Peri-implant Disease

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9.1 Osseointegration: An Almost Perfect Relationship Between Metals and Living Tissues

According to the Centers for Disease Control and Prevention, the number of US adults with complete tooth loss has decreased from 49% in 1960 to 13% in 2012 [1, 2]. In addition, elderly adults are motivated to maintain their dentition since tooth loss has an impact on their oral health-related quality of life [3]. Some benefits to having a full complement of teeth include improved esthetics, function, nutrient intake, and self-esteem. The number of people that are keeping their teeth is on the rise, and when patients are missing individual teeth, implants have become a therapy of choice.

The replacement of missing teeth is one of the most challenging treatment modalities in dentistry. The traditional approach is to maintain the patient's existing dentition for as long as possible prior to

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resorting to tooth replacement strategies. Some of the conventional tooth replacement options include complete dentures, removable partial dentures, and fixed partial dentures. All of these options require rigorous maintenance and repair regimen and fall short of ideal replacement strategies in terms of function and esthetics. One of the functional benefits of implants as opposed to dentures is the continuous mechanical load exerted on the surrounding alveolar bone, resulting in bone maintenance and prevention of bone loss.

In general, loss of functional use and mechanical stress results in gradual resorption of bone, both in terms of height and width [4]. This has been referred to as disuse atrophy, which suggests that the body eliminates bone that is not actively stressed. According to Wolff's law, bone adapts its mass and structure to the mechanical demands placed on it [4]. One of the functional benefits of dental implants is the continuation of the mechanical stress exerted on alveolar bone, resulting in the prevention of bone resorption. While humans have attempted to replace natural teeth with implants for more than 1500 years, implants only became a reliable treatment option during the 1970s [5, 6].

Early dental implant technology consisted of blade and transosteal implants, and it was thought that both of these implant types relied on mechanical retention [7]. A wide array of metals and implant designs were used unsuccessfully. One implant design that is frequently referenced is the subperiosteal blade implant developed by Dahl in the 1940s [8]. This implant was inserted between the bone and the soft tissue and therefore relied on soft tissue anchorage. These implants were fraught with complications and were typically removed soon after placement due to infection, inflammation, and foreign body response [9].

Early endosseous implant studies revealed the remarkable ability of bone to tolerate metal implants and even tightly surround the inserted metal shaft. This phenomenon was first described by Bothe in 1940 and by Leventhal in 1951; however, it was not until 1952 that Per Ingvar Brånemark coined the term "osseointegration" [6, 10, 11]. Brånemark was studying blood flow in rabbits and discovered that titanium chambers placed in the rabbit tibia and fibula could not be removed from the bone after implantation. These studies prompted Brånemark to develop a dental implant fixture using pure titanium screws. Further studies demonstrated that these titanium implants demonstrated predictable long-term results [12].

Years after the original Brånemark implants were produced, Schroeder and Straumann in Switzerland worked with various alloys used in orthopedic surgery to develop their own dental implant [13]. In 1980, Schroeder initiated the International Team for Implantology (ITI), which helped stimulate advances in implant research and development. Several implant designs were developed and tested, including the Core-Vent, Stryker root form, and IMZ implants [7]. After years of testing, mainly through trial and error, some implants left the market and others withstood the test of time. The most popular dental implant designs used today are threaded, root-form implants with various surface treatments to facilitate osseointegration (Fig. 9.1).

The original Brånemark implants had a smooth, machined surface, while most modern-day implants have a roughened surface. The original Brånemark implants called for a 6-month healing time before loading while the modern-day roughened surface implants can be loaded in as little as 6 weeks [14]. The roughened implant surface results in an increase in surface area, allowing for increased bone apposition and better stress distribution along the implant body [15]. It has been shown that a roughened surface promotes bone formation by increasing the proliferation of cytokines, growth factors, and osteoblasts [16]. Some common surface treatments to create this roughened surface include sandblasting, acid etching, anodizing, electrochemical treatment, vacuum treatment, thermal treatment, and laser treatment [17]. Comparing smooth and rough surface implants side by side, it has been demonstrated that soft tissue adheres more readily to a smooth surface while bone tends to favor a roughened surface [18]. This concept has led to the design of a smooth collar at the top of the implant to facilitate soft tissue adherence.

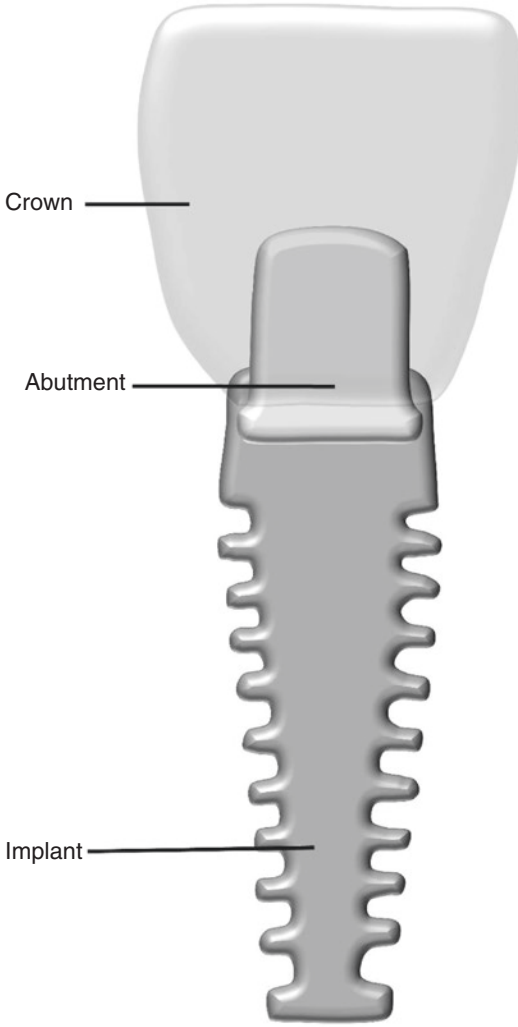

Fig. 9.1 Basic components of a typical dental implant. Dental implants usually consist of an implant fixture that anchors the implant in the bone (Implant), an abutment, that connects the implant fixture with the crown of the tooth (Abutment), and a prosthetic crown, that esthetically and functionally mimics a tooth crown of a healthy tooth (Crown)

The interface between bone and the oral cavity consists of a soft tissue barrier that includes sulcus, epithelial attachment, and connective tissue attachment [19]. This soft tissue barrier provides a protective seal between the bone and the outside world. In health, this soft tissue barrier prevents bacteria and debris from causing bone loss around the tooth. The integrity of this soft tissue seal is compromised in implants. According to Berglundh, the epithelial attachment is similar, while the connective tissue does not attach to the implant surface [20]. Other studies emphasized that the epithelium adheres to the implant via hemidesmosomes, but the connective tissue encircles the implant without attaching to the implant [21, 22]. These studies suggest that a tooth has a stronger biological seal than an implant, resulting in increased susceptibility of implants to invasion by bacteria and other debris.

Titanium became the material of choice for implants in both the dental and medical fields due to its perceived biocompatibility and its ability to form a seamless boundary between bone and implant, the process that Brånemark called osseointegration. Implants were considered biocompatible because of their ability to perform with an appropriate host response in a specific application [23]. Titanium is considered the most biocompatible metal due to its resistance to corrosion from bodily fluids, inertness, and relatively high fatigue limit. From an immunological perspective, implant biocompatibility is based on its containment in a tough, thin, avascular capsule that is quiescent [24].

Originally, the concept of osseointegration implied that bone is in intimate contact with titanium. However, in a typical dental implant, bone is in close proximity to the implant but does not adhere to it [24]. There is a thin biological layer between the bone and the implant, approximately 20–50 nm thick, is referred to as the "zone of tolerance." [25, 26] This zone is composed of a titanium oxide layer, ground substance, and a cloud of zwitterionic forces that create enough friction to prevent implant movement. A zwitterion is a molecule that contains both a positive and a negative charge and therefore serves as a buffer between two dissimilar molecules. The titanium oxide layer is one of the key components responsible for titanium biocompatibility. The oxide layer insulates the titanium and serves as a buffer between the titanium and bone. Without a titanium oxide layer, titanium would become highly reactive and susceptible to corrosion [24].

Most modern-day implants utilize a design known as platform switching in order to maintain alveolar bone height over time. This design

comprises an implant design in which the abutment of the restored implant is of narrower diameter than the implant diameter. For example, if the implant is 6 mm in diameter, the portion of the crown that is attached to the implant is 4 mm in diameter. This concept was accidentally discovered when 3i Implant Innovations used abutments that were narrower than their implants. Lazzara and Porter reported that less bone loss was seen with platform switching [27]. The platform switch allows for the bone to form an implant–bone interface to the very top of the implant without a separate restorative component impinging on the bone to implant connection. This also will allow the oral mucosa to generate a soft tissue seal around the abutment and the crown as opposed to the implant body itself. Studies have demonstrated that platform switching, in contrast to platform matching, results in reduced bone loss after implant restoration [28, 29]. According to these and other studies, platform switched implants reveal minimal bone loss in the first year of service, and bone will even grow back to the coronal portion of the implant over time. Based on a study of platform switched Nobel implants that had been followed for 20 years, Chrcanovic reported that 11% of those implants displayed a gain in bone height and 36% experienced bone loss less than 1 mm [28]. In another study using platform switched implants, Froum detected an average of 0.8 mm of bone loss after 1 year, which decreased to only 0.3 mm of bone loss at 8 years [30].

