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REVIEW ARTICLE

Update on the Taxonomy of Clinically Important Anaerobic Bacteria

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임상적으로 중요한 무산소성 세균의 분류 업데이트

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ARTICLE INFO	ABSTRACT				
Received July 26, 2022 Revised September 28, 2022 Accepted October 14, 2022	The taxonomy of bacteria in the field of clinical microbiology is in a state of constant flux. A large-scale revamping of the classification and nomenclature of anaerobic bacteria has taken place over the past few decades, mainly due to advances in molecular techniques such as 16S rRNA and whole genome sequencing (WGS). New genera and species have been added, and existing genera and species have been reclassified or renamed. A major role of the clinical microbiological laboratories (CMLs) is the accurate identification (ID) and appropriate antimicrobial susceptibility testing (AST) for clinically important bacteria, and rapid reporting and communication of the same to the clinician. Taxonomic changes in anaerobic bacteria could potentially affect the choice of appropriate antimicrobial agents and the antimicrobial breakonints to use. Furthermore, current				
Key words Anaerobic bacteria Taxonomic change Update	taxonomy is important to prevent treatment failures of emerging pathogenic anaerobes with antimicrobial resistance. Therefore, CMLs should periodically update themselves on the changes in the taxonomy of anaerobic bacteria and suitably inform clinicians of these changes for optimum patient care. This article presents an update on the taxonomy of clinically important anaerobic bacteria, together with the previous names or synonyms. This taxonomy update can help guide antimicrobial therapy for anaerobic bacterial infections and prevent treatment failure and can be a useful tool for both CMLs and clinicians.				
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INTRODUCTION

Anaerobic bacteria are considered as etiologic agents in a number of clinical diseases, including aspiration pneumonia, brain abscess, and intra-abdominal infections [1, 2]. As the number of immunocompromised patients has been increased, the clinical importance of anaerobic

Department of Laboratory Medicine, Severance Hospital, Yonsei University College of Medicine, 50–1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea E-mail: msvkim@yuhs.ac ORCID: https://orcid.org/0000-0002-4933-5018 bacterial infections has been extended [3]. The development of molecular technologies including 16S rDNA sequencing and genome sequencing has led to major changes among taxonomy of anaerobic bacteria, as well as aerobic bacteria, in the fields of clinical microbiology [4, 5]. Taxonomic changes potentially affect interpretation of susceptibility testing and reporting for anaerobes, and tracking of new names is important to work toward better improvement of patient treatment and disease management [6]. The Clinical and Laboratory Standards Institute (CLSI) provides the performance standards for AST stated with

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changed taxonomy in their updated guidelines, such as Cutibacterium (formerly Propionibacterium) acnes and Clostridiodes (formely Clostridium) difficile [7]. According to CLSI guideline, clinical microbiological laboratory (CML) may not be necessary to perform the AST for all anaerobic bacteria isolated from culture, because their antimicrobial susceptibility patterns are often predictable. However, antimicrobial resistance in anaerobic infections has been associated with poor clinical outcome due to treatment failure. Recently, the importance of the treatment of *C. difficile* infection has increased in both hospitals and the community, as emerging pathogen with high virulence and resistance of fluoroquinolones [8]. Furthermore, CLSI has published the data of cumulative AST for anaerobes, relatively limited on anaerobic organisms in spite of the clinical importance in guiding empiric therapy. CMLs have problems on identification (ID) of new and unusual species, such as Actinotignum schaalii, a newly recognized uropathogen with resistance of trimethoprime-sulfamethoxazole and ciprofloxacin, and history of treatment failure [9]. This article presents update on taxonomy of clinically important anaerobic bacteria with previous names or synonyms. Current taxonomy is important to perform the accurate organism identification, and antimicrobial susceptibility testing in the aspect of emerging pathogens. The taxonomy update can help guide patient management and prevent treatment failures in both CMLs and clinicians.

