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Microbiologically compromised patients and impact on oral implants

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This paper considers different factors that increase a patient's susceptibility to an infectious process, which can jeopardize the success of endosseous implants. A distinction is made between an early failure (or impaired healing), and peri-implantitis (73). Although an early failure can be caused by different factors (e.g. traumatic surgery, overheating during drilling, etc.), a bacterial origin is commonly diagnosed. Early failures of infectious origin can be due to a preoperative contamination, an infected recipient site or a postoperative hematogenous infection. The term peri-implantitis refers to an ''inflammatory process'' affecting the tissues around an already osseointegrated implant, resulting in loss of supporting bone (4). Occlusal overload, another important etiologic factor for implant failure, and often confused with peri-implantitis, will not be discussed in this paper.

Early failure/impaired healing

Peroperative contamination

Possible sources of direct bacterial contamination during surgery (infection of the implant or the bony socket) are: the surgical instruments, the gloves, the air in the operation room, the saliva in the oral cavity and the peri-oral skin. Such infections can result in an abscess around an implant, possibly accompanied by a fistula (65). The reduction of the salivary flow by intramuscular injection of atropine, the supine position of the patient, and the relative protection of the surgical plane by an orally pediculated flap can avoid contamination of the wound, at least in the anterior part of the oral cavity, especially if two separate surgical aspirations (one for the wound and the other for the mouth) are used (29). Furthermore, the salivary microbial load can be reduced by 95% via a preoperative rinse with chlorhexidine (91). A disinfection of the peri-oral skin with a chlorhexidine–alcohol solution can only partially reduce the microbial load on this surface. Thus to deal with the skin and mucosae of the nares, a perforated cap (Fig. 1) should be installed over the patient's nose (88).

In a prospective multicenter study on the use of osseointegrated oral implants in partially edentulous patients the few early failures were concentrated in subjects with a high plaque and gingivitis index. This indicates a peroperative contamination and/or airborne infections that interfered with the osseointegration process, or an influence (hematogenous infection) from the concomitant gingivitis (87). As such, partially edentulous patients with periodontitis and/or poor oral hygiene can be considered compromised cases when implant surgery is planned.

Infected recipient site

Infections/inflammatory processes within the jawbone – in the immediate vicinity of an integrating implant – such as periapical lesions (79, 85) around neighboring teeth, cysts (which are often underestimated on radiographs) (24, 86), root remnants, or foreign bodies (e.g. endodontic material) (19), seriously interfere with osseointegration. Some implants show a periapical lesion shortly after installation, termed retrograde peri-implantitis or peri-implantitis apicalis (8). These aspects will be discussed in greater detail in a separate chapter.

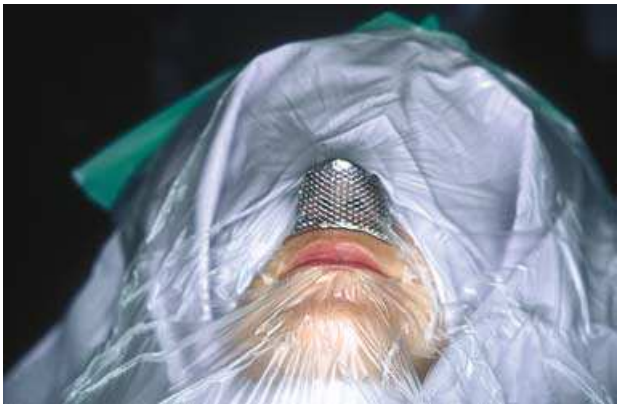

Fig. 1. Sterility measures before implant insertion. After disinfection, the patient's head and body are covered with sterile drapes and a plastic film. A nose guard (metal or plastic mesh) allows the patient to breath freely, but prevents contact between surgical gloves and the nose.

Early infections/inflammation

Signs of infections/inflammation (swelling, fistulae and pain) during the healing period of a submerged 2-stage implant can also be confined to the soft tissues. The most frequently reported causes are a residual suture, a poorly seated cover screw, or soft tissue perforation of a protruding implant after trauma from an inadequately relieved denture or trauma by antagonistic teeth (22, 40, 95).

