



Microbes: The Silent Majority
Global & Not So Global Perspectives

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Howard Hughes

What comes to mind?



Is it a picture of a handsome, vital man, heir to a great fortune, whose exploits as an aviator, a movie producer, a husband of starlets, and a wily businessman?



Is it a lonely figure of an aging, unkempt, drug-addicted recluse, ensconced at vast expense in a Las Vegas hotel suite that he obsessively tried to keep operating-room clean, fretting endlessly that some germ will infect and kill him?



Our Fear

A cluster of translucent, rod-shaped bacteria and a single spherical microbe are positioned in the upper right corner of the slide.

When it comes to germs there is a little Howard Hughes in all of us!

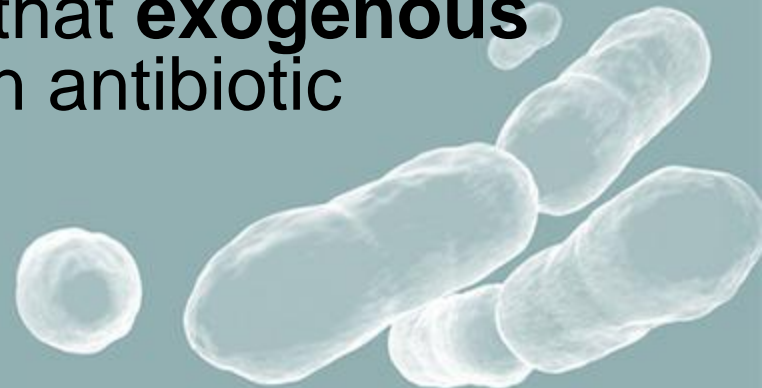
We all have the psychic fear that at any moment, in any setting, invisible agents may as easily give us an incurable, lethal disease as they would the common cold.

Is there just cause for alarm?

A group of translucent, rod-shaped bacteria and a single spherical microbe are positioned in the lower right corner of the slide.

The Threat

- **Globalization** has unleashed germs that were once confined among isolated population groups like HIV, Ebola, West Nile, monkeypox, SARS, Mad-cow, dengue fever, XDRTB, among others. It made it possible to ***spread from anywhere to anywhere***, just like a computer virus on the internet, only much more deadly.
- However, we are probably at a greater risk from our **indigenous** germs rather than **exogenous** ones, especially with the rise in antibiotic resistance.



Top Killers of Man



Year 1900

Germs: #1 killer worldwide

Life expectancy ~ 45y

Year 2010

Germs: #1 killer worldwide

Life Expectancy* ~ 78y

In the US and industrial nations, we've relegated germ caused deaths to 3rd place:

#1: Heart disease**

#2: Cancers***

#3: Germs (infectious diseases)

***Because of (a) sanitation/hygiene (b) vaccines (c) antibiotics**

**Chlamydia pneumoniae

* ** HHSV-8 Kaposi's sarcoma

HPV cervical carcinoma

Peridontitis

Hepatitis B & C carcinoma

Oncoviruses

Hpylori (inflam & carcinoma)

EBV lymphomas;

HTLV-1 leukemia-lymphoma



Of Microbes and Men

- Human body has **10X** more bacterial than human cells
- **90%** of cells that constitute “us” are bacterial
- Approximately **2.5 lbs** of body weight is from bacteria living on external and internal surfaces
- There are more bacteria living in a **tablespoon** of human feces than the number of men whoever walked the face of planet Earth!
- **Combined weight** of Microbes on Earth is **greater** than all other life forms.




Sometimes Germs Get a Bad Rap...



Good vs. Bad Germs

Of the 60,000 microbial groups or types or categories one might encounter from people, animals or the environment only about 1-2% (600-1200) are potentially or overtly pathogenic



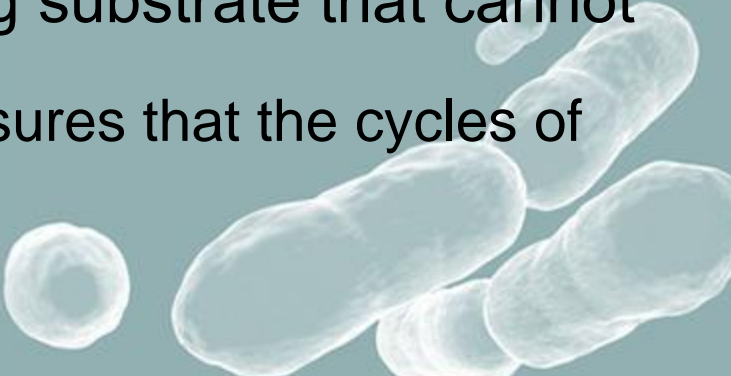
Man vs. Microbe

THE DYNAMIC STRUGGLE:
THE “YIN & YANG”

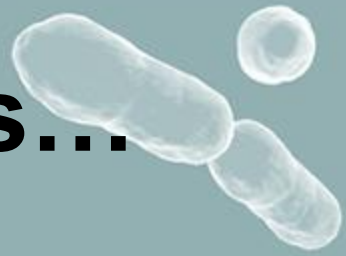


Reality Role of Microbes



- CB are **bottom of food chain** (cyanobacteria make up majority portion of marine plankton approx 100K cells/ml)
 - May one day serve our future protein source as population increases
 - **Convert N₂ to NO₃** – Earth is surrounded by 78% N₂ but not usable by plants (via nitrogen fixing bact)
 - Feed the herbivore animals which in turn feed carnivores and omnivores
 - Produce **>90% of Earth's O₂**
 - Light doesn't penetrate deeper than 320ft (photic zone)
 - **Decompose organics** into inorganics thusly recycling matter (there's no naturally occurring substrate that cannot be degraded by microbes)
 - A most important function which assures that the cycles of life continue
- 

If There Were No Microbes...



There would be:

NO Food

NO Oxygen

NO Nitrates

NO Recycling

NO LIFE!



Cyanobacteria: Food Chain & Oxygen

Long Misidentified as Blue-green Algae

- **Oldest fossilized bacterium (3.5 Billion yrs)**
 - From Archaean period before O₂ accumulated in early Earth atm (Oldest viable bact see next slide)
- **During late Archaean & Proterozoic CB became photosynthetic changing atm to O₂**
 - Have been providing O₂ to this day
 - Unique = Need only sunlight + CO₂ & miniscule salts for survival & photosynthesis
- **During late Proterozoic to Cambrian Era some larger cells engulfed CB, which survives as internalized CB or “chloroplasts”**



Oldest Viable Bacteria



- 1993 endospores of *Bacillus sphaericus* in extinct bee preserved in amber & dated **25 to 40 million years old**
- 2000 scientist Russell Vreeland* found endospores of *Bacillus* spp in **250 million year old** salt deposits that were viable!!!!

*Russell H. Vreeland, et al, Nature 407 (200): 897-900



Spirulina pacifica

a Cyanobacterium spp



Let's have a closer look at this important organism



Cyanobacteria: *Our Future Food Source*



- ***Spirulina pacifica*** - filamentous CB used for centuries as food (grown, sundried, patted into flatcakes to eat directly or to cook (grown worldwide on spirulina farms in Thailand, India, and even U.S.-NASA experimented w this food in spaceflights)
- Nutritionally it has **more beta-carotene** than carrots
- **28x more iron** than beef liver
- Highest conc of **B12** than any known foodstuff
- Per acre **200x more protein yield** than beef
- Consumes **315x less water**
- Its protein is complete –contains **all essential a.a.**



Fossil Fuels:

Oil, Coal, & Methane

- Re: Marine Plankton: dead phyto- & zoo-plankton, as well as, plants, & animals settle to bottom of large bodies of water = anaerobically decomposed by microbes;
- Layer upon layer of decomposing sediment accumulated & compacted over **millions of years** (this material viewed microscopically would reveal **fossilized bacteria**, hence, fossil fuels)
- Heat and pressure caused matter to alter to form *shale, crude oil & methane gas* (shallow water deposits & land degradation became *coal*)




Years of Production Remaining



Estimates Based On Current Level Of Usage

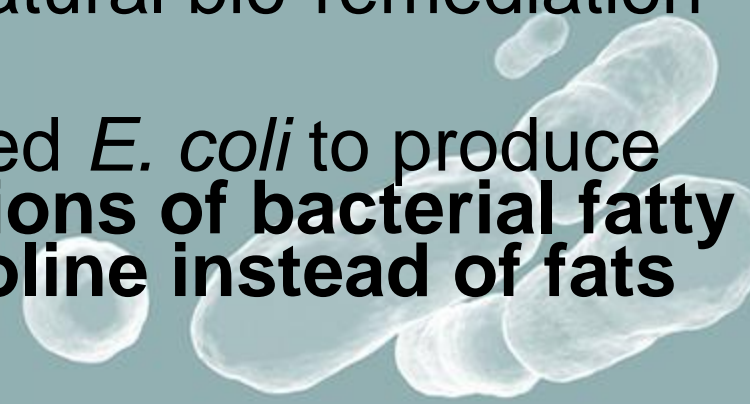
- **Coal:** 148 yrs
- **Oil:** 43 yrs
- **Natural Gas:** 61 yrs