In general, dental implants are regarded as a safe and highly effective treatment option for replacing missing teeth [24]. Compared to traditional modes of tooth replacement, dental implants have several benefits, including maintenance of bone height, stable anchorage for fixed restorations, and preservation of adjacent teeth when compared to bridge or denture-based applications. Moreover, implants allow for superior esthetics and function when compared to alternative tooth replacement options. In an effort to standardize the evaluation of implant health, Albrektsson et al. formulated five essential criteria for implant success in 1986 [31]. The criteria include: (1) immobility of the implant; (2) a lack of peri-implant radiolucency on a radiograph; (3) less than 0.2 mm vertical bone loss after the first year of service; (4) the absence of pain, infection, neuropathy, paresthesia, or violation of the mandibular canal; and (5) a minimum success rate of 85% at 5 years and 8% at 10 years. The authors also considered 1.5 mm of crestal bone loss within the first year a success and attributed this loss to the formation of soft tissue attachment.

Unfortunately, in recent years, the remarkable success rate of dental implants has turned them into a cure for all when only slightly compromised teeth have been replaced by implants without a clear prognosis for the implant to surpass the natural tooth in terms of longevity. A recent article in the *Journal of Dental Research* "Are Dental Implants a Panacea?" [32] asks whether the recent implant epidemic has led to the removal of teeth that could have been salvaged by conservative means. The article suggests that the longevity of even severely compromised teeth may far surpass that of the average dental implant if properly maintained [33, 34]. The readiness to apply dental implants without immediate clinical need raises eyebrows when clinical indicators of peri-implantitis have been reported in up to 45% of implant patients (Fig. 9.2) [35]. These recent studies by Giannobile, Derks, and others [36] have raised concerns about the unreflected use of implants as a means to an end for all dental health concerns regardless of the remarkable clinical success rates in many cases.

In addition to the increased readiness to place implants and potential side effects related to peri-implantitis, another worrisome trend has marred the once-untainted success story of dental implants: the changing training and skill levels of practitioners involved in placing implants. The high commercial profit margin associated with implant procedures has attracted a wide range of clinicians of various skill sets and training levels to participate in the profitable business. The original Brånemark implants were typically placed in a sterile operating room setting by oral and maxillofacial surgeons, while today, most implants are placed

in a private practice setting by a variety of dental professionals. Continuing education courses and dental school curricula include training on the placement and restoration of dental implants (Fig. 9.3). As a result, implants are being placed and restored by individuals with varying educational backgrounds. According to Adell, inexperienced surgeons had a 5-year implant survival rate of 75% while experienced surgeons had a 5-year survival rate of 98% [37]. Lambert found that inexperienced surgeons had implants fail twice as often as experienced surgeons [38]. Da Silva conducted a practice-based research network study where implant parameters were measured over time in multiple general dentists' offices [39]. That study found that after 4 years, 7% of the implants were classified as failures and 18.7% were considered to have excessive bone loss. The authors concluded that implants placed by general dentists have a higher failure rate when compared to those placed by specialists.

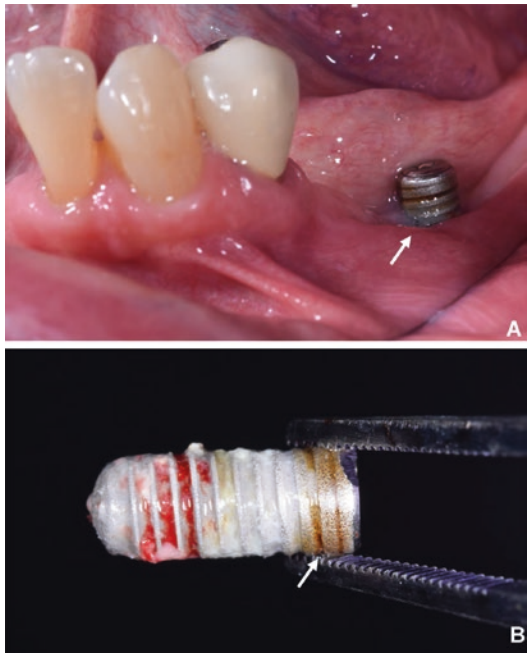

Fig. 9.2 Clinical signs of peri-implantitis. (**a**) Redness of the mucosal tissue immediately surrounding the implant surface (arrow). (**b**) Clinically visible signs of corrosion on the implant surface

According to the American Academy of Periodontics, implants displaying evidence of peri-implant disease suffer from either peri-implant mucositis or peri-implantitis [40]. Peri-implant mucositis entails the inflammation of the soft tissue around an implant without the loss of bone [41]. Peri-implantitis involves inflammation of the soft tissue and progressive bone loss around

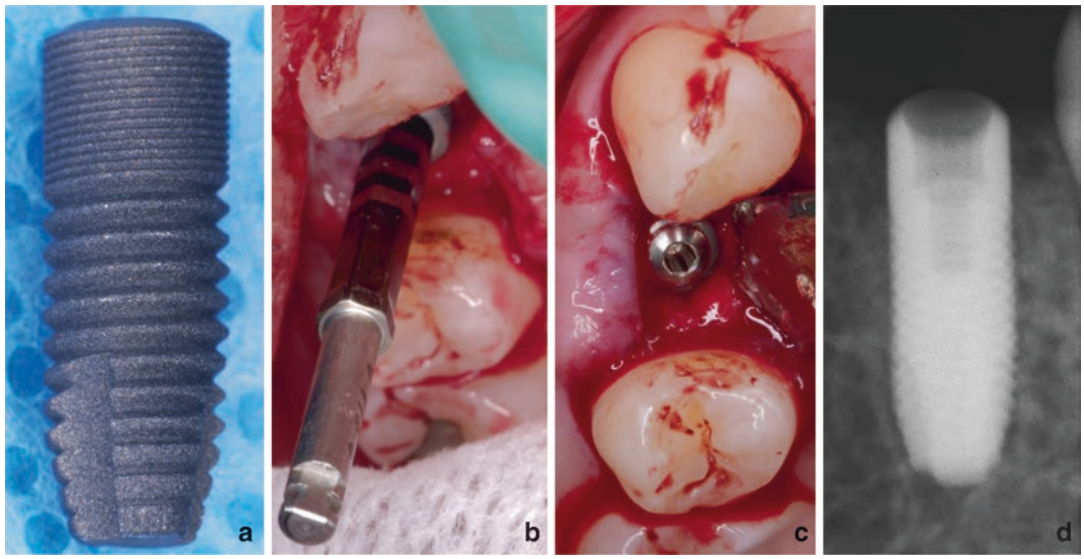

Fig. 9.3 Stages of implant placement. (**a**) Implant fixture, (**b**) insertion of the implant into the bone, (**c**) position of the implant between two adjacent teeth, and (**d**) radiograph of the successfully placed implant

the implant. According to a systematic review by Atieh et al. [42], peri-implant mucositis affects 63% of implant patients while peri-implantitis affects 19% of patients. To aid the clinician in determining the prognosis of a diseased implant, Froum et al. [43] have classified peri-implantitis into three different categories: early, moderate, and advanced. Early peri-implantitits is defined as an implant with a periodontal probing depth of greater than 4 mm, with bleeding upon probing and bone loss of less than 25% of the implant length. Moderate peri-implantitis entails probing depths from 6 to 8 mm with bleeding upon probing and 25–50% bone loss. Advanced peri-implantitis is an implant with a periodontal probing depth of greater than 8 mm, with bleeding upon probing and bone loss of greater than 50% of the implant length.

Peri-implantitis may eventually result in implant failure, which usually requires surgical removal of the implant in order to prevent further pain, infection, and bone loss. Becker et al. [44] described implant failure as the presence of implant mobility and radiolucency around the implant. In addition to these criteria, several other clinical observations such as pain, infection, tissue inflammation, and degree of bone loss help the clinician determine whether the implant is salvageable or needs to be removed.

Several studies have evaluated factors that could contribute to implant failure, yet in many cases the cause remains unknown. The timing of implant failure and an understanding of the healing process are useful tools that aid the clinician in determining the potential causes of failure. Chrcanovic et al. [45] define primary, or early, implant failure as the failure of an implant to osseointegrate after it has been placed in bone (i.e., failed to form a close union between the implant and surrounding bone during healing). Some studies speculate that primary implant failure may be due to overheating of the bone and/or poor surgical technique, even though a cause and effect relationship remains to be established [46, 47].

Chrcanovic et al. [45] call secondary implant failure a process that occurs later than primary implant failure and that is due to progressive bone resorption around the implant (i.e., advanced peri-implantitis). Studies demonstrate that bone loss around an implant could be associated with one or more of the following: poor clinical handling, poor implant design, complex patient medical history, poor oral hygiene, overloading of the implant due to the crown being too high, excess cement, or a response to foreign particles embedded in the tissue [45, 48–51]. Some of the clinical parameters for secondary implant failure include deep probing depths (using a periodontal probe), bleeding upon probing, purulence, pain upon palpation or percussion of the area, and radiographic bone loss.

