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It'll Make Your Skin Crawl — Microbes and Skin Physiology

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by Vanessa Vitug

Introduction

"Ring around the rosy, a pocket full of posies, ashes, ashes, we all fall down." This seemingly innocent children's nursery rhyme actually describes the pustules an infected individual might get when their body is fighting a raging infection of the bacterium *Yersinia pestis*. It is the microbe responsible for the Bubonic plague. The infection causes an inflammation of the lymph nodes that may eventually lead to the development of buboes (swollen lymph glands) and even worse, gangrene. Throughout human history, humans have attempted to fight their invisible enemies – the microbes. As long as stories on the nightly news discuss the latest outbreak of antibacterial resistant bacteria in a hospital, a child inadvertently harmed by *E.coli* contaminated broccoli, or a tourist developing flesh-eating bacteria while on holiday, microbes will continue to have a bad reputation.

Like many people, my students readily turn to television as their main source of science. This is in part due to the success of shows like *Cosmos*, *Mythbusters*, and my two favorites *Dirty Jobs*, and *Monsters Inside Me*. Science shows are easy to digest and frankly, they make for great entertainment. One memorable experience my students and I share occurred when watching a clip of the dirtiest man alive - Mike Rowe. We watched as the fearless Dirty Jobs host swabbed from head to toe. The enthusiastic microbiologists collected the seemingly innocuous swabs, swiped them onto a life-size agar medium, and incubated the agar Mike Rowe. The revelation at the end of the program showing the variety of microbial fauna that grew on the life-size cast is enough to drive the most desensitized microbiologist to grab the largest bottle of disinfectant spray. The life-size agar model was littered with various colors of grown-up microbes clearly showing the extensive harmless microbes that call our skin home.

Today, advances of DNA sequencing techniques, scanning and electron microscopes, and the development of systems and procedures for collecting, handling, and storing microbes have allowed scientists to study them to new heights. New bacterial and viral species are constantly being discovered in places both inhospitable to humans and seemingly inhospitable to any organisms. The diversity of microbes and their often higher rates of mutation and evolution, create endless points of inquiry for scientists, teachers, and students. This curriculum unit is designed to answer a small niche in microbial study – What microbes exist on the human skin? What are their beneficial or pathogenic potentials? What new discoveries will the Human Microbiome Project unveil?

To high school teenagers, the concept of microbes is simply that: "micro". Beyond the rudimentary splashing of their fingers as they depart the bathroom facilities and their vain attempts to not sneeze onto their friends, teenagers are simply unaware of the microscopic world of bacteria and viruses. Humans are a hardy species, withstanding the barrage of microbes attacking our body's systems each day. So, the question is how? How can we survive the onslaught of an enemy whose numbers are far greater than all of human kind itself? One answer is the genius design of the human integumentary system or skin. It is our body's first wall of defense against the "dirty" world we live in.

Background and Rationale

Mt. Pleasant High School is a comprehensive high school located in San Jose, California. Nestled in the foothills of East San Jose it is one of 8 traditional high schools within the 17 schools supported by East Side Union High School District. Mt. Pleasant is a school in transition as it faces the challenges of incorporating Common Core embedded lessons into its current curriculum while facing the challenge of a decreasing enrollment due to the influence of charter schools and fewer school-aged children in the community. Though it has the facilities available to serve a much larger student population, this past year enrollment dropped below 1500. Despite this ongoing issue, Mt. Pleasant continues to serve a population where 66.2% are considered socioeconomically disadvantaged. [1] One asset of the school is the diversity of the population which includes Latino, Asian, Filipino, White, and African American students. Mt. Pleasant also serves a high percentage of students with disabilities. Special needs students make up 14.9% of the school population which requires all staff members to be especially aware of how to serve the neediest of its students. Finally, Mt. Pleasant teachers are conscientious in the creation of lessons and activities that will aide in the success of its English Language Learners which total 47.0% of the school population. [2] The school's Single Plan for Student Achievement focuses on this population since they make the greatest impact on the school's API (Academic Performance Index) score.

Our school is a Title 1 supported school and part of our attempts to reach the broad range of middle-achieving students will be performed by the AVID Program. AVID (Advancement via Individual Determination) has been a part of Mt. Pleasant since 1994 and its history of success like many programs has its peaks and valleys. Within the past year, our school has heavily invested in the program, seeking to improve teaching quality of AVID Methodologies through professional development, and increasing student enrollment in all AVID sections. This unit will support not only Physiology teachers with their content, but also AVID teachers looking for ways to incorporate science in their AVID curricula.

To meet the demands of college admission, students at Mt. Pleasant often choose to take a third and fourth year of science though it is not required for high school graduation. Students take Physiology for foundational knowledge as they plan to pursue majors in nursing, biology, kinesiology, or pre-medicine. Though the course focuses on anatomy and physiology, often pathology becomes a major focal point for our students who consistently relate physiological function to dysfunction. Thus, pathogenesis is often the most direct route for aiding students in their understanding of normal physiological function.

