

# Getting a Knack for the GPACs & GNACs:

*The Basics, and some more...*

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Infectious Disease / Medical Microbiology

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# Disclosures:

- Currently (11/2019) involved in ongoing compensated research projects with Attostar LLC

# Objectives:

- 1: Describe the important organisms in the GPAC and GNAC categories
- 2: Familiarize oneself with the emerging disease associations of clinical relevance
- 3: Understand the importance of the microbiology laboratory identification of these organisms, and the underlying purpose behind identifying them

# Guidepost:

- 1. **Anaerobes**, in general
- 2. **Focusing on cocci:**
  - **GPAC**
  - **GNAC**
- 3. **Laboratory** Considerations
- 4. Current issues of interest



# Anaerobic Bacteriology

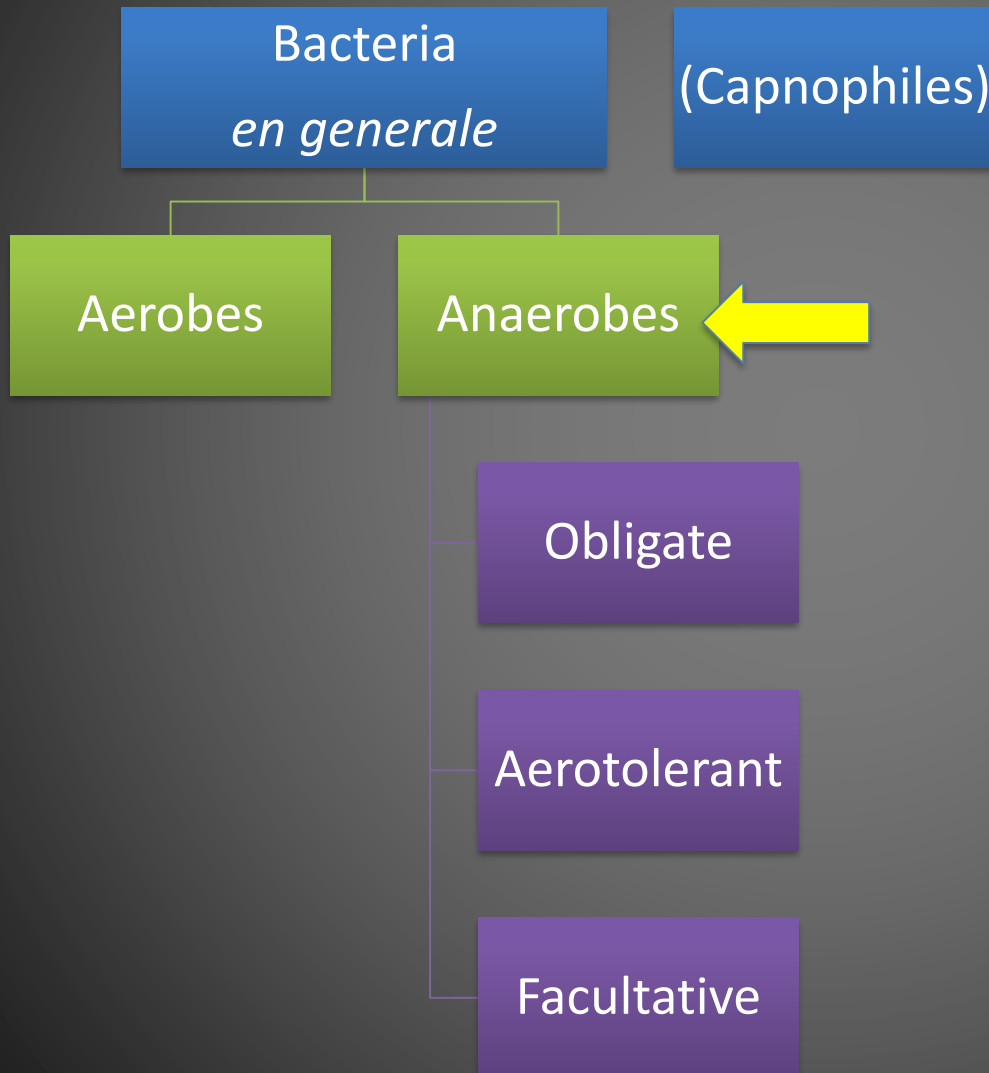


Image: Wikipedia (Leeuwenhoek)

# When invoke anaerobes?

- Reasonable suspicion:
  - Gram stain discordant with culture
  - Infections of the gut, or mucus membrane
    - Trauma, penetrations, procedures, or plastics that cross between these zones
  - Gas production
  - Stinky

*Microb Ecol.* 2019 Apr;77(3):808-820. doi: 10.1007/s00248-018-1231-z. Epub 2018 Aug 23.

## Co-occurrence of Anaerobes in Human Chronic Wounds.

[Choi Y<sup>1</sup>](#), [Banerjee A<sup>2</sup>](#), [McNish S<sup>2</sup>](#), [Couch KS<sup>2</sup>](#), [Torralba MG<sup>1</sup>](#), [Lucas S<sup>1</sup>](#), [Tovchigrechko A<sup>1</sup>](#), [Madupu R<sup>1</sup>](#), [Yooseph S<sup>1</sup>](#), [Nelson KE<sup>1</sup>](#), [Shanmugam VK<sup>3</sup>](#), [Chan AP<sup>4</sup>](#).

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### Abstract

Chronic wounds are wounds that have failed to heal after 3 months of appropriate wound care. Previous reports have identified a diverse collection of bacteria in chronic wounds, and it has been postulated that bacterial profile may contribute to delayed healing. The purpose of this study was to perform a microbiome assessment of the Wound Healing and Etiology (WE-HEAL) Study cohort, including underlying comorbidities less commonly studied in the context of chronic wounds, such as autoimmune diseases, and investigate possible relationships of the wound microbiota with clinical healing trends. We examined chronic wound specimens from 60 patients collected through the WE-HEAL Study using 16S ribosomal RNA gene sequencing. A group of co-occurring obligate anaerobes was identified from taxonomic analysis guided by Dirichlet multinomial mixtures (DMM) modeling. The group includes members of the Gram-positive anaerobic cocci (GPAC) of the Clostridia class (i.e., *Anaerococcus*, *Fingoldia*, and *Peptoniphilus*) and additional strict anaerobes (i.e., *Porphyromonas* and *Prevotella*). We showed that the co-occurring group of obligate anaerobes not only co-exists with commonly identified wound species (such as *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Pseudomonas*, *Corynebacterium*, and *Streptococcus*), but importantly, they could also predominate the wound microbiota. Furthermore, examination of clinical comorbidities of the WE-HEAL specimens showed that specific obligate and facultative anaerobes were significantly reduced in wounds presented with autoimmune disease. With respect to future healing trends, no association with the wound microbiome community or the abundance of individual wound species could be established. In conclusion, we identified a co-occurring obligate anaerobic community type that predominated some human chronic wounds and underrepresentation of anaerobes in wounds associated with autoimmune diseases. Possible elucidation of host environments or key factors that influence anaerobe colonization warrants further investigation in a larger cohort.



# Understanding the microbiome of diabetic foot osteomyelitis: insights from molecular and microscopic approaches.

Johani K<sup>1</sup>, Fritz BG<sup>2</sup>, Bjarnsholt T<sup>3</sup>, Lipsky BA<sup>4</sup>, Jensen SO<sup>5</sup>, Yang M<sup>6</sup>, Dean A<sup>6</sup>, Hu H<sup>1</sup>, Vickery K<sup>1</sup>, Malone M<sup>7</sup>.

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- 7 Infectious Diseases and Microbiology, School of Medicine, Western Sydney University, Australia; Liverpool Hospital, South Western Sydney LHD, Sydney, Australia; Liverpool Diabetes Collaborative Research Unit, Ingham Institute of Applied Medical Research, Sydney, Australia. Electronic address: matthew.malone@health.nsw.gov.au.

## Abstract

**OBJECTIVES:** Rigorous visual evidence on whether or not biofilms are involved in diabetic foot osteomyelitis (DFO) is lacking. We employed a suite of molecular and microscopic approaches to investigate the microbiome, and phenotypic state of microorganisms involved in DFO.

**METHODS:** In 20 consecutive subjects with suspected DFO, we collected intraoperative bone specimens. To explore the microbial diversity present in infected bone we performed next generation DNA sequencing. We used scanning electron microscopy (SEM) and peptide nucleic acid fluorescent in situ hybridization (PNA-FISH) with confocal microscopy to visualize and confirm the presence of biofilms.

**RESULTS:** In 19 of 20 (95%) studied patients presenting with DFO, it was associated with an infected diabetic foot ulcer. By DNA sequencing of infected bone, *Corynebacterium* sp. was the most commonly identified microorganism, followed by *Fingoldia* sp., *Staphylococcus* sp., *Streptococcus* sp., *Porphyromonas* sp., and *Anaerococcus* sp. Six of 20 bone samples (30%) contained only one or two pathogens, while the remaining 14 (70%) had polymicrobial communities. Using a combination of SEM and PNA-FISH, we identified microbial aggregates in biofilms in 16 (80%) bone specimens and found that they were typically coccoid or rod-shaped aggregates.

**CONCLUSIONS:** The presence of biofilms in DFO may explain why non-surgical treatment of DFO, relying on systemic antibiotic therapy, may not resolve some chronic infections caused by biofilm-producing strains.

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# Clinical and microbiological features of bacteraemia with Gram-positive anaerobic cocci: a population-based retrospective study

M. Badri<sup>1</sup>, B. Nilson<sup>2,3</sup>, S. Ragnarsson<sup>4</sup>, E. Senneby<sup>1,2,3</sup>, M. Rasmussen<sup>1,5,\*</sup>  

Editor: S.J. Cutler

 PlumX Metrics

DOI: <https://doi.org/10.1016/j.cmi.2018.09.001>

 Article Info

Abstract **Full Text** Images References

## Abstract

### Objectives

Gram-positive, anaerobic cocci (GPAC) can cause infections in humans. Only a few cases of bacteraemia with GPAC have been reported. We describe the clinical and microbiological characteristics of GPAC bacteraemia.

