

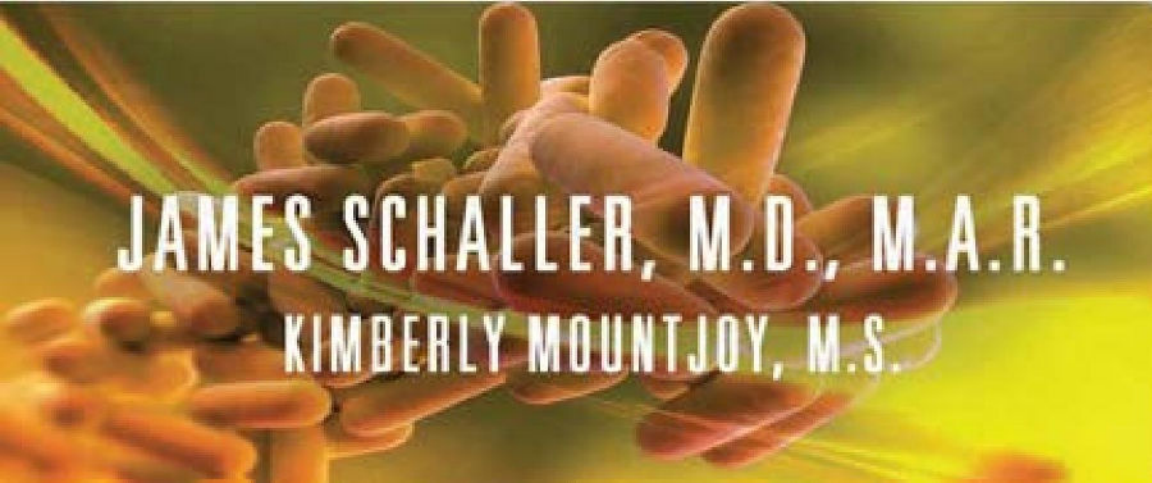


对抗生物膜

为什么您的抗生素和抗真菌药物失败

莱姆病、慢性鼻窦炎的解决方案，
肺炎、酵母菌感染、伤口、耳朵
感染、牙龈疾病、肠道疾病、
口臭、囊性纤维化和植入物

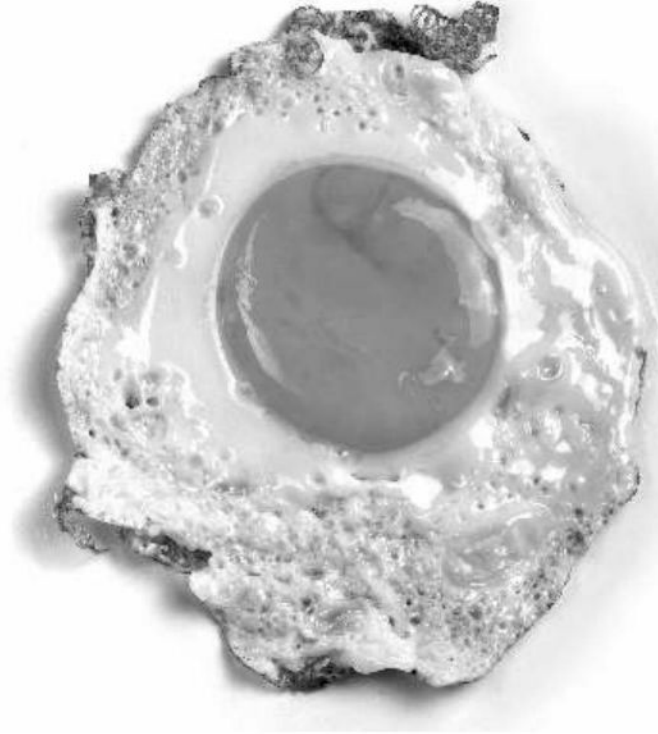
慢性病拼图中的一个重要缺失部分



JAMES SCHALLER, M.D., M.A.R.
KIMBERLY MOUNTJOY, M.S.

什么是生物膜？

简单、科学的生物膜定义：细胞在表面相互粘附的任何微生物群。它们通常位于它们创建的称为“粘液”的层内。



将生物膜与煎鸡蛋进行比较。煎鸡蛋中心的黄色蛋黄是细菌或真菌感染。

蛋黄周围较大的白色部分可称为“生物膜”。它可以保护内部感染或卵黄免受抗生素和人体免疫系统的侵害。

鸡蛋的外缘有一些非常小的炸边。由于鸡蛋的大小，它们很容易被错过。我们将假装它们是抗生素或杀死感染的化学物质。它们毫无用处，因为它们永远不会穿过鸡蛋的外白色边缘。蛋清对他们来说就像一堵墙。

谁患有生物膜感染？

当您了解生物膜常见的地点和情况多种多样,并考虑到这通常是细菌和真菌生物体的常规状态时,您开始意识到任何人都可能患有生物膜感染。

我们在这本书中寻找什么？

以下材料将展示多种突破“蛋清”或生物膜的方法。一旦发生这种情况,通常更容易消除以蛋黄或黄色中心为代表的感染。

生物膜是痛苦和死亡的主要原因

生物膜的身体位置和情况

- 感染持续超过两周
- 6岁以下儿童死亡的主要原因
- 牙菌斑 人类口腔中含有约 25,000 种细菌,其中约 1,000 种存在于牙菌斑生物膜中。

- 酵母菌感染
- 术后感染
- 癌症
- 口臭
- 牙龈疾病或牙周炎*
- 蛀牙 · 肺部感染

- 泌尿系统感染
- 口腔细菌 会损害心脏动脉并导致死亡并增加肠癌的发生

- 慢性耳部感染
- 鼻窦感染**
- 慢性扁桃体炎
- 伤口
- 牙刷头 包括声波摇头类型

- 用于排出尿液的导管
- 人工膝关节、髌关节和其他替代品
- 心脏瓣膜感染
- 损伤或疮口
- 莱姆病
- 任何类型的静脉注射导管
- 导尿管
- 隐形眼镜
- 植入设备 任何植入或插入的设备都可能将细菌传送到大脑、肝脏或肾脏。
- 慢性前列腺感染
- 退伍军人病和许多其他生物毒素细菌会在任何室内水中爆炸
- 霉菌疾病 可能是由任何室内直立水中的霉菌堆积引起的,即洪水、屋顶、地下室或窗户漏水、加湿器、未使用的 Waterpik™ 或其他牙齿清洁设备、交流管道中的冷凝等。 · 囊性纤维化 气道中过量的粘液产生使得铜绿假单胞菌等细菌能够击败生物膜层后面的细菌杀手。
- 失去身体部位
- 皮肤、头发或指甲感染
- 关节炎
- 心内膜炎
- 骨感染
- 痤疮

清单中还可以添加许多其他内容,包括水中生物膜污染的严重问题以及数十种其他与健康相关的生产实践。

*退休牙医大卫·肯尼迪医生感叹大多数美国成年人都患有牙龈疾病 另一种涉及慢性感染的细菌生物膜病症。那么这种隐秘的医疗保健流行病到底有多普遍呢？

**在 Ondine Biopharma,[Richard Longland] 的采访显示,这个国家有 38,000,000 人患有 (或曾经患有)慢性鼻窦问题。

***里卡多·穆尔加;特丽·S·福斯特。生物膜在模型饮用水系统中嗜肺军团菌存活中的作用。微生物学(2001), 147, 3121-3126。

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慢性病之谜中的一个重要缺失部分

James Schaller, 医学博士, 三月
和

金伯利·蒙特乔伊, MS

国际传染病出版社

银行大厦·纽盖特中心 (305 室)

5150 塔迈阿密步道北 [41 号公路]

那不勒斯, 佛罗里达州 34103

制定当前生物膜挽救生命的答案 清澈坚如磐石

现在,您可以在论文、博客和书籍中阅读两年来对抗生物膜的选择。这将花费您 1,000-1,500 小时。您将有多种选择可供提议。以下是您可以在这些论文、博客和书籍中找到的一些选项示例:

避免镁	乙二胺四乙酸	蜂王浆
避免糖和谷物	二甲基亚砷	百里香
NAC	万古霉素	柠檬草
去甲亚精胺	庆大霉素	锯齿肽酶
顺式2-癸烯酸	班德罗尔	2-氨基苯并咪唑
蚓激酶	避免脂肪	棘白菌素

您如何找到合理的营销和对生物膜剂作为解决方案的信心?