The integumentary system is a major focus for Physiology students within the first semester. After an introduction to types of tissues and membranes found in the human body, students study the skin as the first organ system. Helping my students understand that the study of Physiology includes understanding pathology

is the key to keeping them engaged through the year. Thus, an objective for this unit includes, not only, understanding the anatomical and physiological function of the skin, but also to understand etiology of bacterial and viral skin disease. Over the course of the three week unit, students will engage in readings related to normal and resident microbes along with pathogenic microbes affecting the skin. Students will practice critical reading skills that will allow them to better access subsequent readings in their classes.

Beyond the pedagogical challenge of engaging students, reading skills and comprehension is always an obstacle to overcome. Despite the concurrent enrollment of my students in AP (Advanced Placement) classes, many continue to struggle with reading comprehension in order to participate in discussion, engage in activities, and deepen their understanding. This unit is designed to capture student's interests while teaching them foundational skills in critical reading, which I hope will transfer to subsequent chapters throughout the school year.

Finally, a recent WASC (Western Association of Schools and Colleges) visit to our school suggested the need for opportunities to share best practices, alignment of curriculum that is considered rigorous, relevant, and in-line with Common Core State Standards and Next Generation Science Standards. This unit aims to provide teachers with a new approach to teaching Physiology. Its classroom lessons and activities answer the demands of the Common Core State Standards and Next Generation Science Standards with regards to Structure and Function and Interdependent Relationships in Ecosystems. [3] Teachers teaching Biology can adapt the unit and its activities to reflect their students and needs. English teachers can also adopt the readings for their students.

The Human Integumentary System

When I have asked my students, what is the largest organ of the human body? Inevitably, I will get two main answers, liver and intestines. Students often forget that their skin is an organ; in fact it is the largest organ of the human body. Our skin is comprised of different tissues working together with accessory organs to create the Integumentary system. Some of the accessory organs include hair, (sweat) glands, and sebaceous glands (oil glands) which support the three layers of the skin. Skin is actually a cutaneous membrane comprised of three interlocking layers: the epidermis, dermis, and hypodermis.

Epidermis

What we see as skin is actually epithelial tissue (a group of cells which line a lumen or duct). The epithelial tissue is comprised of joined epithelial cells of varying shapes (flat or squamous, square or cuboidal, rectangular or columnar). Layers of cells create different strata. Hence, various thicknesses of tissues can be attributed to epithelial tissue that is stratified. Depending on the type of epithelia that comprise the strata the tissue may be described as stratified squamous, stratified cuboidal, stratified columnar, or pseudostratified. The epidermis consists of 5 distinct layers with the top being the stratum corneum and the bottom being the stratum basale which is the source of mitotically dividing epithelia. [4]

The outer epidermal layer consists of several layers of keratinized epithelial cells which include pigment producing cells known as melanocytes. Because of the protein keratin, the epidermis is impermeable to water and provides the thin layer with strength and flexibility. [5] A major function of this wall of keratin cells is to

provide a barrier to heat, chemicals, and microbes. 90% of epidermal cells are keratinocytes. [6] The process of pushing old keratinized cells upwards to be shed is known as keratinization. Keratinization is an important concept to understand since keratinization is a major factor in maintaining the skin's homeostatic balance between old cells and new cells.

The second most abundant skin cells are melanocytes. Melanocytes are the source of melanin production. The amount of melanin accounts for skin pigmentation along with genetic, environmental, and dietary factors. It is also the lack of melanin that increases one's susceptibility to ultraviolet rays and is the source of a type of skin cancer. Merkel and Langerhans cells also exist in the skin but are few. They are important because they play roles in immune response, sensory perception, and perhaps even the biodiversity of microbes of the skin. [7]

Dermis

Beneath the epidermal layer lie the dermal papillae, the barrier separating the upper epidermis and the lower dermis. Once the wall of the epidermis is passed, the machine factory of the dermal accessory organs becomes visible. Here are the hair follicles, sweat glands, sebaceous glands, blood vessels, and receptor organs. Ducts traverse both epidermal and dermal layers providing exits for sweat, salt, and oil through tiny pores. This layer is thicker than the epidermal layer and is hub for many skin functions. These include production of sweat and the oily moisturizer called sebum secreted by the sebaceous gland. Feeding the needs of the machine are dermal blood vessels that capture carbon dioxide waste products and deliver oxygen necessary for cellular respiration, the energy source for aerobic cells.

Embedded in the dermis are hair follicles, which work with sebaceous glands to promote hair growth. Attached to each hair root is a collection of small muscle fibers known as the arrector pili muscle that reacts to changes in temperature, pressure, and even changes in emotion. The bottom layer, the hypodermis or subcutaneous layer is composed of primarily adipose tissue (fat tissue) and contains lymphatic and vascular tissue. [8]

The Human Skin – An Ideal Microbiome

Beyond the study of Anton van Leeuwenhoek, Antoni Redi, and Louis Pasteur in Biology, very little time during high school science classes is actually spent on microbiology and biodiversity. Though students are still taught the hierarchy of organisms, the debunking of spontaneous generation, and Darwin's theory of natural selection, they spend little time outside of Biology learning about the biodiversity of microbes, their potential for disease and decay, their beneficial roles in nitrogen fixation and photosynthesis, or their useful role in both the food and pharmaceutical industry. This unit attempts to fill some of the gaps that exist in high school microbiology education. Because the unit is intended for Physiology students who are primarily in their third or fourth year of science, students are expected to have some fundamental knowledge of bacterial and viral life cycles, which will not be a focus of this unit. Most studies of bacteria and viruses in relation to the human integumentary system focus attention on pathogenic microbes, when, in fact, benign viruses, fungi, arthropods, and bacteria all call the human skin "home". [9]