Most Optimistic Estimate

- **Coal:** 417 yrs
 - **Oil:** 43 yrs
 - **Natural Gas:** 167 yrs
- 

Unrefined Crude is Toxic




- **Crude poisons marine & terrestrial life; Oil's aromatic hydrocarbons (benzene, toluene, xylene) damage tissue, enzymes & nervous system**
 - But bacteria (*Oceanospirillales*, *Arthrobacter*, *Pseudomonas*, *Rhodococcus*, *Corynebacterium*, *Bacillus*, etc) **view crude oil as carbon-rich & digestible food** and they degrade crude.
 - Albeit a relatively **slow process** for large molecules smaller alkane molecules may degrade faster as evidenced by the recent BP massive oil leaks & such microbes could be part of the natural bio-remediation process for the Gulf region
 - Conversely, researchers tweaked *E. coli* to produce hydrocarbon fuel; minor **alterations of bacterial fatty acid synthesis produces gasoline instead of fats**
- 

Decomposition

Microscopic view of several rod-shaped bacteria, some appearing to be in the process of dividing or budding.

- A rubber eating bacterium has been found living in stagnant water inside a discarded tire
- Over 100 rubber eating bacteria & fungi degrade the 5-8 carbon isoprene units of natural rubber (the “yin” of things)
- Unfortunately the “yang” has also surfaced:

Recently** *Gordonia polyispreivorans* was the cause of pneumonia in a patient; also colonizes catheters*** causing bacteremia & endocarditis (...more environmental bacteria are causing disease)

Microscopic view of several rod-shaped bacteria, some appearing to be in the process of dividing or budding.

**M. Gupta, et al. JID 14(2010): 75-76.

*** usually misidentified as *Corynebacteria*, *Rhodococcus* or *Nocardia*

....Speaking of Rubber

- The Andromeda Strain (Michael Crichton's 1987 book) even ate the rubber gaskets of the enclosures used to contain it.
- In the end, man could not destroy this bug but it disappeared after it mutated to a less virulent form because it destroyed too many hosts (this is much like the bubonic plague, *Yersinia pestis*, bacillus did; and likely HIV will eventually do).

(Note: successful parasites don't kill their hosts)



Michaelangelo's *Pieta*



- **Bacteria can be fine-tuned to clean (decompose) artwork without destroying it***
- *Desulfovibrio vulgaris* laden poultices cleaned debris from marble and *Pseudomonas stutzeri* removes glue from protective coverings used on art work in Italy
- In the future **GMO's** (genetically modified organisms) can be produced to specifically address the needs of conservators, or they can address our needs against disease, hunger or pollution.

* A Mazulak, *Allies & Enemies*, FTPress, 2010



HMS Titanic vs Biofilm



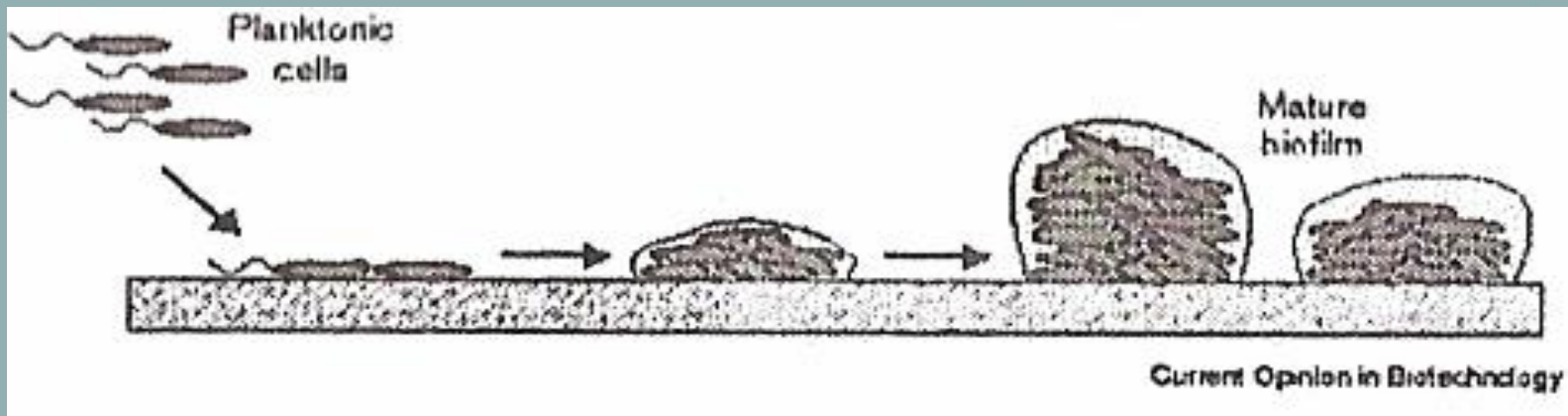
- April 15, 1912 sank 12,850 ft at bottom of the Atlantic Ocean
- Despite incredible barometric pressure, anaerobic conditions, & cold temps, “iron-eating” bacteria decompose >300 kgs of iron each day*
- “iron-eating” bacteria: *Leptothrix* oxidize iron and sulfate reducing *Desulfovibrio* produce sulfur which combine to form iron pyrite in a **biofilm** matrix
- Estimated that by the year 2050 the hull should completely collapse



* A Mazulak, Allies & Enemies, FTPress, 2010

Speaking of Biofilms – What Are They?

- Microbial biofilms are structures where microbes are attached to a surface and **embed in an extracellular polysaccharide matrix**
- Form on virtually **all aqueous environmental interfaces**, including the surfaces of ships, pipes, and sewers, and on living surfaces (ex. respiratory epithelium, heart valves)
- Bacteria growing as biofilms (**sessile**) behave differently to **planktonic** populations: more resistant to antimicrobial agents and display different growth parameters



