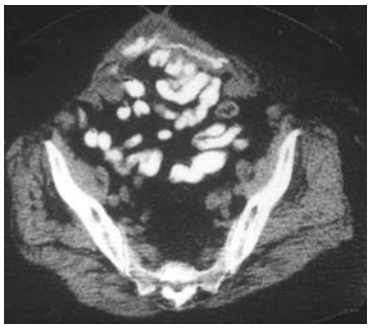

Figure 10 An 83-year-old woman with infected Gore-Tex mesh. Note the soft tissue edema surrounding the mesh. The mesh was removed completely and primary tissue repair performed. There was no recurrence 2 years postoperatively.

Malaise, low-grade fever, drainage, local tenderness, and erythema may indicate an early postoperative infection. Needle aspiration, local exploration, or wound culture may be required for diagnosis.

Vascular graft infections have been studied to show the sequence of healing following placement of prosthesis. A hematoma may take 3 months to resolve. Subcutaneous air can remain 3 to 4 weeks prior to total resorption. Before that time, it is difficult to distinguish early infections from postoperative changes [7]. The finding of perigraft fluid, ectopic gas, persistent perigraft inflammation, and loss of tissue planes beyond 3 months postoperatively is reliable for the diagnosis of a graft infection.

CT is limited in its ability to identify meshes. With the exception of Gore-Tex, the majority of the meshes—prolene, mersilene, and Marlex—cannot be seen distinctly by CT. Gore-Tex's physical thickness and density allow visualization (Fig. 12).

It is not uncommon to see a fluid collection anterior to the mesh following a laparoscopic hernia repair. Excision of the hernial sac is not always included in the laparoscopic repair, as it is in the open repair. In addition, the postoperative fluid collection or hematoma may have a globular, tubular, or multilobular morphology and include an enhancing rim mimicking a complex abscess (Fig. 13). These fluid collections may also be mistaken for bowel with air present, indicating failure of the

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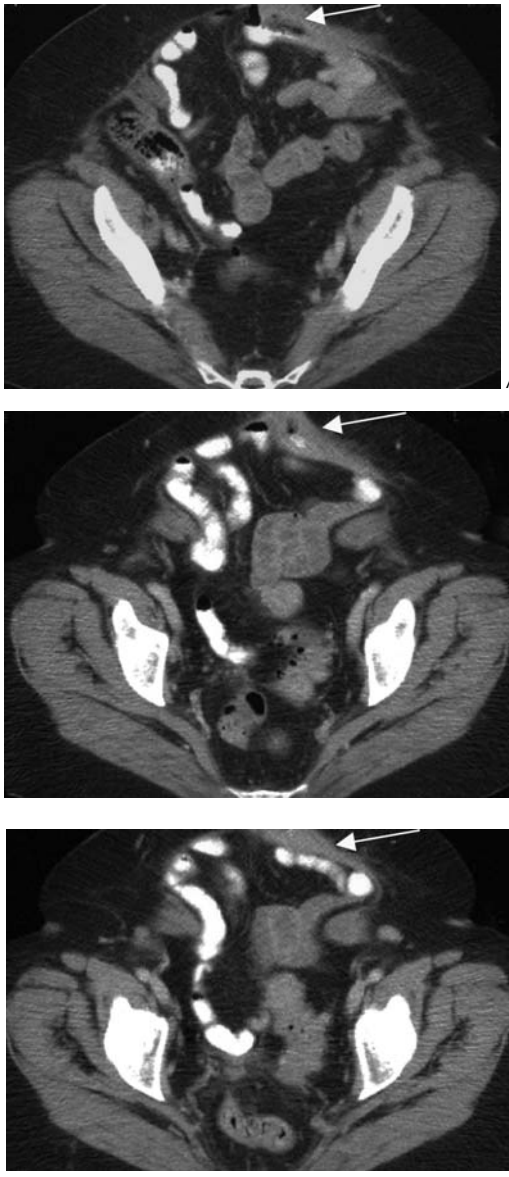

Figure 11 (A) CT of small bowel fistula to Prolene mesh (arrow) (same patient in Fig. 7A and B). (B) CT scan showing contrast in fistula tract (arrow). (C) CT scan showing air in fistula tract (arrow).

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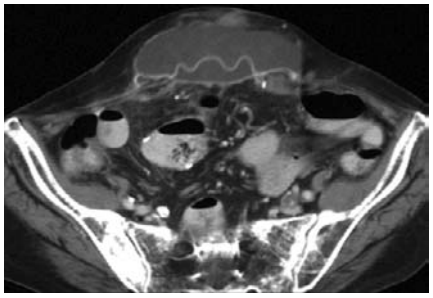

Figure 12 CT scan of Gore-Tex with surrounding seroma. This drained spontaneously and was culture-positive for methicillin-resistant *S. epidermidis* (same patient as in Fig. 5).

repair. As mentioned in the discussion of ultrasound, chronic seromas can form around meshes used for hernia repair.

The herniologist must be aware of the advantages, limitations, and radiographic characteristics of CT in order to correlate them to the clinical picture. Only then can an accurate diagnosis be made.

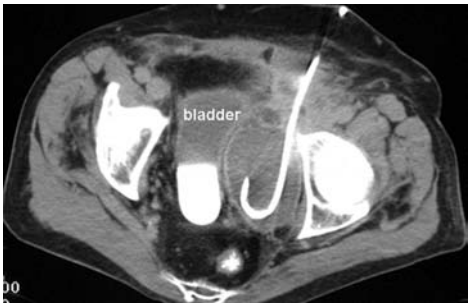

Figure 13 CT scan of postoperative hematoma. The patient had fever and abdominal pain following laparoscopic repair of a multiply recurring inguinal hernia. The patient was on warfarin and was anticoagulated perioperatively. The problem was presumed to be an abscess, but the aspirate and cultures were negative. Note the catheter in the hematoma, which has an enhancing rim mimicking an abscess.

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C. MRI

Magnetic resonance imaging (MRI) is another entirely different imaging technology that is useful for diagnosing mesh infections. A large magnet with an internal diameter large enough to fit an adult is coupled with smaller magnets called *gradient coils*. The force created by these two magnets causes the protons to spin. Additional radiofrequency coils next to the patient provides a counterforce away from the magnets. As the protons spin back toward the magnets, they emit a radiofrequency that, when combined and analyzed by the computer, forms an image. This image is enhanced by the addition of intravenous and oral contrast [12].

Gadolinium is the contrast given during the examination. It is a paramagnetic agent that aids energy transfer to water protons in the magnetic field. Different concentrations display different effects on the protons, producing T1- or T2-weighted images. The presence of graft infections appears with low to medium signal intensity on T1-weighted images and high signal on T2-weighted images [13].

Cellulitis may be confused with an early abscess. The distinguishing change occurs when the abscess's center liquefies and produces an area of signal void on gadolinium-enhanced images (Bennett). Otherwise, developed abscess cavities appear the same on CT; there is hypodense center with air-fluid levels and surrounding tissue edema.

MRI is not traditionally used for the evaluation of mesh infections for several reasons. To complete the examination, older MRIs took time. In the acutely ill, claustrophobic, or otherwise anxious patient, this would not necessarily be feasible. This relative contraindication has been surmounted with newer and faster MRI. However, because of similar appearance of an abscess on both MRI and CT, as well as the great difference in cost and speed, MRI does not offer any significant advantage over CT.

III. OTHER MODALITIES

A. Plain Radiographs and Fluoroscopy

Plain radiographs and fluoroscopy are not routinely used for the evaluation of mesh infections. The meshes currently used are not radio-opaque unless they are calcified or marked with radio-opaque markers. These two modes of diagnosis are excellent for detecting a foreign body.

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The use of plain radiography or fluoroscopy can produce indirect signs of an infection or a foreign body. They have been used to support clinical suspicion of a foreign body. The addition of air in the soft tissue, air-fluid levels in a cavity, or soft tissue edema may support the clinical suspicion of an infection [11].

B. Xeroradiography

Xeroradiography has been used in the past for mammography. Some have tried to use this modality to identify foreign bodies. Woesner and Sanders [14] advocated its use and concluded it to be superior to conventional radiography in the evaluation of foreign bodies. They found that the use of positive-mode xerography was excellent for the diagnosis of most foreign bodies and that negative xerography was excellent for the detection of metal.

In contrast to this conclusion, Charney et al. found that objects seen on conventional radiography could also be identified on xeroradiography [15]. They also demonstrated that objects not highly visible on plain radiographs would not be visible on xeroradiography. In a supporting study by Flom, xeroradiography did not prove to be superior to plain radiography.

Xerography is a specialized diagnostic tool; most physicians do not have experience with it, and it is not available in most hospitals. More ionizing radiation is needed to perform the examination, which does not prove superior to conventional radiography [11].

C. Fistulogram

A fistulogram is not very helpful in the initial diagnostic process to determine the presence of an infection. It is useful in demonstrating a cutaneous connection with a foreign body and size of the cavity to which it is connected. It is also used to monitor the progress of the infection indirectly by evaluating the size of the fistula and cavity. A decreasing size along with clinical improvement indicates resolution of the infection. A fistulogram is useful in confirming that a fistula is associated with a mesh infection.

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D. Gallium Scan

The gallium scan is another modality used to locate areas of occult infection. This is performed by obtaining a sample of the patient's leukocytes and tagging them with a radioactive label. The sample is then reinjected into the patient. At intervals, the patient is then scanned with a camera that can detect radioactivity. Areas of increased leukocyte concentration indicate a possible infectious or inflammatory process.

Because of the normal postoperative inflammatory response, a gallium scan in the immediate postoperative period has limited usefulness. It may, however, be useful in patients who appear to be septic clinically but in whom a source is not readily identifiable. The gallium scan has been successfully used to evaluate vascular and orthopedic prosthesis infections but has not been evaluated for mesh infections.

IV. TREATMENT

The treatment of mesh infections initially involves drainage, antibiotics, and local wound care. If drainage persists and there is no sign of closure, the mesh may have to be excised completely or partially for complete healing.

V. LONG-TERM FOLLOW-UP

Follow-up of mesh infections can be quite long. Weekly physical examinations and subsequent follow-up radiography can be costly. Of all the modalities available for evaluating resolution of an infected cavity, ultrasound is the most practical and economically feasible. It can be performed in the office at any time. It is convenient, fast, easy, without radiation exposure, and noninvasive. Ultrasound has proven to be an invaluable and indispensable tool in our practice. We rely less on CT, although it is essential for deeper infections not visible with ultrasound. Ultrasound is useful to monitor resolution of a fluid collection but does not tell us if the infection is resolved. We rely on clinical examination by looking for purulent drainage, smell, lack of granulation tissue, and so on.

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VI. CONCLUSION

Although there are no formal prospective studies evaluating radiological techniques to identify or diagnose mesh infections associated with hernia repairs, we have presented our own practical approach to identifying, evaluating, and following these prosthetic infections. Much of the formal information on imaging of prosthetic infections is extrapolated from the experience of vascular and orthopedic surgeons as well as from the literature on imaging intraabdominal abscesses. Ultimately, the diagnosis of mesh infections relies on clinical suspicion and physical examination. Ultrasound and other radiological techniques are useful to identify or confirm the diagnosis and to monitor treatment.

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8

Infectious Complications Following Open Inguinal Herniorrhaphy

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I. INTRODUCTION

Approximately 800,000 inguinal herniorrhaphies are performed yearly in the United States. Figures proportional to population density are similar in Europe and Asia, making up a significant portion of what is called general surgery [1–6]. The incidence of wound infection following inguinal herniorrhaphy should run parallel to that in clean surgical cases, which hovers between 1 and 4% or even higher. The impact of this complication upon the general population in the form of human suffering, economic loss, and logistical debit is significant. Furthermore, in the United States in the year 2002, over 85% of these operations involved prosthesis utilization, a policy that is spreading around the world. The critical problem is that wound infections involving prostheses carry a significantly worse prognosis than those following anatomical repairs because their treatment requires multiple additional procedures, turning a simple ambulatory operation into a clinical ordeal [6].

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II. FACTORS RESPONSIBLE FOR POSTINGUINAL HERNIORRHAPHY INFECTIONS

Several factors influence the number of bacteria present in the wound at the end of an inguinal herniorrhaphy: intestinal strangulation, procedure duration, the institution of transcutaneous drainage, extensive dissection required by techniques involving direct tissue approximation, and previous recurrence are all conditions correlating with a higher incidence of postoperative infection. Furthermore, some surgeons believe that femoral herniorrhaphy is also associated with higher infection rates.

Mesh repair adds a foreign body to this equation, multiplying the risk. Most significantly, the mesh's surface physical characteristics and their interaction with the invading bacteria are also relevant: expanded polytetrafluoroethylene (ePTFE) presents a large and microscopically pitted contact area facilitating microbial colonization by hampering leukocyte and antibiotic defenses. Under those circumstances, prosthesis infections are more difficult to treat. On the other hand, infected ePTFE prostheses are easily removed, thus preventing damage to adjacent organs [6].

III. ANATOMICAL FACTORS AFFECTING INFECTION DIAGNOSIS

Mesh inguinal herniorrhaphy infections may appear at different wound depths. Their clinical manifestations are related to the vascularity of the anatomical layer in which they occur, expediting or delaying their discovery.

The subcutaneous tissue, with its poor vascularization, reacts sluggishly to the presence of bacteria, allowing more time for their colonization and for eventual suppuration. Conversely, muscle, with its abundant circulation, may permit faster access of white blood cells and macrophages to the contaminated area, defending it from bacteria. Thus muscle may be able to raise a better and earlier defense. Deep infections are usually detected later than superficial ones because the prosthesis is located in the depths of a multilayered wound, delaying symptom recognition and facilitating widespread bacterial colonization. The development of infections and their capacity for damage also correlate

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with the use of peroperative systemic or local antibiotics—all factors influencing not the entrance of bacteria but their eventual survival [7–14].

IV. DIAGNOSIS AND TREATMENT

A. Superficial Infections

Signs and symptoms of postinguinal herniorrhaphy infection are related to its anatomical location. Superficial subcutaneous infections, limited in depth by the external oblique aponeurosis, usually manifest themselves by increasing wound pain—often pulsating in character—starting 3–5 days postoperatively. The patient recounts that the gradually decreasing postoperative incisional pain changed in character, becoming severe, annoying, and throbbing. *This symptom is often associated with fever, malaise, and leukocytosis. Axillary or oral temperatures are 1°F lower than core body temperature (rectal or tympanic), and these differences should be considered whenever fever is suspected.* This is an important point in the differential diagnosis of infection, as fever is its most sensitive sign. A false-negative temperature recording will provide a dangerously unrealistic sense of security. The wound will be swollen, erythematous, and tender and a purulent exudate may be seen emerging between the skin sutures. No further diagnostic measures are needed at that time except for culture and sensitivity of the pus.

B. Deep Infections

Infections involving layers deeper than the external oblique aponeurosis are associated with a more complicated array of signs and symptoms. The wound may appear normal and swelling may not be evident, particularly in obese patients. Local pain, malaise, and a throbbing sensation may not be significant. At this time the surgeon should institute all possible measures to rule out the presence a deep infectious process jeopardizing the mesh. As a first diagnostic step, it is important to establish the real spatial relationship between the infected anatomical layer and the prosthesis, as this will dictate the significance of the planned drainage procedure. Imaging in the form of computed tomography (CT) scans or sonograms is indicated; however, all these diagnostic procedures should be performed with minimal delay to decrease the risk of widespread mesh contamination by a solidly established bacterial colony. Sonography may demonstrate a liquid phase surrounding the prosthesis. The surgeon can

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further evaluate the nature of the collection by CT scan or sonography-guided needle aspiration. If the colonizing bacteria are other than *Staphylococcus*, the whole processes may carry a threatening prognosis (Figs. 1 and 2).

If the help of a consultant is requested, he or she should evaluate several factors that will dictate the depth of the clinical approach, such as the technique utilized in the original procedure, the possibility of intraoperative bacterial contamination, the immunological status of the patient, and the mesh and suture material utilized. All these elements should be balanced during the planning procedure, as the initial approach to these patients will bear heavily upon the final outcome. At that time, the surgeon's interaction with other physicians may transform a minor incision and drainage procedure into a major surgical undertaking, requiring repeated operations followed by a sequence of long-term complications. It is recommended that as soon as a patient returns to an office or clinic with signs and symptoms suggesting a wound infection, he or she they should be set aside from the usual routine follow-up of uncomplicated patients. The incorporation of such patients into a therapeutic algorithm helps to prevent loss of time, which can facilitate additional bacterial invasion.

C. Superficial Infections

These infections are superficial to the external oblique aponeurosis. They require the removal of all skin sutures, immediately followed by complete opening of the skin and subcutaneous tissue along the whole length of the incision. Failure to do so will result in undrained pus pockets, which significantly delay final healing by secondary intention. A systemic, oral, broad-spectrum antibiotic should be used early and at full dosage for 3–4 days only. We utilize cefadroxil monohydrate, 500 mg every 12 h. Our patients have not experienced any adverse reactions to this. However, the choice of drug will depend on the most commonly found bacteria in a specific nosocomial area. The wound should be dressed with normal saline compresses changed frequently (the patient can be taught to do this). If the wound is irrigated, the solution may contain povidone-iodine. We do not recommend the use of antibiotic-containing fluids because they may lead to the development of bacterial resistance. The dressings should be kept moist at all times, thus facilitating the drainage of contaminated lymph and serum. This accelerates healing, because dry and crusted gauze effectively tamponades the cavity, turning an open into

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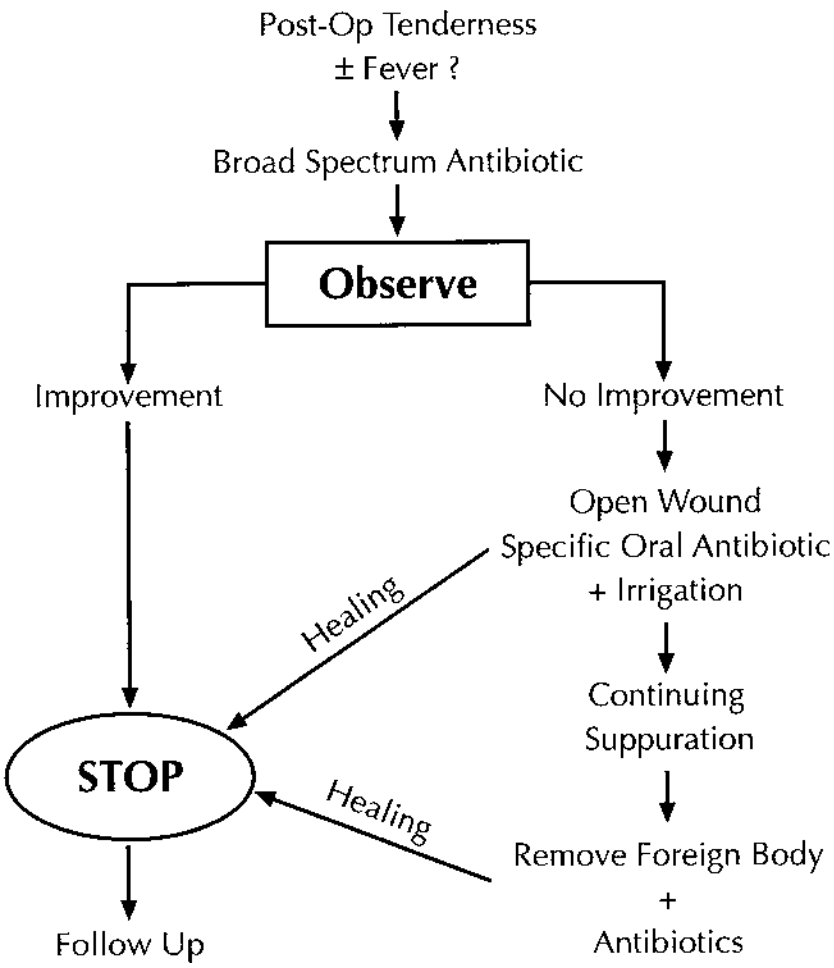

Figure 1 Recommended algorithm to be followed when a postoperative infection is suspected. It is essential to evaluate the patient on a daily basis.

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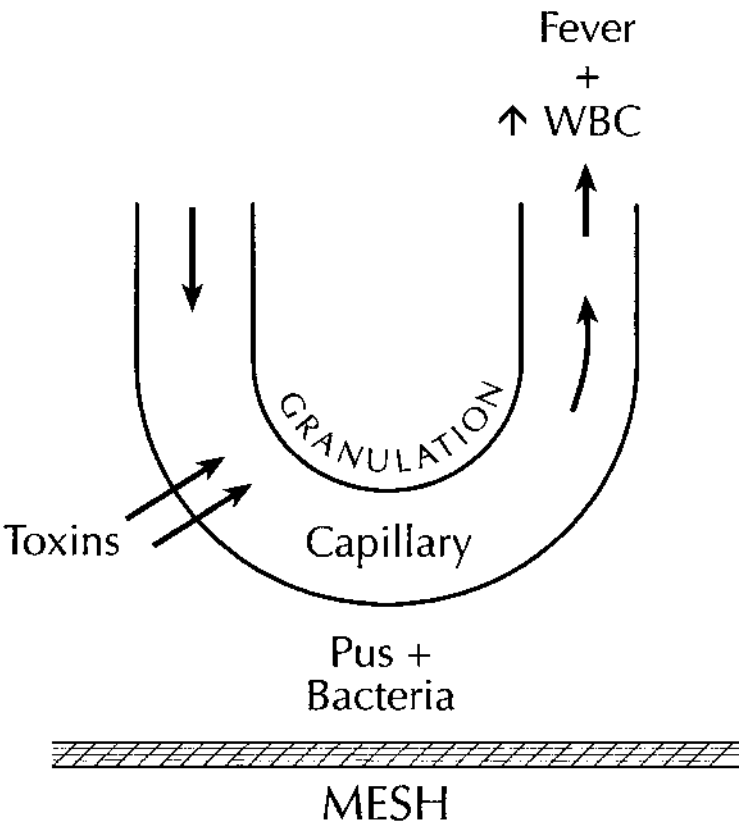

Figure 2 Diagram representing the pathogenesis of fever and an elevated white blood cell count as bacterial toxins penetrate the capillary bed from an infected area.

a closed wound. Rest is recommended with full ambulation. Wound progress should be monitored daily by the operating surgeon or someone familiar with the patient. If the infection is under control, with fever, white cell count, and symptoms all improving, there should be no change in antibiotics even if the sensitivity studies warrant so. If, however, signs and symptoms of infection remain unchanged, the results of the culture and sensitivity should be adhere to and the specific antibiotic utilized. As soon as the suppuration has ceased, the wound edges can be

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approximated—but not sealed—with Steri-Strips. In general these infections do not progress in depth and respond well to therapy.

Unremitting signs and symptoms such as fever, leukocytosis, and the appearance of sinus tracts point to a deeper infection, which should be treated expediently. Harmless as they may seem, superficial infections are evidence that the wound was exposed to an excessive amount of intraoperative bacterial contamination, which may have contacted the prosthesis. The surgeon should be alerted to the fact that a deeper infection may be present and masked by the superficial one.

Consultation with an infectious disease specialist is warranted in order to institute a full course of specific intravenous antibiotics administered on an ambulatory basis to preempt bacterial colonization of the mesh (Fig. 3).

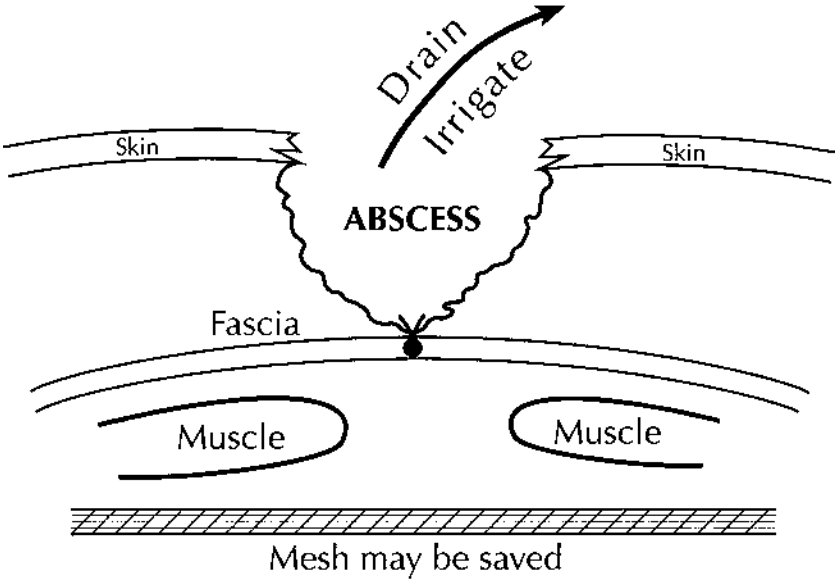

Figure 3 Diagrammatic interpretation of a superficial infection. Note that the abscess cavity reaches but does not penetrate the fascia. Early treatment is necessary to protect the mesh.

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D. Treatment of Infections Involving Deeper Wound Planes and Prostheses

Although there is no sharp anatomical definition between superficial and deep infections, superficial ones can be defined as those that respond to subcutaneous tissue incision and drainage. In contrast, deep postinguinal herniorrhaphy infections will not respond to such therapy. The important clinical difference is that these infections also involve the prosthesis, which then becomes the major site of bacterial colonization [11–15].

Pathologically, we will find the mesh bathed in pus and surrounded by a shell of granulation tissue provided by adjacent structures including the cord. The initial therapeutic goal is an attempt to save the implant. Although infected polypropylene meshes inserted for the repair of ventral hernias may be preserved by wide surgical exposure, irrigation, and systemic antibiotic therapy, their salvage is more difficult in infected inguinal herniorrhaphies because their deep location hinders adequate drainage.

Therefore the initial therapy should include wide exposure to drainage, daily irrigations, and systemic antibiotics. Portions of the prosthesis found to be invaded by healthy granulation tissue—which will eventually evolve into scar—may be preserved or even used as anchoring points for future repairs; they seem to be free from further bacterial colonization. On the other hand, if any doubt exists about their status, they should be completely removed, together with all suture material.

An ePTFE prosthesis suggests a different prognosis because—as bacteria penetrate its microscopic crevasses—they evade white blood cell phagocytosis. Such a prosthesis tends not to be amenable to therapy and should be expediently removed to speed the healing process and permit later repair (Fig. 4).

E. Prosthesis Removal

Prior to reoperation, it is strongly recommended that a full disclosure be made to the patient and next of kin about the risks of testicular ischemia resulting from the inevitable and difficult dissection.

The removal of inguinal prostheses requires solid knowledge of the regional anatomical landmarks, as it involves the meticulous and tedious separation of the mesh fibers from the attached elements of the spermatic cord. The testicles have abundant arterial irrigation, but their plexus pampiniformis is made of thin-walled veins, which tear easily and are

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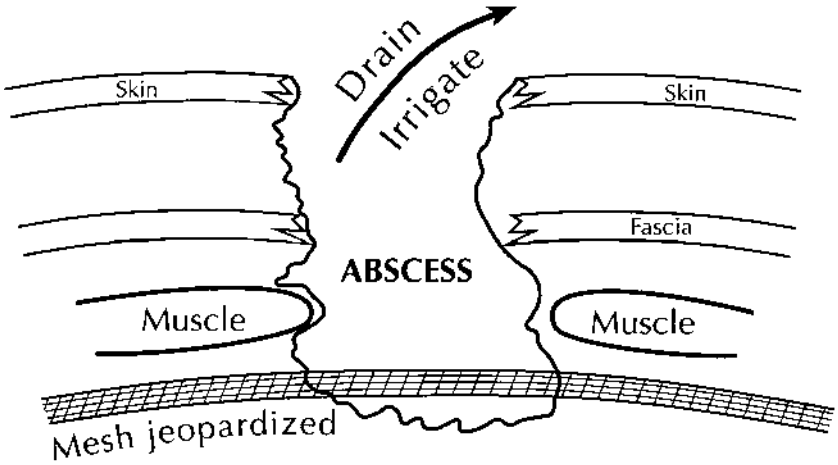

Figure 4 Diagrammatic interpretation of a deep infection involving the prosthesis. An attempt should be made to treat this condition with early incision and drainage plus antibiotics and irrigation in an attempt to save the mesh.

vulnerable to unintentional damage, producing testicular venous ischemic infarcts. The vas deferens may become intimately adherent to the mesh, and its destruction should also be avoided, particularly in the young. The longer the time span between prosthesis insertion and removal, the firmer those adhesions will be, requiring time-consuming dissection. Partial excision of infected polypropylene meshes yields poor results, as the remaining mesh aliquots and suture material produce draining sinuses, demanding further exploration. However, portions of prostheses already invaded by healthy granulation tissue may be allowed to remain in place and become incorporated in the final scar tissue. These areas may be used later as anchoring suture points. Braided or ePTFE sutures material should be removed together with the prosthesis, as the latter requires multiple knots to be secured, behaving like multifilament material.

In an infected femoral hernia, the contaminated prosthesis will be in contiguity with the femoral vein, making its extraction a real threat to limb and life. Prior to the procedure, the surgeon should take advantage of expert assistance and adequate anesthesia. A wide incision will

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facilitate all technical maneuvers necessary to avoid injury to the femoral vein, with its catastrophic implications.

After the prosthesis is removed, the wound should be left widely open with liberal drainage consisting of loosely placed Penrose drains or moist gauze. Tightly packed dry gauze physically obliterates the wound, impeding adequate drainage. The patient should receive a broad-spectrum or specific antibiotic, intravenously if necessary. The treatment may be ambulatory; but as the wound requires daily inspection, hospitalization may be required for the first few days. The healing process should be allowed to progress from ''bottom to surface'' until complete skin closure is achieved. However, residual sinus tracts indicate the presence of remnants of infected mesh or suture material. This requires re-exploration, because these foreign bodies will remain in the wound for months, impeding healing and subsequent reconstruction.

After prosthesis removal, the hernia will recur in almost 100% of cases requiring planning for further repair, which should take place at least 6 months later in order to allow complete wound healing and collagen reorganization. Before attempting reconstruction, we recommend the performance of percutaneous bacteriological wound testing as described in Chapter 16, in order to reassure both surgeon and patient that the new prosthesis has the best chance of survival by not being in contact with an unrecognized contaminated area.

The technique chosen for the repair will depend on the size of the recurrence and its anatomical location. Our procedure of choice for recurrent hernia repair is the use of a preformed polypropylene plug inserted after the recurrent sac's neck is dissected centripetally high, as recommended by Rutkow [9]. This simple and effective technique requires little dissection, avoiding further damage to already traumatized tissues. On occasion and to avoid entering a previously contaminated field, we have inserted a Kugel patch using a preperitoneal approach. This patch does not require suturing and is easily placed in the appropriate anatomical pocket.

F. Late Infections

Commonly, these are infections that, for a variety of reasons, have evaded early detection. The usual cause of such delays is a communication breakdown preventing adequate patient follow-up. These deep infections progress in an occult manner, exhibiting only mild signs and

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symptoms and appearing months or even years after the initial procedure.

In these patients, the infectious process has progressed from the initial inflammatory response to the formation of a real abscess with a well-defined wall of granulation tissue surrounding the prosthesis. Clinical events usually unfold in an uncharacteristic fashion, thus complicating the diagnosis. Following the initial infectious response—characterized by pain and low-grade fever—such patients may develop chronicity, exhibiting only mild local discomfort, low-grade and often undetected intermittent fever and a borderline elevated white blood cell count. The diagnosis is usually made by exclusion on a patient whose discomfort remains at a constant level for weeks, months, or even years after the repair was made.

Occasionally these infections make themselves evident by the appearance of skin sinus tracts which are connected with the offending infected material. In this case the treatment should be preceded by a fistulogram—a test that will help to locate the main infection site.

Reoperation requires complete removal of all suture and prosthetic material, followed by curettage of the granulation tissue lining the abscess cavity. This maneuver will speed up the healing process. Methylene blue dye injected into the track will greatly facilitate the surgical eradication of all infected elements. On occasion, the infection may involve suture material attached to the pubic periosteum or bone, producing a localized area of osteomylitis. This is associated with intense parapubic pain, at times disabling and aggravated by motion.

Imaging in the form of radiograms, CT scans, MRIs, or sonography will reveal a localized focus of osteomyelitis, the contents of which can be tested by CT scans used to guide needle aspiration. The discovery of white blood cells and bacteria in the aspirated fluid leads to the diagnosis of an abscess requiring drainage.

