

Microbe Wars

Who Is Winning ?

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The Second Golden Age of Micro

Previously undiscovered organisms
Newly discovered microbial causes of familiar diseases
Microbial diversity is increasing

The Tooth is not a stone
Many microbe-sized paths and caves

Now we are learning about long-term diseases

Three Great Divisions of Life on Earth

- Eukaryotes
- Bacteria
- Archea

– We just found them
– Most primitive
– Methanobrevibacter
intraorally




Outline:

1. Know your Enemy
2. Our Weapons

Life Forms That → Dental Problems

Bacteria	Old: 350 oral species, now 700-900
Funguses	Viable, Not Cultivable
Spirochetes	New names
Viruses	
Prions	

Bacteria have many ways to defeat antibiotics



- Shut down metabolism
- Community activity (Biofilm)
 - Quorum sensing
 - Gene expression
- Mutation

Bacteria are everywhere

- 2.8 Kilometers below Antarctic ice, with reproduction once every 300 years
- 1 mile below Seattle living only on rocks and water
- Salt mines
- At deep sea vents –
 - very high temperature and pressure
- Bacteria are **Very Promiscuous** w/ their DNA

Funguses

- Hard to kill
 - Same protein metabolism as us
- Candida albicans

Actinomyces – now called a bacteria, was a “fungus”

Geriatric (root) caries

Hard to kill – 4 w. PCN or 5x +1 w. PCN

Spirochetes

- Hard to culture,
- Most every dental sample has lots
 - Dahle, Tronstad & Olsen Oral Microbiol Immunol'93 in all necrotic pulps
 - Baumgartner JOE '03 – 61% of abscess/cellulitis
 - Siqueira JOE '01 – 60% T. denticola in pus
- New PCR methods help

Viruses

- Bacteriophages
 - Transfer DNA between bacteria
- Hepatitis B
 - No longer a problem
- Hepatitis C = 1.6% US population
 - Still a risk, but getting better
 - Many infected patients unaware
 - Liver function ?
 - Maybe not so many in dental aerosol
 - Adam Powell's research at UAB

Prions

- Just a chain of proteins
- Can duplicate itself
- Autoclaving ineffective
 - Alkaline soak before autoclaving
- Bind to steel

Problem:

- Sicker Patients
- Stronger Bacteria

We can fight bacteria

But, they are more evil than suspected

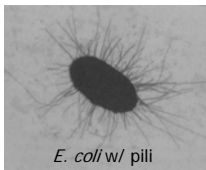
Biofilm

- DNA bank
- Quorum sensing
- Physical barrier

Motility

Anachoresis

Lux & Shi Crit Rev
Oral Biol Med '04



E. coli w/ pili

Endo Landmark

- Kakahashi, Stanley, and Fitzgerald, OOO 1965
- Germ-free rats pulp exposures healed rapidly

Endo Bacteria

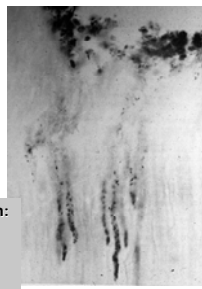
- Caries = aerobes and facultatives
oxygen + sugar → acid
- Penetration into pulp = less oxygen
 - Facultatives and Obligate anaerobes
- Bacteria in tubules
 - Miller 1890; Love (Crit. Reviews, 2002)
 - even in older dentin (Fouad JOE 2009)

Munson's research

JDR 2002

- Used PCR & found 20+ different bacteria types in av. Endo infection
- Kumar found same # in perio infections
- Viable, not Cultivable

Bacteria are smaller than tubules



Chronic canal infection:

More tubules infected

Bacteria go deeper in tubules

Siqueira – Actinomycosis in 5-10% of endo cases

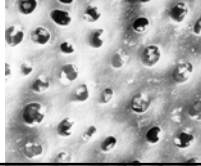
IEJ '02, OOO '03

- Slow growing
- Hyphae
- Tx w/ sx. + PCN x 1w.
- Tx w/ NSRCT + PCN x 4w.

Other antibiotics work too (LeCorn, Vertucci ... JOE '07)
More time is needed - Metronidazole does not work

Pathways to the Pulp

- Bacteria are everywhere
- Anachoresis
- Dentin tubules
 - caries
 - prophy
 - abrasion, etc.
 - "long in the tooth"
- Fractures
- Pulp caps
- Leaking Margins
- Perio disease



Oral Bacteria ↔ Heart Disease

- Non-venereal *Chlamydia*
- *Porphyromonas gingivalis*
- Did the heart bacteria cause perio disease
- What about antibiotic tx for heart disease ?

