

The limburger cheese and socks paper is my favorite of the Chemistry of Stink talk. It demonstrates the overall theme I try to accomplish with most all stories. A singular finding that draws connections to other topics. What can be learned from the discussion of one item and the richness that knowledge provides. Mostly stuff the student already knew about, but hadn't connected together into a wonderful story of how awesome their world is.

Apparently, the anopheles mosquitoes which are a vector for the Plasmodium type malaria use a set of cues that are a little more complicated than our domestic mosquitoes to in order to locate a meal. Well, the girls, at least. It would seem, they prefer the feet and somewhere around 1996-1997 somebody with malarial interests, discovered(?), decided(?) that limburger cheese, smells like nasty feet. As it turns out, the same type of bacteria (corynebacteria) is responsible for the "ripening" of feet and cheese into their stinky counterparts. So the idea of trapping mosquitoes with stinky cheese isn't completely retarded.

My interest in this topic began when I learned ages ago, that pseudomonas bacteria had a characteristic odor. A microbiologist holding a plate of pseudomonas aeruginosa, would say it smells like grapes. Large burns and diabetic feet (poor peripheral circulation and neuropathy) have been described with the characteristic odor of pseudomonas infection, but I haven't found a consistent description of the odor in the mixed environment of the foot or wound. I have asks numerous surgeon folk, and lot of people describe, mostly a vague sweetish odor, others referred to old gym socks. A lot of conflicting and confusing descriptions. MDs will squeeze your ankles but they don't often sniff the toes nearby. Oh well.

Is pseudomonas the likely candidate for everyday day stinky feet? At minimum the sweetish gym sock odors? I thought so, but outside the context of burns and broken skin in the diabetic pseudomonas aeruginosa can't compete or get a foothold. Nor does it make anything that people often associate with bad body odor. (mostly its acetophone-another story, involving corn tortillas and the free-tailed bats.) You do find other forms of pseudomonas in the fridge or on your plants, or in the compost. Stinky vegetable waste is dominated by pseudomonas bacteria and their products. They can use just about anything as a carbon source. As the old legend is told, you can find pseudomonas aeruginosa growing in the dried sludge that collects around the spout of soap dispensers. Woah.

Stinky feet are actually pretty simple compared to the stinky armpit. Armpit odor science seems more confused, despite all the effort devoted to it.

Though staphylococcus and micrococcus, propionabacter, can dominate the skin, they don't appear to have the enzymes necessary to produce the foot/cheese stank. The corynebacteria

is most prevalent with the most stank and also possesses the enzymes needed to turn odorless apocrine secretions into stinky, cheesy, products.

As you may know, *Staph epidermidis*, is commonly found in the skin and is the stuff associated with biofilm infections you find around indwelling medical devices, like central catheters, PICC lines, foley catheters. It can make short chain fatty acids as part of its metabolism, but they don't appear to be a major player in the stinky foot. The corynebacteria culprit has some clinical significance with erythrasma and the so called pitting keratolysis, but nothing very significant, clinically. I think.

The long and the short of it is: (I had to look this shit up) 3-hydroxy-3-methylhexanoic & (E)-3-methyl-2-hexenoic acid are the two major actors with plain vanilla sweaty armpit, sweaty foot stink. A variety of similarly arranged, but sulfur containing sulfanylalkanols contribute the sulfury, oniony, ripe stank. The most important actor being 3-methyl-3-sulfanylhexanol (3M3SH) . The secret sauce to caucasian apocrine gland stench.

The whacky part to all of this is that precursors of these molecules, arrive at the apocrine sweat glands (not the "typical" eccrine sweat glands we associate with sweating, salt, diaphoresis etc) and somehow are enzymatically released out of the gland onto the skin. From there the corynebacteria chomp the above molecules loose from the cysteine-glutamate boat they rode in on. This is done via cysteine b-lyase which is one of those singular methionine synthesis enzymes. I guess corynebacteria need to make their own methionine?

WTF?

From where do these conjugated pre-cursors come from? Beats me. But its a glutathione type conjugate, which I normally associate with the liver functions.