This procedure, which necessitates general or spinal anesthesia, starts with the excision of the skin scar, followed by an in-depth dissection until the abscess cavity is reached. The most superficial aspect of the mesh is identified and secured with clamps; then the separation of all tissues from the prosthesis proceeds bluntly or sharply until its complete removal. Occasionally, a mesh invaded by granulation and scar tissue must be removed piecemeal. After excision of all foreign bodies in the form of meshes, sutures, or staples, the osteomyelitic area is meticulously curettaged until healthy cancellous bone is reached. Failure to do so leads to protracted chronic osteomyelitis. The wound should be

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laid wide open and irrigated daily with an antibiotic solution while the patient receives specific systemic antibiotic therapy. The wound should be kept open by all possible means with Penrose rubber drains or loose gauze packing kept in place until complete—bottom to surface—healing has been achieved. The reappearance of sinus tracts will herald the presence of residual foreign bodies, the removal of which will require further surgery.

During the healing period, wound cultures should be repeated for early detection of resistant bacterial strains; in addition, we strongly recommend a consultation with an infectious disease specialist for the sake of their expertise in choosing specific antibiotics (Figs. 5–7).

G. Removal of Infected Prostheses in Contact with Vascular Elements

Most preperitoneal prostheses, such as those recommended by Stoppa, Wants, or Kugel, are placed in direct contact or in proximity to the external iliac or femoral veins. Made of polyester or polypropylene, these

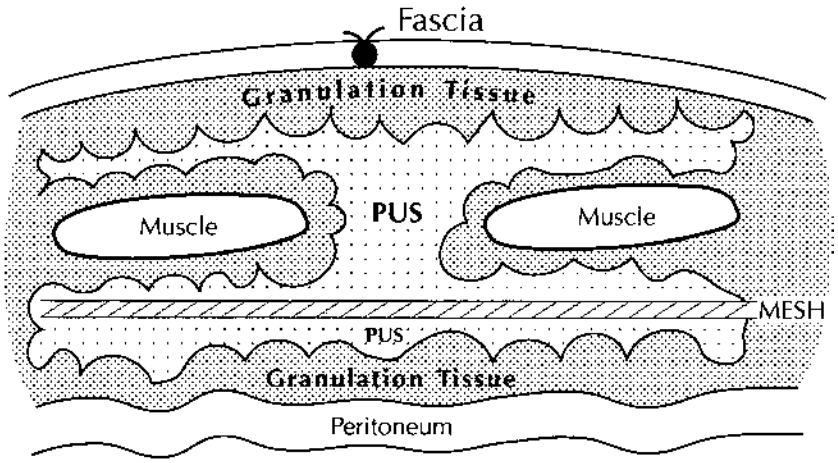

Figure 5 Diagrammatic interpretation of an abscess involving all tissues including the mesh. The cavity is lined by granulation tissue, which requires debridment to accelerate wound healing. It is essential that this area be treated like any other abscess, providing adequate drainage until complete healing is achieved. Persistent sinus tracks are due to leftover infected foreign bodies, which require excision.

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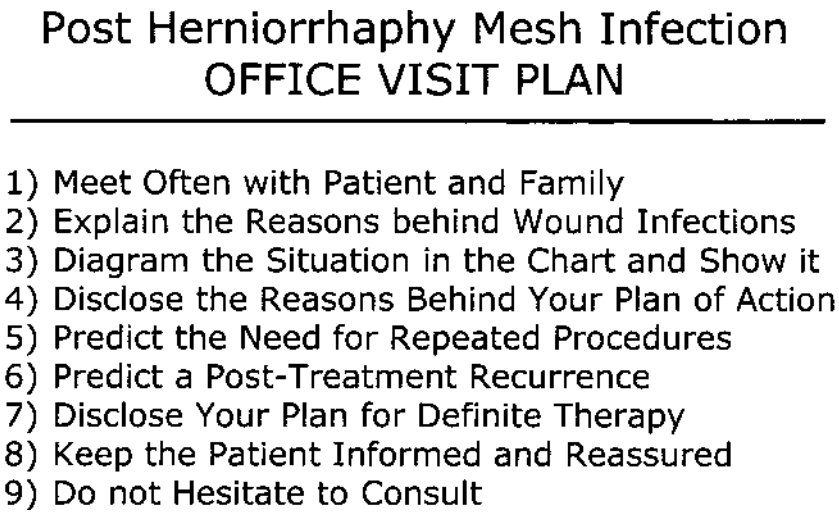

Figure 6 Recommended management plan for disclosure to the patient and next of kin. This should alleviate both the surgeon's and patient's anxiety about the forthcoming repeated procedures. It is recommended that a consult be sought in order to share some of the responsibilities involved.

meshes may adhere to the adventitial layer of those vascular elements [18–24]. Their removal demands highly skilled, meticulous dissection in order to prevent a major vascular accident. We recommend that surgical entrance to that area be initiated through an anatomical plane away from the infected mesh, starting its mobilization from the adventitial layer of noninvolved vein wall until a safe plane of dissection is well established and continuing the separation into the infected area. Because those maneuvers carry the risk of hemorrhage and the possible loss of limb or life, we strongly recommend the assistance and advice of a vascular surgeon, who should actively participate in the procedure.

H. Infections Produced by Proteolytic Bacteria, Streptococci, and Clostridia

Proteolytic bacteria, such as certain streptococcusal or Clostridial strains, can bring about a sequence of events that will startle the best-prepared surgeon. Some types of streptococci may digest large skin areas,

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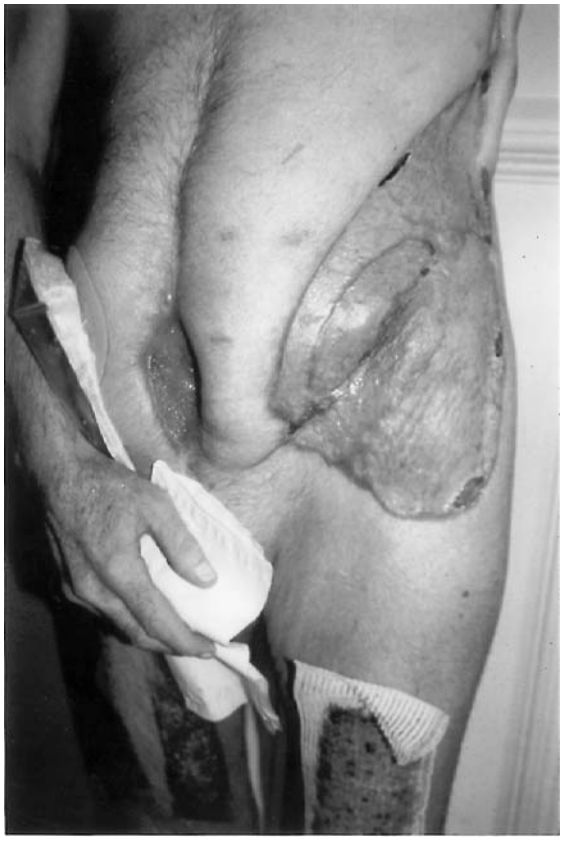

Figure 7 Photograph depicting multiple granulating wounds secondary to massive debridement. This patient suffered a clostridial infection following laparoscopic (TEP) inguinal herniorrhaphy. The inadverdent large bowel injury led to the initial fecal wound contamination. Recovery was complete.

producing full dermal loss requiring intravenous antibiotic therapy and sharp wide debridment of all necrotic skin, followed by grafting. Their onset of action of these infections is often insidious and curiously circumscribed to a small stitch abscess, from whence they grow exponentially. This bacterial species seems to work superficially, and we have not detected it in deep spaces.

Clostridial infections, although rare, carry an ominous prognosis. They have been observed after laparoscopic inguinal herniorrhaphies and

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are the result of an inadvertent and unintentional instrument entrance into a bowel loop, followed by further dissection with a contaminated device. The resulting gas gangrene may lead to septic shock accompanied by sequential organ failure, requiring critical care. Although the incidence of these complications is very low, it should be kept in mind whenever a postoperative patient exhibits disproportionately severe symptoms following an otherwise uneventful procedure. Severe wound pain with crepitus, skin discoloration, fever, or hypothermia and hemodynamic decompensation may be observed. Early recognition should be followed by vigorous emergent treatment, including rapid volume replacement, organ support, massive parenteral antibiotic administration, extensive sharp debridement, hyperbaric oxygenation, and intensive therapy (Fig. 8).

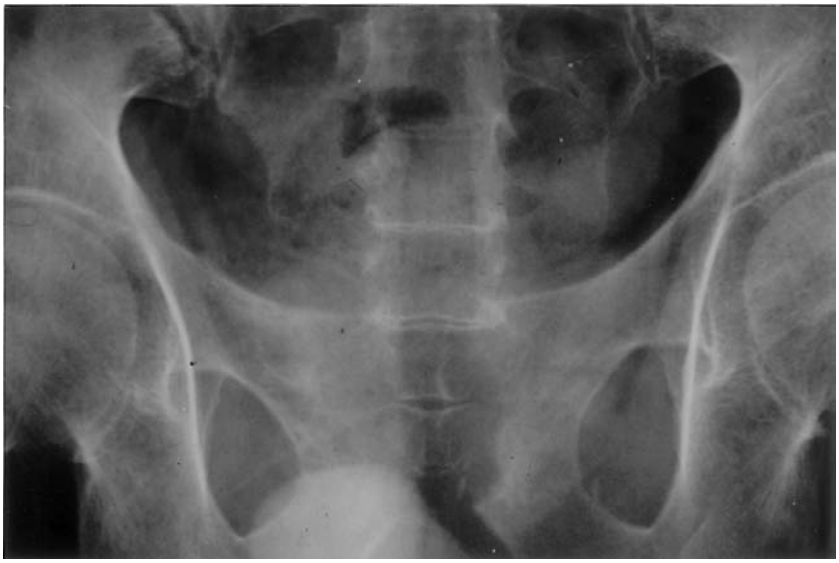

Figure 8 Radiograph showing partial destruction of the os pubis secondary to an infection following an open inguinal herniorrhaphy.

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V. CLINICAL EVOLUTION OF INFECTED POSTINGUINAL HERNIORRHAPHY PATIENTS

A. Patient 1

A 45-year-old male underwent right inguinal herniorrhaphy utilizing an anatomical repair. Three days postoperatively, a 2-mm dark spot was observed in one of the skin sutures; this was disregarded until a week later, when the patient returned with increasing incisional pain and fever. A 10-cm^2 area of necrotic skin was observed. The patient was admitted, started on systemic intravenous antibiotics, and the necrotic skin and subcutaneous tissue debrided up to the external oblique aponeurosis. The resulting granulation tissue surface was skin grafted and the wound healed uneventfully. There was no recurrence. Cultures grew *microphilic Streptococcus*.

B. Patient 2

A 70-year-old male underwent right inguinal herniorrhaphy utilizing an anatomical repair with braided polyester sutures. Five days postoperatively, the wound swelled. The skin and subcutaneous tissue were opened and the patient was placed on oral antibiotics. The culture revealed *Staphylococcus aureus*. Pain and fever continued until a consulting surgeon drained a large scrotal abscess. All suture materials were removed and the wound healed. The hernia did not recur.

C. Patient 3

An 18-year-old mentally disturbed male underwent the anatomical repair of a right inguinal hernia utilizing braided polyester sutures. Seven days postoperatively, the wound was opened because of a deep infection. The culture revealed *Staphylococcus aureus*. The patient was placed on oral systemic antibiotics and required several procedures to remove all suture material. The patient was lost to follow-up

D. Patient 4

A 35-year-old male underwent anatomical repair of a right inguinal hernia utilizing polypropylene sutures. Six days postoperatively, a subcutaneous infection was found and drained. The culture revealed

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Staphylococcus epidermidis. The patient received systemic antibiotics and his wound healed without recurrence.

E. Patient 5

A 55-year-old male underwent the anatomical repair of a right inguinal hernia utilizing polypropylene sutures. Seven days postoperatively, a deep subfascial infection was drained. The culture revealed *S. aureus* and the patient received intravenous antibiotics. The wound healed but the hernia recurred.

F. Patient 6

A 54-year-old male was referred to us with recurrent bilateral inguinal hernias. A year earlier he underwent bilateral inguinal herniorrhaphies, which were followed by bilateral wound infections. The left herniorrhaphy had been allowed to drain and healed but was recurrent. The right side revealed several draining sinuses, which cultured *S. epidermidis*. The patient underwent several procedures during which portions of polypropylene mesh were removed, together with suture material. That side had been reoperated twice before elsewhere, resulting in repeated infections. Percutaneous testing was negative. The right side was repaired by inserting a Kugel patch via a preperitoneal approach in order to reduce the risk of contamination. The left side was repaired with a Rives-stoppa procedure. Six years later there was no evidence of recurrence or infection.

G. Patient 7

A 62-year-old male was referred to us because of recurrent postherniorrhaphy infections. He had undergone the repair of a right inguinal hernia with mesh 1 year earlier. An infection was discovered and the mesh was removed and replaced during the same procedure. This was followed by another infection, which was treated by intravenous antibiotics and drainage in an effort to save the mesh. On physical examination, several sinus tracts were seen, indicating that the infection had recurred. The wound was reopened, all prosthetic material was removed, and the wound was left open to heal secondarily. When healed and after percutaneous testing was found to be negative, the hernia was repaired with prosthesis. Five years later, there is no evidence of infection or recurrence.

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9

Diagnosis and Management of Laparoscopic Inguinal Hernioplasty Infections

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I. INTRODUCTION

Antisepsis, asepsis, and the development of antibiotic therapies have dramatically reduced the infection rate associated with surgical intervention. In a clean, class I surgical wound (open hernia repair), the expected wound infection rate is 1.5% [1]. The usual pathogens for postoperative infection in class I surgical wounds are *Staphylococcus aureus* and *Staphylococcus epidermis*. These organisms usually originate from the operative environment or from the patient's skin flora.

Extremes of age, the presence of coexisting debilitating diseases, the absence of general good health, and other modifying factors have been known to have a deleterious effect on a patient's response to infection. Elek and Conen in 1957 convincingly demonstrated the enhancing effect of a stitch on wound infection. These investigators found that it took 10^6 *S. aureus* organisms injected subcutaneously to produce an infection in healthy human volunteers, but that only 10^2 organisms were required to produce an infection in the presence of suture. In effect, the buried portion of a suture represented a virulence-enhancing effect on infection

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of at least 10,000 times [2]. Bacteria, it seemed, were better able to maintain a defense against phagocytosis after they had gained entrance to the interstices of multifilament suture. Other workers confirmed these findings and showed that monofilament suture appeared to confer an improved resistance to infection when compared to multifilament suture [3].

Bacteria average about 1 μm in size. Macrophages and neutrophilic granulocytes are too large to enter the interstices of suture or pores of synthetic material if these spaces are 10 μm in three-dimensional size or smaller [4,5]. When bacteria are present in the interstices of suture or in pores of prosthetic mesh in which pore size is smaller than 10 μm in three-dimensional size, they are relatively safe from several of the body's defense mechanisms. Proliferation of bacteria within the interstices of braided suture or within the pores of synthetic mesh is the cause of infection associated with implanted prosthetic materials.

Synthetic mesh use for hernia repair can be classified, based on pore size, into four groups or types:

Type I: Prostheses with pores greater than 75 μm. These are totally macroporous materials that will admit macrophages, fibroblasts, blood vessels, and collagen fibers. (Marlex, monofiliment polypropylene meshes) [4,6,7]. Figure 1 depicts polypropylene mesh.

Type II: Prostheses with pore sizes less than 10 μm in at least one of their three dimensions. These—including expanded polytetrafluoroethylene (ePTFE), Dual Mesh and surgical mem-

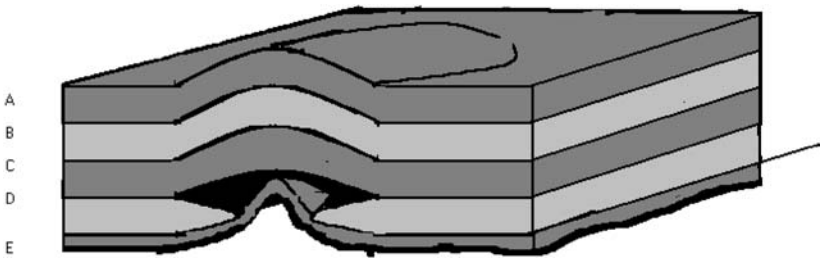

Figure 1 Diagram illustrating the tissue layers in an unrepaired inguinal hernia, from superficial to deep. A. Skin; B. Subcutaneous tissue; C. External oblique aponeurosis; D. Inguinal floor with defect; E. Peritoneum.

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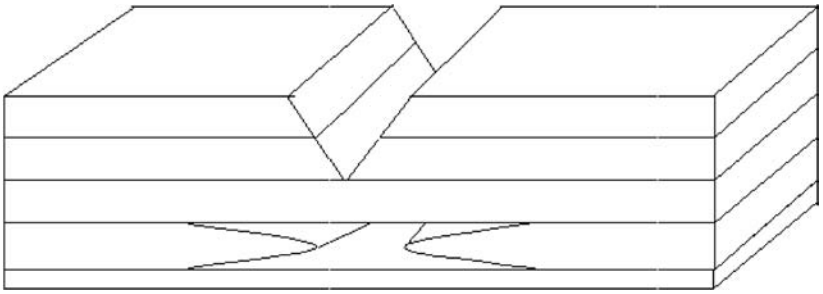

Figure 2 The drawing illustrates the first step in any open hernia repair. The skin incision is generally parallel to and at least as long if not longer than the inguinal canal. The result is a larger area for bleeding more dead tissue, and a larger portal of entry for endogenous and exogenous flora.

brane—are totally microporous prostheses. Figure 2 depicts ePTFE mesh.

Type III: Macroporous prostheses with mutifilamentous or microporous components, including braided Dacron and braided polypropylene. Figure 3 depicts woven Dacron mesh.

Type IV: Biomaterials such as Silastic, with submicron pore size.

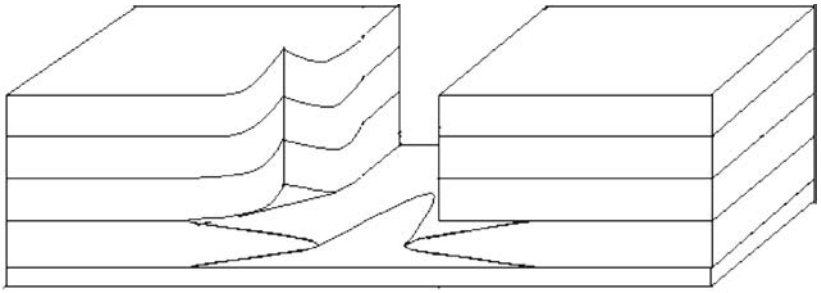

Figure 3 Schematic representation of the dissection of an open hernia repair. The skin incision has been extended through the external oblique aponeurosis. Which has been bluntly dissected from the cord and its structures, creating a large wound with greater potential for bleeding, nonvital tissue, and seroma formation.

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II. OVERVIEW OF THE PROBLEM

Since the introduction of laparoscopy in 1982, numerous authors have published several large series of laparascopic groin hernia repairs. These reports collectively catalogue an astonishingly low infection rate ranging from 0–0.1% [8–11]. Since the discipline of surgery is driven by empirical data, well-designed clinical trials generally form the basis of the fund of knowledge that practicing surgeons use daily to make significant clinical decisions. When such information is scant, however, the surgeon must fall back on his or her knowledge of basic science, surgical technique, and the available literature to formulate a solution. Such is the case with prosthetic infections following laparoscopic groin hernia surgery. With only 20 years' experience with the technique and numerous series of cases reported without a single infection, empirical data concerning the cause and management of an infected graft are scant. This paucity of empirical information can be frustrating for the busy surgeon faced with the possibility of managing such a rare complication. Even personal experience is not a satisfactory guide, as a general surgeon may practice throughout an entire career without encountering this complication.

The purpose of this chapter is to synthesize current clinical and basic science information concerning synthetic graft infection into a set of coherent principles. By reviewing the basic science of prosthetic infection, comparing and contrasting open and laparascopic groin hernia repair techniques, and reviewing what few case reports are available concerning the diagnosis and management of prosthetic infections in the literature on laparoscopy, it will be demonstrated that those characteristics of laparoscopic hernioplasty that result in low infection rates and make it an ideal method for repair also provide the conceptual framework for a sound approach to the management of prosthetic infections when they occur.

III. CAUSES OF PROSTHETIC INFECTION

In most cases of surgical infection, deficiencies in surgical technique or failure to control the bacterial milieu of the surgical wound are frequently cited as causes of wound infection. For instance, delicate handling of tissues, gentle dissection, and meticulous hemostasis are time-honored surgical principles [8]. Adherence to these principles prevents the accumulation of undue amounts of devitalized tissue in the surgical

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wound and decreases the quantity of nutrients available to potential pathogens. It is also well established that biomaterials with interstices greater that 10 μm in diameter are more resistant to infection than those with smaller interstices. Bacteria can find a haven in smaller pores to which macrophages and neutrophils cannot gain entrance [4,12]. Breaks in sterile technique are also frequently cited [12].

IV. EFFECT OF SURGICAL TECHNIQUE ON RISK OF INFECTION

A comparison between open and laparoscopic hernia repair techniques can easily demonstrate the effect of surgical technique on the incidence of infection, as the literature demonstrates. The infection rate in open hernia repairs is estimated at between 1 and 2% [12]. As noted above, laparoscopic hernia repairs with prosthetic material enjoy an infection rate orders of magnitude less—between 0 and 0.1% [8–11].

Open repairs employ a skin incision to gain access to the abdominal wall musculature; this is generally as long as or longer than the inguinal canal. The external oblique aponeurotic layer is also incised and bluntly dissected from the spermatic cord or round ligament. The cord is skeletonized by blunt and sharp dissection, the hernial sac is excised or imbricated, and the hernia is repaired. Figures 1–5 illustrate two current techniques of open prosthetic hernial repair: the Lichtenstein repair and the patch-and-plug technique.

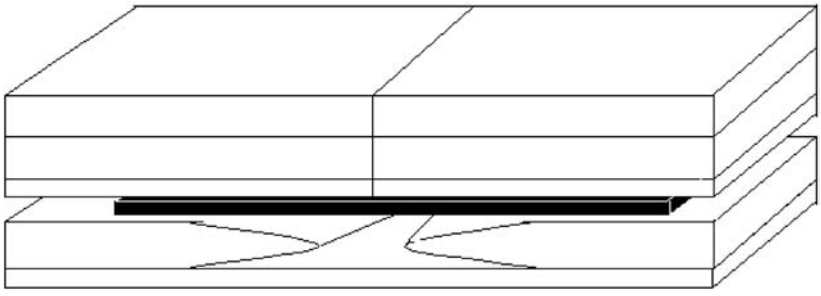

Figure 4 Diagram illustrating a repaired hernia using the open mesh onlay (Lichtenstein) repair.

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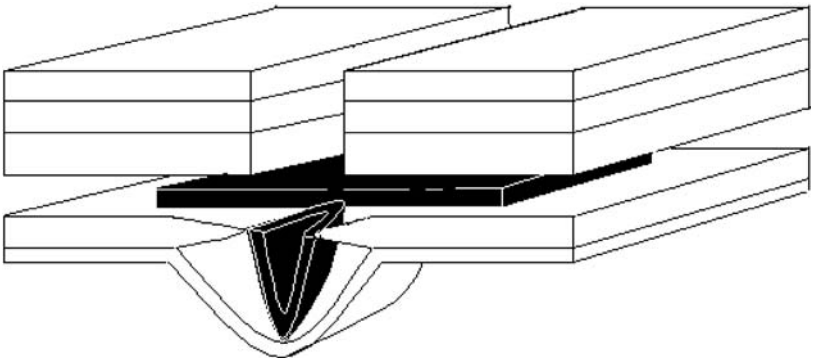

Figure 5 Diagram of open patch and plug repair illustrating the large incision needed for open repair as well as large area of dissection. Additionally, the addition of the plug in the hernia defect is shown to tent the peritoneum, risking erosion through both peritoneum and intra-abdominal viscera. Failure to anchor the plug may increase the risk of erosion as a result of mesh migration. Placement of a preperitoneal plug has also been reported as the cause of hollow visceral fistulization after laparascopic hernia repair.

In contrast, laparascopic hernia repairs employ relatively small incisions that are some distance from the operative site. These smaller incisions make smaller portals of entry for bacteria. The surgical wound, which does not involve division of the abdominal wall musculature, is protected from ambient contamination by a cannula. Dissection is generally carried out in the relatively avascular preperitoneal space. The two most common laparoscopic repair techniques, the transabdominal preperitoneal (TAPP) and the transabdominal extraperitoneal (TEPP), demonstrate this. Each is performed with laparoscopic instrumentation through 5-mm port sites. The TAPP repair approaches the defect from inside the peritoneal cavity. The peritoneum is opened, the hernia reduced, and the sac dissected. Mesh is placed over the myopectineal orifice and secured with staples, tacks, or stitches. The peritoneum is then closed. Figure 6 represents this repair schematically.

The TEPP repair, on the other hand, utilizes a preperitoneal approach. The defect is dissected after the preperitoneal space has been opened and enlarged using an inflatable dissecting balloon. The myopectinal orifice is then covered with prosthetic, which is fixed with

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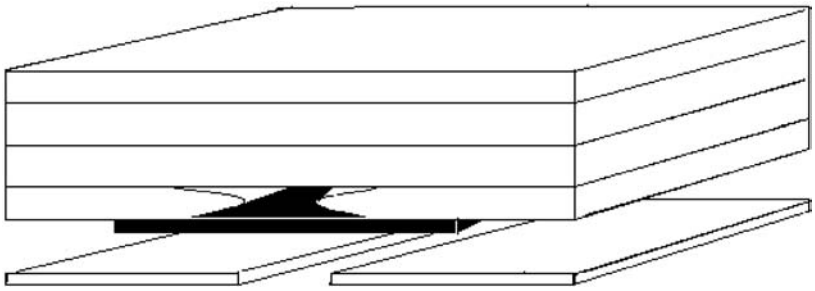

Figure 6 Transabdominal preperitoneal hernia repair. The diagram illustrates the advantages of this type of repair with regard to contamination from exogenous sources. In contrast to open repairs, there is no large incision in direct continuity with the operative site and the prosthetic, nor is there extensive dissection of the skin, subcutaneous tissue, or abdominal wall musculature. Also, the skin incisions are separated from the operative site not only by a small skin incision but also by several centimeters of inert pneumoperitoneum. However, should the mesh migrate or the peritoneal closure be inadequate, the risk of endogenous infection from visceral erosion is quite real.

staples or tacks. No intentional defects are placed in the peritoneum. Figure 7 demonstrates this repair graphically.

V. EFFECT OF CHOICE OF PROSTHETIC MATERIAL ON RISK OF INFECTION

It has been demonstrated that a minimal concentration of bacteria is required to produce infection in a surgical wound [2]. The presence of foreign material reduces this threshold and increases the virulence factor of bacteria several thousandfold. Microbial surface component recognizing adhesive matrix molecules (MSCRAMMs) are elaborated by the bacteria themselves [12,13]. These adhesion molecules recognize and bind to elements of the host's interstitial matrix. The binding process leads to an elaboration of a glycoprotein layer, which impedes the entrance of host bactericidal elements [2]. In the presence of a synthetic graft, bacterial microbial surface components bind to the prosthetic surfaces, which are devoid of a protective cellular layer, competent protective

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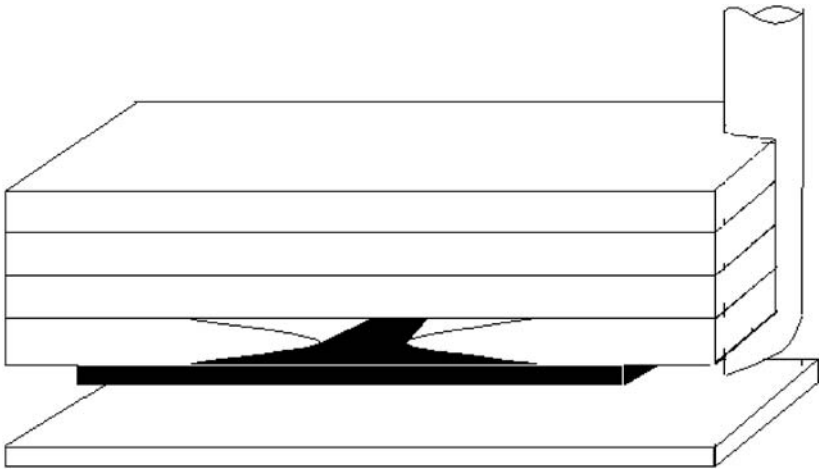

Figure 7 The above diagram schematically illustrates the technique of TEPP repair. The advantages of a small incision are still seen here, but in contrast to the TAPP repair, there is direct communication between the skin incision and the operative site. There is also more dissection than in TAPP but far less than in the open repairs, and it does not involve skin, subcutaneous tissues, and abdominal wall musculature. There is also no peritoneal defect to repair, reducing the risk of adherence to and erosion of intra-abdominal viscera.

extracellular polysaccharride (glycocalyx), or a basement membrane. The lack of these elements promotes bacterial growth [12,13].

The presence of suture material in a contaminated wound decreases the minimal bacterial concentration needed to produce clinical infection [2]. Braided sutures compound this problem because of the presence of very small interstices between the braided strands [12,14]. Even monofilament sutures have interstices between the throws of a knot that can harbor bacteria. Thus the use of sutures to anchor mesh can increase risk of infection and generate a "stitch abscess" [4]. However, laparoscopic hernial repairs are almost universally performed with inert, metal anchoring devices that are minimally reactive and have no interstices.

It follows that current techniques of laparoscopic groin hernial surgery have optimized those conditions, outlined above, that make prosthetic infection less likely. Reducing the potential inoculum with

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small incisions protected by a cannula sleeve minimizes bacterial contamination. The access incisions are remote from the operative site and serve to limit critical numbers of micro-organisms from gaining access to the operative site. Because of the magnification inherent in laparoscopic surgery, dissection is typically more meticulous than in open surgery, and the amount of devitalized tissue available to bacteria is reduced. Complementing these factors is the common use of type I biomaterials (which tend to resist infection) and their fixation with staples or tacks—inert devices that eliminate interstices smaller than 10 μm. The result is a hernia repair that is quite resistant to infection.

VI. DIAGNOSIS AND TREATMENT

Two distinct types of prosthetic infection have been described. The first type is an uncomplicated infection caused by contamination of the prosthetic material at the time of operation from endogenous or exogenous sources. In this type of infection, the source of sepsis is localized and not ongoing. The second type of prosthetic infection, a complicated one, typically results from mesh migration and its erosion into adjacent viscera, as seen in Figs. 8 (migrated mesh) and 9 (explanted mesh plug). In these cases there is an ongoing source of sepsis from the eroded organ. These infections must be differentiated from each other and from other postherniorrhaphy complications (Table 1).

History is key in differentiating complex from simple infections. Because the bacterial source in uncomplicated infections is present from the time of operation, signs and symptoms are present within a few days

Table 1 Differential Diagnosis of Mesh Infection

	Simple	Complicated
History	Early onset of symptoms	Late onset of symptoms
Physical examination	Pain, erythema, suppuration, drainage, swelling	Pain, erythema, suppuration, drainage, swelling
Differential diganosis	Recurrence, hematoma, seroma, orchitis, neuralgia	Recurrence

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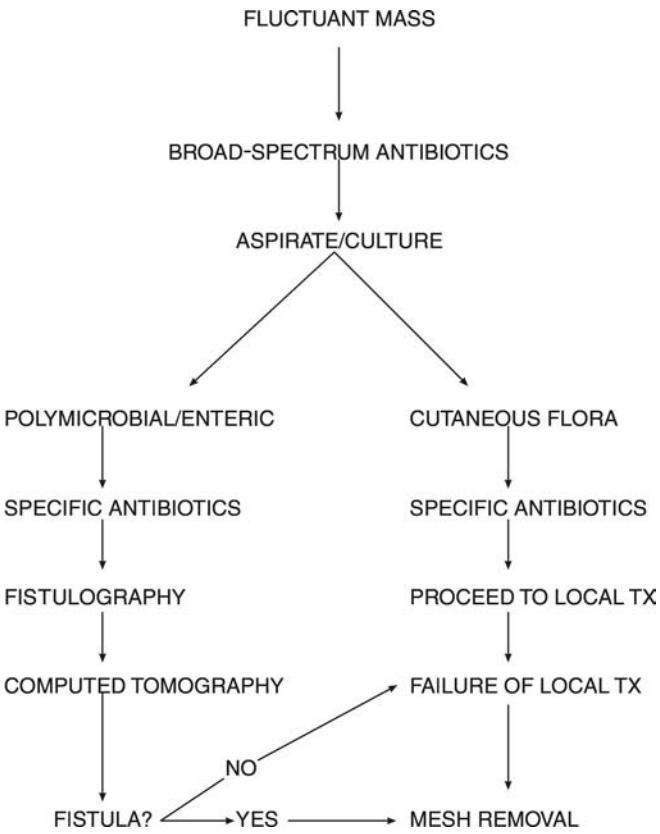

Figure 8 Algorithm for treatment of mesh infection.

to weeks. Therefore, these must be differentiated from other early postoperative complications, such as those listed in Table 1. Complex infections, because they involve migration and erosion of the mesh, take time to evolve and typically present months or even years from the original operation. Late infections should be assumed to be complex until proven otherwise.