Tom 和 Lisa 在博客中表示,产品“x”和处方“d”是破坏慢性疲劳 (CFS) 和纤维肌痛 (FM) 生物膜感染的特殊疗法。

人们很兴奋,因为他们的常规医生没有主要的解决方案,并且对生物膜感染不感兴趣。

问题在于“x”或“d”可能有助于破坏生物膜或帮助克服疾病。但要小心建立快速链接。治疗“a”可能只对十种感染的生物膜有效,而且我们只有证据证明它对三种感染有效。

我们的目标是向您展示好的研究结果,以便您和您的医生可以从事实开始,并能够了解任何可能的生物膜试验背后的原因。

例如,您的感染可能像莱姆病一样使用铁。Saito 和许多其他人报告说,与所有其他已知的生物体不同,莱姆病的病因伯氏疏螺旋体可以在没有铁的情况下生存,而铁是所有其他生命都需要的金属。相反,伯氏疏螺旋体使用锰。

如果将来您发现基于生物膜的疾病在没有铁的情况下也具有同样的能力,该怎么办?这可能意味着破坏莱姆病生物膜的生物膜剂可能对您有效。细菌和真菌感染生物膜往往对生物膜破坏剂具有类似的脆弱性。了解您的感染如何发生可能有助于确定哪种生物膜制剂有效。

<http://phys.org/news/2013-03-scientists-reveal-quirky-feature-lyme.html#jCp>。访问日期:2014年3月26日。

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一场医学革命

生物膜感染理论是感染研究领域的一场深刻革命,感染可能会带来痛苦、致残,而且事实上,根据年龄的不同,感染是头号杀手。

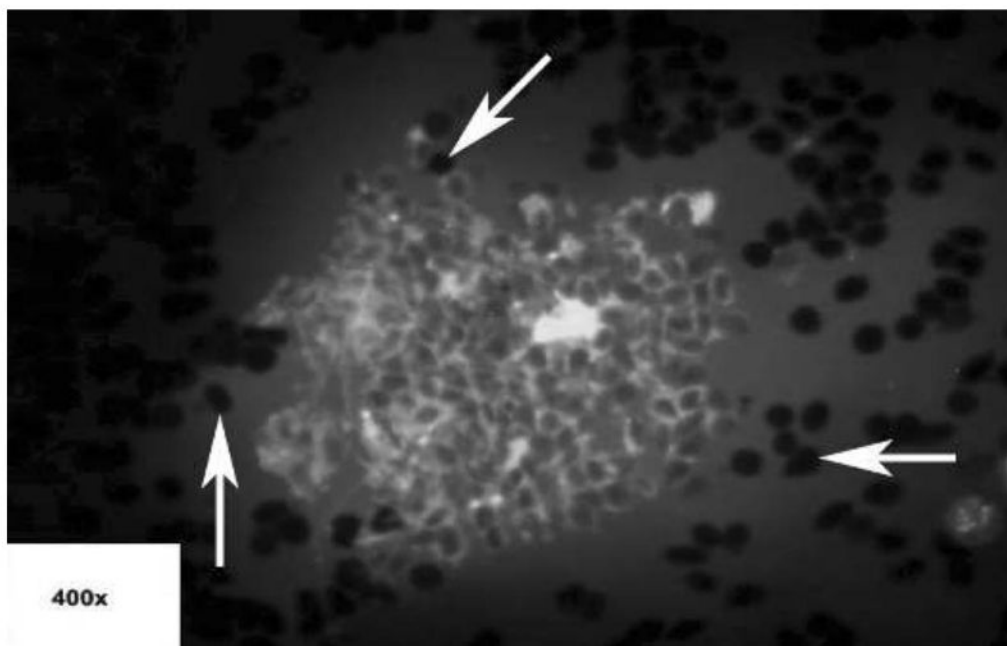
感染开始让我们回到人们因简单感染而死亡的时代。如果发达国家和不发达国家的情况不迅速改变,新的生物膜感染世界可能会比第一次世界大战和第二次世界大战造成的死亡人数加起来还要多。由于对生物膜重要性的认识缓慢,因此,医生对新生物膜解决方案的采用缓慢,即使是最先进的医生也可能只有在证明更多的人因生物膜而致残和死亡时才会认真对待生物膜。目前,大多数人都忽略了生物膜是痛苦和死亡的原因。因此,没有解决方案的生物膜就像19世纪没有疫苗的脊髓灰质炎一样严重,就受害者人数而言,其破坏性远比艾滋病毒/艾滋病更具破坏性。

大多数细菌生活在通常具有独特保护性生物膜的群落中。感染人类或影响人类生命的细菌有 1% 是单独漂浮的,当它们出现在血液中时,不会与任何生物膜粘液一起被发现。

美国国立卫生研究院估计,人体内 80% 以上的微生物感染是由生物膜引起的,其中许多会造成慢性和反复出现的问题。或者,Glowacki 正确吗?99% 的细菌都生活在生物膜中?无论您使用 NIH 的 80% 还是 Glowacki 的 99% 作为估计值,生物膜都是感染中需要认真考虑的因素。

G owacki R, Strek P, Zagórska-Swiezy K, Sk adzień J, Ole K, Hydzik-Sobocińska K, Miodoński A. [慢性鼻炎患者的生物膜。形态扫描电镜研究]。[波兰语文章]。耳鼻喉科波尔。 2008; 62(3):305-10。

介绍性生物膜图像



一种新的基因独特的产生生物膜的单细胞寄生虫,名为 FL1953 或风湿原粘虫。(这种特殊的涂片是检测人体内这些单细胞寄生虫的最佳方法,因为 DNA 或 PCR 检测并不总是呈阳性)。

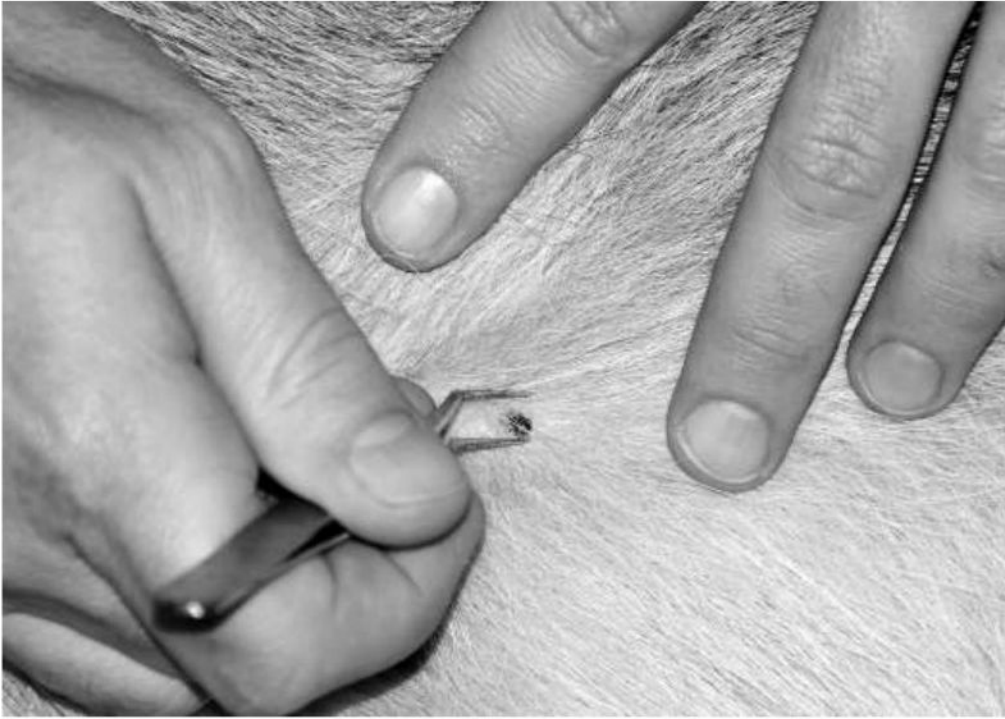
上图所示图像外侧的一百个黑色椭圆形是 8 微米大小的红细胞 (RBC)。中心物质是一个生物膜球,生物膜团中有许多红细胞。

