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Editorial

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This issue of JHS brings forth not just topics to ponder over, but essentials to read & understand……..

Mini Review Section – Lactobacilli are members of the lactic acid bacteria, a broadly defined group characterized by the formation of lactic acid as a sole or main end product of carbohydrate metabolism. Lactobacilli are important in the production of foods that require lactic acid fermentation, notably dairy products (yogurt and cheese), fermented vegetables (olives, pickles, and sauerkraut), fermented meats (salami), and sourdough bread. Lactobacilli clearly offer microbiologists exciting research prospects, both for biomedical applications and for acquiring fundamental knowledge of how bacterial cells function in the gut ecosystem.

Current Trends Section - The World Health Organization (WHO) has published "Guidelines on Hand Hygiene in Health Care" recommending2 hand rub formulations based on 80% vol/vol ethanol or 75% vol/vol isopropanol for local production in healthcare settings where commercial products are not available or are too expensive. In 2009, the World Health Organization (WHO) published "Guidelines on Hand Hygiene in Health Care," which recommended the use of alcohol-based hand rubs for both hygienic and preoperative hand treatment.

In Profile - Werner Arber is a Swiss microbiologist and a geneticist who was awarded the Nobel Prize in Physiology or Medicine for his work on the discovery of the process by which enzymes could be used to break down the DNA molecules into smaller fragments without losing their inherent characteristics and could then be studied easily. He shared the prize with two other American scientists named Daniel Nathans and Hamilton Othanel Smith who collaborated with him in the experiments.

Bug of the Month - *Shigella sonnei* was first successfully isolated from a 5 year old patient in Japan. It is a bacterium that is closely related to *E. coli*. *Shigella sonnei* is a non-motile, nonspore-forming, facultative anaerobic Gram-negative bacterium. Its natural habitat is in a low pH environment such as the human gastrointestinal tract. In both developed and developing countries, the enteric infectious disease shigellosis, caused by *Shigella sonnei* infection, has been the most common cause of endemic in those areas. *S. sonnei* continues to be a major food-borne threat to public health in many developed countries where the issues of sanitation are closely monitored.

Did You Know? - Genetically engineered (GE) crops were first introduced commercially in the 1990s. After two decades of production, some groups and individuals remain critical of the technology based on their concerns about possible adverse effects on human health, the environment, and ethical considerations. At the same time, others are concerned that the technology is not reaching its potential to improve human health and the environment because of stringent regulations and reduced public funding to develop products offering more benefits to society.

Best Practices - Candidiasis is a fungal infection due to any type of *Candida* (a type of yeast).[2] When it affects the mouth, it is commonly called **thrush.** Systemic fungal infections, including those by *C. Albicans*, have emerged as important causes of morbidity and mortality in immunocompromised patients. Invasive *Candidiasis* occurs when excess *Candida* enters the bloodstream and causes an infection. Invasive *Candidiasis* is most likely to happen in hospital patients or residents of nursing homes. If you are in an intensive care unit or are using a catheter, you are at risk of invasive *Candidiasis*. Having a weakened immune system, low neutrophil, or diabetes can also put you at risk.

Our JHS team is thankful to all our readers for their increasing appreciation that has served as a reward & motivation for us. Feedback & suggestions are always welcomed.

A Special Fondness for Lactobacilli

Lactobacilli are members of the lactic acid bacteria, a broadly defined group characterized by the formation of lactic acid as a sole or main end product of carbohydrate metabolism. The lactobacilli are gram-positive, non-spore-forming rods or coccobacilli with a G+C content usually below 50 mol%. Eighty species of lactobacilli are recognized at present. They are strictly fermentative, aerotolerant or anaerobic, aciduric or acidophilic, and have complex nutritional requirements (carbohydrates, amino acids, peptides, fatty acid esters, salts, nucleic acid derivatives, vitamins). Using glucose as a carbon source, lactobacilli may be either homofermentative (producing more than 85% of fermentative products as lactic acid) or heterofermentative (producing lactic acid, carbon dioxide, ethanol, and/or acetic acid in equimolar amounts). The nutritional requirements of lactobacilli are reflected in their habitats, which are rich in carbohydrate-containing substrates: they are found on plants or material of plant origin, in fermented or spoiled food, or in association with the bodies of animals.

Lactobacilli are important in the production of foods that require lactic acid fermentation, notably dairy products (yogurt and cheese), fermented vegetables (olives, pickles, and sauerkraut), fermented meats (salami), and sourdough bread. The use of lactobacilli in the food industry has a long history, and the functions of the bacteria in the industrial setting have been well studied. Lactobacilli that inhabit the bodies of animals, however, are much less known, despite an almost continuous interest by scientists spanning about 100 years.

Elie Metchnikoff (1845-1916), winner of a Nobel Prize for his pioneering descriptions of phagocytosis, was interested in the ageing process. While modern research on this topic concentrates on the maintenance of non-mutated DNA sequences, Metchnikoff focused on the gut microbiota as a source of intoxication from within. According to Metchnikoff, the bacterial community residing in the large bowel of humans was a source of substances toxic to the nervous and vascular systems of the host. These toxic substances, absorbed from the bowel and circulating in the bloodstream, contributed to the ageing process. Gut bacteria were thus identified as the causative agents of "autointoxication." The offending bacteria were capable of degrading proteins (putrefaction), releasing ammonia, amines, and indole, which, in appropriate concentrations, were toxic to human tissues. Low concentrations of toxic bacterial products could escape detoxification by the liver and enter the systemic circulation. His solution for the prevention of autointoxication was radical: surgical removal of the large bowel. A less frightening and more popular remedy, however, was to attempt to replace or diminish the number of putrefactive bacteria in the intestine by enriching the gut microbiota with bacterial populations that fermented carbohydrates and had little proteolytic activity. Oral administration of cultures of fermentative bacteria would, it was proposed, "implant" the "beneficial" bacteria in the intestinal tract. Lactic-acid-producing bacteria were favored as fermentative bacteria to use for this purpose, since it had been observed that the natural fermentation of milk by these microbes prevented the growth of non-acid-tolerant bacteria, including proteolytic species. If lactic fermentation prevented the putrefaction of milk, would it not have the same effect in the digestive tract if appropriate bacteria were used? Eastern Europeans, some of whom were apparently long-lived, consumed fermented dairy products as part of their daily diet. This was taken as proof of efficacy, and milk fermented with the "Bulgarian bacillus" of Metchnikoff subsequently enjoyed some vogue in Western Europe: the birth of probiotics. First coined in an entirely different context by Lilley and Stillwell to describe substances secreted by one type of microorganism that stimulated the growth of another (probiotic to contrast with antibiotic), the term "probiotic" was subsequently used to describe "organisms and substances which contribute to intestinal microbial balance". Fuller's definition, "a live microbial feed supplement which beneficially affects the host animal by improving its intestinal balance," has been widely used. "Living micro-organisms which upon ingestion in certain numbers exert health benefits beyond inherent general nutrition" has been suggested, as well as the formulation "Probiotics contain microbial cells which transit the gastrointestinal tract and which, in doing so, benefit the health of the consumer". So, too, have the following: "defined, live microorganisms administered in adequate amounts which confer a beneficial physiological effect on the host"; "live microorganisms which when administered in adequate amounts confer a health benefit on the host"; and "microbial cell preparations or components of microbial cells that have a beneficial effect on the health and well-being of the host".

Probiotic products, many of which contain lactobacilli, are actively promoted by the dairy, food, and "self-care health" industries and have been accepted uncritically by food scientists as well as the general public. However, claims of the efficacy of probiotics in relation to human health benefits do not result from rigorous, unbiased evaluations such as would be required by the U.S. Food and Drug Administration for pharmaceutical products. In other words, these claims have not been subjected to the usual four phases of assessment of efficacy.

Metchnikoff's view that consumption of bacterial cells in food would alter the proportions in which certain populations were present in the gut microbiota overlooked one of the most powerful forces in nature: homeostasis. Put in simple terms, homeostasis is the force in nature by which, although everything changes, everything stays the same. Homeostasis of bacterial communities is represented by a steady state that is generated by the organisms themselves. Competition for nutrients and space, the inhibition of one group by the metabolic products of another group, and predation and parasitism all contribute to the regulation of populations in particular proportions, one to the other. Because all of the ecological niches are filled in a regulated bacterial community, it is extremely difficult for allochthonous (formed in another place) microbes, accidentally or intentionally introduced into an ecosystem, to establish themselves. This phenomenon is referred to as "competitive exclusion". The newly introduced bacteria have no way of earning their living in the ecosystem, since all possible niches have been filled. The composition of the human gut microbiota, as shown by the examination of fecal samples, has a remarkable stability. The genetic fingerprint (denaturing gradient gel electrophoretic profiles) of this bacterial community remained constant in

samples collected during long-term studies, even of 18 months' duration. For many of the humans who have been studied, this stability extended beyond genera and species, even to the level of bacterial strains. Competitive exclusion is relevant to the introduction of probiotic bacteria into the gut. These bacterial cells are allochthonous to the bacterial community of the bowel, and as demonstrated in several studies, they have only a transient existence in the gut ecosystem. To take one study as an example, *Lactobacillus rhamnosus* DR20 was administered in milk to human subjects daily for 6 months. The probiotic strain was detected only while the probiotic product continued to be consumed. Once consumption of the probiotic product ceased, so too did excretion of the bacteria in the feces. Moreover, levels of the probiotic strain were relatively low (105 to 106 organisms per gram of feces), and it was detected only irregularly in samples collected from about 40% of the subjects who had preexisting, stable *Lactobacillus* populations resident in their guts. The remainder of the subjects did not have stable *Lactobacillus* populations, and the probiotic strain could be detected in all of their fecal samples during the period of probiotic consumption, because the probiotic cells were not outnumbered by those of resident lactobacilli.