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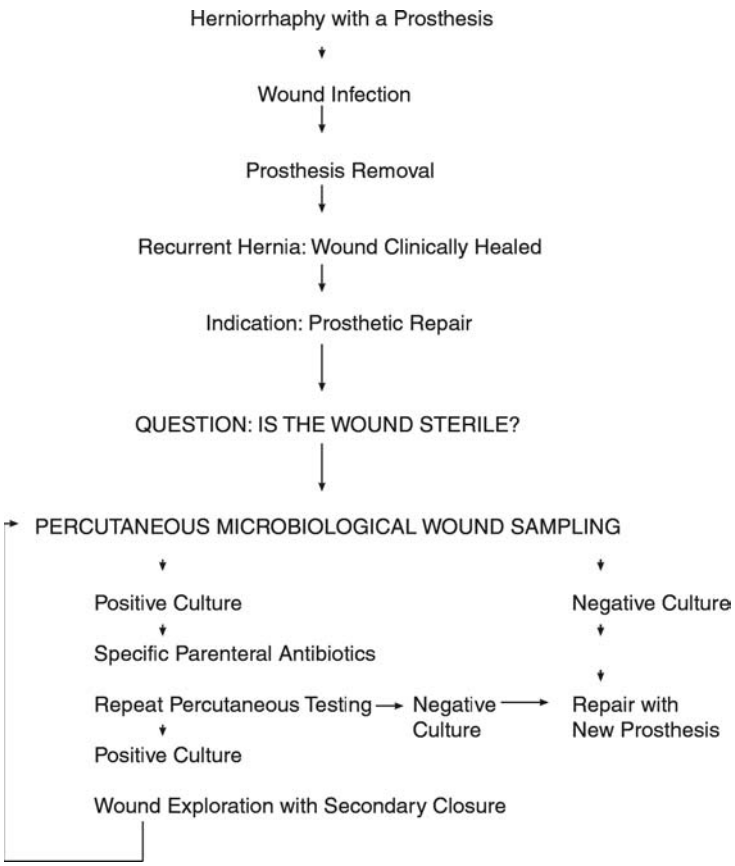

Figure 9 Algorithm for treatment of postherniorrhaphy infection.

VII. SIMPLE PROSTHETIC INFECTIONS

Uncomplicated infection may present as simply as a mass in the groin, persistent postoperative pain, or as dramatically as a chronically draining sinus tract or large fluctuant mass in the groin.

Early recurrence after laparascopic inguinal hernia repair can present with swelling at the operative site, pain, obstructive symptoms, and skin discoloration. Differentiating recurrence from the other types of complications is important, because diagnosing and appropriately

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treating mesh infections depends in large part on the results of bacteriological studies of the material aspirated or drained from the operative site. Swelling localized to the operative site may be either a fluid accumulation or recurrent hernia. Aspiration or incision and drainage of the visceral contents of a recurrent hernia could prove disastrous. Differentiation between the two may be determined by physical examination. Ultrasound and computed tomography are useful to rule out early recurrence as a cause of prolonged groin swelling or pain if physical examination is equivocal. Radiographic evidence of recurrence does not rule out infection but does mandate reoperation.

Once recurrence is ruled out, the differential includes not only infection but also seroma, hematoma, and ischemic orchitis on the one hand and neuralgia on the other. Seroma and hematoma can be managed expectantly, as both will typically resolve within 6–12 weeks without active intervention. Persistent hematomas can be drained and confidently expected to resolve. Ischemic testicular orchitis is a serious complication thought to arise from ischemia secondary to thrombosis of the testicular veins [15]. There is swelling of the testicle initially that may be confused with infection. The swelling is usually painless and associated with an indurated or "woody" enlargement of the testicle that slowly subsides with or without antibiotic. There is no effective treatment after testicular ischemia has been established, and the patient will commonly present with an atrophic testicle within 1 year.

Mesh inguinodynia may be due to direct injury of a major sensory or mixed motor-sensory nerve of the groin (iliohypogastric, ilioinguinal, or lateral femoral cutaneous) with a suture, tack, or staple. It is thought that mesh inguinodynia can arise from entrapment of the nerve in the fibrous reaction induced by the prosthetic mesh. The latter may require removal of the mesh to alleviate symptoms; the former can generally be managed with local injections of corticosteroid to relieve discomfort or by removal of the offending fastener.

Diagnosing postoperative neuralgia may be as simple as noting that the patient clearly has pain in the distribution of the ilioinguinal, iliohypogastric, genitofemoral, or lateral femoral cutaneous nerves on physical examination. The pain has been present since surgery, there are no systemic signs or symptoms of sepsis (i.e., fever, leukocytosis, eleveated erythrocyte sedimentation rate), and radiographic imaging has been normal. Delayed presentations have been reported and may be diagnosed as neuralgia with the additional aid of specific nerve blocks. Treatment is mesh removal with or without neurectomy.

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Swelling from hematoma and seroma and orchitis must be differentiated from mesh infection. The absence of warmth, erythema, fluctuance, and purulent drainage on physical examination as well as the absence of fever or leukocytosis are reliable signs that infection is not present. If physical examination is equivocal and computed tomography or ultrasound reveals no bowel or bladder in the mass, aspiration of fluid with bacteriological culture is advisable. In the absence of a positive culture, seroma and hematoma can be managed expectantly.

VIII. COMPLEX PROSTHETIC INFECTION

Distinguishing between uncomplicated and complicated infections may be difficult but is essential for appropriate management. In those cases where a perforation is contained or walled off, the signs and symptoms of infection can be muted. In addition, the clinical signs and symptoms of infection are not necessarily specific to mesh infection and may be indistinguishable from other postherniorrhaphy complications such as recurrence, hematoma, seroma, ischemic orchitis, and neuralgia.

Once infection is suspected and recurrence ruled out, aspiration of the fluid collection with appropriate bacteriological studies should be done. Additionally, culture of any drainage from chronic sinus tracts should be obtained. Aspiration of purulent fluid should prompt open drainage and administration of a broad-spectrum antibiotic with good gram-negative and anaerobic coverage [12]. Polymicrobial infections or growth of enteric organisms should raise the suspicion of a visceral complication and prompt radiographic investigation [12,18–20].

Erosions of laparoscopically placed mesh into the small bowel, colon, and urinary bladder have been reported [8,18,20,21]. Clinically, the character of the drainage can be helpful in identifying the eroded organ. Frank stool would clearly point to the colon as the source of ongoing infection. Bilious drainage would suggest the small bowel. Clear drainage high in creatinine would point to the urinary bladder. If clinical examination provides few clues, a systematic search should be undertaken.

Fistulography, the direct injection of contrast into the external fistulous opening, is the diagnostic study of first choice. This should be followed by contrast enema and or small bowel follow-through if the results of the fistulogram are inconclusive. Retrograde cystography rounds out the diagnostic evaluation. Radiographic evaluation is

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complete when the entire fistulous tract is delineated. Colonoscopy or cystoscopy may be used to localize an erosion site in either the colon or urinary bladder if all contrast radiographs have failed to localize a fistula.

IX. TREATMENT

Infection complicated by graft migration requires surgical intervention for removal of the mesh and management of the enteric source of sepsis [2,9,18–20].

Intervention should be planned as soon as a definitive diagnosis of graft migration and visceral perforation has been made. Graft migration without visceral injury is an elective intervention for recurrent hernia. In many instances, the migrated prosthetic is markedly scarred to surrounding tissues and there is little value in removing it. Hernial repair is all that is required, and it may be performed laparoscopically or by open techniques.

Infections that are not the result of ongoing contamination from bowel or urinary bladder (i.e., that are the result of a skin contaminant or break in surgical technique and involve type I biomaterials) are generally readily treatable by exposure of the prosthesis, removal of stitches or any unincorporated mesh, and local wound care. Since the source of sepsis is not ongoing, opening the wound and allowing it to heal by secondary intention is all that is needed. Good results have been nearly universally reported using this technique [12,14].

Type II prostheses may need to be removed under these circumstances, as tissue incorporation is impaired in the presence of infection. However, a trial of local therapy with antibiotics, exposure, and local wound care is warranted. The method of mesh removal should be individualized. Type I materials tend to incorporate more fully than type II materials; their excision may be difficult and time-consuming. Type II prosthetics, on the other hand, do not incorporate well in the presence of infection and are easier to remove. Also, experience with type II prosthetic infections has shown these infections to be more resistant to conservative management. Drainage of the operative site along with antibiotic coverage should be initiated. However, persistence of infection usually demands removal of the prosthesis. In the case of ventral hernial repair, it may be beneficial to remove only the portion of mesh that is exposed and continue with local hygienic measures and antibiotic coverage. If the patient does not improve, then complete removal of

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the prosthesis is indicated, with definitive repair after all evidence of infection has resolved.

Enteric fistulas, in contrast, will not respond to local care and require removal of the mesh as well as repair of the fistula. There are increasing reports of mesh migration and erosion [18–20]. The operative approach for mesh removal and fistula repair in these cases has varied from open incision and drainage of the groin to laparotomy. Alternatively, a laparascopic intervention may be attempted if the operator has sufficient skill and experience. Depending on the organ injured, laparotomy may be performed via an infraumbilical, midline, or groin incision. A standard bowel prep (GoLytely and neomycin/erythromycin) is indicated if a large bowel lesion has been identified or is suspected. Urological consultation should be considered in the case of bladder involvement. The operative site is explored and the visceral injury (bowel or urinary bladder) identified. Usually, with long-standing infection, the fistulous tract and injury site are mature, with only localized contamination. The injured site is resected and primary anastamosis or repair is performed. With infection, mesh usually becomes unincorporated from the operative site and is not difficult to remove. The operator's experience and judgment guide the choice of approach, whether it be laparosocopic or an open laparotomy. Given the rarity of this condition and potential for complications arising from intervention, surgeons early in their experience may be advised to refer these cases to a tertiary center for definitive management.

X. SUBSEQUENT REPAIR

As described above, it is rare for mesh to be removed because of an infectious complication. Also, when mesh is removed posthernioplasty, recurrence seems to be infrequent [14]. However, when mesh must be replaced because of infection, care must be taken to avoid recurrent infection. Deysine has outlined an approach to this problem based on the orthopedic experience with implantable prostheses (Fig. 9) [12].

XI. CONCLUSION

As has been demonstrated, laparoscopic hernioplasty results in a remarkably low prosthetic infection rate because laparoscopic technique

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and materials minimize those factors that predispose to infection. When infection is suspected or confirmed, consideration must be given to breach of technique as a cause of the problem. For uncomplicated infections, suspect suture, knots, or mesh with small pore size as the primary site of the infectious process. Remove these sites when feasible. If local therapy fails, excise the mesh and close the wound over a drain. In many cases the hernia will not recur. Should a hernia recur after mesh removal, ensure the sterility of the wound prior to reinsertion of any prosthetic material and adhere to sound operative principles. If possible, perform the procedure through a virgin tissue plane. Be mindful that an infection may be the result of a visceral fistula caused by mesh migration, with erosion into the bowel or urinary bladder, especially if the presentation is months to years after the index operation. Removal of the migrated mesh and repair of the injured organ is mandated in this situation. In this instance, reimplantation of mesh is guided by the same principles as in uncomplicated infections. Also, it should always be kept in mind that mesh infections after laparoscopic hernia repair are exceedingly rare; their management is based not on experience gained from treating large numbers but rather from the application of knowledge and judgment. Liberal consultation for second opinion or referral are legitimate options for dealing with mesh infection after laparoscopic hernia repair.

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10

Treatment of Infections After Open Ventral Herniorrhaphy

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Today mesh materials are essential for abdominal wall hernia repair. Unfortunately, these synthetic materials are associated with higher rates of infection than in comparable procedures where mesh is not employed [1–5]. Correspondingly, we saw 8 infections after suture repair in 215 incisional hernia patients (3.7%) in comparison to 20 out of 239 repaired with mesh (8.4%) (1986–1999). Inspite of the fact that infection rates following mesh repair are quite low, the onset of such a situation leads to a clinical dilemma. The challenging question after the occurrence of infection is whether or not the mesh must be removed. Removal of the mesh appears to be unavoidable in the presence of extended necrosis of the adjacent tissue or after dislocation of the mesh associated with an uncovered hernia gap. However, prosthesis explantation leads to a significan number of concomitant problems, such as large residual defects in the abdominal wall (''open abdomen''); closure of an attenuated abdominal wall fascia in the presence of infection, leading to secondary wound healing; physical impairment by the persisting open wound; and, finally, a high risk of recurrence. Whether the prosthesis must be removed or not depends on different factors, such as the type of infection and the mesh material utilized. Whereas an abscess formation around the mesh—frequently seen with infected polytetrafluoroethylene (PTFE) material—

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Table 1 Infection Rates Associated with Various Mesh Materials[a]

Mesh	Polymer	*N*	Infected	%
Mersilene	PET	29	7	24.1
Marlex	PP	76	19	25.0
Prolene	PP	70	17	24.3
Atrium	PP	47	12	25.5
Gore-Tex	EPTFE	19	4	21.1
Vypro	PP/PG	9	3	33.3
Total		250	62	24.8

[a] Collection of explanted meshes. The Centre of Excellence for Implant Pathology, Aachen.

usually demands mesh explantation, a slight tissue swelling associated with scant infiltration of serous fluid together with an incompletely incorporated polypropylene-type mesh can be treated conservatively.

In regard to the surgical therapy, two kinds of infection must be distinguished: the early-onset infection, occurring during the first postoperative days, or the late infection, observed after a long postoperative interval. On occasion, these infections can be observed years after surgery (Fig. 1).

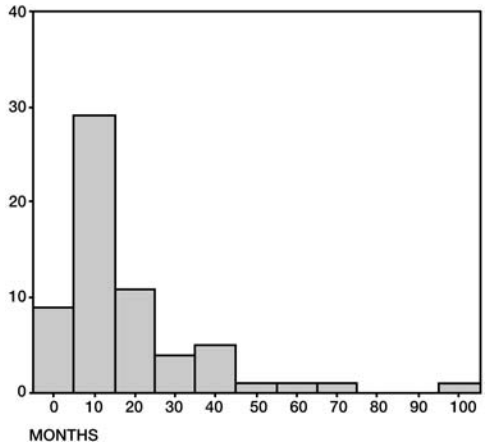

Figure 1 Interval in months between operation and revision for infection ($n = 62$ mesh explants).

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I. EARLY POSTOPERATIVE INFECTION

In the first days following the implantation of polypropylene meshes, a slight physiological inflammatory reaction is frequently seen. This is the expression of an unavoidable foreign-body reaction characterized by a slightly raised temperature ($38.0 \pm 0.3^{\circ}C$) (Fig. 2), cutaneous erythema, induration, and usually an accompanying sterile seroma. This is not associated with signs of systemic inflammation, although an histological persistence of the inflammatory reaction over the years can be proven [6]. Depending on the weight of the mesh and its structure, this reaction is mainly characterized by granuloma formation around the polymer filaments plus an excessive fibrosis occurring in between the mesh fibers and associated with increased cell turnover, resembling a "chronic wound."

The diagnosis of a relevant infection is for the most part a clinical one, with the classical signs of local tumor, dolor, rubor, and calor. This finding can be practically supplemented by ultrasound, although ultrasound cannot differentiate between seroma and bacteria-containing liquids. An ultrasound-guided needle aspiration of the fluid around the prosthesis is a simple way of obtaining a representative aliquot. Volumes of more than 5 mL can be obtained and sent for microbiological assessment to detect bacterial contamination. If the liquid turns out to be sterile, expectant management can be chosen. The local application of ice

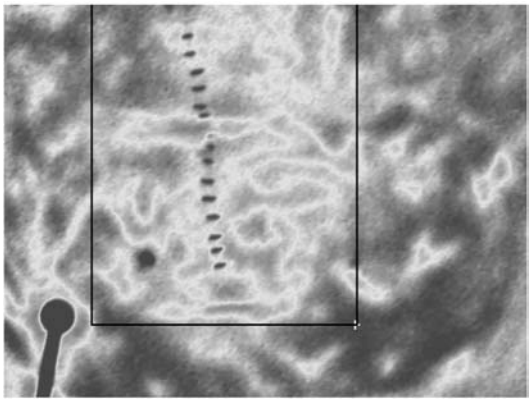

Figure 2 Infrared videography visualization of the inflammatory hyperemia after mesh implantation. (Hot spots = red, low temperature = blue; original in color. Temperature is increased within the mesh area on both sides of the skin staples.)

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cold compresses to the wound and nonsteroidal anti-inflammatory drugs (e.g., ibuprofen 200 mg three times a day) may be helpful. The wound's clinical appearance should improve within 12 h and the symptoms should disappear within a week.

If the aspirated fluid from the subcutaneous layer reveals bacterial contamination, an attempt at antibiotic treatment is justified (e.g., 1000 mg amoxicillin and 250 mg clavulanic acid three times a day or, in the presence of penicillin allergy, ciprofloxacin 200 mg twice daily). If mesh contamination is suspected or if the subcutaneous infection is progressive, the woud should be opened for at least 10 cm and irrigated with 0.9% NaCl solution. Only in rare cases, with additional signs of general infection or generalized sepsis, should a local wound exploration be performed under general anesthesia; at such time, removal of sutures or unincorporated mesh may be necessary. Film-like meshes such as SurgiPro or PTFE usually show little or no tissue ingrowth and can easily be removed. In contrast, all porous meshes are almost inseparably embedded into strong, dense scar tissue. If a polypropylene or porous mesh was implanted, its removal at this stage is usually not indicated, even if it was used in a preperitoneal position. In our experience, mesh removal is not necessary in cases of early infection. The wound and even the fascia can be left open and covered with an adequate wound dressing (gauze soaked in 0.9% NaCl solution) and the growth of granulation tissue can be observed (Fig. 3). After the infection has been controlled and the wound has granulated into the mesh, secondary closure of the wound can be carried out with sutures or skin staples.

In those patients in whom a PTFE-mesh has beeen used, mesh removal is again dependent on the overall clinical findings. If there are signs of a generalized infection lacking improvement after 24 h of conservative therapy or bacterial contamination of the mesh is proven, removal of the prosthesis is unavoidable in most cases. Usually, the mesh no longer shows attachment to the surrounding tissue and, due to its microscopic pores, physiological clearance of the mesh surface with complete elimination of bacteria by macrophages may be unachievable. Thus the patient must be returned to the operating theater, where the wound will be fully explored and all mesh material removed. Due to the absence of tissue ingrowth into these film-like mesh materials, the prosthesis can usually be extracted with little effort (Fig. 4). Only in mild forms, when the infection is limited to the subcutaneous layer, may a conservative approach to management be possible, as personal reports have indicated (Lammers et al., Düsseldorf, unpublished). After mesh

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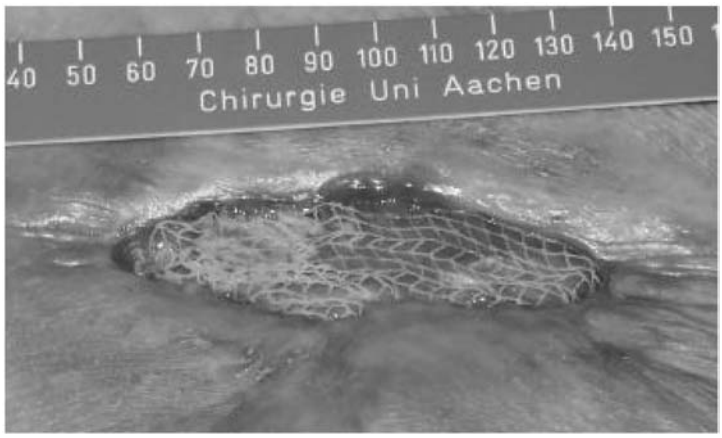

Figure 3 Secondary healing with visible mesh structures after local infection following mesh repair of a laparostomy and overgrowth of granulation tissue from the borders. Healing was complete after 6 weeks.

explanation, the abscess area is generally cleaned thoroughly, followed by excision of the abscess capsule. A temporary closure is then performed with absorbable sutures. This will be followed by a recurrence of the incisional hernia, which should be repaired in a second step after at least 6 months have elapsed. The use of a belt or a corset may improve the patient's comfort but will not alter the natural course of events leading to recurrence.

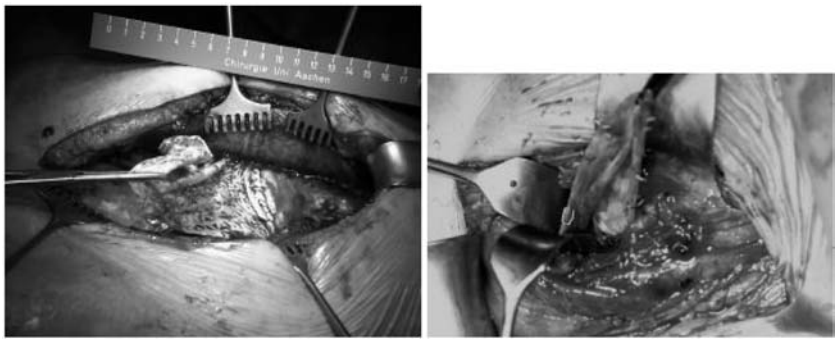

Figure 4 Infection of PTFE prosthesis.

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II. DELAYED MESH INFECTION

Recently, various reports of delayed infection with all kinds of mesh material have been published [3,7–9]. Accordingly, our experience shows a mean interval between implantation of the mesh and its extraction of 17 months (2–98 months). Clinical signs can include the sudden development of fistulas with putrid secretion, the appearance of pain, or the local signs of an inflammatory process. In the presence of symptoms of a generalized infection, the search for the focus, either by ultrasound or computed tomography (CT), usually reveals an abnormal mass in the area of the mesh. It is important to remember that delayed infections can occur years after the mesh is implanted, and at that time they present a more complicated problem requiring specific management. In such a case, the presence of an intestinal fistula creates a veritable clinical challenge.

If, after polypropylene mesh implantation, an infection occurs without evidence of fistula formation, conservative treatment should be attempted. Ultrasound-guided puncture-aspiration of possible fluid collections together with systemic antibiotic treatment is the first therapeutic option (Fig. 5). If, after an appropriate time, this fails to control the infection, we then recommend open treatment including vigorous wound irrigation, removal of suture material, and excision of redundant or nonincorporated mesh. The open wound with the inlaying

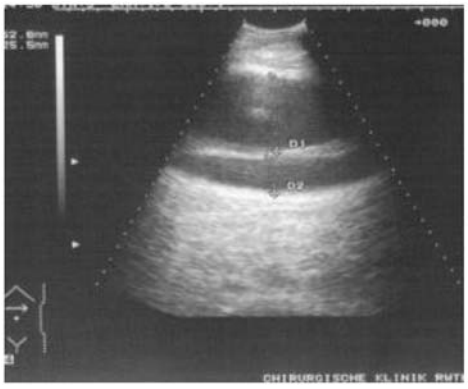

Figure 5 Ultrasound visualization of a periprosthetic mesh infection (*S. aureus*) 17 months after implantation. Mesh is visible as dense line surrounded by liquid. The infection disappeared after percutaneous drainage and 4 weeks of drug therapy.

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mesh can then be allowed to granulate secondarily. Although every open wound must be regarded as contaminated, the granulation tissue seems able to achieve local infection control with significant bacterial eradication. This turn of events may avoid the need for the implantation of a new mesh. If a recurrence follows, reoperation for the implantation of a new mesh should be postponed for at least 6 months.

If the infection occurred in a mesh placed in the depth of the preperitoneal space, closure of the overlying layers performed around large drains might be sufficient to allow healing. Concomitant antibiotic therapy is imperative. If a permanent improvement of the local wound can be seen, ambulatory treatment is possible. The drains are removed when the amount of secretion is less than 10 mL per day.

If, however, this conservative management fails, the mesh must be explanted. The resulting defect can be temporarily bridged by direct tissue approximation or by establishing a laparostomy (Fig. 6) using an absorbable mesh. This policy is continued until the infection is under control. The recurrent hernia can be managed by a second operation with replacement of a polypropylene mesh at least 6 months following resolution of the infection.

In our experience, if a of PTFE-mesh becomes infected, only its removal will assure complete control of the infection.

The onset of an infection as a consequence of an enteric fistula is the most severe complication after mesh hernia repair and demands the

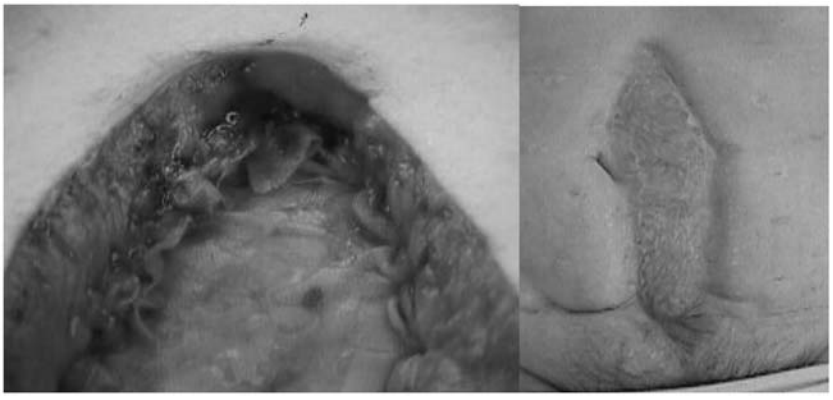

Figure 6 Temporary closure of the abdominal wall with an absorbable mesh after infection, creating a laparostomy for secondary healing.

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immediate and complete removal of the prosthesis, usually combined with a resection of the responsible bowel segment. In the presence of a severe peritonitis, any anastomosis must be avoided and an enterostomy of some type established until the infection is controlled. Otherwise, if the infection is limited to the abdominal wall, an intestinal anastomosis can be performed with absorbable sutures followed by careful drainage of the infectious area.

In our center and up to now, 14 cases of of intestinal fistula were observed, all following the insertion of heavyweight polypropylene meshes. Under those conditions and after mesh excision, the abdominal wall was closed with a single suture repair or, if the asssociated peritonitis was severe, it was managed with a laparostomy using an absorbable mesh (Fig. 6). This policy avoided damage to the fascial structures and prevented evisceration. The absorbable mesh was sutured to the fascia with continuous absorbable sutures (size 0). A transparent sheath was used as a wound dressing. Within 2–3 weeks, the mesh was covered by granulation tissue. Depending on the size of the wound, complete epithelialization can take several months to occur, but the process can be accelerated by grafting with meshed skin. However, this type of management usually leads to a recurrent hernia, which can be treated by a second, definitive operation with repositioning of a mesh at least 6 months after the infection has been brought under control. During that time, ultrasound or CT scans may be used to rule out the presence of residual infection. We do not recommend a one-step replacement of the infected mesh.

In general, any mesh infection should be treated according to well-established principles of wound care, including surgical drainage of the putrid liquids and elimination of its sources. Explantation of the prosthesis can frequently be avoided by fairly long-term antibiotic use, particularly when a monofilament polypropylene mesh has been used. If the mesh infection persists and the prothesis becomes a persistently infected foreign body, it must be removed and a temporary mesh-free, direct tissue approximation procedure performed as a bridge until a definitive repair can be made.

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11

Diagnosis and Treatment of Infections Related to Laparoscopic Incisional and Ventral Hernia Repair

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I. INTRODUCTION

Laparoscopic repair of incisional and ventral hernias is gaining popularity. It has been shown to be associated with fewer complications, a shorter postoperative recovery, and improved cost-effectiveness as compared with the open prosthetic repair [1–3]. As expected with other surgical procedures, an occasional infectious complication will occur; within this scenario, a wound infection will be particularly troubling given the fact that this technique requires the insertion of a prosthesis in nearly all cases. The management of these complications can be difficult and frequently requires the removal of the prosthetic biomaterial. This chapter attempts to provide guidance for the management of this turn of events.

II. PREVENTION

It is readily apparent that prevention of infection is the initial goal. The majority of the infections will involve the skin flora such as *Staphylo-*

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coccus or *Streptococcus*. The preoperative use of a first-generation cephalosporin antibiotic will nearly always provide the patient with adequate prophylaxis. If the patient is allergic to this drug, I use a quinolone.

Special considerations are recommended for the patient who experienced an infection after a previous repair of the same incisional hernia. This event is more significant if the recurrent hernia has occurred following the removal of an infected prosthesis, as the patient will be at greater risk for a recurrent infection at that site. To minimize this peril, I generally defer surgery for 6–9 months after the infection has been completely eliminated. Additionally, at the second repair, I institute prophylaxis using the same antibiotic that successfully treated the prior infection for a minimum of 3 days postoperatively.

The published literature that deals with laparoscopic hernia repair recommends the use of expanded polytetrafluoroethylene (ePTFE) patches impregnated with antimicrobial agents (DualMesh Plus, W. L. Gore and Associates, Flagstaff, AZ), and that is my prosthesis of choice. This material contains silver and chlorhexidine; the former agent gives the prosthesis its characteristic brown color. Many surgeons choose not to administer a prophylactic antibiotic when this product is used. There are no long-term studies documenting the efficacy of these meshes; however, one study demonstrated that the impregnating antibacterial agents did not produce adverse reactions [4].

The majority of the patients who undergo a laparoscopic ventral herniorrhaphy will develop a sterile seroma above the biomaterial; however, the majority of these collections are not clinically significant and will be resorbed within a 2- to 3-month period, depending upon the size of the fascial defect and the hernial sac's surface and volume. I do not recommend the aspiration of these seromas because of the risk of contaminating them. This can produce an infection, that could spread to the underlying biomaterial, creating the need for prosthesis removal. The majority of the infections involving the biomaterial followed the aspiration of postoperative seromas. In our own series, clinically significant seromas requiring detailed follow-up occurred in 7–8% of our patients [5].

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III. TYPES OF INFECTIONS

A. Inflammatory Response

Postoperatively, it is important to distinguish a common inflammatory response from a wound infection. About 5–7 days postoperatively, approximately 15% of all patients will develop a significant and characteristic dermal erythematous reaction at the site of the hernial sac (Fig. 1). This is due to an inflammatory response that develops as a consequence of the endoscopic dissection and the energy sources utilized during that phase of the procedure. Typically these patients would have required a wider dissection due to a large hernial defect containing bowel and/or omentum. Remnants of fatty tissue previously lodged within the hernia may necrose and undergo resorption, causing the inflammatory reaction. No treatment is necessary for this occurrence, which is self-limited (4–8 weeks) and is not associated with pain, fever, or leukocytosis.

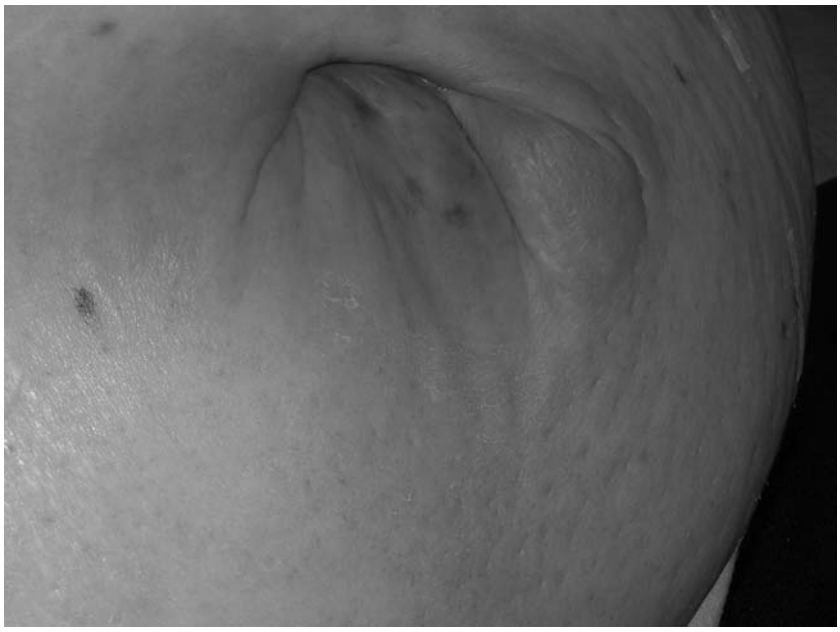

Figure 1 Noninfectious erythematous inflammatory response after laparoscopic incisional hernia repair.