上图所示的生物膜常见于蜱传感染患者,例如非常常见的巴尔通体、莱姆病伯氏疏螺旋体和致命的巴贝虫。虽然某些蜱传疾病可能比其他疾病更严重或更常见,但除非根除,否则所有疾病都可能致命。上图所示的这种寄生虫是一种与巴贝虫和疟疾相关的单细胞感染,当它的生物膜被剥离时,它看起来就像未成熟的疟疾。据疾病控制中心称,这是一种独特的原生动植物。它既不是巴贝虫病,也不是疟疾。这种感染称为 FL1953 或风湿原粘菌。它产生大量的生物膜,图中巨大的中心质量包含数百个红细胞。



当我们研究不同的器官和生物膜的成因时,我们不应忽略至少三大洲 200 多种生物所携带的生物膜感染载体——蜱虫。它携带至少两种重要的生物膜制造者:FL1953和高度复杂的基因先进的莱姆病细菌。我们仍在了解它携带的所有可能的感染。

请注意,头发看起来像大草,所以这个蜱虫只是这个大小的一小部分。当你将隐形与含有止痛药、抗组胺剂、抗凝剂和抗炎剂的叮咬结合在一起时,你就拥有了一个隐形感染携带者。蜱唾液中的一种化学物质,Sialostatin L,是一种很好的免疫抑制酶,可以抑制哮喘(Horka 2012)。



狗可以是人类最好的朋友,但如果你触摸它们的唾液,或者它们把蜱虫或跳蚤带进你的家或车里,那就不行了。假设生活在城外的每只狗和猫都可能被蜱虫或跳蚤叮咬。



清除“生物膜”

生物膜就像橄榄油池中心的一角硬币,油的外缘是代表感染杀伤细胞的胡椒。他们不能进去破坏一毛钱。生物膜细菌群落是大多数人类感染的常见状态。我们被告知感染是漂浮在周围的孤立细菌,这是一个严重的错误。

它表明,如果细菌的主要形式

生物膜细菌群落 是一个新的但至关重要的概念。2004年,当我列出了25种杀死生物膜的选择时,并没有引起多大兴趣。

如今,无法通过多种选择破坏生物膜实际上是一场健康灾难。

编写和出版本书的目的是提供一套负担得起的基于研究的选项以及其他可能的选项,呈现一本纯粹的解决方案书,为数百种相关疾病提供最新的可能的当前和最新的解决方案与生物膜。生物膜的屏障完全不可能通过医生、感染专家、自然疗法、替代医学学校、精油从业者、针灸师、护士或草药师使用的常规方法去除或穿透。

通过这本书,我们希望通过探索现在可用的选择来为您和您的医生/治疗师提供服务。我们检索了PubMed(医学科学的大型数据库)过去五年的出版物

用于“生物膜处理”。选项的范围令人印象深刻,但并不总是您所期望的。本书旨在为您提供广泛的选择,以防止您遭受痛苦、残疾甚至死亡。

经过多年的研究和学习,我逐渐意识到,生物膜方面的传染病“专家”可能早已输掉了这场战争,而且事实上,许多人可能从未意识到所有的战斗。帕-

非常短的人体和生物膜样本

2004年,理查德·朗兰 (Richard Longland)在脊柱手术后患上了一种神秘疾病,恢复情况非常糟糕。在接下来的几个月里,他出现了许多问题 头痛、关节痛,后来出现心脏和大脑问题、极度疲劳和思维困难。

医疗系统反对他,但最终在 2007 年,他接受了支原体治疗,该支原体来自可能的手术过程,无论是在医院的任何地方还是在公共场所或蜱虫。

我的大多数患者在来找我之前已经看过 3 到 200 名医生。我理解他的经历。朗兰先生不得不去看二十多位医生才能做出诊断。在这个困难时期,他创作了一部优秀的电影,名为《我为什么这么病?》他是使用药物和自然疗法药物清除体内全身细菌生物膜的患者冠军。

爱德华现年 78 岁,有三个女儿和八个孙子。他因呼吸急促被送往医院。他患有严重肺炎或肺部感染。他的情况越来越糟。使用能够击败许多生物膜保护的肺炎的药物,人们已经康复。

琳达多年来一直感到疲倦,并且在学校方面遇到了麻烦。我最近发现她患有多种蜱虫感染,导致超过 15 个实验室结果出现异常。昨天她打电话来,由于她膝盖后面疼痛,我让她去急诊室。不到一天的时间,她的肺部和腿部被发现有23个血栓。她怀疑是巴贝虫、炎症和FL1953。我们有一些特工杀死了这些特工,包括 2006 年的 FL1953。

It would be an error to say that nattokinase, lumbrokinase, serrapeptidase, EDTA, gentamicin, vancomycin, Samento, Banderol, olive products, poorly known herbs with fair lab testing in humans, clove bud oil, diet, chelation, three to four part amino acid mixes, NAC, Rife, diet changes or a vast range of other options not listed, will **work for all biofilms**. For example, an elderly patient dying of a lung infection or another person with painful and treatment-resistant sinus infection *will not* have the same biofilm.

As a trend, trying different options to destroy a biofilm is less dangerous than allowing it to spread.

A Brief Word on Biofilms in Lyme

At times, individuals who have tick- and flea-borne infections, like Bartonella, Babesia and Borrelia (Lyme disease), can feel their treatment is minimal or incomplete. Debates rage over the diagnosis and treatment of Lyme and tick-borne diseases; whether the pain is from residual dead infection incorporated into tissue or one of the many infections carried by the I. scapularis tick, we still have patients' misery.

After writing **twelve books** which include many pages on non-Borrelia infections, “Lyme testing” seems like alphabet testing in which ***one only looks for the vowel “a.”*** Due to the lack of acceptance of the number and complexity of tick-borne infections, there is a lack of up to date education, leaving quality medical doctors to evaluate tick and flea infections in the ***abstract***, by which I mean that they very falsely and sadly do not realize the full magnitude of ***“the alphabet.”***

Specifically, they “diagnose” by ignoring inflammation alterations, nutrient changes, hormone deficits, immunity changes caused by tick-borne infections, and chemicals made or suppressed by direct tick and flea infectious agents. I discuss these in my three most recent tick and flea infection books. All are available in English. All can be found free through inter-library loan, for less than \$20 USD, or at www.personal-consult.com under the “free books” button. No one can expect to become an expert in this massive area after reading any guide or merely going to ten conferences, because these cluster infections impact twenty areas of medical and scientific knowledge.

In the last four years, researchers like **Dr. Eva Sapi have shown Lyme is like some other spirochetes—it has biofilms. These are very tough biofilms to defeat unless caught in the “acute stage.”** A tough, “mature biofilm” allows organisms to **“laugh at” many antibiotics.**

Some medical professionals interested in Lyme often ignore the immune suppressing Bartonella bacterium, which is more common than Lyme. Ignoring coinfections may increase the risk of fatality with Babesia and possibly **FL1953**. These healers also may not realize that the highly

genetically complex Lyme spirochete appears to have a troublesome biofilm. Performing a simple direct test at laboratory companies whose testing kits have reduced sensitivity will probably result in more negatives for tick-borne diseases. The ultimate result is anti-science and anti-truth. Searching for tick infections with one test is like writing in “Lincoln” at the next presidential election.

Lyme Disease (*Borrelia*) and Biofilms

Several researchers believe *Borrelia burgdorferi*, the active agent of Lyme disease, has biofilms. Lyme organism biofilms have been found in culture and in the tick gut. Lyme cysts and biofilms have also been noted in patient skin biopsies using focus floating microscopy according to Dr. Eisendle publishing in the *American Journal of Pathology*.