Allochthonous lactobacilli are commonly introduced into the gut ecosystem because they are ubiquitous in nature. They are part of the microbiota of many foods, and these food-derived *Lactobacillus* species can be detected transiently and unpredictably in human feces. In contrast, as noted above, a proportion of human subjects harbor autochthonous (formed where found) lactobacilli. First postulated in relation to the gut ecosystem by Dubos and colleagues, the concept of autochthony was subsequently defined by Dwayne Savage: "Autochthonous microbes are characterized as indigenous microorganisms that colonize particular regions of the tract early in life, multiply to high population levels soon after colonization, and remain at those levels throughout the lives of healthy well-nourished animals. Autochthonous microorganisms should be found in essentially all individuals of a given animal species, irrespective of their geographical location".

As a result of further reflection on observations made in recent studies of *Lactobacillus* ecology, the following concise definition could be proposed: "An autochthonous species has a long-term association with a particular host species, forming a stable population of characteristic size in a particular region of the gut, and has a demonstrable ecological function." This definition could be considered as a working hypothesis and a basis for further discussion.

Autochthonous *Lactobacillus* species can be clearly identified in the case of broiler chickens raised under commercial conditions. Lactobacilli become established in the crops of the birds soon after hatching and persist throughout the life of the host despite the common administration of antimicrobial drugs in the poultry feed (long-term association with a particular host species). At least some *Lactobacillus* strains adhere to the crop epithelium and proliferate to form a biofilm. The metabolic activities of the lactobacilli that persist in this way influence the pH of the digesta, which, in turn, inhibits the proliferation of enterobacteria (demonstrable ecological function). Shed from this site, *Lactobacillus* cells provide an inoculum of the digesta, which is then rich in lactobacilli throughout the remainder of the gut (stable populations of characteristic size). A major proportion of the microbiota of the ileal contents, for example, is composed of lactobacilli). Moreover, species succession is detectable within the total *Lactobacillus* population of the chicken gut. While members of the *Lactobacillus acidophilus* group and *Lactobacillus reuteri* are early colonizers, *Lactobacillus salivarius* is consistently detected only in older birds. The mechanistic regulation of this succession would be fascinating to study, because it would appear that prior conditioning of the habitat by other lactobacilli, or by changes in chicken physiology or dietary composition, is required for *L. salivarius* to become established and persist in the avian gut. A similar *Lactobacillus* succession occurs in the crop and the ileum, suggesting that colonization of the crop determines the composition of the microbiota of the idealdigesta with respect to the *Lactobcaillu*s population.

L. reuteri is autochthonous to the rodent gut, as evidenced by the facts that it has been detected there in several studies; adheres to the nonsecretory epithelium of the forestomach, thus forming a biofilm; persists at constant population levels throughout life in the guts of formerly Lactobacillus-free mice inoculated by mouth with a pure culture on a single occasion; and influences small bowel biochemistry. *L. reuteri* and the gut ecosystem of mice therefore provide an excellent paradigm for study of the molecular basis of autochthony. In the past decade, promoter-trapping technologies have been developed to overcome the limitation of in vitro models for study of the traits that enhance ecological performance in complex ecosystems. For example, in vivo expression technology (IVET) was developed by Mahan and coworkers to study gene expression by *Salmonella enterica*serovar Typhimurium during infection of mice. IVET has also been used to identify in vivo-induced (ivi) genes for a number of other pathogens, and mutations within a subset of these ivi genes resulted in a decrease in virulence. IVET recently identified *L. reuteri* strain 100-23 genes that were specifically induced in the murine gut. A plasmid-based system was constructed containing 'ermGT (which confers lincomycin resistance) as the primary reporter gene for selection of promoters active in the guts of mice treated with lincomycin. A second reporter gene, 'bglM (encoding beta-glucanase), allowed differentiation between constitutive and in vivo-inducible promoters. Application of the IVET system using *L. reuteri* and formerly Lactobacillus-free mice revealed three genes induced specifically during colonization. Sequences showing homologies to xylose isomerase (xylA) and methionine sulfoxide reductase (msrB) were detected. The third locus showed homology to a protein of unknown function. Xylose is a plant-derived sugar commonly found in straw and bran and is introduced into the gut via food. Xylose in the gut could be derived from the hydrolysis of xylans and pectins by other members of the gut microbiota. The selective expression of xylose isomerase suggests that *L. reuteri* 100-23 meets its energy requirements in the gut at least partly by the fermentation of xylose or isoprimeverose (the main component of xyloglucans). Methionine sulfoxide reductase is a repair enzyme protecting bacteria against oxidative damage caused by reactive nitrogen and oxygen intermediates. Nitric oxide is produced by epithelial cells of the ileum and colon and possibly acts as an oxidative barrier, maintaining intestinal homeostasis, reducing bacterial translocation, and providing a means of defense against pathogens. This pioneering IVET study showed the utility of the technology in investigating the molecular basis of autochthony and identified bacterial properties that may be essential for *L. reuteri* persistence in the

gut. Indeed, there is now a strong case to be made for carrying out genomic comparisons between *L. reuteri* 100-23 and a strain of the same species that does not colonize the murine gut. Strain 100-23 clearly has properties that allow it to form a biofilm and to persist on the forestomach epithelia of mice. Moreover, this strain can be manipulated genetically and will express heterologous genes introduced in vitro (by electrotransformation) or by horizontal gene transfer into the gut ecosystem. Genomic comparisons of *L. reuteri* strains in relation to the ecological phenomena with which they are associated in the murine gut could reveal the molecular bases of autochthony.

It has been the hope of some microbiologists that lactobacilli could be genetically modified so that their cells would produce substances of biotechnological, and perhaps therapeutic, value. Rather than use these recombinant bacteria in industrial fermentors, the aim has been to use the bacterial cells in the gut as in situ factories that would deliver a bioactive substance to a particular region of the gut. This work has been impaired by the use of allochthonous species of lactobacilli, resulting in little progress in achieving the overall goal. The recognition of autochthonous species associated with different animal hosts makes it more likely that recombinant lactobacilli that will have at least some likelihood of metabolizing, and perhaps persisting, in the gut can be produced. The work of Lee and colleagues, in which recombinant vaginal lactobacilli that synthesized and secreted the first two domains of human CD4 were developed and shown in vitro to competitively block infection of target cells by the human immunodeficiency virus, provides a good example of a rational approach to this type of research. Although an autochthonous *Lactobacillus* species was used in these experiments, whether the recombinant bacteria have the ability to persist after instillation into vaginas remains speculative.

The interactions of lactobacilli with their hosts and their impact on host characteristics continue to fascinate microbiologists. Clues as to the influences of bacteria on the mammalian host have been obtained from comparisons of the biochemical and physiological characteristics of germfree and conventional mice, but comparative research of this type can now be performed at a sophisticated level because of the advent of genome sequencing of animals and the consequent manufacture of DNA microarrays that feature sequences representative of the entire genome of the animal. The potential for obtaining exciting knowledge of mechanistic influences of the microbiota on the host by this approach has been demonstrated by the pioneering work of Hooper and colleagues, who studied the impact of colonization of formerly germfree mice by Bacteroidesthetaiotaomicron. But monoassociation experiments with formerly germfree mice are not representative of what occurs in the natural ecosystem. A single bacterial strain colonizing the gut of a gnotobiote usually attains a much higher population level than it does in a conventional animal, where the microbe is faced with intense competition from the other members of the microbiota. Physiological differences between germfree and conventional animals can also influence colonization patterns. The wash-out effect of small bowel motility confines the bacteria to the more static terminal ileum or large bowel of conventional animals, but this restriction disappears in the monoassociated animal because of the slower peristalsis characteristic of the gnotobiotic host. Additionally, in the complex conventional ecosystem, the up-or down-regulation of host gene expression induced by the presence of one bacterial species could be negated by the impact of another species. Thus, a more ecological view would favor abandoning the additive approach (germfree animal plus bacterial species) and adopting a subtractive approach (conventional animal minus bacterial species). Mice that lack lactobacilli yet are colonized by a complex microbiota functionally equivalent to that of conventional mice have been produced and would appear to offer the ideal model in which to determine the impact of both allochthonous and autochthonous lactobacilli on the regulation of expression of host genes.