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1. Trocar Site Infections

This is an infrequent problem, occurring in less than 1% of all patients. Patients exhibit a localized erythema around the site of trocar insertion that may on occasion drain pus and should be treated early in its development. One must be cautious when continuous drainage is seen, because that may signify that the infection actually originated from the underlying prosthesis rather than from a simple superficial infection at the trocar site. It may be difficult to differentiate these entities clinically. When in doubt, I recommend the performance of either an ultrasound or computed tomography (CT) scan to evaluate this area. The CT examination is my test of choice. The presence of air or air-fluid levels is indicative of an abscess.

2. Transfascial Suture Site Infections

These are less frequent than trocar site infections. Most of the surgical literature recommends the use of nonabsorbable transfascial sutures to secure fixation of the prosthesis [5–7]. The skin incisions used generally measure 2–3 mm. In the case of infection, one will typically note an indurated area at the site of the suture incision within 7 days postoperatively, associated with erythema and/or drainage. The significance of these findings is difficult to evaluate and, because the possibility of an underlying prosthesis infection, diagnostic and therapeutic measures should be initiated as soon as possible to avoid progression of the infection.

3. Deep Infection Not Involving the Biomaterial

This is a rare occurrence, as invariably this type of infection will involve the prosthetic biomaterial. It is difficult and controversial to postulate how this might not involve the patch, but it will be more likely that the infection is caused by an organism of low virulence that is highly sensitive to antibiotic therapy. These patients will have increasing pain associated with erythema, fever, and leukocytosis. Alternatively, the "infection" may actually represent the inflammatory reaction described above.

4. Deep Infection Involving the Biomaterial

This is, of course, the most feared complication of this procedure (other than enterotomy) and it has been reported to occur in up to 5% of patients [3,5,7,8]. Generally, however, the incidence of this complication

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is 1% or less. These patients will usually exhibit indolent, slowly progressing signs and symptoms consisting mostly of pain localized to the operated area.

This insidious evolution complicates the diagnostic process, as these infections may not manifest themselves for several months. Their diagnosis is frequently suspected when the patient's pain is located at the site of the hernial defect rather than at the periphery of the sites of patch fixation. Skin erythema may not become evident in the early stages of the infection; however, a persistent fever should be a significant and relevant early warning. Leukocytosis will also be present in these patients.

If at any time in the postoperative period I suspect this kind of complication, I request a complete blood count (CBC) and a CT scan. The latter is the most sensitive test with which to diagnose and evaluate infection, and it may demonstrate the presence of fluid either above or below the biomaterial. It must be remembered that a seroma is a very frequent finding after this operation, which may complicate the patient's management. Therefore, the discovery of a fluid collection does not preclude an investigation of its nature and composition. In other words, one should rule out the presence of a purulent exudate. In some cases air within the hernial sac can be detected by imaging as late as 10 days postoperatively. Parenthetically, residual carbon dioxide from the peritoneal insufflation should remain in place for up to 3 days. Physical examination of the patient significantly aids in its overall assessment.

In addition and most significantly, if air or fluid is detected within the hernial sac, the surgeon must rule out the presence of a missed enterotomy as the source of the infection. There is significant difficulty in determining the presence of an enterotomy because, in the early postoperative period, these patients often exhibit signs of ileus without an associated elevation of their white blood cell count. This dilemma may be particularly troublesome and requires repeated and frequent patient evaluation. An early CT scan will aid in the differential diagnosis, perhaps revealing the presence of a fair amount of free peritoneal fluid, which in this case may be heavily contaminated with bacteria. Accordingly, if a missed enterotomy is present, these individuals will rapidly become gravely ill and will require emergent operative intervention to prevent septic shock and its progression to sequential organ failure.

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B. Differential Diagnosis of Postoperative Infections

The patient's clinical condition will indicate the presence of an infection and, of course, the physical examination will be a most important asset for the initial evaluation. Under these circumstances and immediately postoperatively, these patients will have the expected low-grade temperature elevation commonly associated with atelectasis. However, these relatively benign and self-limited infections seldom produce fevers above 101°F. In the presence of higher core body temperatures, the surgeon should become suspicious of a wound infection. An active fever workup consisting of appropriate laboratory tests and chest radiographs is indicated to rule out, without delay, the usual postoperative concerns, such as bronchitis, pneumonia, urinary tract infection, and so on. As after any other surgical procedure, persistent pain may be an early indicator of infection, and this symptom requires dedicated evaluation.

Postlaparoscopy pain differs in intensity and quality from the pain observed after open hernia repairs, becoming more severe than anticipated in the presence of an infection. Its differential diagnosis may be more difficult, particularly if the surgeon is relatively inexperienced with this method of herniorrhaphy. Under normal conditions, uncomplicated postlaparoscopic herniorrhaphy pain is characterized by a burning or "pulling" sensation located at the periphery of the inserted biomaterial. This is caused by the fixation technique utilized, be it staples, tacks, or sutures. This pain is fairly intense for the first 5–7 days postoperatively and then tapers off, as in the case of other surgical procedures. Most patients do not experience significant discomfort at the trocar sites. Therefore, increasing rather than decreasing levels of pain should alert the physician as to the source of the complaint.

In our experience, postoperative pain can also be more intense in patients in whom the hernia was repaired utilizing either polypropylene (PPM) mesh or a composite made of polypropylene and ePTFE. The exact etiology of such a phenomenon is currently unexplained; however, one can speculate that this may be due to the scar contraction and maturation commonly occurring with the macroporous meshes. We have seen this happen also with the plug-and-patch devices used in the inguinal hernia repair [9]. On some occasions we had to remove composite PPM and ePTFE biomaterials that were used in the open repair of incisional hernias because of persistent pain [10], which did not abate post-operatively, as expected, and became chronic. These complaints were not

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associated with fever, leukocytosis, or abnormal radiological studies; pain was the only finding, and it was relieved by the removal of the prosthetic material. In none of these instances of prolonged pain was an infection encountered. The resulting defect was then repaired either by an open or a laparoscopic technique utilizing ePTFE.

As mentioned above, there are several tests that can be performed to evaluate these patients. In cases involving relatively minor infections (i.e., not entailing the prosthetic material), no testing will be necessary; however, the standard CBC would be the logical starting point to evaluate the possibility of an infection. A normal white blood cell count, however, does not exclude an infection. In diabetics, a change in glucose management requiring more insulin may be an early indication of infection. Cultures of any fluid, if available, will be helpful.

Radiological studies are not always useful early in the infectious process, and they are rarely indicated if the infection is limited to the sutured incisions or the trocar sites. Imaging studies should be performed if an infection involving the biomaterial is suspected. Ultrasound may not be useful in the absence of a fluid collection. It is my observation that under those circumstances it may be difficult for the radiologist to recognize the subtle subcutaneous tissues changes that might indicate an infection. The tissue swelling present early in the postoperative period is usually interpreted as either ''postoperative changes'' or ''normal tissue,'' with the usual statement that ''clinical findings must be correlated.''

My preference is to obtain a CT scan whenever I believe that any problem exists involving the organs within the abdominal cavity. It is the easiest and most informative examination that can be performed because it will reveal very early, subtle changes that may indicate infection. With a CT scan, small air pockets within the hernial sac will be accurately detected, as well as the phlegmonous changes noted within the subcutaneous tissues. In the absence of air, the high incidence of seroma formation in these patients can be confusing. Seroma noted beneath the patch (i.e., in the preperitoneal position) seldom represents an infection. The CT scan can also be used to closely follow the progress of the ensuing treatment. If the examination of the patient reveals the development of a significant amount of unexplained ascites, one should assume, until proven otherwise, that a bowel injury exists.

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C. Treatment of Postoperative Infections

1. Inflammatory Response

This represents a physiological event and, as such, requires no treatment. The major reason that this is mentioned again is to stress the importance of this finding. One must not assume that it represents an infection, but it should prompt a high index of suspicion that an infection may be developing.

2. Trocar Site Infections

This type of infection will present itself within the first 5–7 days postoperatively. If one can be sure that this event does not represent a more complicated process, its treatment is relatively simple. In the presence of a simple cellulitis, an antibiotic that provides adequate coverage for the skin flora will usually suffice. Typically, one would feel comfortable with a 7-day course of antibiotics for such an infection. However, because of the presence of a foreign body within the wound, I prefer to extend the treatment for at least 10 days if the patient is not immunologically compromised.

If there is a subcutaneous collection of fluid or pus, it must be aspirated and cultured. If frank pus is encountered, open drainage is necessary. The skin incision should be reopened and, if necessary, extended to provide adequate drainage of that site. The standard surgical principles for the treatment of infection should be applied. A first-generation cephalosporin should initiate the treatment, followed by the appropriate antibiotic choice based on the results of the cultures.

3. Suture Site Infections

This problem is generally evident within the first postoperative week and may be associated with erythema. The patient may experience greater pain than expected at that site and may need stronger pain medication to control the symptoms. This should suggest to the surgeon that a significant problem may exist. Aspiration of the site may be helpful but is seldom productive. The pre-emptive and empirical use of antibiotics based on common skin flora is preferable to waiting for clearer evidence of infection, such as pus. The nonabsorbable transabdominal suture located at this site can become a nidus of infection, potentially seeding the prosthesis with bacteria. Such an event can have disastrous

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consequences. A first-generation cephalosporin is generally adequate here, and the choice should be similar to that used for trocar site infections.

Obviously, if aspiration is performed and pus is identified, open drainage is indicated. This can be accomplished through the original skin incision, which may have to be enlarged to provide for adequate drainage.

D. Deep Infection Not Involving the Biomaterial

If the surgeon suspects this possibility, then aggressive evaluation is necessary to prove or disprove the presence of an associated infected prosthesis. These events are rare and usually encountered late in the patient's course, when significant tissue ingrowth into the biomaterial has taken place, thereby sealing and protecting the prosthesis from the infection.

The surgeon should follow these patients with serial CBCs, sedimentation rates, CT scans and continue to be suspicious that the infection may involve the patch. If it appears that the infection is separate from the prosthesis, the patient should be maintained on intravenous antibiotics for approximately 1 month. Aspiration of any fluid collection or seroma at this site with subsequent Grams stains and cultures should provide guidance for further medical management. If the patient does not respond adequately or if his or her condition seems to be worsening, one should be quick to assume that the infection includes the prosthetic biomaterial. Under this circumstance, the surgeon should administer broad-spectrum gram-positive and gram-negative coverage for the infection, because it may be difficult to positively identify all the bacteria present at that site. Therefore antibiotics that provide coverage for both these types of organisms are necessary. If *Pseudomonas* or methicillin-resistant *Staphylococcus* is a problem within your institution, then appropriate choices of antibiotics should be made quickly.

E. Deep Infection Involving the Prosthetic Biomaterial

This is nearly the worst infectious complication associated with this operative procedure. A very significant factor must be ruled out if this infection is suspected: the possibility of an unrecognized bowel injury. If there is no such injury, the therapeutic measures outlined below can be implemented.

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The infection may present itself with a variety of signs and symptoms. Erythema with or without fever may be seen early after the operation. Tenderness or pain at the site of the hernial defect may be increasing rather than decreasing. Drainage from a trocar site may be evident despite appropriate treatment, as described above. Occasionally, a patient may present on an emergency basis with clinical sepsis. After the diagnostic workup has confirmed that the infection involves the prosthetic biomaterial, several options are available based on a variety of possibilities.

If the patient is not in extremis, a conservative approach without prosthesis removal may be attempted. This is particularly true if the biomaterial used was polypropylene. This will infrequently be an option. But if so, one may try a treatment similar to that of an infection subsequent to the open procedures. The presence of pus indicates the need for open drainage performed in the operating room. The incision should be made directly over the patient's midline so that adequate exposure will be available should there be a need to explore further for an intra-abdominal infection. This setting will allow for an excellent inspection of the prosthesis and close scrutiny of any areas of potential detachment from the fascial edges. The wound should be left open and treated with frequent dressing changes; the antibiotic of choice will be based on culture results. Empirical gram-positive, gram-negative, and anaerobic coverage should be started until this is available.

The wound will granulate successfully in over 90% of these cases. The use of a vacuum-assisted suction apparatus on the wound may speed up the healing process considerably. One may complete the wound closure by covering the prosthesis with a skin graft. Occasionally this is not necessary and the skin edges can be approximated primarily. It is generally preferable to leave the prosthetic biomaterial in place rather than attempting to excise it. The PPM prosthesis and other polyester products are all associated with an intense adhesive reaction to the intestinal organs. Attempts at removal of these can be associated with a significant risk of bowel injury and resultant fistulization. This problem greatly complicates management of the abdominal organs and abdominal wall.

The laparoscopic repair of incisional and ventral hernias will usually involve placement of a product that is either a solid sheet of ePTFE or a composite product that contains ePTFE and polypropylene on opposing surfaces. For the purposes of this discussion, these products may be considered identical, due to the need to treat the ePTFE

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biomaterial. However, the utilization of a single prosthetic biomaterial for the repair may simplify matters significantly. Nevertheless, the use of the ePTFE biomaterial and its high surface tension limits the effectiveness of the antibiotic and drainage procedure tried as mentioned above. When an infection is seen following the use of ePTFE, an aggressive attempt at open drainage may occasionally be successful when combined with appropriate antibiotics.

The wound should be opened and drained. Frequent dressing changes will initially allow the surgeon to assess the possibility of success with this therapy. If the infected biomaterial is noted within the depths of the wound, the chance of success in saving the patch are severely diminished.

Occasionally only the midportion of the ePTFE prosthesis will be infected. This is usually apparent when only that portion exhibits a lack of tissue penetration and the rest of the patch is firmly adherent to the tissues. In this *rare* instance, an attempt may be made to excise the central portion of the involved prosthesis with primary closure of the biomaterial. This should only be done in the operating room using pressure lavage during the operative procedure. The subcutaneous tissues should be loosely approximated and the skin very loosely closed. One should attempt to cover the biomaterial with some kind of soft tissue, avoiding its exposure to the air. Continued antibiotic coverage for 4 weeks will be necessary if it appears that this regimen is effective. It may be successful in a small percentage of the patients. But if they continue to exhibit purulent drainage with positive bacterial cultures, prosthetic excision will become necessary.

If it appears that the entire prosthetic is infected, which is usually the situation, then the quickest remedy is to proceed with removal of the entire patch. This situation is problematic, as there is generally a large fascial defect that will remain following the removal of the biomaterial used in repairing of the hernia. In the smaller hernias (e.g., those less than 4 cm in diameter), one may be able to effect a primary closure of the defect with a monofilament nonabsorbable suture. If this is attempted, I will generally close the bascial defect utilizing interrupted suture in a "figure-of-eight" pattern, with very wide margins. I will then close the midline again over these sutures or incorporate within these a running closure of the fascia with another of nonabsorbable monofilament suture. This will create tension on the repair, and the fact that a high percentage of these patients will have a recurrence will have to be accepted. In larger defects, the rate of recurrence is magnified. Additionally, there is a risk of

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creating an abdominal compartment syndrome if this maneuver significantly increases the intra-abdominal pressure following closure of the fascial defect. In the latter condition, the surgeon cannot reapproximate the midline without compromising the respiratory function of the patient's diaphragm.

There are a few options that can be chosen to resolve this situation, and the clinical status of the patient will dictate the choice. If the patient is maintaining a good hemodynamic status, a sequential excision of the patch may allow for the reconstitution of the midline primarily. In this scenario, the patient is returned to the operating theater at scheduled intervals to undergo wound debridement and lavage, followed by the excision of approximately 25–33% of the central portion of the prosthesis. This should be followed by a primary closure of the patch at the end of each procedure. If the patient continues to improve clinically, he or she can be returned to the operating room within 5–7 days for a repeat of the above. If, under those conditions, there is a concern about the development of too much intra-abdominal pressure following a closure, then less than 25% of the prosthesis can be removed. After a few such interventions, the midline may be closed primarily with a nonabsorbable monofilament suture as described above. The use of retention sutures is advisable at the full closure of the abdomen. However the patient will still incur the risk of a future 25–50% recurrence rate. The above option can certainly be modified depending on the condition of the patient. The advantage of the ePTFE product is that the reoperation will usually not be complicated, with the intense adhesions that are seen with the macroporous meshes. If the patient is exhibiting signs of severe sepsis as a consequence of the biomaterial, then the surgeon will be forced to remove it earlier in the phases of treatment. This creates a difficult situation, but there are still a few options to be explored.

One may choose to leave the entire abdominal cavity open and institute treatment with the vacuum suction apparatus. The Vac-Pac is used by placing a specially designed sponge onto the abdominal organs. This is then covered with an occlusive adhesive dressing. Direct continuous suction is then applied to the sponge to evacuate the tissue fluids. This enhances the speed of granulation of the wound and contraction of the wound edges. Typically, these patients will have developed significant adhesion between the bowel loops, so the chance of evisceration is minimal. Close scrutiny is mandatory, of course. These devices can be used on an outpatient basis and are changed two to three times per week. I have observed quite impressive results with the use of

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such therapy. This mode of therapy will work best in those patients who have undergone multiple intra-abdominal procedures, resulting in significant enteroenteric adhesions. As stated above, in the presence of PPM, the patient's skin may be closed primarily or the granulation tissues can be covered with a skin graft. In general this will be followed by a recurrence, which will have to be corrected later after the 6- to 9-month interval.

Occasionally, the surgeon may have to use a PPM prosthesis to repair the resulting large fascial defects. This is a useful and often lifesaving maneuver if the patient develops a compartment syndrome as the surgeon attempts to close the abdomen. Under those circumstances, the surgeon should leave the wound open to allow drainage and minimize the risk of reinfection. Granulation will finally cover the mesh and permit the placement of the skin graft at the appropriate time. Generally, I would suggest that this option be used sparingly due to the risk of postoperative obstruction or fistualization. If this option is chosen, I recommend that either the Wittman Patch (Starsurgical, Inc., Burlington, WI) or the DualMesh Plus (W. L. Gore and Associates, Inc., Flagstaff, AZ) be used [11]. Neither of these materials will allow the migration of granulation tissue; they will serve as a bridge covering the abdominal contents and will allow the surgeon to gradually excise the midportion of the biomaterial as described above, facilitating the closure of the resulting gap.

Some surgeons have used absorbable prosthetics to create a bridge over the fascial defect. This may be successful with the smaller hernias, but larger defects will generally exert too much tension upon the product, so that these biomaterials will disintegrate rather rapidly. Nevertheless these materials can be used early in the treatment of the ill patient while close*ly* monitoring the fascial edges, with plans to provide other methods of closure.

A new option that seems to have promise is the use of the absorbable product Surgisis Gold (Cook Medical Inc., Bloomington, IN). This is a natural biomaterial consisting of porcine small intestinal submucosa. It is available in large and multilayered sizes (i.e., up to eight layers of the submucosa bonded together) to provide strength. This material is designed to allow the migration of the patient's fibroblasts into the product's collagen fibers. The patient will then deposit native collagen to create a "neofascia," which will provide a permanent closure of the defect. This prosthesis can also be used to bridge the fascial margins and effectively close the gaps (Fig. 2). Surgisis Gold is relatively

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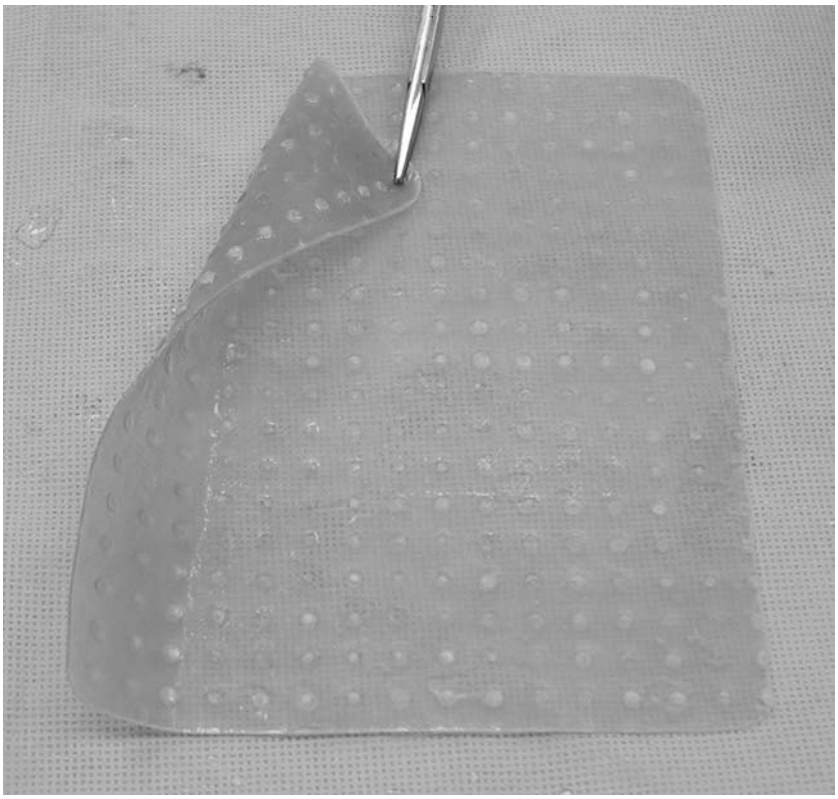

Figure 2 Surgisis Gold

new and there are no published reports related to its use in this manner. This material cannot be used in the presence of an intestinal fistula, as this will result in resorption of the product. The general concept, however, may prove to be useful in the future.

The surgeon could also request the services of a plastic surgeon to provide coverage of the abdominal contents will a large "free flap" of tissue that may contain skin, subcutaneous tissue, and muscle. This procedure is a significant undertaking in aged and ill patients and may not constitute a practical option.

Finally, the surgeon could simply close the available skin over the hernia. This would guarantee a recurrence, as the hernial defect is not

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repaired by this technique. This option may be particularly useful if the patient is significantly ill, requiring a rapid solution.

Once the infection is successfully treated, the patient can be returned to the operating room after several months and a new prosthesis inserted. Longer-term antibiotics prophylaxis is then recommended.

F. Long-Term Expectations and Prognosis

The long-term results following an infection that involves a foreign biomaterial, whatever the type, depends in large part upon the original need for the operation, the type of biomaterial utilized, and the success of the treatment of the subsequent infection. If one is successful in not removing the prosthetic, the risk of recurrent herniation is less than if the prosthetic is removed. In spite of this, there will be a significant number of patients who will develop a new hernia—usually at the prosthetic/fascial interface, as the infection will have dislodged the ingrowth of the biomaterial, resulting in a recurrence. This defect can be repaired laparoscopically. As stated earlier, it would be best to wait for at least 6–9 months to reduce the risk of recurrent infection.

If the prosthetic has been removed, the risk of recurrent herniation approaches 50–75%, and when a hernia develops, the waiting period should also be observed. The defect will typically be larger than the original hernia and the number of adhesions encountered can be significant. Despite this, the laparoscopic method can again be chosen, particularly if the surgeon is proficient in advanced laparoscopic techniques. The prosthetic biomaterial and method of fixation should be identical to the original laparoscopic methodology utilized, as previously described [5]. The repair of the new hernia should be long-lasting.

The repair of any of these hernias could also be undertaken with the open technique. And the tissue repair options are those of Welti and Eudel, Clotteau and Prémont, or Judd [12]. Following an infection, it will be necessary to insert another prosthetic biomaterial. In this instance, the Chevrel repair may be a better alternative [13]. If feasible, I would prefer the Rives-Stoppa technique; this alternative may be of questionable use because the available peritoneal tissue will undoubtedly be thinned or disrupted by the previous operative dissection required to release the adhesions. The placement of the prosthesis will then be in the intraperitoneal position and fixed with transfascial sutures. ePTFE biomaterial would be the preferred choice in this situation. Either of these

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methods used for the repair of a recurrence should yield good results, but the risk of recurrence will be slightly higher than that following the original operation.

IV. CONCLUSION

The incidence of postoperative infection following laparoscopic incisional and ventral herniorrhaphy is low, and this complication rate can be lowered by the use of antibiotic prophylaxis as well as possibly by the utilization of the antimicrobial-impregnated DualMesh Plus. If an infection develops, the above described steps should lead to a satisfactory outcome. This will involve additional surgery as well as appropriate antibiotic treatment. The risk of the development of a recurrent hernia is significant despite the best treatment utilized and particularly if the prosthesis is excised. As with all surgical procedures, prevention of infection is the best treatment.

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12

Absorbable Mesh in Closure of Infected Abdominal Wall Defects

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I. INTRODUCTION

One of the most difficult scenarios the abdominal surgeon is ever likely to encounter is closure of the abdominal wall in which there is loss of fascia from necrosis or trauma or massive visceral edema precluding a tension-free fascial closure. In most cases, there is massive infection or contamination, which often precludes placement of a permanent nonabsorbable prosthesis. Often the closure comes at the completion of a difficult, emotionally draining procedure, after which a careful fascial closure is less likely to occur. Occasionally, the novice surgeon fails to adequately debride infected, necrotic fascia because of concerns that he or she may be unable to perform a primary fascial closure. Alternatively, an attempt may be made to close fascia under tremendous tension despite the risks of the suture breaking, fascial necrosis, or abdominal compartment syndrome. Violation of the fundamental principles of a tension-free, viable fascia closure virtually guarantees a trip to the operating room to manage a fascial dehiscence, thus requiring the unfortunate patient to start over again to heal the abdominal wall defect.

The experienced surgeon who performs an adequate debridement of necrotic fascia back to healthy tissue or recognizes at the conclusion of

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the case that it will not be possible to bring the fascia back together without tension is left with a real dilemma: how does one deal with an uncloseable abdomen? Some may merely pack the abdomen with laparotomy pads until the viscera are "stuck down" enough to prevent evisceration. The obvious disadvantages of this approach are that the patient is consigned to bed rest for an extended period of time, with attendant concerns about thromboembolic phenomena, bed sores, muscle wasting, contractures, and general body weakness. Others may utilize a temporizing approach, often referred to as a "vac pac," in which surgeon's towels are placed in the abdomen to restrain the viscera and a clear adhesive sheet (ViDrape) is placed on the skin on both sides of the defect to prevent evisceration. The latter technique is adequate for a few days, but the patient must be completely immobilized and usually has to be taken back to the operating room in 72 h for more definitive management.

Some advocate the use of a nonabsorbable mesh in this setting and quote literature supporting the placement of permanent mesh in an infected field [1–5]. While nonabsorbable mesh may heal and be incorporated in a few patients with massive contamination, the majority face potentially serious complications and almost certain eventual mesh removal [6–8].

In a few cases, major abdominal wall reconstruction utilizing flaps created by plastic surgeons has been tried. However, that technique is associated with morbidity and often causes significant deformity of the remaining abdominal wall. For an already desperately ill surgical patient, this approach is rarely used in the acute setting.

One of the simplest, quickest, and most effective management options for this difficult clinical scenario is use of absorbable meshes to provide a temporary closure while the infection resolves. The patient heals somewhat and the nutritional status improves. While patients will almost always develop a hernia after use of the absorbable mesh, it provides temporary support of the abdominal wall, restrains viscera until it is "fixed," and allows the patient immediate mobility to avoid the sequelae of prolonged bed rest.

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II. INITIAL MANAGEMENT OF THE INFECTED ABDOMINAL WALL DEFECT

Extensive experience has demonstrated that management of the desperately ill patient whose abdominal wall appears to be uncloseable should always adhere to certain principles. Foremost among these is management of the primary process that caused the sepsis. Clearly, before attention should be given to a fascial closure, drainage of any abscesses, including any loculations, is critical for the overall well-being of the patient. After drainage of abscesses, one should focus on surgical removal of the organ responsible for the problem. For example, a patient with a fistula should have resection of that portion of the small bowel, a necrotic gallbladder should call for a cholecystectomy, and a perforated colon should require resection of the perforation. After removal of the diseased organ, copious irrigation should ensue until the irrigant returns clear. Additional debridement of any devitalized tissues is critical. After cleaning the abdomen, a decision about stoma versus primary anastomosis is indicated where intestine is concerned. Generally, a conservative approach to intestine is always warranted in the desperately ill patient. A stoma is always a safe management principle if there is any question about nutrition and healing capacity. After those decisions are made, if there is residual omentum, a wise management principle is to cover the viscera with remaining omentum. Similarly, in any loculated areas, a drain should be placed prior to exiting.

The next general principle is to decide on some sort of temporary fascial support or strategy to prevent evisceration. Often, this means bringing the patient back at a second operation to do a definitive closure. Similarly, one frequently has to worry about skin coverage, and this may be accomplished by primary skin closure or even skin grafting after adequate granulation has occurred. Intravenous antibiotics are indicated in virtually all of these patients to assist in eliminating the infectious process.

In most cases, one simply has to wait for a length of time for infection to resolve, granulation to begin, and viscera to become somewhat fixed in the peritoneal cavity. Additionally, improved nutritional status is consistent with rapid healing. Very often in patients on steroids, a rapid steroid taper is indicated to accelerate healing.

The decision to go back into the abdomen to do the definitive fascial closure is a function of all of the elements mentioned above.

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Nevertheless, a simple but accurate test that can be applied in determining whether a patient is ready to return to surgery for definitive fascial closure is the texture of the abdomen on deep palpation. For the patient who has firm, brawny edema throughout the abdomen, reoperation is hazardous because of bloody adhesions and an incomplete healing process. When the patient's abdomen is soft and all induration has resolved such that the abdomen feels like "a jelly belly," one can be certain that reoperation can be safely considered.

III. USE OF NONABSORBABLE MESH IN INFECTED HERNIAS

The search for a nonabsorbable prosthetic for use in hernia repairs in a clean field has been extensive and complex. Even more difficult has been the search for an ideal prosthetic in a contaminated field. A host of agents have been studied over the years that were felt to be possible substitutes for abdominal wall loss. Such materials as Silastic, preserved human dura, nylon woven mesh, polyester fiber mesh, braided carbon fiber, stainless steel mesh, polytetrafluorethylene, and polypropylene have all been studied. At one time or another, all of them were felt possibly to satisfy the criteria of an ideal prosthetic. After years of study, polypropylene mesh has emerged as the nonabsorbable prosthetic of choice because of its strength, low reactivity, and relatively low cost. While there are reports in the literature as far back as 1900 that recommend various prosthetic agents [9,10], it was the report by Usher and Wallace in 1958 that established a near ideal prosthetic material which was consistently successful in the repair of fascial defects [11]. In that report, Usher and Wallace introduced polypropylene as their agent of choice, an agent that is used extensively even today. Their report stipulated that the mesh should be placed in a clean field, as infection rates quadrupled when the mesh was placed in a contaminated field. For this reason, in the early experience, polypropylene mesh was not used in infected fields.

The first report in the literature describing the successful use of Marlex mesh to repair grossly contaminated abdominal wall defects was 1967. This paper, by Schmidt and Grinnan [1], reported on three Vietnam War patients with massive abdominal wall contamination and loss of abdominal wall substance. Polypropylene mesh was placed in these three

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patients, granulation tissue grew through the mesh, and grafts were subsequently placed. Many investigators have confirmed the findings of Schmit and Grinnan, although most with only short-term follow-up. Eng and colleagues [2] report a case of clostridial myonecrosis of the anterior abdominal wall in a patient who had resection of the abdominal wall followed by polypropylene mesh placement and subsequent skin grafting. Wouters et al. reported on the use of polypropylene mesh in 20 patients with massive contamination and organ failure [4]. In their report, polypropylene mesh was used for wound closure, but it was incorporated into the wound in only 5 of the 20 patients. Gilsdorf and Shay [3] reported on six patients with wound dehiscence who underwent abdominal wall closure with polypropylene mesh in a massively septic abdominal wall defect. Two of the six had successful incorporation of the mesh into the field. Finally, the report by Boyd [5] details the use of polypropylene mesh in an abdominal wall defect that had become infected, also describing 4 of 8 patients in whom the mesh was successfully incorporated. These reports make it clear that sometimes polypropylene mesh can be successfully used in a contaminated field. However, as mentioned above, most of the series reported in the early literature were small and did not include long-term follow-up.

When long-term follow-up is conducted on patients who have mesh placed in a contaminated field, it usually demonstrates that, while nonabsorbable mesh may be successfully used in a contaminated field on a short-term basis, a number of serious complications are associated with its long-term use, including the development of intestinal fistulas, erosion of the mesh through the skin, bleeding, and infected, chronically bleeding sinuses [6–8]. Two recent large series and one small series with long-term follow-up demonstrate the above. For example, in the study by Voyles and coworkers [7], 20 of the 24 patients who had Marlex mesh placed under contaminated conditions had to have the mesh removed because of long-term complications. Similarly, the study by Stone et al. [6] demonstrated that of 124 patients who had mesh placed in a contaminated field, 101 had their mesh removed because of complications. The review by Jones and Jurkovich [8] in 1989 demonstrated that of 5 patients who had had polypropylene mesh placed in an infected field, 4 developed small bowel fistulas, and wound dehiscence occurred in 1. The four patients who had complications eventually had the mesh removed. This review also cited 14 studies reporting on a total of 125 patients who had had polypropylene mesh placed in a contaminated setting; the overall complication rate was 55% and patients who did not have skin coverage

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had mesh extrusion (44%) and enteric fistulization (23%). The authors concluded that, while the surgeon will occasionally be able to place polypropylene in a contaminated setting, the unacceptable complication rate argues for alternative methods of wound care in these difficult cases.