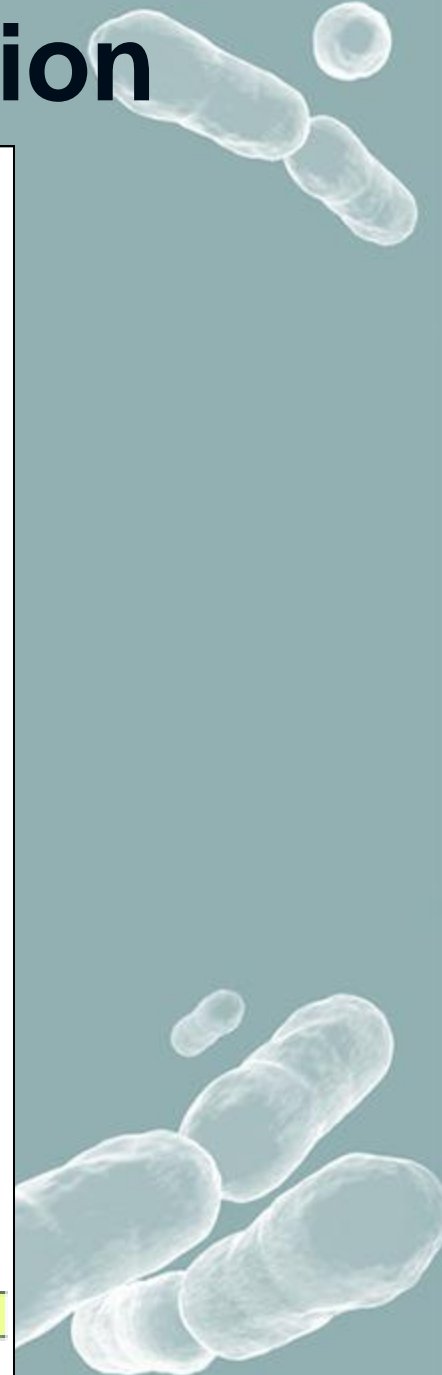
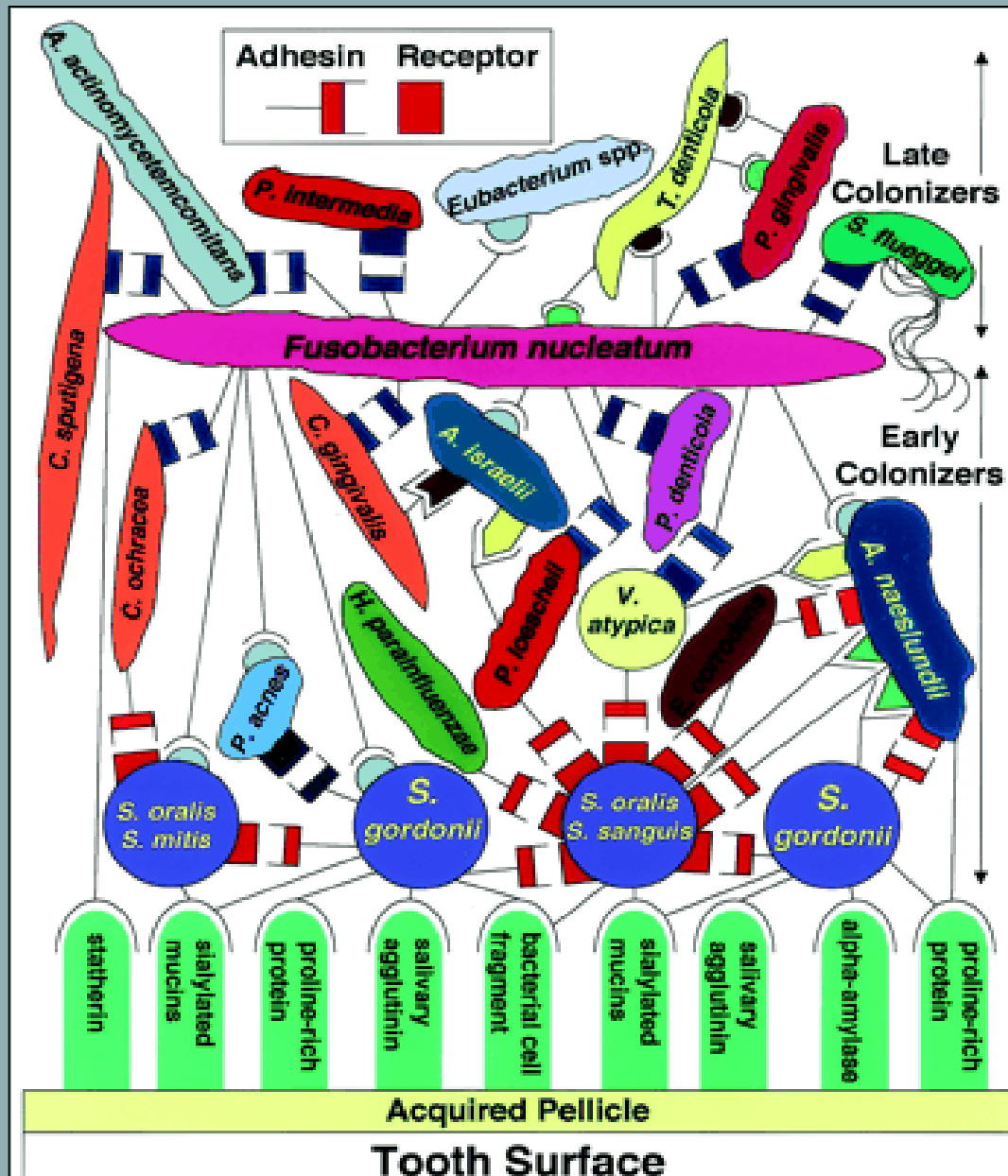
Biofilms



- Biofilms can be of one species
 - Example: *Pseudomonas aeruginosa* within bronchi of CF patients
- Biofilms can also be of mixed genera/species
 - Example: Dental plaque = the quintessential biofilm!



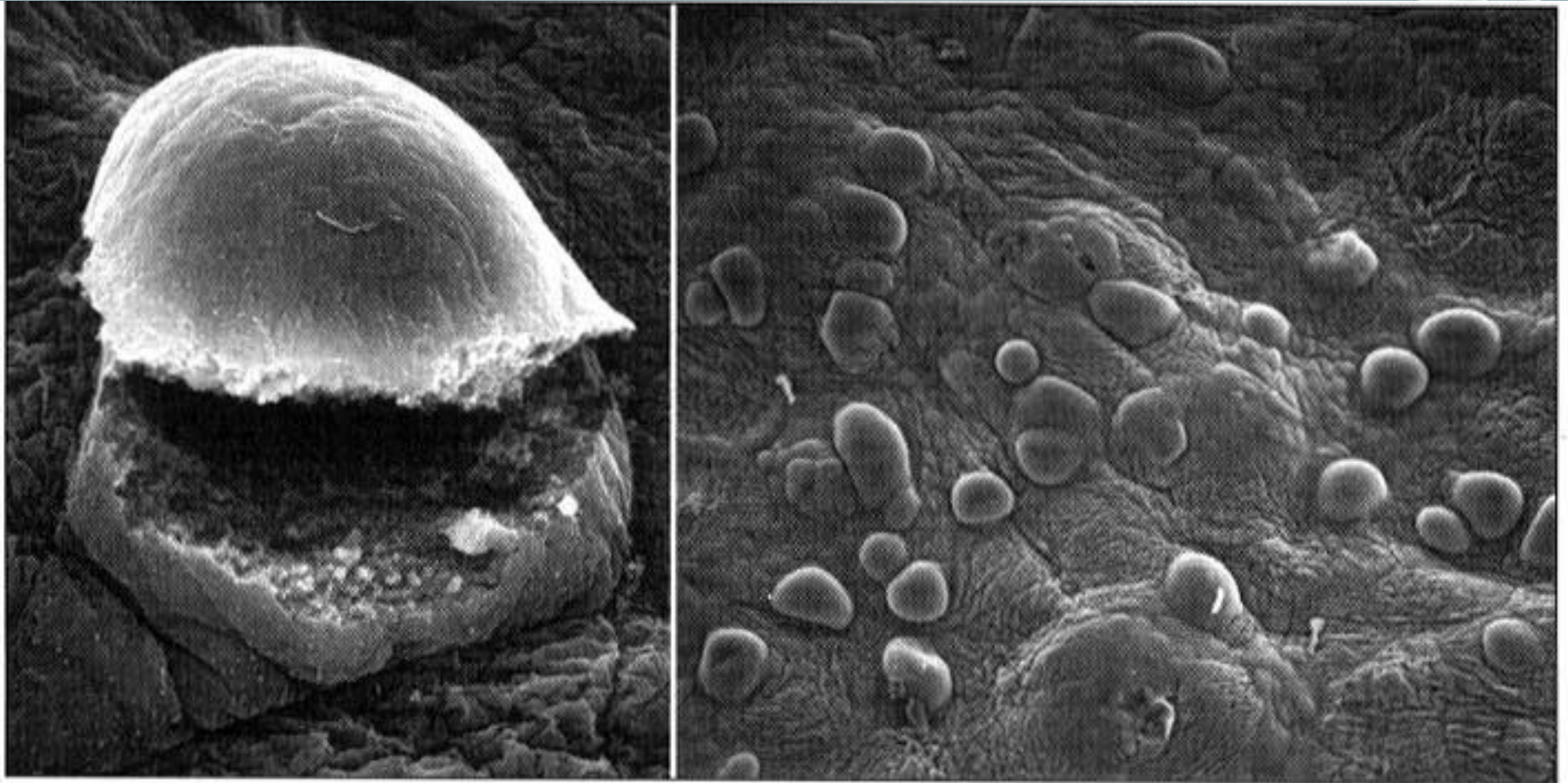
Oral Bacterial Colonization



Examples of Biofilm-Related Diseases

DISEASE	ORGANISM
Dental caries	viridans streptococci
Periodontitis	Gram(-) anaerobic oral bacteria
Otitis media	Nontypable strains of <i>H. influenzae</i>
Musculoskeletal infections	Gram-positive cocci (staphylococci)
Necrotizing fasciitis	Group A streptococci
Biliary tract infection	Enteric bacteria (ex. <i>Escherichia coli</i>)
Osteomyelitis	bacterial and fungal species (mixed)
Bacterial prostatitis	<i>E. Coli</i> and other Gram (-) bacteria
Pulmonary disease (CF)	<i>Pseudomonas aeruginosa</i>
Nosocomial Sutures, catheters and prosthetic devices ICU pneumonias	<i>S. epidermidis</i> or <i>S. aureus</i> Gram-negative rods


E.Coli Intracellular Plaque



E. coli forms biofilm-like communities inside bladder cells. (left) A pod on the surface of the bladder, as seen by scanning electron microscopy. The top of the cell is broken revealing the intracellular biofilm inside. The biofilm has completely engorged the bladder cell. (right) Low-magnification scanning electron micrograph depicting the abundance of pods which cover the bladder surface. Each round bump represents an individual pod, filled with an intracellular biofilm. (Micrographs courtesy of S. Hultgren.)

Properties of Bacteria in Biofilms

A cluster of translucent, rod-shaped bacteria, some appearing to be in a chain, set against a light blue background.