From a pragmatic point of view, the impact of *Lactobacillus* metabolism on the nutrition and physiology of farm animals is an important area of study. Although antimicrobial drugs have been added to the food of farm animals for several decades, the precise mechanism by which the growth rate of the animal is augmented and feed conversion is improved is unknown. Feighner and Dashkevicz reported that antimicrobial supplementation of the food of broiler chickens resulted in decreased bile salt hydrolase activity in the ilea of the birds. This may have been a particularly important observation because, at least among members of the gut microbiota of mice, lactobacilli are responsible for much of this enzyme activity. Bile salt hydrolases catalyze the cleavage of an amino acid from the steroid nucleus of conjugated bile salts. It is not clear why lactobacilli produce an enzyme with this property, because they would not gain energetically from the deconjugation process, but it may be an essential property enabling the bacteria to survive transit through the small bowel, into which relatively high concentrations of conjugated bile acids are released. The deconjugating activity of the lactobacilli could be important to the host, because deconjugated bile salts are less effective in emulsification of dietary lipids and micelle formation. Thus, the bile salt hydrolase activity of lactobacilli in the small bowel could impair lipid digestion and absorption by the host and could have implications in the poultry and pig industries, where rapid growth and efficient feed conversion are required for profitability. Much attention has recently been paid to the phylogeny of the gut microbiota, but little has been paid to the microbial physiology of complex bacterial communities or their individual components. It is time that this imbalance was rectified. Lactobacilli could provide model bacteria for such physiological studies because their relationship with the farm animal host (chickens, pigs) is much better defined than that of other members of the microbiota.

A large proportion of the immune cells of the body are associated with the gut. In the healthy host, the presence of the microbiota is tolerated by the immune system, although the mechanisms involved are not precisely known. Nevertheless, it can be inferred that tolerance toward the microbiota exists, because human patients with inflammatory bowel diseases and experimental animals with dysfunctional immune systems suffer from chronic, immune-mediated inflammation of the bowel mucosa. Much evidence points to the presence of the microbiota as the fuel for this smoldering inflammation. The autochthonous microbe-immune system relationship in healthy animals must therefore be one of tolerance and requires mechanistic investigation. The allochthonous microbe-immune system relationship is presumably quite different, at least initially, because the immune system will experience novel antigenic complexes with each encounter with a different bacterial strain. Continuous close encounters with the same strain, either serendipitous (food microbiota) or intentional (probiotic), could, one supposes, eventually engender tolerance. Lactobacilli have been shown to

invoke responses from immune cells, but much of the research reported has failed to establish a natural consequence for the host of such responses should they occur in vivo. Specifically, we do not have measurements of the impact of lactobacilli on the immune systems of healthy humans in the community with respect to resistance to disease, apart from preliminary studies on the prevalence of diarrhea in high-risk groups. While probiotics seem not to have a major effect in altering the composition of the gut microbiota, they may have a role in manipulating the immune system in relation to specific diseases that have an immunological etiology, such as inflammatory bowel diseases and allergies. It must be noted that the titillating reports that have appeared in this respect are reports of small studies emanating from single research groups. Where medical outcomes are involved, there is a need for large, comprehensive trials to prove efficacy in very well defined patient groups, in varied geographical locations with different ethnic mixes and cultural values.

Lactobacilli clearly offer microbiologists exciting research prospects, both for biomedical applications and for acquiring fundamental knowledge of how bacterial cells function in the gut ecosystem. As model gut bacteria, they may provide lessons in the molecular mechanisms that define autochthony as well as in understanding bacterial physiology in relation to host welfare. For these reasons, lactobacilli are set to remain the fond favorites of many microbiologists.

REFERENCES

1. Alander, M., R. Satokari, R. Korpela, M. Saxelin, T. Vilpponen-Salmela, T. Mattila-Sandholm, and A. von Wright. 1999. Persistence of colonization of human colonic mucosa by a probiotic strain, Lactobacillus rhamnosus GG, after oral consumption. Appl. Environ. Microbiol. 65:351-354. Abstract/FREE Full Text
2. Alexander, M. 1971.Microbial ecology.John Wiley and Sons, New York, N.Y.
3. Barrow, P. A., B. E. Brooker, R. Fuller, and M. J. Newport. 1980. The attachment of bacteria to the gastric epithelium of the pig and its importance in the microecology of the intestine. J. Appl. Bacteriol. 48:147-154. CrossRefMedline
4. Chaillou, S., B. C. Lokman, R. J. Leer, C. Posthuma, P. W. Postma, and P. H. Pouwels. 1998. Cloning, sequence analysis, and characterization of the genes involved in isoprimeverose metabolism in Lactobacillus pentosus. J. Bacteriol. 180:2312-2320. Abstract/FREE Full Text
5. Chang, T. L.-Y., C.-H. Chang, D. A. Simpson, Q. Xu, P. K. Martin, L. A. Lagenaur, G. K. Schoolnik, D. D. Ho, S. L. Hillier, M. Holodniy, J. A. Lewicki, and P. P. Lee. 2003. Inhibition of HIV infectivity by a natural human isolate of Lactobacillus jensenii engineered to express functional two-domain CD4. Proc. Natl. Acad. Sci. USA 100:11672-11677. Abstract/FREE Full Text
6. Christensen, H. R., C. Wang, G. Qian, and B. Zhu. 2003. Lactobacilli differentially modulate expression of cytokines and maturation surface markers in murine dendritic cells. J. Immunol. 168:171-178.
7. Dal Bello, F., J. Walter, W. P. Hammes, and C. Hertel. 2003. Increased complexity of the species composition of lactic acid bacteria in human feces revealed by alternative incubation condition. Microb. Ecol. 45:455-463. CrossRefMedline
8. De Boever, P., and W. Verstraete. 1999. Bile salt deconjugation by Lactobacillus plantarum 80 and its implication for bacterial toxicity. J. Appl. Microbiol. 87:345-352. CrossRefMedline
9. Dubos, R., R. W. Schaedler, R. Costello, and P. Hoet. 1965. Indigenous, normal, and autochthonous flora of the gastrointestinal tract. J. Exp. Med. 122:67-76. Abstract
10. Duchmann, R., I. Kaiser, E. Hermann, W. Mayet, K. Ewe, and K.-H. Meyer zumBuschenfelde. 1995. Tolerance exists towards resident intestinal flora but is broken in active inflammatory bowel disease (IBD). Clin. Exp. Immunol. 102:448-455. Medline.

Current trends in hand rub formulations

The World Health Organization (WHO) has published "Guidelines on Hand Hygiene in Health Care" recommending 2 hand rub formulations based on 80% vol/vol ethanol or 75% vol/vol isopropanol for local production in healthcare settings where commercial products are not available or are too expensive. Previous investigations have shown that neither formulation meets the ef?cacy requirements of European norm (EN) 12791, which is the most stringent available norm for surgical hand rub preparations. Even when modi?ed with approximately 5% higher alcohol content, the formulations proved to be inferior to the reference of the norm when measured after 3 hours.

Objective: Because the high glycerol content of the formulations was suspected to negatively in?uence their ef?cacy, additional investigations were performed with varying glycerol content.

Method: Modi?ed formulations with higher alcohol concentration (mass instead of volume percentage) and lower glycerol concentration (0.725% instead of 1.45%) or without the addition of glycerol were evaluated for their conformity with the ef?cacy requirements of EN12791, which demands noninferiority in comparison with a reference hand antisepsis procedure immediately and 3 hours after treatment on volunteers' hands.

Results: Reducing the concentration of glycerol or omitting it completely rendered both WHO formulations non inferior to the reference, both immediately and 3 hours after surgical hand antisepsis.

Conclusions: Both WHO-recommended formulations meet the ef?cacy requirements of EN 12791 by increasing their alcohol concentrations by 5%, prolonging their application to 5 minutes and reducing the glycerol concentration to 0.725%.

In 2009, the World Health Organization (WHO) published "Guidelines on Hand Hygiene in Health Care," which recommended the use of alcohol-based hand rubs for both hygienic and preoperative hand treatment. For local production in healthcare settings where commercial products are not available or too expensive, the guideline recommended 2 different hand rub formulations based on either ethanol 80% vol/vol (WHO I) or isopropanol 75% vol/vol(WHO II) as active agents. Additionally, low concentrations of hydrogen peroxide (0.125% vol/vol) are incorporated in the formulations to destroy potentially contaminating bacterial spores during storage. Furthermore, glycerol (1.45% vol/vol) is added as an emollient to improve dermal acceptability.

Previous investigations have shown that neither formulation meets the ef?cacy requirements of the European norm (EN) 12791, which is the most stringent in vivo laboratory assay for testing products with respect to their bactericidal ef?cacy in surgical hand treatment.

This norm requires that the reduction of skin bacteria from the hands of volunteers caused by the product shall not be inferior to that achieved with a standard reference procedure, rubbing n-propanol 60% (vol/vol) onto the hands of the same subjects for 3minutes. The 2009 WHO guideline itself reported that WHO I did not exceed the ef?cacy of the norm in 2 test laboratories and that WHO II did not exceed the ef?cacy of the norm in 1 of 2 test laboratories.

To improve the bactericidal ef?cacy of the formulations, we modi?ed both formulations by increasing their alcohol concentrations by approximately 5%, changing their volume percentage into weight percentage, and prolonging the duration of application from 3 to 5 minutes, which is the longest duration of application allowed by the norm. It is of note that a mass concentration of 80% ethanol equals a volume concentration of approximately 85% ethanol, whereas a mass concentration of 75% isopropanol is equivalent to a volume concentration of approximately 80% iso-propanol. These modi?cations were earlier shown to render the immediate effect of both formulations non inferior to the reference of EN 12791 on an ungloved hand tested immediately after antisepsis.

Because the high glycerol concentration (1.45% vol/vol) of the formulations was suspected to exert a negative in?uence on their 3-hour ef?cacy, we performed additional studies in which the glycerol was reduced by half or omitted entirely. 3-hour effects of both formulations lacking glycerol proved signi?cantly stronger than that of the reference.