In fact, a careful review of the literature demonstrates the fate of nonabsorbable mesh placed in contaminated hernia repairs in series with long follow-up. Table 1 demonstrates that when long-term follow-up does occur, over 75% of patients who require placement of nonabsorbable mesh under contaminated conditions will require removal if the mesh was initially placed in a dirty field. Of significance is the fact that removal of the mesh in that setting is always a difficult surgical procedure, associated with bleeding, fistula, hernia, bowel resection, and recurrent infection. Because of the high incidence of complications associated with nonabsorbable mesh in an infected field, surgeons began to consider the use of absorbable meshes. While a number of commercially available meshes have been tested by surgeons, those that

Table 1 Fate of Nonabsorbable Mesh in Contaminated Hernia Repair

Author	Mesh	No. Patients with Mesh Removed	No. Patients with Mesh Placed	Mesh Removal, (percent)
Ger	Marlex	3	3	100
Blom	Marlex	0	1	0
Lewis	Marlex	1	2	50
Kaufman	Marlex	0	2	0
Eng	Marlex	1	2	50
Morgan	Mersilene	1	1	100
Schmitt	Marlex	1	3	33
Gilsdorf	Marlex	2	4	50
Wouters	Marlex	15	20	75
Boyd	Marlex	4	8	50
Voyles	Marlex	20	24	83
Stone	Marlex	21	23	91
Stone	Prolene	80	101	80
Bauer	Gore-Tex	1	2	50
Jones	Marlex	4	5	80
Total		154	200	77

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are composite meshes and include one side of absorbable mesh and the other side nonabsorbable mesh are not considered here, as it is felt that any product used in this setting should be purely absorbable. The two principal absorbable meshes initially described included a polyglycolic acid mesh (Dexon) and polyglactin mesh (Vicryl). The Dexon mesh developed by Davis and Geck is a soft, stretchable mesh that is biodegradable and disappears within 50–60 days. The interstices of the polyglycolic acid mesh are large and allow the passage of fluid that drains after a contaminated case. Conversely, the polyglactin mesh is a tightly woven mesh with small interstices, inelasticity, and less likelihood of allowing viscus fluids to drain. However, it is also very strong and biodegradable, much like polyglycolic acid mesh. Initially, it was theorized that these absorbable meshes would serve as a template for collagenization while the wound was healing and thus allow closure of the abdominal wall defect without infection and the subsequent need to remove it. However, extensive experience has shown that both of these meshes, if used in closure of an abdominal wall defect, will virtually always result in a hernia. Thus, neither of these meshes would be a good candidate for use in a clean abdominal wall closure in which a permanent prosthesis is needed to close the defect. The earliest studies regarding use of Dexon mesh in an animal model were published by Delaney in 1982, when he demonstrated that polyglycolic acid mesh could be used to wrap injured dog spleens and successfully stop the parenchymal bleeding [12]. A study by Lamb et al. [13] demonstrated that repaired clean rabbit abdominal wall defects closed with Vicryl mesh at three weeks would be as strong as nonabsorbable meshes. However, at 12 weeks, the bursting strength of the polyglactin repair was significantly less than that of nonabsorbable meshes. In addition, a full 40% of the animals whose wounds were repaired with polyglactin mesh developed a ventral hernia. The authors believe that inadequate fibrous tissue incorporation into the mesh occurred before hydrolysis. Their final conclusion was that polyglactin mesh is an inadequate material for permanent repair of abdominal wall defects. Conversely, Jenkins and colleagues [14] used polyglactin mesh to repair uncontaminated abdominal wall defects in rats and found no difference in bursting strength in the first 8 weeks when polyglactin mesh was compared with polypropylene, polytetrafluoroethylene, silicone rubber, and preserved human dura. Additionally, the absorbable mesh provided the best long-term protection against adhesions of any of the prosthetic substitutes. Unfortunately, this study included a follow-up of only 8 weeks. Additional follow-up would likely

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demonstrate results similar to those of Lamb et al., cited above. In 1989, Tyrell et al. [15] conducted a study in which they compared polypropylene and polytetrafluoroethylene, as well as polyglactin and polyglycolic acid meshes, with respect to histological appearance, development of adhesions, tensile strength, and occurrence of hernias in rabbits in which defects of the abdominal wall were repaired with the meshes. They observed that the inflammatory response was minimal with all prosthetic products. However, adhesions were more marked with the nonabsorbable agents. No such difference was seen in the absorbable meshes. In vitro tensile strength at 10 weeks demonstrated that Marlex was superior to the other materials. A comparison of the absorbable meshes revealed that polyglactin was superior to polyglycolic acid. Initially, no abdominal wall hernias were observed with the nonabsorbable meshes, but all of the rabbits repaired with absorbable meshes had ventral hernias by the tenth week. The investigators also concluded that absorbable meshes are not indicated when prolonged tensile strength is required. They thought that they might be useful for other purposes, including the temporary repair of fascial defects, since evisceration was not detected. As noted above, a multitude of studies have been conducted in laboratory animals in an attempt to demonstrate decreased adhesions from bowel to nonabsorbable mesh, prolong absorption time of absorbable mesh, or strengthen absorbable mesh to lessen the likelihood of hernia formation. Composite grafts have been one approach to this problem. In 1998, Klinge and colleagues added polyglactin to nonabsorbable polypropylene and found that there was less adhesive attachment to the nonabsorbable mesh, with no decrease in mesh strength [16]. Similarly, Dasika et al. [17] demonstrated, in a study using rats, that lining polypropylene mesh with polyglactin mesh reduced intraperitoneal adhesions.

Novel approaches to strengthening absorbable mesh were also described by Zieren and colleagues in 1999 [18]. Their study compared rats that had received polyglycolic acid mesh only with those that had polyglycolic acid mesh plus added fibrin and platelet releasates. They found that the group that had added fibrin and platelet releasates had higher herniation pressures, higher hydroxyproline content, and increased fibroblast and collagen fibers found at the time of animal sacrifice. A second study by Klinge and colleagues [19] compared rats that had polypropylene placed to fix an abdominal wall defect that was either coated with polyglactin or into which fibrils of polyglactin were woven. The presence of polyglactin coating actually inhibited incorpora-

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tion of the permanent mesh. Conversely, the addition of polyglactin filaments or fibers appeared to favorably affect the mesh, such that fewer adhesions to the underlying small intestine occurred.

IV. CLINICAL STUDIES WITH ABSORBABLE MESH

The first use of absorbable meshes in human beings was described by Delaney et al. in 1985 [20], when they reported on the use of a polyglycolic acid mesh for splenorrhaphy. The absorbable mesh was wrapped around the fractured spleen, holding its segments together and thus preserving the spleen and obviating splenectomy. Other authors have since used polyglycolic acid mesh for the repair of injured spleen and kidney. Additionally, Delaney [21] described the use of absorbable mesh to construct a pelvic sling that would hold the intestinal contents out of the pelvis for a limited time while radiation was being utilized to treat the pelvis following the resection of pelvic cancer.

The first description of absorbable mesh used to repair contaminated abdominal wall defects occurred in 1986, when Dayton and colleagues [22] described placement of the mesh in eight patients. Their study reported four patients with previously placed polypropylene mesh that had become infected and was draining pus. The other four patients had massive abdominal wall sepsis and loss of abdominal wall substance. In this report, polyglycolic acid was placed as the initial mesh with generally good results. Unlike the polypropylene mesh, which was rigid and inflexible, the polyglycolic acid mesh used in these cases was soft, pliable, and stretchable. It was also surprisingly strong. In seven of the cases, the mesh was sutured to the fascia along one side of the abdominal wall, pulled slightly to place it under mild tension, and then sutured to fascia on the opposite side. A single layer of the mesh was used and was sewn to the fascia using an absorbable suture. It was initially felt that an abdominal binder should be used for support until healing had taken place. But subsequent experience has demonstrated that no binder is necessary. Four of the eight patients had initial skin coverage, which made wound management easy; that is, the skin was closed over the absorbable mesh without any difficulties and healed without a problem. However, the other four patients had had some loss of abdominal wall substance and the skin could not be closed over the mesh. These patients required moist gauze packing of the wound until a granulating field was produced. After adequate granulation, split-thickness skin grafts were

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placed and the wounds healed nicely. The authors originally hypothesized that the mesh would persist long enough to allow collagenization and thus obviate the development of an abdominal wall hernia. However, over time, it became clear that the mesh absorbed completely, and the majority of the patients developed large abdominal wall hernias within 60 days.

After analyzing this clinical scenario, the authors concluded that, in spite of the development of the hernias, a case could be made for placing absorbable mesh in patients who are critically ill with contaminated wound defects, allowing the wound to heal and contamination to resolve and subsequently repairing any hernia that developed postoperatively with a nonabsorbable mesh and/or full-thickness skin flaps. In follow-up experience, 17 additional patients underwent placement of the absorbable mesh with the intent to use its placement as a temporary staging procedure until contamination resolved and the patient could undergo subsequent, successful, permanent mesh placement. In that follow-up series, 19 patients had necrotizing abdominal wall infections, 4 had infected Marlex mesh from the previous repair, 1 had an extensive electrical burn of the abdominal wall, and 1 had a hernia covered by a chronically infected scar. Defect sizes varied from 8 by 15 cm to 45 by 37 cm. In 10 of the original 25 patients who developed large hernias at the site of the mesh placement, a mean interval of 10 months elapsed before reoperation and placement of a permanent mesh. In this group, reoperation involved identification of the fascia and repair with polypropylene mesh in the standard fashion. Reoperating after the polyglycolic acid mesh had been placed revealed complete mesh resorption. Specifically, there was no evidence of mesh-induced complications, such as dense adhesions, hypervascularity, obstruction, or residual infection.

In patients who had placement of split-thickness skin grafts on bowel covered with granulation tissue, a fine adventitial layer developed over time between the bowel surface and the skin. This allowed relatively easy, bloodless removal of all skin from the bowel surface on reoperation. All of the 10 patients described who had reoperation and operative placement of a permanent mesh recovered without complication and remain free of complications today.

Subsequent reports in the literature have documented the effectiveness of using absorbable meshes in an emergency setting. For example, in 1998, McGahren et al. described the use of absorbable polyglactin mesh to close the abdomen of an infant who had a large neuroblastoma

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resected and whose viscera became massively edematous [23]. The temporary mesh allowed the abdomen to be closed until the edema resolved and a permanent mesh was finally placed. Smith and colleagues [24] described 13 patients whose fascia could not be closed after life-threatening trauma. Five of these patients were closed with absorbable mesh, which gave the abdominal wall stability until visceral edema had resolved and a subsequent permanent mesh could be placed. These authors, however, favored simply closing skin over the visceral mass with towel clips, returning a few days later to approximate fascia after the edema had resolved.

A study by Buck et al. [25] documented the use of polyglycolic acid mesh in the emergent setting in 26 critically ill patients who had placement of absorbable mesh as part of an emergent laparotomy. They found that mesh placement allowed drainage from contaminated abdominal wounds, was strong enough to allow ambulation, and generally improved recovery in this group of patients. They noted, like other authors, that while none of the patients had to be reoperated on for dehiscence, there was frequent hernia formation. Gentile et al. [26] described the use of polyglycolic acid mesh for abdominal access in patients with necrotizing pancreatitis. They found the mesh particularly helpful in those patients who required multiple reoperations for debridement and abdominal cleaning. In their series, some patients even underwent repeat drainage procedures in the intensive care unit. They concluded that polyglycolic acid mesh is a useful adjunct in the surgical care of selected patients with necrotizing pancreatitis. Chendrasekhar [27] described the use of local anesthetic and bedside placement of polyglycolic acid mesh in uncomplicated and localized abdominal dehiscence to prevent evisceration.

Use of a staging approach in the care of these extremely complicated hernia patients has been advocated by others. For example, Fabian et al. [28] suggested that the first stage (stage I) involves prosthetic insertion; the second stage (stage II) prosthetic removal; the third stage (stage III) skin grafting of any large defect; and fourth stage (stage IV), 6–12 months later, definitive reconstruction. Their study described 88 cases, of which 27 had polyglactin mesh placed as a temporary prosthesis until the wound cleaned up. The authors concluded that the staged approach was associated with low morbidity and no technique-related mortality. They also concluded that absorbable mesh provided the advantages of reasonable durability, easy removal, and relatively low cost. They concluded that it had become the prosthesis of choice in this

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setting. Greens and associates [29] agreed with Fabian et al. A polyglycolic acid mesh was used in 59 critically ill patients to bridge abdominal wall defects and prevent evisceration after trauma laparotomy. They noted that the mesh was infiltrated by granulation tissue within 2–3 weeks and that, 2–3 months after insertion, the material was absorbed, resulting in a hernia. They were then, some months later, able to perform definitive hernia repair. They concluded that absorbable polyglycolic acid mesh was useful for achieving secure, tension-free closure of abdominal wounds on a temporary basis.

Ramadwar et al. [30] described another novel approach in 1997. Their study involved coating the Vicryl mesh with a layer of collagen in an attempt to prolong the absorption life of polyglactin mesh. This preparation was used to repair diaphragmatic defects. However, because of recurrent diaphragmatic defects, the authors were less than enthusiastic about this material. Carachi and associates [31] used collagen-coated polyglactin mesh in 28 patients who needed repair of thoracic and abdominal wall defects, and their use of this new mesh was quite encouraging.

As previously mentioned, the use of composite prostheses is also an interesting area of study. Unfortunately, most of the composite prostheses use a nonabsorbable mesh attached to an absorbable polyglactin mesh. Barie et al. [32] describe the use of this mesh to close a Spigelian hernia using a laparoscopic approach. Additionally, Porter [33] described the use of polyglactin and Marlex mesh to close the abdominal wall in five patients with complex problems. He observed that Vicryl mesh prevents enterocutaneous fistulas and adhesions and that Marlex mesh prevents late ventral hernia.

An additional area of study that has stimulated significant interest is the use of adhesion-preventing materials to obviate the formation of intra-abdominal adhesions to absorbable meshes. Recently, the U.S. Food and Drug Administration (FDA) approved a material composed of carboxymethylcellulose and hyaluronic acid (Seprafilm), which has been demonstrated to reduce adhesions in the abdomen. Theoretically, placement of this material immediately adjacent to a nonabsorbable mesh would inhibit adhesion formation to that mesh. Alponat and colleagues [34] used this agent in an animal study and demonstrated that it virtually eliminated adhesions to the prosthesis. At the author's institution, this same material has been placed underneath absorbable mesh as well as absorbable mesh, and it is thought to lessen adhesions to the posterior surface of the mesh. This would obviously make it much

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easier to enter the abdomen if reoperation became necessary for either mesh removal or definitive repair after bowel edema had resolved. Similarly, the FDA has approved a material that is coated on its undersurface with this material. This mesh (Sepramesh) is currently being studied in the United States.

V. SPECIFIC INDICATIONS FOR USE OF ABSORBABLE MESHES

A. Abdominal Wall Necrosis with Massive Contamination

One of the most clear-cut indications for the absorbable meshes is the patient who has sustained massive loss of abdominal wall substance (Fig. 1). This may be due to wound dehiscence, necrosis of the fascia, abdominal wall fasciitis, and any disease process that causes a loss of abdominal wall substance, such as processes associated with fistulas, radiation, and so forth. Absorbable mesh has been used to close complicated abdominal wall defects at the author's institution in over 110

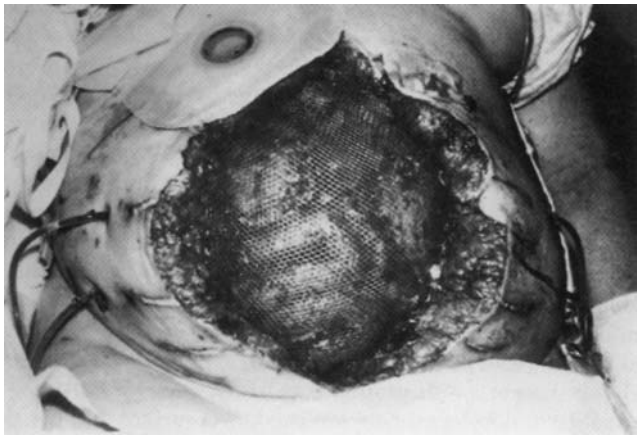

Figure 1 This patient underwent aggressive debridement of abdominal wall due to necrotizing fasciitis. Her reconstruction with absorbable mesh is shown here along with a colostomy and mucus fistula. The wound was regularly dressed using saline-moist gauze. (From Ref. 36, p. 295.)

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patients. The absorbable meshes are thought to be best used in the staged repair of these complicated, contaminated abdominal wall defects. After adequate debridement of infected and nonviable tissue, the fascia is identified and the polyglycolic acid mesh is sewn to the fascia using a #1 absorbable suture in a running fashion. It is always optimal to close the skin over the Dexon fascia if it can be appropriately mobilized without any tension. However, if there is any question, mere packing of the wound with saline moist gauze works very well. If there is significant loss of skin with the disease process, it must be debrided back and allowed to heal by secondary intention. Over time, granulation buds grow up through the interstices (Fig. 2). When the defect is large, a split thickness skin graft can be placed when the granulation bed is healthy. Once

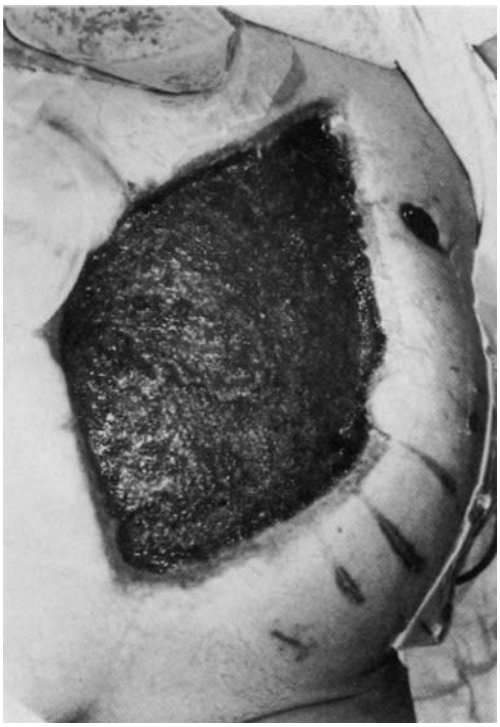

Figure 2 Patient in Fig. 1 is seen 7 weeks later as extensive granulation has grown through the mesh interstices, has coalesced, and is now ready for skin grafting. (From Ref. 36, p. 296.)

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epithelialization of the defect is complete and there is no longer any infection, one should probably wait 10 months before considering going back to place a permanent mesh.

Patients who have primary skin closure over the absorbable mesh can have definitive repair done in a simple standard fashion. A cautious incision is made through the skin until viscera are encountered. Fascia is identified and mobilized. An appropriately sized section of polypropylene mesh is then sutured to the fascia using nonabsorbable sutures in an interrupted fashion. Skin is then closed over the permanent mesh, with closed suction drains used to keep the flap stuck to the prosthesis. The drains can be removed in 3–7 days, and it has been our practice to keep the patient on appropriate antibiotics until the drain is removed. Using this strategy, we have had very few problems with seromas. Those patients who require a split-thickness skin graft on granulation tissue that is immediately adjacent to bowel pose a more complicated problem. Experience has demonstrated that, over time, an adventitial layer develops between the skin graft and the bowel, allowing one to easily peel the skin away from the bowel when returning to do the definitive repair. Permanent mesh is placed as previously described, and skin is then extensively mobilized to bring over the nonabsorbable mesh in the midline. Closure of that skin layer should be done in three to four layers to obviate contamination and breakdown of the midline incision. Again, placement of a closed suction drain also helps the skin flap stick down, so that seromas and hematomas do not form.

B. Infected Mesh from Previous Hernia Repairs

One of the most common indications for a placement of temporary, absorbable mesh is the patient who has had a previous repair of an abdominal wall hernia which has become infected (Fig. 3). Obviously, the massive contamination of the old mesh precludes placement of a permanent mesh in an attempt to repair this terrible problem. The patients usually present with foul-smelling fluid draining from the infected mesh. Virtually always, the entire mesh along with the overlying skin has to be resected to resolve the problem. In many cases, the overlying skin is a skin graft that has become chronically infected along with the mesh. The technique involves complete removal of the infected skin and mesh, mobilization of healthy fascia, and suturing the absorbable mesh to the fascia, as previously described (Fig. 4). In most cases, the skin can be mobilized to be brought over the temporary mesh

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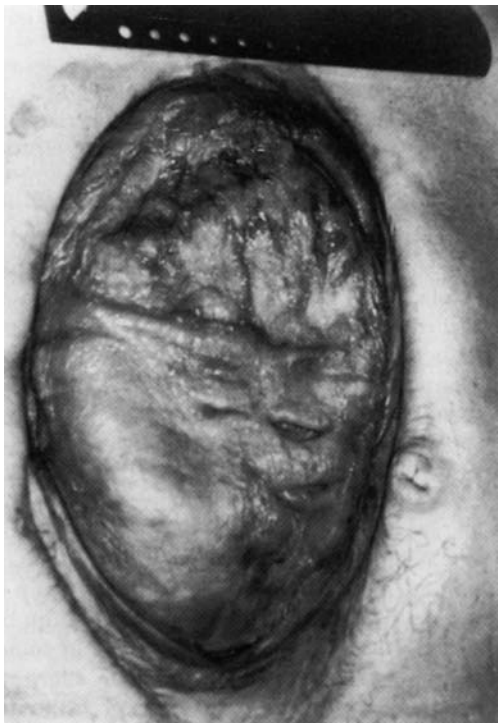

Figure 3 Patient presented with infected, foul-smelling wound in which polypropylene mesh had been placed in an infected defect, granulation occurred, and skin grafting was done. The wound broke down and drained continuously as mesh became exposed. (From Ref. 36, p. 296.)

and closed primarily with a closed suction drain placed (Fig. 5). An attempt to mobilize the skin and achieve primary skin closure over the temporary mesh is always desirable, as it makes the definitive repair 10 months later much easier, with a greater likelihood of success.

It is imperative to emphasize that all infected mesh has to be removed in this setting. Failure to do so will result in inadequate healing and possible reinfection when definitive repair is attempted months later.

C. Infection in a Pre-Existing Hernia

Patients with a pre-existing large abdominal wall hernia who develop peritonitis or infection comprise a third group of patients who benefit from

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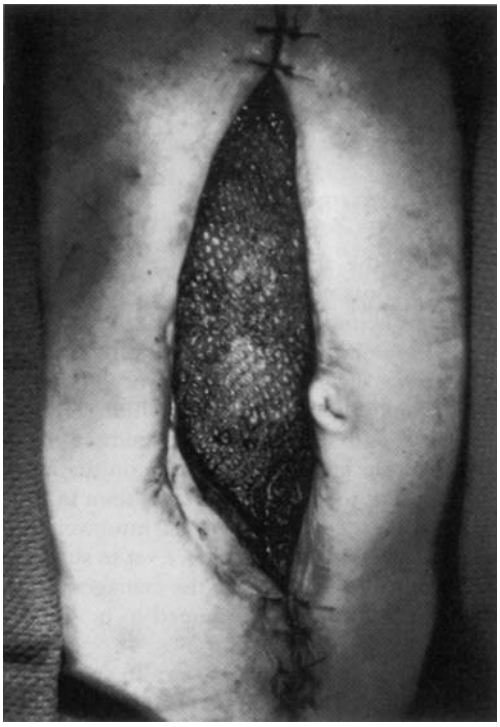

Figure 4 Patient in Fig. 3 has had resection of the infected mesh and overlying skin, mobilization of the fascia, and temporary closure with absorbable mesh. (From Ref. 36, p. 297.)

staged repair of the defect with an absorbable mesh. Management of this difficult clinical problem would involve treatment of the primary disease process, copious irrigation, drainage of all abscess cavities, and subsequent mobilization of the fascia and placement of absorbable mesh with attachment to the fascia, utilizing absorbable suture in a running fashion. Again, attempts should be made to close the skin over the temporary mesh.

Other patients who would fall into this category are those with abdominal wall loss due to multiple enterocutaneous fistulas from Crohn's disease, trauma, or irradiation. Again, successful management of this problem always involves treatment of the primary condition before using the Dexon mesh to temporarily close the abdominal wall defect.

Another clinical scenario that falls into this general area is the setting in which tumor involves the abdominal wall and results in bowel

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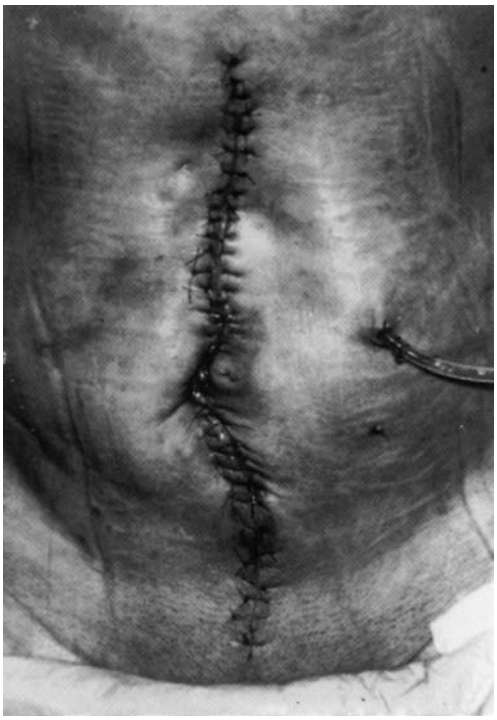

Figure 5 Patient in Fig. 3 had mobilization of the skin with primary skin closure over the temporary mesh placed in Fig. 4. This patient will develop a hernia in 2–3 months, which can then be permanently repaired with polypropylene mesh with healthy skin coverage. (From Ref. 36, p. 297.)

resection that grossly contaminates the wound. Use of absorbable mesh in a contaminated setting such as this allows the surgeon to resect a wide margin and not compromise the cancer operation. The absorbable mesh can be placed until the wound heals and contamination resolves, allowing permanent repair at a later date.

D. Abdominal Wall Loss with Contamination Secondary to Major Trauma

Another indication for use of absorbable mesh is the trauma patient who has sustained significant loss of abdominal wall substance with massive contamination. Such mechanisms as electrical burn, shotgun injuries,

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explosions, and machine trauma are included in this group. It has been the experience at the author's institution that these extremely ill patients—who may be unstable and who have sustained loss of abdominal wall substance associated with massive contamination—can be closed quickly and effectively using absorbable mesh. The absorbable mesh appears to be even safer in this setting because it can be more quickly and safely placed than a permanent mesh, which the surgeon should not use in the setting of this kind of contamination.

Clearly, after treating the primary trauma—including bowel resection, solid organ resection, and any other traumatized organ—is of foremost importance. After management of those problems, if primary closure of the fascia can be accomplished, it is always the first choice. However, if the trauma has resulted in loss of both skin and abdominal wall substance, the wound can be quickly closed using an absorbable mesh, with a plan to return another time and place permanent mesh after the contamination has resolved and the patient has healed and is more stable.

E. Massive Bowel Edema After Major Sepsis or Trauma

A great deal of experience has now accrued with use of absorbable mesh in the setting of the patient who has life-threatening sepsis with massive contamination who requires aggressive resuscitation. These patients, as well as trauma patients, often have associated massive bowel wall edema due to aggressive resuscitation after a complicated intra-abdominal procedure. Upon attempting to close the fascia, in spite of efforts to decompress the bowel, the fascia cannot be closed or would be closed only under significant tension. In this setting, where there is difficulty in closure of the abdominal wall, absorbable mesh can be used as a temporary closure by merely stapling it to the skin or sewing it to the fascia with absorbable suture until the bowel wall edema resolves in 7–10 days. As the edema resolves, the viscera can then be returned to the peritoneal cavity and a primary fascial closure effected. In some of these cases, we have found that it is not necessary to attach absorbable mesh to fascia to provide temporary support of the bowel. That is, in some cases, we have stapled absorbable mesh directly to the skin, and the mesh has provided strong support until reoperation could result in primary closure of the fascia.

However, one important point should be noted. If the surgeon waits too long to reoperate, the polyglycolic acid mesh will become tenaciously

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adherent to the serosa of the small bowel, so that its removal will be almost impossible. On the few occasions when this was a problem, the author found that it is better to simply leave fragments of the mesh attached to the bowel wall surface rather than try to remove it. Certainly, one of the obvious advantages of the absorbable mesh is that it does not have to be removed when reoperating. There is also evidence from Edlich et al. [35] that the mesh may provide some element of antibacterial effect as it breaks down.

F. Additional Considerations

As experience with the absorbable mesh and closure of the abdominal wall in a contaminated setting has increased, additional considerations are being evaluated. Because it is somewhat difficult to remove the polyglycolic acid mesh when used short-term, some authors have suggested that a layer of Seprafilm, an adhesion-inhibiting absorbable film, might make the mesh easier to remove. A few patients at the author's institution have had placement of Seprafilm immediately before the polyglycolic acid mesh was sewn in. Although the use of the adhesion-reducing Seprafilm intuitively seems like a good idea, there is little experience to suggest that it will truly make a difference in the management of these patients. Clearly, further studies need to be done to see if it might find some use.

VI. SUMMARY

The use of absorbable mesh has revolutionized the management of infected abdominal wall defects or defects that are under too much tension to be closed. Although the absorbable meshes do not appear to meet the definition of an ideal prosthesis, they are soft, nontraumatic, strong, noninflammatory, sterilizeable, and noncarcinogenic. Their use is associated with hernia development in virtually all cases. However, while the absorbable meshes would never be indicated in the clean, uncomplicated large hernia repair, they have some unique and specific advantages when used as temporary prostheses to repair defects in grossly contaminated operative fields. The mesh is soft and easy to work with in this group of patients, who are often very ill at the time of placement. The meshes are extremely strong, allowing the patient to ambulate and be mobile almost immediately after operation. They can be

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placed in a grossly infected field and do not exacerbate the infection or make it more difficult to resolve. More importantly, they maintain their strength long enough to provide abdominal wall support until the field is covered by skin that is free of infection. An additional obvious feature is that because the mesh is resorbed, reoperation to remove it is never required. The author and others now recommend that absorbable meshes be used as a temporary prostheses in a staged process to close the abdominal wall. The absorbable mesh is a temporary prosthesis that serves to close a contaminated wound until the wound is cleaned and epithelialized, thus allowing eventual reoperation and placement of a permanent mesh. Patients who have had infected or contaminated defects repaired with this mesh can be safely reoperated, at which time a permanent mesh can be placed with low morbidity and mortality.

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13

Bacterial Colonization of Implanted Devices

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I. INTRODUCTION

There are two primary states in which bacteria can exist and grow—namely, as free-floating cells or as sessile communities attached to surfaces [1–3]. Surgeons are most familiar with the free-living, single-cell form of bacterial growth, the "planktonic" state, typical of liquid cultures and believed to be the cause of most acute infections. Because these bacteria are mobile, they can travel from one body site to another and from one patient to another, thus potentiating the spread of infection. Their growth as individual organisms, however, allows for easy isolation and identification in pure culture and leaves them more exposed to the effects of antibiotics and host defenses (antibodies and phagocytic cells). The clinical picture produced when such organisms invade patients is one of an illness that either develops rapidly into an overwhelming disease or one that is brought under complete control by antimicrobials and host defenses.

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Less familiar to the average surgeon is the sessile mode of bacterial growth, which defines a multicellular community known as a biofilm. This is actually the predominant form of bacterial growth in nature, but appreciation of its importance is lacking because of the technical difficulties inherent in assessing and characterizing the diverse physiological states of these organisms. When bacteria assume a sessile state by adhering to inert surfaces or tissue, they generally form microcolonies. As the colonies grow, they may begin to synthesize a protective matrix of extracellular polymeric substance (EPS) primarily composed of carbohydrates. Although this matrix, or glycocalyx, limits further motility of the attached bacteria, it also provides a shield against host immune responses and antimicrobial agents. The low rates of metabolism and growth associated with some of these biofilm cells now produce a clinical picture that is chronic rather than acute, with high rates of recurrence once therapy is discontinued. In addition, EPS may also provide binding sites for the attachment of additional microbes of similar or different species. The community that eventually forms may be quite diverse; and when heterogeneous species are present, the by-products of metabolism of one species may support the growth of another in ways that increase the overall viability of the community.