### Methods

A retrospective population-based study of GPAC bacteraemia 2012–2016 in southern Sweden was performed. GPAC were identified using matrix-associated laser desorption ionization time-of-flight mass spectrometry or 16S rRNA gene sequencing. Etests were used to determine antibiotic susceptibilities. Data on patient and infection characteristics, treatment, and outcome were collected from the medical records.

### Results

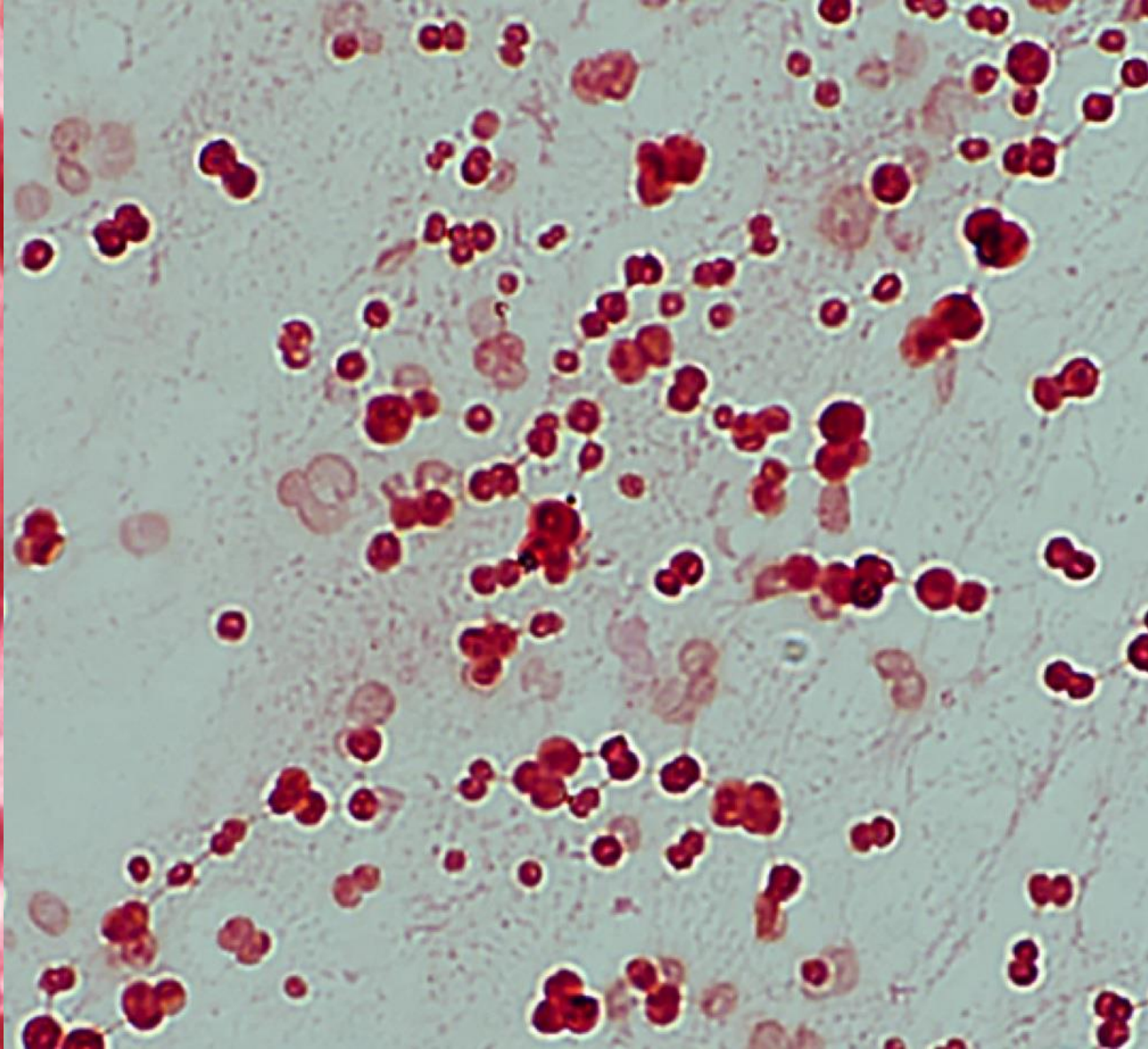
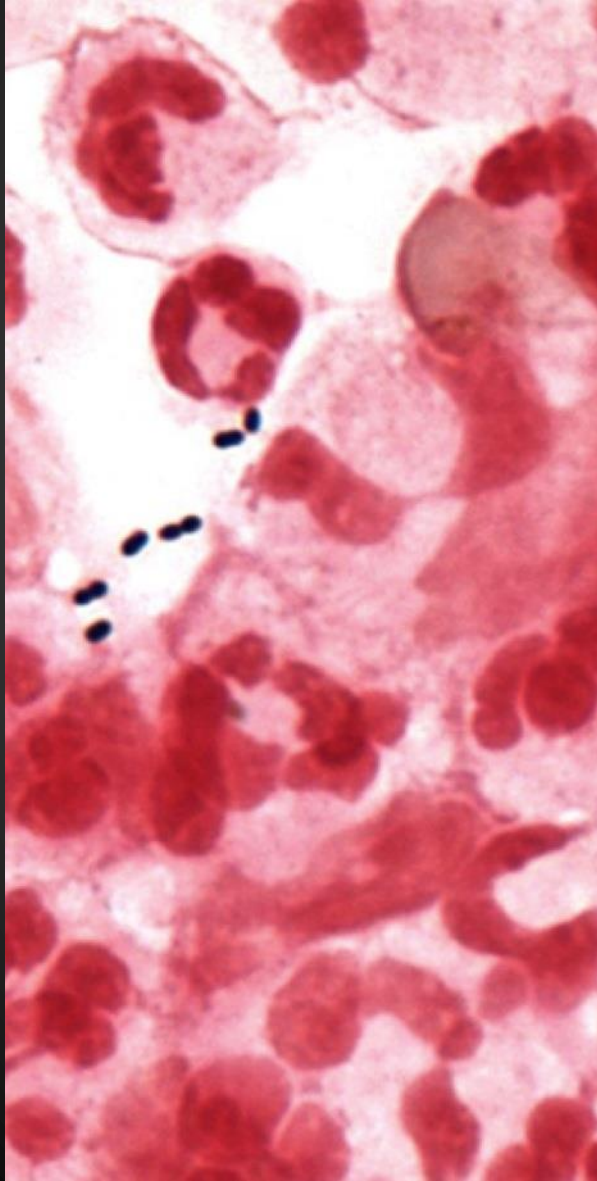
A total of 226 episodes of GPAC bacteraemia in adults were studied; this corresponds to an annual incidence of 3.4 cases per 100,000 persons per year. The bacteria identified were *Anaerococcus* spp. ( $n = 43$ ), *Atopobium* spp. ( $n = 7$ ), *Blautia* spp. ( $n = 1$ ), *Fingoldia* spp. ( $n = 15$ ), *Parvimonas* spp. ( $n = 100$ ), *Peptoniphilus* spp. ( $n = 52$ ), *Peptostreptococcus* spp. ( $n = 2$ ), and *Ruminococcus* spp. ( $n = 9$ ) of which 200 isolates were identified to the species level. Resistance to imipenem and piperacillin was not identified, whereas resistance among the 229 isolates to penicillin was detected in four, to metronidazole in six, and clindamycin in 16 isolates. The median age of patients was 73 years (55–83, IQR), 57% were male and comorbidities were common. Fifty-one per cent of infections were polymicrobial. In 60% of cases a focus of infection was identified. Forty per cent of patients had either organ dysfunction or shock. The 30-day mortality was 11%, and nosocomial infections were over-represented among the deceased.

### Conclusions

GPAC bacteraemia is much more common than previously reported. GPAC-bacteraemia is a condition with significant mortality mainly affecting elderly persons with comorbidities.



# Gram Stain Rules All:



# *Two Groups to Discuss:*

- **Gram Positive Anaerobic Cocci (GPACs)**
  - The vast majority of organisms of clinical consequence today
- **Gram Negative Anaerobic Cocci (GNACs)**
  - Occasional players in select circumstances