MAIN ISSUE

1. Anaerobic Gram-positive cocci and other anaerobic cocci

The anaerobic gram-positive cocci (AGPC) are part of the commensal flora of humans and are also associated with a variety of human infections [10]. AGPC belongs to the *Firmicutes* phylum, and the taxonomy of AGPC has undergone extensive changes of new genera and species (Table 1). Most clinical isolates of AGPC were described in the genus of *Peptococcus* and *Peptostreptococcus*. In 1983, four *Peptococcus* species (*P. asaccharolyticus*, *P. indolicus*, *P. prevotii* and *P. magnus*) were transferred to the genus

Table 1. Taxonomic changes of anaerobic gram-positive cocci isolated from humans

Phylum and genus	Species or subspecies	Previous name(s) or synonym	References
Firmicutes			
Anaerococcus*	A. hydrogenalis	Peptostreptococcus hydrogenalis	[14]
	A. lactolyticus	Peptostreptococcus lactolyticus	[14]
	A. octavius	Peptostreptococcus octavius	[14]
	A. prevotii	Peptostreptococcus prevotii	[14]
	A. tetradius	Peptostreptococcus tetradius	[14]
	A. vaginalis	Peptostreptococcus vaginalis	[14]
Anaerosphaera*	A. aminiphila	New species	[15]
Atopobium*	A. parvulum	Streptococcus parvulus	[17]
Blautia*	B. producta	Peptostreptococcus productus, Ruminococcus productus	[18]
Finegoldia*	F. magna	Peptostreptococcus magnus	[12]
Gallicola*	G. barnesae	Peptostreptococcus barnesae	[14]
Murdochiella*	M. asaccharolytica	New species	[16]
Parvimonas*	P. micra	Peptostreptococcus micros, Micromonas micros	[12, 13]
Peptococcus	P. niger		[11]
Peptoniphilus*	P. asaccharolyticus	Peptostreptococcus asaccharolyticus	[14]
	P. harei	Peptostreptococcus harei	[14]
	P. indolicus	Peptostreptococcus indolicus	[14]
	P. ivorii	Peptostreptococcus ivorii	[14]
	P. lacrimalis	Peptostreptococcus lacrimalis	[14]
Peptostreptococcus	P. anaerobius		[12]

*New genus.

Peptostreptococcus leaving Peptococcus niger as the single species in the genus Peptococcus [11]. Since 1998, the genus Peptostreptococcus has been divided into several novel genera. Peptostreptococcus magnus and P. micros were transferred to two new genera, Finegoldia and Micromonas, respectively [12]. The genus Micromonas has more recently been replaced by Parvimonas [13]. For the remained peptostreptococci, three new genera were proposed; Peptoniphilus, Anaerococcus and Gallicola [14]. In addition, two novel genera have been proposed; Anaerosphaera, with the type species A. aminiphila, most closely related to species of the genus Peptoniphilus [15] and Murdochiella, with the type species *M. asaccharolytica*, most closely related to Parvimonas micra and Finegoldia magna [16]. Among the other AGPC, Streptococcus parvulus has been changed to the genus Atopobium, as A. parvulum [17]; Ruminococcus productus (formerly Peptostreptococcus productus) was reclassified in a new genus Blautia, as B. product [18].

The anaerobic gram-negative cocci (AGNC), including the genera *Veillonella*, *Acidaminococcus*, *Megasphaera*, *Anaeroglobus*, and *Negativicoccus*, which was the recently described, have been classified in a single family, the *Acidaminococcaceae* [19]. Of the genus of *Veillonella*, *V. dispar*, *V. parvula* and *V. atypica*, have so far been isolated from human flora. Currently, the species *V. alcalescens* was abolished [20].

2. Anaerobic Gram-positive rods

The anaerobic gram-positive rods (AGPR) are widely distributed among the phylum *Actinobacteria* and *Firmicutes*. More recently, taxonomic reclassification of AGPR has undergone changes of new genera within these two phyla (Table 2).

1) Phylum Actinobacteria

The genera *Actinomyces*, *Actinobaculum*, *Actinotignum*, *Mobiluncus*, and *Varibaculum* belong to the family *Actinomycetaceae*. Important taxonomic reclassification has occurred within the genus *Actinomyces*, such that *A. naeslundii* has been reclassified within the genus *Actinomyces*, which is previously considered "*A. naeslundii* genospecies I", and *Actinomyces oris* and *A. johnsonii* have been represented as novel species [21]. *Actinobaculum schaalii* and *A. urinale* of the genus *Actinobaculum* have been reclassified into the novel genus *Actinotignum* and *Actinotignum sangunis* has been described as a novel species [22]. Recently, *Actinotignum schaalii* is recognized as an uropathogen with resistance of antimicrobials, but other *Actinotignum* species are less associated with human infections [9]. *Actinobaculum massiliense* and *A. suis* are remained in the genus *Actinobaculum* [23, 24].