The skin contains many different types of "environmental niches" The various anatomical locations of the skin allow for a mini-planet of different ecosystems. Like earth, the skin has it desert regions which are dry and arid, its tropical regions which are moist and warm, its deciduous forest regions which are hotter at some times of the year and cooler at others, and the skin even has savannah regions which are vast areas of the skin that are subjected to wind and other elements. Depending on the location of the skin (scalp, armpit, head and neck), the surface may be cooler, warmer, drier, wetter, acidic, or basic creating environments in which a

variety of microbes may thrive. These different areas allow for development of 19 different phyla and more than 1000 bacterial species. [10] In addition, the different microenvironments allow for different strains of bacteria to develop and thrive. However, different microenvironments are not the only factors that contribute to microbial diversity. Other factors include a person's gender, age, and preferred diet, which factor into the types of microbes that appear in the skin. [11]

It is well known that the diversity of microbes has allowed for their presence in all areas of earth including the most environmentally extreme areas like salt flats, hot geysers, and frozen tundras. [12] Schommer and Gallo present the reason for microbe success on human hosts in their article, "Structure and function of the human skin microbiome." They claim that humans and microbes have co-evolved and are co-dependent upon each other. This evolution has allowed for microbes to adapt to new environmental conditions. The article, "Skin Microbiota: A source of disease or defense," further asserts that healthy skin is dependent on a balance between host cells and microbial presence. [13] If an imbalance occurs, it would cause the host to be ill or weakened reducing the microbes' own chances for survival. This is a striking argument, which one could conclude is in part the reason why humans can be found in just about every corner of the earth. Could microbes really be the reason why humans are such a successful species? Or are microbes driving and allowing humans to develop and adapt so that they can use humans as a vehicle to prevent themselves from dying?

Unfortunately, despite how perfect the skin might be for cultivation of microbes, imbalances of the skin-host equilibrium are major contributing factors to disease. The host factors that contribute to dysbiosis or imbalance of the host-microbe equilibrium include one's "age, sex, use of medication, lifestyle, and hygiene." [14] Factors like the pH, thickness of the skin, the rate of sebum, sweat, and hormone production add to reasons for dysbiosis. How often one cleanses their skin, the manner in which they do, and the cosmetic products they use or avoid also contribute to the potential imbalance. Schommer and Gallo also indicate that where we live on earth, how we live, the uses of modern conveniences, and our choices of birth delivery drive differences in our microbiome and of course health. [15]

The Skin's Defenses against Microbial Pathogens

Michael Wilson in *Microbial inhabitants of humans: ecology and role in health and disease* asserts that the skin's first line of defense against an environment teeming with microbes is actually airflow over the surface of the skin. This flow acts as barrier from airborne microbes which cannot settle so easily on the skin. It is similar to a piece of paper in a room with a rotating fan; as long as there is airflow and little resistance, the paper will float as it is blown by a fan until there is no airflow. Because the upper layers of the stratum corneum are covered with products of the sweat and sebaceous glands, tiny little cracks and gaps between the keratinized cells are filled to create a tough wall not easily breached by microbes. [16] Thus, epidermal layers of the skin are tough walls that act as a physical barrier to water loss, mechanical damage, and assault by UV rays. While the lower layers are acidic, making the environments much less hospitable to some microbes that are resistant to pH changes. All the while chemicals are released on the skin's surface that further inhibit the implantation or prevent the proliferation of some microbial organisms. [17] Wilson cites that chemicals such as free fatty acids, lauric, and myristic acids are "the most effective antimicrobials and have a wide spectrum of activity against members of the resident microbes." [18] Microbes such as *S. aureus*, *P. acnes,* and *S. pneumonia* can be inhibited by such chemicals contributing to the skin's defense mechanisms.

Furthermore, the production of sweat and deposit of sodium chloride on the epidermis also deters some

microbes. The increased osmolarity of the epidermis creates an inhospitable environment against gram negative bacteria like Acinetobacter species. In "Antimicrobial Defence Mechanisms of the Skin", Wilson includes evidence that sweat is a natural antibiotic by the presence of dermicidin which acts against strains of *Escherichia coli*, *Staphylococcus aureus*, and *Candida albicans* preventing their growth in sudoriferous glands. [19] The implication of this statement is an intriguing discussion for students. Would the public be open to sampling their armpits, for example, to find new strains of bacteria that might prove to be a better antibiotic than those that are synthetically developed?

Bacteria of the Skin

With a market flooded with antibacterial products, humans and bacteria seem to be a part of a never ending fight. It is well understood that antibacterial products often do more harm than good if a person has a basic understanding of Darwin's natural selection theory of survival of the fittest. So, what are bacteria and how do they influence skin health?