# Isolation of oxidase-positive Gram-negative cocci not belonging to the genus *Neisseria* from the urogenital tract

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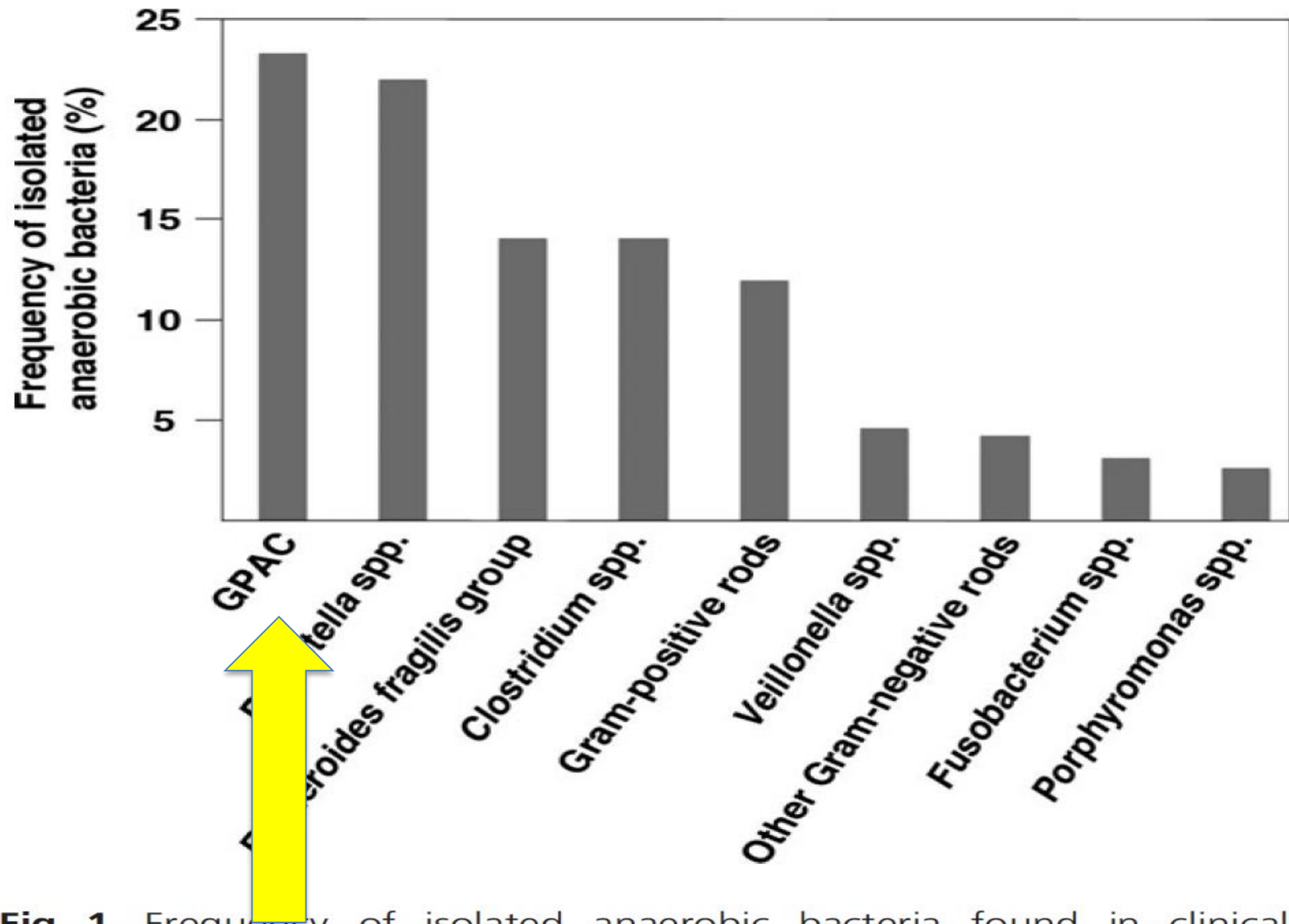
**SYNOPSIS** In a 12-month period, oxidase-positive, Gram-negative cocci showing similar characteristics in biochemical tests have been isolated from the urogenital tract of 39 male and female patients. Although these organisms superficially resemble *Neisseria gonorrhoeae*, biochemical characterization and the results of DNA base composition analysis indicate that they do not belong to the genus *Neisseria*. The relationship of these organisms to the genera *Neisseria*, *Achromobacter*, and *Pseudomonas* is discussed.

The isolation of *Neisseria* spp other than *Neisseria gonorrhoeae* from the urogenital tract has been reported (Wilkinson, 1952). More recently, Jephcott and Morton (1972) have reported the isolation of *N. lactamicus* from a genital site, and *N. meningitidis*

rectum were inoculated on to a modified Thayer Martin medium (Riddell and Buck, 1970) and incubated in candle extinction jars at 37°C for 48 hours.



## Interactions of GPAC with the host



**Fig. 1.** Frequency of isolated anaerobic bacteria found in clinical infection (1994–2004). Figure adapted from (Mikamo *et al.*, 2011).

# Groups: GPAC

- **GPAC** (Gram Positive Anaerobic Cocci):
  - *\*Peptostreptococcus*
  - *Peptococcus*
  - *\*\*Finegoldia*
  - *Parvimonas*
  - *Peptinophilus*
  - *Atopobium*
  - *Anaerococcus*

## Antibiotic resistance

G

- Variably called “Peptostreptococcus”
  - 25-33% of GPAC
  - Usually penicillin sensitive
  - May stain gram positive
  - Metronidazole sensitive
- Frequent pathogens
  - Surgical infections
- Fairly tolerant to antibiotics

In general, GPAC have variable resistance to penicillins (7–10%), clindamycin (7–20%), and metronidazole (5–10%), whereas these bacteria are more susceptible to  $\beta$ -lactam/ $\beta$ -lactamase inhibitors, cephalosporins, carbapenems, and chloramphenicol (Hecht, 2006). Also, resistance to tetracycline and erythromycin has been reported (Brazier *et al.*, 2003; Boyanova *et al.*, 2004). Data describing differences in antimicrobial susceptibility between various species of GPAC are increasing (Bowker *et al.*, 1996; Brazier *et al.*, 2003, 2008; Koeth *et al.*, 2004; Roberts *et al.*, 2006; Könönen *et al.*, 2007) and are described in more detail for the major groups below.

Regarding the continuous rise in antibiotic resistance amongst GPAC and anaerobes in general, more surveillance testing will be needed. Moreover, due to differences in antibiotic susceptibility between GPAC species, it is important to identify isolates in clinical specimens for susceptibility testing to adapt the correct antibacterial therapy.

# Proposal of the genera *Anaerococcus* gen. nov., *Peptoniphilus* gen. nov. and *Gallicola* gen. nov. for members of the genus *Peptostreptococcus*

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Members of genus *Peptostreptococcus* have previously been found to be distantly related to the type species, *Peptostreptococcus anaerobius*, on the basis of 16S rDNA sequence similarities. They were divided into three major phylogenetic groups, and their peptidoglycan structure and biochemical traits differed between groups. The reclassification of the species of these three groups into three new genera, *Peptoniphilus* gen. nov., *Anaerococcus* gen. nov. and *Gallicola* gen. nov., is proposed. The genus *Peptoniphilus* gen. nov. includes the following butyrate-producing, non-saccharolytic species that use peptone and amino acids as major energy sources: *Peptoniphilus asaccharolyticus* comb. nov. (type species), *Peptoniphilus lacrimaris* comb. nov., *Peptoniphilus harei* comb. nov., *Peptoniphilus indolicus* comb. nov. and *Peptoniphilus ivorii* comb. nov. The genus *Anaerococcus* gen. nov. contains the saccharolytic, butyrate-producing species *Anaerococcus prevotii* comb. nov. (type species), *Anaerococcus tetradius* comb. nov., *Anaerococcus lactolyticus* comb. nov., *Anaerococcus hydrogenalis* comb. nov., *Anaerococcus vaginalis* comb. nov. and *Anaerococcus octavius* sp. nov. The genus *Gallicola* gen. nov. contains a single species, *Gallicola barnesae* comb. nov.

**Keywords:** *Peptostreptococcus*, taxonomy, *Anaerococcus*, *Peptoniphilus*, *Gallicola*

Fig  
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Case report



## Septic arthritis in a native joint due to *Anaerococcus prevotii*

[S Jain<sup>1</sup>](#), [V Bui<sup>2</sup>](#), [C Spencer<sup>2</sup>](#), [L Yee<sup>1</sup>](#)

[Author affiliations](#) +

### Abstract

A 37-year-old injecting drug user presented with signs and symptoms of septic arthritis. *Staphylococcus aureus* was grown from his blood cultures. Despite treatment with flucloxacillin and fusidic acid his condition continued to deteriorate. Echocardiography showed no signs of endocarditis. Culture of his knee aspirate grew *Anaerococcus prevotii* after 5 days of incubation. Metronidazole was added to his treatment regime. A collection of pus (800 ml) was drained from the right thigh and *A prevotii* was isolated. His condition improved gradually and he was subsequently transferred to a drug rehabilitation unit after completing his antibiotic course. The importance of anaerobic streptococci in septic arthritis, as a very rare cause, is highlighted.

[View Full Text](#)



# A newly discovered Anaerococcus strain responsible for axillary odor and a new axillary odor inhibitor, pentagalloyl glucose.

Fujii T<sup>1</sup>, Shinozaki J, Kajiura T, Iwasaki K, Fudou R.

## Author information

1 Frontier Research Laboratories, Institute for Innovation, Ajinomoto Co. INC., Kanagawa, Japan.

## **Abstract**

Skin surface bacteria contribute to body odor, especially axillary odor. We aimed to investigate anaerobic bacteria that had not been previously studied for axillary odor formation. A new anaerobic Anaerococcus sp. A20, that releases 3-hydroxy-3-methyl-hexanoic acid (HMHA, main component of axillary odor) from its glutamyl conjugate, was discovered from axillary isolates. This strain showed strong resistance to the antimicrobial agents, triclosan and 4-isopropyl-3-methylphenol; therefore, we screened plant extracts that inhibit the A20 strain. We discovered that pentagalloyl glucose (PGG) extracted from the Chinese Gall plant exhibited both antibacterial and inhibitory activities against HMHA release by the A20 strain. As the excellent antibacterial activity and inhibitory effect of PGG against HMHA release were seen in vitro, we conducted an open study to evaluate the deodorant effects of PGG on axillary odor. The sensory tests on odor strength showed that application of the PGG solution could reduce axillary odors in vivo. Although there was a small change in axillary microbiota, the microbial count of A20 significantly reduced. These results strongly indicate PGG as a new innovative deodorant material that only affects odor-releasing bacteria in the axillary microbiota.