- Because bacteria are embedded in polysaccharide polymer **specific Ab is impeded & ineffective**
 - Programmed release of planktonic cells (**continual nidus for infection**)
 - Bacteria become resistant to antibiotic because failure to penetrate Bf or is slow growing (need up to **1500X MIC** to kill sessile form)
 - **New phenotypes emerge** (ex. change in gene expression)
 - ***Respond to Quorum Sensing (can be used to defeat infection – ex. anthrax toxin production)***
- 
- A cluster of translucent, rod-shaped bacteria, some appearing to be in a chain, set against a light blue background.

Why Quorum Sense?

- Bacterial population can coordinately control gene expression of **entire community**
- Allows single celled bacteria to act as a **multicellular** organism
- Keep **bacteria invisible to host defenses** until enough bacteria are present to overwhelm host (bacterial army does not display its weapons until troops have amassed and are prepared to attack!)



Quorum Sensing Communication

A cluster of translucent, rod-shaped bacteria of varying lengths and a few smaller spherical cells are visible in the upper right corner of the slide.

- **Intraspecies communication:**

- G+ detect own density via peptide phermones = AIP (autoinducer peptide)
- G- utilize buildup of diffusible small MW molecules
AHL = acyl homoserine lactone

- **Interspecies communication:**

- Autoinducer-2 (AI-2) is a furanosyl borate diester
Produced by both G+ and G- bacteria and is detected by all (esp important for complex biofilms like dental plaque)

Note: Both types of communication systems are potential drug targets




Man has helped create & spread an additional problem= MDRO: 3 Interconnected** Issues In The U.S.

1. Overuse of antibiotics by clinicians
2. Use of antibiotics in agriculture
3. Rising nosocomial infection rate

*****The problems of improper antibiotic usage & use of antibiotics in agriculture causing MDRO are compounded by a rising nosocomial infection rate in hospitals (where MDRO are likely to be found and heavy antibiotic usage occurs). Many of these infections are caused by poor aseptic technique, poor cleaning practices. These MDRO can also find their way into the community.***

Issue #1: Drivers of Resistance = Antibiotic Usage



- Approximately 4 Billion Rx written in USA
 - About half of these are for antibiotics
 - CDC estimates about a third to half antibiotic Rx's are deemed unnecessary.
 - **3 million lbs.** antibiotics used on Rx disease (with heavy inappropriate and improper use)
 - U.S. agriculture puts **25 million lbs.** production into livestock feed and other non-medicinal uses.
 - Antibiotic resistance costs U.S. tax payers \$5 billion/yr.
- 

Issue #2: MDRO Found in the Community

- A recent Un of Arizona Veterinary Dept report found 40% of packaged meats sampled tested positive for C diff; reported 30% of samples of ground beef, pork, turkey & ready-to-eat meats tested positive for C diff strains identical to those strains found in hospitals
- MDRO Salmonella, Campylobacter spp, & E. coli found in livestock & poultry meats
- MRSA, VRE, KPC & other MDRO Enterobacteriaceae found in general community

THE WALL STREET JOURNAL

WSJ.com

HEALTH INDUSTRY | JUNE 29, 2010

FDA Warns on Antibiotics in Livestock

By SCOTT KILMAN

The Food and Drug Administration, worried about the rise of drug-resistant bacteria, issued a guidance document Monday to discourage the use of human antibiotics in farm animals.

The agency took an official position in a draft guidance paper that the use of antibiotics to healthy hogs, chickens and cattle, commonly done because it tends to speed their growth.

While the FDA's guidance isn't legally binding, it sets the stage for the agency to take regulatory action. The paper also is likely to heighten public concern about antibiotics in meat production, which in turn could make more restaurant chains and supermarkets squeamish enough to ask for changes from meatpackers. In 2003, McDonald's Corp. prohibited its suppliers from using human antibiotics solely to promote the growth of food animals.



FDA vs. antibiotics for animal growth

Updated 12h 16m ago

By Elizabeth Weise, USA TODAY



By Matthew S. Gunby, AP

Rules against antibiotics are more strict for milk cows than for beef cows.

The Food and Drug Administration issued a document Monday stating that antibiotics important for human health shouldn't be used to help animals grow faster. Officials say it's the beginning of a process to halt their use in meat production. But critics say the agency has made similar statements before, yet nothing came of it.

FDA will then use those comments to consider its next move, Sharfstein says. "We're seeking guidance on how to achieve those principles."

However, public health advocates working to preserve the power of antibiotics say the FDA document is pretty much the same testimony Sharfstein gave before the House a year ago, with summaries of other reports tacked on.

"We were really disappointed because it's not really a plan for action," says Steven Roach, with Keep Antibiotics Working, a coalition of public health, consumer and animal welfare groups. "It describes what they would like to do, but they don't have any description of what they plan on doing or how they plan on doing it."

Low doses of antibiotics, more generically called antimicrobials, are given to animals either to make them grow more quickly or so they require less feed to get to market weight. They are commonly used in meat animals such as chickens, pigs and beef cattle, but not in milk cows or laying hens, because of restrictions on antibiotic residue in milk and eggs. In meat animals, the antibiotics must be stopped in time for the drugs to leave the animals' bodies.

The agency can either change its rules to end antibiotic use as a growth promoter, or get companies to do it voluntarily. "They're still trying to get the industry to make the problem go away voluntarily," Roach says. "The problem is the companies aren't going to voluntarily give up their profits."



Issue #3: Nosocomial Infections in USA



2.5 million infections annually
with 100,000 deaths:

70,000: Co-caused
30,000: Primary cause

Estimated cost = \$4.5 billion

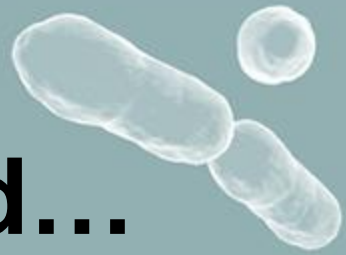
***Many of these infections are caused by poor aseptic technique,
and poor cleaning practices.***



A MODEL: Denmark, Holland, Finland...

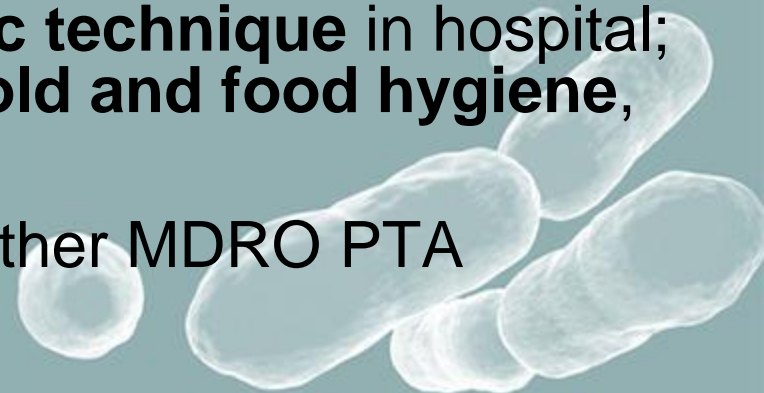
***Epitome of good hygiene &
sound preventive measures***

- Managed to bring HAIs under control (~1%) via “search and destroy” practices:
 - Rigorous hand hygiene
 - Meticulous cleaning & disinfection of rooms and equipment between patient uses
 - Testing incoming patients for MRSA as well as other resistant bacteria (i.e., GNB)
 - Proactively taking precautions to prevent transmission to other patients
 - No routine agricultural use of antibiotics
 - Antibiotic stewardship



Possible Remedies

- **Use antibiotics cautiously & judiciously**
- Many institutions use **antibiotic stewardship** programs to control usage
- **Eliminate** or drastically reduce use of **antibiotics in agricultural industry (i.e., for Rx disease only)**
- **Judicious use germicides in both hospital and community environments, for both routine and terminal cleaning**, to reduce the transfer and reservoir of R-bugs (many institutions established “**clean teams**” to assure process)
- Always practice **appropriate aseptic technique** in hospital; as well as **good personal, household and food hygiene**, to reduce transport of R-bugs
- **Test incoming Pts** for MRSA and other MDRO PTA