Bacteria are single celled organisms that lack a nucleus, differentiating them from eukaryotes. They also lack the organelles or compartmentalized inner structures of the eukaryotic cell but do contain genetic material in the form of a single loop of DNA (Deoxyribonucleic Acid). Some bacteria are specialized and contain one or more loops of DNA known as plasmids. In Physiology, students are taught the hierarchy of an organism's level of organization, beginning with atoms to whole organisms. Students therefore understand that human cells take on a variety of shapes and forms to create a tissue. This can be related to bacterial forms and shapes. Bacteria come in a variety of shapes from spherical (i.e. Staphylococci), rods (Lactobacillus), to corkscrew (spirochaetes). [20]

Bacteria make their homes on specific human tissues because of tissue tropism. Tissue tropism is the preference of bacteria for certain tissues due to the nutrients and growth factors that exist on the tissue. Another reason for a bacterium's specificity for a tissue is due to the interaction of the proteins on the bacterium's surface to the receptors on the host's cell membrane. The different adhesion molecules on the surface of a bacterium will prevent or allow a bacterium to attach to mucosal surfaces, such as the lungs, intestines, or the conjunctiva of the eye.

As previously mentioned, skin is an ideal location for microbes to thrive. Christensen and Brggemann state that the most abundant bacterial species found on the human skin include various species belonging to four genera. The most prevalent bacteria found on the skin are: Actinobacteria (51.8%), Firmicutes (24.4%), Proteobacteria (16.5%) and Bacteriodetes (6.3%). [21] This finding was possible because of the development of DNA sequencing techniques that could decipher genetic differences between bacteria, without having to grow them in the laboratory.

Host – Bacteria Interactions

It is well known that the human body is teeming with microbes and yet people are still surprised when they learn that the vast majority of bacteria that exist on our skin's surface is actually beneficial and function to prevent the proliferation of pathogenic bacteria. The normal or "indigenous micro-biota" are the results of thousands of years of mutations, evolution, infections, survival, and resistance to other microbes. The

remaining microbes are those best adapted to their current host. Humans and indigenous bacteria have, for the most part, a commensal relationship, where neither party is harmed or benefits from the presence of the other. Of the three types of interactions between hosts and microbes, the most infrequently found relationship is that of commensalism. In this unit both commensalistic and parasitic interactions will be discussed in a sample bacterium.

Staphylococcus epidermidis

One example of well-studied host-bacterium commensalism is the role of gram negative *Staphylococcus epidermidis* interacting with humans. *S. epidermidis* is a commonly found aerobic bacterium of human microbiota. Typically the bacteria are found in the head, neck, and armpit skin regions. There are several reasons for the bacterium's success on the skin. Michael Otto in *Nature Reviews Microbiology* describes *S. epidermis's* ability to exist on the surface of the skin because it can sustain extreme salt concentrations and osmotic pressure. This is due to the high number of Na+ exchanger channels on its cellular membrane. [22]

Additionally, *S. epidermidis* provides host defense mechanisms by a complementary system of barriers that prevent other organisms from proliferating in the tissues of its host. Cogen et al. summarize these complimentary systems by stating that *S. epidermidis* helps its host establish a physical barrier and a hostile surface pH. Furthermore, *S. epidermidis* actively synthesizes genes that produce host defense molecules like natural antibiotics against other microbes. [23] Their review specifically states *S. epidermidis* produces lantibiotics or bacteriocides which are toxic against other bacteria, thus reducing competitive bacteria from proliferating. Surprisingly, studies have shown that one lantibiotic produced by *S. epidermidis* inhibits methicllin-resistant *S. aureus*, showing a competitive superiority of one species over the other. Incredibly, the hosts' immune system actually allows for the bacterium to proliferate on the skin in order to prevent pathogens from dwelling and developing in the same cutaneous tissue where *S. epidermidis* lies. The immune system does this by increasing the proliferation of keratinocytes which increases the skin's ability to shed the top most layers and thereby trapping potentially pathogenic bacteria. [24] Schommer and Gallo also show that the immune system's T-cells are modulated by the bacteria to control inflammatory responses, supporting the idea that *S. epidermidis* and its human host interact with one another in a commensalist manner. [25] Finally, Wang, in his articles on the probiotic potential of *S. epidermis,* states that *S. epidermis* colonies prevent growth of *Propionibacterium acnes*, the microbe responsible for some acne problems. [26] Imagine, instead of using Clearasil or Neutrogena, teenagers may one day wipe *S. epidermis* colonies on their face each night before they sleep!

However, if *S. epidermidis* accidentally becomes pathogenic it is because the host is immune-comprised, or became compromised because they are drug abusers, were born as premature babies, or were implanted with a medical device like a catheter. In-dwelling implants increase the chance for *S. epidermidis* infections. While relatively innate on the human skin, in-dwelling medical devices must be carefully monitored because of the bacteria's potential for proliferation on the device's surface. [27] Typically, *S. epidermidis* creates a biofilm that shields the bacteria from the immune systems of its hosts. *S. epidermidis* fools its hosts using a variety of mechanisms including intercellular adhesion to proliferate, and production of immune evasion chemicals that hide its presence to the hosts' immune cells. If the host is unable to break through the biofilm that coats the growing infectious bacteria, the host may develop sepsis which is a severe inflammatory infection due to the spread of the bacteria into the bloodstream. Thus far, it is unclear how to distinguish between *S. epidermidis* strains that are a part of our normal biomes from those causing severe infections. However, Christensen and Brggemann state that *S. epidermidis* is less problematic than *S. aureus* in terms of the amount of toxins and

degradative enzymes produced by the bacterium. [28] Though *S. epidermidis* is generally harmless and infections are treatable, if the bacterium infects the lower layers of the skin then it can be difficult to treat with penicillin and methicillin. [29] This presents a concern because of the rise of methicillin-resistant bacteria, which prevent physicians from being able to treat these seemingly innocuous bacteria.