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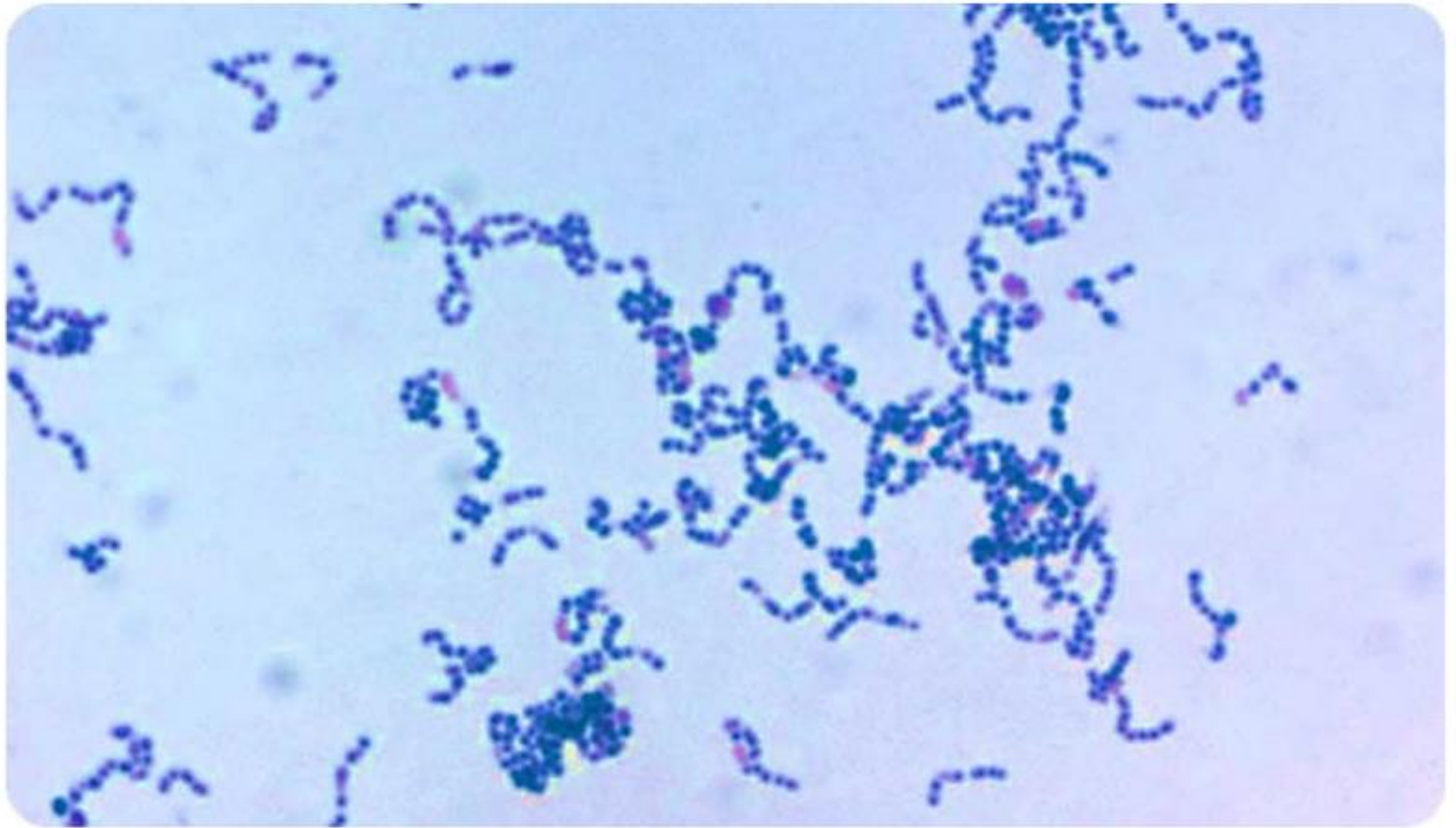
**KEYWORDS:** 3-hydroxy-3-methyl-hexanoic acid; Anaerococcus; axillary odor; pentagalloylglucose; skin microbiota

PMID: 24784923 DOI: [10.1111/1574-6941.12347](https://doi.org/10.1111/1574-6941.12347)

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Age old microbiology: if it smells, there's anaerobes!



**Fig. 1** *Atopobium vaginae* culture, Gram stain, magnification 100 × (courtesy of M. Vaneechoutte, Belgium)

# Infective endocarditis due to *Atopobium vaginae*: a rare association between genital infection and endocarditis of the tricuspid valve

[Josephine Mansell<sup>1</sup>](#), [Yannis Gourtsoyannis<sup>2</sup>](#), [Nehal Draz<sup>3</sup>](#), [Ruaridh Buchanan<sup>4</sup>](#)

[Author affiliations](#) +

## Summary

*Atopobium vaginae* is an anaerobic gram-positive organism associated with genitourinary infections. Bacteraemia is rare, with only two cases reported in the literature. This case describes an 18-year-old type 1 diabetic, presenting with sepsis and haemoptysis, on a background of poor dental hygiene and recurrent hospital admissions. Blood cultures grew *A. vaginae* and echocardiogram revealed a large tricuspid valve lesion. Despite medical therapy, symptoms of pulmonary emboli continued and she therefore underwent surgical resection of the lesion. Histopathological findings were of a vegetation; culture of the lesion was negative but 16S ribosomal PCR was positive, detecting 16S rRNA of *A. vaginae*. The patient was treated with 4 weeks of vancomycin and made a good recovery. To our knowledge, this represents the first report of infective endocarditis due to this organism. We also provide a review of the literature, including comparing published drug susceptibility data with consensus breakpoints for antimicrobial agents.



# *Peptococcus*

- Lonely *Peptococcus niger*  
– Others reclassified elsewhere

FEMS Microbiol Lett. 1990 Sep 1;59(1-2):139-43.

## **The phylogenetic position of *Peptococcus niger* based on 16S rRNA sequence studies.**

Ludwig W<sup>1</sup>, Weizenegger M, Dorn S, Andreesen J, Schleifer KH.

### **Author information**

1 Lehrstuhl für Mikrobiologie, Technische Universität München, F.R.G.

### **Abstract**

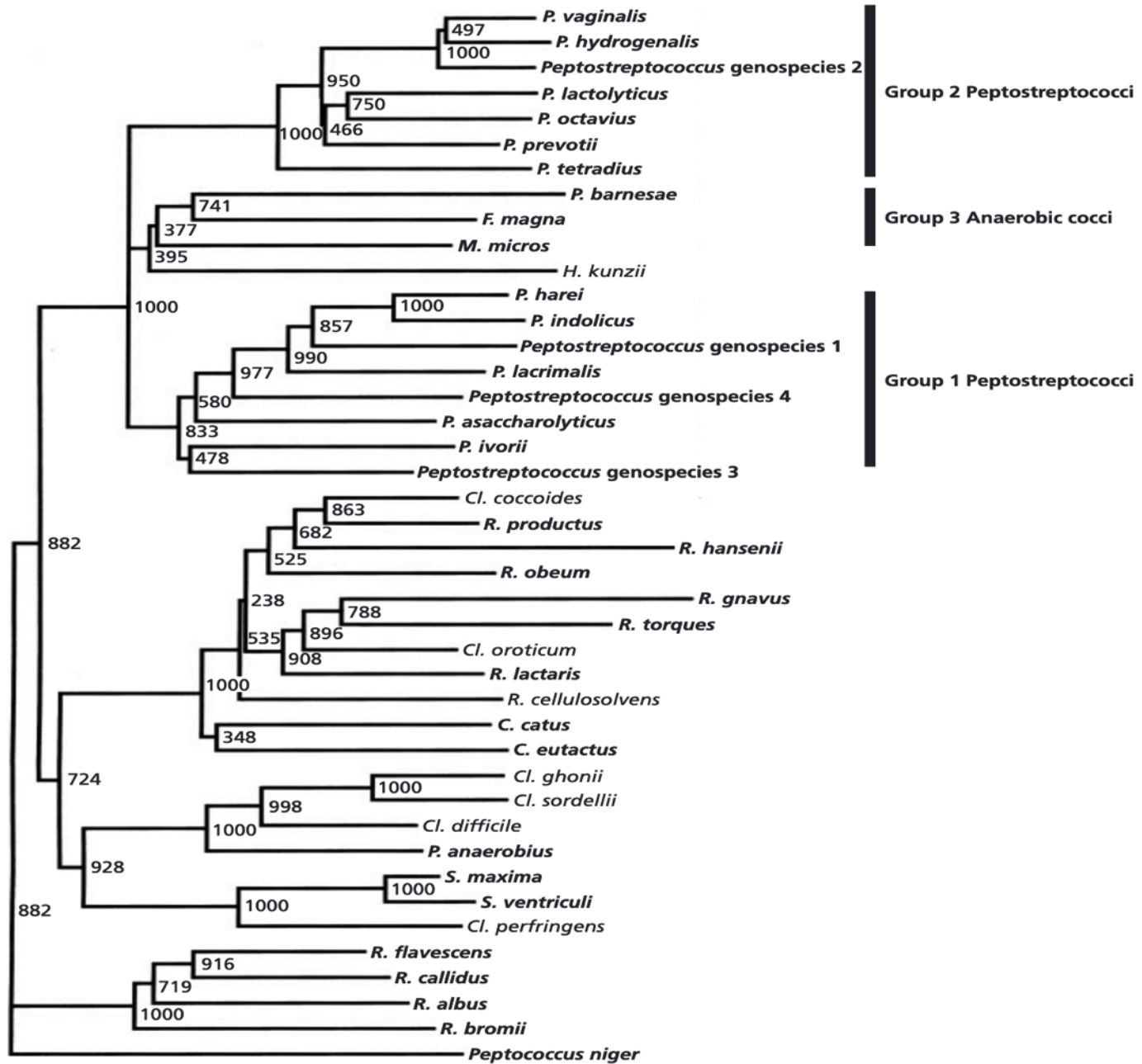
A 1330 base-pair fragment of a 16S rRNA gene has been amplified, cloned and sequenced. Comparison to other 16S rRNA sequences of eubacteria showed that *P. niger* represents a deep branch within the subdivision "Gram-positive with Gram-negative cell walls". It is not related to peptostreptococci, representatives of this genus studied so far are more closely related to clostridia.

PMID: 1703504 DOI: [10.1111/j.1574-6968.1990.tb03812.x](https://doi.org/10.1111/j.1574-6968.1990.tb03812.x)

[Indexed for MEDLINE]

# *Peptostreptococcus*







# *Peptostreptococcus* (genus)

- Several representatives:
  - *Peptostreptococcus anaerobius*

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, June 2007, p. 2205–2207  
0066-4804/07/\$08.00+0 doi:10.1128/AAC.00056-07  
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## Antimicrobial Susceptibilities of *Peptostreptococcus anaerobius* and the Newly Described *Peptostreptococcus stomatis* Isolated from Various Human Sources<sup>∇</sup>

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Received 15 January 2007/Returned for modification 1 February 2007/Accepted 21 March 2007

*Peptostreptococcus anaerobius sensu lato*, currently including two closely related species, *P. anaerobius* and *P. stomatis*, is known to be more resistant than other gram-positive anaerobic cocci. We reidentified potential *Peptostreptococcus* isolates and tested their susceptibilities to eight antimicrobials. Notably, *P. anaerobius* had constantly higher values for the MIC at which 50% of the isolates are inhibited (MIC<sub>50</sub>) and the MIC<sub>90</sub> than *P. stomatis*.

## Primary sternal osteomyelitis due to *Peptostreptococcus anaerobius*.

Chen YL<sup>1</sup>, Tsai SH, Hsu KC, Chen CS, Hsu CW.