Systemic factors versus impaired healing

Diabetes mellitus, a metabolic disease that influences wound healing and jeopardizes the immune reaction to infections (reduced chemotactic and phagocytic functions of neutrophils) slightly increases the risk for early implant failure, especially in patients that are not metabolically controlled (9, 25, 58, 80). Shernoff et al. (80), for example, reported an early failure rate of greater than 10% in diabetic patients. Whether this increased failure rate is related to a reduced immune response, to a more pathogenic oral flora or to an impaired healing capacity in these patients remains partially unanswered. While early studies on periodontitis showed possible differences in subgingival bacterial colonization between diabetic and nondiabetic patients, more recent research failed to confirm these observations (17), pointing towards other factors for compromising these patients for implant surgery.

Another study on 1,263 Brånemark implants correlated early implant failures with chemotherapy for cancer, radiotherapy and claustrophobia (the latter pointing to inappropriate asepsis during surgery), as well as with poor bone quality and quantity (90). The increased failure rate due to chemotherapy is, however, in contrast to the data of a large-scale study by Kovács (35).

Recent studies have shown that subjects with early implant failures (before or at abutment connection) often demonstrate low serum antibody avidity to *Bacteroides forsythus* and low serum antibody titers to *Staphylococcus aureus* (37, 38). These data indicate that patients with early implant failures might be unable to mount protective serum IgG titer levels to pathogenic species (thus an unfavorable immune response) that contaminated the area during surgery or soon afterwards via penetration through the wound or via a bacteremia. This observation is in line with data of previous studies indicating that serum IgG antibody avidity levels to periodontopathogens are lower in subjects with periodontitis than in periodontally healthy subjects (46). The reduced IgG production may be either the consequence of host genetic immune defects, acquired immune deficiency through smoking etc. and other diseases, the effect of bacterial genotype and virulence factors (37, 38).

Peri-implantitis

The term peri-implantitis refers to an ''inflammatory process'' affecting the tissues around an already osseointegrated implant, resulting in bone loss (4). This inflammatory process has been associated (e.g. in animal studies, cross-sectional and longitudinal observations in man) with a microbiota comparable to that of periodontitis, but this association does not necessarily prove a causal relationship. Some large-scale clinical follow-up studies seem to indicate that implant failures cluster within patients, with increased odd ratios for a second implant failure in patients that have already lost one implant (90, 93). These observations indicate that within-patient or systemic factors are important in the identification of compromised patients.

Subgingival flora around failing implants

Table 1 summarizes the most significant microbiological data on failing implants. Healthy peri-implant pockets are characterized by high proportions of coccoid cells, a low anaerobic/aerobic species ratio, a low number of gram-negative, anaerobic species, and low detection frequencies for periodontopathogens (3, 14, 28, 41, 59). Implants with peri-implantitis

Table 1. Microbiota around successful and failing implants (late failures only). Considered are dark field microscopy data (proportions), the proportion of gram-negative anaerobic rods, and culture data (detection frequency or proportion) and sorted by intra- or intersubject comparison

Authors	Edentulism	Study design	Implant information		Probing pocket depth in mm	Darkfield microscopy in %				% gram-negative anaerobes	Specific bacteria: % flora/frequency			
			Status	Parameters used for failure		Cocci	Other morphotypes	Motiles	Spirochetes		*A. actinomycetemcomitans*	*P. gingivalis*	*P. intermedia*	*F. nucleatum*
Mombelli et al. (54)	Full	Intra subj	Failed	Pocketdepth, suppuration, radiographical	8.5	48.7	32	7.9	11.4	42.1	0%[c]	0%	5.7%	15.3%
			Success		3	59.5	34.4	4.8	1.3	23.4	0%	0%	1.1%	7.0%
	Full	Inter subj	Success		3.8	82.1	16.6	1.3	0	15.4	0%	0%	0.9%	6.5%
Alcoforado et al. (5)		–	Failed	questionable definition: pocketdepth, radiographic or suppuration							0/10[c]	0/10	4/10	4/10
Mombelli et al. (52)	Full/ partial	Intra subj	Failed	pocketdepth, culture, radiographic	5.9	–	–	7/9	7/9	39.8		1/9[c]	5/9	7/9
			Success		≤3	–	–	–	0/9	19		0/9	5/9	4/9
Sbordone et al. (77)	Partial	–	Failed	pocketdepth, suppuration, radiographic, mobility	6.4	42.1	40	12.3	5.6	50.4	0/13[c]	8/13	10/13	13/13
Augthun et al. (7)		–	Failed	Radiographic							16/18[c]	–	5/18	4/18
Leonhardt et al. (43)	Partial	Inter subj	Failed	Radiographic							9/29[c]	1/29	19/29	
			Success								1/35	1/35	9/35	
	Full	Inter subj	Failed								1/8[c]	2/8	3/8	
			Success								0	0	0	
Rutar et al. (75)	Partial	Inter subj	Failed	pocketdepth, suppuration, radiographic		37.7	44.5	3.2	14.6					
			Success			36.9	51.2	3.1	8.9					