The genus *Propionibacterium* contains bacteria isolated from human sources and dairy products. Recently, important taxonomic reclassification has occurred in the cutaneous species of the genus. *P. acnes, P. granulosum, P. avidum*, and *P. humersii* have been reclassified into the novel genus *Cutibacterium*. *P. propionicum* has been reclassified as *Pseudopropionibacterium propionicum* [25]. *Bifidobacterium* and the closely related genera *Alloscardovia* [26], *Parascardovia*, and *Scardovia* [27] belong to the family *Bifidobacteriaceae*. There are currently 50 *Bifidobacterium* species, of which 11 species have been isolated from the human gut and oral cavity. *B. logum* including the former species *B. infantis* and *B. suis* is reclassified as three subspecies [28].

The genus *Atopobium* was proposed for *Lactobacillus minutus, Lactobacillus rimae* and *Streptococcus parvulus,* reclassified as *A. minutus, A. rimae* and *A. parvulum* [17]. The genus *Collinsella* has been proposed for *Eubacterium aerofaciens* with one species, *Collinsella aerofaciens* [29]. Other genus *Eggerthella* includes *E. lenta* and *E. sinensis,* and *E. hongkongenesis* is now reclassified as the only member of the novel genus *Paraeggerthella* [30].

Phylum and genus	Species or subspecies	Previous name(s) or synonym	References
Actinobacteria			
Actinobaculum*	A. massiliense	Actinomyces massiliae	[23]
	A. suis	Actinomyces suis	[24]
Actinomyces	A. johnsonii	New species, A. naeslundii genospecies WVA 963	[21]
	A. naeslundii	A. naeslundii genospecies 1	[21]
	A. oris	New species, A. naeslundii genospecies 2	[21]
Actinotignum*	A. sangunis	New species	[22]
-	A. schaalii	Actinobaculum schaalii	[22]
	A. urinale	Actinobaculum urinale	[22]
Alloscardovia*	A. omnicolens	New species	[26]
Bifidobacterium	B. logum subspecies infantis	New subspecies, <i>B. infantis</i>	[28]
	B. logum subspecies longum	New subspecies, <i>B. logum</i>	[28]
	<i>B. logum</i> subspecies <i>suis</i>	New subspecies, <i>B. suis</i>	[28]
Collinsella*	C. aerofaciens	Eubacterium aerofaciens	[29]
Cutibacterium*	C. acnes	Propionibacterium acnes	[25]
	C. avidum	Propionibacterium avidum	[25]
	C. granulosum	Propionibacterium granulosum	[25]
	C. humersii	Propionibacterium humersii	[25]
Paraeggerthella*	P. hongkongenesis	Eggerthella hongkongenesis	[30]
Parascardovia*	P. denticola	Bifidobacterium denticolens	[27]
Pseudopropionibacterium*	P. propionicum	Propionibacterium propionicum	[25]
Scardovia*	S. inopinata	Bifidobacterium inopinatum	[27]
Firmicutes			
Anaerostipes*	A. hadrus	Eubacterium hadrum	[32]
Atopobium	A. minutus	Lactobacillus minutus	[17]
	A. rimae	Lactobacillus rimae	[17]
Clostridioides*	C. difficile	Clostridium difficile	[34]
Clostridium	C. maximum	Sarcina maxima	[31]
	C. moniliforme	Eubacterium moniliforme	[31]
	C. tarantellae	Eubacterium tarantellae	[31]
	C. ventriculi	Sarcina ventriculi	[31]
Dorea	D. formicigenerans	Eubacterium formicigenerans	[33]
Eubacterium	E. sulci	Fusobacterium sulci	[55]
Filifactor	F. alocis	Fusobacterium alocis	[55]
Hathewaya*	H. histolytica	Clostridium histolyticum	[31]
	H. limosa	Clostridium limosum	[31]
	H. proteolytica	Clostridium proteolyticum	[31]
Hungatella*	H. hathewayi	Clostridium hathewayi	[37]
Paeniclostridium*	P. sordellii	Clostridium sordellii	[36]
Paraclostridium*	P. bifementans	Clostridium bifementans	[36]
Terrisporobacte*	T. glycolicus	Clostridium glycolicum	[35]

Table	2.	Taxonomic	changes	of	anaerobic	gram-positive	rods	isolated	from	humans

*New genus.