### Author information

1 Department of Emergency Medicine, National Defense Medical Center, Taipei, Taiwan.

### **Abstract**

Primary sternal osteomyelitis (PSO) is a rare syndrome. In adults, it usually occurs with underlying predisposing factors, such as immunodeficiency, or intravenous (IV) drug abuse. The infecting organism in these patients is usually *Staphylococcus aureus* or *Pseudomonas aeruginosa*. *Peptostreptococcus* species are Gram-positive anaerobic cocci and are part of the normal flora of human mucocutaneous surfaces. *Peptostreptococcus* infection can occur in all body sites, including the central nervous system, head, neck, chest, abdomen, pelvis, skin, bone, joint, and soft tissue. Here, we report on a 32-year-old previously healthy Chinese man who was diagnosed with PSO and *P. anaerobius* was yielded in the bacterial culture. He was treated empirically with antibiotics, but these failed. After additional limited surgical intervention with debridement, the PSO was cured.

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# Efficacy of tedizolid against methicillin-resistant *Staphylococcus aureus* and *Peptostreptococcus anaerobius* in thigh mixed-infection mouse model

Yuka Yamagishi<sup>a,b</sup>, Hiroshige Mikamo<sup>a,b</sup>, Hideo Kato<sup>b,c</sup>, Naoya Nishiyama<sup>a,b</sup>, Nobuhiro Asai<sup>a,b</sup>, Yusuke Koizumi<sup>a,b</sup>, Daisuke Sakanashi<sup>b</sup>, Hiroyuki Suematsu<sup>b</sup>, Katsuhiko Matsuura<sup>c</sup>, Mao Hagihara<sup>a,b,c,\*</sup>

PlumX Metrics

DOI: <https://doi.org/10.1016/j.jiac.2017.02.013> | 



Article Info

Abstract

Full Text

Images

References

## Abstract

### Objective

The purpose of this study is to compare the antimicrobial activity of human simulated exposures of tedizolid 200 mg daily, and linezolid 600 mg every 12 h for the treatment of complicated skin and skin structure infection (cSSSI) caused by MRSA and *Peptostreptococcus anaerobius* in both the neutropenic mice thigh mixed-infection models.

### Material and method

Tedizolid phosphate and linezolid were used for all *in vivo* testing. A total of one MRSA and two *P. anaerobius* isolates were utilized. Antimicrobial efficacy was calculated for each isolate as the change in bacterial numbers ( $\Delta\log_{10}$  CFU/ml) obtained in the treated mice after 24 h compared with the numbers in the starting control animals (0 h).

### Results

The tedizolid and linezolid MICs for MRSA was 0.25 and 2  $\mu$ g/ml. Tedizolid MIC for *P. anaerobius* was 0.12  $\mu$ g/ml, and linezolid MICs for two *P. anaerobius* isolates were 0.5 and 1  $\mu$ g/ml. In mixed infection model, tedizolid therapy showed similar antimicrobial activities for one MRSA and two *P. anaerobius* isolates evaluated, compared with linezolid therapy. Additionally, when comparing the activity of tedizolid and linezolid monotherapy between single infection and mixed infection model, antimicrobial activities of both antimicrobials were attenuated when mixed infection model was used.

### Conclusion

In the neutropenic murine thigh infection model, human simulated exposures of tedizolid and linezolid resulted in similar efficacies against MRSA, even though single and mixed infection models were used. These data support the clinical utility of tedizolid for use against MRSA and *P. anaerobius* in the treatment of cSSSI.

EDITOR

# caused by *Saccharolyticus*

M<sup>1</sup>, Carvalho P<sup>1</sup>, Silva J<sup>1</sup>, Malcata A<sup>1</sup>

016;41:271-272

nes & Wade, 2006). Metronidazole is the most effective antibiotics against *S. spp.*. However, the nitroimidazole *rimB* – has been found in 31% of *S.* in another study (Theron *et al.*, 2010). Metronidazole resistance in *Peptostreptococcus* should be monitored in the future.

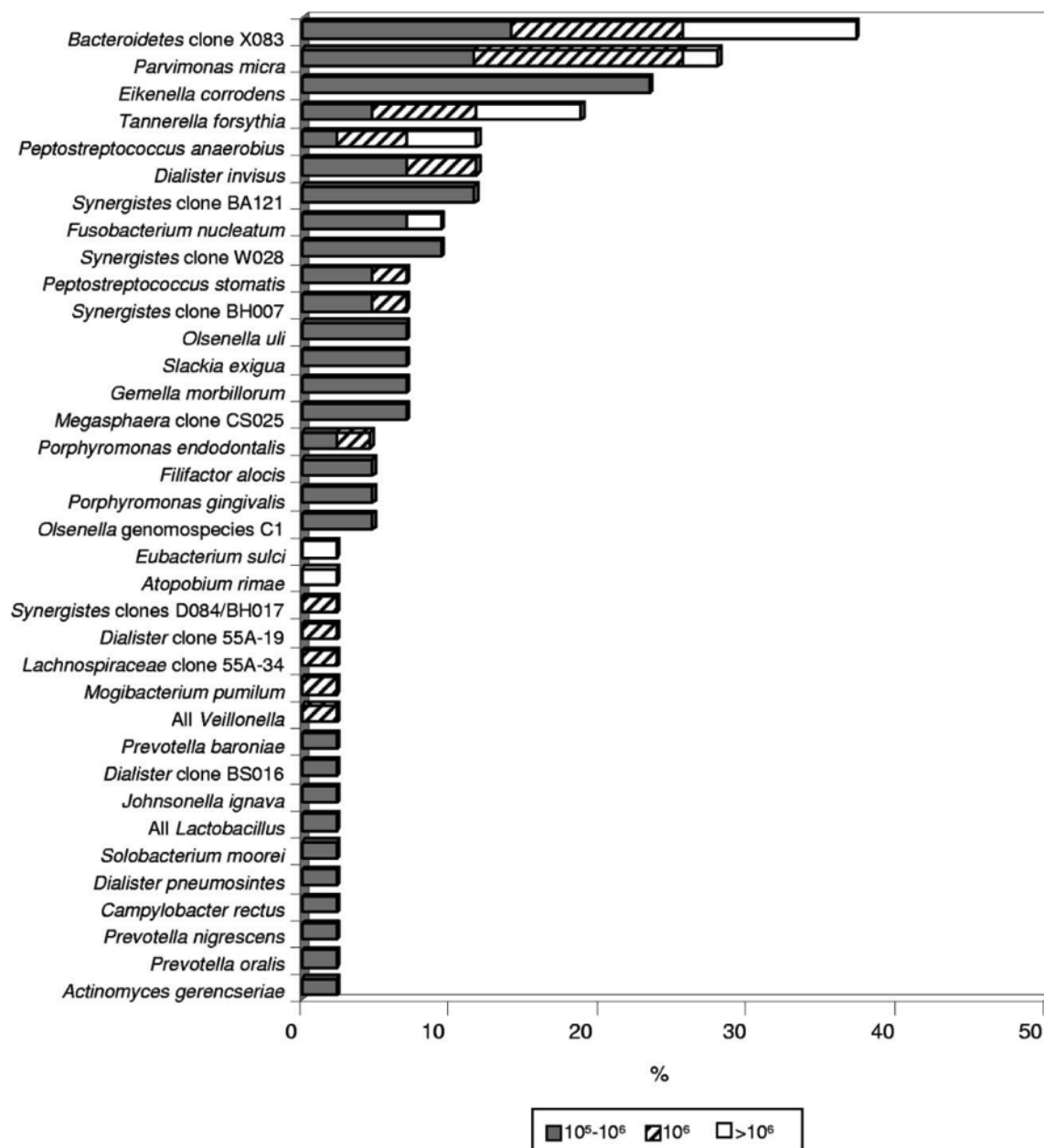
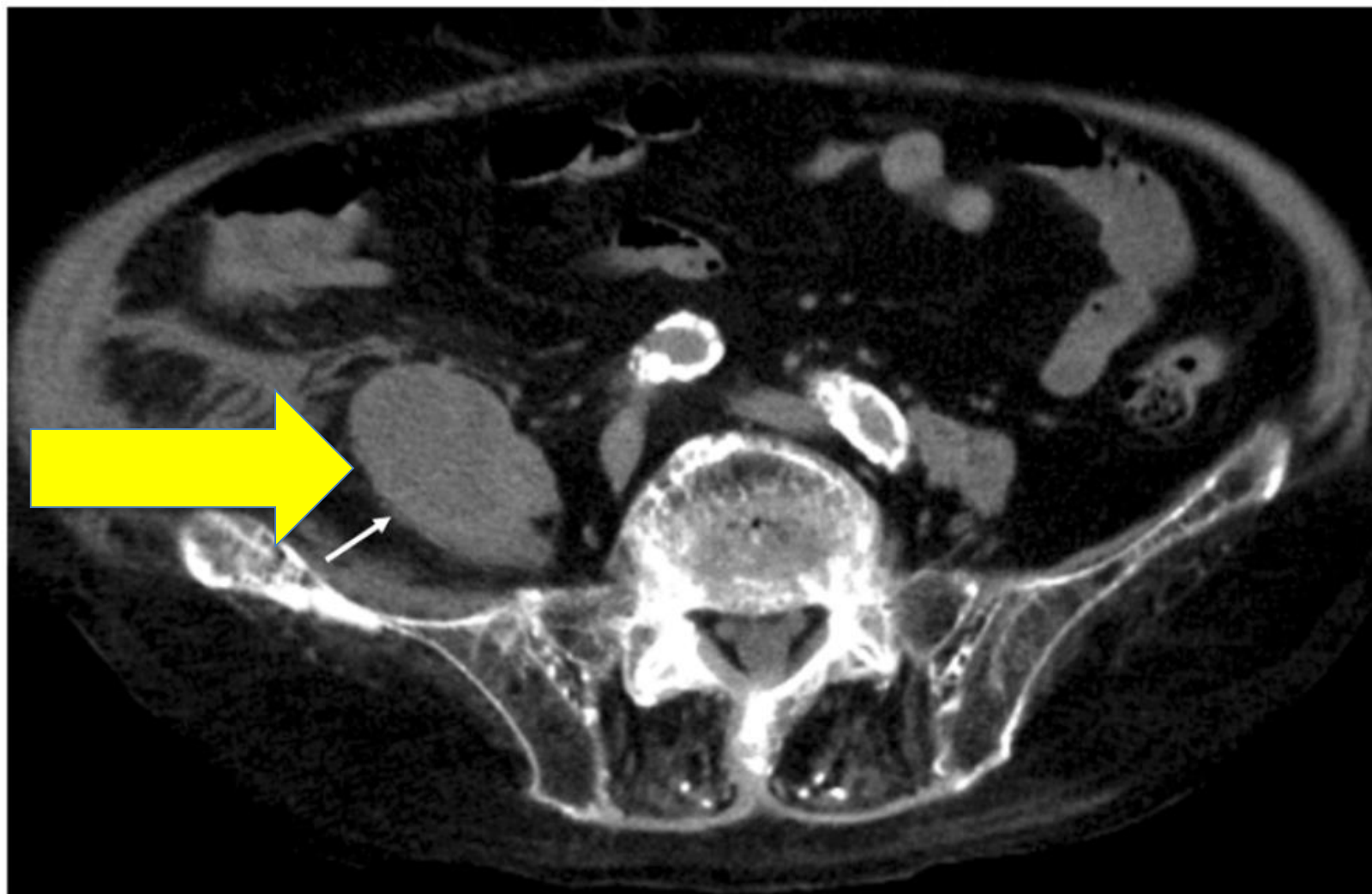


FIG. 2. Stacked bar chart of frequency of detection of bacterial species and phylotypes in root canal samples at levels above  $10^5$ . Different shades within each bar indicate the percentages of samples containing different levels of the species.