Further, we see in Lyme that biofilm formation is dependent on cyclic di-GMP expression and we see that in Lyme (Stricker and Johnson).

Brihuega B, Samartino L, Auteri C, Venzano A, Caimi K. In vivo cell aggregations of a recent swine biofilm-forming isolate of *Leptospira interrogans* strain from Argentina. *Rev Argent Microbiol*. 2012 Jul-Sep;44(3):138-43. PMID:23102459

Cogoni V, Morgan-Smith A, Fenno JC, Jenkinson HF, Dymock D. *Treponema denticola* chymotrypsin-like proteinase (CTLP) integrates spirochaetes within oral microbial communities. *Microbiology*. 2012 Mar;158(Pt 3):759-70. Epub 2012 Feb 7. PMID:22313692

Sapi E, Kaur N, Anyanwu S, Luecke DF, Datar A, Patel S, Rossi M, Stricker RB. Evaluation of in-vitro antibiotic susceptibility of different morphological forms of *Borrelia burgdorferi*. *Infect Drug Resist*. 2011;4:97-113. Epub 2011 May 3. PMID:21753890

Stricker RB, Johnson L. Lyme disease: the next decade. *Infect Drug resist*. 2011; 4: 1-9. PMID: 21694904

Sapi E, Bastian SL, Mpoy CM, Scott S, Rattelle A, Pabbati N, Poruri A, Burugu D, Theophilus PA, Pham TV, Datar A, Dhaliwal NK, MacDonald A, Rossi MJ, Sinha SK, Luecke DF. Characterization of biofilm formation by *Borrelia burgdorferi* in vitro. *PLoS One*. 2012;7(10):e48277. Epub 2012 Oct 24. PMID:23110225

lease of bacteria in the human body will be like a dangerous tornado in a field. It is a wise concern.

For these two problems regarding biofilm-held infections suddenly being released, here are useful solutions:

1. You need many infection killing options for use since more is better to prevent “seeding” of dispersed infection.
2. You want the biofilm killing options to destroy biofilms by different mechanisms. This makes the dispersed seeded infections naked to the immune system.
3. Biofilm tools are given initially at low doses and then increased gradually to large doses since often in the beginning patients have massive inflammation and a drastic increase in killing of biofilm organisms in a short time could cause trouble with bone marrow, liver, heart, eye, or kidney issues, or merely create more dead infectious debris resulting in patient misery.
4. You may need to pulse (use every other day) or fully stop this treatment because once a wave of biofilm eroding agents strips off or severely damages a biofilm of an infection, the same antibiotics that were useless in the past can become very effective.
5. There is no single master biofilm destroyer, yet some are broader than others.

Bartonella and Babesia Biofilms?

Most people have heard of the profoundly common tick infection Lyme disease, but they may not know Bartonella is more common than Lyme and is carried by far more vectors (Breitschwerdt). Babesia decimated the cattle population in the southern United States many decades ago and is more dangerous in humans than Lyme.

Currently, we have no solid data showing Bartonella and Babesia have biofilms.

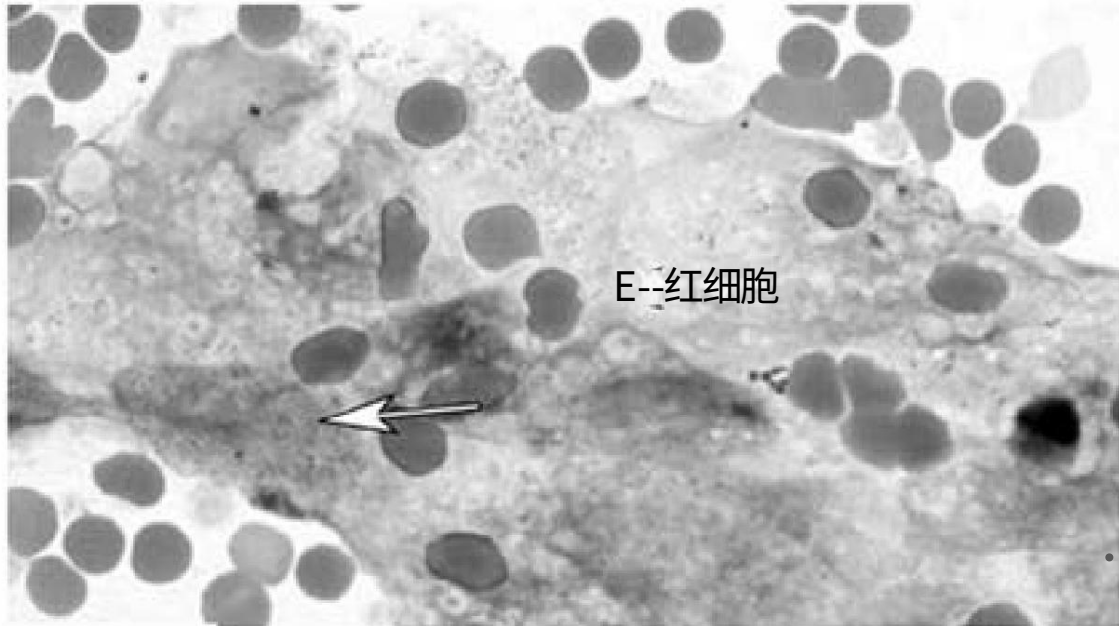
Tick and Flea-Borne Biofilms Conclusion

Below you will see that mouth spirochetes routinely have biofilms. Another spirochete is Leptospira which is able to make biofilms in many environments and may contribute to lost pregnancy in mammals (Brihuega).

In terms of tick and flea infection biofilms, I would focus on **FL1953** (Protomyxzoa) and Lyme, since both have been known and treated by us since 2006, though the former was killed without knowing its genetic uniqueness. We are learning what decreases their biofilm pathology and have agents that should work if one is open to look at diverse approaches. A synthetic “antibiotic only approach” to biofilms, including antibiotics targeted to hit biofilms, might be similar to typing with one finger.

There are herbalists, such as Stephen Buhner, who propose selected herbs to treat some tick infections. And, in terms of **primary treating herbs to kill organisms**, there are also credible options that are not always herbal in use for a tick or flea infection. We will continue to use **advanced lab testing**, typically only allowed under physician supervision, to determine by serious extensive **indirect blood exam** biochemistry tests to see which infection is actually destroyed in people experiencing benefit from herbal therapy. In any event, I enjoyed this line from Buhner: *“I can’t really say what will clear all biofilms.”*

另一个生物膜图像样本



黑暗的IOWld oVlls ai:e红血 “°Us (-blade upp«乌鸦) ,Tho “片”diat从
lllo右低 “ ° 11«开始,朝左上oomer移动,生病了生物填充,\rnllffial
IOW\ll mow ia poi11i11g 到一个小 bam:rium。 (Piy Labaratoriea)

丁子香酚基础知识

丁子香酚存在于许多精油和草药中。例如,它在丁香花蕾精油中具有很高的效力,但在肉桂叶及其精油中的剂量也较低。据 PubChem 称,它还存在于多椒、月桂、黄樟、马苏树皮油、樟脑油和 chamchwi 植物中。效力和浓度根据来源和提取方法的不同而有很大差异。此外,这不仅是一种强大的生物膜剂,而且是一种有效的生物膜剂。它具有其他惊人的特性,例如抗病毒作用和抗癌作用。



例如,Tragoolpua 和 Jatisatiendr 表明,丁子香酚对口腔和生殖器疱疹的影响取决于物种、菌株和其他因素。他们明确表示,精油比简单的提取物更有效。事实上,口腔和生殖器疱疹 (HSV-1 和 HSV-2)在丁子香酚存在下无法繁殖。谢里夫已显示出显著的癌症效果。非常低的浓度 ($2 \mu\text{M}$)对不同的乳腺癌细胞具有特定的毒性。这种杀伤作用是通过诱导癌细胞死亡路径并降低 E2F 1 和生存素 (这两种对细胞生存至关重要的分子)的水平来介导的。它还可以预防乳腺癌

genes. Importantly, these anti-proliferative and pro-cancer cell death effects were also observed inside body grafts placed in non-human animals.