Which begs the question: Do people suffering from tylenol/acetaminophen poisoning, with a horribly damaged and glutathione deficient livers...do they not get stinky feet/armpits?

Dunno.

Would N-acetyl-cysteine bring the stinky back?

Dunno!

Crazier still, was the discovery of an ATP binding cassette (ABC transporter) that is actually necessary for the sulfur secret sauce part of this endeavour. Apparently ABCC11 is the transporter and some folk in the far East have an isoform that spares them from the stank and for added value, gives them a characteristic scanty, dry earwax. Something about cholesterol or steroid transport.

Us white folk? We get to smell bad.

The corynebacter is what gives us the stinky feet/stinky cheese connection. Beyond the cheese or acid odors, it doesn't seem simple. Example:the armpit

Do sweaty sock or limburger cheese attract mosquitoes? Depends, but yeah.

Often the question "Why do feet smell worse, when you wear no socks?" I suspect this is a nutrition issue. You leave a lot more dead skin behind when there is no sock to trap it. The predominating bacteria in socks vs no socks stinky feet, hasn't been examined, as far as I know.

I have heard rumors that newborn babies can have feet that smell "like feet". I bet they colonized with cooties, just like grownups, even if they don't wear shoes. And just like their fat heads, newborn baby feet are crazy out of proportion huge compared to the rest of the baby skin apocrine real estate. When you next see a cute little newborn, sniff its feet, and re-evaluate the cute.

How to get rid of the stink?

Change your socks, wash your feet. Gets rid of the bacteria, and removes most of the nutrition (dead skin). Occlusive footwear is associated with stinky feet and fungal infections as airtight shoes promotes the jungle conditions where stank best thrives, as well as leading to skin maceration "pruniness" which compromises the barrier qualities of intact skin, leading to fungal establishment.

Foot powders? Here its a mixed bag of products. Often you find things with talc and deodorant, which seems to help

Baking soda? It works. It forms salts from the volatile acids that stink. Do salts evaporate? No. That why they don't smell. I don't know to what extent the alkaline pH the carbonate forms upsets the bacterial growth. Since its a direct titration, more acid stank, requires more baking soda.

Incidentally, baking soda for the kitty litter box. A damned lie. Ammonia is too alkaline to react with carbonate irreversibly.

Sometimes you find a quaternary ammonium compound such as benzalkonium chloride which is a good antimicrobial agent.

The Gold bond powder with its zinc oxide and menthol works. Menthol has some antimicrobial activity, reminiscent of the classic "carbolic acid" Phenol! which was the first antiseptic agent used to great effect by Joseph Lister. The zinc oxide would appear to help too, as it can form a weak acid, shifting H⁺ equilibrium to the acid side of things, something that gram + skin bugs don't like very much. What pH is achieved? I dunno. There is also some evidence that the zinc ion may have antimicrobial activity, but I'm not convinced of this yet.

Lastly, antifungal powders deserve mention, as they are quite common in terms of foot powders. Like other powder compositions, they try to achieve a drier less microbe friendly jungle but they contain the secret sauce to the sticky feet lecture. Ketoconazole, clotrimazole, miconazole etc make life difficult for the eukaryotic invaders yeast and fungi. Of the millions of species of yeast and fungi, perhaps only a half dozen? are pathogens in a person with a reasonable functioning immune system. They drive the antigen presenting cells of the "innate immune system" crazy, giving rise to the profound inflammation and itching that are associated with fungal skin infections. If found inside the organism, they tend to form granulomas, again due to pissed off macrophages and the like. Mostly macrophages. Angry, constipated macrophages. Pathologists call them epithelioid macrophages since they kinda-sorta resemble epithelial cells when all riled up in granulomas, usually flogged by a ring of lymphocytes, encircling the whole constipated mess.

So what? Well, it turns out that miconazole, while an effective antifungal, it also possesses significant activity against quite a few of the gram + skin bacteria. Consider that added value for your stinky foot purchases. The other azole antifungals do possess some antibacterial activity, but not as much as miconazole.

Oh ho!. Andy just saved you some money. Use the miconazole powder for fungus, AND for stinky feet. Staph aureus, staph epidermidis and a few others don't dig the miconazole, making for fresher smelling toe jam.