**Fig. 1** Abdominal computed tomography on admission showed a low-density mass in the right iliopsoas muscle (*white arrow*)

**keyworas:** Primary iliopsoas abscess, *Parvimonas micra*, CT-guided percutaneous drainage, Ampicillin/sulbactam



# Multiple Hepatic Abscess from *Parvimonas micra*: An Emerging Gastrointestinal Microbe



**Figure 1.** Contrast-enhanced abdominal computed tomography: (A) transverse image showing multiple rim-enhancing lesions in both hepatic lobes; (B) coronal image showing thick enhancing septations of hepatic abscesses.

# An Unusual Presentation of *Parvimonas micra* Infective Endocarditis

Dawn Ho <sup>1</sup>, Grace Ang <sup>1</sup>, Chaozer Er <sup>2</sup>, Siew Fei Yap <sup>3</sup>, Veeraraghavan Meyyur Aravamudan <sup>4</sup>

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Disclosures can be found in Additional Information at the end of the article

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## Abstract

*Parvimonas micra* has been identified as a prominent oral pathogen. This organism has been implicated in periodontal, soft tissue and bone infections. It causes a subacute presentation with high morbidity. We present a case of severe infective endocarditis caused by *Parvimonas micra* requiring valvular surgery despite appropriate antibiotics. To our knowledge, this is the second case report of *Parvimonas micra* infective endocarditis since its reclassification in 2006.

## **Parvimonas micra bacteremia following endoscopic retrograde cholangiopancreatography: A new route of infection.**

Boattini M<sup>1</sup>, Bianco G<sup>2</sup>, Cavallo R<sup>2</sup>, Costa C<sup>2</sup>.

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- 2 Microbiology and Virology Unit, University Hospital Città della Salute e della Scienza di Torino, Turin, Italy.

### **Abstract**

*Parvimonas micra* is an anaerobic, Gram-positive coccus belonging to oral, gastrointestinal and genital flora, rarely causing infections in humans. It was mainly deemed to cause bacteremia, septic bone and cerebral infections in patients which have undergone dental procedures or with suboptimal dental hygiene. We report the first case of *Parvimonas micra* bacteremia following endoscopic retrograde colangiopancreatography performed due to choledocholithiasis in a patient with good oral health. Identification of *P. micra* was finally performed by Matrix-assisted laser desorption ionization-time of flight mass spectrometry (VITEK MS system, bioMérieux, Marcy l'Étoile, France). All cases reported in english language of *Parvimonas micra* infections after medical procedure are reviewed in order to alert clinicians about new possible routes of infection of this emerging pathogen.

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**Infections following device emplacement, instrumentation, and procedures will continue to be evolving issues (and drive a multi-billion dollar industry in the direction of disposal devices (e.g. endoscopes)**

# Peptoniphilus

## Bloodstream infections due to *Peptoniphilus* spp.: report of 15 cases

K. Brown<sup>1</sup>, D. Church<sup>1,2,3</sup>, T. Lynch<sup>2,3</sup> and D. Gregson<sup>1,2,3</sup>

1) Department of Medicine, 2) Department of Pathology and Laboratory Medicine, University of Calgary, and 3) Calgary Laboratory Services, Calgary, AB, Canada

### Abstract

- Increasing player in ch
- ? Sinus disease
  - Fluoroquinolone resist

JOURNAL OF CLINICAL MICROBIOLOGY, Mar. 2011, p. 1189

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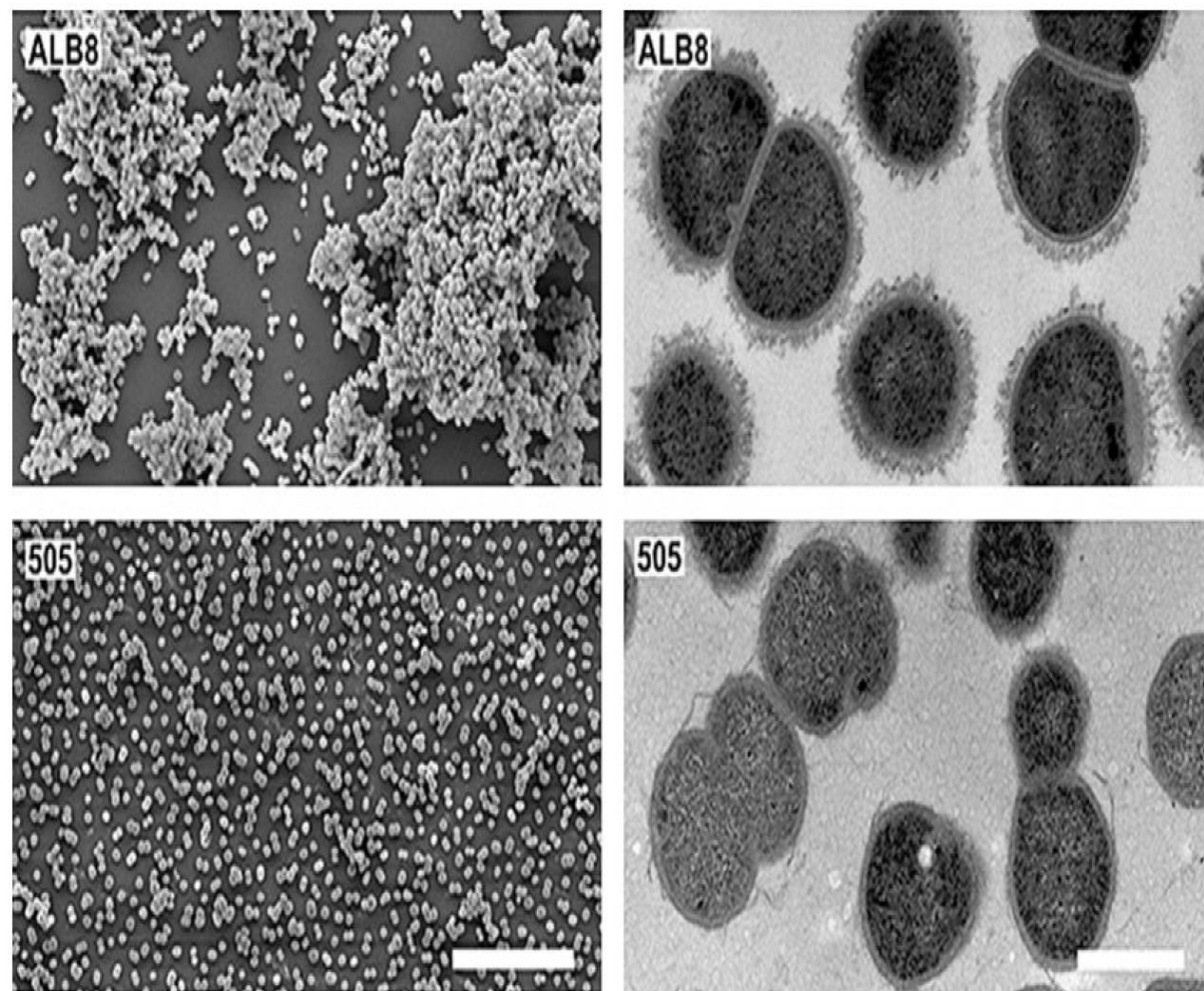
Vol. 49, No. 3

## Mistaken Identity of *Peptoniphilus asaccharolyticus*<sup>▽</sup>

*Peptoniphilus asaccharolyticus* is a commonly isolated Gram-positive anaerobic coccus (GPAC) (7). However, the type strain, ATCC 14963, is not representative of the species. Huss et al. (4) described the DNA-DNA homology between the type strain and clinical isolates as being <25%.

each other phenotypically. Holdeman-Moore et al. (3) commented in 1986 that one should be cautious in reporting on isolation and incidence of *P. asaccharolyticus*. In our opinion, this caution still stands. The fact that the type strain of *P. asaccharolyticus*, ATCC 14963, is atypical of clinical isolates (Y07839). *Peptoniphilus* is a rare but important cause of BSI.





**Fig. 4.** Electron microscopy images of *Finegoldia magna* ALB8. Left: Scanning electron micrographs of *F. magna* strains ALB8 (top row) and 505 (non-FAF expressing strain) (bottom row) Bar represents 10  $\mu\text{m}$ . Right: Transmission electron micrographs of same. Bar represents 5  $\mu\text{m}$ . Reproduced with permission from (Frick *et al.*, 2008).

# *Finegoldia magna*

- Formerly *Peptostreptococcus magnus* (et al)
- Increasingly becoming the “big player” in the who’s-who of anaerobes
  - Most common GPAC of consequence from skin, soft tissue, bone, and subcutaneous specimens
  - Implicated in a wide variety of disease states
    - Frustrated by slow growth, commingling, and sample bias
- Multiple virulence factors
  - May be the “*Staphylococcus aureus*” of the GPACs



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Contents

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Anaerobe

Volume 42, December 2016, Pages 145-151



Review article

Pathogenesis and Toxins

Molecular biology, genetics and biotechnology  
Identification of pili on the surface of  
positive anaerobic cocci

Molecular Microbiology (2014) 94(2), 403–417 ■

## Identification of molecular *magna* to penetrate and co

Elizabeth C. Murphy,<sup>1\*</sup> Matthias Mörgelin,<sup>1</sup>  
Dieter P. Reinhardt,<sup>2</sup> Anders I. Olin,<sup>1</sup> Lars Björk  
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H3A 2B2, Canada.