II. THE NATURE OF BIOFILMS

There are three components of a classically defined biofilm: a surface or substratum, surface-attached microbes, and the presence of an EPS matrix in which the microbes are embedded. A biofilm probably has a selective advantage in nature because nutrients in aqueous solution tend to accumulate near surfaces and exposure to predation is minimized. Once adherence occurs, aggregates develop through cell division. These organisms are bound to one another by adhesion molecules and by the EPS matrix. As the colony grows, the internal environment changes. Nutrients that were plentiful at the surface become less abundant due to restricted diffusion and/or utilization by competing organisms. Waste products may also accumulate, adversely affecting both pH and the O_2/CO_2 balance. These changes may reduce the metabolic and growth rates of the microbes, especially those cells located within the central areas of the biofilm. Although these ''internal'' organisms may benefit from reduced exposure to environmental hazards and may also benefit from accumulation of utilizable metabolic products of neighboring

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bacteria, diffusion limitations affecting other critical external substrates may be detrimental. Thus, in this scenario increased scarcity probably leads to more modest growth, but growth with greater security.

In saturated environments, the EPS matrix itself is mainly composed of water, and there appear to be sizable water channels within a fully hydrated matrix structure. Because the glycocalyx is predominantly anionic, it forms a scavenging system for minerals and small nutrient molecules. However, larger molecules such as antibiotics and antibodies and predators such as protozoans or human phagocytes are prevented from entering the matrix.

Recent evidence suggests that chemical communication occurs among biofilm bacteria via the production of small signaling molecules such as homoserine lactones. This "quorum sensing" is a concentration-dependent phenomenon that may, for example, promote timely secretion of enzymes to maximize utilization of available nutrients or act to limit the production of virulence factors until a large enough microbial population is reached, in effect reducing the chance that the host will notice the infection until sufficient numbers of bacteria are present to mount an effective invasion. Thus, bacteria can respond as a community to changes in their environment by altering gene transcription. In addition, under localized conditions of stress, it is believed that quorum sensing may effect detachment of cell aggregates and/or the release of newly mobile, planktonic bacteria for colonization of more favorable sites.

III. BIOFILMS IN NATURE

Biofilms are widespread in nature and are familiar to anyone who has had to clean the slime from a clogged drain. The slime is, in fact, a macroscopic example of a complex, mature biofilm, the slimy texture being conferred by the EPS matrix. Biofilms disrupt many industrial processes and have a deleterious impact in the biocorrosion of concrete, natural stone, and metal surfaces. Biofilms are also present on many household surfaces and have been implicated in the transmission of food-borne disease. Conversely, many biofilms are benign or beneficial. For example, different biofilm communities give the multicolored appearance to rock surfaces in thermal springs. They also exist on plant leaves and roots and probably contribute significantly to nutrient uptake. In addition, biofilms in soil are

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responsible for the biodegradation of organic contaminants in soil and water and have been used to form biobarriers that assist in secondary oil recovery as well as to minimize acid mine drainage and the spread of groundwater pollutants.

Although most people are probably aware of the necessary digestive functions that naturally occurring human gut bacteria perform, all human body surfaces that have contact with the environment represent sites potentially open to biofilm formation. Fortunately, the shedding of surface epithelium can disrupt biofilm formation in healthy humans—a process that can contribute to the removal of pathogenic bacteria as well as other benign species. Historically, dental plaque was the first biofilm identified by Anton van Leeuwenhoek, the father of modern microscopy, who scraped some plaque from his teeth and observed small ''animalcules'' within it [2,3]. More recently, biofilm formation has been documented on skin, in the vaginal area, in the nares, and in the middle ear. In the case of vaginal biofilms, aggregates of *Lactobacillus* sp. may be beneficial in preventing human cell contact with harmful species. Thus, indiscriminant use of antibiotics may actually mitigate this beneficial effect.

Evidence now suggests that many exposed surfaces of the human body are colonized by biofilm-associated bacteria, even in healthy individuals. However, much is yet to be learned about the nature of host cell/biofilm interactions. It is currently held that these human-colonizing biofilms generally demonstrate relatively little virulence and cause difficulties mainly of a localized nature, such as dental caries or gingivitis, when preventative treatment is minimal. Occasionally, however, more virulent manifestations appear, usually when there is interference with shedding of the outer surface bacteria, when biofilms become buried beneath the surface tissue as in the cases of infected cysts or when there is entrapment in fibrotic tissue, when there is tumor overgrowth [8,13,14], when the human host is immunocompromised, or by introduction of pathogenic bacteria during invasive medical procedures. Detached bacteria from existing biofilms may then invade other epithelial tissues, producing acute inflammation and perhaps eventually causing even more serious problems by invasion of deeper tissues. Understandably, the potential for systemic release of opportunistic, pathogenic bacteria that may become dislodged by disruption of biofilm during normal dental procedures, for example, requires application of appropriate antibiotic treatments to protect patients with vascular prostheses or damaged cardiac valves.

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Human health problems associated with bacterial biofilms usually occur when normal host defenses have been altered either by disease or excessive use of medications or when a surface amenable to biofilm formation remains indwelling or is implanted and becomes contaminated. Sometimes these latter two conditions exist simultaneously—for example, when an implantable catheter is used to administer chemotherapeutic drugs. Virtually all synthetic surgical devices have been shown to be colonized by bacterial biofilms. These devices include orthopedic tools, vascular grafts, mechanical heart valves, penile prostheses, and virtually all indwelling catheters, venous, urinary, and biliary.

IV. MECHANISM OF ANTIBIOTIC RESISTANCE IN BIOFILMS

Although the exact mechanisms of biofilm-conferred resistance to antibiotics are considered to be somewhat complex, they probably involve at least three important phenomena: binding and inactivation of the antibiotic by the EPS matrix, reduced activity of the antibiotic due to chemical alterations of microenvironments within the EPS matrix (e.g., changes in pH and/or pCO_2), and reduced activity/growth rate of at least some of the associated microbes, making them less susceptible to the effects of antibiotic agents [1–3,7].

A number of studies have shown that planktonic bacteria are three to four orders of magnitude more sensitive to bactericidal agents than biofilm-associated cells. In fact, adding extracts of the EPS matrix to bacterial cultures can also increase their resistance, indicating the neutralizing effect this matrix material can have on antimicrobial agents. The effects of the chemical microenvironment are largely conjectural, but the importance of pH is in line with known effects of acidosis on decreasing antibiotic effectiveness. However, most surgeons are probably familiar with the relationship of bacterial growth rate to antibiotic susceptibility. The fact that abscesses need surgical drainage is due primarily to the relatively slow growth of organisms within the abscess, which limits their sensitivity to the effects of antimicrobial agents, rather than to the lack of penetration of the abscess by these same agents.

Exacerbating the problem of antimicrobial resistance is the added role that biofilm matrices play in limiting the effectiveness of host immune responses. The EPS matrix not only limits exposure of enclosed

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bacteria to phagocytic cells but also prevents the binding of antibodies in a way that will allow biofilm bacteria to be opsonized. As a result, host defenses and antibiotics may be able to eradicate those organisms breaking away from the surface of the biofilm but will have little effect on bacteria residing deeper within the microcolonies.

V. BACTERIA RESPONSIBLE FOR INFECTIONS

Catheters and other indwelling surgical devices may be colonized by somewhat complex biofilms, including both bacteria and fungi. Usually, the type of biofilm that forms is dependent upon the microflora commonly present in or around the orifice or area being treated. For implanted materials, including implanted venous catheters and ports, the infectious organisms most commonly involved are the gram-positive bacteria, *Staphylococcus epidermidis* and *Staphylococcus aureus*. *S. aureus* is a familiar foe to general surgeons, accounting for many of the acute pyogenic infections that are initiated via surgical drainage devices. Because *S. aureus* produces a number of toxins including coagulase, few infections with these organisms remain subclinical for long. Nevertheless, under the right circumstances, even virulent strains of *S. aureus* can be incorporated into existing biofilms and produce recurrent chronic infections. Common examples of recurrent disease are associated with suture abscesses and graft infections, which can be controlled for a time with antibiotics but which rapidly recur once therapy ceases. Because of its virulent nature, *S. aureus* seldom lies dormant for long, even when associated with a biofilm, since bacteria detached from biofilm surfaces make their presence known within days of interruption of antimicrobial therapy. Removal of the implant is a necessary step for the eradication of such infections [4].

In contrast, *S. epidermidis* causes few clinical infections, even though it is a virtually ubiquitous colonizer of human skin and mucous membranes [5]. In fact, until recently, *S. epidermidis* was thought to be a strictly saprophytic organism. Clinical infections, when they occur, usually do so in an immunocompromised host. This nonvirulent tendency in *S. epidermidis* is thought to be primarily due to a lack of toxin-encoding genes. When *S. epidermidis* colonizes an implanted device, such as a venous catheter, clinical symptoms can often be suppressed with antibiotics for long periods of time, even indefinitely if the patient is otherwise healthy. Bacteremias tend to recur when host defenses fail, as

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recurrent disease or chemotherapy lowers white blood cell counts below critical levels, so that bacteria escaping from the biofilm surface are unchecked. If the host can be kept immunologically intact, implants containing viable *S. epidermidis* organisms may often be left in place for prolonged periods without producing clinical disease [6]. Therefore, implant removal for maintenance of patient health is related to the balance between the virulence of the colonizing organism and the strength of the host defenses. This balance may be maintained for prolonged periods, only to be disrupted by disease progression or by the exogenous introduction of destabilizing factors, such as drugs.

Other organisms have also been identified in infections associated with hernia mesh. These microbes include *Mycobacterium fortuitum* [20] and group A streptococcus (GAS), which can cause streptococcal toxic shock syndrome (Strep TSS) [18].

VI. EVOLUTION OF MATERIALS USED IN HERNIA REPAIR

Within the last decade, hernia surgery has emphasized the use of different types of mesh repair rather than suture repair [15]. Prosthetic mesh greatly reinforces abdominal wall repair and is now widely used because of its ease of placement and the relatively low recurrence of herniation [22]. The ideal prosthetic mesh material must not be modified by exposure to tissue fluids and must not initiate an inflammatory response or be carcinogenic or allergenic, yet it must also be chemically inert, resist mechanical stress and sterilization, and be able to be manufactured in the required functional shapes. Although the first meshes were composed of silver filigrees or stainless steel, more nonmetallic and nonabsorbable synthetic materials including nylon, Silastic, polytetrafluoroethylene, polyesters, and polypropylene have been developed for use in meshes [8]. In addition, absorbable meshes primarily made of polyglycolic acid and polyglactine 910 are increasingly used. Generally, polyester, polypropylene, and polytetrafluoroethylene seem to best fulfill the above criteria for the ideal mesh material [8].

A number of physical and chemical factors that contribute to the overall design of mesh material have been shown to affect mesh performance, especially as performance is related to colonization by bacterial biofilm. The importance of this issue should not be surprising

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given that the waste-water treatment industry has spent much time and energy in optimizing some of these same types of mesh for use as biofilm support systems (BSS) for maximizing the biodegradation of water-borne contaminants [10]. In addition, reporter gene technology has been used to demonstrate that Teflon mesh represents one substratum that allows biofilm formation, as evidenced by the upregulation of genes controlling alginate production [12]. Alginate is one of the primary components of the EPS matrix associated with classic bacterial biofilms. The physical factors that have been shown to affect mesh performance include mesh size, the types of filaments used, and total surface area. For example, macroporous meshes have been shown to cause erosive phenomena and viscera/mesh adhesions [8,21], whereas a small mesh size seems to foster bacterial colonization and more rapid stent occlusion [13]. In vivo, the adherence of bacteria is positively correlated to surface area, which favors the use of monofilament mesh material over multifilament types [15]. Finally, it has been shown that prosthetic rejection phenomena are also positively correlated to surface area of the synthetic tissue [8].

Whether or not performance of different mesh materials can be traced to physical or chemical characteristics, it is clear that different mesh materials do perform differently with regard to provoking immune responses, allowing biofilm development, and in the occurrence and recurrence of infections. For example, sling intolerance was shown to vary between 1% for Prolene mesh and 31% for Gore-Tex, while abdominal sacrocolpopexy rates varied from 1.7% for Prolene and 20% for Teflon [8]. In another study, no difference in resistance to bacterial colonization was observed between fluorinated polyester and polytetrafluoroethylene; however, the former mesh material performed much better with regard to ease of manipulation and showed more rapid and sustained incorporation and neovascularization. Conversely, copolymer and wire mesh stents demonstrated significantly less biofilm formation than a more traditional stent material [11]. Mesh coatings have also been shown to affect performance. Although both Sepramesh (Seprafilm-coated polypropylene) and Parietex composite (collagen-coated polyester) prevented bowel adhesions, the latter mesh material also increased infection rates [21]. No doubt future materials will be developed to address problems that now occur with existing mesh materials. For example, a microfibrous metal mesh coated with titanium dioxide is now only used in air filtration, but it has the interesting properties of being self-sterilizing and self-cleaning through the use of a UV light–induced photocatalytic regeneration process [9].

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VII. MESH INFECTIONS AFTER HERNIA REPAIR

Little research has examined synthetic materials used for hernia repair to determine whether biofilm formation occurs in the absence of an induced inflammatory response. Such a study would necessarily require examination of control samples of mesh material removed from apparently healthy individuals. However, studies do suggest that biofilm formation on implanted mesh generally does produce an immune response. For example, one study of biofilm morphology and ultrastructure of an in vitro *Pseudomonas aeruginosa*–colonized, Silastic subdermal implant reported that, after in vivo implantation of the device and subsequent removal, that the bulk of the biofilm was host-generated, dominated by polymorphonuclear neutrophils with lesser numbers of erythrocytes, macrophages, and fibroblasts [14]. These results suggested that inactivated phagocytes trapped in fibrin may actually embed bacterial microcolonies and thus inhibit contact with other active phagocytes. In a similar study using *S. aureus*–colonized implants, no difference in infection rate was observed with either monofilament or multifilament mesh material when compared to control mesh without *S. aureus* contamination [15]. However, subclinical local inflammation and fibrosis were induced by the *S. aureus* biofilm, which was still detected 1 week after implantation. Therefore it is the persistence of *S. aureus* biofilm that may be the critical factor eventually leading to mesh-related infections months to years after surgery. Nevertheless, when these materials do become clinically infected, the clinical picture is similar to that of other biofilm infections. After an acute episode, inflammation will resolve with drainage and antibiotics, only to recur once treatment stops. Sometimes the wound will even close completely, but usually it will reopen and drain again over time. Patients may be able to tolerate this condition for months or years with little effect on their general health other than the aggravation that comes from continually having to clean the area and keep it covered. Ultimately, the only way to resolve such infections may be to remove the foreign material. Typically, biofilm is observed on the removed mesh (Fig. 1). Unless more synthetic mesh is needed to keep the hernia in check, prompt healing usually occurs subsequent to removal of the infected material.

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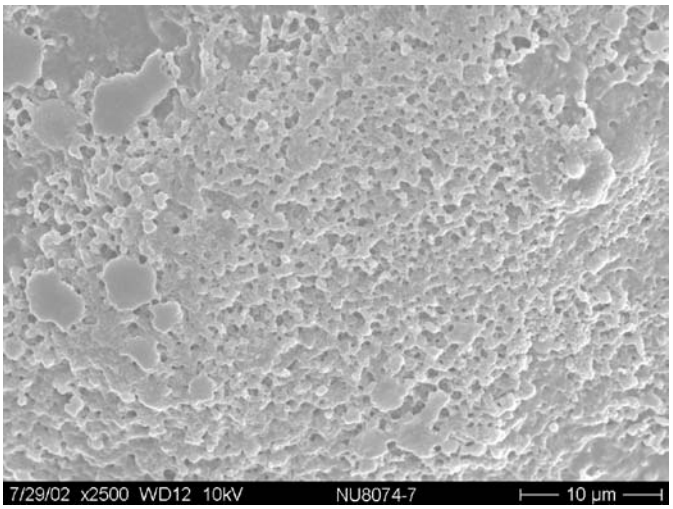
(A)



(B)

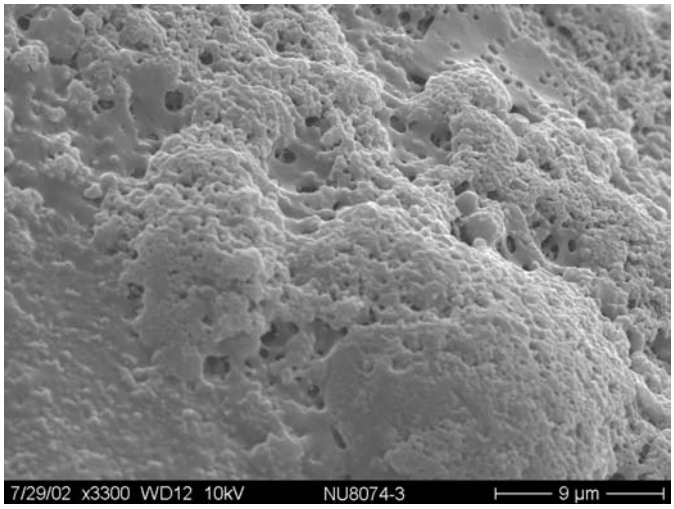


Figure 1 Scanning electron micrographs of bacterial biofilm colonizing an implanted hernia mesh that was explanted because of chronic sinus drainage. Two morphotypes that were observed include (A) a rather homogeneous coverage by biofilm and (B) a much thicker biofilm in characteristic ''cauliflower-like'' colonies.

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VIII. STRATEGIES TO PREVENT OR CONTROL BIOFILM INFECTIONS

Commonly used prevention strategies for biofilm control include the following: administration of antibiotics at the time of implantation (prophylaxis), incorporation of antibiotics onto devices to be implanted, other alterations of the chemical or physical properties of implant surfaces, and/or use of biological materials into which host cells can migrate. Preoperative administration of prophylactic antibiotics to perfuse tissues prior to incision is currently the only strategy for which effectiveness has been established. For example, one study investigated a number of variables with potential effects on local septic infection, and the two statistically significant factors were antibiotic prophylaxis (using either cephalosporins or amoxicillin-clavulanic acid) and the number of risk factors associated with the patient [23]. In this study, only 13.6% of patients receiving antibiotic prophylaxis developed surgical wound infection, compared to 26.3% who had not received antibiotic treatment. The two most frequently occurring risk factors were diabetes and obesity. Again, the positive correlation observed between patient risk factors and wound infection stresses the special considerations that must be given to immunocompromised patients. Ceftriaxone has also been shown to be an effective preoperative antibiotic [24].

Other potential means of infection prevention are not as consistently effective. For example, no convincing data support surface alterations of invasive devices as an effective means of preventing graft infection. As indicated previously, one potential problem with this approach is that serum may coat and condition implanted surfaces, actually making the device more receptive to bacterial adhesion and negating any effect of other surface alterations. Again, minimizing the surface area of the device may indirectly lower wound infection rates simply by providing less sites for bacterial colonization. Precise surgical technique and keeping the operative field dry and free of hematoma and serum may help prevent infection by reducing this surface conditioning. Seroma or hematoma is a frequent complication of laparoscopic or open repair of ventral hernias. Aspiration of this seroma includes the risk of introducing infectious bacteria, ultimately causing recurrence of the hernia. Cauterization of the hernial sac by monopolar cautery or harmonic scalpel was shown to prevent seromas and reduce the necessity for subsequent surgery [17]. Although prosthetic biomaterials are thought

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to perhaps encourage better incorporation by host tissue, they also have been associated with higher rates of infectious complications. One study reported, however, that outside exposure of the implanted mesh was the critical factor leading to a methicillin-resistant *S. aureus* infection [16]. The open wound was subsequently successfully treated without removal of the implanted material by a combination of intravenous antibiotics, wound debridement, vacuum-assisted closure of the wound, and soft tissue coverage of the mesh.

It has been appreciated for some time that autologous veins used as vascular grafts are more resistant to infection in contaminated conditions than are synthetic materials. The precise mechanism for this resistance is unclear, but it could be related to an increased efficiency of host cells in preventing biofilms from achieving a critical mass. Other biological material, in the form of processed collagen matrix, is being evaluated as a substitute for synthetics and may offer an additional strategy to overcome this difficult problem.

Although most cases of infection of repaired hernias occur outside the hospital setting, nosocomial infection by group A streptococcus (GAS) has increased in the past 10 years. In one epidemiological study, it was shown that the surgeon performing the hernia repair was an asymptomatic nasal carrier of the identical strain of GAS isolated from the postoperative wound infection [18]. Results such as this point to the necessity of adhering to appropriate surgical practices that minimize exposure of wounds to potential sources of infection. Another potential source of contamination in some hernia surgeries is open bowel exposure. However, one study involving 24 patients reported that only minor wound infections or cellulitis occurred in 21% of patients in which slightly less than half of the cases were considered contaminated as opposed to clean-contaminated [22]. No patients in this study required mesh removal, and only one patient had a recurrent hernia. Therefore, when appropriate surgical practices are followed, success in minimizing infection can be achieved even with placement of permanent mesh in contaminated fields. No doubt wound healing is critical to the success of any invasive surgery. In one postoperative survey of over 100 patients receiving hernia repair, 95% reported normal primary wound healing without infection [25]. Although there was no statistically significant correlation between wound healing, type of hernia, patient age, length of hospital stay, surgeon, or method of operation, it was concluded that using the tracer "wound healing after groin hernia repair" provided an inexpensive approximation for follow-up and quality control.

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Once mature biofilms are established, the best method for eradication is by removal of the colonized surfaces. For example, successful treatment of a persistent *Mycobacterium fortuitum* infection after hernia repair involved not only prolonged therapy using sulfamethoxazole but also multiple surgical debridements and complete removal of all the mesh material [20]. Since this may entail the loss of a device that is important to the continued health of the patient, other strategies need to be considered. Unfortunately, prevention is the only other strategy currently available, although suppression may work temporarily, as discussed previously.

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14

Postherniorrhaphy Mesh Infections: Microbiology and Treatment with Antibiotics

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I. INTRODUCTION

The principles applied in the diagnosis and treatment of wound infection are the same whether a prosthesis is present or not. Nevertheless, the presence of prosthetic material adds the additional challenge of trying to eradicate an invading organism that may have a privileged site within the matrices of the foreign material or in a loculated adjacent space. It is important that a standard definition of infection be used, especially if one is to discriminate between surgical wounds that have become infected at a superficial level and those that involve deep infection. The Centers for Disease Control (CDC) has published guidelines for defining infection [1]. This definition takes into account the signs and symptoms of infection as well as whether or not there is culture-proven infection; it is used as the definition of infection in this review.

It is well documented that the source of bacteria that lead to wound infection is most often from the environment at the time of the initial procedure. However, one must be aware of the possibility that bacteria may come from distant sites, either via the hematogenous route or by contamination of the site. Therefore the infectious agent may vary

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depending on the patient and his or her comorbidities and pre-existing disease. In a patient with a clinical surgical-site infection (pain or tenderness, erythema, edema, heat and/or drainage) but where no organism has been identified, it is worth considering several different scenarios:

A. ELECTIVE CLEAN PROCEDURES

Infection that occurs after elective clean procedures in otherwise healthy patients is usually caused by gram-positive bacteria, most often *Staphylococcus aureus* [2]. When cultures are not available, it is reasonable to start administering antibiotics with good gram-positive coverage, such as the first-generation cephalosporins: for example, cefadroxil monohydrate 500 mg twice a day orally or, in more severe cases, cefazolin 1 g IV every 8 h. Alternatives are ceftriaxone sodium 1 g IV per day. If the infection seems massive, one can start with ampicillin sodium/sulbactam sodium at a dose of 3 g IV every 6 h. If a gram-negative organism is suspected, a quinolone may be indicated (e.g., levoquim 500 mg IV daily or cefadroxil). If the patient gives a history of penicillin allergy, vancomycin hydrochloride, 1 g IV every 12 h or levoquin 500 mg IV once a day may be used, or clindamycin phosphate 900 mg IV every 8 h. As last resort, Xyvox may be utilized.

B. The Compromised Host

Patients who have a compromised immune response are more likely not only to develop infection but also to have infections with mixed flora. Therefore, empirical therapy in the compromised host should start with broad-spectrum coverage for both gram-negative and gram-positive organisms. One may start with ticarcillin disodium and potassium clavulanate 3.1 g IV every 6 h or, if combined flora are suspected, piperacillin sodium 12–18g IV per day in divided doses given every 6–8 h.

C. Distant Infection Site/Previous Infection Site

Urinary tract infection or low-grade pulmonary infection (e.g., bronchitis in a patient with chronic obstructive pulmonary disease) can be unrecognized source for seeding of the operative site and has been documented to increase the risk of infection [3]. Careful evaluation of a

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patient with wound infection occasionally reveals previously unrecognized sources of infection. Antibiotics for the treatment of the organisms, usually gram-negative, associated with these sites should be used after the specific organism is found by cultures and sensitivity.

Placement of prosthetic material in the site of a previous infection carries the risk of ''reactivating'' the previous infection. Tissue has been shown to harbor the same organism for years after an infection. This is more common when there was residual necrotic tissue or permanent braided suture material in the wound. In such cases antibiotics used for therapy should include activity against the original organism. Careful record review is then recommended in order to provide adequate and effective coverage.

D. Recent Antibiotic Exposure/Hospitalization

Organisms that have developed multiple resistance to antibiotics may begin to appear in patients by the time they reach the operating room. This appears to be due to the overuse of antibiotics in the outpatient setting, transmission of hospital-acquired bacteria, or persistence of bacteria acquired in the inpatient setting. In initiating therapy, it should therefore be recognized that resistant organisms may be present. When surgical site infections do not respond to therapy within 24–48 h, it is likely that the wound harbors a resistant organism. The offending bacteria is usually methicillin-resistant *S. aureus*, which requires vancomycin or rifampin to be administered by an infectious disease consultant. Resistant bacteria may require further treatment with Zyvox, tetracyclines, or choramphenicol.

II. IDENTIFICATION OF THE ORGANISM

Specific identification of the infecting organism and determination of its sensitivity to antibiotics should always be the goal in treating any wound infection that is more than just a superficial and localized. Superficial-site infections that do not respond promptly to antibiotic treatment should be opened and the drainage sent for Gram's stain and culture for the presence of aerobic and anaerobic organisms. This is particularly important when the infection is established in a deep incisional site in the presence of prosthetic material. Initial therapy is directed by the

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findings on Gram's stain and modified by, first, identification of the organism and, second, determination of its sensitivities.

Bacteria associated with prosthetic materials may take advantage of their glycocalyx [4], such as that of *Staphylococcus epidermidis* [5], and are adherent to the matrix of the graft. In order to isolate the organism, a portion of the mesh should be sonicated prior to culturing the material.

In difficult-to-diagnose infections or to determine whether infection persists, evaluation of tissue from the wound can be a valuable adjunct to the culturing of wound drainage. The biopsy is done after cleansing the wound with saline (not antimicrobials). The tissue, which must be viable, is handled in a sterile manner; it is recommended that it be assessed either by quantitative wound culture or by a combination of qualitative wound culture and microscopic evaluation [6]. The finding of 100,000 or more organisms per gram of tissue from a quantitative culture confirms invasive infection; therapy is based on identification of the organism that is isolated from the quantitative analysis. If histological evaluation is performed, the diagnosis of invasive infection is made when bacteria are identified in viable tissue. The treatment is then guided by the results of the qualitative culture. Repetition of this procedure may be of assistance in persistent infections or in those that do not respond to antimicrobial therapy.

III. PERSISTENT INFECTION

In a majority of cases, good local wound care with adequate drainage of local fluid collections and use of appropriate antimicrobials will lead to resolution of the infection and preservation of the mesh. When there is evidence that there is ongoing infection, the challenge is to determine whether mesh is involved. In the absence of other evidence of a deep-site infection, such as chronic drainage or a fluctuant mass, indium-labeled white blood cell scanning may assist in determining whether deep tissues are involved. This approach has provided the insight to allow selective wound exploration when there is a question of infection in vascular grafts [7]. This test, however, is difficult to interpret in the perioperative period and is best reserved for use in evaluating patients who had their repair more than 3 months prior to the examination. Although some have advocated early removal of Gore-Tex mesh because of the difficulty in eradicating infection associated with this material, attention to the local

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wound with irrigation, excision of exposed graft, and culture-based antimicrobial use is advocated even in this difficult situation.

Persistent sinus tracts are a sign of residual infection and lack of incorporation of the mesh into the surrounding tissues. A sinogram that shows a space around the foreign body will confirm the lack of incorporation [8]. When local or systemic signs of infection persist even in the absence of drainage, one must suspect that there is an undrained collection at the site of the mesh. A computed tomography scan or ultrasound evaluation should be used to determine whether collections persist; it can also be used to direct catheters for the drainage of collections.

IV. PROGNOSIS FOR THE REPAIR AND THE MESH

In order to assess the anticipated outcome from infection in wounds of patients with a mesh-based hernia repair, peer-reviewed published articles were examined and divided into the categories of incisional and inguinal hernia repair. The 3429 cases collected from the reports of 12 different authors were summarized by type of mesh, the incidence and number of infections, and by the incidence and number of times the mesh needed to be removed. In these studies, the definition of infection was not routinely described, nor were there sufficient data to determine whether the authors used the CDC guideline for separating surgical site infections into superficial and deep types. The overall infection rate was 4.1%, with an incidence of 6.3% for incisional hernia repair and 1.7% for inguinal procedures. The overall risk of having to have mesh removed because of infection was 0.79%, with rates of 1.1 and 0.49% for incisional and inguinal hernia reconstruction, respectively. These data support the anecdotal reports indicating that, in a majority of cases, judicious use of antibiotics and local wound care will proceed to eradication of infection with the mesh left intact.

The data are insufficient to evaluate the relative risk of infection associated with different types of mesh. However, it is of interest to note that in every instance when expanded polytetrafluoroethylene mesh was associated with infection, it had to be removed. This was not true for the polyester- and polypropylene-based meshes. It is not clear whether the Gore-Tex grafts were removed in every case because of the recognition of their characteristic pore size, which provides a protected niche for

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bacteria to evade inflammatory cells [9], or whether these clinical findings support the previous evidence.

V. CONCLUSION

In order to be consistent and to communicate effectively, the CDC definitions of surgical site infection should be used. Prompt recognition and early therapy of wound infection will lead to resolution of a majority of surgical site infections. A recognition of the flora present, the patient's history, and his or her comorbidities provide a basis for empirical therapy. Once an organism is identified, antibiotics should be changed if the empirical coverage is inadequate. Persistence of signs of infection should lead to a search for undrained collections or involvement of the mesh in the process. If the acute process cannot be controlled within 2–3 days or if signs of sepsis are present, the wound should be explored and drained. The chronic wound with continuing localized signs and with persistent collections or sinus drainage over a 3- to 4-week period should be explored with the expectation that mesh removal will be necessary. The possible need for repeat operations has been outlined by Deysine [10], who also developed an algorithm that outlines the approach to infection after herniorraphy.

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15

Utilization of Bioactive Prosthetic Materials for Hernia Repair in Infected Fields

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I. INTRODUCTION

Synthetic meshes for abdominal hernia repair were first commercially available over 40 years ago, and the history and evolution of their development reads like a history of hernia surgery itself. The development of the "ideal" mesh remains just as elusive as the "ideal" hernia operation. It has been stated that the ideal prosthetic material should be chemically inert, noncarcinogenic, capable of resisting mechanical stress, capable of being fabricated in the form required, and sterilizable yet not be physically modified by tissue fluids, incite an inflammatory response or foreign-body reaction, or induce a state of allergy or hypersensitivity [10,24]. From steel to Silastic to polyester to polypropylene, polytetrafluorethylene (PTFE), and polyglactin, the number of different synthetic meshes rivals the number of different techniques for hernia surgery. Prosthetic meshes for hernia repair have gained widespread acceptance as a means of buttressing a weak musculoaponeurotic layer of the

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abdominal wall and have by and large reduced hernia recurrence rates. In the event of incarcerated/strangulated hernias and other potentially contaminated fields, however, placement of prosthetic material remains controversial because of increased risk of infection. While there are reports of placement of polypropylene mesh in infected fields with satisfactory results, the perfect prosthetic mesh has yet to be described.

In 1967, Schmitt and Grinnan were the first to describe the successful use of polypropylene mesh in a contaminated wound [25]. Since that time there have been numerous publications describing the successful implantation of polypropylene mesh in large, contaminated abdominal wall defects [6,7,12–14,27,30,31]. While these repairs healed well initially, they were fraught with long-term complications such as chronic infection, fistula formation, and erosion into bowel or through skin grafts [7,17,26,27,29,31]. In 1989, Jones and Jurkovich reviewed 14 studies reporting on 128 patients in whom polypropylene mesh was placed following intra-abdominal sepsis, necrotizing fasciitis, wound dehiscience, or traumatic tissue loss [16]. The overall complication rate was 55%, with enteric fistulization being the most common complication in 23% of the patients reviewed. Anywhere from 50–90% of those patients in whom nonabsorbable mesh is placed in an infected field will require removal of the mesh at some time in the postoperative period [11].