This begs the question: Will a dash of miconazole foot powder ruin my limburger cheese project? Good question. I bet it would. More added value. Save your feet and sabotage the stinky cheese industries of your enemies.

But wait. Does that mean you could use that foot powder to prevent the skin infections commonly associated with cellulitis, erysipelas, impetigo etc? I think so, miconazole is that cool. Check it out. Sprinkle some in your skin creases, scalp etc or under the panniculus of

bigger folk, and tell me if it spares you some keflex or bactrim. Of course, soap and water works too, but I'm not letting that fact ruin my sales pitch here.

From mosquito traps in malaria country, we learn about stinky cheese and stinky feet. Commonality of corynebacteria give us unifying incite to stanky feet and cheese. A common antifungal powder can do double duty, killing fungi and the foot stank, also giving you a tool to sabotage your enemy's cheese and possibly prevent staphylococcal and streptococcal skin infections in an austere environment, where usual soap and water washing may be lacking.

You may recall the somewhat apocryphal tale, I told, of factory workers, working around PCBs. (or was it benzene?) From the Drugs and Human behavior book, by Tibor Palfai. The chronic PCB exposure induced expression of cytochrome p450 in the liver, a form of cellular organelle hypertrophy. This extra microsomal enzyme achieves more prompt removal of the offending PCBs but causes cross tolerance with other substrates for the same enzyme. The workers supposedly had profound tolerance to alcohol on their weekends off, but if challenged with a beer during the work week, they'd been in trouble. Metabolic trouble.

Why PCBs? PCBs were good solvents, oils and dielectrics for capacitors and the like. Back then, capacitors were bigger can shaped things filled with oil, PCB oil. Carbon-Chlorine bonds are very stable. Super-duper stable. So stable, that you need crazy UV light from the upper atmosphere to bust those molecules apart. Of course, the free chlorine that is produced, reacts with all the ozone up there, making a big hole. Oops.

Why benzene? A good solvent too, and very very stable. Extremely reactive reagents and conditions are needed to do any chemistry with benzene.

Ah, both are super stable, but our liver has no problem busting those molecules up. The power of enzymes! As a result, both are really bad for your liver (and kidneys). Oops.

For example, carbon tetrachloride, the chlorine version of methane, in completely non flammable. ie. those carbon-chlorine bonds won't react with oxygen, even with heat. In addition to being a dry cleaning solvent, it was used as a fire extinguisher. You squirted this inert oil stuff on the fire, smothering it, and the carbon tet was volatile enough that it wouldn't leave things a mess for long. Sometimes it was sealed into a glass sphere, to be used as a fire extinguishing "grenade". Unfortunately, just like PCBs, the liver creates reactive radicals with these things, which deplete glutathione and causes fantastic hepatotoxicity similar to the chaos Tylenol/acetaminophen is famous for. NAC N-acetylcysteine would be appropriate here as well. Similar chaos occurs in the tubules of the kidney and carbon tet was a classic animal model for inducing ATN acute tubular necrosis.

Interestingly, the kissing cousin to carbon tet, carbon trichloromethane (chloroform), is impossible to set afire, is a bit more volatile, and has the added history of being a general anaesthetic, which for a time, was seen as a replacement for diethyl ether anesthesia. It was faster in its induction of surgical anesthesia and recovery from it. Unfortunately it was also associated with toxicity in multiple organs, again the liver and kidneys especially. Interestingly, there is a sexual dimorphism in chloroform's toxicity. Men are worse off than the ladies. It also had the habit of producing a bradycardia during the initial moments of anesthesia induction, with the more than occasional ectopic activity which stop the heart...kaput. Atropine was used to combat this, but ultimately chloroform was abandoned.

James Young Simpson, the obstetrician who was credited with introducing chloroform anesthesia, had a terrible time, and ultimately committed suicide, aided by chloroform, but mostly with a sharp razor. It was a sad story I told back then.