2) Phylum *Firmicutes*

The genus *Lactobacillus* belongs to the order *Lacto-bacillales* and family *Lactobacillaceae*. Although numerous others have been assigned to other genera, the phylogenetic relationship between the diverse species is complicated and poorly defined not yet.

The genus *Eubacterium* is phylogenetically diverse, and many *Eubacterium* species, which have been assigned to other genera, are now widely distributed within the phylum *Firmicutes. Eubacterium moniliforme* and *E. tarantellae* was reclassified to the genus *Clostridium* as *C. moniliforme* and *C. tarantellae*, and additionally *Sarcina maxima* and *S. ventriculi* was reclassified as *Clostridium maximum* and *C. ventriculi* [31]. The family *Lachnospiraceae* includes a number of former members of the genus *Eubacterium. Eubacterium hadrum* was reclassified as *Anaerostipes hadrus, E. formicigenerans* as *Dorea formicigenerans* [32, 33].

Among the genus *Clostridium, Clostridium difficile* and *C. mangenotii* were reclassified to the new genus *Clostridioides,* as *Clostridioides difficile* and *Clostridioides mangenotii* [34]. *C. glycolicum* was reclassified to the new genus *Terrisporobacte*, also changed to *T. glycolicus* [35]; *C. bifementans*, and *C. sordellii* were reclassified to the new genus *Paraclostridium* and *Paeniclostridium*, respectively [36]; *C. hathewayi* was reclassified to *Hungatella hathewayi* [37]; *Clostridium histolyticum, C. limosum* and *C. proteolyticum* were reclassified to the new genus *Hathewaya* as *H. histolytica, H. limosa* and *H. proteolytica* [31].

3. Anaerobic Gram-negative rods

Most of anaerobic gram-negative rods (AGNR) belong to the phylum *Bacteroidetes*, including the families *Bacteroidaceae*, *Porphyromonadaceae*, *Prevotellaceae*, and *Rikenellaceae*, and to the phylum *Fusobacteria* including the families *Fusobacteriae* and *Leptotrichiaceae*. The taxonomic changes have occurred within the phylum *Bacteroidetes*, especially those of the genus *Bacteroides*; new species have been described and some species have been transferred to other genera, since 2006 (Table 3).

1) Bacteroides and Parabacteroides

The genus *Bacteroides*, consisting of saccharolytic, bile-resistant, and nonpigmented species, is limited to species within the *Bacteroides fragilis* group, which now more than 20 species. The other species within the *B. fragilis* group are more resistant to many antimicrobials than *B. fragilis* and exclusion of the more resistant species in a published data of susceptibility may provide misleading results [38]. Some former *Bacteroides* species have been reclassified in the genus *Prevotella* and *Porphylomonas* [39, 40]. The genus *ParaBacteroides* consists of three former *Bacteroides* species, which are *P. distasonis*, *P. goldsteinii*, and *P. merdae*, and in addition, *P. gordonii* and *P. johnsonii* [41-43]. The latest new species is *P. chongii*, isolated from blood of a patient with peritonitis [44].

2) Prevotella and Porphyromonas

The genus *Prevotella* consists of moderately saccharolytic, bile-sensitive, predominantly oral species of formerly classified in the genus *Bacteroides* [39]. Novel *Prevotella* species, *P. micans* and *P. nanceiensis*, have been isolated not only from the oral cavity, but also from other sites of the body [45, 46]. The nonpigmented former *Mitsuokella dentalis* and *Hallella seregens*, which are associated with endodontic and other oral infections, have been reclassified as *Prevotella dentalis* [47].

The genus *Porphylomonas* consists of asaccharolytic, pigmented species of formerly classified in the genus *Bacteroides* [40]. Among *Porphyromonas* species which are frequently detected in humans, *P. gingivalis* and *P. endodontalis* (formerly *Bacteroides gingivalis* and *B. endodontalis*) are closely related to the acute symptoms in endodontic infections [48]. The newly described species of human origin are *P. pasteri*, isolated from human saliva [49], and *P. pogonae* isolated from clinical specimens [50].