Propionibacterium acnes

The bane of adolescent and teenage life is the dreaded A word – Acne. Beyond the social stigma that develops and self confidence that reduces when a teenager develops signs of acne, acne is problematic because so many factors contribute to its development. *Propionibacterium acnes* is the bacterium that causes acne. Cogen et al. describes the bacterium as aero-tolerant gram positive anaerobe that thrives in the sebaceous glands of the skin. It is responsible for the irritation of the sebaceous duct, the clogging of its pore, and local folliculitis. If the bacteria were to spread to tissues beyond the dermal layer they may lead to systemic infections include endocarditis. [30]

An example of dysbiosis is the proliferation of *P. acnes* in the human hair follicle and pore, its mechanism of pathogenesis will be discussed though this disease is not completely understood. [31] Due to increased levels of androgen induced sebum levels, altered keratinization, inflammation, and changes to facial skin bacterial colonies, *P. acnes* tend to create the well known symptoms, of red, inflamed, raised, and irritated pilosebaceous (hair and oil) pores. Essentially, *P. acnes* is able to create clogged sebaceous pores by the production of free-fatty acids which irritate the hair follicles' wall, causing inflammation. 80% of adult skin infections are due to P. acnes proliferation. Current microbial studies into *P. acne* have shown that acne was not due to an increased proliferation of the bacteria but rather the development of different strains of the bacteria. [32] Another study points to acne development due to an increased stimulation of the production of bacteriocins, preventing the sebaceous duct from other harmful, more pathogenic bacteria since bacteriocins act like natural antibacterial chemicals. [33]

As commonplace as acne infections are to the general public, some people are never affected by acne. People living in Papua New Guinea and Paraguay do not show signs of acne. Schommer and Gallo present the reason for this as the diet consumed in those regions. Papua New Guineans and Paraguayans do not eat foods with high glycemic loads thereby reducing the androgen induced trigger for acne. Treatments for Acne Vulgaris include a host of commonly known antibiotic products, benzoyl peroxide, and sulfur based ointments. Most common treatments included antibiotics. Tetracycline, erythromycin, and clindamycin were readily prescribed but have contributed to *P. acnes* growing resistance against some antimicrobial treatments. [34]

Viruses of the Skin

Viruses are well known as obligate parasites and, similar to bacteria, receive much attention when a viral outbreak occurs. From SARS (Severe Acute Respiratory Syndrome), to HIV (Human Immunodeficiency Virus), to Smallpox, viruses are everywhere and are potentially nearly ancient as earth itself. Most viruses are smaller than bacteria, ranging between 20 nm to 300 nm. Mimiviruses are one exception who can be as large as 440nm. Viruses are considered obligate intracellular parasites because they rely so heavily on their host for reproduction of viral structures. Like other microbes such as bacteria, viruses seek the opportunity to

reproduce. Finding the right host and complementary cell is important in a virus's ability to deposit its genome, and have it successfully instruct the cell to make virus copies. It has been said that viruses are a bag of genetic material of either DNA or RNA with no concrete organelles unlike eukaryotes with their defined nucleus and mitochondria. Surrounding the virus's genetic material is its capsid made of proteins. Capsids mostly occur in two shapes: cylindrical or spherical, while many bacteriophages (viruses that infect bacteria) have a similar shape to the lunar lander. [35]

The life cycle of viruses involves the attachment of the virus to a host cell where it can penetrate the cellular membrane and inject its genes into the cell. Viral genes commandeer the host cell's transcription and translation process to make copies of its proteins necessary for building more viruses. Once the host cell pops open or lysis occurs, new viruses are expelled. The nature of a virus is to take control of its host's protein synthesis machinery in order to reproduce, thus when host cells rupture, viral clones can easily spread to neighboring cells causing eventual tissue damage in a multicellular host such as humans. If the virus is not cleared by its hosts' immune system, latent viral infections may occur. For example the herpes virus and the influenza virus are examples of latent viral infections since it has the ability re-emerge after lying dormant and asymptomatic in their host's tissues. Viruses can infect their hosts in different ways. Passage through the skin is only one mode of entry into the host. [36]

In "Human Skin Microbiota" authors Foulogne et al. assert that through the use of high throughout sequencing (HTS) scientists are now able to show the diversity of cutaneous resident or transient viruses. In fact with HTS, more and more scientists are able to produce DNA sequence data that previous attempts could not. The results of these experiments include the identification of new viral strains on the surface of the skin. One of these new strains is the Gyrovirus, which is found in 4% of people with healthy skin. With viral samples taken from healthy and unhealthy individuals Foulogne et al. were able to show the diversity of viruses on the human skin. One result showed the presence of bacteriophages (bacteria infecting viruses) which were present in direct correlation with the type of bacterial species present in the area tested for viral presence. Though very little is known about viruses that are beneficial to humans, research is available that shows that the human skin plays host to bacteriophages known to control Staphylococcus, Pseudomonas, and Propionibacterium species. [37] Exactly how the phages interact with the skin is unknown.