Discussion

As shown previously by Kampf et al, both of the original WHO-recommended formulations containing EtOH or Iso do not meet the ef?cacy requirements of the forthcoming amendment of EN 12791 for surgical hand preparations. Even prolongation of the application to 5 minutes, which is the longest duration of application allowed by EN12791, did not result in a favorable outcome for these formulations.

From the results of several of our earlier studies, we know that the bactericidal ef?cacy of alcohol-based handrubs varies, not only with the type of alcohol and contact time, but also with the alcohol concentration.

Recently, we have shown that pure ethanol met the ef?cacy requirement of EN 12791 at a concentration of 85% (vol/ vol), whereas it failed to meet that requirement at 75% (vol/vol).

In another study by Kampf et al, a hand rub based on 80% wt/wt ethanol was also found to be as effective as the reference of EN 12791. As with ethanol, the isopropanol concentration (75%

vol/vol) seemed to be too low in the original WHO II–recommended formulation.

Rotter et al have shown that a 70% (vol/vol) isopropanol-based hand rubs was not as effective as the reference alcohol in the EN. In another study, pure n-propanol 60% (vol/vol) proved to be more ef?cacious than isopropanol 70% (vol/vol) when applied for a similar duration.

In a recent study, we found that increasing the volume percentage concentrations of both alcohols by approximately 5% (by changing to weight percentage concentrations), together with a prolonged application time of 5 minutes, rendered the immediate effect of the 2 modi?ed WHO formulations noninferior to the reference, thus conforming to the ef?cacy requirement of the norm.

Unfortunately, this was not the case with the 3-hour effect, which remained inferior to the reference. This surprising result raised the suspicion that glycerol may be the reason for this phenomenon, at least in the given concentration of 1.45%.

Glycerol is often added to hand hygiene preparations as a humectant or emollient to increase the acceptability, because frequent use of pure alcohol can cause dry skin. A positive effect of glycerol in alcohol-based hand rubs on skin condition and user acceptability has been shown by some authors.

Kampf et al found that the addition of a mixture of emollients containing 0.81% (wt/wt) glycerol to a propanol-based hand rub resulted in signi?cantly less dryness and erythema after frequent application. However, the in?uence of glycerol on the bactericidal efficacy of the alcohol- based hand rubs tested here has, to the best of our knowledge, not been investigated before. The original WHO-recommended formulations contain 1.45% vol/vol glycerol, which is a high concentration when compared with commercially available preparations. We suspected that this may have reduced the bactericidal ef?cacy that we and other authors have observed.

Indeed, as shown by the results of our study, reducing the glycerol concentration in the formulations or completely omitting glycerol increased the bactericidal efficacy, especially that of the isopropanol-based formulation, such that it conformed to the EN 12791 standard. The immediate effect of the isopropanol formulation without glycerol was even signi?cantly stronger than that of the reference, which suggests suf?cient ef?cacy when the application duration is shorter than 5 minutes. The 3-hour effect of both formulations with reduced glycerol content (0.725%), compared with the original WHO-recommended formulations, was successfully rendered noninferior to the reference; the ef?cacy of the glycerol-free preparations was even signi?cantly stronger than that of the reference. Thus, it appears that the glycerol concentration in formulations for hand hygiene are critical. If it is too low or absent, frequent use may lead to skin dryness, but if it is too high, hands may feel sticky, and, more importantly, the hand rub bactericidal performance may be unfavorably in?uenced. The cause for this latter phenomenon is still unknown.

In conclusion, as shown by recent investigations, the original WHO-recommended formulations do not comply with the ef?cacy requirements of EN 12791. It may seem debatable that, in this of?cial European norm, n-propanol, which is the most ef?cacious of the alcohols used in hand hygiene, is included as a reference, because it is only sparsely used in clinical practice worldwide, and there is no evidence that its ef?cacy as a reference ?nds a clinical correlate.

However, it is to be considered that it is used only as a laboratory standard and serves as the yardstick for high-level bactericidal ef?cacy of surgical hand preparations.
It is of note that an increase in the alcohol concentration has also been shown to be bene?cial for the modi?ed WHO formulations in their application as hygienic hand rubs, because their bactericidal ef?cacy has been proven to conform to another European standard for testing the bactericidal ef?cacy of hygienic hand rubs (EN1500) when applied even for only 30 seconds, rather than 60 seconds, which is the duration of application necessary to comply with the original WHO-recommended formulations.
This shortening of the necessary exposure time may help medical personnel to comply with hand hygiene. With regard to the limitations of our study, it should be indicated that our results have not yet been con?rmed by other laboratories and that inter laboratory variation is possible. Furthermore, the study was conducted only with the aim of harmonizing the bactericidal ef?cacy of WHO-recommended formulations with the requirements of EN 12791, although there is no evidence to date that better test performance is associated with better clinical outcome.

Nevertheless, we feel that changing the original ethanol- based formulation WHO I to 80% (wt/wt) ethanol, 0.125% (vol/vol) hydrogen peroxide, and 0.725% (vol/vol) glycerol should be considered. Likewise, we suggest that the original isopropanol-based WHO II formulation be recomposed to contain 75% (wt/wt) isopropanol, 0.125% (vol/vol) hydrogen peroxide, and 0.725% (vol/vol) glycerol.
Although both new formulations were successfully tested for 5-minute application, one may speculate from our results that they could meet the ef?cacy requirements of the norm even with a 3-minute duration of application, which is more convenient and, at present, the most common duration of application for preoperative hand rubs in Europe. Additional studies of the in?uence of glycerol on the ef?cacy of pure ethanol, isopropanol, and n-propanol are being conducted atthis time. It is of importance to note that information on the dermal tolerability and healthcare workers' acceptance of the modi?ed formulations proposed here is not yet available.

Adoption of the modi?ed formulations for regular use in healthcare settings should be based on ?eld testing, which is presently in progress in collaboration with the WHO.

Product Selection
The following information is the current evidence available to assist healthcare facilities in choosing an appropriate ABHR (Alcohol based handrub):

Type of Alcohol
Isopropanol and ethanol both have in-vitro activity against bacteria, fungi and viruses. When tested at the same concentration, isopropanol is more efficacious than ethanol, however ethanol has greater activity against viruses than isopropanol.

Alcohol-only ABHR versus alcohol-chlorhexidine ABHR
Although alcohols are rapidly germicidal when applied to the skin, they have no appreciable persistent or residual activity. The addition of a low concentration of chlorhexidine to an ABHR results in significantly greater residual activity than alcohol alone and therefore potentially improves efficacy. Notably, most published clinical studies that have demonstrated reductions in healthcare-associated infections (HCAIs) with the use of ABHR, have been associated with the use of ABHR that contains at least 70% v/v alcohol (isopropanol), 0.5% chlorhexidine and a skin emollient.

Alcohol Concentration
There is a clear positive association between the extent of bacterial reduction and the concentration of alcohol contained in ABHR products. Furthermore the concentration for maximum efficacy is different for isopropanol than ethanol – e.g. ABHR containing 60% v/v isopropanol is associated with similar cutaneous bactericidal activity as ABHR that contains 77% v/v ethanol. Overall, however, the ideal ABHR is one that has an alcohol content of ≥ 70% v/v.
When comparing alcohol concentrations it is important to look at the unit of measure, not just the numerical value of the concentration. Alcohol concentrations can be reported in a number of ways:

- Volume / Volume (V/V)
- Weight / Weight (w/w)
- Weight / Volume (w/V)

Conversion tables are available for comparison between V/V and w/w for ethanol only. A sample of ethanol labelled with a concentration of 70% V/V is equivalent to an ethanol sample labelled as 62.39% w/w.
Significant differences in the efficacy of ABHRs appear to be related primarily to a product's overall concentration of alcohol with higher concentrations being more efficacious.

Solutions versus Gels versus Foams
Laboratory studies have found that ABHR solutions are more effective than ABHR gels that contain an equivalent concentration of alcohol. Usually gels contain approximately 10% less effective alcohol than a similar solution. For example, an ABHR gel containing 60% alcohol has similar effective alcohol activity as a 50% ABHR solution. Technically it has proven difficult to develop ABHR gels that contain≥70% alcohol without the gel becoming less viscous and more solution-like. Thus the first generations of gel formulations have reduced antimicrobial efficacy compared with solutions.

There is some evidence to suggest gels are preferred to solutions, and have a trend towards improved compliance. Recent evidence suggests that the efficacy of alcohol based gels may depend mainly on concentration and type of alcohol in the formulation, rather than on product consistency.

Foams are new to the ABHR market and to date are used less frequently. There is currently minimal clinical evidence available for the use of alcohol based foams. Further clinical tests are encouraged.

ABHR Volume and Drying Time
The volume of hand rub dispensed is important. One ml of alcohol has been shown to be substantially less effective than 3 ml. The effective volume of ABHR (2-3 mL; 1-2 squirts from most ABHR dispensers) generally takes 15-20 seconds to dry on hands – hence ABHR drying time is a convenient indicator that sufficient ABHR has been applied. It is important to follow the recommendations of the manufacturer which are usually found on the ABHR bottle.

In clinical practice often smaller volumes are used than what is recommended in the testing of ABHRs. Unless high concentration products are used there is no significant reduction in contaminants with small volumes of ABHR.