Dichloromethane, also known as methylene chloride, doesn't burn either. It was tried as an anesthetic as well. It worked, but the metabolism of dichloromethane generates a carbon monoxide molecule, which in turn reacts with hemoglobin to form methemoglobin and the less than optimal tissue oxygenation that results when you muck around with hemoglobin's oxygen affinity. Oops.

Today, it remains in use as "brake cleaner" since it evaporates quickly with no residue, which is desirable on car brakes. Other solvents like toluene, xylene etc are too "oily" to be trusted on brakes, and find use as carb/choke cleaner of the engine. Dichloromethane is an unusual solvent in that it is safe around most rubber and plastic. Xylene, toluene and the like tend to swell and soften rubber and many plastics. On the other hand, chloroform will dissolve most plastics you previously thought were indestructible. Don't ask me how I know. Oops.

I don't think a monochloromethane exists. Hmm.

Where was I? Oh yeah, inducing hepatic cytochrome p450, an enzyme commonly associated with the smooth endoplasmic reticulum, with one agent or toxin, which will also create cross tolerance with other drugs/toxins. Barbiturates and alcohol, PCBs etc.

The 2015 version of that story would involve azole antifungals and stinky feet. In the late 1980's a new antihistamine Seldane was introduced, and since it did not cross the blood brain barrier, it didn't create the drowsiness and mental stupid associated with every other antihistamine known previously. It was wonderful stuff if you were an atopic sneezy hayfever guy like me. Unfortunately a couple people died suddenly. Both were taking Seldane. One had erythromycin on board, the other ketoconazole. It was quickly determined to be a result of competition for, or inhibition of, cytochrome p450, in this case cyp3a4. Decreased cyp3a4

enzyme activity let the other actors achieve more toxic levels. Seldane was actually a pro-drug that was oxidized into its active form, what we call Allegra today.

Why didn't they just start with the Allegra? I dunno.

The Seldane pro-drug had some antagonist activity against a particular voltage gated K⁺ potassium channel. Occupying or inhibiting the cyp3a4 enzyme allowed the pro-drug to reach a concentration in the blood much higher than normally achieved, inhibiting the aforementioned potassium channels and inducing arrhythmias. Oops.

A long QT interval was the big clue. I think macrolides like erythromycin, actually have some potassium channel antagonism as well, so the toxic effect is probably worse, perhaps synergistic. The azoles just tie up the enzymes, letting the pro-drug Seldane circulate longer.

Lengthening of the QT interval and possible torsade de pointes? Not too healthy. Hence the current day warning about mixing azole antifungals with other drugs metabolized by cyp3a4. Taking macrolides with birth control, grapefruit etc etc etc.

The other cytochrome p450 often mentioned is cyp2e1, which has such a profound affinity for ethanol that you can actually displace things like methanol from the enzyme. This is the isoform of cyp450 that was the actor in my PCB/ benzene factory worker story, years ago.

Drinking methanol makes you go blind?

Well yeah, some gets oxidized in the retina, (another story) to formaldehyde, formic acid, which starts cross linking proteins in there. The most immediate worry in methanol poisoning is actually metabolic acidosis, with ethanol being an antidote. Weird, eh? Of all the xenobiotics your liver is exposed to, it really really really, wants to get rid of ethanol first. Does that mean something?

Anyways, updating the PCB+alcohol cytochrome p450 story with cyp3a4, and zole antifungals brings us to a BUT.

But what?

Exactly!

Is there a downside to Andy's can of mighty miconazole? His go to stinky foot remedy.

Well...the classic example of drugs lengthening the QT interval...Antimalarials. The medications you take when in areas endemic with malaria, places where people try to trap mosquitoes with stinky cheese and old sweaty socks. Miss Shereen mentioned she is doing something with malaria. Hopefully this stinky feet lecture, will enrich her experiences surrounding the plasmodium parasites and their impact on mankind, and the individual.

Science! Can you dig it?

Of course, quinidine, quinine, chloroquine have been used as antiarrhythmics as well as antimalarials. class 1 antiarrhythmic? I'm not really familiar with that stuff, but I tend to think ion channels/ion concentration with these things. Hypokalemic patient? ECG shows a long QT interval and maybe U waves? Think! Think stinky feet! Stinky cheese. How to combat the cheese, the feet, the gram positive cocci of cellulitis and erysipelas, erythrasma...cytochrome p450. Something is delaying depolarization at the level of the ion channels, just like the QT interval with antimalarials...