Biofilm Problem

- Can form outside root
- Quorum sensing
- Persister cell (like submarine)
- Problem for Implants
 - Joints
 - Penile implants ? Dental
 - Breast implants OK



Antibiotics Prior to Endo Appointment ?

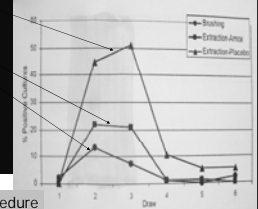
- Yes, if infected, without drainage
- Will not help pulpitis without necrosis
- American Academy of Orthopedic Surgeons 2009: **All** joint patients should get prophylactic antibiotics before invasive dental tx. - **No time limit** after sx.
- Vasculature around joint is very different

New Research on Bact. Endocarditis

- Lockhart et al. *Circulation* 2008;117:3118.
- Lit review:
 - 170 oral species in blood
 - 275 species caused IE
 - Merging lists → 98 species
- N = 290 patients for dental extraction
 - Gr. 1 Brushing alone (extraction after study)
 - Gr. 2 Amox, ext. after 1 hour
 - Gr. 3 Ext. w/ antibiotic

Results: IE-causing Bacteremia

- Extraction worst
- Reduced w/Antibiotic
- Brushing only

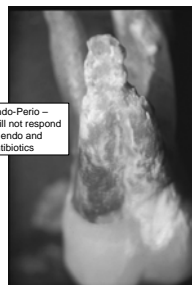


Prophylactic Antibiotics ?

- Cochrane Reviews
 - Sickle cell pts. w/ antibiotic = fewer pneumococcal infections
 - C-sections pts. w/ antibiotics = fewer infections
 - CF pts. w/ antibiotics = no difference in groups
 - Bronchitis pts. w/ antibiotics = slightly better
 - Pulpitis w/ antibiotics = same pain (Did the coverage keep the pulpitis from progressing into an abscess?)

Biofilm challenges our therapy

Costerton says 1000 X antibiotic concentration needed to kill all biofilm bacteria



Biofilm = Genetics changes Bacteria

- Planktonic form = free swimming
 - What we grow in lab
- When attached, they choose different genes from their DNA and thus behave very differently



Much of change we see is actually already there

That is:
Bacterial adaptability is less from mutation than from gene expression

Biofilm

- Attaches w/ holdfasts
- Slime = extracellular food storage
- Tumbleweed-like mats
- Outer layer = protection
- Quorum sensing
- Gene swapping

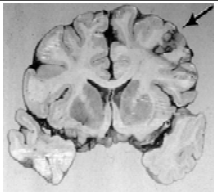


How do Obligate Anaerobes survive from one site to the next ?

• Biofilm

- Core cells survive
- Cell membrane shuts pores
- Metabolism stops

Dental microbes cause brain abscess



Copyright 1993 by The Journal of Bone and Joint Surgery, Incorporated
 Late Infection after Total Hip Replacement, Caused by an Oral Organism after Dental Manipulation
 A Case Report*
 Sullivan, 1990, J Bone Joint Surg

Can bacteria go thru vessel wall
 (Can one tooth's infection spread to another?)

Lemierre's Disease = *Fusobacterium necrophorum* from neck infection spreads into jugular vein to cause a clot. Also spreads into mediastinum (lungs)
 Enterococcus faecium (flesh eating bacteria)

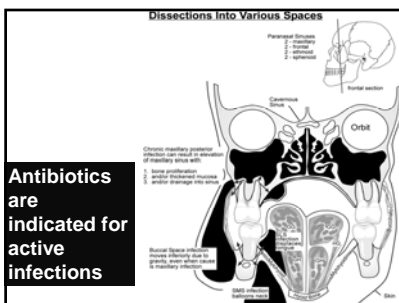
Lemierre's Disease

Bacteria grow through jugular

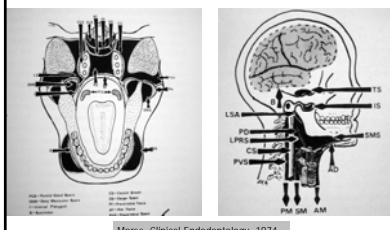
- Acute lung infections
 - Dental
- Source – Shiota Chest '02