Host – Viral Interactions

Most of what is known of viruses on the human skin is greatly focused on pathogenic viruses. With the advent of technology that is able to collect, culture, and study these microbes, scientists were able to focus their study of viral pathogens simply because non-pathogenic viruses were not as important for study as those causing illness and death in humans. The interactions between human hosts and viruses can be classified into three categories. They are virus-specific, host-specific, and environment-specific. Like with some bacteria, human hosts and their viruses can maintain a homeostatic balance allowing both to exist without hurting each other; however, once there is an imbalance between the two, problems and disease may arise. [38]

Lecuit and Eloit question why some viruses make human skin their home. They suggest that viruses may reside on their host so that these become vehicles for future transmission. Their findings lead to further points of inquiry: Could viruses promote keratinocyte proliferation and shedding as a means to transmit their viral genomes? Could further investigations into host-virus relationships lead scientists to find uses for viruses in the production of antimicrobial, anti-inflammatory, and immunosuppressive therapy? [39]

Human Papillomaviruses

With high throughout sequencing (HTS) techniques, scientists have found strains of human papillomaviruses (HPV) in the epidermal layers of the skin as well as a Polyomaviridae virus, and Merkel's virus. [40] HTS studies of HPV have shown that there are several strains of HPV that typically reside in the skin and shed as part of the skin's normal processes. Areas of the human body where viruses tend to thrive include the hair follicles where Foulogne et al. have shown chronic asymptomatic shedding of HPV. Their presence and eventual shedding from keratinization show little to no tissue damage from the proliferation of HPV. [41]

Papillomaviruses are the culprits of skin diseases like warts. They appear as double-stranded DNA with a cubed capsid. 100 different strains of papillomaviruses are known and the warts that they cause on the epidermal and dermal layers of the skin are host specific. Specifically, the basal squamous epithelia of the epidermis are affected where the virus infects the host cell's cellular processes to increase the rate of cellular division. This increase of cellular division helps the production of viral DNA, viral assembly, and release. [42]

Human papillomaviruses are responsible for genital warts associated with the sexually transmitted disease known as HPV infection. Though HPV warts are an obvious skin abrasion, signs of the infection are not always visible. Furthermore, transmission of the virus can occur with contact of an infected skin through unprotected intercourse, oral sex, and bodily fluid exchange. [43] Because HPV infections are asymptomatic in many people, the virus can easily be transmitted and the newly infected have no idea that they have acquired the virus. Surprisingly, 20 million people in the U.S. have HPV [44] and the majority are in the age range of 15-49 years which tend to be the years that people are the most sexually active.

Variola Virus

A well studied example of virus that has nearly wiped out the native peoples of South America, Mexico, and West Indies is the Variola Virus, which caused smallpox disease. Historically smallpox disease is well documented in ancient Egyptians, ancient Chinese, and of course New World Native Americans, who all suffered from the disease. Because of vaccine-pioneer Edward Jenner's work in the late 1700s and subsequent scientists in the 20 th century, smallpox has all been eradicated with the creation of the smallpox vaccine. However, smallpox continues to be an important and pivotal example of the pathogenic potential of a microbe. [45]

Those affected by the Variola Virus show initial signs of infection with the presence of a fever, lethargy, muscular aches and pains, and the beginnings of a rash on the skin. This rash spreads throughout the body which develops into sores. Once the sores break open, the virus is in its most contagious peak. Over the period of four days the sores become dry and are known as pustules. The skin is raised and protruding. Once a scab develops, new epidermis is generated and will replace the dried pustules and scabs. During the period between the initial appearance of the rash to the scab formation, Variola virus is contagious. Desiccation and shedding of the scab represents the point at which the virus is no longer infectious. [46]

Student Goals and Activities

Physiology classes at Mt. Pleasant High School are structured around an organ system of focus. A typical unit includes a combination of lectures in a flip-classroom fashion, daily discussions, activities, labs, mini-project, and assessment. In this unit students will be asked to relate their understanding of the Human Integumentary System and Microbiology.

Beyond day to day activities, students will be assigned a microbe, which may be a part of the normal flora or may be pathogenic. As a homework assignment they will be asked to find two scientific articles on their assigned microbe. In their search, students will have to relate their assigned microbe to a skin disease and explain its symptoms, the virulence and pathogenesis within the two articles they will bring to class. Because our school does have wireless and many students bring their tablets, smart phones, and laptops to class they will be encouraged to utilize their technology as a means to complete this initial assignment.

Once students return with their articles, they will be asked to write no more than twenty-five words to describe their microbe as a means to get the "gist" of their microbe, its relation to skin, symptoms, and pathogenesis. Within the framework of a pair-share activity students will share their twenty-five word gist summary. After which, they will defend their chosen words to their partner. This type of activity will help students focus on the essential words that have "the most bang for their buck." Select students will then be allowed to share their list to the whole class and the whole class will decide on the top five which will be featured as a "Today's Microbe."During the second week of this unit students will be asked to do some research related to everyday microbes. In a similar fashion as the first week's focus, students will research microbes commonly found on classrooms, cell phones, bathrooms, and bedrooms. Surely, by the end of this exercise my students' skin will feel like it is crawling.