It is essential that the team in charge of implementing the ABHR educate their staff about the correct use of the product. Specific education is required to ensure the correct dose is administered: it is important to use a two handed action to operate the dispenser, and to recognise that the number of squirts required for the ABHR to be effective may differ between products, or the size of the HCW's hands. ABHR should never be applied to gloves.

If hands are wet when ABHR is applied
The antimicrobial efficacy of alcohols is very sensitive to dilution with water and is therefore vulnerable to inactivation, especially if only small volumes of ABHR are applied. For instance, if 60% isopropanol were rubbed onto wet hands in two portions of 3 mL (each for 1 minute), the mean log bacterial reduction achieved is 3.7, as compared to 4.3 with dry hands. Thus, it is recommended that ABHR be applied to dry hands.

Triclosan
Triclosan (chemical name 2,4,4'–trichloro-2'-hydroxydiphenyl ether) is known commercially as Irgasan DP-300. It is a nonionic, colourless substance developed in the 1960s; it is poorly soluble in water, but dissolves well in alcohols.

Concentrations ranging from 0.2% to 2% have antimicrobial activity. Triclosan has been incorporated in detergents (0.4% to 1%) and in alcohols (0.2% to 0.5%) used for hygienic and surgical hand antisepsis or preoperative skin disinfection; it is also used for antiseptic body baths to control MRSA. This agent is incorporated into some soaps (at a 1% w/v concentration) and a variety of other consumer products (deodorants, shampoos, lotions, etc.), as well as being integrated also into various dressings and bandages for release over time onto the skin.

Triclosan enters bacterial cells and affects the cytoplasmic membrane and synthesis of RNA, fatty acids, and proteins. Recent studies suggest that this agent's antibacterial activity is attributable in large part to binding to the active site of enoylacyl carrier protein reductase.
Triclosan has a fairly broad range of antimicrobial activity but tends to be bacteriostatic.

Minimum inhibitory concentrations (MICs) range from 0.1 to 10 µg/ml, while minimum bactericidal concentrations are 25–500µg/ml. Triclosan's activity against Gram-positive organisms (including MRSA) is greater than against Gram-negative bacilli, particularly P. aeruginosa.
The agent possesses reasonable activity against mycobacteria and Candida spp., but has little activity against filamentous fungi and most viruses of nosocomial significance. Triclosan (0.1%) reduces bacterial counts on hands after a 1-minute hygienic handwash.
In a number of studies, log reductions achieved have been lower than with chlorhexidine, iodophors or alcohol-based products.

Similar to chlorhexidine, triclosan has persistent activity on the skin. Its activity in hand-care products is affected by pH, the presence of surfactants or humectants, and the ionic nature of the particular formulation.
Triclosan's activity is not substantially affected by organic matter, but may be inhibited by sequestration of the agent in micelle structures formed by surfactants present in some formulations. Most formulations containing less than 2% triclosan are well tolerated and seldom cause allergic reactions. A few reports suggest that providing HCWs with a triclosan-containing preparation for hand antisepsis has led to decreased infections caused by MRSA.

Increased tolerance (i.e increased MICs) to triclosan due to mutations in efflux pumps has been reported in E.coli and P. aerugninosa.
Laboratory studies involving exposure of some microorganisms to sub inhibitory concentrations of triclosan have resulted in increased triclosan MICs. However, the clinical relevance of increased triclosan MICs generated in the laboratory is unclear, since affected strains remain susceptible to in-use concentrations of triclosan.
Further research dealing with the relationship between triclosan use and antimicrobial resistance mechanisms is warranted, and surveillance for triclosan-resistant pathogens in clinical and environmental settings is needed.

References:

https://www.researchgate.net/publication/236316784_Modified_WHO_handrub_formulations_comply_with_European_efficacy_requirements_for_pre-operative_surgical_hand_preparations
http://apps.who.int/iris/bitstream/10665/44102/1/9789241597906_eng.pdf
http://www.ncbi.nlm.nih.gov/books/NBK144054/
http://www.hha.org.au/About/ABHRS/product-selection/product-selection.aspx

Werner Arber

FAMOUS AS: Microbiologist & Geneticist
BORN ON: 03 June 1929 AD
AGE: 86 Years
BORN IN: Gränichen, Aarau, Aargau, Switzerland
SPOUSE: Antonia
CHILDREN: Silvia, Caroline
AWARDS: 1978 Nobel Prize in Physiology or Medicine

Werner Arber is a Swiss microbiologist and a geneticist who was awarded the Nobel Prize in Physiology or Medicine for his work on the discovery of the process by which enzymes could be used to break down the DNA molecules into smaller fragments without losing their inherent characteristics and could then be studied easily. He shared the prize with two other American scientists named Daniel Nathans and Hamilton Othanel Smith who collaborated with him in the experiments. His main research involved enzymes present in bacteria that have been infected by a virus and how the enzymes change the DNA of the virus to protect the bacteria. He had initially started out as an assistant in a biophysics laboratory who was required to maintain electron microscopes in proper working condition. During his job he was also required to prepare biological samples to be viewed under the microscope by other researchers. While doing this job he grew familiar with the fundamental aspects of genetics and 'bacteriophage physiology' and became interested in a totally new field of research on 'bacteriophage'. The opportunity made Arber give up his job involving electron microscopy and change over to research in genetics which became a passion with him over the years.

Childhood & Early Life

Werner Arber was born on June 3, 1929 in Granichen, in the Canton of Aargau in Switzerland. He studied at the public schools in Granichen until he was 16. He next joined the gymnasium at the 'Kantonsschule Aarau' from where he received a B-type maturity in 1949. He then enrolled at the 'Swiss Federal Institute of Technology' located in Zurich under the 'University of Geneva' and studied physics and chemistry for his diploma in 'Natural Sciences' from 1949 to 1953. During the last part of his studies he first became interested in fundamental research while trying to isolate an isomer and study its characteristics.

In November 1953 he took up the job of an assistant for electron microscopy at the 'Biophysics Laboratory' at the 'University of Geneva'. He helped to keep the two electron microscopes in good working condition and spent a lot of time helping in the preparation of biological specimens to be viewed with the microscopes. While doing this he became familiar with the basic issues related to genetics and the physiology of 'bacteriophages'.

He was also inspired by the lectures given by Jean Weigle who had been a professor of experimental physics at the 'University of Geneva'. Weigle had become a biologist doing research on 'bacteriophage lamda' while studying at the 'Department of Biology' under the 'California Institute of Technology, Pasadena'.

He received his PhD from the 'University of Geneva' in 1958 in which his thesis was on the characteristics of 'bacteriophage'.

Career

Werner Arber and some more scientists had already started work on the findings of another Nobel laureate named Salvador Luria during the late 1950s and early 1960s. Luria had found that the viruses that infect bacteria known as 'bacteriophages' are themselves affected by hereditary mutations while inducing hereditary mutations in their hosts. His work was centered mainly on the protective nature of some of the enzymes in the bacteria that prevent the growth of the 'bacteriophages'.

He received an offer from the 'University of Southern California' in Los Angeles in the summer of 1958 after completing his PhD to work with Joe Bertani who had collaborated earlier with Jean Weigle in the research on 'bacteriophages'. Arber started to work with Joe Bertani on a 'bacteriophage' of the E. Coli virus which Bertani had isolated a few years earlier. He received many offers from various laboratories for post-doctoral work as his doctoral thesis was highly appreciated by the genetics fraternity. He was also invited by Eduard Kellenberger to return to Geneva for research on the effect of radiation on micro-organisms.

Before returning to Geneva at the beginning of 1960, he spent a few weeks working at the 'Gunther Stent' laboratory in Berkeley, the 'Joshua Lederberg' laboratory in Stanford and the 'Salvador Luria' laboratory at the 'Massachusetts Institute of Technology' in Cambridge. After returning to Geneva he started working on the bacteriophage of E.Coli. Within a year of research he was able to establish the fact that DNA of both the 'bacteriophage' and the cell had been affected by modification and strain-specific restrictions.

In 1961 Arber and another geneticist, Daisy Dussoix, reported this phenomenon to the scientific community for the first time during the 'First International Biophysics Congress' which was held in Stockholm.

In 1962 Arber presented the findings more elaborately to the 'Science Faculty' at the 'University of Geneva' for which he was awarded by the university.

In 1963 he spent one year at the 'Department of Molecular Biology' under the 'University of California, Berkeley' as a visiting 'Miller Research Professor'.

In 1965 he was promoted to the post of 'Extraordinary Professor for Molecular Genetics' by the 'University of Geneva'.

From 1965 to 1970 he was able to procure financial help from the 'Swiss National Science Foundation' to carry out fundamental research. This was when direct financial help was not available from the Swiss federal government.

In 1968 he received an offer of professorship at the 'University of Basel'. He joined the 'University of Basel' in 1971 and worked there as a professor of microbiology up to 1996. He became one of the first few people who started work at the 'Biozentrum' which had been recently constructed to house the different departments of microbiology, biophysics, biochemistry, cell biology, pharmacology and structural biology.

In 1981 he became a member of the 'World Knowledge Dialogue Scientific Board' and also a member of the 'Pontifical Academy of Sciences'.