3) Fusobacterium

Based on the 16S-23S rDNA internal transcribed spacer regions (ITS), Fusobacterium species were composed of three phylogenetic clusters; the first cluster (all nonoral) included F. mortiferum, F. varium, and F. ulcerans; the second cluster (all oral) contained. F. nucleatum subspecies, F. naviforme, F. simiae, and F. *periodonticum*; the third cluster (all invasive potential) included F. necrophorum subspecies and F. gonidiaformans [51]. F. nucleatum, the most commonly encountered in oral infection, is very heterogenous and currently classified as four subspecies including subsp. nucleatum, polymorph, vincentii, and animalis. F. nucleatum subspecies fusiform is a later synonym of subspecies vincentii [52]. In more recent, analyses using the genome sequences strongly suggest that four F. nucleatum subspecies should be reclassified as Fusobacterium species [53]. Fusobacterium equinum, a new species that is phenotypically similar to F. necrophorum, has been described from the normal oral cavity

Phylum and genus		Species or subspecies	Previous name(s) or synonym	References
Bacteroidetes				
Bacteroides	В.	<i>fraailis</i> group		[38]
Parabacteroides	Р.	chonaii	New species	[44]
	Р	distasonis	Bacteroides distasonis	[41]
	P	aodonii	New species	[42]
	P	godorni goldsteinii	Bacteroides goldsteinii	[41]
	, . Р	iohnsonii	New species	[43]
	, . Р	merdae	Racteroides merdae	[41]
Pornhvromonas	, . Р	asaccharolytica	Bacteroides asaccharolyticus	[40]
, espinyrennende			Bacteroides melaninogenica subspecies asaccharolytica	[40]
	Р	endodontalis	Bacteroides endodontalis	[40]
	, . Р	oingivalis	Bacteroides cincivalis	[40]
	, . Р	nasteri	New species	[49]
	, . P	podonae	New species	[50]
Prevotella	, . P	bivia	Racteroides hivius	[39]
1101010110	, . P	buccae	Bacteroides burcae Bacteroides ruminicola subspecies brevis	[30]
		Succue	Bacteroides capillus Bacteroides pentosaceus	[00]
	P	buccalis	Bacteroides huccalis	[39]
	, . P	corporis	Bacteroides cornoris	[20]
	, . P	dentalis	Mitsuokella dentalis. Hallella seregens	[00] [/17]
	, . P	denticola	Bacteroides denticola	[39]
	, . P	disiens	Bacteroides disiens	[39]
	, . P	henarinolytica	Bacteroides henaringlyticus related to <i>B</i> fragilis group	[39]
	, . P	intermedia	Bacteroides intermedius	[20]
	, .	momoda	Bacteroides melaninogenica subspecies intermedius	[00]
	P	micans	New species	[45]
	, . P	loescheii	Racteroides loescheii	[30]
	, . P	melaninogenica	Bacteroides melaninogenica	[39]
	, .	melannegernea	Bacteroides melaninogenica subspecies melaninogenicus	[00]
	Р	nanceiensis	New species	[46]
	, . Р	oralis	Racteroides oralis	[39]
	γ. Ρ	oris	Bacteroides oris Bacteroides ruminicola subspecies brevis	[39]
	, . Р	oulorum	Bacteroides oulorum Prevotella oulora	[39]
	P	veroalis	Bacteroides veroalis	[39]
	P	zooaleoformans	Bacteroides zoogleoformans related to B fragilis group	[39]
Fusobacteria		2009/00/01/10/10		[00]
Fusobacterium	F.	eauinum	New species	[54]
	F	nucleatum subspecies animalis		[52]
	F	nucleatum subspecies necleatum		[52]
	F	nucleatum subspecies polymorphum		[52]
	F	nucleatum subspecies vincentii	Later synonym of <i>F nucleatum</i> subspecies <i>fusiform</i>	[52]
	F	pseudoperiodonticum	New species	[56]
Dialister	י. ת	invisus	New species	[57]
Dianotor	D.	pneumosintes	Bacteroides pneumosintes	[57]
Selenomonas*	S	sputiaena	·····	[58]
Proteobacteria	0.	,		[50]
Bilophila*	В.	wadsworthia	New species	[60]
Sutterella*	S.	wadsworthensis	Campylobacter gracilis, Bacteroides gracilis	[59]

Table 3. Taxonomic changes of anaerobic gram-negative rods isolated from humans

*New genus.