<http://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=3314>

Tragoalpua Y, Jatisatiennr A. Anti-herpes simplex virus activities of *Eugenia caryophyllus* (Spreng.) Bullock & S. G. Harrison and essential oil, eugenol. *Phytother Res.* 2007; 21(12):1153-8.

Al-Sharif I, Remmal A, Aboussekhra A. Eugenol triggers apoptosis in breast cancer cells through E2F1/survivin down-regulation. *BMC Cancer.* 2013 Dec 13;13(1):600. [Epub ahead of print]

Eugenol and Biofilms

Recently, Dr. Zhou has reminded us of a special process that is involved in the formation of dangerous biofilms. Basically, many bacteria have a “chatty” way of talking to other cells such as other bacteria. So, bacteria use chemicals or cause other bacteria to make chemicals to help them survive and often act to harm you or a loved one.

Eugenol is so effective that at very low amounts, it still disrupted bacteria chemical communication. This is very important in a biofilm destroying agent. If cells cannot communicate, it is doubtful they can form communities. Biofilms are community creations. **Further, eugenol at very low doses, called “sub-inhibitory concentrations” inhibited biofilm formation.**

One type of biofilm research being conducted compares biofilm killers head to head. The results are not always the same, perhaps in part because the infections are not always the same. Note that in an Epub abstract before publication, Malic explains that the best essential oil for urinary catheters, with or without biofilms, against fourteen different bacteria was eugenol. This is why I believe this substance is a “double killer.” It can defeat many biofilms, and then kill the organism making the biofilm. Finally, in this study, eugenol did better than tea tree oil.

Linalool

According to the Merriam-Webster dictionary, the word linalool is derived from a Medieval Latin phrase meaning “wood of the aloe.” Linalool has a nice smelling alcohol and essential oils. It is used in perfumes, soaps, and flavoring materials.

In terms of biofilms, it seems to be most effective when **the essential oil part** is used, which has **the most evidence of killing Candida albicans**. (Candida albicans is the cause of yeast infections.) Yet, again, it is the essential oil fraction that not only **inhibits the growth** of Candida albicans but also of the bacteria Lactobacillus casei, Staphylococcus aureus, Streptococcus sobrinus, Porphyromonas gingivalis and Streptococcus mutans cell suspensions, all of them associated with oral cavity disease, according to Alviano and Mendonça-Filho. Yet, Budzyńska reported this essential oil did not fully remove biofilms formed by Staphylococcus aureus (ATCC 29213) and Escherichia coli (NCTC 8196) on the surface of routine medical materials such as urinary catheters, infusion tubes and surgical mesh.

Hsu found that linalool could be effective against Candida albicans due to its many genetic blocking effects. For example, using a scanning electron microscope and other technology, many signs of the effect of linalool to destroy Candida or inhibit its growth could be noted. Hsu found blocking actions against genes involving adhesion production and the formation of “branches” or the mold’s hyphae were both decreased by linalool.

<http://www.merriam-webster.com/dictionary/linalool>

Budzyńska A, Wieckowska-Szakiel M, Sadowska B, Kalemba D, Różalska B. Antibiofilm activity of selected plant essential oils and their major components. Pol J Microbiol. 2011;60(1):35-41. PMID:21630572

Alviano WS, Mendonça-Filho RR, Alviano DS, Bizzo HR, Souto-Pradón T, Rodrigues ML, Bolognese AM, Alviano CS, Souza MM. Antimicrobial activity of Croton cajucara Benth linalool-rich essential oil on artificial biofilms and planktonic microorganisms. Oral Microbiol Immunol. 2005 Apr;20(2):101-5.

Reserpine

Reserpine is a substance found in the roots of some types of Rauwolfia that has been made into a traditional medicine. It is used to lower high blood pressure and help with psychotic symptoms, but side effects have limited its use.

While it may not be comfortable to use at modest or high dosing, very low dosing, according to Magesh, showed it to be profoundly powerful against *Klebsiella pneumoniae*. In one report, he used reserpine and was able to stop biofilms in this pneumoniae infection at a fraction of the dose thought to inhibit growth.

Specifically, a tiny fraction of this drug, a mere 0.0156 mg/ml, stopped biofilm production in *Klebsiella pneumoniae*. So, it may be possible that we have another example of a medical truth I use every day:

“Change the dose and you change the drug or herb.”

In this case, perhaps it is possible that 1/10th of the lowest size tablet, 0.1 mg, could harm *Klebsiella* and other infections and be safe for the patient. However, the raw materials for making it may be hard to find some months according to ASHP who tracks pharmacy shortages.

Magesh H, Kumar A, Alam A, Priyam, Sekar U, Sumantran VN, Vaidyanathan R. Identification of natural compounds which inhibit biofilm formation in clinical isolates of *Klebsiella pneumoniae*. *Indian J Exp Biol*. 2013 Sep;51(9):764-72.

<http://www.ashp.org/DrugShortages/Current/Bulletin.aspx?id=975>

“Stacking” Biofilm Killers

While physicians may ponder the problems caused by biofilms in practice, I rarely encounter the doctor who understands that it is usually better to have more than one treatment. In the article below, **oral bio-film infections were controlled best by three agents, not merely one.** For example, Alves explains that when you are going to irrigate or clean a root canal area, that two mouth bacteria infections protected by their biofilms have these same film barriers decreased significantly by treatment with farnesol, xylitol and lactoferrin together.

The same results were found in wounds. One of the best treatments for wounds is the use of a silver-based wound dressing or bandage, together with a gel containing xylitol and lactoferrin (Ammons).

Alves FR, Silva MG, Rôças IN, Siqueira JF Jr. Biofilm biomass disruption by natural substances with potential for endodontic use. *Braz Oral Res.* 2013 Jan-Feb;27(1):20-5. PMID:23306623

Ammons MC, Ward LS, James GA. Anti-biofilm efficacy of a lactoferrin/xylitol wound hydrogel used in combination with silver wound dressings. *Int Wound J.* 2011 Jun;8(3):268-73. Epub 2011 Apr 1. PMID:21457463

Terpenoids

I would like to mention a class of options that come from a familiar substance, chemicals from tea tree oil. We have already mentioned linalool which is part of this class individually, since it comes up as a leading biofilm killer. According to Raut, as many as 14 terpenoids derived from tea tree oil inhibit biofilms, and α -terpineol, nerol, isopulegol, carvone, linalool, α -thujone and farnesol are worthy of special note. Eight terpenoids have effects on **mature** yeast biofilms (*Candida albicans*).

A study by Ramage shows tea tree oil (TTO), terpinen-4-ol (T-4-ol), and α -terpineol displaying potent activity against 69 biofilm-forming *Candida* strains, of which T-4-ol and α -terpineol displayed rapid kill action.

Of these three, T-4-ol displayed no significant toxicity to cells. These data provide further laboratory evidence that TTO and its derivative components, specifically T-4-ol, exhibit strong antimicrobial properties against fungal biofilms. Further, T-4-ol appears to possess safety advantages over the complete essential oil (TTO) and may be suitable for prevention and treatment of established oral and upper throat cavity candidosis. Certain terpenoids are components of spices or food ingredients generally regarded as safe (GRAS) (Pauli 2006).

In another study, several chemicals from plants were tried against two very common bacteria (Budzyńska), *Staphylococcus aureus* (ATCC 29213) and *Escherichia coli* (NCTC 8196), both with biofilms on the surface of **routine** medical products, i.e., urinary catheter, infusion tube and surgical mesh. All three are present in most advanced hospitals and other settings. Surgical mesh was the surface most prone to persistent colonization since the biofilms that formed on it, both by *S. aureus* and *E. coli*, were difficult to destroy.