reveal a complex microbiota encompassing conventional periodontal pathogens. Species such as *Actinobacillus actinomycetemcomitans*, *Porphyromonas gingivalis, B. forsythus, Peptostreptococcus micros*, *Campylobacter rectus, Fusobacterium* and *Capnocytophaga* are often isolated from failing sites, but can also be detected around healthy peri-implant sites (Table 1). These bacteria are also commonly associated with progressive periodontitis and possess virulence factors, which could be pertinent to peri-implantitis (81). Other species such as *Pseudomonas aeruginosa*, *Enterobacteriaceae* species, *Candida albicans* or staphylococci are also frequently detected around implants (5). These organisms are uncommon in the subgingival area, but have been associated with refractory periodontitis (82). High proportions of *S. aureus* and *Staphylococcus epidermidis* have been reported in other papers on oral implants (74). The relative resistance of these organisms to commonly utilized antibiotics (83) suggests that their presence might represent an opportunistic colonization secondary to systemic antibiotic therapy.

Susceptibility for peri-implantitis versus periodontitis

Two case reports described an unsuccessful implant therapy in a partially edentulous patient suffering from rapidly progressing periodontitis (23, 48). Many authors misquoted these papers to prove that patients susceptible to periodontitis are also susceptible to peri-implantitis. Several other publications, however, proved the opposite (57, 72, 89). The latter studies, together with the observations in long-term clinical studies (2, 3, 44, 87), indicate that some implant configurations and surfaces may be even more resistant to loss of ''attachment'' than teeth. This might, for example, not be true for implants with a very roughened surface (15, 21). Thus some implant types inserted in patients prone to periodontitis may pose an increased risk for marginal soft and hard tissue problems.

The subgingival biofilm as compromising factor

Presence and periodontal status of teeth

Several papers have suggested an intraoral translocation of pathogenic bacteria from the periodontal to the peri-implant pockets in partially edentulous patients. Studies in the early 1990's by Apse and co-workers (6), and Quirynen & Listgarten (68) illustrated that the pockets around remaining teeth in partially edentulous patients act as ''reservoirs'' for the colonization of recently installed abutments on implants. This similarity in microflora between teeth and implants with comparable probing depths has been confirmed by several studies (Table 2) and appears soon after abutment insertion. Leonhardt and coworkers (43) detected periodontopathogens in the subgingival peri-implant environment within a month after abutment connection. All the studies in Table 2 corroborate the concept that the microflora in the oral cavity prior to implant insertion determines the composition of the establishing microflora around the artificial abutments. Consequently, the periodontal status of the remaining teeth also influences the composition of the subgingival flora around implants (70, 71, 76). When partially edentulous patients are compared with fully edentulous patients (without remaining teeth in both jaws but rehabilitated with implants) the impact of the remaining teeth becomes even more striking. Rehabilitated fully edentulous patients (Table 3) are characterized by significantly lower proportions of motile organisms (3% vs. 11.4 %) and spirochetes (0.9% vs. 2.7%), and very low detection frequencies for pathogenic species (6, 18, 53, 55, 61, 68). In these six studies on fully edentulous patients rehabilitated with implants, *P. gingivalis* and *A. actinomycetemcomitans* were never detected (0/75). The detection frequency for *P. intermedia* (7/75) also seems to be reduced, in contrast to *F. nucleatum*.

Probing pocket depth

A positive correlation between probing depth and pathogenicity of the subgingival flora in peri-implant pockets has been reported for both one- and two-stage implants (31, 32, 36, 41, 53, 60, 61, 71). This observation justifies a reduction of the probing depth (by trimming the mucoperiosteal flap and/or by using a post-surgical healing pack to maintain some pressure during healing). Such trimming should, however, not go beyond 3 mm, since in animals, at least, the existence of a minimal biologic width has been well documented (11).

