Foreigners in our body

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"...equipments are used for the management of many serious illnesses but, in fact, they are foreigners in our body. These foreigners ... can ... be problematic, resulting in many complications, the most serious and devastating of which is an infection."

New developments in technology and in modern medicine have provided us with various medical equipments, including indwelling vascular catheters, cardiac pacemakers, prosthetic heart valves, chronic ambulatory peritoneal dialysis catheters and prosthetic joints [1]. These equipments are used for the management of many serious illnesses but, in fact, they are foreigners in our body. These foreigners may be comfortable but can also be problematic, resulting in many complications, the most serious and devastating of which is an infection [2].

The diagnosis of foreign-body infections is important, and management of these infections is often very difficult because most of them result in high mortality and morbidity. Frequently, patients are managed with a long period of hospitalization, which requires many courses of antibiotics, as well as surgical interventions, all of which can negatively impact on patients' quality of life. These medical cases are also associated with increased costs to healthcare systems [3].

There are various types of foreign body that are used for different aims, yet we do not have consensus definitions or guidelines of what constitutes an infection and its severity, nor do we have any well-designed large studies supporting methods of investigation and management of these infections.

A foreign-body infection often involves a host immune response to one or more microbial pathogens on an indwelling implant. Logical and scientific management requires understanding the pathogenesis of these infections. First, the microorganisms attack the surface of foreign material and, subsequently, colonization begins. Complicated steps follow the colonization, which result in biofilm formation [4].

The biofilm layer protects the microorganisms and, if antimicrobial therapy were to be used alone, it may be ineffective. With the assistance of the biofilm layer, microorganisms cause local damage and proliferate. Fever, embolic events and severe systemic inflammatory response syndrome can occur and result in the loosening of implanted devices, wound dehiscence or disruption of prosthetic valves [4].

Clinical manifestations of foreign-body infections vary depending on the virulence factors of the pathogen, host immune response and the affected component of the foreign body. The time period after foreign-body implantation is very important in choosing the most suitable empirical antimicrobial therapy, based on the signs and symptoms that have developed. Microbiologic specimens are the keys for therapy. Although the infected foreign body should be removed, some studies have investigated methods for the salvage of foreign bodies. However, we have no defined indications as to which salvage therapy may be warranted. In practice, many patients do not want further surgical interventions, so sophisticated prevention strategies and definite suppressive antimicrobial therapy must be considered [5].

During the past two decades, in order to lower the risk of infectious complications in foreign-body infections, laminar airflow with ultra-clean air in operating rooms, routine antimicrobial prophylaxis, short operating times, the use of antibiotic-bonded cement and antimicrobial-coating of foreign bodies have been applied in most

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hospital settings, especially in orthopedics [5]. However, despite all prevention strategies, there are no apparent or proven methods for reducing foreign-body infections. Over the past few years, orthopedic implants have become the most important component of modern medicine. In the USA and the UK, more than 200,000 and 50,000 total hip replacements are performed annually, respectively [6]. Together with the rapidly rising elderly population in industrialized countries, the requirement for many orthopedic foreign bodies increases. Nearly 15 million people have at least one interne fixation and 12 million have an artificial joint [7].

Pathogenesis and the occurence of the biofilm layers are part of foreign-body infections. There is not an internationally accepted classification system for implant infections. A frequently used classification system is based on the time when infection occurs [8]. Early postoperative infection is a type of acute surgical-site infection, occuring 2–4 weeks after surgery. Persistent pain after surgery, fever, sweating, redness and swelling at the implanted area are the signs and symptoms of an early postoperative infection. In the acute phase, *Staphylococcus aureus* and coagulase-negative staphylococci are the most commonly isolated microorganisms [9]. The diagnosis should be conducted carefully between the superficial or deep implant infections. For suspected early infections, salvage therapy can be the solution but the clinician should evaluate the characteristics of the patient and the infection carefully [9].

Late chronic infection is the second type of postoperative infection and frequently originates at the time of surgery. The onset is between 16 months and 2 years after surgery. Persisting pain can be the only symptom. Coagulase-negative staphylococci, *Propionibacterium* species and anaerobes are the responsible pathogens [9]. The surgical removal of the implant or the extensive debridement with aggressive antimicrobial therapy are the available choices for treatment [9].

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The last type of postoperative infection is the hematogenous infection, which occurs 2 years after the surgery. The signs and symptoms are the same as the early postoperative infection after a long period of good health. Streptococci, *S. aureus* and Gram-negative bacilli are the most frequently isolated microorganisms. Immunosupressive or transplant patients are at particular risk of this infection because it results in hematogenous spreading of the pathogens [9].

Salvage of an implant can be considered if the onset of acute infection is under 28 days, if their is a stable implant with no signs or symptoms for loosening, only one microorganism is isolated from multiple specimens by aspiration or intraoperative culture of surgical debridement and the pathogen is susceptible to antimicrobials. Salvage can also occur in patients who accept long-term antimicrobial therapy [9].

There are many limitations for this treatment strategy, the most important of which are the long time period required and the strict rules regarding the treatment. Limitations for this strategy include the patients requiring frequent visits, possible prolonged time without a cure, adverse reactions of antimicrobial therapy and the difficult adaptation period for long-term antimicrobial therapy, which oblige patients to change their doctors. Other limitations are the patients' underlying illnesses and advanced age, both of which can interfere with the treatment.

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The required time for this prospective type of research is 2–6 years because one should follow all the patients and, if necessary, one should perform debridement and modification of antimicrobial therapy, as well as follow the adverse events of this therapy [10]. There is a necessity for close collaboration between surgeons, infectious-disease specialists, microbiologists and pathologists for the diagnosis and management of these infections. The specialist should carefully evaluate the patient, their underlying diseases, the type of implant and the quality of the bone stock for the successful management of such infections.

Together with the developments of orthopedic surgery, new terms appear, such as 'orthopedic implant infections' or 'orthopedic foreign-body infections'. If one searches for orthopedic foreign-body infections in Medline/PubMed, there are many reviews and articles. Most of these are regarding implant infections, such as their demographics, pathogenesis and, especially, diagnosis and treatment. What about the other foreigners in orthopedics, such as external and internal fixators, and intramedullary nails, plates and rods? Are there any differences between these, especially for the definition, management or the treatment of these infections?

In conclusion, foreign-body infections, especially those due to orthopedic implants, are increasing in our country and worldwide, while there are inadequate studies to define these infections. In order to define and substantially reduce these infections, there need to be specific guidelines providing evidence-based recommendations for each type of foreign-body infection and comprising of both technological and nontechnological strategies for their prevention.

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