Melaleuca alternifolia is the source of Tea Tree Oil (TTO). *Lavandula angustifolia* yields Lavender, English Lavender and True Lavender (LEO). *Melissa officinalis* is Lemon balm (MEO). Tea Tree oil, Lemon balm, α -terpineol and terpinen-4-ol showed stronger anti-biofilm

Allicin and Garlic

Garlic has been used as a medicine throughout human history. Allicin is considered one of the medically useful components of garlic. Other useful components are discussed in Chinese language pharmacology texts.

As early as 2003, the use of allicin against *Staphylococcus epidermidis* had reported effects on biofilm formation at low dosing. Pérez-Giraldo reported that lab testing showed that allicin diminished biofilm formations.

Lihua reported ten years later that allicin impacts *Pseudomonas aeruginosa* biofilm. This is hardly casual information, since *P. aeruginosa* is likely resistant to multiple antibiotics, and this resistance may be due to biofilms. Organosulfur allicin has been shown to inhibit surface-adherence of bacteria and Lihua demonstrated that allicin could inhibit early bacterial adhesion which is a first step to bacterial community formation, usually just before biofilm production.

Other researchers isolated various components of garlic and tested the most active components. The following three components were examined:

1. garlic extract
2. allicin
3. diallyl sulfide (DAS)

They were tested against the serious mouth and dental infection *Aggregatibacter actinomycetemcomitans*, the primary cause of severe aggressive periodontitis and other non-oral infections.

Lumbrokinase

We appreciate that some people interested in progressive medicine feel this enzyme, Lumbrokinase, is a useful substance. Some have suggested it is useful in the removal of biofilms. If that is true, we had trouble finding the evidence for that position. However, it does seem that some researchers see a potential for this enzyme to “digest” pathological clots. This possibility seems to have some support, and at this time we will only wait for further research. Since we are only proposing biofilm options that are supported by research and since human use is just starting in research settings, we do not promote this agent at this time.

Ryu GH, Park S, Han DK, Kim YH, Min B. Antithrombotic activity of a lumbrokinase immobilized polyurethane surface. *ASAIO J.* 1993 Jul-Sep;39(3):M314-8. PMID:8268550

Kim JS, Kang JK, Chang HC, Lee M, Kim GS, Lee DK, Kim ST, Kim M, Park S. The thrombolytic effect of lumbrokinase is not as potent as urokinase in a rabbit cerebral embolism model. *J Korean Med Sci.* 1993 Apr;8(2):117-20. PMID: 8397927

Mihara H, Sumi H, Yoneta T, Mizumoto H, Ikeda R, Seiki M, Maruyama M. A novel fibrinolytic enzyme extracted from the earthworm, *Lumbricus rubellus*. *Jpn J Physiol.* 1991;41(3):461-72. PMID:1960890

Wang KY, Tull L, Cooper E, Wang N, Liu D. Recombinant Protein Production of Earthworm Lumbrokinase for Potential Antithrombotic Application. *Evid Based Complement Alternat Med.* 2013;2013:783971. Epub 2013 Dec 12. Review. PMID:24416067

Cao YJ, Zhang X, Wang WH, Zhai WQ, Qian JF, Wang JS, Chen J, You NX, Zhao Z, Wu QY, Xu Y, Yuan L, Li RX, Liu CF. Oral fibrinogen-depleting agent lumbrokinase for secondary ischemic stroke prevention: results from a multicenter, randomized, parallel-group and controlled clinical trial. *Chin Med J (Engl).* 2013 Nov;126(21):4060-5. PMID:24229674

Huang CY, Kuo WW, Liao HE, Lin YM, Kuo CH, Tsai FJ, Tsai CH, Chen JL, Lin JY. Correction to Lumbrokinase Attenuates Side-Stream-Smoke-Induced Apoptosis and Autophagy in Young Hamster Hippocampus: Correlated with eNOS Induction and NFκB/iNOS/COX-2 Signaling Suppression. *Chem Res Toxicol.* 2013 Jul 15;26(7):1126. Epub 2013 Jun 7. PMID:23746067

tract also made the pneumonia far more susceptible to the antibiotic tobramycin. Further, genes involved with resistance to antibiotics were down-regulated.

- Bag published that highly resistant urine organ infections were more vulnerable to treatment with *T. chebula* but proposed this is due to its ability to collect iron, since adding iron reduced its effect. However, Bag only tested one of many chemicals from this fruit, and I would suggest other components may have antibacterial action and work by other means.
- Four carefully chosen antibacterial plants (*P. guajava*, *T. chebula*, *A. aspera*, and *M. elengi*) are combined with four solvent extracts (hexane, ethyl acetate, ethanol, and methanol) by Kamal Rai Aneja, who initially evaluated their anti-cavity activity against *S. mutans*. All four of the plants showed activity against *S. mutans*. Ethyl acetate extracts of the four plants showed high antibacterial activity against *S. mutans*, superior to the other solvent extracts. Further, *T. chebula* ethyl acetate extract acts as an effective anti-cavity agent by inhibiting *S. mutans* and *C. albicans*. However, we were unable to find evidence if the benefit of these chemicals involved biofilm removal.

In conclusion, we appreciate that this medicine is proposed to both dissolve Lyme biofilms and also destroy the underlying Lyme bacteria. We offer no opinion on this belief. We do not want to oppose or support its use in terms of biofilm ability. It appears this fruit does act on the bacteria biofilm of *P. aeruginosa*, but Lyme bacteria are not the same as *P. aeruginosa* bacteria. Lyme is also profoundly more genetically complex than a “relative” spirochete bacterium, syphilis.

Therefore, while we do note that this medicine has antibacterial and cell protection actions, and **we accept some patients feel better**, we presently cannot say it is due to biofilm removal in those with tick-borne infections.

Cancer

Cancer has many causes. Some things increase your risk and other things can decrease your risk. It is rarely pure genetics, even in those with genetic vulnerability. We know some types of plastics increase rates of breast cancer. We know the 200 poisons in cigarettes cause lung cancer. We know various chemicals made by various companies can increase cancer, despite the reality that most US and international chemicals have limited or no top research on their safety.

I like my dental hygienist. And, I like making sure my gums and teeth are “safe.” Why? At first it was because I want to have teeth in twenty years. But, she correctly reminds me that heart attacks are increased by gum disease which is routine in many countries.

Yet, even this passionate healer was not aware of the role of biofilms in cancer. Yes, I said cancer. We are only beginning to understand the role of infections in triggering cancer diseases.

Many years ago, I was working with a physician who asked me to help research possible cures for his cancer. Eventually, that cure was found and written up, taking over 200 hours and many months to complete, with the help of a top medical editor in North America—the former editor of the *Journal of the American Medical Society* and forty other journals, specifically, George Lundberg, who worked feverishly to get this death disorder cure in print ASAP (Schaller).

Years later, he asked me to write a follow up, and we had found that over eight top infection specialists in the United States had missed Babesia, a common parasite that is harder to kill than malaria and which can occasionally increase eosinophils (Schaller). The patient’s trouble included the fact that he had so many eosinophils, his blood could clot quickly. The point? Eosinophils are a type of white blood cell designed to kill parasites. The man’s disorder (HES) Idiopathic Hypereosinophilic Syndrome, which is often fatal and means that eosinophils reproduce out of control, was primed by a Babesia infection. Not all patients with HES also have a Babesia infection, but after writing six books which

Lactoferrin Xylitol Combination Treatment

In a fascinating look at this proposed double treatment, Mary Ammons shares that treatment of *Pseudomonas aeruginosa* biofilm with both lactoferrin and xylitol inhibits the ability of bacteria to respond to damage resulting from lactoferrin iron chelation.

Pseudomonas aeruginosa has been identified as the most common biofilm-forming infection in chronic wounds. The immune stimulating molecule lactoferrin and the rare sugar alcohol xylitol, together, were effective in the lab against *P. aeruginosa* biofilms.

How? Lactoferrin iron chelation was identified as the primary means by which lactoferrin undermines the bacterial membrane. Amazingly, this combination showed huge alterations in the expression of the bacteria's genes, but these changes are too complex for a summary. The findings mean that critical chemicals made by *P. aeruginosa* had changed.