In January 2011 he was made the president of the 'Pontifical Academy of Sciences' by Pope Benedict XVI. This made him the first Protestant to hold the post of president in an otherwise Catholic institution. For the last several years he has been involved in the study of 'transposons' and 'insertion elements' and their activities in providing the driving force required for the evolution of micro-organisms.

Awards & Achievements

Werner Arber received the 'Plantamour-Prevost' prize from the 'University of Geneva' in 1962. Werner Arber was awarded the Nobel Prize in Physiology or Medicine in 1978.

Personal Life & Legacy

Werner Arber married Antonia in 1966. They have two daughters, Silvia and Caroline, who were born in 1968 and 1974 respectively.

Trivia

When Werner Arber's daughter Silvia heard of his discovery after he got the Nobel Prize she made a story out of the discovery which received wide publicity. In the story the DNA has been named as the King ruling over a kingdom of subjects who are the bacteria. The enzymes are servants who use scissors to cut a foreign king entering the kingdom into pieces to learn his secrets without harming their own king.

JOKES

An Angry Wife To Her Husband 0n Phone:
"Where d Hell Are You ...?"
Husband: Darling You Remember That Jewellery Shop Where You Saw The Diamond Necklace n Totally Fell In Love With It n I Didn't Have Money That Time n I said "Baby It'll Be Yours 1 Day ... "O:)
Wife, With A Smile & Blushing: Yeah I Remember That My Love!
Husband: I'm in the Pub Just Next To That Shop

A man came home late at night after a party.
His wife yelled: "how would you feel if you don't see me for two days?"
The man couldn't believe his luck: 'that would be great'!
Monday passed and he didn't see her.....
Tuesday and Wednesday passed too.....
On Thursday his swelling became better
And now he could see her from the corner of one eye.

A: I have the perfect son.
B: Does he smoke?
A: No, he doesn't.
B: Does he drink whiskey?
A: No, he doesn't.
B: Does he ever come home late?
A: No, he doesn't.
B: I guess you really do have the perfect son. How old is he?
A: He will be six months old next Wednesday.

Sardar joined new job. 1st day he worked till late evening on the computer. Boss was happy and asked what you did till evening.
Sardar: Keyboard alphabets were not in order, so I made it alright.

Tourist: Whose skeleton is that?
Sardar: An old king's skeleton.
Tourist: Who's that smaller skeleton next to it?
Sardar: That was same king's skeleton when he was a child.

Son:- Mom when I was on the bus with dad this morning he told me to give up my seat to a lady.
Mom:- Well, you have done the right thing.
Son:- But mom, I was sitting on daddy's lap

Cricket Fever
Husband was busy watching Ind vs Pak match..
Wife Came in a New Dress & Asked Him: Main Kaisi Lag Rahi Hu ??
Husband Jumped, Clapped n Shouted
.
.
.
'CHHAKKA'
.
.
His visiting hrs in the hospital are between 4 to 7!!

Sardar was busy removing a wheel from his auto.
A man asks sardar why are you removing a wheel from your auto.
Sardar : Cant you read the board.
Parking is only for 2 wheeler

Hey U Know Which is the best day to propose a girl..
April 1
U Know Why??
If she accept its your luck otherwise just tell April Fool.

A person who surrenders when he's WRONG, is HONEST.
A person who SURRENDERS when not SURE, is WISE.
A person who surrenders even if he's RIGHT, is a HUSBAND.!

Rich Man: Today, I have 14 Cars, 18 Bikes, 4 Bungalows, 3 Farm Houses
What do you have?
Poor Man: I have a boy
whose Girl Friend is
.
.
Your Daughter..!

Shigella Sonnei

Classification

Kingdom: Bacteria
Phylum: Proteobacteria
Class: Gammaproteobacteria
Order: Enterobacteriales
Family: Enterobacteriaceae
Genus: *Shigella*
Species: ***S. sonnei***

Description and significance

Shigella sonnei is a non-motile, nonspore-forming, facultative anaerobic Gram-negative bacterium. Its non-motile characteristic means that this species doesn't have flagella to facilitate its movement like many other human enterobacteria. *Shigella sonnei* is a rod-shape bacterium and is lactose-fermenting bacterium causing dysentery. *Shigella sonnei* is extremely fragile in experimental settings. Its natural habitat is in a low pH environment such as the human gastrointestinal tract. Its optimal environmental temperature is 37 degrees Celsius, similar to the temperature in the human body. Therefore, human's gastrointestinal tract appears to be the only found natural host of *Shigella sonnei* that we know so far.

Shigella sonnei was first successfully isolated from a 5 year old patient in Japan. It is a bacterium that is closely related to *E. coli*. It was known from the beginning that *Shigella sonnei* is related to *E. coli*, however, Shigella has evolved from many different strains of *E. coli*. Since the evolutionary route away from the similarities of the *E. coli* genome, Shigella has been classified as another species. Due Shigella's highly evolved genome, it has become a highly specific human pathogen due to its extensive evolutionary progress involving its continual gain and loss of function comparative to *E. coli*.

In both developed and developing countries, the enteric infectious disease shigellosis, caused by *Shigella sonnei* infection, has been the most common cause of endemic in those areas. *S. sonnei* continues to be a major food-borne threat to public health in many developed countries where the issues of sanitation are closely monitored. This enterobacterium is generally transmitted by uncooked food or contaminated water. In the U.S., 70% cases of Shigellosis are caused by *Shigella sonnei* .

Genome structure

Shigella sonnei has a circular DNA genome. It uses both chromosomal and plasmid coded gene for its virulence. This species has been subjected to complete genome sequencing. It has a ~4Mb size genome. *Shigella sonnei*'s chromosome has the same replication origin and terminus as those of *E. coli*; this not only means that they are evolutionarily related but suggest that they most likely use the same cellular mechanism to replicate. There are very few biochemical properties that can distinguish *Shigella sonnei* from *E. coli*. In all Shigella genomes, the rRNA operons, a sequence that is highly conserved among the prokaryotes, map to approximately the same relative positions as in *E. coli* indicating that *Shigella sonnei* and *E. coli* did not go through DNA recombination between the rRNA operons.

The most fascinating feature about the strains of *Shigella sonnei* and all the other species of Shigella is that their genomes are highly dynamic. They exhaust the use of insertion sequence element (IS-element) in characterizing their genome dynamic in terms of causing constant DNA rearrangement such as deletions, translocation, and inversions. It is through the use of IS-elements that *E. coil* differs from other Shigella species. It is evident that Shigella chromosome has inversions sites at its origin of replication sites and termini that can be possible recombination "hotspots" for the insertion of other bacteria's mobile genome elements. It is also through the use of IS-element that *Shigella sonnei* and other Shigella species can be characterized as highly virulent. Like all the other Shigella species, *Shigella sonnei* has plasmids that increase in the toxicity of the microbe to their host or other organisms around them. They produce a toxin called the "Shiga toxin". It is a unique kind of toxin that works its toxicity in the body in multiple ways that will bring potential harm to the neurons, cytoplasm of the cells and enteric epithelial cells.

Cell structure and metabolism

Shigella sonnei is a rod-shape, Gram-negative bacterium. Its outer membrane is filled with lipopolyscharride (LPS), a common characteristic of Gram-negative bacteria. The O-antigen component of LPS in *Shigella sonnei* is characterized differently among the other species of Shigella. Moreover, LPS of this bacterium play an important role in the bacterial virulence.

So far we only know that *Shigella sonnei* can survive in the human body, therefore, its mechanism of infection defines *S. sonnei*'s ability to live. *S. sonnei*, like most Shigella species, spends most of the time intracellularly during infection and is very mobile within the cells by polymerizing actin.

Unlike many other pathogenic bacteria, *S. sonnei* does not use flagella for its chemotoxicity and tissue invasion. Without flagella, *S. sonnei* can often escape the human immune system of the TLR-5 (toll-like receptor) that usually mediate the innate and adaptive immunity by detecting the conserved domain on many bacteria that use flagellin for motility. Although *S. sonnei* cannot be considered as a motile bacterium as it lacks flagellin for movement, nevertheless, it facilitates movement by using an atypical mechanism of motility, by polymerizing actin. Such a mechanism is not recognizable to the human immune system and also is a type of motile mechanism that saves energy.

Metabolism:

Lactose fermentation is a biochemical property commonly used for to distinguish Shigella from the closely related bacterium *E. coli*. However, *S. sonnei* isolates ferment lactose at a lot slower process than other species of Shigella. The unique biochemical property of *S. sonnei* can be explained genetically. In genome Sd197 and Ss046 the key gene lacZ, encoding beta-D-galactosidase, is attached to lacY gene encoding for galactose transport function. Many of the genes in *S. sonnei* are categorized as pseudogenes. Pseudogenes are genetic sequences sporadically located in the *S. sonnei* genome. They are subject to decay at any given time. The nature and purpose of pseudogene still remains elusive. The result of this sporadic lost of galactoside transport functional gene in *S. sonnei* explains the slow lactose fermentation process due to the fact that pseudogene is subject to constant decay from its original site of the initial encoded region.

Much of the *S. sonnei*'s metabolic mechanism remains elusive

because it is considered to be a more evolved species than other Shigella serogroups. *S. sonnei* is known to be less virulent than other Shigella species because it doesn't kill its host immediately. Perhaps this also explains why *S. sonnei* is now the most common Shigellosis causing species that pervades most the developed countries.