# Virulence arsenal of the most pathogenic species among the Gram-positive anaerobic cocci, *Finegoldia magna*

Lyudmila Boyanova , Rumyana Markovska, Ivan Mitov

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<https://doi.org/10.1016/j.anaerobe.2016.10.007>

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## Highlights

- *Finegoldia magna* is a highly successful opportunistic pathogen.
- Factors like sortase-dependent pili and FAF act at the start of the infection.
- Infection severity can be linked to superantigen protein L, capsule and enzyme.
- FAF, SufA and biofilms can lead to infection chronification.
- Antibiotic therapy can be hampered by biofilms and antibiotic resistance.



## Abstract

This review focuses on the virulence arsenal of the most pathogenic species among Gram positive anaerobic cocci, *Finegoldia magna* according to recently published data from 2012 to 2016. **Virulence factors** like **sortase** dependent **pili** and *F. magna* **adhesion** factor (FAF) facilitate the start of the infection. **Albumin binding protein** (PAB) enhances *F. magna* survival. FAF, subtilisin-like extracellular **serine protease** (SufA) and **superantigen protein L** protect the bacteria from factors of innate defense system. SufA, capsule and tissue-destroying enzymes provide a deep **penetration** or spread of the infections and the protein L is associated with infection severity. Biofilm production results in infection chronification and complicated treatment as well as to persistence of multi-species biofilms. Resistance rates to **quinolones** (13.0-70%) and **clindamycin** (0–40.0%) are important, and resistance to **penicillins** (<4%), **chloramphenicol** (7.0%) and **metronidazole** (<7%) has been reported. *F. magna* should not be overlooked when present in mono-infections or mixed infections in humans.



# Finegoldia magna

- Common player
  - Diabetic Foot Ulcers
    - Avid biofilm former
  - Mixed anaerobic infections
  - (anaerobic) Prosthetic Infections



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## *Finegoldia magna* Isolated from Orthopedic Joint Implant-Associated Infections

Bo Söderquist,<sup>a,b</sup> Sanna Björklund,<sup>a</sup> Bengt Hellmark,<sup>a,b</sup> Anders Jensen,<sup>c</sup> Holger Brüggemann<sup>c</sup>

School of Medical Sciences, Faculty of Medicine and Health, Örebro University, Örebro, Sweden<sup>a</sup>; Department of Laboratory Medicine, Clinical Microbiology, Örebro University Hospital, Örebro, Sweden<sup>b</sup>; Department of Biomedicine, Aarhus University, Aarhus, Denmark<sup>c</sup>

**ABSTRACT** The anaerobic Gram-positive coccus *Finegoldia magna* is a rare cause of infections of bone and joints. The aim of this study was to describe the microbiological and clinical characteristics of orthopedic implant-associated infections caused by *F. magna*. We retrospectively analyzed samples consisting of anaerobic Gram-positive cocci and samples already identified as *F. magna* from patients with orthopedic infections. The isolates found were determined to the species level using matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS). The antibiotic susceptibility pattern was determined by Etest. Whole-genome sequencing (WGS) was performed. Clinical data were extracted from each patient's journal. In nine patients, orthopedic joint implant-associated infections were identified as being caused by *F. magna*. The isolates were susceptible to most of the antibiotics tested, with the exception of rifampin and moxifloxacin in a few cases. Five of the nine infections were monomicrobial. The most common antibiotic used to treat the infection was penicillin V, but five of the nine patients received a combination of antibiotics. Eight patients underwent surgical treatment, with extrac-

# A case of necrotizing fasciitis caused by *Finnegoldia magna* in a patient with type 2 diabetes mellitus

360 | M. Scapatucci, S. Marchetto, A. Nardi, et al.

**Figure 1** - Patient at admission presented necrotizing fasciitis of the forefoot, anterior (A) and posterior view (B).



# **Finegoldia magna (formerly Peptostreptococcus magnus): an overlooked etiology for toxic shock syndrome?**

Rosenthal ME<sup>1</sup>, Rojtman AD, Frank E.

## **– Author information**

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## **Abstract**

*Finegoldia magna* is an anaerobic Gram positive coccus, previously classified as *Peptostreptococcus magnus*. It is normal flora of the gastrointestinal and genitourinary tract, and can be isolated from skin and the oral cavity and is often regarded as a contaminant in cultures. As the most frequently isolated anaerobic coccus, it is implicated in a range of mono- and polymicrobial infections, including skin and skin structure, bone and joint (native and prosthetic joints), infective endocarditis (native and prosthetic valves), necrotizing pneumonia, mediastinitis and meningitis. Recently, whole genome sequencing furthered the understanding of the pathogenicity of this organism by elucidating both chromosomally encoded and mobile plasmid mediated virulence factors. Although no cases of toxic shock syndrome have been attributed to *F. magna*, we present a case of a fatal monomicrobial *F. magna* bacteremia and hypothesize that superantigen activity, mediated via Protein L binding the variable domain of the  $\kappa$  light chains of IgG, resulted in the syndrome observed in our patient. Additionally, we suspect the overall significance of this pathogen is underestimated and with more sensitive detection methods, this organism will be identified more frequently in clinical cultures and associated with true infection.

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PMID: 22571938 DOI: [10.1016/j.mehy.2012.04.013](https://doi.org/10.1016/j.mehy.2012.04.013)

Most likely, the incidence of *F. magna* is highly underestimated due to problems of obtaining good quality anaerobic clinical specimens. For instance, detection of *F. magna* in blood cultures was found to be dependent on the blood culture system used (Bassetti *et al.*, 2003).

- A In this case of prosthetic valve endocarditis caused by *F. magna*, several blood cultures incubated in BacT/ALERT (BioMérieux) and BACTEC 9240 (Becton Dickinson) systems were negative despite growth of *F. magna* from biopsies of the aortic wall of the patient (Bassetti *et al.*, 2003). Additional tests demonstrated that the isolated strain did grow in other blood culture systems like SEPTI-CHEK BHI-S (Becton-Dickinson) and ISOLATOR (Du Pont Co.) or in thioglycolate medium and on blood agar (Bassetti *et al.*, 2003). This is consistent with other reports on prosthetic valve endocarditis caused by *F. magna*, where the bacterium could only be detected in cultures from the infected valve (Pouëdras *et al.*, 1992; van der Vorm *et al.*, 2000). Thus, the relevance of *F. magna* as the infectious agent in patients with apparent culture-negative endocarditis has to be considered. Inter-

in a car

st



# *Finnegoldia magna*

- Antibiotic resistance:
  - An emerging, worsening problem

*Finnegoldia magna* in PJI

Journal of Clinical Microbiology

**TABLE 1** Distribution of MIC values for eight antibiotics, using *Finnegoldia magna* isolated from patients with orthopedic implant-associated infections ( $n = 9$ )

Antimicrobial agent <sup>a</sup>	No. of isolates with MIC ( $\mu\text{g/ml}$ ):													
	0.002	0.004	0.008	0.016	0.032	0.064	0.125	0.25	0.5	1.0	2	4	8	>32
PG				4	2	3								
AC				1	2	4	1		1					
CM					2	1	2	2	1	1				
MZ				2	4	1	2							
LZ							1		1	1	5		1	
RI	3	1				3		1						1
VA							2	7						
MXF				1	1	3		1				1		2

<sup>a</sup>PG, benzylpenicillin; AC, amoxicillin; CM, clindamycin; MZ, metronidazole; LZ, linezolid; RI, rifampin; VA, vancomycin; MXF, moxifloxacin.

# Bonus GPAC: *Fastidiosipila sanguinis*



CASE REPORT

## First Human Case of *Fastidiosipila sanguinis* Infection

Clémence Beuruelle,<sup>a</sup> Hervé Le Bars,<sup>a</sup> Laurence Pougnet,<sup>b</sup> Ludovic Lesecq,<sup>c</sup> Philippe Buisson,<sup>d</sup> Geneviève Héry-Arnaud<sup>a,e</sup>

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***Fastidiosipila sanguinis* is a Gram-positive anaerobic coccus. We report the first case of osteitis implicating this species. The strain was accurately identified by 16S rRNA sequence analysis, matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) identification having failed. The reservoir remained unclear; an endogenous origin is suspected.**

# Groups: GNAC

- **GNAC** (Gram Negative Anaerobic Cocci):
  - \**Veillonella*
  - *Acidaminococcus*
  - *Megasphaera*
  - *Anaeroglobus*
  - *Negativicoccus*

# Veillonella

- GNAC
- Normal flora of GI / GU tract
  - High quantities in **saliva, and on tongue**
- Generally sensitive to antimicrobials:
  - Penicillin G
  - Clindamycin
  - Metronidazole
    - Can be confused with *Dialister* (nim!)



# Veillonella

- A Real Case:
  - 47 YO transgender female with AIDS (CD4 ~22), off HAART, undomiciled, admitted for dysphagia, dysphonia, and ? Hemoptysis
    - Erosive esophagitis on EGD, ?? Candida
    - Tissue from esophagus grew:
      - *Lactobacillus* spp x 1 specimen, scant
      - *Veillonella* (multiple spp) x 3 specimens, heavy
    - Improved dramatically with Augmentin

# *Megasphaera*

- Probably belongs with the Clostridia
- Many species
  - *Megasphaera micronuciformis*
- Implicated in **Bacterial Vaginosis**
  - ? Relapsing/recurrent BV in **WSW**?