...Hmmm Miconazole. The mighty bottle of miconazole nitrate foot powder you bring with yourself everywhere. Yes, everywhere. Why? Would you really want to be without the tools needed to sabotage the manufacture of the delicious stinky cheese consumed by your enemies, if the need arises?

Of course not!

Could you predict the time for such an extraordinary occasion?

Of course not!

Be prepared! Don't let your enemies have the stinky cheese!

What if, in defiance, they eat the defeated cheese, with its poor flavor and baby fresh scent? Hello Torsades! Their day will be ruined, either way. All the while your feet are stink free.

So...Umm...Is there a downside to the mighty can of miconazole?

Nope. The above story applies to oral/systemic administration of ketoconazole etc,

Phew!

But hopefully, when you come across an XYZ-azole, you'll think:

"Hmm there is something about these antifungals that make them noteworthy...something about sabotaging cheese and fatal heart arrhythmias..."

A note on dyes: with a focus on microbiology

Mannitol salt agar is really salty, and this selects for staphylococcus, and micrococcus. Ages ago, (1980's) salt water gargles were recommended for sore throat. I never knew the reasoning behind this. Was it based on the fact that streptococcus don't like high salt concentrations? Dunno. But it should get one thinking...

You may remember. long ago I did a demonstration with methylene blue. Soda bottle almost filled with water, a pinch of methylene blue power, or a squirt of the methylene blue you can get for your fish tank, some glucose, and sodium hydroxide. At the time, I had to get the glucose in Chinatown (glucolin brand) , and pure lye was available as "Red Devil" lye. Red Devil lye is no longer available, but some drain cleaners are still available with pure sodium/potassium hydroxide. I claimed all the ingredients for the blue bottle demo could be found by the student, and tried to keep all of the demonstrations that way. I learned of the blue bottle demo from the Bassam Shakhshiri books. During the very first MESH (in Bldg 66) was the first time I demonstrated the blue bottle. Nearby building 56 was being gutted and the teaching labs abandoned. I managed to find the methylene blue, glucose and sodium hydroxide, among the ruins.

Mixed up, you had a dark blue solution that gradually became colorless. Vigorous shaking brought the blue back, only to fade again. Oxygen. Redox. In the alkaline environment, reduction is promoted, and the reducing sugar glucose, reduced the methylene blue to the colorless leucomethylene blue. Fructose is a reducing sugar as well, and easily found in corn syrup, but I never tried it, preferring a powdered sugar, for convenience and consistency with story telling. The reducing activity of glucose and fructose come from a free aldehyde group, which often reacts with the sugar molecule itself to form the "ring" version of these sugars. In solution, in particular, alkaline solutions you can get an equilibrium which favors the free aldehyde. What I needed for the blue bottle.

Aldose hemiacetal pyranose ring ketose to aldose

Anyways...

Methylene blue turns out to be neat redox indicator due to this simple color change. Blue when oxidized, colorless when reduced. I will try to illustrate its utility in a bit.

Question: How did I remember that chain of events in the blue bottle reaction?

Because of the other glucose reduction stories. I didn't have the resources for it at the time, but I really wanted to do some silver nitrate/oxide mirror reactions. ie. Tollens reagent. An ammonia laden solution of silver nitrate, and redissolved silver oxide will precipitate pure

silver against the wall of the container, forming a mirror, when glucose (or formaldehyde) is added.

Beautiful stuff. Again described well, by Shkhashiri.

Another glucose reduction demonstration: Fehlings solution. Leave a copper penny in strong ammonia water for several days, a blue solution will result. When reduced, pure copper (or is it copper oxide?) will precipitate. The poor man's mirror demo. It makes a pile of coppery sludge instead of the lovely silver mirror coating.