Ecology

The primary host and natural reservoir known at this point for *Shigella sonnei* and among all other species of Shigella is the human gastrointestinal tract. Shigella can survive in fecal contaminated material but has a low survival rate without the optimal acidic environment in the intestinal tract as its surrounding. The bacterium is known to be able to survive in soiled linen for up to seven weeks. In fresh water environments, it can live up to 5 days and in salt water for 12-30 hours. It has been recorded that *Shigella sonnei* can not survive on the smooth surfaces of tomatoes.

No known cases of another natural reservoir have been proven to be the natural host *Shigella sonnei* other than human's intestinal tract. Some investigations have researched the possibility of free-living amoebae engulfing Shigella bacteria as a mode of harvesting *Shigella sonnei* in an environment outside of the human host. Amoebas are unicellular microscopic life forms that have the ability to live in the environment without a host. They can change shapes and engulf other cells. Much is not yet known about of the origin and the formation of these phenomenal cells. It has been shown experimentally that free-living amoebae Acanthamoeba species have the ability to uptake virulent and non-virulent *S. sonnei*. These amoebas can promote growth of many different pathogenic bacteria inside their cysts in experimental settings, which gives the pathogenic bacterium like *Shigella sonnei* a microhabitat that protects them from the outside environment. However, natural finding of fee-living amoebae harvesting*Shigella sonnei* has not been found; therefore, the possible host for *Shigella sonnei* other than the human GI tract still remains an elusive factor.

Pathology

Shigella sonnei cause an enterobacterium disease called Shigellosis. *Shigella sonnei* is the Shigella species has been responsible for most of the large shigellosis endemic in industrialized countries. *Shigella sonnei* is spread mostly by means of fecal-oral transmission. Other possible modes of transmission can be from ingestion of contaminated food or water, and subcutaneous contact with inanimate objects and, most rarely, sexual contact. Food prepared by the contaminated person may easily become contaminated with Shigella bacteria.

Shigella sonnei infection is characterized by invasion of the intestinal mucosa. *S. sonnei* bacterium utilizes the common enteric Gram-negative pathogen's Type III secretion systems to inject designated Invasion Plasmid Antigen (Ipa) protein into the invaded cell. Ipa BC protein complex can cause the lysis of epithelial cell vacuoles and increase the uptake of *Shigella sonnei* by M cells and other epithelial cells. The infection stays locally at the colon and rectal mucosa site where the bacteria cause major inflammatory destruction of the mucosal wall. *Shigella sonnei*'s infectivity dose is very low; as few as 100-200 bacteria are needed to cause a clinical infection, shigellosis.

Shigella pathogenic mechanism is very complex due to its different mechanisms that cause destruction to the intestinal wall. *Shigella sonnei*, like all the other Shigella species, excrete shiga toxin that causes inflammatory response to the enteric cell wall and necrotic cell death of the colonic epithelium. The necrotic cell death is an extremely messy death for the cell due to the massive spill-out of all the intracellular content upon its death; as the result, it attracts the body's cytokine-mediated immune response to clean up the mess; however, the cleaning up process of cell debris also causes a large local enteric inflammatory response that contributes to the shigellosis disease progression.

Once *Shigella sonnei* enter into the colonic cell wall they can also invade other cells in the intestinal tract. After they enter into the intestinal tract, Shigella bacteria lyse the phagocytic vacuole and enter the epithelial cell's cytoplasm where they multiply and move to invade other cells. Shigella is known for its promiscuity in terms of their ability to infect different cell types, such as enterocytes and M cells, and the intestinal epithelial cells. Shigella bacteria multiply within colonic epithelial cells, causing mucosal ulceration, inflammation and bleeding.

Shigella sonnei's virulence can be largely understood in its genome versatility. *Shigella sonnei* unlike the species of most enteric pathogens, has no known natural reservoir other than human, therefore, this enterobacteria is highly expected to undergo gene transfer and selective pressures in the human intestinal tract. It has been found through genome sequence analysis that *S. sonnei* contains site of several different mobile genetic elements including plasmids, transposons, and integron involving gene cassettes that are all important factors in *S. sonnei* incorporation of antibiotic resistance abilities and increase its virulence. It has been found that *S. sonnei* bacteria can use contact-dependent conjugative plasmid transfer in obtaining antibiotic resistance factor from other bacteria.

Shigella sonnei has a circular chromosomal DNA and a large plasmid that contribute largely to its virulent factors. Class 1 and 2 integrons have been detected in *S. sonnei* encoding recombinase to induce the site of incorporation for the gene cassettes that can contribute to the virulence of the bacterium chromosomal genome. The gene cassettes are usually integrated between the two conserved segments at the 5' and 3' ends at the attI1 site. As for the large plasmid genome of *S. sonnei*, one encoded ability is cellular invasion. This large plasmid encodes for *S. sonnei*'s outer membrane protein, VirG (IcsA) to elicit polymerization of filamentous actin that's involved in intra and intercellular movement for the bacterium. This is one of the main mechanisms that *S. sonnei* use to form protruding pores at the colonic epithelial cell wall in order to invade other neighboring cells in the colon.

Knowing the many mobile genetic elements markers on the *Shigella sonnei* plasmid and chromosomal DNA, it would be expected that strains of *Shigella sonnei* would be resistant to multiple antibiotics; however, resistant to multiple antibiotics strains is quite uncommon in the United States. Clinical symptoms of shigellosis cause by *Shigella sonnei* in the United States are similar to all other the dysenteric diseases. The most common symptom is bloody stool and small to severe diarrhea. Other symptoms on some people are mild to high fever, malaise, and tenesmus. Tenesmus is the constant feeling of the need to empty the bowel, accompanied by pain and cramping. The passage of stool excretion can go for 3 or more per day either chronically or last for several days.

Application to Biotechnology

Shigella sonnei is the cause of a human enteric infectious disease, shigellosis. Its natural reservoir is in the human intestinal tract, therefore, *S. sonnei* is only known for its disease causing ability. *S. sonnei* is not use for any known biotechnology to benefit

society. Much is still needed to investigate the evolutionary development from *E. coli* to the Shigella species, in order to answer questions on the nature of Shigella choice of reservoir in the human intestinal tract.

Current Research

S. sonnei's disease causing ability has given much attention to recent research on the epidemiology of the bacteria and the techniques to disinfect the disease causing bacteria on food products. New outbreaks and disease patterns of the different strains of *Shigella sonnei* have been detected and updated by epidemiologists around the world. Most recent research papers on shigellosis outbreak cause by *Shigella sonnei* are from countries outside the United States.

The shigellosis outbreak that happened in Taiwan during 2001 to 2003 has now been found to be a *Shigella sonnei* strain outside of Taiwan. The Taiwanese researchers and epidemiologists have been using the technique of pulse-field gel electrophoresis (PFGE) technique to genotype and tract the bacteria's mobile genetic element marker, the IS sites, on the large plasmid virulent factor of *S. sonnei*. After the genotyping and characterization of *S. sonnei*'s genome, they found that the first wave of the outbreak happened in 2001 was a foreign strain. In the year 2007, this particular ancestral strain from the 2001 outbreak continues to be widespread in the central region of Taiwan even though there are several new strains that have arisen from the 2001 outbreak. The Taiwanese epidemiologists are on watch for the new emerging strain to arise in Taiwan to cause another outbreak.

The Korean epidemiologists have recently published a paper on the tracking of their own shigellosis endemic cause by *Shigella sonnei. Shigella sonnei* first appeared in Korea in 1951 and since then there have been sporadic reports of the bacteria causing the disease shigellosis over many decades. Looking at the trends of the disease since the first emergence of *S. sonnei* in Korea, the scientists saw that *S. sonnei* disease causing ability have been zoning in and out of the Korean population. Current genotyping of the recent antibiotic resistance strains of *S. sonnei* using PFGE technique have revealed the genetic changes of *S. sonnei* over the decade of shigellosis emergence in Korea. The scientists have found multiple antibiotic resistance strains of *S. sonnei*. A high proportion of the resistant strains were found to be resistant to some of the most commonly used antibiotics such as tetracycline and streptomycin. These reports have alerted the Korean epidemiologists to develop a more comprehensive report of the genetic changes in *S. sonnei* since the beginning of its emergence in the 1951, knowing that the use of many antibiotics that we currently have pervasively today throughout the world will soon become obsolete.

It was previously known by the Spanish epidemiologists that several shigellosis outbreaks in Spain were caused by the consumption of fresh-cut vegetables. Since then fresh produce has been treated with chlorine-based agents to kill the *Shigella sonnei* bacteria responsible for the outbreaks since the beginning. However, most recent reports have been found that chlorine-based agent treatment of fresh produce can be carcinogenic. Therefore, new techniques have been investigated in Spain to find an alternative approach to decontaminate. A research study of quality, safety and bioactivity of plant foods under the Spanish department of Food Science and Technology has found that ozone can inactive *S. sonnei*. The research group inoculated *S. sonnei* on lettuce and in water and exposed them to UV-C. As the result of this experiment, the growth of *S. sonnei* bacteria was halted. This means that there is a safer alternative to decompose *S. sonnei*'s toxic products from fresh produce.