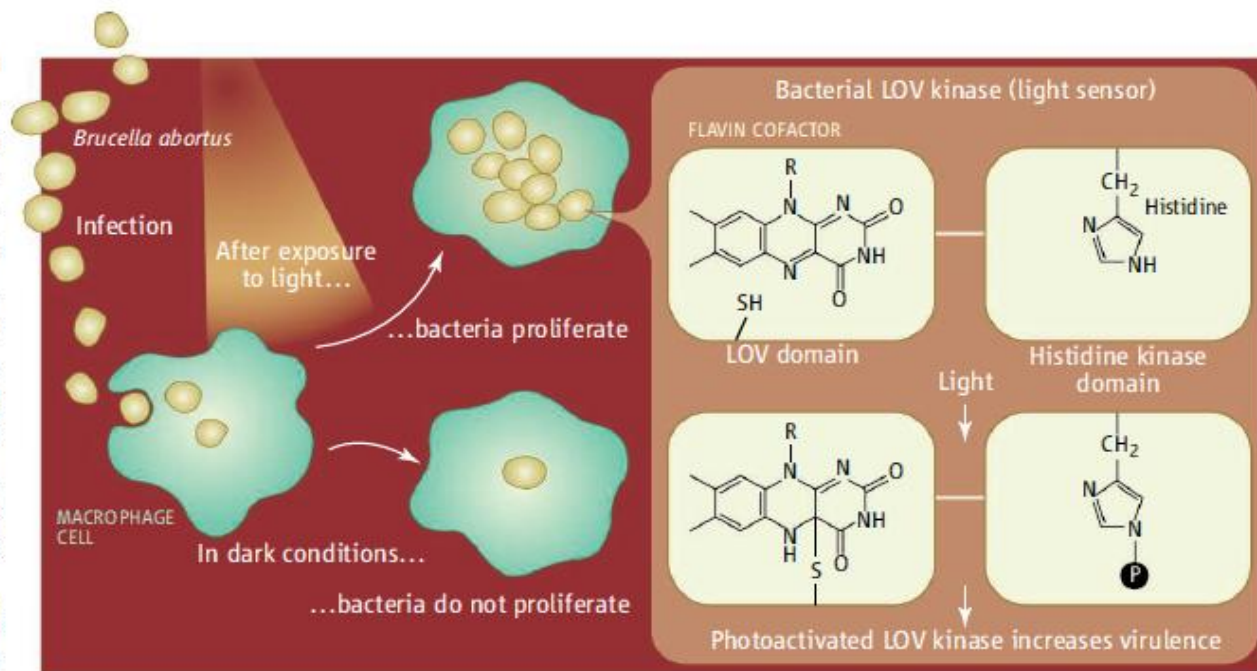
MICROBIOLOGY

A Bacterial Pathogen Sees the Light

John T. M. Kennis and Sean Crosson

Light, a nearly ubiquitous environmental signal, regulates myriad developmental and behavioral responses in plant, fungal, bacterial, and animal cells. Photosensitive proteins abound in the bacterial kingdom, but their cellular functions often remain a mystery. On page 1090 in this issue, Swartz *et al.* (1) identify a functional role for a new type of light sensor in bacteria—light, oxygen, or voltage (LOV) histidine kinase. In the notorious pathogen *Brucella abortus*, light increases the enzymatic activity of this kinase, which, remarkably, increases virulence of the bacterium. Related LOV histidine kinases are conserved across a range of bacterial taxa, suggesting that this virulence pathway could be one of many new photosensory pathways regulating bacterial physiology.

LOV domains belong to the PAS (PerArnt-Sim) protein domain superfamily (2), and were initially described as the light-



Infectious light. Infection of cells by the pathogenic bacterium *B. abortus* is accentuated by visible light. Absorption of light by a photosensory histidine kinase causes a change of its chemical and physical properties that increases virulence.

An unusual photosensitive kinase is discovered in bacteria, where it increases virulence in response to light.

Bacterial “Eyes”

- LOV (light, O₂, voltage) domain proteins possessed by >100 spp (function unknown)
- Recently *Brucella abortus* shown to respond to light (like a primitive eye) when outside body
- **hv activates enzyme histidine kinase** (only found in bacteria as eucaryotes have serine/threonine kinase) which causes rapid cell division & **expression of virulence & adherence factors to better infect a new host**



The Fidelity of Initial Acquisition of Mutans Streptococci by Infants from Their Mothers

Y. Li* and P.W. Caufield

Department of Oral Biology, School of Dentistry, Box 13, University of Alabama at Birmingham, Birmingham, Alabama 35294; *to whom correspondence and reprint requests should be addressed

Abstract. Previous cross-sectional studies using bacteriocin profiles, serotyping, or genotyping suggest that mothers are the principle source of mutans streptococci (MS) to their infants. This study determined the commonality of MS genotypes between mothers and their infants at the time of initial acquisition. Oral bacteria of mothers and their infants were monitored from birth for approximately 3 years at three-month intervals. Genotypes of MS in infants appeared identical to those present in mothers in approximately 71% of 34 mother-infant pairs studied. Interestingly, female infants acquired MS genotypes identical to their mothers' with significantly greater fidelity than male infants (88% *vs.* 53%). Homology of genotypes between mothers and their infants at initial acquisition strongly suggests that MS

Introduction

The mutans streptococci (MS) are considered major etiologic agents in dental caries in humans. Because the presence of teeth or other non-desquamating surfaces is a prerequisite for stable colonization of MS, infants acquire MS after their teeth emerge (Berkowitz *et al.*, 1975; Stiles *et al.*, 1976; Caufield *et al.*, 1993). The question as to how and from whom infants acquire MS has not been definitively answered because most studies showing homologies among strains are cross-sectional and thus compare isolates after their initial acquisition. Moreover, the methods used for showing MS strain homology varied widely in their application and interpretation.

Delivery Method May Determine the Bacteria Babies Acquire

Finding may explain why C-section babies seem more likely to develop allergies, asthma, study suggests

By **Randy Dotinga**
HealthDay Reporter

MONDAY, June 21 (HealthDay News) -- Babies who are born vaginally pick up different bacteria than those who are delivered by cesarean section, potentially affecting how their immune systems develop, a new study suggests.

The findings could provide more insight into why babies born through cesarean sections appear to be more at risk of allergies and asthma, researchers say. The bacteria they're exposed to at birth may help explain the relationship, since coming into contact with germs seems to help babies build defenses against them.

"We want to understand what the differences are and how they are important for the baby's health," said study author Maria G. Dominguez-Bello, an associate professor in the department of biology at the University of Puerto Rico.

The research is preliminary, she said, but it could help determine whether babies will benefit by being exposed to germs at birth that they otherwise wouldn't encounter.

While germs may sound like a bad thing, they're often beneficial to the body.

"We are all colonized -- our skin, mouth, intestines, vagina, ears -- by bacteria that have evolved with man," Dominguez-Bello said. "We are just now starting to unveil what these bacteria are, what they do, why they are important for organs to function." Colonization means the organism is present but not causing infection

In the new study, researchers aimed to determine what types of germs colonize the bodies of babies as they're born. (The womb itself is free of germs, Dominguez-Bello noted.)

The researchers tested bacteria from the skin and mouths of 10 babies within a day after their birth. They also tested bacteria from their mothers.

Those who were born vaginally clearly picked up bacteria from their mothers since the germs matched. Those germs, which were linked to vaginal infections, gum disease and the digestion of milk, appear to have been acquired as they passed through the birth canal.

"It's very clear that the moms give the bacteria to the newborn babies. The babies are like magnets," Dominguez-Bello said.

The babies born by C-section harbored germs linked to skin infections, acne, diphtheria and food poisoning.

Bacteria sent to space come back more infectious

(AFP) – Sep 24, 2007

WASHINGTON (AFP) — Microbes that cause salmonella came back from spaceflight even more virulent and dangerous in an experiment aboard the US space shuttle Atlantis, according to a study published on Monday.

The experiment by microbiologists at Arizona State University sent tubes with salmonella bacteria on a shuttle flight in September 2006 to measure how space flight might affect disease-causing microbes.

The salmonella sample that travelled millions of kilometers (miles) in orbit changed their pattern of certain genes compared to identical bacteria back on Earth, said the study in the journal Proceedings of the National Academy of Sciences.

Following the shuttle flight, studies using mice showed the salmonella bacteria aboard the shuttle were "almost three times as likely to cause disease when compared with control bacteria grown on the ground," said a university statement outlining the study.

After about three weeks, 40 percent of mice fed the salmonella from Earth were still alive while only 10 percent of those given the bacteria from space survived, according to the study.

The professors who carried out the research, Cheryl Nickerson and lead author James Wilson, said the results of the research could help advance understanding of salmonella and other infectious diseases -- in space and on Earth -- possibly paving the way for development of new treatments.



The Space Shuttle Atlantis lifts off from launch pad 39A on its way to the International Space Station, June 2007 from Kennedy Space Center in Cape Canaveral Florida. Microbes that cause salmonella came back from spaceflight even more virulent and dangerous in an experiment aboard the US space shuttle Atlantis, according to a study published on Monday.