Siderophore detection verified that xylitol is the component of this unique double treatment that inhibits the ability of the bacteria to produce siderophores under conditions of iron restriction. Siderophores sound complicated—here is the simple meaning: they are some of the strongest iron binders in the world and they are made by bacteria, viruses and fungi.

The study concludes with two points:

1. Lactoferrin treatment of *P. aeruginosa* biofilms results in destabilization of the bacterial cell membrane through iron chelation.
2. Combining lactoferrin and xylitol inhibits the ability of *P. aeruginosa* biofilms to respond to environmental iron restriction.

Access to iron is profoundly hard for bacteria when this combination is used.

Erythritol

Erythritol is an amazing sugar. For example, when it was given to children head-to-head with xylitol or sorbitol it was clearly superior. Here is a summary of the research:

Runnel writes: “Three-year consumption of erythritol-containing candies by initially 7- to 8-year old children was associated with reduced plaque growth, lower levels of plaque acetic acid and propionic acid, and reduced oral counts of mutans streptococci compared with the consumption of xylitol or sorbitol candies.”

In a similar way, Japanese researchers show highly advanced reasons for erythritol superiority over xylitol and sorbitol (Hashino). While this study is very dense, let me at least try to list the stunning findings:

1. By advanced confocal microscopic observations, the most effective sugar used to reduce *P. gingivalis* accumulation onto an *S. gordonii* substratum was erythritol, as compared with xylitol and sorbitol.
2. In addition, erythritol moderately suppressed *S. gordonii* monotypic biofilm formation.
3. To examine the inhibitory effects of erythritol, they analyzed the metabolomic profiles of erythritol-treated *P. gingivalis* and *S. gordonii* cells. Metabolome analyses showed that a number of critical bacteria chemicals were decreased by erythritol.
4. Next, metabolites of erythritol- and sorbitol-treated cells were examined. Erythritol significantly decreased the levels of *P. gingivalis* dipeptides. They tended to be increased by sorbitol.

Amazingly, it appears erythritol has inhibitory effects on two diverse species with biofilms, and it acts by at least five very distinct mechanisms.

Dowd reported that biofilm formation was completely inhibited in a standard wound approach by 10% erythritol in either of the two San-

Does Magnesium Deprivation Hinder Biofilms?

Before we decide to remove an element that is used in vast numbers of important enzymes, we have to have a foundation. First, in some basic physiology texts, calcium displaces magnesium inside human cells. My impression of this research is that suboptimal magnesium increases systemic inflammation, vascular death such as heart attacks, and cancer. Dibaba shows that the higher the magnesium in diet the lower C-reactive protein. This protein is associated with inflammation. If you lower inflammation you decrease deaths.

Qu pooled studies of approximately a half a million people to examine the results. The greatest risk reduction occurred when magnesium intake increased from 150 to 400 mg/day. A significant inverse association was found between dietary magnesium intake and total cardiovascular events. Serum magnesium concentrations are linearly and inversely associated with the risk of cardiovascular troubles such as heart attacks and brain strokes. Since magnesium is poorly absorbed even when chelated to an amino acid, it is perhaps useful to note the useful dose was 400 mg, when compared to minimal benefit from 150 mg orally.

Del Gobbo also examined vast studies and wrote: “Clinical hypomagnesemia and experimental restriction of dietary magnesium increase cardiac arrhythmias.” Deadly ischemic heart disease, in which a person dies due to poorly oxygenated blood reaching the entire heart, was more common in those with no magnesium supplementation or very low oral magnesium dosing. Simply, “circulating and dietary magnesium are inversely associated with [cardiovascular disease].” Further, Qu shows, in another study, a significant drop in intestinal cancers with a reasonable magnesium intake. While we may not know the mechanism for these useful findings, they are not felt to be due to chance.

Song and Leff clearly show why a small number of scientists and physicians have pondered lowering human magnesium Mg^{2+} levels. They remind us that Mg^{2+} can influence bacterial adhesion, which is part of biofilm process. In their study, the bacterium *Pseudomonas fluorescens* was used to investigate the influence of Mg^{2+} on biofilm growth.

Nitroxoline

We are not going to spend significant time on this fifty year-old antibiotic because it is not used in many countries, and it is a quinolone, and quinolones all seem to have serious risk of tendon damage. For example, it is possible nitroxoline has the same risks as other quinolones (www.drugbank.ca/drugs/DB01422).

Quinolones easily enter cells and are often used to treat intracellular pathogens such as *Mycoplasma pneumoniae*.

The FDA has increased warnings regarding side effects since the drugs were first approved. I just want to focus on three side effects that might not be routine but are possible risks with many quinolones:

- **Damage to nerves outside the brain:** This could present as sensory nerve or muscle nerve injury causing paresthesias, hypoaesthesias, dysesthesias, and weakness. New pain, burning, tingling, numbness and/or weakness, or new decreased abilities to detect light touch, pain, temperature, position sense, vibratory sensation, and/or motor strength are basic nerve functions and show damage; these are reasons to stop taking the drug.
- **Tendon damage:** While some focus on the Achilles tendon, actual tears of tendons have occurred in the hand, the shoulder, the thigh, or other locations. Some are helped with surgery. Other patients feel the surgical or other treatment still leaves them with damage. It is believed by some that the use of prednisone and other cortical steroids meant to drop inflammation increases the risk of tendon damage. Perhaps this is especially true in older seniors. Surprisingly, tendons can rupture after the medication is stopped. Some have suggested that IV, transdermal or sublingual magnesium might decrease the risk, but I am not aware this hypothesis has been proven (Schaller).

Aspirin and NSAIDS

We have previously said it is best to see biofilms like a key, and using AIDS as an example, it was only after AZT in 1996 with **the arrival of protease inhibitors that those quickly dying, experienced a “Lazarus effect,” in which AIDS patients who looked to be ready to die recovered markedly in 30 days.** Medications used in AIDS are tough medications, even if they are miracles. Some may question offering a section on the tough medications aspirin and NSAIDS.

While we appreciate that aspirin and various other over the counter NSAIDS may not be optimal, perhaps due to concerns of liver, kidney or ulcer issues, we are discussing infections that invade and cannot be stopped by your body. You might need all the help you can get. So we offer some synthetic options here that may offer help against a top killing and disabling problem—**biofilm-protected** infections.

For example, fluconazole-resistant *Candida* is increasing worldwide. Fluconazole is also called Diflucan. Biofilms are one reason for a decreased effect in treatment. Aspirin, diclofenac, ketoprofen, tenoxicam, and ketorolac all undermined biofilms or their processes. They all reduced fungal adhesion, and increased biofilm detachment with low concentrations of anti-inflammatory agents. Microscopic examination confirmed the tested drugs had a significant effect on reduction of *Candida* adhesion and biofilm development. The drugs also made fluconazole work more effectively against fluconazole-resistant *C. albicans* (Abdelmegeed).

Another useful way to involve aspirin is by teaming it up with the chelation chemical EDTA. Both aspirin and EDTA possess broad antimicrobial activity for biofilm cultures. Aspirin used for 24 hours was successful in eradicating *P. aeruginosa*, *E. coli* and *C. albicans* biofilms. Moreover, exposure to the Aspirin-EDTA combination completely destroyed bacterial biofilms after only four hours in simulation lab testing (Al-Bakri).

Azithromycin (Zithromax)

This medication is almost a household name and is known as the “Z-Pak” which contains brand name Zithromax pills that are still in use today. Despite being in use many years and used very routinely, this medication still has a strong use in addressing biofilms.

For example, Maezono showed that azithromycin was markedly superior compared to other routine antibiotics in killing gum infection bacteria. Specifically, azithromycin at **very low dosing** undermined four strains of *Porphyromonas gingivalis*. This determination involved the use of two fascinating techniques.

Azithromycin dropped the bacteria “gasoline” or ATP in the bacteria, which means the bacteria had decreased function or were dead. Cyanide kills humans in part due to dropping ATP levels—it is not a trivial substance. Further, the power of azithromycin was seen clearly with a confocal laser scanning microscope, which has the ability that the long name suggests—seeing the decreased amount of bacteria.