[54]. The *Fusobacterium alocis* and *F. sulci*, belonged to Clostridium cluster XI, have been reclassified as *Filifactor alocis* and *Eubacterium sulci*, respectively[55]. The latest proposed new species is *F. pseudope-*

riodonticum isolated from oral cavity based on the whole-genome analysis, most closely related to *F. periodonticum* [56].

4) Other anaerobic gram-negative rods

Among the genus *Dialister*, *D. invisus* and *D. pneumosintes* (formerly *Bacteroides pneumosintes*) isolated from the oral cavity [57]. *Selenomonas sputigena* of the genus *Selemonas*, as type species, is found in specimens from oral infections [58]. *Sutterella wadsworthensis*, new species of the genus *Sutterella*, formerly *Campylobacter gracilis* (*Bacteroides gracilis*), has been isolated from clinical specimens [59]. The genus *Bilophila* in the family *Desulfovibrionaceae* includes one human species, *Bilophila wadsworthia*, which is a important pathogen in humans [60].

CONCLUSION

Anaerobic bacteria are part of the commensal microbiota of humans in multiple sites of the body as opportunistic pathogens in many infections. The anaerobic taxonomy has undergone considerable changes over the years, mainly due to the increased widespread use of molecular technologies, including 16S rRNA sequencing and WGS. Existing genera and species have been reclassified or renamed and new genera and species have been added, resulting in changes of taxonomy. A subset of these changes is relevant to the field of anaerobic clinical microbiology, particularly in the context of accurate ID and appropriate AST, and epidemiology of emerging infections. The taxonomic updates are necessary to keep track of new names to aim at better description and recognition of the bacterium-disease associations. As the large percentage of the new species described are based on a single isolate of a new species, which was recovered from stool of a healthy person, taxonomic updates are necessary to determine the clinical importance. Furthermore, Current taxonomy is important to work toward better improvement of patient treatment and disease management, because antimicrobial resistance and misidentification of emerging pathogenic anaerobes. such as A. schaalii and Cutibacterium difficile, can be caused the inappropriate empiric therapy. Therefore,

CML should periodically update the taxonomic changes of anaerobic bacteria and properly inform clinicians of these changes. This article presents taxonomic changes of clinically important anaerobic bacteria. The update on taxonomy of anaerobic bacteria can help both CML and clinician guide empiric therapy for patient care and prevent treatment failure.

요 약

임상미생물학 분야에서 세균의 분류는 끊임없이 변화하는 상 태에 있다. 무산소성 세균의 대규모 분류와 명명법은 지난 수십 년 동안 발생되었는데, 주로 16S rRNA 염기서열 분석 및 전체 게놈 염기서열(WGS) 분석과 같은 분자 기술의 발전 때문이다. 새로운 균속과 균종이 추가되었고, 기존 균종과 균속은 재분류 되었거나 재명명되었다. 임상미생물검사실의 주요 역할은 임상 적으로 중요한 세균의 정확한 동정 및 적절한 감수성 시험, 그리 고 신속한 보고 및 임상의와의 의사 소통이다. 무산소성 세균의 분류학적 변화는 진단적으로 적절한 보고 항균제의 선택과 항균 제 감수성 해석 기준의 적용에 잠정적으로 영향을 미칠 수 있다. 이는 신흥 병원성 무산소성 세균의 항균제 내성 및 잘못된 동정 은 환자 치료에 있어서 부적절한 경험적 치료를 유발할 수 있기 때문이다. 따라서, 임상미생물검사실은 주기적으로 무산소성 세균의 분류학적 변경 사항을 업데이트하고, 임상의에게 이러 한 변경 사항을 적절하게 알려야 한다. 이 논문에서는 임상적으 로 중요한 무산소성 세균의 분류에 관한 업데이트을 제시하였 고, 이전의 균명 또는 동의어을 함께 기술하였다. 무산소성 세균 의 분류 업데이트는 무산소성 세균 감염에 대한 항균제 요법을 안내하고, 치료 실패를 예방하는데 임상미생물검사실과 임상의 모두에게 도움이 될 수 있다.

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