# A Few Words on **BV**:

- A hot topic in microbiology, microbiomics, and in the wake of rising STD rates worldwide:
  - By definition, a “**dysbiosis**”
    - Lactobacillus (H<sub>2</sub>O<sub>2</sub>), pH, stability of the ecosystem
    - Switch to anaerobiosis = problems
  - **Increases risk for infections (HIV, STDs, PID)**
  - Negative implications in Obstetrics
  - **Recalcitrant problem** in some women

# Oral Microbiome in HIV-Infected Women: Shifts in the Abundance of Pathogenic and Beneficial Bacteria Are Associated with Aging, HIV Load, CD4 Count, and Antiretroviral Therapy

Tyler Lewy, Bo-young Hong, Barbara Weiser, Harold Burger, Andrew Tremain, George Weinstock, Kathryn Anastos, and Michael D. George [✉](#)

Published Online: 5 Mar 2019 | <https://doi.org/10.1089/aid.2017.0200>

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## Abstract

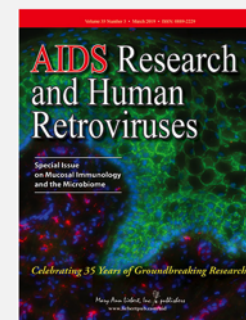
Human immunodeficiency virus (HIV)-associated nonacquired immunodeficiency syndrome (AIDS) conditions, such as cardiovascular disease, diabetes, osteoporosis, and dementia are more prevalent in older than in young adult HIV-infected subjects. Although the oral microbiome has been studied as a window into pathogenesis in aging populations, its relationship to HIV disease progression, opportunistic infections, and HIV-associated non-AIDS conditions is not well understood. We utilized 16S rDNA-based pyrosequencing to compare the salivary microbiome in three groups: (1) Chronically HIV-infected women >50 years of age (aging); (2) HIV-infected women <35 years of age (young adult); and (3) HIV-uninfected age-matched women. We also examined correlations between salivary dysbiosis, plasma HIV RNA, CD4<sup>+</sup> T cell depletion, and opportunistic oral infections. In both aging and young adult women, HIV infection was associated with salivary dysbiosis characterized by increased abundance of *Prevotella melaninogenica* and *Rothia mucilaginosa*. Aging was associated with increased bacterial diversity in both uninfected and HIV-infected women. In HIV-infected women with oral coinfections, aging was also associated with reduced abundance of the common commensal *Veillonella parvula*. Patients taking antiretroviral therapy showed increased numbers of *Neisseria* and *Haemophilus*. High plasma HIV RNA levels correlated positively with the presence of *Prevotella* and *Veillonella*, and negatively with the abundance of potentially

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### Keywords

HIV oral microbiome saliva  
 opportunistic infection aging  
 disease progression



# GPAC/GNAC Specimens:

- **Proper specimen is imperative!**
  - Vary in their aerotolerance
  - Vary in their proportion in mixed infections
  - Clinicians may need to be reminded that anaerobes exist, cause disease, grow “differently”, and have special considerations for sensitivity testing and identification on the back end

# Performance of two blood culture systems to detect anaerobic bacteria. Is there any difference? ☆



Manica Mueller-Premru <sup>a</sup>, Samo Jeverica <sup>a, \*</sup>, Lea Papst <sup>b</sup>, Elisabeth Nagy <sup>c</sup>

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## ABSTRACT

We studied the performance characteristics of two blood culture (BC) bottles/systems, (i) BacT/ALERT-FN Plus/3D (bioMérieux, Marcy l'Étoile, France) and (ii) BACTEC-Lytic/9000 (Becton Dickinson, Sparks, USA) for detection of growth and time-to-positivity (TTP) against a balanced and diverse collection of anaerobic bacterial strains ( $n = 48$ ) that included reference strains ( $n = 19$ ) and clinical isolates ( $n = 29$ ) of 32 species (15 Gram-negative and 17 Gram-positive). Standard suspension of bacteria was inoculated to each bottle in duplicates and incubated in the corresponding system. Overall, 62.5% ( $n = 30$ ) of strains were detected by both BC bottle types. Comparing the two, 70.8% ( $n = 34$ ) and 79.2% ( $n = 38$ ) of strains were detected by BacT/ALERT-FN Plus and BACTEC-Lytic bottles, respectively ( $p = 0.38$ ). Among Gram-negative anaerobes ( $n = 25$ ) the detection rate was 76.0% ( $n = 19$ ) vs. 92.0% ( $n = 23$ ) ( $p = 0.22$ ), respectively. Among Gram-positive anaerobes ( $n = 23$ ) the detection rate was 65.2% ( $n = 15$ ) in both bottles ( $p = 1$ ). The average TTP per bottle was calculated only for the strains detected by both systems ( $n = 30$ ) and was 40.85 h and 28.08 h for BacT/ALERT-FN Plus and BACTEC-Lytic, respectively ( $p < 0.001$ ). The mean difference was 12.76 h (95% CI: 6.21-19-31 h). Six anaerobic strains were not detected by any system, including Gram-negative *Porphyromonas gingivalis*, and five Gram-positive strains: *Fingoldia magna*, *Peptostreptococcus anaerobius*, *Propionibacterium acnes*, *Clostridium novyi* and *Clostridium clostridioforme*. Furthermore, *Eggerthella lenta* and *Prevotella bivia* were detected only by BacT/ALERT-FN Plus, while *Prevotella disiens* and *Prevotella intermedia* were detected only by BACTEC-Lytic bottles. There were no major differences in detection rate among clinical and reference strains. Anaerobic bacteria represent a minority of BC isolates, however, far from ideal detection rate was observed in this study for both tested bottle/system combinations. Nevertheless, in those cases where both gave positive signal, BACTEC-Lytic was superior to BacT/ALERT FN Plus with 12.76 h shorter mean TTP. Improvements of media in blood culture bottles available for detection of anaerobes are warranted.

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no major differences in detection rate among clinical and reference strains. Anaerobic bacteria represent a minority of BC isolates, however, far from ideal detection rate was observed in this study for both tested bottle/system combinations. Nevertheless, in those cases where both gave positive signal, BACTEC-Lytic was superior to BacT/ALERT FN Plus with 12.76 h shorter mean TTP. Improvements of media in blood culture bottles available for detection of anaerobes are warranted.

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**Perhaps blood cultures are not the ideal means for identifying GPACs/GNACs**, though in all cases the proper specimens (transport, storage, etc) assure a higher probability of correctly isolating the organisms

MALDI-TOF's usefulness is generally in proportion to the degree of curation of the databases used...

...but that won't be the end of anaerobic identification in the modern era (much now being done with metagenomics, shotgun sequencing, and microbiomics approaches)

Clinical Microbiology

## Burden of emerging anaerobes in the MALDI-TOF and 16S rRNA gene sequencing era

Bernard La Scola <sup>a, b</sup>  , Pierre-Edouard Fournier <sup>a, b</sup>, Didier Raoult <sup>a, b</sup>

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<https://doi.org/10.1016/j.anaerobe.2011.05.010>

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### Abstract

The isolation of **anaerobes** from patients has declined in recent years, whereas their detection by molecular techniques has increased. In the present work, we analyzed the application of **matrix-assisted laser desorption ionization time-of-flight mass spectrometry** (MALDI-TOF MS) and **16S rRNA gene** sequencing to routine identification of anaerobes in **clinical microbiology** laboratory. We identified 544 isolates of 79 species by routine culture from deep samples in our hospital. **MALDI-TOF MS** allowed identification of 332 isolates (61%). The remaining 212 (39%) were identified by 16S rRNA gene sequencing, allowing identification of 202 at the species level. The most common anaerobes were *Propionibacterium* spp. (12%), *Fingoldia magna* (4%), *Fusobacterium* spp. (6%) and *Bacteroides* spp. (6%). However, among the 79 identified species, seven were **new species or genera**, including two *Prevotella* conceptionensis, a species previously detected by our team by amplification and sequencing, five *Anaerococcus* sp. and one *Prevotella* sp. Beyond the identification of these new species, we also identified several uncommon or previously not described associations between species and specific pathologic conditions. MALDI-TOF MS-based identification, which will become more effective with future spectra database improvement, will be likely responsible of a burden of emerging anaerobes in clinical microbiology.



# Anaerobic Sensitivities?

- **Generally a good idea if:**
  - Agent selection is critical for disease control
  - Long-term antibiotics are anticipated
  - Anaerobe(s) found in a **sterile site**
  - Usual regimen has failed
  - Strict anaerobiosis is presumed (i.e. no aerobes)
    - Microaerophile GPACs problematic
  - Honorable mention:
    - **When a good reason exists to do them**
      - Eye, Brain, valve, endograft, prosthetic, transplant, ? PJI

FUTURE MICROBIOLOGY, VOL. 14, NO. 12 | SPECIAL REPORT

## Multidrug resistance in anaerobes

Lyudmila Boyanova  , Rumyana Markovska & Ivan MitovPublished Online: 30 Aug 2019 | <https://doi.org/10.2217/fmb-2019-0132> [View Article](#) [Tools](#)  [Share](#)

Multidrug resistance (MDR) in anaerobes is not a well-known topic. *Bacteroides fragilis* group isolates have numerous resistance determinants such as multidrug efflux pumps, *cfiA* and *nimB* genes and activating insertion sequences, and some isolates exhibited extensive drug-resistant patterns. MDR rates in *B. fragilis* group were from 1.5 to >18% and up to >71% in *cfiA* and *nimB* positive isolates carrying insertion sequences. MDR was present in >1/2 of *Clostridioides difficile* isolates, most often in epidemic/hypervirulent strains and unusually high metronidazole or vancomycin resistance has been reported in single studies. MDR was found in *Prevotella* spp. (in ≤10% of isolates), *Fingoldia magna*, *Veillonella* spp. and *Cutibacterium acnes*. Resistance in the anaerobes tends to be less predictable and anaerobic microbiology is required in more laboratories. New hopes may be new antibiotics such as eravacycline, cadazolid, surotomycin, ridinilazol or *C. difficile* toxoid vaccines; however, more efforts are needed to track the MDR in anaerobes.

**Keywords:** anaerobes • anaerobic cocci • *Bacteroides fragilis* • *Clostridioides (Clostridium) difficile* • mechanisms • multidrug resistance • prevalence • *Prevotella* • rates

# Final Words:

- GPACs/GNACs will continue to play an evolving role in Infectious Disease
- The medical laboratorian will need to stay abreast of changes in taxonomy, diagnostics, drug sensitivity, and impact on clinical cases

Thank you!

Inquiries?

*also sent to my email; will reply in a few days, or so...*