As an alternative to *nonabsorbable* meshes such as polypropylene, studies involving the repair of hernias with *absorbable* materials such as polyglactin 910 (Vicryl) and polyglycolic acid (Dexon) have been performed. In 1986, Dayton et al. used polyglycolic acid mesh to repair infected abdominal wall defects in 8 patients [11]. While there were no infections and no fistula formation in follow-up studies up to 18 months, 6 of the 8 patients (75%) developed hernias at the site of the absorbable mesh repair. Dayton et al. concluded that postoperative hernia development is probable in patients whose defects are repaired with absorbable mesh; however, this complication must be balanced against the severe complications of sepsis, fistula, bleeding, skin erosion, and drainage, which require removal of nonabsorbable prostheses in a large percentage of cases when the latter are used in contaminated areas. Lamb and colleagues repaired clean rabbit abdominal wall defects using Vicryl mesh and found, at 3 weeks, that the bursting strength of the grafts was comparable to that of nonabsorbable meshes; however, at 12 weeks, the polyglactin 910 repair was significantly weaker [18]. In addition, 40% of the animals repaired with Vicryl mesh developed hernias. In contrast, Jenkins et al. compared prosthetic materials in rats for abdominal wall

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repair and found *no* difference in bursting strength, up to 8 weeks when Vicryl mesh was compared with Marlex and Gore-Tex prostheses [15]. However, their 8-week follow-up may not have been sufficiently long to detect hernia recurrence following absorption of the Vicryl mesh. Absorbable repair materials have the advantage of host tissue invasion and subsequent absorption of the implant, leaving behind only host tissue. However, these materials are not generally indicated when prolonged tensile strength is required [28].

II. SURGISIS MESH

Surgisis (Cook Biotech, Inc., West Lafayette, IN) is a new biologically active four-ply prosthetic mesh for hernia repair derived from porcine small intestinal submucosa (Fig. 1). Once harvested, the small intestinal submucosa (SIS) is minimally processed to lyse all resident cells and remove cellular debris. SIS consists of a trilaminar portion of the small intestine, including the stratum compactum layer of the tunica mucosa,

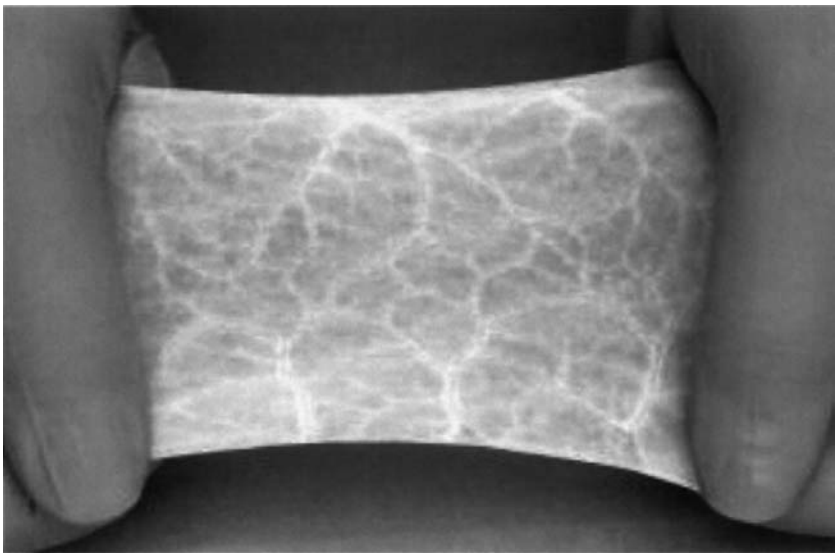

Figure 1 Four-ply Surgisis ES mesh derived from porcine small intestinal submucosa.

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the tunica muscularis mucosa, and the tunica submucosa. It is relatively acellular and the bulk of the material consists of extracellular connective tissue matrix. The intact cells present in SIS consist of occasional fibrocytes and the endothelial cells that line the vascular channels which once coursed through these layers of intestine. SIS biomaterial is terminally sterilized using a proprietary method that includes treatment with ethylene oxide.

SIS is a naturally occurring extracellular matrix that is easily absorbed, supports early and abundant new vessel growth, and appears to foster cellular differentiation, serving as a template for the constructive remodeling of many tissues [3,19,20,23]. In contrast to other absorbable materials, extracellular matrix scaffolds such as SIS show rapid degradation, with associated and subsequent remodeling to a tissue with strength that exceeds that of the native tissue when used as a body wall repair device. Using a standardized ball-burst test in a canine model, Badylak et al. were able to compare burst strengths of the normal canine abdominal wall, the SIS mesh prior to implantation, and the SIS after implantation [2]. The strength of the SIS hernia repair device prior to implantation was 73 ± 11 lb. The mean value for strength of the SIS mesh following implantation decreased to a nadir of 40 lb at 10 days, followed by a progressive increase in strength to 157 lb at 2 years. The strength of the normal canine abdominal wall is 32 lb when evaluated by the same ball-burst test procedure. A study by Clarke et al. compared SIS with polypropylene mesh for abdominal wall repair in dogs, finding that the SIS maintained sufficient strength while serving as a temporary scaffold for host tissue ingrowth and remodeling [9]. The SIS implants were totally replaced by organized collagenous tissue by 4 months, leaving no foreign material but apparently retaining tensile strength.

In none of the preclinical implantation studies was there evidence of the pronounced, chronic foreign-body reaction often seen with synthetic implants. In a full-thickness rat skin replacement study, no acute or delayed hypersensitivity reactions were observed [21]. The absence of adverse immunological reaction is thought to be related to the acellular condition and significant collagen composition of the SIS material. Additionally, the lack of permanent foreign material at the Surgisis implant site coupled with host tissue growth may decrease the risk of mesh infection. Badylak and colleagues deliberately challenged SIS and expanded polytetrafluoroethylene (ePTFE) infrarenal aortic grafts with *Staphylococcus aureus* [1]. After a 30-day follow-up period, none of the SIS grafts were infected as determined by clinical observation, clinical

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pathology, bacterial culture, and histopathology. Conversely, there was evidence of infection in all ePTFE grafts. The authors surmised that the apparent infection resistance of SIS in this vascular graft study may have been due to rapid capillary penetration of the SIS (2–4 days) and delivery of body defenses to the local site early in the healing process. Encouraged by these results, we postulated that SIS mesh might be an ideal candidate for repair of hernias in infected fields.

III. RESEARCH STUDY

From November 2000 through May 2002, a total of 25 patients (11 male, 14 female) at the Texas Endosurgery Institute underwent placement of Surgisis mesh for either ventral or inguinal hernia repairs in a grossly or potentially contaminated setting and were studied in a prospective, nonrandomized fashion. A total of 25 hernia repairs were performed in our patient population (Fig. 2). Fourteen procedures (56%) were performed in a *potentially contaminated* setting (i.e., with incarcerated/strangulated bowel within the hernia or coincident with a laparocopic cholecystectomy/colectomy). Eleven repairs (44%) were performed in a *grossly contaminated* field (i.e., gross pus or fecal spillage), including one in which an infected polypropylene mesh from a previous inguinal hernia repair was replaced with Surgisis mesh (Fig. 3) and one in which dead bowel was discovered within the hernial sac. Intraoperative cultures were obtained to confirm contamination in those sites with gross pus or enteric spillage.

Incisional/Ventral Hernias	19
Inguinal Hernias	6
Total Hernia Repairs	25

Figure 2 Distribution of hernia repairs.

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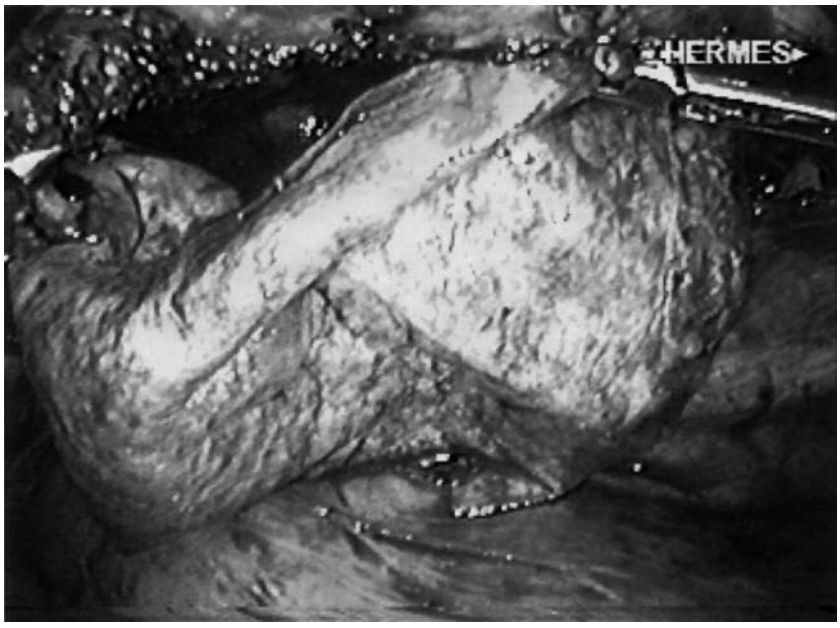

Figure 3 Infected polypropylene mesh is removed and replaced with Surgisis mesh implant.

Surgisis ES mesh comes in four-ply sheets of either 7×10 or 7×20 cm. Because of the physiological construct of the porcine-derived mesh itself, it cannot be made wider than 7 cm when manufactured into a four-ply sheet. This can present problems with larger hernias, where it is essential to have a 3-cm margin of mesh surrounding the defect. In these instances, more than one sheet is used, with at least 1 cm of overlap of one piece of mesh over the other. Currently, an eight-ply Surgisis Gold mesh is available, which is much larger (15×13 cm) than the four-ply sheet and provides even greater tensile strength to the repair.

In general, the surgical technique with regard to placement of the mesh was similar for each operation. Once the hernia was identified and reduced, its borders were cleared of any adhesions so as to allow the placement of mesh over the defect with at least a 3-cm margin in all directions. Using sterile technique, a four-ply Surgisis mesh (7×10 or 7×20 cm) was placed in a sterile dish and trimmed to fit the abdominal

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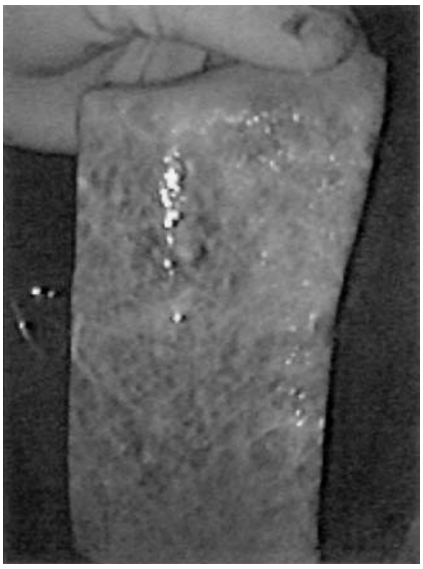

Figure 4 Mesh rehydrated with normal saline.

wall defect. The mesh was rehydrated with normal saline for at least 10 min and subsequently introduced into the abdomen via a 10-mm trocar (Fig. 4). The Surgisis mesh was then stapled securely into place with an intracorporeal stapler. For all inguinal hernias, the mesh was placed laparoscopically by the intraperitoneal onlay mesh (IPOM) technique. When possible, omentum was interpositioned between the abdominal contents and the mesh repair. We do not routinely use drains secondary to mesh placement only unless otherwise indicated. The 10-mm trocar site was closed with the aid of a Carter-Thomason (Louisville Laboratories, Inc., Louisville, KY) suture passer and the abdomen was then desufflated. The skin was closed with 3-0 Monocryl (Ethicon, Inc., Somerville, NJ) subcuticular stitches.

IV. RESULTS

All procedures were completed laparoscopically and there were no conversions to open. Median follow-up is 15 months with a range of 1–20

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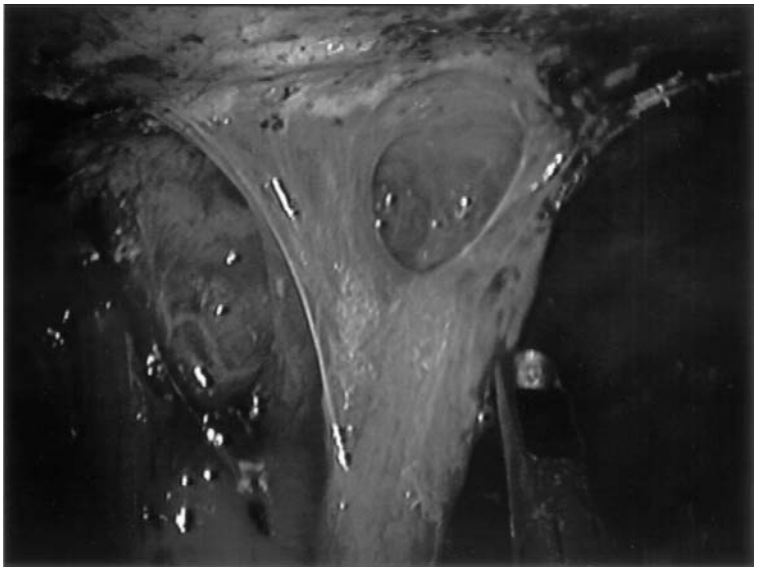

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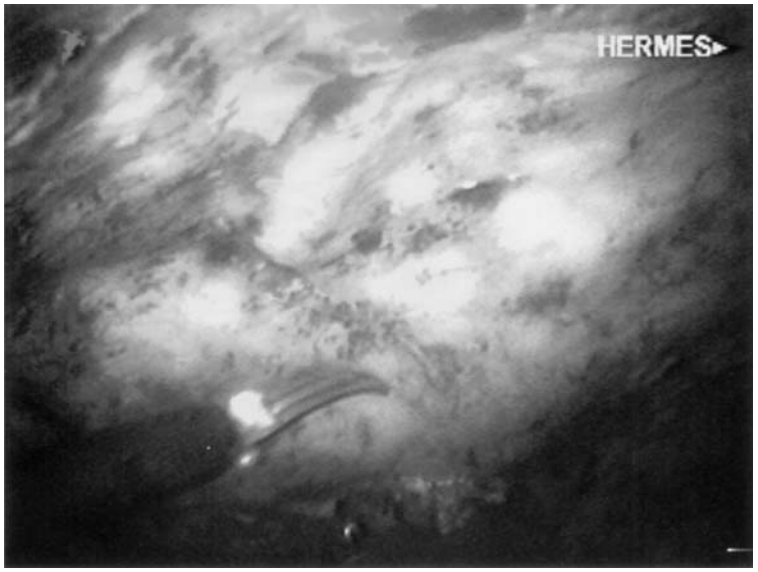

B

Figure 5 A. Benign adhesions to Surgisis mesh. B. Good incorporation of mesh within healing plate.

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months. Of the 25 total repairs, there has been one wound infection complicated by enterocutaneous fistula in a patient originally operated on for ischemic bowel. The fistula was in a location independent of the Surgisis mesh. There have been *no* mesh-related complications or recurrent hernias in our early postoperative follow-up period.

Three patients with Surgisis mesh hernia repairs have had subsequent laparoscopic procedures performed by our group for unrelated reasons. At the time of laparoscopy, the areas of mesh repair had only minimal benign adhesions and near complete incorporation of the mesh by the surrounding tissues, with abundant ingrowth of collagen material (Fig. 5A and B). In one of these patients the Surgisis mesh implantation site was biopsied and sent for histological analysis. As expected, there was microscopic confirmation of good incorporation of the mesh within a healing plate and profound ingrowth of collagen fibers (Fig. 6A and B).

V. CONCLUSION

The use of prostheses for hernia repair has gained widespread acceptance as a means of reinforcing a weak musculoaponeurotic layer. In the event of incarcerated/strangulated hernias and other potentially infected fields, however, placement of prosthetic material remains controversial because of the increased risk of infection. To our knowledge this is the first reported series investigating the placement of Surgisis mesh into grossly or potentially contaminated abdominal wall defects in human patients. The results of these 25 patients are encouraging and suggest that porcine small intestinal submucosa may be a viable alternative for placement of mesh in contaminated wounds. In our short follow-up period, SIS appears to possess the clinically important tensile strength characteristic of the nonabsorbable meshes while retaining the benefits of absorbable meshes, such as fewer infectious complications and decreased adhesion formation.

Surgisis is significantly more expensive than polypropylene mesh with a 7×10 cm four-ply sheet costing \$500 and the 7×20 cm sheet going for \$650, according to the Cook Surgical brochure. However, the cost of the Surgisis mesh is more than compensated for by the fact that it obviates the need for a second surgical procedure, whether it be to remove an infected polypropylene mesh placed in a contaminated setting, repair a recurrent hernia secondary to placement of an absorbable mesh,

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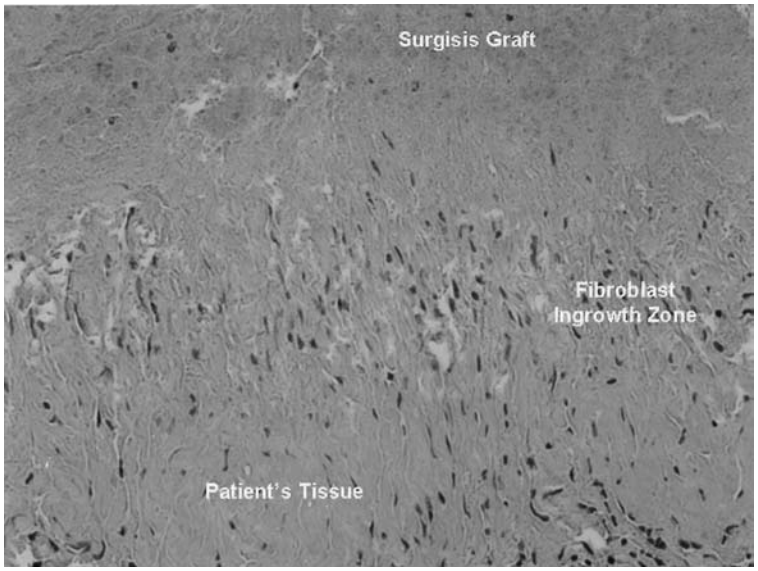

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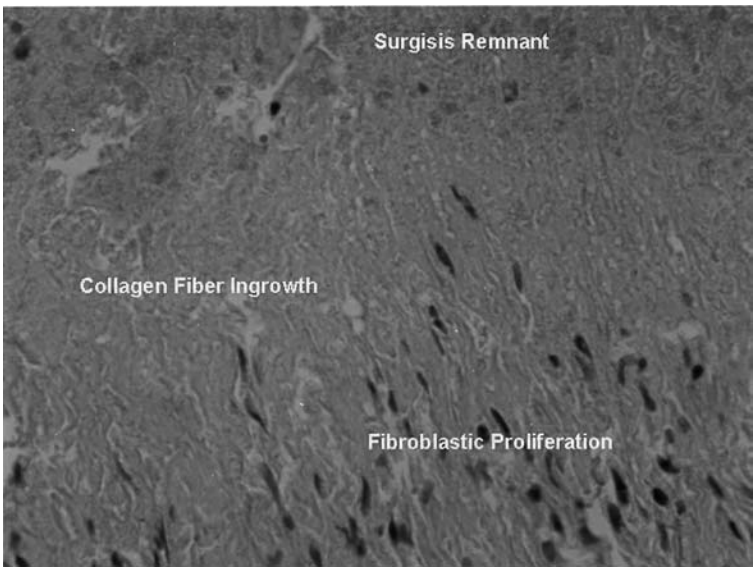

B

Figure 6 A. Low-power view of Surgisis mesh implant demonstrating good incorporation of the mesh, with fibroblastic proliferation and abundant ingrowth of collagen fibers. B. High-power view.

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or to simply perform a hernia repair that was postponed because of gross contamination of the original surgical field.

While further human studies are still required to establish the long-term efficacy of the Surgisis mesh implant, initial investigation appears to parallel the current animal data with reference to strength of repair and decreased infectious complications. Porcine-derived small intestinal submucosa is a naturally occurring extracellular matrix that is easily absorbed, supports early and abundant new vessel growth, and appears to serve as a scaffold for organized collagen deposition. In stark contrast to other absorbable materials, SIS shows rapid degradation with subsequent remodeling to a tissue with strength exceeding that of the native tissue when used as a body wall repair device. As such, we feel SIS mesh is clinically indicated for the repair of ventral and inguinal hernias in potentially or grossly contaminated fields, where the tensile strength of a nonabsorbable mesh is desired and the infection resistance of an absorbable implant is required.

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16

Percutaneous Bacteriological Testing Before Mesh Reinsertion After a Wound Infection

Patient–Surgeon Personal and Clinical Interaction

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One of the most complicated clinical dilemmas facing a surgeon is the necessity to reinsert a prosthesis into an abdominal wall in which an infection existed—an endeavor posing a significant risk of a recurrent infection. As the number of ventral and inguinal hernias repaired with mesh increases and in view of our present infection rate, this situation may be encountered more often than expected. Nowadays, the surgeon can utilize technology geared to diminish the risk of reinfection.

I. CLINICAL SCENARIO

After removal of an infected mesh, the surgical field is usually left open with appropriate drainage and allowed to heal by secondary intention while the patient receives specific antibiotic therapy. This healing process

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may take several weeks or even months until the skin incision is closed and no further external evidence of infection in the form of purulent sinuses is observed [1]. However, there is a possibility that an area of infection may remain active in the deep wound recesses, not easily reached by the surgeon during the mesh removal procedure. These areas consist of residual granulation tissue or abscesses that may or may not contain leftover foreign bodies. Parenthetically, the patient will be clinically asymptomatic without local or systemic evidence of infection; the wound will appeared healed, without skin sinus tracks. The only significant problem will be an enlarging, recurrent hernia requiring repair.

This situation produces a significant patient–doctor dilemma. The former will be psychologically and physically fatigued. After undergoing the primary repair which led to infection, it was necessary for the patient to endure several journeys to the operating table for wound exploration with mesh removal and drainage, followed by a protracted care involving further debridments, lavage, and so on. If successfully performed, all of these procedures lead to wound healing, accompanied by the inevitable recurrent herniation. The surgeon, on the other hand, is taxed by having to implement these repeated procedures, which never seem to lead to ultimate success. The surgeon is also aware of the fact that post-operatively delayed mesh infection is a real possibility, and that conclusive and complete healing may be problematic [2,3].

This situation is similar to that occurring with orthopedic patients in whom, after the removal of an infected prosthesis, a new one must be inserted. In the past, these procedures were associated with high reinfection rates. Orthopedic surgeons met this diagnostic challenge by performing percutaneous aspiration and bacteriological testing of the apparently healed wound, carried in an operating theater and utilizing all the antiseptic precautions of a regular orthopedic operation. Under those circumstances, percutaneous bacteriological testing gave the surgeon a reasonable idea of the bacterial sterility of the surgical field that would have to be crossed in order to insert a new prosthesis. This technology has entered into the routine management of postarthroplasty infection and has been adopted with a few modifications by the author, following the guidelines of Dr. Eduardo A. Salvati [2].

Accordingly, we have routinely performed percutaneous needle aspirations in patients in whom mesh repair was followed by an infection requiring prosthesis removal and who later required mesh reinsertion because of a recurrence. This policy was established and adhered to after

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the fortuitous discovery of a 2 mm^2 abscess located in the preperitoneal space of a wound from which an infected mesh had been excised 6 months previously. The operated site was clinically healed and the patient was asymptomatic, afebrile, and with a normal white blood cell count. During re-exploration for the purpose of inserting a new mesh and after the anatomical planes had been completely dissected, the abscess was discovered. This alarming finding created a significant problem for the patient, who was obese and also had chronic pulmonary disease. Nonetheless, the possibility of a secondary mesh infection was real, and it was decided to excise the infected area and drain it with a Jackson Pratt device emerging through the skin directly above the site. The wound was closed without repairing the defect, and the patient was placed on specific antibiotic therapy. He was then discharged to be readmitted at a later time for a definitive repair. From that time on, there always remained the concern that, under similar circumstances, an abscess might have remained undetected in the depth of a wound. This concern prompted us to test previously infected wounds percutaneously.

II. PATIENT DISCLOSURE

The reinsertion of a mesh in a previously infected field for the purpose of correcting a recurrent hernia demands complete disclosure of possible complications to both the patient and the family. The need for repeated surgical procedures must be carefully and patiently delineated to a group already taxed by the occurrence of the infection. It is important to make them aware that the surgeon cannot completely eliminate the possibility of reinfection and that percutaneous testing may avert further complications or even a catastrophic event. It should be stressed that this procedure will delay the final repair. In my experience, patients were appreciative of this dialogue and became compliant. (See Table 1.)

III. TECHNIQUE

In an operating theater, under aseptic conditions, after preparing and draping the skin with the same precautions undertaken for a regular operation, a 22-gauge 3 1/2-in. needle is inserted into random areas on both sides of the previous incision. The needle should penetrate the fascia, reaching the muscle layer. The skin areas over the puncture sites

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Table 1 Postherniorrhaphy Mesh Infection Management Plan

1.	Meet *often* with patient and family.
2.	Explain the reasons behind wound infections.
3.	Diagram the situation in the chart and show it.
4.	Disclose the reasons behind your plan of action.
5.	Predict the need for repeated procedures.
6.	Predict a post-treatment recurrence.
7.	Disclose your plan for definite therapy.
8.	Keep the patient informed and reassured.
9.	Do not hesitate to consult.

are numbered with an indelible pen and the specimens labeled accordingly so as to facilitate further wound exploration. The aspirated fluid, blood, serum, or pus is placed in broth and taken immediately to the laboratory for culture and sensitivity testing. If there is any doubt about the reliability and expediency of this transport, I recommend that the surgeon deliver the specimen to the microbiologist personally in order to avoid common delays and errors of the sort that can produce a false-negative result.

IV. MANAGEMENT

If the results of percutaneous testing are negative, the surgeon may proceed with the repair. If they are positive for bacteria, the patient should undergo treatment of the infection with a specific antibiotic under the guidance of an infectious disease specialist. Three weeks later, the percutaneous testing is repeated in the areas where the infection was found; if the results are then negative, there is a good chance that no further treatment will be necessary and surgery can be completed. If, however, the test is again positive, the wound should be explored and all recesses debrided, curetted, or excised, followed by adequate drainage and/or secondary closure. The skin labeling will facilitate the search. I recommend a pre-exploratory set of imaging tests such as computed tomography (CT) or ultrasound, which may help to delineate the infected area. After complete healing is achieved, the percutaneous wound testing should be repeated (Fig. 1).

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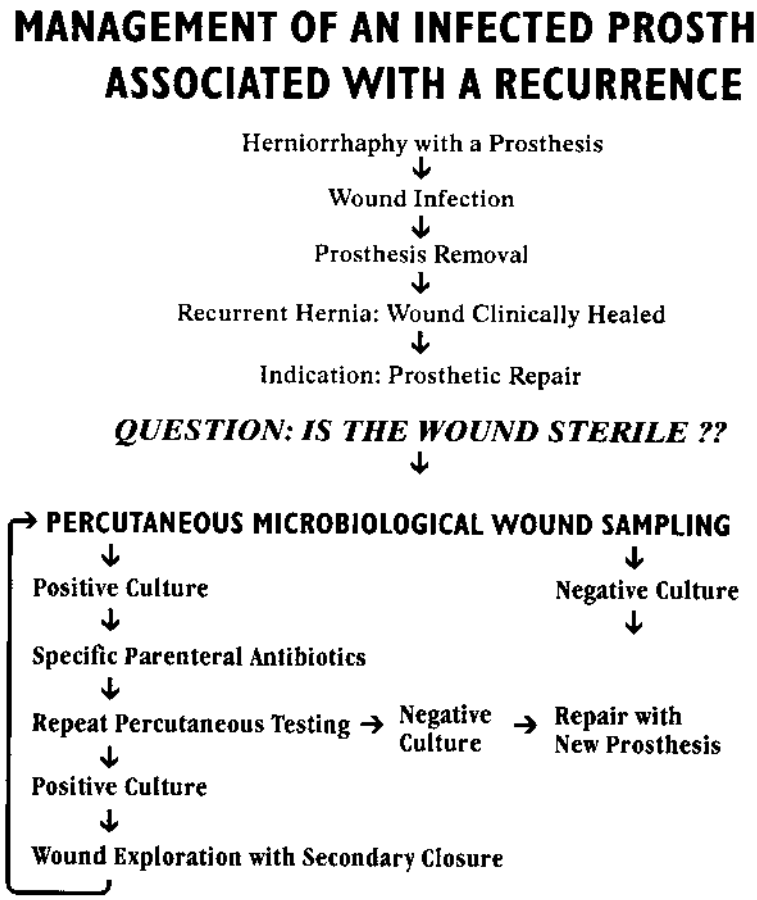

Figure 1 Algorithm depicting the recommended course to be followed in the presence of a recurrent hernia appearing in a previously infected site. The major stumbling block for prosthesis reinsertion under these circumstances is the possible uncovering of a bacterial colony, which would contraindicate the procedure. Although time-consuming, this diagnostic procedure enables the surgeon to estimate the sterility of the surgical field.

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V. OUR EXPERIENCE

We utilized this technique in 12 patients who consulted us with a history of infection following mesh repair, requiring mesh removal. All the wounds were clinically healed without sinus tracts or erythema, and the hernia had recurred. All the percutaneous tests were negative, and after mesh reinsertion, all wounds healed uneventfully. A follow-up of 6 years revealed one recurrence, requiring site reinforcement, and no further infections.

VI. COMMENTS

Although this form of management may seem cumbersome and time-consuming, it is the only way to reasonably assure the patient and the surgeon that the insertion of a new mesh has the best chance of success under the previously described circumstances. ''Best chance'' does not mean absolute assurance. However, we are not aware of any other technique that may solve this problem.

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17

Prevention

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I. INTRODUCTION

The preceding chapters have described the pathogenesis and natural history of hernia mesh infection, demonstrating that the overwhelming majority of these complications emanate from exogenous bacteria. Having established this fact, we now survey their sources, recommending measures to impede their invasion, diminish their food substrate, and finally exterminate them. Our goal is to persuade the reader that adequate infection control can diminish or even eliminate infection in mesh hernia surgery.

In essence, the formation of a wound infection requires a critical bacterial mass plus a measure of organic material to nourish it, permitting the bacteria to survive after contamination. On the other hand, healthy tissues coated by extracellular space fluid seem to resist bacteria well [1].

Today, over 80% of herniorrhaphies are performed with prostheses, and although synthetic materials seem to be inert, as discussed by Bryers (in Chap. 6) and Gupta and DeBord (in Chap. 5), they interact with host tissues at their surface atomic level, facilitating or inhibiting adhesion, integration, inflammation, and immune responses, which depend on a variety of surface factors.

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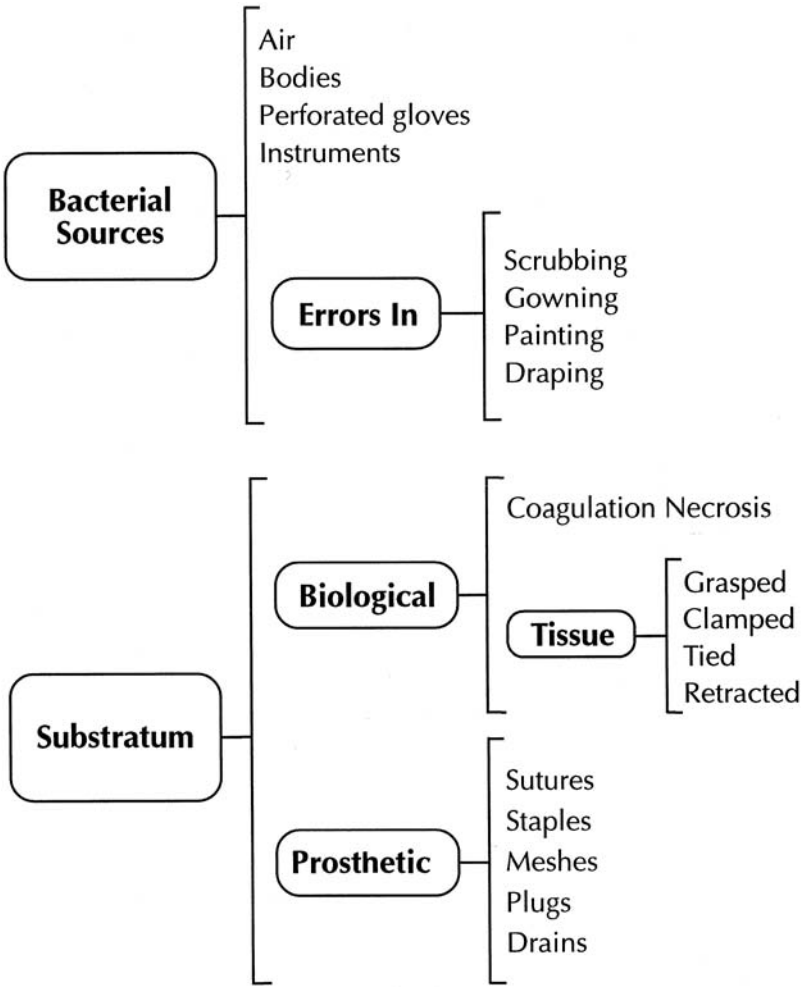

Figure 1 List of potential sources of bacterial wound invasion and the wound substratum from which they feed, colonize, and reproduce. Although none of these factors is solely responsible for an infection, their addition or combination greatly enhances its possibility.