Bacteria Take Flight Into Outer Space



- Aboard *Atlantis* (9/06) Salmonella took a flight and amazingly Zero-gravity caused:
 - Expression of **167 genes** making Salmonella 3x more deadly
 - **Grew in biofilm in space** but not on Earth (caused by low fluid-shear conditions of 0 gravity). Longer the journey more concern for Astronauts
 - Gives us new insight into virulence control

Bottom line: what we do to the microbes environment can also affect its pathogenic potential.



Speaking of what we do : Look At What Manufacturers Got Away With Over The Decades...



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You'll enjoy Camels for the same reasons so many doctors enjoy them. Camels have mild, cool satisfaction, pack after pack, and a flavor unmatched by any other cigarette. Make this available test: Smoke only Camels for 30 days and see how well Camels please your taste, how well they soothe your throat as you steadily smoke. You'll see how enjoyable a cigarette can be!

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For 30 days, test Camels in your "T-Zone" (T for Throat, T for Taste).

www.StrangeCosmos.com

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**NO
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FRIENDS FOR A
FAIR FORM

Easy To
Swallow!

Prepared By
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New York

SEND NO
MONEY
PARTICULAR
MAILED
FREE

No Ill
Effects!

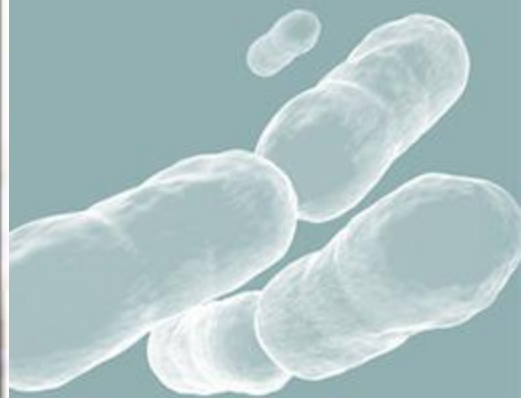
The advertisement features a central illustration of a woman in a long, flowing dress and a dark hat, holding a small object. She is surrounded by a large, chaotic pile of various food products, including cans of 'CASWELL'S NATIONAL CEREAL', 'ALPINE MILK', 'PRIMES', 'ROYAL MARGARINE', and 'GOLDEN HONEY'. In the top left corner, there is a small inset illustration of a person with the text 'NO CANCER'. The background is a solid yellow color.



THEY'RE HAPPY
Because they eat
LARD



Issued by the Lard Information Council





"Held in a web of indifference . . ."

Day after heartbreaking day I was held in an unyielding web . . . a web spun by my husband's indifference. I couldn't reach him any more! Was the fault *mine*? Well . . . thinking you know about feminine hygiene, yet

trusting to *now-and-then* care, can make all the difference in married happiness, as my doctor pointed out. He said never to run such careless risks . . . prescribed "Lysol" brand disinfectant for douching—always.



"But I broke through it!"

Oh, the joy of finding Tom's love and close companionship once more! Believe me, I follow *to the letter* my doctor's advice on feminine hygiene . . . always use "Lysol" for douching. I wouldn't be satisfied now with

salt, soda or other homemade solutions! Not with "Lysol," a proved *germ-killer* that cleanses so gently yet so thoroughly. It's *easy* to use, too, and *economical*. The very best part is—"Lysol" *really works!*

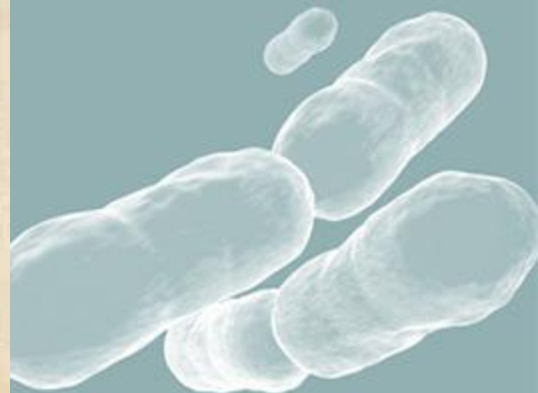
Many doctors recommend "LYSOL" for Feminine Hygiene . . . for 6 reasons

Reason No. 5: DEPENDABLE UNIFORMITY . . . Uniform in strength, "Lysol" is made under continued laboratory control—is far more effective than homemade douching solutions.

Note: Douche thoroughly with correct "Lysol" solution . . . always!

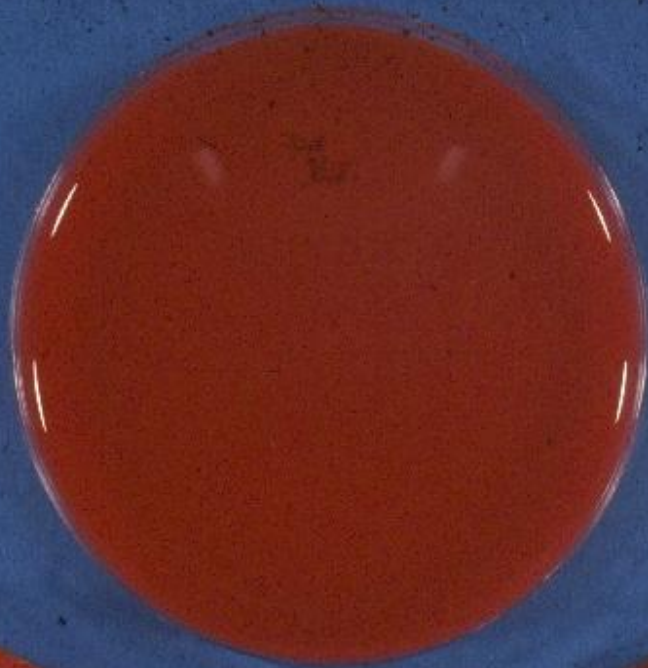


For Feminine Hygiene use "Lysol" always!



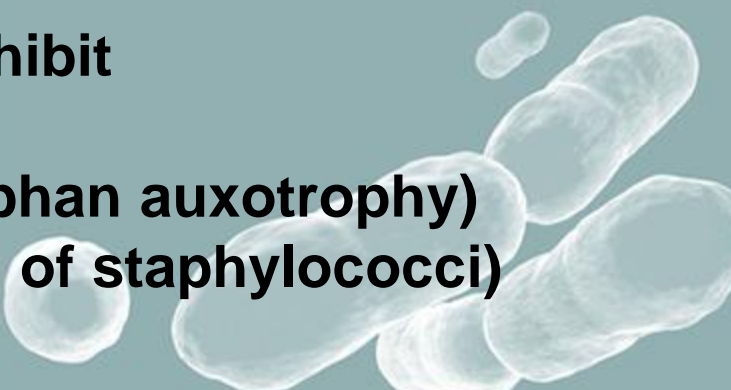
**Circa 1980 manufacturers were still getting away with things:
Synthetic Tampons = manufacturers greatest "faux par"**





TOXIC SHOCK SYNDROME



- **Ecologic factors affecting the production of toxic shock syndrome toxin 1 by strains of *Staphylococcus aureus*:**
 - **Physical environment**
 - High viscosity
 - Increased surface area
 - Adsorbing and absorbing capacity
 - **Protein concentrating capacity of fiber**
 - **Oxygen = 20%; carbon dioxide = 5%**
 - **Protein: menstrual blood = 4%; semen = 4%**
 - **pH = 7, Eh = +100 mV**
 - **Temperature = 40 C**
 - **Staphylococcal strain variability**
 - **Leachables: some stimulate, some inhibit**
 - **Interspecies competition**
 - **Interspecies cooperation (e.g., tryptophan auxotrophy)**
 - **Ionic composition (e.g., Na⁺ selection of staphylococci)**
 - **In vivo vs. in vitro growth conditions**
- 

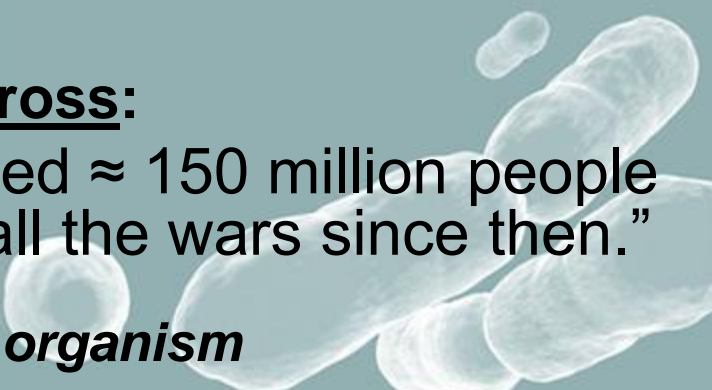
Top Germ-Related Killers Worldwide



1. Acute lower respiratory infections
2. **AIDS:**
 - 3.5M deaths/yr
 - 40M infected/yr
3. **Diarrheal diseases:**
 - 2.2M deaths/yr
 - 100'sM infected/yr
4. ****Tuberculosis:**
 - 2M deaths/yr
 - 2.2 Billion infected
5. **Malaria:**
 - 2.7M deaths/yr
 - 300-500M infected

International Red Cross:

“AIDS, TB and malaria alone have killed \approx 150 million people since 1945, vs. 23 million killed in all the wars since then.”