9.2 Risk Factors Contributing to Implant Disease

Several patient-related risk factors are known to contribute to peri-implant disease, including smoking, diabetes mellitus, and pre-existing periodontal disease (Fig. 9.4). Smoking and its relationship to periodontal destruction has been discussed extensively in the literature [52, 53]. A longitudinal study by Miller et al. conducted statistical analyses of several variables that may contribute to tooth loss and found that smoking was the most important risk factor for tooth loss [54].

Several mechanisms by which smoking affects wound healing are discussed by Rivera-Hidalgo [55]. Nicotine decreases the proliferation, attachment, and chemotaxis of periodontal fibroblasts. Fibroblasts are a key cell that function in the healing and turnover of periodontal tissues. Smokers also suffer from decrease in oxygen delivery to the periodontal tissues, which leads to an increase in anaerobic bacteria. In smokers, polymorphonuclear leukocytes (PMN) cells have decreased motility and function, resulting in decreased periodontal immunity. Smokers typically experience severe xerostomia, which facilitates an increase in bacterial adhesion to the soft tissue and inadequate salivary flushing mechanisms. Smoking also reduces blood perfusion in the small capillary network of the periodontal soft tissues. As a result, periodontal connective tissues do not receive enough nutrients and are not able to rid themselves of waste products. Budunelli et al.

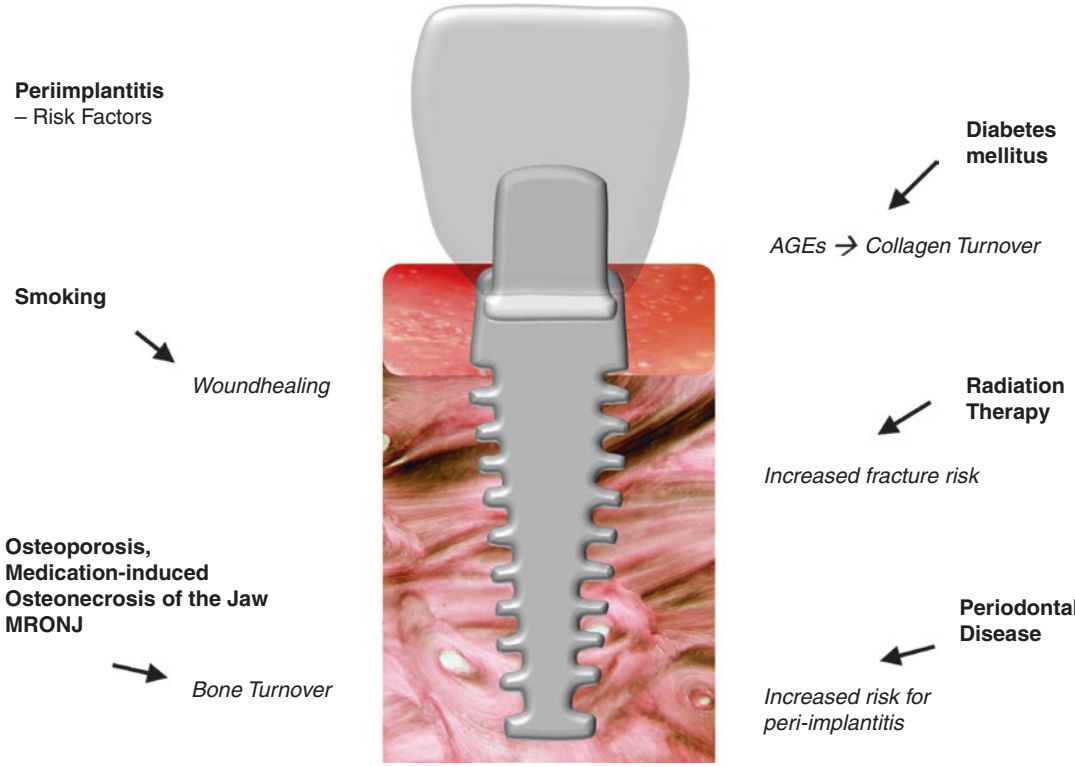

Fig. 9.4 Risk factors contributing to peri-implant disease. Factors contributing to peri-implant disease include diabetes, smoking, radiation therapy, periodontal disease, and osteoporosis and osteonecrosis

found that smokers have an altered RANKL to osteoprotegrin ratio [56]. RANKL is an acronym for receptor activator of nuclear factor kappa-B ligand, which binds to RANK in order to trigger bone resorption. Osteoprotegrin is a protein that can bind RANKL in order to minimize its effects. As a result, the catabolic bone resorption signaling surpasses the anabolic aspect of new bone formation in smokers, resulting in an imbalance of the bone regenerative periodontal homeostasis toward the katabolic aspect. Finally, a smoking-related increase in advanced glycation end-products (AGEs) results in a decrease in oxygen delivery to periodontal tissues and a decrease in collagen turnover [57].

Smoking appears to have a similar impact on dental implant health as well. Karbach et al. demonstrated that smoking was the most important risk factor for the formation of peri-implant mucositis [58]. It has also been reported that bone loss around implants in smokers is twice as high as in nonsmokers [59]. Chung et al. studied a variety of implant designs in smokers and nonsmokers placed over a 21-year period [60]. They found that smokers had almost 3 times more annual bone loss than nonsmokers. Another study that examined long-term results of implants found that the rate of implant failure was higher in smokers than in nonsmokers [61]. The authors concluded that the higher failure rate in smokers was due to a reduced healing capacity among patients who smoke.

Curiously, implant surface modifications may improve implant longevity more so in smokers than in nonsmokers. One study compared machined implants and oxidized implants in smokers and nonsmokers [62]. This study demonstrated that bone loss around machined implants was twice as high in smokers as in nonsmokers while there were similar bone levels and failure rates between smokers and nonsmokers when oxidized implants were used. In another

study, Balshe and coworkers found that rough surface implants in smokers had no significant failure rate, while there was a significant failure rate associated with smooth surface implants [63]. While some studies show reassuring results with rough surface implants, smoking is still considered a risk factor for peri-implant disease.

The effect of diabetes mellitus on periodontal health has been well established [64, 65]. There is evidence of a bidirectional relationship between diabetes and periodontal health in which the stability of one disease influences the other. Löe was the first to suggest that periodontal disease is the sixth complication of diabetes [66]. Some of the common complications found in diabetics include cardiovascular disease, neuropathy, nephropathy, retinopathy, and vascular changes. When a patient has prolonged elevated blood glucose, there is an increase in advanced glycation end-products (AGEs), which results in diminished oxygen delivery to tissue, poor collagen turnover, and reduced healing capacity. Prolonged diabetes is also associated with decreased PMN leukocyte motility and function, decreased fibroblast function, and increased RANKL/osteoprotegerin ratio [65]. A patient with well-controlled diabetes will typically have fewer of these sequelae and will hence heal better than an uncontrolled diabetic.

Elevated blood glucose as it occurs in diabetic patients and its level of control affect both periodontal therapy and implant therapy. In animal models, diabetic pigs have less bone-to-implant-contact and rats injected with AGEs exhibit a slower rate of osseointegration [67, 68]. Another study on diabetic rats reported decreased bone density around the implants [69]. Studies in humans have identified a correlation between uncontrolled diabetes and bleeding upon periodontal probing around implants, but they did not report an increase in bone loss or implant failure among diabetics [70–72]. Other studies in humans have suggested that periodontal wound healing occurs at near physiological levels in a well-controlled diabetic (Hemoglobin A1C ≤ 7) [73].

Based on their effect on bone density, osteoporosis and bisphosphonate treatment of osteoporosis and cancer have been tested for their relationship with implant failure. Osteoporosis is known for causing a decrease in bone density and is typically found in postmenopausal females [74]. In general, multiple cohort and meta-analysis studies have identified a slight correlation between osteoporosis and implant failure, but the correlation is weak and not statistically significant [75, 76]. Many osteoporosis and cancer patients are prescribed bisphosphonates, which decrease bone loss by inhibiting osteoclasts. Osteoclasts are bone cells that degrade bone into its mineral components. Without the help of osteoclasts, the jawbone is lacking in healing capacity and is therefore susceptible to a condition known as bisphosphonate-related osteonecrosis of the jaw (BRONJ). Several other medications, such as RANK ligand inhibitors and antiangiogenics, induce a similar phenomenon and so the term has been changed to medication-related osteonecrosis of the jaw (MRONJ) [77]. Some bisphosphonates, such as intravenous (IV) and nitrogen-containing oral bisphosphonates, are associated with a higher incidence of MRONJ [77]. Shabestari et al. conducted a case series on 21 patients taking oral bisphosphonates and reported that bisphosphonates had no effect on implant health [78]. A retrospective study on 362 patients treated with dental implants found no correlation between bisphosphonates and implant failure, but there was a correlation with implant thread exposure over time [79]. Together, these studies indicate that bisphosphonates do not have a substantial effect on implant failure.