Surface roughness of transmucosal part of the implant

Supra- as well as subgingivally, rough abutments harbor significantly more bacteria and a higher proportion of pathogens (13, 69, 70). A smoothing of the surface (roughness $R_a \leq 0.2$ μm) resulted in significant reductions in the periodontal pathogenicity of adhering bacteria, so that this value was suggested as

Table 2. Intrasubject comparison of subgingival flora around implants and teeth in partially edentulous patients. Considered are dark field microscopy data (proportions), and culture data (detection frequency for specific bacteria)

Authors	Abutment	Probing pocket depth in mm	Bacterial morphotypes in %				Detection frequency of specific bacteria			
			Cocci	Other morphotypes	Motiles	Spirochetes	*A. actinomycetemcomitans*	*P. gingivalis*	*P. intermedia*	*F. nucleatum*
Lekholm et al. (41)	Implant	3.3	30.7	45	25	0	0[c]	0	0	
	Tooth	2.3	17.8	54.4	23.5	0.9	0	0	0	
Apse et al. (6)	Implant	3.5	87	8	3	4	1/28[c]	5/28	1/28	
	Tooth	2.6	87	7.5	4	9	3/19	1/19	1/19	
Quirynen et al. (70)	Implant	2.9	65.8	29.8	2.3	2.1				
	Tooth	2.7	56.6	34.9	4.9	3.6				
Koka et al. (34)	Implant						-	2/4[i]	2/4	1/4
	Tooth						-	3/4	3/4	1/4
Leonhardt et al. (42)	Implant	2.2					4/17[c]	4/17	9/17	
	Tooth	2.7					5/17	8/17	11/17	
Kohavi et al. (33)	Implant	3.1					9/29[c]	20/29		
	Tooth	3.5					11/29	16/29		
Mombelli et al. (56)	Implant				15	25	0[c]	2/20	7/20	12/20
	Tooth				23	28	1/80	6/80	32/80	41/80
Papaioannou et al. (62)	Implant	4.7	40	46.3	12.5	1.2	0/2[d]	0/2	0/2	2/2
	Tooth	7.3	13	47	21.5	18.5	0/3	3/3	1/3	2/3
	Implant	5.5	38.5	30.5	21.5	10	0/2[d]	2/2	2/2	2/2
	Tooth	8.3	21.5	29.5	25	24	0/3	3/3	3/3	3/3
Mengel et al. (51)	Implant		79.9	8.2	10.7	1.3	0[d]	0	1/5	-
	Tooth		80.8	9.5	9.4	0.2	0	0	1/5	-
Sbordone et al. (78)	Implant	3.3	80.5	14	5	0.5	3/25[c]	10/25	4/25	4/25
	Tooth	3	76.3	15.7	5.2	2.8	4/25	5/25	3/25	1/25
Hultin et al. (30)	Implant	1.9					4/43[d]	7/43	8/43	12/43
	Tooth	1.5					0/31	3/31	3/31	6/31
Overall mean	Implant		60.3	26	11.4	2.7	21/181	52/185	34/156	33/96
Standard deviation			23.4	16.3	9	3.5				
Overall mean	Tooth		50.4	28.4	13.4	8.4	24/222	48/226	58/197	54/146
Standard deviation			32.3	18.4	9.5	9.3				

Microbial analyses: [c] = culture, [d] = DNA, [i] = immunoblot assay.

Table 3. Subgingival flora around implants in fully edentulous patients. Considered are dark field microscopy data (proportions), and culture data (detection frequency for specific bacteria)

Authors	Probing pocket depth in mm	% bacterial morphotypes				Detection frequency of specific bacteria			
		Cocci	Other morphotypes	Motiles	Spirochetes	*A. actinomycetemcomitans*	*P. gingivalis*	*P. intermedia*	*F. nucleatum*
Mombelli et al. (55)		94	6	0	0	0/8	0/8	1/8	2/8
Apse et al. (6)	3	84	6	8	4	0/13	0/13	0/13	
Quirynen et al. (68)	2.6	71.3	28.4	0.4	0				
Mombelli et al. (53)	2.9	83	11	6	0	0/34	0/34	4/34	4/34
Papaioannou et al. (61)	3.1	67.7	31.5	0.7	0.1				
Papaioannou et al. (61)	3.6	57.7	38.3	2.8	1.2				
Danser et al. (18)	3.6					0/20	0/20	2/20	20/20
Overall mean		76.3	20.2	3	0.9	0/75	0/75	7/75	26/62
Standard deviation		13.1	14.2	3.3	1.6				