*****Causes highest # of infections by single organism***

An Ounce of Prevention...

Preventing Infection Eliminates

Need to treat

Worry of antibiotic resistance

- In terms of loss of life and money spent, the costliest diseases in U.S. are:
 - AIDS
 - Food-borne illnesses
 - Nosocomial infections (HAI)
- More than half of deaths in these three categories could be eliminated by
 - (a) Safer sex
 - (b) Proper food hygiene
 - (c) Hand washing/proper asepsis/disinfection



(a) Safer Sex

- Primarily use of condoms
- Educate people on how STD's are transmitted
- Eliminate or reduce promiscuity

These could eliminate a large portion of STD's



(b) Proper Food Hygiene



Not Only Ordinary Household Kitchen Hygiene

ALSO...

- From growing crops and raising livestock to processing and packaging
- Livestock slaughtering, meat inspections, cleaning and packaging techniques leave much to be desired from the point of view of hygiene.



(c) Hand Washing



- 80% of all infections** are transmitted through **contact** (direct and indirect)
- In U.S. alone \approx 100,000 deaths can be attributed to nosocomial infections

With above factoids, the bottom line is that clean hands can be the single most powerful weapon on Earth.

***** 20% infections transmitted via vector, common-source, & airborne***



Hygiene Hypothesis (HH)

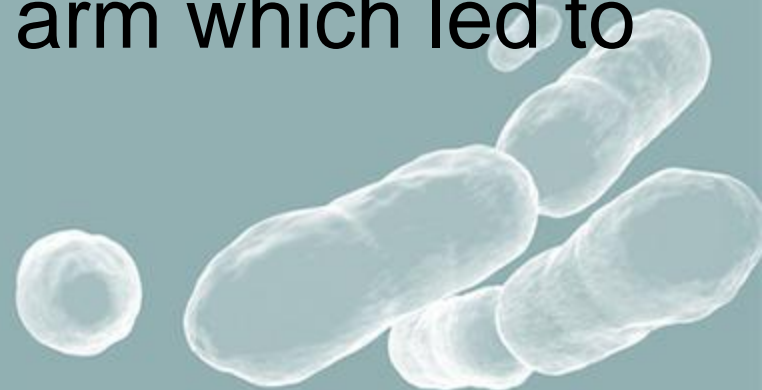


- 1989 Strachan suggested cause of atopic (allergic) diseases is explainable by lower incidence of infection in early childhood caused by transmission from unhygienic contact with older siblings
- He assumed trend towards smaller family size didn't allow for sufficient unhygienic contact
- Term has been broadened by many interpretations that are **NOT** supported by scientific evidence (some **erroneously** translated this to “are we too clean for our own good”)
- Bjorksten (2004) suggests term “**microbial deprivation hypothesis**” which does not preclude practice of good hygiene.



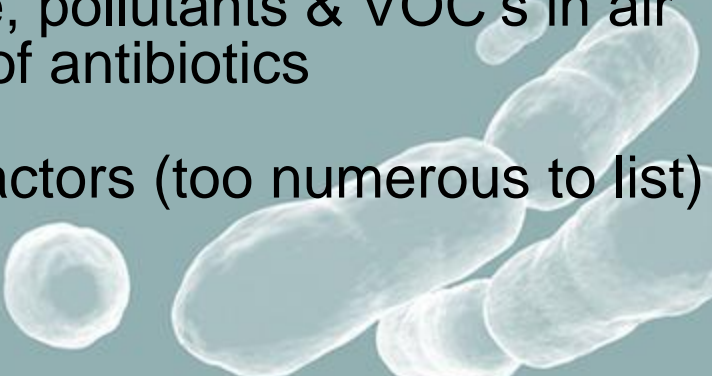
Hygiene Hypothesis *(cont'd)*

- Allergic disorders are caused by inappropriate immunologic response to harmless antigens driven by Th-2 mediated immune response
- Counterpart is Th-1 immune response which down regulates Th-2
- HH states insufficient stimulation of Th-1 arm led to overactive Th-2 arm which led to allergies



Hygiene Hypothesis *(cont'd)*



- Scientific evidence does not support the “too-clean hypothesis”, in fact, that evidence reports the following are involved in atopia:
 - Genetic variations, mutations & polymorphisms
 - DNA damage
 - Environmental factors (i.e., mold, household dust expos, etc)
 - Western diet, obesity, sedentary and other lifestyle issues
 - Allergens in processed foodstuff
 - Vaccine administration; as well as getting vaccine vs wild microbe i.e., chickenpox
 - Vitamin D deficiency; folate excesses or deficiencies, etc
 - Defects with cytokine production like IL-33, IL-10, IL-17
 - Low levels of dendritic cells (i.e., immune dysfunction)
 - Use of aerosols like hairsprays; smoke, pollutants & VOC's in air
 - Early childhood (<2yo) administration of antibiotics
 - Vaginal delivery vs C-section birth
 - Numerous other non-microbiological factors (too numerous to list)
- 

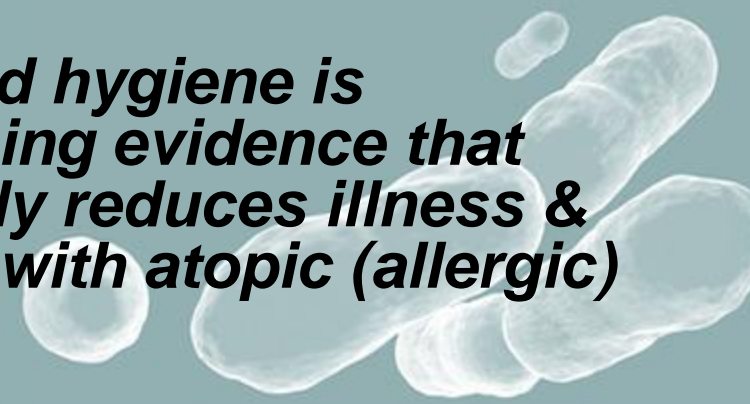
Hygiene Hypothesis *(cont'd)*



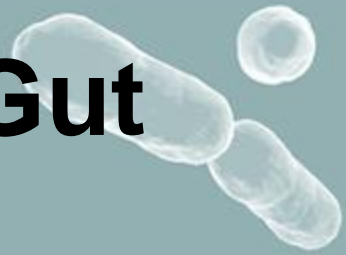
BOTTOM LINE = 3 THINGS ARE EVIDENT:

1. The issue of the Th-1 and Th-2 imbalance is far from simple
2. The body of scientific evidence debunks connection between use of cleaning agents, disinfectants and soaps & prevalence of atopia
3. There is no “cause and effect” relationship between practice of good hygiene & atopia

Note: In fact, it is clear that reduced hygiene is detrimental. There is overwhelming evidence that practice of good hygiene not only reduces illness & mortality but does not correlate with atopic (allergic) disease.



Antibiotics (Abx) and the Gut



- Newly published research:
 - Mice receiving abx have poor PMN response (innate immunity) to killing *S. aureus* & *S. pneumoniae* vs. mice not receiving abx
 - Mutant mice without Nod1 receptors on PMN's are ineffective at killing *S. aureus* & *S. pneumoniae* vs. those with Nod 1 receptors



Mechanism: Kill Off Normal Flora Thereby Lose “Priming”



- Data show peptidoglycan (Pg) fragments are translocated from gut and act systemically to prime PMN in bone marrow
- Host cells respond to Nod1 receptors* which recognize Pg fragments from bacterial cell walls
- Pg fragments shed from *normal flora*** travel via blood to PMN cells in bone marrow which then prime innate immune cells

* *Nod1 recognizes muramyl tripeptide (GNB) & Nod2 the recognizes muramyl dipeptide (found in most bacteria)*

** *Up to 1000 species can be isolated from different people in GI tract (~160 spp live there at any one time)*



Recall Nod2 Function (self vs non-self)