Radiation therapy is often administered for the treatment of head and neck cancer [74]. This treatment can result in severe dry mouth and altered function of the bone and soft tissue. Similar to MRONJ, a history of radiation therapy can result in a condition known as osteoradionecrosis of the jaw. A systematic review based on 10,150 implants determined that implants placed in irradiated bone had a 174% higher chance of failure [80]. Thus, caution is advised when implant placement in irradiated bone is considered.

Periodontal disease not only affects the attachment and retention of natural teeth but is also implicated in the loss of implants due to peri-implantitis. Periodontal disease has a wide array of causes and risk factors but is most commonly

associated with bacterial plaque and the host immune response [81]. Periodontitis and peri-implantitis are both typically associated with a certain bacterial profile, namely, gram-negative anaerobic bacteria [82]. In addition, certain patients may be more susceptible to the deterioration of the periodontium due to individual variables such as medical history, social history, bacterial flora, and genetic profile [81].

A cross-sectional study including 109 volunteers resulted in a significant correlation between implant failure and periodontitis [83]. Swierkot et al. conducted a prospective long-term study on patients with a history of generalized aggressive periodontitis, formerly known as juvenile periodontitis [84]. Despite the fact that the aggressive periodontitis was controlled prior to implant placement, these patients were more susceptible to peri-implantitis, peri-implant mucositis, and implant failure when compared to healthy control patients [84]. Another longitudinal cohort study on adults reported a significant correlation between severe chronic periodontitis and late implant failure [85]. Costa et al. noted an increased likelihood to develop peri-implantitis when patients with peri-implant mucositis did not attend regular maintenance appointments [86]. Together, these studies established a significant correlation between periodontitis and peri-implantitis.

Based on these findings, the dental professional must remain abreast of current research with regard to risk factors for developing implant disease and implant failure. Smoking, diabetes mellitus, antiresorptive therapy, antiangiogenic therapy, radiation therapy, and periodontal disease are some of the more common risk factors discussed in the literature. Of these risk factors, several studies suggest that smoking and periodontal disease are the most prevalent risk factors for developing implant disease [82, 83, 85, 87].

9.3 Etiology: Bacterial Plaque

One of the most controversial and highly studied questions in dentistry is "what causes implant disease?" [41, 42] Many authors consider a multifactorial etiology for peri-implant disease (Fig. 9.5). Assuming that all risk factors

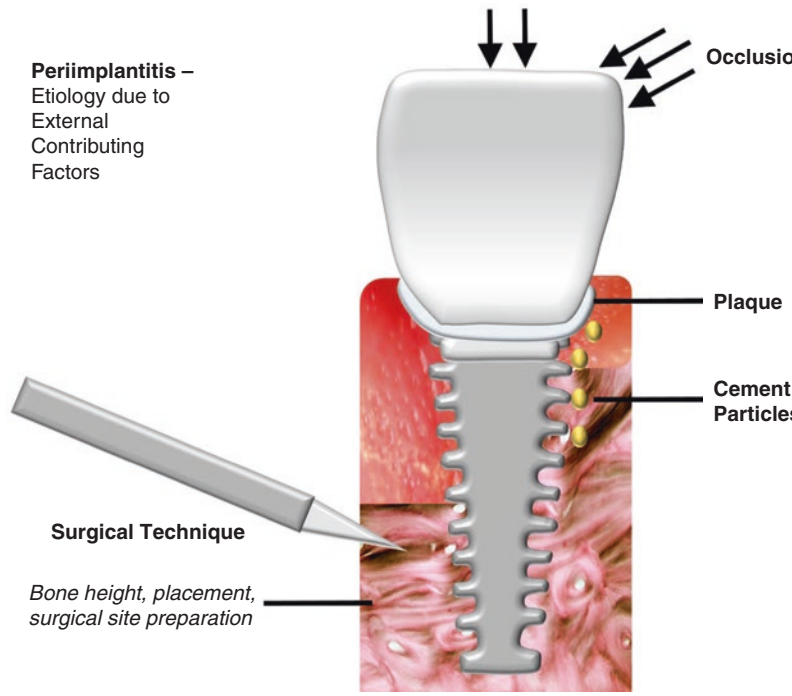

Fig. 9.5 External factors causing peri-implant disease. External factors contributing to the etiology of peri-implant disease include surgical technique, occlusion, plaque, and cement particles

are controlled and the patient is healthy, patients may still develop implant disease or implant failure due to yet-to-be-defined etiologies.

Bacterial plaque is among the most commonly discussed primary etiologies for gingivitis, periodontitis, and peri-implant disease. A well-organized biofilm on an implant surface appears to initiate and propagate peri-implant disease and peri-implant mucositis in a similar fashion as biofilms on the tooth surface cause gingivitis and periodontitis [41]. The early stages involve soft tissue inflammation and a shift from gram-positive aerobic bacteria to gram-negative anaerobic bacteria. If this early lesion is left unclean and uncontrolled, the plaque matures and the inflammation progresses and ultimately results in bone and tooth loss.

In 1965, Löe demonstrated in humans that the accumulation of bacterial plaque on teeth leads to gingivitis and that gingivitis resolves once oral hygiene is reinstituted [88]. Pontoriero et al. conducted a similar study on implants, using teeth in the same patients as a comparison [40]. After 3 weeks of plaque accumulation, the teeth and implants both displayed similar changes in bleeding, swelling, probing depth, and bacterial profile. There was no statistically significant difference between the teeth and implants after plaque accumulation. The teeth developed gingivitis as expected, and the implants developed peri-implant mucositis. Unfortunately, the authors did not take measurements after the patients resumed oral hygiene and therefore did not demonstrate whether peri-implant mucositis is a reversible process. Salvi et al. conducted a similar study and included clinical measurements 3 weeks after the reinstitution of oral hygiene [89]. Gingivitis and peri-implant mucositis were found to be reversible at the biomarker level, but the clinical parameters had not yet reached the pre-experimental levels. These parameters did, however, show trends toward resolution in both teeth and implants.

The term "peri-implantitis" was first used by Mombelli in 1987 when he discovered that implants with bone loss harbored gram-negative anaerobic rods, black-pigmented bacteroides, fusobacterium species, and spirochetes [90]. When evaluating the microbiota of healthy implants in the same patients, Mombelli reported predominantly coccoid cells. He referred to peri-implantitis as a site-specific infection, which has many features in common with periodontitis.

Peri-implantitis is thought to be initiated in a manner similar to periodontitis, namely, by a mounting bacterial insult and a host response [41, 42]. Some studies document a similar bacterial profile for both peri-implantitis and periodontitis, while others reveal a unique profile for peri-implantitis [91]. An independent study group of 30 clinical experts met in Italy to systematically review the literature on peri-implantitis [91]. They concluded that peri-implantitis is not comparable to periodontitis since several anatomical differences exist between the periodontium and the peri-implant environment. Among potential microbes associated with peri-implantitis, the review lists gram-negative anaerobes, opportunistic microbes, Epstein-Barr virus, anaerobic gram-positive rods, and *Staphylococcus aureus*. Some papers have identified *S. aureus* as the microbe that initiates peri-implantitis, but this notion was refuted by the aforementioned review in Italy [92, 93].

Other similarities between periodontitis and peri-implantitis include similar inflammatory cascades [41]. Both inflammatory processes exhibit an upregulation of proinflammatory cytokines such as interleukin (IL)-1, IL-6, IL-8, IL-12, and tumor necrosis factor (TNF)-α [41]. However, peri-implantitis typically progresses more rapidly than periodontitis, most likely due to a less robust protective barrier around implants when compared to teeth. More specifically, teeth are protected through a connective tissue attachment and complex defense mechanism, while implants lack a connective tissue attachment and the interface between the implant and the bone is occupied by an avascular mucosa layer. A recent comparison noted a self-limiting process in teeth that separates the inflammatory lesion from bone through a protective connective tissue capsule, while such a separating barrier does not exist around implants [94].

Most modern implants feature a rough implant surface due to surface modifications including

sandblasting and surface etching. This roughened surface was introduced to enhance implant anchorage, adhesion, and stability. However, when it comes to plaque adhesion, the roughened surface provides a niche for bacterial plaque to firmly attach to the implant and create a mature bacterial colony [95]. Ultrasonic and hand instruments were designed to remove the majority of the plaque from a natural tooth, but they usually do not remove all of the hard deposits known as calculus [96]. Removal of bacterial plaque and calculus from implant surfaces is substantially more challenging due to the topography of the implant surface. Once the bacterial plaque has reached the implant itself, plaque removal becomes a challenge for the clinician, and there is a lack of universally accepted approaches for plaque removal from implant surfaces. Some implant companies supply "tissue-level" implants with a polished collar at the very coronal portion of the implant. This polished titanium is much easier to clean and allows for soft tissue adhesion. The drawbacks of this approach are poor esthetics and difficulties for crown design as it emerges from the implant.