UAB's Dr. Centor: 10% of sore throats are *F. necrophorum*, more deaths recently

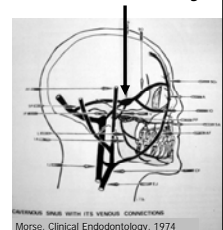


Danger – Up or Down



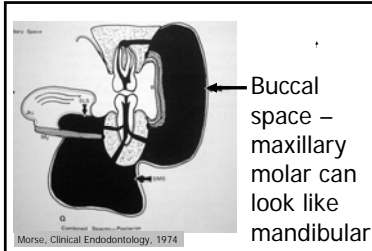
Canine Space Swelling into Cavernous Sinus

35% mortality



Sublingual - Submandibular

- **Sublingual Space**
 - Above mylohyoid muscle, displaces tongue
- **Submandibular space**
 - Below mylohyoid muscle, into neck
- **Mylohyoid has no posterior boundary, infection can get into neck easily**



Active Tuberculosis

- **Patients cannot be treated in your office**

Clinical Warning:

- **New strains of *Mycobacterium tuberculosis* are resistant to all antibiotics**
- **Tuberculosis bacteria are suspended in aerosols for hours**
- **Dental treatment creates these aerosols**

Others Harmed

Clostridium difficile

- Most common cause of abc. → diarrhea
- 1978-83, we blamed clindamycin
- 1983-2003 worst was cephalosporins
- Now, cases harder to treat Bartlett Ann Int Med '06
- Tx.: metronidazole 250 qid or 500 tid x 10 d.
- Not Vancomycin b/c VREF

IV Bisphosphonate Patients Take Penicillin Continuously



Outline

1. Know your Enemy
2. **Our Weapons**

Our Weapons

- **Techniques**
- **Disinfectants**
- **Antimicrobial drugs**
- **Probiotics**
- **Culture and Sens. Test**

Recent Changes

An MRSA variant repels Vancomycin action by buttressing its cell wall

Sieradzke and Tomasz Antimicrob Agents Chemo 2006; 50:527-533

Vancomycin interferes with cell wall synthesis

Our techniques

- **Handwashing is 10 X better than disinfectant hand rub** (Clinton, unpublished)
- **Change gloves after rubber dam placed** (Luckey)

Jeff Luckey's Study

- J Endodontics, 2006, p.646
- Our exam gloves in box = very low bacteria count, even after a week in the operatory
- Very high bacteria count after exam, anesthesia
- Should change to new gloves after rubber dam placed and tooth disinfected

Stephen Thomas – UAB

- **H₂O₂ killed intracanal anaerobe much faster than air exposure**

Endo Technique

- **We really should use better sterile technique for endo**

- Barrier for x-ray machine ?
- Film packet to darkroom ?

Dirty Area on Tray

- Keep a dirty area for used items
- Dixie cup of disinfectant for used files
 - Protection from stick injury

Incision for Drainage

- Block anesthesia
- Consider anatomy
- Consider gravity
- Cut to bone
- Many need to open bone
- Consider in-dwelling drain
- Antibiotic ?

Anesthesia for I & D

- *Block*
 - Infiltration into acidic pH = poor*
 - Wand = poor*
 - Pressure from anesthetic = poor*
- *Freeze*

1500 B.C.



Drain by Aspiration



Disinfectants

- Kill quickly
 - No problem with resistance
- Damage host cells
 - Keep in canal



Antibiotics vs. Disinfectants

- Antibiotics attack only bacteria
 - Metabolic differences
 - Structural differences
 - Spare host cells
- Disinfectants
 - Kill fast (no resistance)
 - Host cells harmed too

Routine Canal Irrigants

- Clorox
- Chlorhexidine 2%
- Iodine-potassium iodide
- EDTA
- MTAD
 - Tetracycline, citric acid, detergent

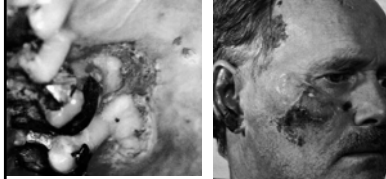
Remove Smear Layer = get to bacteria in tubules

*Shahnavan JOE 2007 Syst. Review (EDTA, various acids, Tetra.)