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Hernia prostheses can be either hydrophobic or hydrophilic, and their capacity to attract or reject water molecules makes them more or less amenable to bacterial binding [2].

Bacterial wound invasion is produced by mechanisms that can be significantly curtailed by the application of proven principles. Based on reliable data, bacterial entry, adherence, and colonization in a herniorrhaphy wound are not chance occurrences but expected events, and their reduction should be a high priority for the surgeon [3]. It is of importance to notice that the frequent suggestion that meshes can be rejected by immune mechanisms is not supported by scientific facts; neither is the opinion that prostheses by themselves can produce infections in susceptible individuals. Prostheses are rejected through a process of suppuration after becoming colonized by bacteria. (See Figs. 3 to 6.)

II. THE SIGNIFICANCE OF FOREIGN BODY INSERTION

The surgical insertion of large foreign bodies began when Charnley popularized hip and knee replacements. However, these procedures were initially associated with high infection rates, prompting surgeons to implement a methodology to reduce them [4]. The subsequent orthopedic data clearly demonstrated that prothesis implantation should be undertaken only if the operating theater provides means to diminish the number of environmental bacteria entering the wound [5]. We believe that prosthetic herniorrhaphy should be performed under the same conditions of antisepsis and asepsis, because the total surface area of a large propylene mesh used for a ventral herniorrhaphy far exceeds the surface of any orthopedic prosthesis. This situation is magnified when expanded polytetrafluoroethylene (ePTFE) material is utilized, because its real surface vastly exceeds that of polypropylene.

Mesh insertion performed without the utilization of the highest degree of protection available against bacterial colonization exposes the prosthesis to infection. These realities emphasize the need to persuade surgeons to perform mesh hernia surgery in state-of-the-art operating theaters [6].

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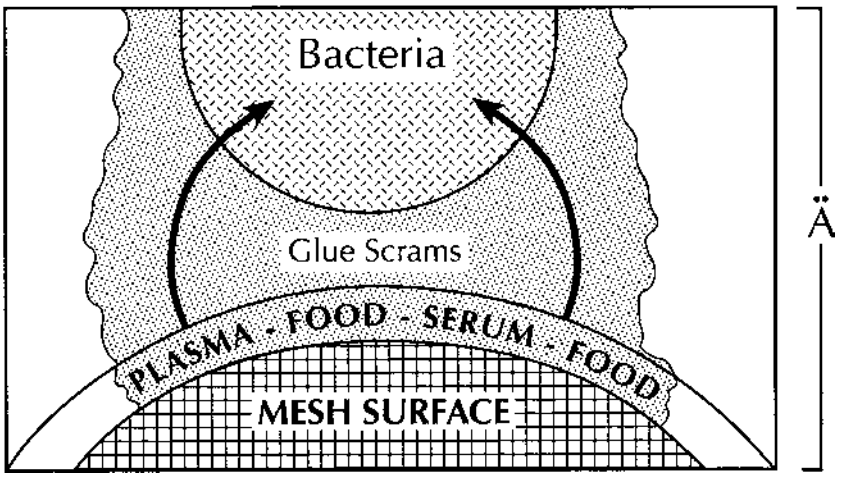

Figure 2 Diagram depicting the Darwinian capacity of bacteria to first adhere to the mesh surface, to commence feeding, and finally to colonize it. Unseen by the naked eye, mesh contamination will ensue unless it is avoided by the use of systemic and local antibiotics.

III. INFECTION CONTROL IN THE OPERATING THEATER

Since Von Bergman, surgeons have attempted to isolate the operative wound from the outside air, with varying success [7]. There is strong evidence that bacteria can enter a wound from a diversity of sources within the operating theater, and, as in other infection-control situations, this is a controllable variable [5]. The contemporary surgical team has at its disposal new and relevant information about bacterial biology as well as gadgets, antiseptics, and other equipment designed for bacterial control. It is the surgeon's responsibility to enforce and persuade his or her team about the need for strict antisepsis. Although no single defense element can be responsible for success, the combination of all will yield improved and acceptable results [8].

What follows is a description of measures that can be implemented to prevent infection.

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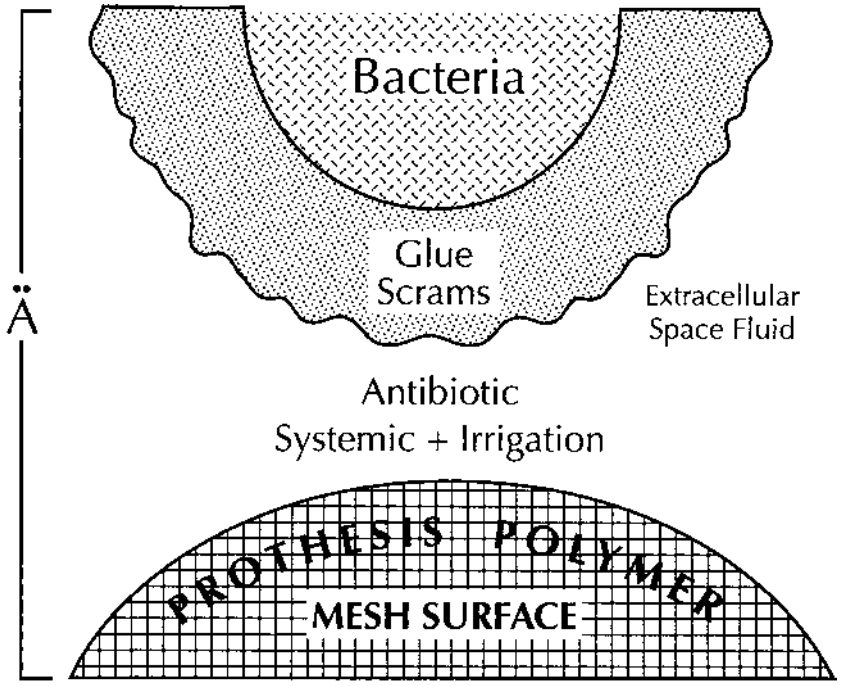

Figure 3 Diagram depicting the elements that will be in contact with a prosthesis, depending on circumstances. Fibroblast contact leads to healthy healing by collagen deposition. Initial bacterial contact with the biomaterial leads to colonization. The surgeon can avoid such contamination by using local and systemic antibiotics.

IV. MEASURES DEALING WITH SKIN BACTERIA

Normal human skin and its sweat glands contain bacteria, particularly in the vicinity of natural cavities. Accepted methods of skin preparation do not completely eliminate such micro-organisms, the presence of which constitutes a constant challenge for the surgical team. Skin shaving just before surgery decreases postoperative infections by eliminating bacterial colonization of nicks and cuts produced by the razors.

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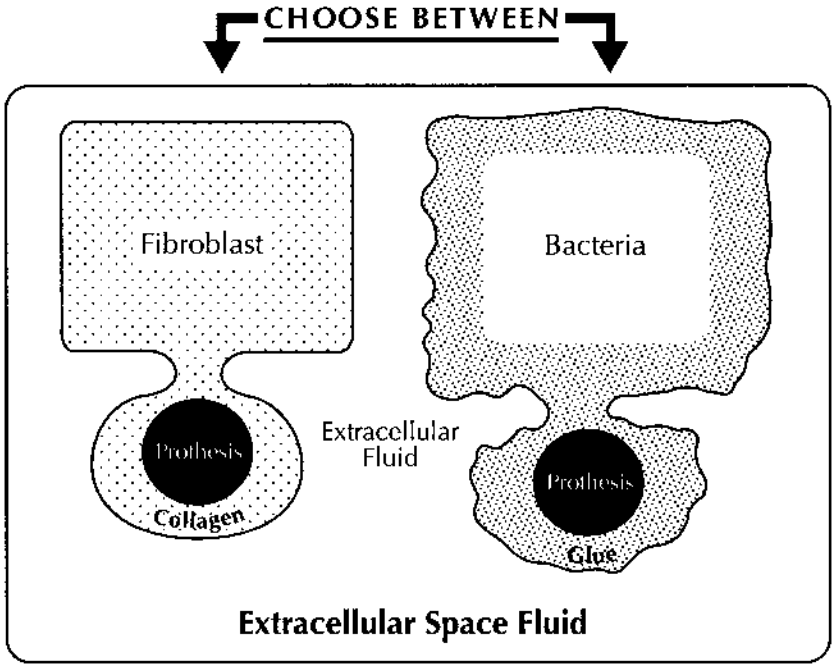

Figure 4 Diagram depicting alternative wound scenarios. Surgeons have the choice of drastically reducing bacterial mesh contamination by allowing healthy fibroblasts to contact the prosthesis first. The alternative gives bacteria a chance to succeed.

A. Recommendations

We shave our patients on the operating table just before surgery. Skin preparation should include a vigorous scrub with an antiseptic soap, followed by painting with antiseptic solutions. The painted area should generously exceed the margins of the planned incision so as to prevent wound contamination from adjacent unprepared skin, the margins of which may be reached when the surgeon is retracting or extending the cut.

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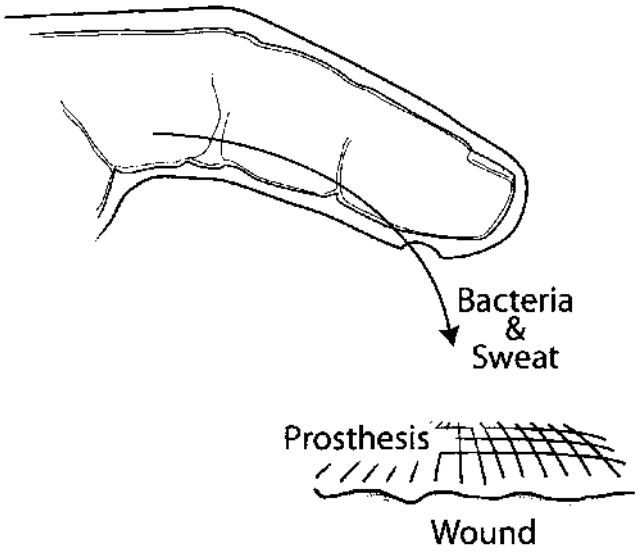

Figure 5 Diagram depicting sweat contaminated with bacteria entering the wound through a perforated glove. This problem is perhaps the most important source of bacterial wound contamination and can be prevented by double gloving and minimizing hand contact with the wound.

V. CONTROL OF BACTERIA ENTERING THE WOUND FROM THE AIR

Operating rooms generally receive an unfiltered outside air supply, which transports bacteria. In essence, the air circulating in ordinary operating rooms may be as contaminated with bacteria as that of the rest of the hospital. Logistical and economic factors have prevented many hospitals from constructing operating theaters that control air filtration, direction, and rate of flow. Studies by Charnley demonstrated the causative role that operating room air may play in infections, and his team has instituted environmental changes geared to change air flow filtration and direction. His results were confirmed by Ayliffe, who reported that operating room air should ideally be changed 25 times per hour [9].

Subsequently, M.J. Hubbell demonstrated that ultraclean (filtered) laminar airflow reduced the infection rate after hip and knee replacement by 50% [10]. Supporting this finding, Lidwell, in a multicenter study of

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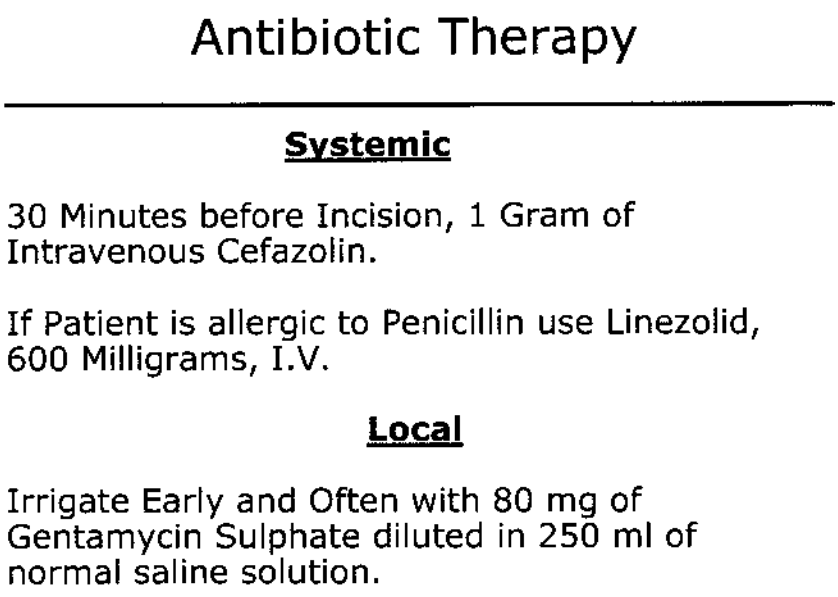

Figure 6 Recommended program of prophylactic systemic and local antibiotics designed to prevent postoperative infections. Since the inception of this protocol in 1981, no further infections were seen in over 4000 external abdominal wall repairs.

8000 total hip replacements, found that air and wound bacterial counts and subsequent infection rates were significantly lowered by the utilization of ultraclean air systems; these figures improved when antibiotic prophylaxis was added [5].

A. Recommendations

If your present operating room does not meet such standards, it is recommended that the specific hospital committee should take steps to implement the necessary alterations.

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VI. BACTERIAL SHEDDING FROM THE BODIES AND GOWNS OF TEAM MEMBERS

Body motion produces bacterial shedding into the wound, adding to that already due to the air [11]. In conventional theaters, if caps and masks are omitted and cotton gowns are used, the wound bacterial count rises sixfold [12]. Attempts by Cox et al. to prevent such contaminated air from coming in contact with a wound by operating through plastic bubbles proved to be cumbersome and unsuccessful [13]. As demonstrated by Charnley, shedding of micro-organisms by the operating room personnel can be curtailed by the introduction of ventilated personnel hoods, which reduced the infection rate from 9 to 1% [14]. In addition, Hubble in 1993 demonstrated that if the surgeon leans forward over the wound, bacterial wound contamination increases 27-fold and also recommended the use of body-exhaust suits [11].

A. Recommendations

Mesh hernia surgery should be performed utilizing body exhaust suits in utraclean rooms, which filter and direct the incoming air.

VII. BACTERIA ENTERING THE WOUND FROM SURGICAL ERRORS

Throughout the years, surgeons have developed a series of motions utilized during skin painting, draping, gowning, gloving as well as changes in position during the operation, all geared at avoiding contamination of the operative field. Unrehearsed or careless draping may lead to contamination as drapes are allowed to drag over nonsterile areas. Departures from these almost ceremonial routines increase the possibility of contamination.

A. Recommendations

Gowning and gloving should be performed with carefully rehearsed maneuvers under the surveillance of the whole team to prevent well-documented but often undetected contamination. New and inexperienced

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personnel should be drilled in their performance before they are allowed to become involved in an operation. Equally important is that gowned personnel avoid contact with nonsterile objects and people.

VIII. BACTERIA FROM THE TEAM'S HANDS AND THE LIMITATIONS OF GLOVE PROTECTION

Since Semmelweis correlated hand-carried bacteria with puerperal sepsis, surgeons have utilized a variety of methods to decrease such contamination, with limited success [15].

The work of Dineen and others emphasized that hand scrubbing should be adequate and conscientiously done. However, despite all efforts made to sterilize the surgeon's hands with bactericidal detergents containing povidone-iodine, chlorhexidine, or alcohol compounds, it is virtually impossible to eliminate micro-organisms from the depths of sweat glands from whence they will eventually resurface. Residual antibacterial product remaining on the skin surface reduces the bacterial flora but does not eliminate it.

Glove utilization has evolved from serving to protect the surgeon from infected patient matter to providing a barrier against the transmission of bacteria from the surgeon's hands to the wound. Today, gloves also protect hospital personnel from HIV infection. The surgical team should remember that the bacterial count on gloved hands increases with time. Furthermore, after 2 h of work, gloves develop micropunctures, allowing micro-organisms to escape and virtually irrigate wounds with bacteria-laden sweat. Gloves should be considered an ephemeral measure in preventing wound infection. Watson-Jones recommended minimal hand manipulation of the wound. He considered only the business ends of the instruments to be sterile [16–21]. There is increasing evidence that double gloving reduces bacterial leakage into the wound from 59 to 25% [22]. An additional problem is that gloving requires some form of friction-reducing agent. Talcum powder, abandoned because of its tendency to produce granulomas, was replaced by cornstarch, a substance that also induces a tissue inflammatory reaction and thus increases the chances of infection [22–25].

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A. Recommendations

Surgeons should double glove and rinse gloves frequently in normal saline solution to remove clots and fat. It is important to avoid touching the wound and the business end of the instruments with one's gloved hands. Finally, the wound irrigation removes residual lubricating materials left by the gloves.

IX. BACTERIA FROM TRANSITING NONGARBED PERSONEL

It is a common occurrence that personnel not involved with the procedure transit through the operating room for a variety of reasons. Even if gowned, those individuals carry bacteria from dirty to clean areas, presenting a real logistical challenge for those who strive for a cleaner operating environment [26].

A. Recommendations

The rule against such transit should be strongly enforced by the circulating nurse, as the rest of the personnel are busy with the procedure itself and cannot see who is moving around. The operating room personnel should present at all times a polite but adversarial attitude toward those who transit into their territory.

X. BACTERIA ENTERING THE WOUND FROM DRAINS

Regardless of whether atmospheric pressure or suction is utilized for wound drainage, these devices establish an open connection between the outside bacteria and the wound. Micro-organisms in such devices would vigorously defend their utilization because it assures them a constant food supply. Protracted drainage constitutes an invitation to infection. Drains are seldom utilized in inguinal herniorrhaphy, but their employment in ventral repairs is widespread and should be restricted to a short postoperative period.

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A. Recommendations

Drains should be used only when absolutely necessary. They should be well covered by sterile dressings and removed as soon as their function has ended.

XI. INCORPORATION OF ENDOGENOUS BACTERIA INTO THE WOUND

The overwhelming majority of wound infections emanate from exogenous bacteria. However there is evidence in the orthopedic literature suggesting that bacteria originating from sources such as tooth cavities or other septic foci may eventually reach the wound, producing a time-delayed infection. Immune-suppressed patients are very susceptible to such infections, as are those receiving prolonged corticosteroid therapy.

A. Recommendations

Prophylactic peroperative antibiotics and particularly systemic antibiotic therapy used during the manipulation of septic foci may diminish endogenous infections. This group of patients will benefit from consultation with an Infectious disease specialist who can offer advice about the antibiotic of choice. Most importantly, every attempt should be made to curtail corticosteroids before elective surgery is undertaken. If surgery is emergent, patients should receive empirical perioperative and postoperative antibiotic coverage.

XII. MEASURES TO DISCOURAGE THE WOUND SUBSTRATE FROM FEEDING BACTERIA

Once in the wound, bacteria will rely on some form of nourishing substrate on which to feed and ultimately reproduce. It is the task of the operating team to reduce this food supply.

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XIII. REDUCTION OF THE AMOUNT OF TISSUE CRUSHED BY CLAMPS, RETRACTORS, AND OTHER INSTRUMENTS

The surgical act exposes the tissues to varying degrees of stretching, compression, and shearing; forces that may produce cell death or vascular disruption, creating necrotic material. Cell damage produced by retractors, clamps, and forceps is proportional to the amount of the forces applied over a given surface:

$$\text{Pressure} = \frac{\text{force applied by the instrument}}{\text{the instrument's active surface}}$$

Accordingly, small-end forceps produce significantly more trauma than broad-end ones. Equally so, the pressure generated by retractors during a time period is relative to the number of dead cells left in the wound. Such areas of necrotic bacterial substrate can be minimized by the judicious and minimal utilization of crushing instruments of all kinds.

A. Recommendations

Although it is difficult to eliminate such factors from the surgical act, an attempt should be made to minimize the use of crushing instruments. Tissue handling by instruments is best kept at a minimum, and instruments that have the broadest working ends should, as far as possible, be chosen. Also, the repeated use of forceps over a singular tissue area is best avoided. If a portion of tissue seems devitalized, it should be excised.

XIV. TISSUE STRANGULATED BY LIGATURES AND SUTURE LINES

Ligatures, sutures, and tight suture lines constrict capillary circulation, producing areas of compromised tissue vitality that lead to necrosis at the sutured edges. These areas become a suitable media for bacterial colonization [3].

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A. Recommendations

Except when suture is involved in the repair itself, reabsorbable suture material should be used. Hemostatic ligatures or ties should be cut short to diminish the amount of nonviable material. Braided non reabsorbable suture materials should be avoided as they provide niches for bacterial survival. Prosthetic tension-free techniques markedly diminish this problem. However, the surgical team should be aware that undue force while tying knots or in continuous suturing creates the same problem.

XV. TISSUE NECROSIS FROM WAVE ENERGY

The electrocautery hemostasis of smal vessels is an indispensable element for the completion of a surgical procedure. At the same time, the electrocautery produces in-depth coagulation tissue necrosis similar to a third-degree burn, generating abundant food substrate for bacteria. The depth of such destruction depends on the integration of energy multiplied by the surface, all factors under surgeon control [27–31]. Manufacturers of radiofrequency units claim less in-depth damage, but this may be related to the intensity and the time during which the energy source is utilized, not on the type of wave [32].

A. Recommendations

Although these adjuvants have simplified surgery, they should be utilized with discretion to avoid creating an ideal medium for bacterial growth. On the other hand, scissors or scalpel produce a thin layer of cell necrosis. We recommend that electrocautery utilization be restricted to the gentle coagulation of bleeding vessels and not for cutting.

XVI. TISSUE NECROSIS FROM DESICCATION

Tissue dissection exposes a large number of live cells to dry and heated operating room air. The vitality of those exposed cells, essential for uneventful postoperative healing, depends on the hydration they can obtain from the underlying tissues. If allowed to die by desiccation, these cells will provide nutrition for the invading bacteria.

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A. Recommendations

The surgical team can significantly reduce cell death due to desiccation by frequent wound irrigation with isotonic fluids preferably containing an antibiotic. Equally beneficial is the covering of exposed tissues with towels soaked in those solutions.

XVII. WOUND FLUID EMERGING FROM EXTRAVASATED BLOOD, SERUM, AND LYMPH

Tissue dissection divides blood and lymph capillaries, the fluid from which then enters the wound. Such extravasation continues after the wound is closed, thus adding to the edema fluid created by trauma. This protein-rich aliquot is available for bacterial consumption.

A. Recommendations

Wound fluids should be rendered bactericidal by mixing them with antibiotic irrigation; otherwise its presence in the wound will permit bacteria to feed on a virtually ideal substrate.

XVIII. PATHOGENESIS OF BACTERIAL COLONIZATION

A. The Invasion

As discussed by Bryers, soon after their wound entrance, bacteria produce substances designated as microbial surface components recognizing adhesive matrix molecules (SCRAMS). These compounds recognize and adhere to fibronectin, fibrinogen, collagen, and heparin-related polysaccharides, all components present in host fluids that will eventually bathe the inserted prothesis. SCRAMS behave like an exchange resin through which bacteria can both feed and eliminate waste [33,34].

On the atomic level, prosthetic surfaces posses binding sites that will acquire and share a film of glycolproteinacious material available to host living cells, prosthetic molecules, and bacterial surfaces. Given enough time, this process will allow molecular cross-linking between bacterial SCRAMS and either host tissue or the prosthesis, producing an

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almost irreversible attachment by adhesion [35,36]. This combination of tissue fluids, bacterial glues, and prosthetic surface molecules forms a layer that antibiotics cannot reach, strongly supporting bacterial survival.

It is therefore important to accept the following concepts:

1. Bacteria will enter the wound.
2. The wound provides an organic substrate for bacterial nourishment.
3. Once in the wound, bacteria will undergo a series of Darwinian evolutionary events leading to their survival by feeding, reproduction, and eventual colonization of devitalized tissue or prothesis.
4. These events will produced an inflammatory response seeking to eliminate the bacteria by suppuration, creating a clinical infection [3].
5. Present knowledge about bacterial biology, the utilization of the available armamentarium, plus attitude modification can eliminate mesh hernia infection.

XIX. FACING REALITY

A. The Conflict

At the tissue level, these events suggest similarities between the bacterial–wound conflict and human wars. In both instances, it is a well-known fact that the best way to maintain peace is prevention, because the consequences of war are grave and long-lasting.

We believe that in dealing with what are called "clean wounds," infection is a preventable event as long as the surgical team is conscious that it is within its power to diminish the number of bacteria entering a wound and the amount of food substrate left in it. Once the biological counterattack occurs in the form of an inflammatory reaction, collateral prosthetic damage will occur from suppuration. As described elsewhere in this book by LeBlanc, DeBord, Chevrel, Kavic, Dayton, and Schumpelick [37–42], the long-term result of this conflict may require mesh removal, leading to hernia recurrence and protracted surgical treatment.

Both tension-free and conventional anatomical repairs produce a significant cytokine response within the inflammatory response [43].

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B. The Battle

1. Measures Recommended to Kill Bacteria After They Reach The Wound

Antibiotic Wound Irrigation During Surgery. Acknowledging the fact that a "clean wound" will contain bacteria, the surgeon can diminish their quantity, wound surface adherence, and reproduction by the use of systemic and local antibiotics. These have been extensively utilized by orthopedic and ophthalmological surgeons with encouraging results. Since 1984 and following the occurrence of five consecutive postinguinal herniorrhaphy wound infections, the author started to irrigate all of his herniorrhaphy wounds with a solution of 80 mg of gentamicin sulfate dissolved in 250 ml of normal saline or multiples thereof. The irrigation was initiated during the dissection of the deep planes and continued intermittently until the skin was closed. During the repair of large ventral hernias, the exposed tissue flaps were covered with towels soaked in this solution, in which the prothesis was kept until its insertion.

We empirically chose gentamicin because the literature around 1984 revealed that wound irrigation with neomycin, bacitracin, cephalosporins, and other agents did not eliminate infections in clean orthopedic wounds [44]. Later on, several orthopedic investigators utilized gentamicin beads, incorporated into cement or pin sleeves for the treatment of orthopedic wound infections. The pharmacodynamics of gentamicin release from polymethylmethacrylate beads placed in wounds was studied by Dirschl et al. [44] and Wahlig et al. [45] and from pin sleeves by Voos et al. [46]. Rutten et al. found that gentamicin could also lower the infection rate of contaminated surgical wounds [47]. That effect was reproduced in intraocular surgery by Dickey et al. [48]. Lately, Yamamoto et al. were able to prevent neurosurgical infections by irrigating their wounds with gentamicin [49]. Closer to our field, Musella et al. significantly diminished the infection rate in prosthetic hernia repair by inserting a gentamicin-impregnated collagen tampon in front of the prosthesis [50].

We were concerned about the side effects of gentamicin; however, blood levels of the aminoglycoside could not be detected 1 h after the end of eight inguinal herniorrhaphies during which gentamicin irrigation solution was used. Furthermore, none of the approximately 5500 patients in whom this solution was utilized (the group also included a variety of

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general surgical cases) exhibited evidence of systemic effects. These results coincide with those of Salvati et al. [51]. In 1996, Troy reported that topical cefazolin and bacitracin significantly decreased the quantitative growth of bacteria found in tissue from herniorrhaphy wounds. In their hands, topical and intravenous antibiotics seem to be equally effective [52].

2. *Peroperative Antibiotics*

The administration of peroperative prophylactic antibiotics is still controversial; however, several investigators encourage their utilization. In a 1991 supplement covering the subject, Archer et al. suggested that the hospital staff constituted a nosocomial reservoir for resistant organisms [53]. Reddington et al. stated that the goal of prophylaxis should be to provide serum levels of free antibiotic above the minimum inhibitory concentration (MIC) for the entire surgical procedure [54]. Waldogel and collaborators emphasized that because clean wounds are undoubtedly contaminated, the critical period of infection development is short. Thus, infection control becomes more of a quantitative than a qualitative problem. They further recommended that the time span of peroperative antibiotic administration should not exceed 24 h [55]. Hopkins provided clinical evidence that antibiotic prophylaxis in herniorrhaphy may decrease infections by 50%, advising caution on their utilization [56]. Hill, on the other hand, found that although prophylactic cefazolin was effective when used in regular operating theaters, he could not corroborate that effect in ultraclean ones [57]. Later on, Classen, Lazorthes, Wong-Beringer, and Abramov recommended perioperative utilization of antibiotics [58–61]. On the other hand, Gilbert, in a cooperative study, did not find enough evidence to support their use [62].

We administer a single 1-g dose of a second-generation cephalosporin (cefazolin, or Ancef) half an hour before the incision is made. After its utilization in over 4300 herniorrhaphies, we have not detected systemic or local evidence of bacterial overgrowth. If the patient is allergic to penicillin, antibiotics are either withheld or, for those at higher risk for infection because of a compromised immune system or long-term corticosteroid treatment, we recommend a single perioperative dose of linezolid, a new oxazolidinone. This agent has been found by Stevens et al. to be as effective as oxacillin-dicloxacinin in the treatment of soft tissue infections, and it can be utilized in penicillin-allergic patients [63].

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In our hands these measures have eliminated wound infections in over 4000 inguinal and 400 ventral herniorrhaphies performed over the last 18 years.

3. *Bacterial Killing by Binding Antibacterial Agents to the Meshes*

In order to diminish bacterial mesh colonization, several investigators have attempted to change the physical and chemical properties of the prosthetic materials by several approaches: DeBord et al. found no adverse human reactions after the utilization ePTFE patches impregnated with silver and chlorhexidine [64]. As reported by Zdanowsky, the adherence of *Staphylococcus aureus, S. epidermidis*, and *Escherichia coli* to ePTFE, Dacron, Dacron impregnated with gelatin, double-knitted velour Dacron impregnated with bovine collagen, or Dacron externally coated with bovine collagen was lower than in untreated Dacron or ePTFE. Coating with human plasma reduced bacterial adherence to woven Dacron and increased the adherence to ePTFE [65]. Montdargent and Letourneur found that the fibronectin-promoted in vitro adhesion of *S. epidermidis* to fibronectin-coated surfaces could be inhibited by derivatized dextrans, which function as heparin-like molecules [66]. These findings were reproduced in vivo by Rojas et al., opening a new horizon on the development of protheses resistant to bacteria [67]. The release of antibody from a polyurethane hydrogel coated with bioactive antibodies cast on a polymer biomaterial imparted enhanced bacterial killing, reduced bacterial adhesion, and increased infection resistance to *E. coli* [68]. These findings support the idea of creating a prosthetic polymer that by itself can prevent bacterial colonization, thus diminishing the risk of infection.

XX. IMMUNE THERAPY IN THE FORM OF VACCINES

Recently, Shinefield and colleagues successfully utilized a *S. aureus*–conjugated vaccine to prevent infections in 1804 patients receiving hemodialysis for end-stage renal disease. This afforded a 40-week period of immunity, halving the number for bacteremic episodes. Under those circumstances, *S. aureus* are killed by polymorphonuclear neutrophils and antibody-mediated opsonophagocytosis. In vitro data from that study showed that both methicillin-resistant and antibiotic-sensitive strains of *S. aureus* are killed by the same mechanism. The investigators

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stress the fact that ''because patients receiving hemodialysis are among the less likely to have a response to inmunoprophylaxis, the efficacy of the vaccine may be at least similar or perhaps greater in other patient populations.'' These promising results suggest that, in the future, patients could be preoperatively immunized against the bacteria that commonly colonize our protheses. If these findings are confirmed, they may open a new chapter in the prevention of wound infection [69].

XXI. SUMMARY

The present armamentarium allows the surgeon to drastically diminish bacterial volume and nutritional substrate, both elements involved in the pathogenesis of wound infection. However, behavior modification is needed to reach this goal, and the teaching of it should commence early during residency training, emphasizing the fact that the present infection rate should be considered unacceptable and a major subject for academic scrutiny.

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