9.4 Etiology: Occlusion

Occlusion is another potential factor that might contribute to implant disease and implant failure. While the effects of occlusion on teeth have been extensively studied, there is still a paucity of evidence regarding the effects of occlusion on implants [97]. A healthy tooth is suspended within its bony housing by the periodontal ligament (PDL). The PDL serves as a shock absorber, which distributes forces along the root [98]. The PDL also contains mechanoreceptors, which provide sensory feedback for the level of bit force and possibly monitor fine tuning. Implants, on the other hand, lack a PDL and are simply positioned in close proximity to the bone. As a result, implants lack the shock absorber effect of the PDL and do not provide occlusal feedback for microadjustments when the patient is chewing [99]. As another consequence of implant design, occlusal forces are concentrated at the crestal bone around implants [98]. Once loaded, teeth move between 25 and 100 micrometers (μm) in vertical direction and 56 and 150 μm in horizontal direction, while implants move only 3 and 5 μm vertically and 10 and 50 μm horizontally. The clinician is therefore faced with the challenge of creating a fine-tuned occlusal scheme that prevents excessive forces when the implants are in function.

The absence of a periodontal ligament as a resilient anchorage between implants and bone causes occlusal forces to directly affect adjacent bone. As a result, mechanical forces exerted on the implant supporting bone may either be physiological, relatively too high, or relatively too low. The level of forces transduced on implant carrying bone is of importance as bone is a tissue extremely susceptible to mechanical loading. To this date, Wolff's law about the responsiveness of bone to mechanical stresses holds true [4]. Elaborating on Wolff's law, Frost reported bone deposition or bone resorption depending on the direction and magnitude of the forces applied to bone [100]. Specifically, Frost determined that a very low amount of strain may result in disuse atrophy, a mild amount of strain maintains a "steady state," and an increased level of strain results in bone resorption and even bone fracture.

The resulting tissue damage from excessive occlusal forces on natural teeth and their supporting structures is called occlusal trauma. Occlusal trauma may result in bony changes, occlusal wear, widened PDL, and tooth mobility [101]. The effect of excessive occlusal forces on implants is called occlusal overload. Occlusal overload occurs when either normal function or parafunctional habits result in structural or biological damage, including damage to the prosthesis, implant, or surrounding bone [102]. It has been suggested that peri-implantitis and occlusal overload are the two most common causes of late implant failure [97]. Several authors have correlated occlusal overload with crestal bone loss [103]. Kozlovsky et al. demonstrated in a dog model that occlusal overload with uninflamed mucosa resulted in a slightly reduced marginal bone level [104]. However, bone loss beyond the implant neck only occurred in the presence of both occlusal overload and peri-implant inflam-

mation. Other consequences of occlusal overload include prosthetic screw loosening, screw fracture, prosthesis failure, and implant fracture [105, 106]. Implant fracture can lead to peri-implant bone loss, resulting in complete implant failure [107].

A dentition that no longer relies on natural teeth but rather on implants requires an appropriate occlusal design to maximize implant longevity and to prevent costly implant repair and replacement procedures. From a biomechanical perspective and according to Wolff and Frost, occlusal designs to support implant integration will minimize the amount of cantilever forces [4, 100]. In other words, vertical bite forces are preferred over torqueing forces as these push heavily on one side of the implant. Cantilever forces are minimized by using an implant prosthesis that is slightly narrower than a normal tooth. Occlusal designs that do not extend too far in any direction beyond the diameter of the implant itself are preferable [97]. Non-axial shearing forces resulting from the cusp inclination of the crown should be minimized.

There is no general agreement about the implant length necessary to support a crown that matches adjacent teeth in length and width [108]. A number of authors have reported equal success rates when using short versus long implants, while others have found inferior results with short implants [109, 110]. Authors who favor a short implant base argue that the apical length is less important since the majority of the forces exerted on the implant occur at the cervical bone–implant interface. A consensus to this debate remains to be seen, but most clinicians and implant companies prefer implants that are at least 8 mm in length [111].

In addition to narrow crown designs to avoid torque forces, optimal implant design from an occlusal perspective also includes very light or no occlusal contact with the opposing tooth when the dentition is in maximum intercuspation (i.e., biting down) [107, 112]. Such design compensates for the lack of PDL around the implant. When a dentition transitions from a physiological bite to a heavy bite, the PDL will allow the teeth to compress, but the implant will remain stationary. In addition, when the patient is moving their jaw in a lateral or excursive direction, there should be no contact on the implant crown. Parafunctional habits must also be considered during implant therapy. Patients who brux (grind their teeth) or clench their teeth have a higher risk of implant failure [113]. These patients may benefit from wearing an occlusal night guard in order to prevent excessive forces from parafunctional habits. An optimized occlusal design will have a profound impact on wear patterns and on the longevity of teeth and implants alike.

9.5 Etiology: Surgical Technique

Another potential factor contributing to peri-implant disease is the clinical technique used during implant therapy. The great demand for dental implant treatment and the high profit margins have led some practitioners to place implants in ways that do not follow the biological, surgical, and mechanical principles that were adhered to during the early years of implant treatment.

One of the key requirements for successful implant placement is the presence of a stable bony ridge to support the implant. Implants will be at a high risk for failure if the implant is not placed into bone of sufficient quality and quantity [111, 114]. Primary stability is also a requirement for osseointegration. A number of bone classification systems have been developed to aid the clinician in implant planning. Leckholm and Zarb distinguished between type I bone as compact cortical bone, type II as dense trabecular and cortical bone, type III as dense trabecular bone with thin cortical bone, and type IV as low-density trabecular bone surrounded by thin cortical bone [115]. Seibert created a classification system for the shape of the defect in edentulous sites [116]. A class I defect entails a loss of defect width, class II is a loss of defect height, and class III is a loss of both width and height. The maxilla typically has less dense bone than the mandible, and the posterior jaws are typically less dense than the anterior regions. As a result, the mandible typically has higher implant success rates and the posterior maxilla has higher failure rates [117].

The condition of the soft tissue is another critical variable for implant therapy. The soft tissue crevice around implants does not compare well to the highly differentiated attachment apparatus of healthy teeth. As a result, the mucosal periphery surrounding implants lacks the resistance against bacterial infection, resulting in inflammation of the healthy periodontium. In addition, some studies emphasize the need for a keratinized mucosa surrounding implants. The lack of keratinized tissue (gingiva) surrounding teeth has been demonstrated to result in inflammation, recession, and even tooth loss [118]. It is not clear to what extent the presence of a keratinized mucosa is a requirement for implant health. Wennström demonstrated that health can be maintained around both implants and teeth that do not have keratinized mucosa [119]. These results were obtained in patients with adequate homecare and periodic professional cleanings. Others have reported a greater degree of plaque accumulation and mucosal inflammation even though the lack of keratinized mucosa did not affect implant survival [120]. Block et al. demonstrated that a lack of keratinized mucosa was associated with crestal bone loss of 2 mm or more and that the presence of keratinized mucosa was directly correlated with soft and hard tissue health [121]. Therefore, the lack of keratinized mucosa due to anatomical or surgical conditions may affect implant health.

Surgical trauma during implant placement should be minimized in order to maximize the likelihood of proper healing. Bone is a living tissue, sensitive to heat, and overheating of bone during the preparation of the site for an implant can lead to necrosis [122]. The clinician must use the proper drilling sequence, and cooling aids to minimize trauma to the bone. Occasionally, the surgeon will inadvertently create a fenestration in the bone, resulting in a direct contact between implant and soft tissue during healing [111]. Such a condition may negatively impact the osseointegration of the entire implant.

Reports of bacteria associated with failed implants underscore the need for rigorous aseptic surgical conditions during implant therapy. An aseptic surgical field will help minimize bacterial contamination and will result in lower implant failure rates as well [111]. The widespread trend for implants to be placed by practitioners lacking proper surgical training may thus be one contributing factor to the rise in peri-implant disease. It is recommended that any practitioner placing implants uses sterile instruments, proper draping, and careful handling of the implant after removal from its package.

The flapless strategy for implant placement has become a popular surgical technique due to its simplistic approach and potential for better healing and esthetics. This technique typically entails creating a small hole in the soft tissue and then preparing the implant bed through this hole. Other benefits of this approach include less post-operative pain and less trauma to bone and soft tissue [111]. Froum et al. conducted a study comparing flapless and flap protocols for implant placement [30]. Contrary to popular belief, there was no difference in bone levels, probing depths, bleeding on probing, or papilla height 8 years after implant placement. The authors concluded that both protocols were equally successful. However, with advances in radiology and three-dimensional implant planning, it is feasible to use the flapless protocol as long as proper surgical technique is exercised.

Two approaches toward implant placement are commonly distinguished: the one-stage and the two-stage protocol. The one-stage protocol entails placing an implant and a transmucosal healing abutment at the same time. This allows the implant to osseointegrate and the surrounding tissue around the abutment to heal. With the two-stage protocol, the implant is buried underneath soft tissue and later uncovered for the attachment of a healing abutment. The benefits to the one-stage protocol are reduced time, money, and surgical trauma [111]. The healing abutment also allows for the early formation of a mucosal barrier while the implant is healing. The drawbacks to the one-stage protocol are the potential for bacterial contamination of the implant during healing and the potential for trauma to the implant by the patient. With the two-stage protocol, the implant is allowed to completely integrate prior to its exposure to the bacterial flora and mechanical forces of the oral cavity. Several studies have

reported a decreased risk of implant failure using the two-stage protocol; however, since the two-stage protocol involves additional time, money, and surgical trauma, it is up to the patient to choose one option over the other [123, 124].