Intracanal meds

- One visit or Two ?
- Phenolics ?
- Calcium hydroxide
 - selects for *Enterococcus faecalis*
 - pH dissipates to cementum, & with time
 - may help external resorption
- $\text{Ca}(\text{OH})_2$ + another disinfectant

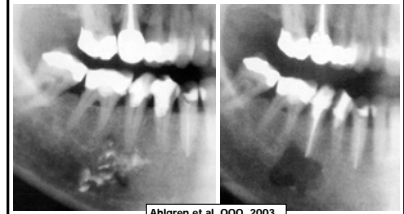
Calcium hydroxide is dangerous



Endo #31

Lindgren, J Oral Max-F 3X, 02

$\text{Ca}(\text{OH})_2$ #29 Paresthesia / surgery



Ahlgren et al. OOO, 2003

Calcium hydroxide needs a second disinfectant

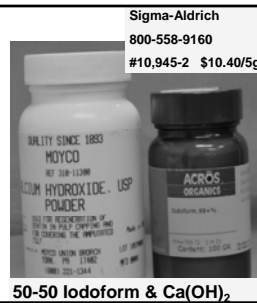
and Time too



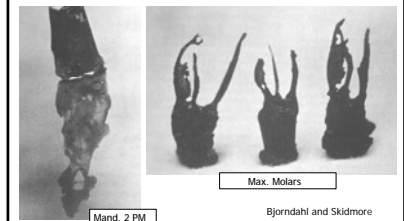
Powder = pH 12

Commercial versions = pH 10

Calcium Hydroxide Needs a second germicide



Clorox needed to dissolve tissue



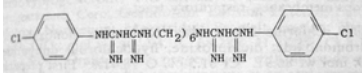
Max. Molars

Mand. 2 PM

Bjorndahl and Skidmore

Chlorhexidine ?

- Substantivity w/ dentin



CHX + NaOCL

Para-chloroaniline precipitate

- Brown color (even @ 0.19% Clorox)
- Unknown implications

- Leakage
- Systemic → methemoglobinemia

Basrani et al. (Toronto) JOE Aug. 2007

Clorox + Chlorhexidine

- A carcinogenic, brown-staining precipitate forms



MTAD ?

- Tetracycline
- Citric acid
- Detergent
- 5 minute soak after instrumentation

Laser - Radiosurgery

- Kill bacteria
- Live bacteria and viruses in smoke plume

No technique kills everything

Summary: Everything works, but nothing kills everything

Nair (TEM & LM) fins harbor many bacteria / pulp, even after 5.25% Clorox

Disinfectants for perio biofilm ?

- Chlorhexidine works
- Listerine works
- Paul Keyes
 - 1970'S
 - H₂O₂ + baking soda

Why Give Antibiotics

- Patient demand
- Treat existing infection
- Prevent infection (pain)

Endo Tip: Is patient swollen ?
Febrile ?

Rapid Worsening Airway ? Headache / vision ?



My Regimen

- Monitor signs / symptoms, including fever
- Bactericidal drug, change if no better w/ 24 hours
- Bacteriostatic drug, change if no better w/ 48 hours



Low-Dose Antibiotics OK ?

- Periostat – anticollagenase = antitumor ?
- Azithromycin used in sub-lethal dose = breaks up biofilm without killing *Pseudomonas*
- Topical antibiotics – FDA = OK
- Intracanal antibiotics ?
- No, get mutations: Kohanski Molec. Cell 2010

News from the Research Lab

- Tigecillin (Tigacil) new IV tetracycline has FDA approval
- Scripps Institute changed only one atom in vancomycin and got a much broader kill spectrum, including Vancomycin Resistant Enterococcus (VRE)
- New antibiotic substitutes bad protein in bacterial membrane (Srinivas, Sci 19 Feb '10)
- Zeftera – anti MRSA drug OK in Canada '08
- More will follow shortly

Probiotics – Fight bad bugs w/ good bugs

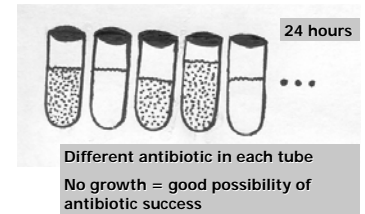
- Great hope
- Some out compete pathogens
 - Adherence
 - Fight for groceries
 - Make antibacterial products

Dentists Culture ???

U of L – UAB system

Needle aspirate,
Inoculate culture,
Shake,
Divide culture in vessels w/ antibiotic disks,
Incubate,
Read in 24 and 48 hours

Immediate inoculation – No O₂



Our System Avoids Oxygen



Anaerobe Systems
Morgan Hills, CA
408-782-7557

Summary

- Bacteria are everywhere and resistance is rising
- Patients are less healthy
- We must use antibiotics (wisely)
- Return to scrupulous sterile technique
 - More time for chemo-