The actual Fehlings solution has cream of tartar in it, tartaric acid salts, but the ammonia & penny works too. Used to test for reducing sugars and for deciding if something is an aldehyde or a ketone. Aldehydes reduce, ketones don't do much. Toss a raisin in there and copper will precip out. Ta Da! Glucose reduces again!

You can use either Tollens or Fehling to test for glucose in urine, glycosuria, one sign of diabetes.

Question: Is it used in glucose urine test strips?

It turns out to be glucose oxidase in those test strips. They isolate it from yeast or mold or some such. I couldn't tell you what the color change reaction is. But the enzyme is specific for glucose and therefore less likely to give false positive reactions, when compared with the Tollens and Fehlings Benedict's reagent

Are these solutions useful in an austere environment?

Dunno, probably not. Those test strips are probably more handy, stable, accurate.

Errant results can be had with Fehling's solution when Vitamin C (ascorbate) is in the urine. Ascorbate, an antioxidant, a reducing agent just like glucose and aldehydes.

Ascorbate on peeled fruit, the fruit will not turn brown in the air until the ascorbate is exhausted. It will also complex with halogens such as iodine or chlorine rendering disinfected water better in taste. Iodine solutions will turn colorless, with enough added ascorbate.

Does glucose do that on fruit?

Not really. Ascorbate has a fantastic affinity for oxygen, compared to glucose, which explains why small amounts excreted in the urine, will turn our glucose test reagents positive. Making mirrors (Tollens reagent) or copper oxide sludge (Fehling reagent)

In case you haven't made the connection yet, ascorbate (Vitamin C) will reduce methylene blue and decolorize it.

Anyways...methylene blue: It turns up as a counterstain in the acid fast bacteria stain, which is usually used to detect mycobacteria such as tuberculosis. It turns out that methylene blue has some antimicrobial activity. The microbiology folk are familiar with EMB agar (Eosin, Methylene Blue) which will actually inhibit gram (+) growth and select for gram negatives of the entero type. Ah ha. This is how we will distinguish our stinky feet bacteria.

Want to grow bacteria from that stinky sewer of a mouth? Not a problem. Want just the gram negative bacteria? Use EMB agar. Just a tad of methylene blue and eosin will suppress gram positive growth.

Will gargling with eosin+methylene blue destroy the streptococcus pyogenes you have in your throat?

Good question. Worth a try.

Why is not used as a topical antimicrobial? Dunno. People played with it long ago. The blue has something to do with it I guess. It makes a mess of things. Of course, there is gentian violet (crystal violet), an old remedy for thrush and a key component to the gram stain, used to distinguish gram(+) vs gram (-). Gram (+) stain with the crystal violet, and gram (-) do not. Hmm, maybe it likes bacteria, just not the coated ones?(gram neg.) Come to think of it, another gram component is lugols iodine or grams iodine (more dilute). Interesting...

If students wanted to replicate the blue bottle demo on their own, I'd tell them their best bet for finding methylene blue is the pet shop, near the fish supplies. There are other products available to kill bacteria in your fish tank, but methylene blue can still be found as a fish tank "antibiotic", disguised by some catchy product name. Read the labels.

Gentian violet is still sold in some places. In the old days, for nursing mothers with thrush. Coat the nipple, let the baby suckle. Baby gets treated, mommy gets treated. I see it on the shelves at CVS, Walgreens and Walmart sometimes, but not consistently.

Crystal violet (gentian violet) is also useful for collecting fingerprints off of the sticky side of tape. Pretty neat.

clinical connections:

Both gentian violet and methylene blue appear to be making a comeback in some wound dressings, and being used in combination. Antibiotic resistant *Staph aureus* sucks, and with diminishing antibiotic options, these old school curiosities of a hundred years ago are getting another look. Especially in the context of slowly healing wounds/ulcers. Oddly enough, methylene blue is a phenothiazine (see Tibor Palfai) just like chlorpromazine (Thorazine) and promethazine (phenergan). Both have antihistamine activity. Does methylene blue? Good question. I dunno. The anticholinergic effects of both chlorpromazine and promethazine also reduce nausea vomiting.(antiemetics) Somehow these have been replaced by Zofran. Dunno why. Zofran interacts with a different receptor type (serotonin 5-HT?)