A third surgical approach toward implant placement involves placing the implant into a fresh extraction socket and is commonly referred to as an immediate implant [111]. Benefits of this approach include a reduced number of surgeries and a faster result when compared to conventional therapy. The drawbacks to this procedure include increased risk of infection, low bone to implant contact, more bone resorption, and a higher risk of implant failure [125]. It is also likely that implant placement on the same day will further traumatize the alveolar ridge and the surrounding soft tissue after already suffering initial trauma due to the tooth extraction procedure. This enhanced trauma on the surrounding bone and soft tissues are likely the cause for the increased bone resorption and failure rates associated with immediate implant placement versus delayed implant placement [126]. A benefit to immediate implants that is worth noting is the ability to create a temporary crown or custom healing abutment on the implant. This will help to preserve the soft tissue dimensions that were present around the tooth prior to extraction. Nonetheless, implants placed using the immediate approach are more prone to implant failure than implants placed using delayed strategies.

Surgical technique is especially important to remove inflammatory tissues from the implant site prior to implant placement. One example are the periapical lesions that often occur at the apex of extracted teeth. Proper surgical protocol requires thorough debridement and cleaning of the lesion prior to implant placement. However, many dentists have successfully placed immediate implants in sockets containing periapical lesions, and randomized controlled trials have shown similar failure rates when implants were placed immediately in sockets with periapical lesions compared to those placed in healthy sockets [127, 128]. However, a concern about primary stability and osseointegration in such inflamed sites remains. Interestingly, a periapical lesion on a tooth adjacent to the implant poses a high risk for infection around the apex of the implant [129]. Thus, proper surgical site preparation is an important strategy to prevent future implant infection and failure.

9.6 Etiology: Cement

The prosthetic components that attach to an implant comprise an abutment, which screws directly onto the implant, and a crown or bridge prosthesis. Two types of implant surgeries are generally distinguished: the one-stage and the two-stage implant procedure. For the two-stage implant, the prosthesis is cemented onto the abutment in the clinic, while for the one-stage implant, the prostheses including the abutment are fabricated as one piece in the lab. The one-piece prosthesis is also referred to as screw-retained implant since it can be screwed directly into the implant without the need for dental cement. Both cement and screw-retained prostheses are used routinely in the dental office, but some dentists prefer the cement-retained approach since it is typically more affordable. The screw-retained prosthesis is distinguished by a hole in the final crown for access to the screw. The location of the screw access hole relies heavily on proper implant placement so that the hole does not affect the cosmetics or function of the restoration.

The drawbacks to a cement-retained prosthesis include difficulties for crown removal after cementation and a potential for extrusion of excess cement into the surrounding tissue. This excess cement is very difficult to remove and may be inadvertently left embedded in the soft tissue. In 1999, Pauletto et al. reported four cases in which excess cement was associated with inflammatory lesions around the implants [130]. Deep probing depths, bone loss, and purulence were noted during surgical removal of the excess cement, and the lesions resolved after cement removal. Another case report demonstrated implant failure that occurred 1 month after crown cementation [131]. During surgical removal of the failed implant, significant bone loss was detected adjacent to an area with excess

cement and inflamed granulation tissue. Wilson conducted a case-control study in which he compared 42 test implants with peri-implantitis to 20 healthy control implants [48]. He used a dental endoscope to explore the condition of the peri-implant mucosa. Excess cement was found in none of the controls and in 34 of the test sites. 30 days after removal of excess cement, 25 of 33 test sites had no clinical signs of inflammation. The author concluded that excess cement was associated with peri-implant disease.

Burbano et al. studied 19 human biopsies that were taken from implants with peri-implantitis and cement-retained crowns [51]. These biopsies were analyzed using scanning electron microscopy and elemental analysis in order to determine the presence of dental cement embedded in the soft tissue. All 19 of the specimens displayed evidence of cement in the soft tissue, and findings were correlated with five different commercially available cements. Penarrocha-Oltra et al. studied the presence of different bacteria present around screw-retained and cement-retained implants [132]. After sampling 55 cement-retained implants and 46 screw-retained implants, the authors detected a significantly higher bacterial load in the cement-retained group.

An in vitro study by Rodriguez et al. studied the effects of different dental cements on human gingival fibroblasts (soft tissue–forming cells) and on pre-osteoblasts (bone–forming cells) [133]. In this study, various dental cements displayed only minute effects on pre-osteoblasts, while effects on fibroblasts were significant. There was a statistically significant decrease in the number of human gingival fibroblasts when exposed to all cements with a singular exception. The cement with a lesser effect on fibroblasts contained zinc oxide noneugenol, with the trade name "Temp-Bond." Studies reviewed so far indicate that dental cement affects soft tissue health, bacterial load, and bone height in the implant periphery. The effect of cement on soft tissue inflammation would suggest a correlation between cement and implant failure; however, three different controlled clinical studies reported no correlation between cement-retained crowns and implant failure [134–136]. Thus, excess cement may have an effect on implant health, but not necessarily on implant failure.

9.7 Etiology: Titanium Allergy

Since its inception, titanium has been regarded as an extremely inert and biocompatible material. However, more recently, titanium has been associated with allergies, foreign body reactions, and particle release (Fig. 9.6). Reports related to allergic reactions to titanium have been on the rise [137]. The most common allergic reactions to titanium including types I, III, and IV. Type I hypersensitivity reactions are reactions in which the patient has been previously exposed to the allergen (i.e., titanium) and will mount a specific immune response to the allergen via IgE antibodies upon secondary exposure. This classic allergic reaction typically occurs within a short period of time. Type III hypersensitivity reactions are characterized by an excess of antigen-antibody complexes, which the body is unable to clear them from an affected area. This type of reaction develops within days or weeks. Type IV hypersensitivity reactions are cell-mediated and not antibody-mediated. Cell-mediated immune reactions occur when T helper cells recognize an allergen and secrete cytokines that cause a chain of events to occur. As a result of this immune reaction, the environment is infiltrated with aggressive and destructive cells such as macrophages, T lymphocytes, and mast cells, which cause damage to the surrounding area. Type IV reactions are delayed and take several days to develop.

Several authors have reported allergic reactions against orthopedic titanium implants associated with implant failure [137]. Examples include allergic symptoms in patients after the placement of titanium plates for fixation of bone fractures [138]. These patients were characterized by discoloration and titanium fragments surrounding these titanium plates as well as T lymphocytes and macrophages indicative of a type IV reaction in the proximity of the fracture prosthesis. In another study in patients with failing prosthetic hips, tissue samples once more contained T cells and macrophages indicative of

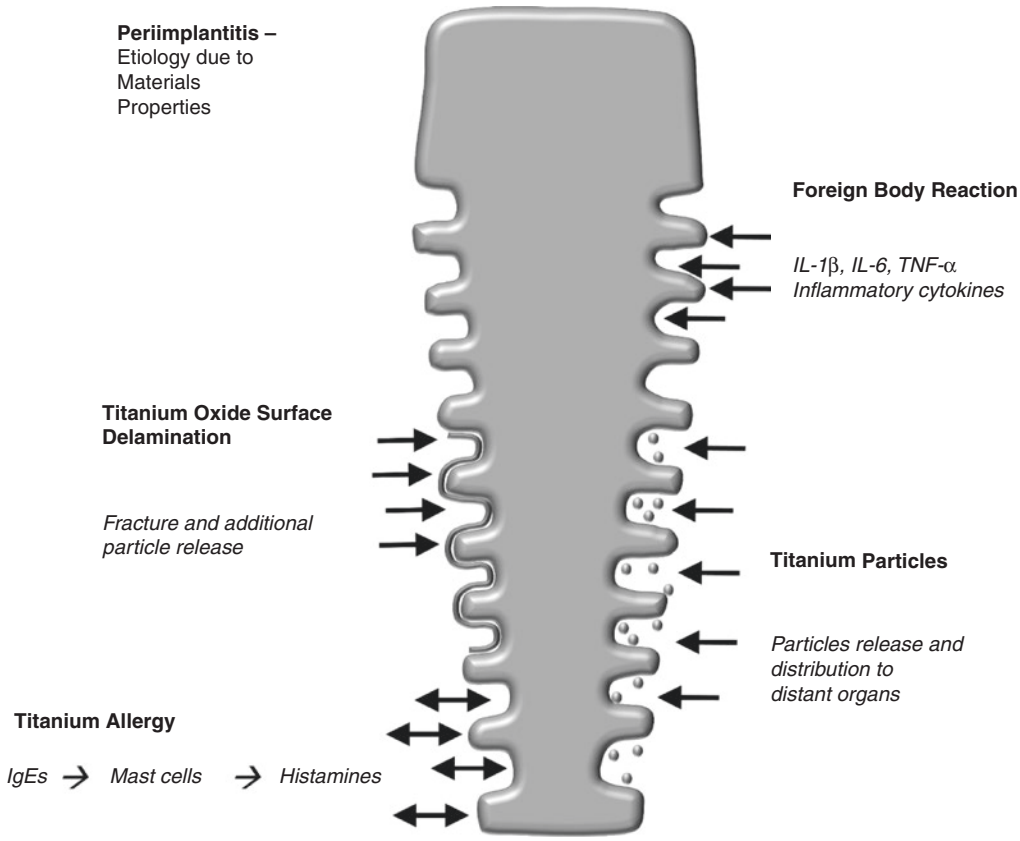

Fig. 9.6 Factors causing peri-implant disease related to the materials properties of the titanium surface. Several factors directly related to the metal implant and its major component, titanium, that have been attributed to play a significant role in the etiology of peri-implant disease, including implant surface delamination, titanium particles, foreign body reaction, and titanium allergy

a type IV allergic reaction [139]. Interestingly, all five of these patients revealed a negative result to a skin patch test using titanium. However, a titanium ointment test yielded positive results in two of these patients [139].