a threshold surface roughness below which bacterial adhesion cannot be further reduced (13). The limited hardness of commercially pure titanium abutments explains the risk for surface roughening during habitual or professional cleaning (26, 49, 50, 84). Application of a fluoride prophylactic agent can also result in a significant increase of the R_a through pitting corrosion by hydrofluoric acid or the combination of fluoride and hydrogen ions from the acid (66). The use of an air-powder abrasive system cannot be advocated because it may result in severe marginal bone loss around implants (10). The above-mentioned studies all dealt with the permucosal part of the implants. It is evident that due to marginal bone loss, because of overload or peri-implantitis, the endosseous part of the implant will one day come into contact with the subgingival flora. From that moment on, the variety in surface roughness between implant systems becomes even more relevant (16, 92).

Intraoral exposure time

The impact of intraoral exposure time on the composition of the subgingival flora around implants is different for partially and fully edentulous patients (34, 36, 39, 53, 55, 61, 78). Especially in partially edentulous patients, and to a lower extent in fully edentulous patients, changes do occur with time, resulting in:

- an increase in the number of colony forming units.
- an increase in the proportion of motile organisms and especially of spirochetes.
- a slight additional increase in the detection frequency of other pathogenic species.

As such, time can be considered a potential risk factor.

Foreign body reaction in peri-implant pocket

Peri-implantitis can be provoked by the subgingival impaction of a foreign body. Cement remnants can lead to an acute peri-implantitis process with local swelling, soreness, exudation on probing, and significant bone destruction (63). After the removal of the excess cement, the healing will often be uneventful, although the bony defect can remain for a while.

The abutment material is critical for both the location and the quality of the soft tissue seal and the underlying bone. In dogs, abutments from gold alloy or porcelain led to a significant marginal bone loss until the soft tissue barrier could be established on the titanium implant surface (1).

Oral hygiene

The patient's oral hygiene has a significant impact on the stability of the marginal bone around osseointegrated implants. Even in fully edentulous patients, poor oral hygiene has been related to increased peri-implant bone loss, especially in smokers (44).

Smoking

Smoking significantly changes the equilibrium between microbial load on implants and the human host response, and as such jeopardizes the longevity of oral implants. First and foremost, smoking has an immunosuppressive effect on the host. Peripheral blood polymorphonuclear leukocyte motility, chemotaxis, and phagocytosis are significantly impaired (27, 47) and antibody production, especially IgG_2 (67), is decreased. Smokers also represent decreased neutrophil levels (64). Periodontopathogens can now escape specific and non-specific immune clearance mechanisms, allowing them to become established as subgingival peri-implant inhabitants. Finally, alteration in the physical subgingival environment, such as decreased oxygen tension, will allow the overgrowth of an essentially anaerobic flora (45). In addition, smoking increases bacterial adhesion to epithelial cells (20). It is therefore not surprising that smokers in general harbor higher levels of periodontopathogens (94) and can be considered microbiologically compromised.

Conclusion

Scientific data support the impact of the oral status, the implant configuration and the surface in particular on the pathogenicity of the peri-implant biofilm. The role of the subgingival flora in peri-implantitis within compromised patients (diabetes, immunocompromised subjects, etc.) has not yet been fully established. Whether osseointegration is at risk depends on the host defense mechanisms, the duration of the infection, the implant design and surface characteristics. Some implants seem to be more at risk for occlusal overload, while other systems are more prone to plaque build-up. Basic research and long-term clinical trials are needed to obtain a better differential diagnosis of the cause of marginal bone loss. Implants in partially edentulous patients, in contrast to fully edentulous subjects, will easily be colonized by putative periodontal pathogens. It seems therefore reasonable that all partially edentulous patients receive appropriate periodontal screening and treatment prior to implant placement and are maintained on an individualized recall schedule for supportive periodontal therapy. It is still unknown whether a past history of periodontitis is a significant risk factor for implant survival in a given patient.

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