Embedded as a daily in-text reading activity, students will read several articles on their assigned microbe in order to practice their text interaction skills. Having taught the AVID (Advancement via Individual Determination) Program for many years, it is apparent that one reason why students do not comprehend the text they are reading is due to not having the skill to interact with it. Students in Physiology will practice this skill using the AVID Critical Reading Approach to Marking the Text on multiple pieces of text that they themselves will find. Students will be asked to read short 1-2 page science news articles related to a microbe that is beneficial or deleterious for human skin health. Utilizing the microbe articles, students will be asked to employ the strategy of "Writing in the Margins." [47] A sample activity that students will engage in will be to make comments in the margins of their notes and assigned readings. The six components are: Visualize, Summarize, Clarify, Connect, Respond, and Question. [48] The six marking the text components include several questioning prompts that ask students to communicate their different levels of understanding of the given text. Sample questions related to the assigned readings include:

1. What are the ideas that you can connect back to the anatomy and function of the skin?
2. Would it be plausible to create or modify the skin's barrier system in order to make it more efficient? And would this really be beneficial or would it be detrimental to the overall balance of the skin's microbiome?
3. What is the author's motive for this article? Should the reader be skeptical of their claims?

Another activity that would allow students to integrate elements of history and English is a "Microbe vs. Skin" battle scenario. Students will take part in strategizing how best to protect their skin against the attack of a

microbe. Students will have to use a set of vocabulary terminology that must be employed within their story. They will be prompted by the following statement: "Your team represents the integumentary system. A new microbe has come to your attention and you must find a way to mitigate the threat of infection. Propose a solution to your problem." Though students will be asked to solve the microbial infection problem, they will however be given limitations for their solutions, for example, one group of students may not be able to produce an inflammatory response, another may not be able to recognize the microbe as non-self, and a third may be immunosuppressed, lacking the ability to call upon the immune system to help with the potential attack. Similarly, student teams will be given a microbe with different capabilities. A virus might have the ability to specifically attack melanocytes; another may mimic the actions of healthy keratinocytes, or commandeer the mechanisms of dermal blood vessels to deliver nutrients to the tissue. Thus, students will need to creatively decide which integumentary organs will be necessary to prevent infection or allow for the development of new relationships between the host and the microbe, thus mimicking similar host-microbe interactions already in existence.

The challenge will be for students to purposefully communicate their defense structures and mechanisms in order to "purchase/develop new mechanisms" of defense from other groups who represent different skin locations. For example one team that represents the skin found on scalp may have a better ability to produce sweat and sebum, whereas a team from the palm of the hand may have a thicker epidermal layer making them stronger against everyday microbes found on surfaces like a table or cell phone.

As their teacher, I hope students will try creative solutions to meet the necessity of both the microbe and the skin needing to thrive. Creative students might make a pact to not destroy each other, or to make agreements with the host to house the microbe. Though it will cause some depletion of the host's resources, perhaps the host will benefit because the microbe it houses will allow the host to defend itself against a far more virulent attack. By inciting students' competitive nature, classroom engagement and motivation will increase, helping the students to understand their topic in depth, while employing critical thinking, inquiry, and design in the curriculum. Thus, the activity will require students to understand the background content related to skin physiology and anatomy, but also to have a basic understanding regarding the difference between a bacterial vs. a viral infection of the skin. It will also provide them a venue to be creative and to practice their critical thinking skills in order to win the battle between microbes and the skin. A second alternative to this activity is the Skin Care Brochure Project attached in Appendix B.

Finally, this unit is written to aide my students' understanding of the necessity for microbes. Rather than turning to the first bottle of antibacterial gel or hand lotion before each lunch hour, I hope my students make wise decisions that some bacteria are good and necessary for human skin health. Though my students immediately think of the HPV-2 infected Dede Kosawa (aka Treeman) when I say, "Name a skin disorder," by the culmination of this unit I hope my students grasp the idea that the human microbiome is a delicate balance of both good and bad microbes. That, in fact, the presence of microbes may benefit humans. Although they may never subject themselves to an ointment or salve teeming with bacteria as an effective moisturizer, perhaps they will be more accepting of the dirt they find in their nails the presence of dust on keypads, and the film of skin and oil on their cell phones as they proudly exclaim Kelly Clarkson's motto of, "What doesn't kill you makes you stronger!"

Notes

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6. Ibid, 51

7. Ibid, 52

8. Ibid, 53-54

9. Nina Schommer and R. L. Gallo "Structure and function of the human skin microbiome," 661

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11. Ibid, 661

12. G.D. Hannigan and E. A. Grice. "Microbial Ecology of the Skin in the Era of Metagenomics and Molecular Microbiology

13. A.L Cogen, V. Nizet, and R.L. Gallo "Skin Microbiota: A Source Of Disease Or Defence?" and Nina Schommer and R. L. Gallo "Structure and function of the human skin microbiome."