A cohort study evaluated 1500 implant patients in Spain for potential titanium allergies [140]. Thirty-five of these patients were suspected of having a titanium allergy based on a history of multiple allergies and a clinical appearance of an allergic reaction. Sixteen of these patients displayed allergic symptoms after implant placement or unexplained implant failure. Nine of these patients displayed positive reactions to a titanium allergy tests. Based on these findings, the authors calculated an estimated titanium allergy prevalence of 0.6% [140].

Implant surface modifications may further affect the allergic effects of titanium implants on surrounding soft tissues and bone. For example, a titanium nitride–coated implant abutments has been associated with an allergic reaction, and the allergic reaction subsided after the removal of the titanium nitride abutment [141]. There have also been reports of exfoliative cheilitis (exfoliation of the lips) after implant placement [142]. Implant placement has also resulted in facial eczema, while implant removal resolved the eczema, confirming the positive relationship between implant materials and allergic reactions [143]. These allergic reactions are somewhat surprising in light of the widespread use of titanium oxide in dermatological products, toothpaste, icing, salad dressing, chewing gum, candy, milk, tattoo ink, and paints [144].

9.8 Etiology: Foreign Body Reaction

All titanium implants trigger foreign bodies in humans, regardless how well they might integrate. The "zone of tolerance" between the bone and the implant provides an equilibrium between the implant and the human body [145]. In some cases this equilibrium is shifted from normal osseointegration to a foreign body reaction. Supportive of the concept of the implant as a foreign body, a study comparing the levels of periodontal pathogens and pro-inflammatory cytokines around healthy teeth and healthy implants demonstrated approximately twice as many pro-inflammatory cytokines around healthy implants as around healthy teeth [146]. The most prominent cytokines around implants included IL-1ß, IL-6, IL-8, and TNF-α. Cytokine levels in the periphery of healthy teeth and implants were higher when bacteria were detected.

The presence of bacterial plaque around failing dental implants makes it difficult to determine with certainty whether inflammatory reactions in the implant periphery are due to foreign body reactions or microbial-triggered inflammation caused by dental plaque. In contrast, orthopedic implants are not exposed to a microbe-rich environment and thus are fairly free of bacterial contamination. Loss of osseointegration in orthopedic implants is thus due to some form of "foreign body reaction." [147] Albrektsson et al. claim that initial marginal bone loss around implants is a reaction to treatment and not a disease process [148]. They state that the initial foreign body response can be sustained and aggravated, leading to significant bone loss and implant failure. In these cases, once severe bone loss has occurred, a secondary bacterial infection may follow. The authors suggest that marginal bone loss around an implant should not be regarded as a periodontitis-like disease, but instead as a "disbalance" caused by a foreign body response.

9.9 Etiology: Titanium Particles

The foreign body reaction against a titanium implant may either be directed against the entire implant or against the small titanium particles on the implant surface. Titanium ions have been located in the tissues surrounding both dental and orthopedic implants, and these in turn have been associated with tissue discoloration and foreign body reactions to these particles [137, 149]. Once an implant has been placed, the presence of titanium particles may not be limited to the immediate implant periphery but, by ions, may also migrate to distant organs through the blood vessels in the nearby soft tissue and bone. One study reported a slight increase in titanium within the lungs and regional lymph nodes after implant placement in sheep mandibles [150]. Two of these implants failed, resulting in a much higher level of titanium in the lungs and lymph nodes (7–9.4 times the levels in controls). In the orthopedic literature, numerous articles have discussed the possibility of metal debris traveling to distant organs, often referred to as "metallosis." [147, 151] A study on human cadavers with joint replacements determined metallic wear particles in the lymph nodes near the aorta in 68% of the patients [152]. An additional 38% had metallic particles in their liver and/or spleen. These particles were detected in aggregates surrounded by macrophages, a cellular response to rid the body of debris. These particles were more prevalent in patients with failed implants, similar to the findings in the sheep mandible study mentioned above.

Titanium particles can be released from the implant surface in numerous ways. Titanium can simply dissipate from the implant surface during and after placement, it can flake off of the implant due to mechanical forces, and it can exfoliate due to oxidative corrosion of the implant surface. Titanium particles released from implants vary in size from small ions to large titanium pieces [152].

It is not clear whether titanium exfoliates from the implant during surgical placement. Most modern-day implants have a surface that is treated and roughened, a process which has the potential to facilitate the exfoliation of small pieces of titanium. Senna et al. inserted three different implant designs (Nobel, Straumann, and Astra) into bovine ribs to evaluate the presence of loose titanium particles [153]. In this study, all three implant designs revealed a decrease in both surface area and

surface roughness after insertion into bone. Loose titanium and aluminum particles were observed, mainly at the crestal portion of the bone. A separate study on the titanium plasma sprayed (TPS) implant surface reported titanium granules in the soft tissue and bone after implant insertion [154]. Suarez et al. studied five different implant surfaces with the outcome that the grit blasted surface resulted in the greatest degree of titanium exfoliation during placement into bovine ribs [155]. Sridhar et al. simulated surgical placement of Straumann dental implants into foam blocks of varying densities designed to match different bone densities seen in the mouth [50]. The authors of this study reported that implant insertion did not result in exfoliation of titanium particles into the surrounding osteotomy site.

Localization of titanium particles in tissues surrounding implants poses the question whether particles were exfoliated during or after implant placement. Some studies have detected titanium particles in the surrounding soft tissue after the implant has been in function. Olmedo et al. conducted exfoliative cytology of the periimplant mucosa and detected metal particles embedded in the soft tissue of both healthy and diseased implants [156]. The diseased implants displayed a higher concentration of metal within the soft tissue. Another study screened the plaque around healthy and diseased implants for titanium particles [157]. All of the implants screened displayed titanium particles within the plaque, but the diseased implants exhibited significantly more titanium per unit area of plaque. However, it is not clear whether these titanium particles were exfoliated during implant placement, as a result of metal fatigue, or simply dissolution of the titanium surface over time.

A phenomenon known as fretting corrosion occurs at the interface of two closely fitting surfaces when they are subjected to repeated micro-motion or vibration [151]. In the dental field, fretting corrosion may occur between the implant and the abutment that is attached to it [158]. Modern implant designs have attempted to minimize this micro-motion [159]. A very small gap between the implant and abutment, known as the microgap, allows for metal fatigue over time.

Fretting corrosion results in surface irregularities on both the implant and the abutment and leads to metal exfoliation into the surrounding tissue. When metal-on-metal wear occurs, there is a chance that the titanium oxide layer on the implant will be mechanically destroyed [151]. The implant will then be at risk for true oxidative corrosion, and only a newly formed titanium oxide layer on the implant surface would counteract oxidative corrosion. Tawse-Smith et al. collected exfoliative cytology samples from the tissue of implants restored with zirconia abutments and crowns [160]. Elemental analysis revealed that in these samples, high numbers of titanium particles were present at the implant abutment interface and in the soft tissue adjacent to the crown. Other studies demonstrated that the implant is at risk for a galvanic reaction between dissimilar metals when nonprecious metals are used for the abutment, resulting in corrosion and a loss of the titanium oxide layer [161].

The original Brånemark implants were made of commercially pure titanium, while modern implants are alloyed with other metals, including iron, aluminum, and vanadium. Iron is added for corrosion resistance, aluminum is added for increased strength, and vanadium acts as an aluminum scavenger to prevent corrosion [162]. Steineman has demonstrated that titanium alloys (TiAlV) are not as well integrated as pure titanium and have an enhanced corrosion rate [145]. According to Khan, titanium alloys have a better combination of corrosion and wear resistance, while pure titanium shows better corrosion resistance but inferior wear characteristics [163]. Modern titanium alloys are touted to be highly resistant to corrosion, but the extent to which stress and wear accelerate the corrosion rate of titanium remains understudied [24].

Continuous loading, micro-motion, and acidic environments may result in a permanent loss of the titanium oxide (TiO_2) layer on the implant surface and eventual corrosion of the implant [158]. Oxidative corrosion involves losing metal due to a chemical reaction that takes place with an electrolyte or acid as the metal repassivates or reforms an oxide layer [151]. Tribocorrosion refers to the combination of both fretting corrosion and oxida-

tive corrosion. With metals in general, this phenomenon occurs either along the entire surface or only in select locations. Typically, the majority of the titanium implant is stable and only a select area that lost its TiO_2 layer will experience corrosion. This phenomenon is referred to as pitting corrosion since it forms small pits in the areas that experience corrosion. Olmedo et al. installed both sterile titanium implants and implants with pitting corrosion into rat tibiae [164]. The implants with pitting corrosion displayed decreased bone–implant contact, and corrosion products were detected within the bone.