Lastly...

The Methylene blue reductase test is an old assay to determine if milk has spoiled. A certain amount of methylene blue is added to a certain amount of milk and observed for a time. If the blue turns colorless within a short time, that indicates a fair amount of bacteria are present. I don't think milk bacteria actually make a methylene blue reductase enzyme, but some reductase activity from the bugs will turn methylene blue colorless. Short duration of blue color in milk?= spoiled milk that isn't sour yet.

Long time blue=Good to go milk.

Good for an austere environment? Dunno. I don't think they drink a lot of milk in Africa.

Back to feet. I hope you like this memory lane jog..

Remember the blue bottle now? No? Punks.

recap:

Stinky cheese smell like stinky feet. Plasmodium carrying Anopheles mosquitoes seem to favor the feet as a target for their vampirism. Can you catch mosquitoes with cheese instead of feet? Depends. That's what the Limburger cheese paper was trying to determine.

Are stinky feet and stinky cheese a coincidence, or a marvel of nature and its economy of methods to produce stank? Among the various gram (+) positive cocci you find growing on

skin, the Corynebacteria are the connection. In the case of feet, the corynebacteria convert odorless materials secreted from the apocrine sweat glands into stinky sulfanylalkanols, whose metabolic origins escape my understanding. In the case of limburger cheese, its part of the recipe, necessary for the ripening of the final product. In both cases, corynebacteria are needed to produce the characteristic stinky cheese odors. They got the enzymes. Staph and strep apparently do not.

Of the various foot care products available for stinky, ripe, feet, miconazole was mentioned as having antifungal and significant antibacterial activity against gram (+) organisms. (staph, strep and the corynebacteria, among others) ie. It can kill the bacteria responsible for the stinky cheese and cheesy feet. And possibly the bacteria responsible for cellulitis, erysipelas, erythrasma etc. (topically)

Miconazole can sabotage the stinky cheese. Efforts to isolate and grow stinky feet bacteria lead to the memory of selective growth media for gram (+) and gram (-) bacteria. Mannitol salt agar and EMB agar. Ah, methylene blue, one of my first demonstrations at the first MESH. A delightful redox indicator. A crowd pleaser

Similar reactions to the blue bottle reaction are used to detect glucose, (Tollens reagent, Fehling's reagent) and rely on the redox reactions of glucose's aldehyde group. Fructose? That works too. Confounding results can be had if ascorbate is present, and limits the utility of these reactions as an assay for glycosuria (glucose excreted in the urine.)

The selectivity of EMB agar comes from the antimicrobial activity of methylene blue and eosin. By itself, methylene blue has antimicrobial activity. Sometimes used as an antimicrobial in fish tanks. Very similar to gentian violet (used for thrush/Candida albicans) in that regard, and both are used in combination for some wound dressings, as antibiotic resistant organisms that produce skin infections, become more of a problem.

Ergo, both methylene blue and gentian violet could be used to kill stinky foot bacteria and to sabotage your enemies stinky cheese manufacture. Both will leave things blue/purple though.

Lastly, we can milk one more reaction out of methylene blue. The methylene blue reductase test. A simple assay to determine milk spoilage. Bacterial concentration in milk will determine the rate at which methylene blue will be turned colorless. A quick and dirty assay for checking on the milk, before it turns sour, or into clumps of cheese.

Cheese.

Cheese?

That reminds me of limburger cheese, stinky cheese. Didya know Anopheles mosquitoes dig feet and cheese...?

Shaking that bottle of liquid, and watching the blue color appear as you mix more air into the solution, can tell you a thing or two about redox, microbiology, cellulitis etc. Just like the stinky feet and limburger cheese can lead you down these paths as well. If you had zero microbiology background, you get a teaser introduction. If you are already experienced in the ways of gram (+) vs gram (-) bacteria, hopefully you've learned something useful too.

The next day would be...

As hinted at above and previously, Gram (+) bacteria have clinical significance. *Strep. pyogenes* is a weird little cootie in that it remains sensitive to penicillin and the other beta-lactam antibiotics, macrolides too. *Staph. aureus* on the other hand...