14. Schommer and R. L. Gallo "Structure and function of the human skin microbiome," 662

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16. M. Wilson, 55

17. G.J.M. Christensen, and H. Brüggemann. "Bacterial skin commensals and their role as host guardians," 201

18. M. Wilson ,56

19. Ibid, 57

20. Todar's Microbiology, 1

21. Schommer and R. L. Gallo "Structure and function of the human skin microbiome," 660

22. M. Otto, Staphylococcus epidermidis – the "accidental" Pathogen

23. A.L Cogen, V. Nizet, and R.L. Gallo "Skin Microbiota: A Source Of Disease Or Defence?", 5

24. Ibid, 6-7

25. Schommer and R. L. Gallo "Structure and function of the human skin microbiome," 662

26. Wang et. al, S. epidermidis in human skin

27. Ibid, 665 and M. Otto. "Staphylococcus epidermidis - the "accidental" pathogen

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29. M. Otto, Staphylococcus epidermidis – the "accidental" Pathogen

30. A.L Cogen, V. Nizet, and R.L. Gallo "Skin Microbiota: A Source Of Disease Or Defence?" 8

31. Schommer and R. L. Gallo "Structure and function of the human skin microbiome,"663

32. Ibid, 663

33. A.L Cogen, V. Nizet, and R.L. Gallo "Skin Microbiota: A Source Of Disease Or Defence?" 8

34. M. Wilson, 99

35. K. Ryan, G.C. Ray, J.C. Sherris, Sherris Microbiology, Chapter 6

36. Ibid, Chapter 7

37. Schommer and R. L. Gallo "Structure and function of the human skin microbiome,"664

38. N. Popgeorgiev, S. Temman, D. Raoult, and C. Desnues, "Describing the Silent Human Virome with an Emphasis on Giant Viruses," 2

39. M. Lecuit, and M. Eloit, "The human virome: new tools and concepts." 5

40. Ibid, 2

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Throughput Sequencing.

42. K. Ryan, G.C. Ray, J.C. Sherris, Sherris Microbiology, Chapter 19

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45. Zimmer, p. 81

46. CDC Smallpox overview

47. AVID Critical Reading, "Marking the Text"

48. Ibid

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Appendix A - Implementing District Standards (Common Core and Next Generation Science Standards)

Molecules to Organisms: Structures and Processes

Within the context of discussions related to the skin as microbiome, article readings, and the development of the students' approach to the Battle Scenario the following standards will be addressed.

Students who demonstrate understanding can:

- Develop and use a model to illustrate the hierarchical organization of interacting systems that provide specific functions within multicellular organisms.
- Plan and conduct an investigation to provide evidence that feedback mechanisms maintain homeostasis.

Biological Evolution: Unity and Diversity

As the pathology of microbes in disease and the development of host-microbe interactions are discussed the following standards will be covered.

- Construct an explanation based on evidence that the process of evolution primarily results from four factors: (1) the potential for a species to increase in number, (2) the heritable genetic variation of individuals in a species due to mutation and sexual reproduction, (3) competition for limited resources, and (4) the proliferation of those organisms that are better able to survive and reproduce in the environment.
- Construct an explanation based on evidence for how natural selection leads to adaptation of populations.
- Evaluate the evidence supporting claims that changes in environmental conditions may result in: (1) increases in the number of individuals of some species, (2) the emergence of new species over time, and (3) the extinction of other species.

Common Core Standards in English Language Arts and Reading: Information Text

The CCSS will be address and practiced in students' interaction with their assigned article readings and pair-share collaborations.

Key Ideas and Details:

- Cite strong and thorough textual evidence to support analysis of what the text says explicitly as well as inferences drawn from the text, including determining where the text leaves matters uncertain.
- Determine the central ideas or conclusions of a text; summarize complex concepts, processes, or information presented in a text by paraphrasing them in simpler but still accurate terms.
- Range of Reading and Level of Text Complexity:

- Students will be asked to utilize varying levels of nonfiction texts within the confines of their skin microbial disease and microbial uses.
- By the end of grade 11, read and comprehend literary nonfiction in the grades 11-CCR text complexity band proficiently, with scaffolding as needed at the high end of the range.
- By the end of grade 12, read and comprehend science/technical texts in the grades 11-CCR text complexity band independently and proficiently.

Appendix B - Skin Care Brochure Project

Student Background:

You have been hired by ILUVMINK Beauty Co. As the senior product researcher for your company it is your job to evaluate new and existing products. Your current project is to evaluate one existing or emerging beauty product, gather consumer reviews, discuss its effects on the integumentary system, and present your findings in the company brochure. Your supervisor is looking for solid research, evaluation, and in-depth knowledge of the integumentary system. As a bonus, your project manager has offered you a bonus on your next pay check if you are able to find a new "organic & natural" product. Your project manager (PM) has a background in microbiology and loves all things microbes. Impress your PM and you are sure to earn that bonus!

Your success with this project will be evaluated by the following criteria:

Informational Brochure with

1. Product Review (through a two-week personal review) – 10 pts
2. Consumer Reviews (online- research based) – 5 pts
3. Pictures/ Graphics/ Statistics -10 pts.
4. Discussion of the Integumentary System – 20 pts.
5. Creativity/ Neatness / Typed/ in color – 5 pts

Timeline

1 day – team brainstorm and distribution of responsibilities

3 days – research and summary of findings

2 days – graphic search and compilation of statistics and reviews

1 day – team midpoint check and discussion of research accuracy & team accountability

3 days – drafting, designing, and editing of brochure

1 day – presentation of findings (brochure assessment)