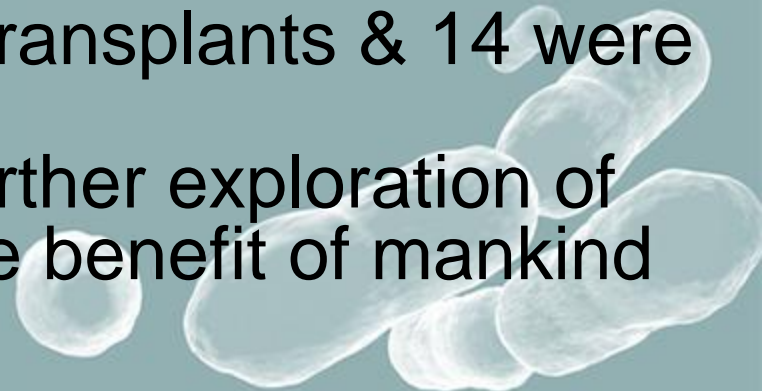
- **Nod2 protein enable WBC's to distinguish between normal gut flora (which they ignore) and invaders (which they destroy)**
- **Nod2 activates NF-kB (nuclear factor kappa B) and I-kappaB supresses NF-kB**
- **When pathogens are present their activity interferes with I-kappaB thereby allowing NF-kB to be released which destroys the invading bacteria**



Fecal Transplantation

(mini-case)

- 2008 GI MD Khoruts @ U Minn had pt w a refractory C.difficile
- Pt lost 60 lbs over 8mts & became confined to a wheelchair
- Microbiomic analysis was done on her gut flora & found she was colonized by all sorts of misfits
- Did same analysis on husbands stool and found he had more **normal array of GI bacteria**
- A fecal transplantation of husbands stool in saline resulted in cure and re-establishment of more normal flora
- Dr K performed a total of 16 transplants & 14 were cured of C diff
- Emphasizes importance of further exploration of metagenomic research for the benefit of mankind



Metagenomic Research




- Although over **1000 different species** live in human gut but, on average, only about **170** live there at any one time, half of which are shared by everyone
 - Entire **human genome** contain only about **20,000 genes** but microbial genes collected from stool (using 124 individual samples) displayed **3.3 million genes**
 - Washington Un scientists discovered **thousands of intestinal viruses** mainly as stable prophages modifying bacteria they inhabit (80% were previously unknown)
 - Further the composition of these gut **viruses are unique** to every individual **even identical twins**
-bottom line = there is much to learn*

Metagenomic Research continued...

- Scientists at Imperial College UK: found *obese* people have *different set of microbial spp* than people of normal weight
- They also found that *lungs of healthy volunteers* harbor ~128 spp (2000/cm)
- And 500-1000 species of microbes ID'd in mouth live there at any given moment
- Even *each surface of the each tooth has different flora*
- Further comparison of 2 different peoples hands show only 13% species are same.
- And only 17% of species on L hand can also be found on R hand

We are only beginning to understand the true impact of metagenomic research in human health and disease & its benefit to mankind


Global Health Care-Associated Infection (HAI): Scale and Cost

A cluster of translucent, rod-shaped bacteria with rounded ends, some showing internal structures, set against a light blue background.

- *Hundreds of millions of people worldwide* are suffering from infections acquired in hospital
- Between **5% and 10%** of patients admitted to modern hospitals in the **developed** world acquire one or more infections
- In some **developing countries**, the proportion of patients affected by an HAI can exceed **25%**



Global Health Care-Associated Infection (HAI): Scale and Cost *(cont'd)*




- In developing countries the situation is even more stark with **4,384 children dying every day of HAI, equating to a plane crashing with 183 passengers every hour.**

Ex. - In Brazil and Indonesia, more than half of the babies housed in neonatal units are affected by HAI, with a fatality rate between 12% and 52%.




Global Health Care-Associated Infection (HAI): Scale and Cost *(cont'd)*




- Every year, worldwide, ***unsafe blood transfusion causes***
 - 16 million hepatitis B infections
 - 5 million hepatitis C infections
 - 160,000 cases of HIV





Global Health Care-Associated Infection (HAI): Scale and Cost *(cont'd)*



- In 2000, ***reuse of contaminated syringes (6 billion injections given)*** in developing and transitional countries caused an estimated
 - **21 million hepatitis B virus** infections: 33% of new infections (China alone = 2/3 of 1.26 billion have Hep. B)
 - **2 million hepatitis C** infections: 40% of new infections
 - **96,000 HIV infections**: 2% of new infections
- 

Global Health Care-Associated Infection (HAI): Scale and Cost *(cont'd)*

A cluster of translucent, rod-shaped bacteria with rounded ends, some showing internal structures, set against a light blue background.

- In some parts of the world, ***up to 96% of people seeking primary health care receive injections***, of which over ***70% are unnecessary*** or could be replaced by an oral formulation.
 - 1.3 million deaths could be ***prevented*** globally
- 
- A cluster of translucent, rod-shaped bacteria with rounded ends, some showing internal structures, set against a light blue background.

Global Health Care-Associated Infection: Scale and Cost

- Approx 2.2 million young children **die** every year just from **diarrheal diseases**
- *Hygiene education and promotion of hand washing can lead to a reduction of diarrhea cases by more than **50%***



Global Clean Water



- 40% world's population (2.5 billion) has ***no access to clean water and proper sanitation*** (*Every 5 sec someone dies from contaminated water*)
- WHO estimates ***cost at \$10 billion*** to bring clean water and sanitary sewage to developing world (*\$10 billion = **half** of U.S. purchase of pet food and **same amt** Europeans spend on ice cream.*)



The U.S. Isn't Spared....

- Within the U.S. **1 in 7 adults** live in poverty (14.3% of population in 2009; up from 13.2% in 2008)
- In U.S. **1 in 5 children** live in poverty
- A total of 44 Million Americans live in poverty

*We are so wasteful a society such that by simply **eliminating waste & judicious planning**, we can literally take care of our poor!*

Global Infection: "From Anywhere To Anywhere"

- Bottom Line: The global practice of *all aspects* of simple Good Hygiene, including good **personal hygiene** (especially hand-washing) as well as good **food hygiene and household (home) hygiene** (including targeted surface disinfection), can significantly reduce infectious diseases.
- **Educating people of both developed and developing countries** about proper hygiene and the ways to prevent infection would be more valuable to enhance health, and lower in cost, than any forms of treatment



Man's Best and Last Resort: Hygiene

A cluster of translucent, rod-shaped bacteria with rounded ends, some appearing to be in the process of dividing or budding. They are set against a light blue background.

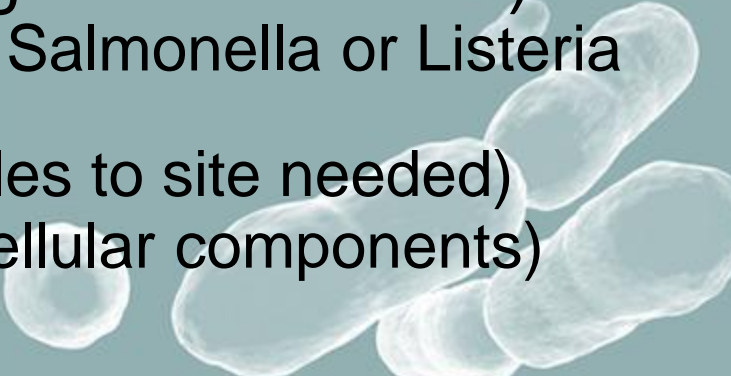
From a **Public Health** perspective the world's population is truly **one big family**. If past history is any indication of future trends, it is easy to predict that infectious diseases—both old and new—will continue to emerge, periodically challenging the world's medical and scientific infrastructures. We must be better prepared as a united world at meeting that challenge.

It can truly be said that an ounce of prevention is worth a pound of cure.

A group of translucent, rod-shaped bacteria, similar to those in the top right, but more numerous and overlapping. They are set against a light blue background.

Changing Paradigm for RX ID

Microscopic view of several rod-shaped bacteria, some appearing to be in the process of division or budding.

- Prevention (ounce of prevention....)
 - Antisense Drugs (inhibit protein synthesis)
 - Probiotics (ex yogurt mollifies RSV)
 - Decoys/Blocking Agents (polymer blocks attachment)
 - Multiheaded Antibiotics (resistance difficult)
 - Biopharming (ex, in potato is Norwalk vaccine)
 - Genetic Engineering & Genetic Therapy (surrogates deliver genes/engineer to kill)
 - Botanical Drug Development (50% green now but inc)
 - Bacteriophage Therapy (phage kills infection)
 - Immune Modulation (sub lethal Salmonella or Listeria activate immunity to kill cancer)
 - Nanotherapy (deliver micro particles to site needed)
 - New wave Vaccines (use subcellular components)
- 
- Microscopic view of several rod-shaped bacteria, some appearing to be in the process of division or budding.

Some Final Words...



“Isn’t it strange yet fitting that the future of nature’s greatest creation, man, depends upon an intimate cooperation with nature’s least, the germ!”

“These smallest of creatures may actually allow us to resolve the most pressing human problems of disease, hunger, & pollution that we face”

“The young science of microbiology, a mere century old, is now only beginning to scratch the surface of the mysteries that govern the most powerful life force on earth, germs!!”
(Tierno 2001)