One of the most common hospital infection risks is MRSA; it causes a number of potentially deadly diseases. This “MRSA” simply means routine staph aureus is no longer able to be killed or it is resistant to methicillin, so it reproduces unchecked. Azithromycin is proposed as one solution to MRSA based partly on its biofilm defeating abilities at very low dosing.

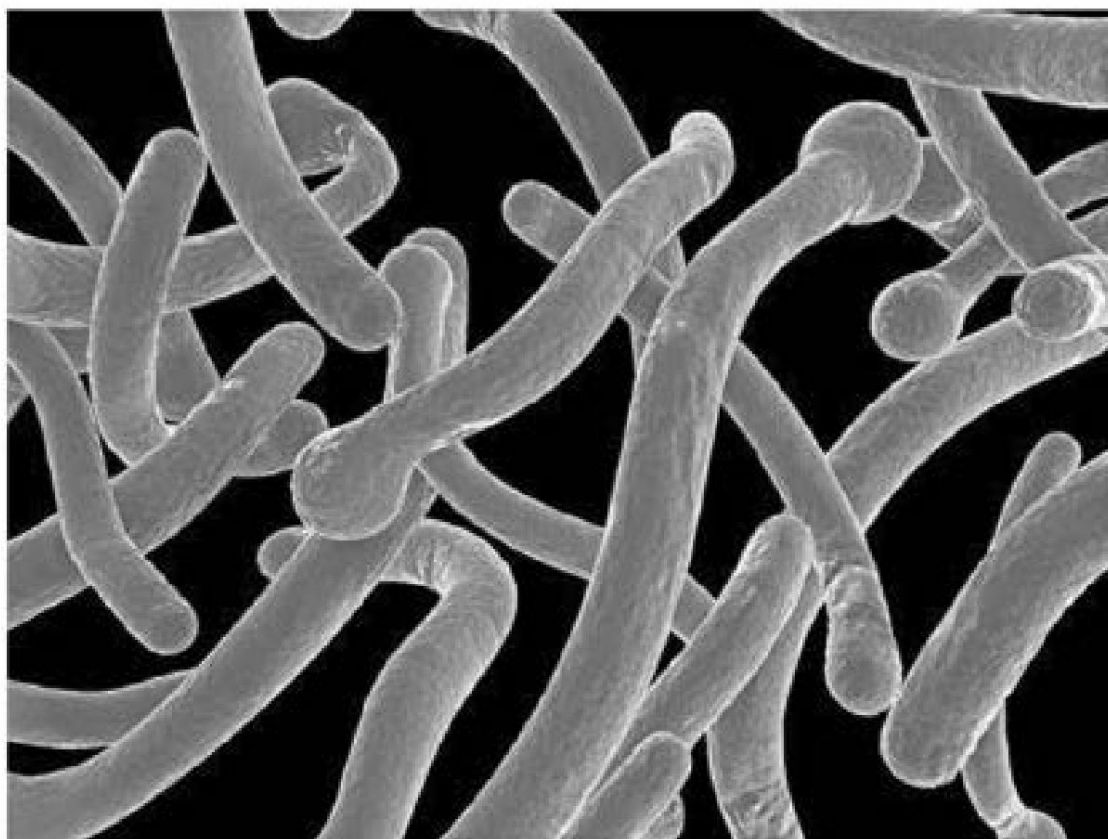
Gui shows that azithromycin was active against methicillin-resistant *Staphylococcus aureus* (MRSA) strains. It reduced the production of α -hemolysin and biofilm formation at very low “sub-inhibitory” concentrations. So, azithromycin may be useful in the treatment of α -hemolysin-producing and biofilm-forming MRSA infections.

Maezono H, Noiri Y, Asahi Y, Yamaguchi M, Yamamoto R, Izutani N, Azakami H, Ebisu S. Antibiofilm effects of azithromycin and erythromycin on *Porphyromonas gingivalis*. *Antimicrob Agents Chemother*. 2011 Dec;55(12):5887-92. Epub 2011 Sep 12. PMID:21911560

银

用于对抗伤口生物膜的银治疗显然是有效的。事实上,1% 的银霜已成功用于治疗 and 预防世界各地烧伤患者的感染。

国际伤口感染研究所的一项审查显示,数据仍然表明银是最佳治疗方法。例如,蒙泰罗测试了胶体银对抗真菌生物膜的效果。这项工作的结论非常明确:无论研究中使用的浓度如何,银都会影响念珠菌生物膜的基质组成和结构。



白色念珠菌的 3 维渲染特写。

Cumanda and Biofilms

Dr. Eva Sapi and her colleagues found in their superior laboratory that cumanda had some mild killing effects on the Lyme bacteria, but more importantly for this book, Lyme **biofilm** communities grown in her lab were reduced 43% by this herb at low dosing. The dosing for a dynamic human or animal body was not explored or proposed by this researcher or any other researcher as of February 2014. Searching by its Latin and popular name did not yield any articles relevant for use on infections.

Finally, while Lyme disease is a common and disabling infection, it is hardly the only infectious agent in the many infections carried by Ixodes ticks. While this preliminary research is very useful, it is possible cumanda may have impact inside a body for Lyme and Bartonella treatment. More study is needed. I regret that we only examined cumanda for Bartonella and not Lyme.

Our conclusion was that cumunda hindered Bartonella more than Levofloxacin (levofloxacin), Zithromax (azithromycin), Rifabutin (mycobutin) and other proposed options. To determine treatment effect one needs to know **the indirect actions of Bartonella, Babesia, FL1953, Lyme, inflammation systems, etc. by lab analysis using different companies.**

Theophilus PA, Burugu D, Poururi A, Luecke DF, Sapi E. Effect of Medicinal Agents on the Different Forms of Borrelia burgdorferi Lyme disease or Lyme borreliosis is a tick-borne multisystemic disease caused by different species of Borrelia. <http://healthyats-nl.blogspot.com/2013/07/effect-of-medicinal-agents-stevia-and.html>

Erythromycin

Gomes found that erythromycin at low doses actually enhanced the growth of biofilms in *C. diphtheriae*. Penicillin acted the same way. Of further concern is that not only did these antibiotics increase biofilm formation but in this case they enhanced infections by strains of *C. diphtheriae*. Diphtheriae is a very dangerous infection without access to effective antibiotics. It is dangerous enough with good ones.

Returning to biofilm-promoted gum disease such as gingivitis, in the United States, over 50% of adults had gingivitis on an average of 3 to 4 teeth. Adult periodontitis, measured by the presence of periodontal pockets ≥ 4 mm, was found in about 30% of the population on an average of 3 to 4 teeth. Lost gum attachment to teeth of at least 3 mm was found in 40% of the population (Oliver).

The density of adherent *P. gingivalis* cells were significantly decreased by using erythromycin at very low dosing called “sub-MIC levels.” One strain was not affected by erythromycin. Finally, erythromycin was not effective for inhibition of *P. gingivalis* biofilm cells at very low dosing.

Erythromycin Key Findings

- Low doses actually grew some biofilms
- Penicillin also grew some biofilms
- It enhanced strains of dangerous *C. diphtheriae*
- Gum disease from *P. gingivalis* cells was much less sticky at very low dosing.
- Erythromycin was not effective for inhibition of *P. gingivalis* biofilm cells at very low dosing.

Contacting Dr. Schaller

Should you wish to talk to Dr. Schaller he offers individualized education consults, which can be arranged by calling 239-263-0133. Please leave all your phone numbers, a working email and a fax number. These consults are typically in 15 minute units and can last as long as you wish. All that is required is the completion of a short informed consent form.

If you would like a full diagnostic consult or to see Dr. Schaller as a patient, know he treats patients from all over the USA and from outside the country. He meets with you first and then does follow-up care with you by phone.

If you would like to fly in to see Dr. Schaller, his staff are very familiar with all the closest airports, and we have special hotel discounts.