The microbe-rich oral cavity constitutes a challenging environment for implant placement, completely different from the sterile environment that prevails during the placement of orthopedic implants. Dental implants are constantly exposed to a variety of insults on a daily basis. Dental implants are susceptible to corrosion once exposed to an acidic environment and in the presence of micro-motion. There are two known situations in the oral cavity in which a dental implant is exposed to an acidic environment: acidic byproducts of oral bacteria and decontamination solutions used by the dentist or patient [165, 166].

Lactic acid is a waste product of the oral bacterial metabolism. The release of lactic acid may result in dental caries, gingivitis, periodontitis, or, in this case, peri-implantitis. Sridhar et al. immersed sterile dental implants into either a bacterial medium or a control medium in vitro [166]. In this study, the bacteria created a sustained acidic environment, leading to discoloration, deformation, corrosion, pitting, and rusting of the implant surface. In a follow-up study by the same authors, physiological mechanical forces on the implant in combination with a bacterial medium resulted in accelerated corrosion and dissolution of metal ions [159]. These results were corroborated by a University of Washington study that detected elevated levels of titanium within the plaque around implants with peri-implantitis when compared to the plaque around healthy implants [157]. In an in vitro study, implants were exposed to healthy human saliva for incremental lengths of time, resulting in significant dissolution of metallic particles already after 1 week [167]. Interestingly, trace amounts of vanadium were detected as well, questioning the stability of the TiAlV alloy used in modern implants.

Acidic medicaments used to decontaminate the implant surface provide another potential mechanism for implant corrosion. Wheelis et al. conducted an in vitro study to evaluate the corrosive effects of several detoxification solutions on Ti and TiAlV dental implants [165]. The solutions included citric acid, hydrogen peroxide, chlorhexidine gluconate, tetracycline, doxycycline, sodium fluoride, peroxyacetic acid, and CO_2 laser treatment. The treatments consisted of either immersing the implant in the solution or rubbing the implant with a cotton swab soaked in solution. Implants that were immersed in a solution with a pH less than three displayed corrosion and pitting of the implant surface. The authors also noted a color change in the acidic solutions, suggesting that titanium exfoliated from the implant. When rubbing was used, any solution with a pH less than 5.5 caused significant discoloration and pitting. The cotton swabs after solution administration contained remnants of titanium. Commercially pure Ti displayed less corrosion compared to the TiAlV alloy when subjected to the immersion protocol. These results suggest that the safest treatment modalities for implant surface decontamination include sodium fluoride and 3% hydrogen peroxide application as well as CO_2 laser treatment. Chlorhexidine may be applied to the implant surface but may lead to corrosion if it is burnished with a cotton swab.

Another source for titanium particles may be due to implant surface delamination. Delamination refers to the exfoliation or cleavage of a portion of the implant surface, resulting in the formation of a large titanium layer in the vicinity of the implant surface and exposure of the underlying implant body to corrosive environments. Rodrigues et al. reported corrosion in conjunction with surface delamination in both orthopedic and dental implants [158, 168]. Delamination of dental implants may be caused by micro-motion in an acidic environment, resulting in the exposure of the inner titanium body and accelerated dissolution [158]. After implant surface delamination, the underlying titanium body is unable to form a tita-

nium oxide layer if it is not exposed to oxygen. This results in a highly reactive surface that will interact with nearby acids and electrolytes in order to stabilize. Sridhar et al. determined that cyclic occlusal forces may result in surface delamination as well, providing additional evidence for the occurrence of micro-motion and fretting corrosion as causative factors for implant disintegration [159].

Based on the present data, there are several mechanisms contributing toward titanium dental implant corrosion (Fig. 9.7). At this point, it is not clear whether a corroded implant surface

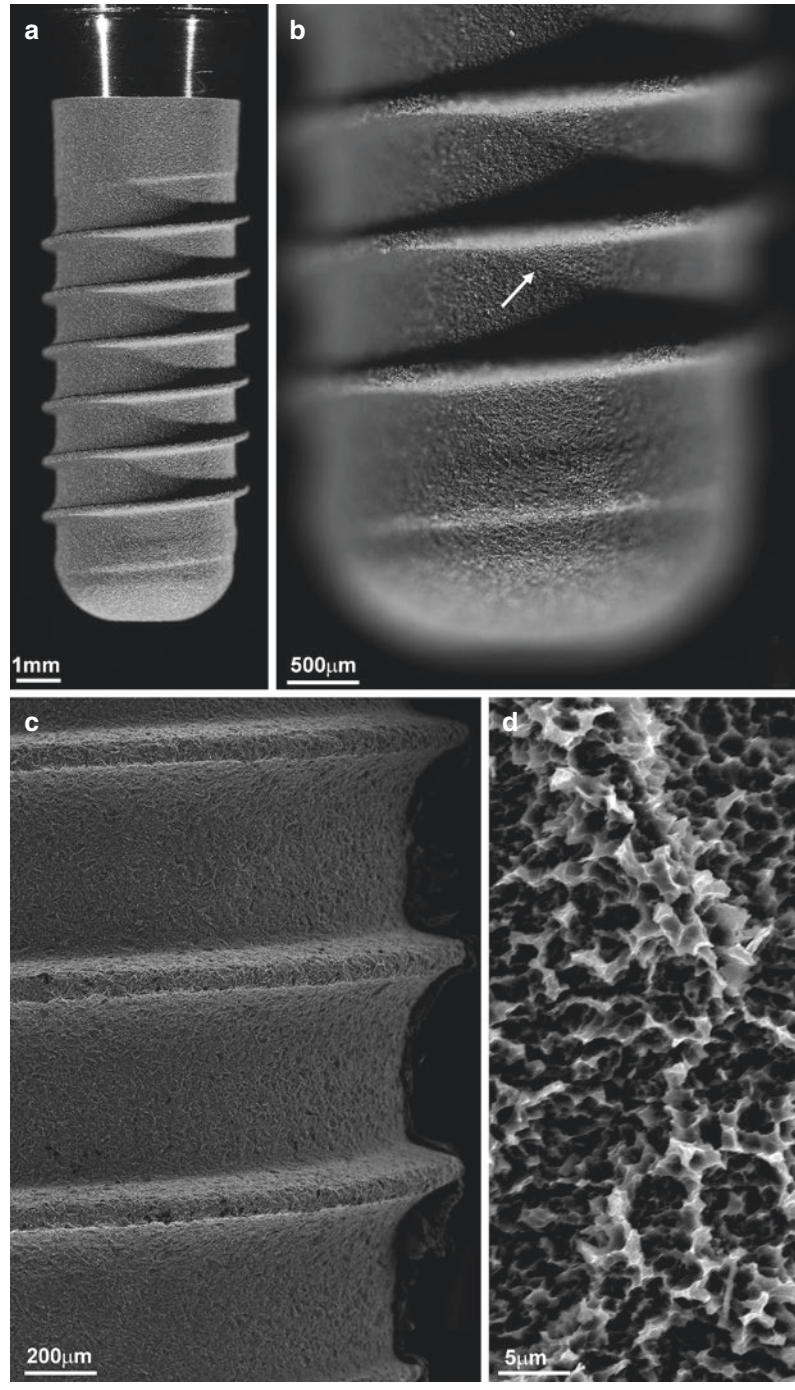

Fig. 9.7 Microscopic structure of a titanium implant surface (straumann standard plus implant). (**a**, **b**) are light micrographs and (**c**, **d**) are scanning electron micrographs. The arrow points to the roughened implant surface structure

is compatible with a healthy implant. However, there is emerging evidence suggesting that foreign particles embedded in the tissue provoke an inflammatory response. A study of orthopedic implants has demonstrated that metal debris trigger inflammation in vivo [169]. Wilson et al. obtained soft tissue biopsies around dental implants with peri-implantitis and evaluated them with light microscopy and SEM [49]. In this study, titanium and/or dental cement were detected in 34 of 36 biopsies, and particles were surrounded by plasma cells, giant cells, and other inflammatory cells. Another study demonstrated that titanium debris trigger a DNA damage response in oral epithelial cells [155]. Together, these studies suggest that foreign debris around titanium implants are not well tolerated and provide a baseline explanation for dental implant failure.

9.10 Summary: Osseointegration—Wishful Thinking or Oxymoron?

In the early years of implantology, osseointegration was the perfect term for the seemingly ideal junction between a living tissue, bone, and a block of metal, titanium. However, decades later, research demonstrated that the very interface between bone and metal became the cause for biological reactions against titanium particles and inflammation of the surrounding tissues, ultimately leading to bone loss and implant failure. While until today approximately 80% of all implants are considered clinically successful, even after 10 years, dentists are now seeking clinical solutions to treat peri-implant disease, how to prevent per-implantitis in the first place, and asking the question how safe titanium implants are for the health of their patients overall. While titanium implants remain a highly successful and lucrative treatment option, it is no longer clear whether the concept of osseointegration truly reflects the highly reactive interface between bone and titanium over the long time period of their exposure to the oral cavity.

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