Genetically engineered crops: Experiences and prospects

An extensive study by the National Academies of Sciences, Engineering, and Medicine has found that new technologies in genetic engineering and conventional breeding are blurring the once clear distinctions between these two crop-improvement approaches. In addition, while recognizing the inherent difficulty of detecting subtle or long-term effects on health or the environment, the study committee found no substantiated evidence of a difference in risks to human health between current commercially available genetically engineered (GE) crops and conventionally bred crops, nor did it find conclusive cause-and-effect evidence of environmental problems from the GE crops. However, evolved resistance to current GE characteristics in crops is a major agricultural problem.

A tiered process for regulating new crop varieties should focus on a plant's characteristics rather than the process by which it was developed, the committee recommends in its report. New plant varieties that have intended or unintended novel characteristics that may present potential hazards should undergo safety testing -- regardless of whether they were developed using genetic engineering or conventional breeding techniques. New "-omics" technologies, which dramatically increase the ability to detect even small changes in plant characteristics, will be critical to detecting unintended changes in new crop varieties.

The committee used evidence accumulated over the past two decades to assess purported negative effects and purported benefits of current commercial GE crops. Since the 1980s, biologists have used genetic engineering to produce particular characteristics in plants such as longer shelf life for fruit, higher vitamin content, and resistance to diseases. However, the only genetically engineered characteristics that have been put into widespread commercial use are those that allow a crop to withstand the application of a herbicide or to be toxic to insect pests.

The fact that only two characteristics have been widely used is one of the reasons the committee avoided sweeping, generalized statements about the benefits and risks of GE crops. Claims about the effects of existing GE crops often assume that those effects would apply to the genetic engineering process generally, but different characteristics are likely to have different effects. A genetically engineered characteristic that alters the nutritional content of a crop, for example, is unlikely to have the same environmental or economic effects as a characteristic for herbicide resistance.

The committee examined almost 900 research and other publications on the development, use, and effects of genetically engineered characteristics in maize (corn), soybean, and cotton, which account for almost all commercial GE crops to date. "We dug deeply into the literature to take a fresh look at the data on GE and conventionally bred crops," said committee chair Fred Gould, University Distinguished Professor of Entomology and co-director of the Genetic Engineering and Society Center at North Carolina State University. In addition, the committee heard from 80 diverse speakers at three public meetings and 15 public webinars, and read more than 700 comments from members of the public to broaden its understanding of issues surrounding GE crops.

In releasing its report, the committee established a website that enables users to look up the places in the report that address comments received by the committee from the public, and also find the reasoning behind the report's main findings and recommendations. "The committee focused on listening carefully and responding thoughtfully to members of the public who have concerns about GE crops and foods, as well as those who feel that there are great benefits to be had from GE crops," said Gould.

Effects on human health. The committee carefully searched all available research studies for persuasive evidence of adverse health effects directly attributable to consumption of foods derived from GE crops but found none. Studies with animals and research on the chemical composition of GE foods currently on the market reveal no differences that would implicate a higher risk to human health and safety than from eating their non-GE counterparts. Though long-term epidemiological studies have not directly addressed GE food consumption, available epidemiological data do not show associations between any disease or chronic conditions and the consumption of GE foods.

There is some evidence that GE insect-resistant crops have had benefits to human health by reducing insecticide poisonings. In addition, several GE crops are in development that are designed to benefit human health, such as rice with increased beta-carotene content to help prevent blindness and death caused by vitamin A deficiencies in some developing nations.

Effects on the environment. The use of insect-resistant or herbicide-resistant crops did not reduce the overall diversity of plant and insect life on farms, and sometimes insect-resistant crops resulted in increased insect diversity, the report says. While gene flow -- the transfer of genes from a GE crop to a wild relative species -- has occurred, no examples have demonstrated an adverse environmental effect from this transfer. Overall, the committee found no conclusive evidence of cause-and-effect relationships between GE crops and environmental problems. However, the complex nature of assessing long-term environmental changes often made it difficult to reach definitive conclusions.

Effects on agriculture. The available evidence indicates that GE soybean, cotton, and maize have generally had favorable economic outcomes for producers who have adopted these crops, but outcomes have varied depending on pest abundance, farming practices, and agricultural infrastructure. Although GE crops have provided economic benefits to many small-scale farmers in the early years of adoption, enduring and widespread gains will depend on such farmers receiving institutional support, such as access to credit, affordable inputs such as fertilizer, extension services, and access to profitable local and global markets for the crops.

Evidence shows that in locations where insect-resistant crops were planted but resistance-management strategies were not followed, damaging levels of resistance evolved in some target

insects. If GE crops are to be used sustainably, regulations and incentives are needed so that more integrated and sustainable pest-management approaches become economically feasible. The committee also found that in many locations some weeds had evolved resistance to glyphosate, the herbicide to which most GE crops were engineered to be resistant. Resistance evolution in weeds could be delayed by the use of integrated weed-management approaches, says the report, which also recommends further research to determine better approaches for weed resistance management.

Insect-resistant GE crops have decreased crop loss due to plant pests. However, the committee examined data on overall rates of increase in yields of soybean, cotton, and maize in the U.S. for the decades preceding introduction of GE crops and after their introduction, and there was no evidence that GE crops had changed the rate of increase in yields. It is feasible that emerging genetic-engineering technologies will speed the rate of increase in yield, but this is not certain, so the committee recommended funding of diverse approaches for increasing and stabilizing crop yield.

Regulation Should Focus on Novel Characteristics and Hazards

All technologies for improving plant genetics -- whether GE or conventional -- can change foods in ways that could raise safety issues, the committee's report notes. It is the product and not the process that should be regulated, the new report says, a point that has also been made in previous Academies reports.

In determining whether a new plant variety should be subject to safety testing, regulators should focus on the extent to which the novel characteristics of the plant variety (both intended and unintended) are likely to pose a risk to human health or the environment, the extent of uncertainty about the severity of potential harm, and the potential for human exposure -- regardless of whether the plant was developed using genetic-engineering or conventional-breeding processes. " -omics" technologies will be critical in enabling these regulatory approaches.

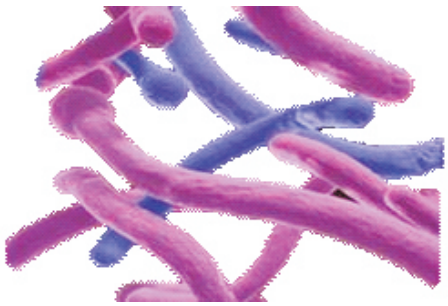
The United States' current policy on new plant varieties is in theory a "product" based policy, but USDA and EPA determine which plants to regulate at least partially based on the process by which they are developed. But a process-based approach is becoming less and less technically defensible as the old approaches to genetic engineering become less novel and as emerging processes -- such as genome editing and synthetic biology -- fail to fit current regulatory categories of genetic engineering, the report says.

The distinction between conventional breeding and genetic engineering is becoming less obvious, says the report, which also reviews emerging technologies. For example, genome editing technologies such as CRISPR/Cas9 can now be used to make a genetic change by substituting a single nucleotide in a specific gene; the same change can be made by a method that uses radiation or chemicals to induce mutations and then uses genomic screening to identify plants with the desired mutation -- an approach that is considered to be conventional breeding by most national regulatory systems. Some emerging genetic engineering technologies have the potential to create novel plant varieties that are hard to distinguish genetically from plants produced through conventional breeding or processes that occur in nature. A plant variety that is conventionally bred to be resistant to a herbicide and one that is genetically engineered to be resistant to the same herbicide can be expected to have similar associated benefits and risks.

Regulating authorities should be proactive in communicating information to the public about how emerging genetic-engineering technologies or their products might be regulated and how new regulatory methods may be used. They should also proactively seek input from the public on these issues. Not all issues can be answered by science alone, the report says. Policy regarding GE crops has scientific, legal, and social dimensions.

For example, on the basis of its review of the evidence on health effects, the committee does not believe that mandatory labeling of foods with GE content is justified to protect public health, but it noted that the issue involves social and economic choices that go beyond technical assessments of health or environmental safety; ultimately, it involves value choices that technical assessments alone cannot answer.

To prevent candidiasis in healthcare



Candida albicans is an opportunistic fungus (or form of yeast) that causes various types of infections in humans. This microorganism belongs to the genus *Candida*. The *Candida albicans* yeast is a part of the normal gut flora, a group of microorganisms that live in your mouth and gastrointestinal tract and is present in up to 80% of the human population. It normally does not cause harmful effects; however overgrowth of the fungus can result in candidiasis (candidosis). Candidiasis is often observed in immunocompromised individuals, such as patients infected with HIV.

The most common infections caused by members of the Candida species include:

1) Thrush: a thick, white growth on the mucus membranes of the mouth and throat.
2) Genital yeast infections: a painful inflammatory condition of the genital area that causes ulceration and a whitish discharge. Candidiasis in the vagina is commonly referred to as a "yeast infection."
3) Cutaneous candidiasis: occurs in moist areas of the skin due to rub and in neonates and burn patients.

These infections are usually easily cured in people who are not immunocompromised.

Healthcare-associated candidemia:

Systemic fungal infections, including those by *C. Albicans*, have emerged as important causes of morbidity and mortality in immunocompromised patients. Problems start when a person experiences some alteration in:

- Cellular immunity (i.e., chemotherapy or HIV)
- Normal body flora (i.e. the loss of normal bacterial flora due to antibiotics or steroid therapy)
- Normal physiology (i.e. cardiac surgery or indwelling catheters)
- *candida* yeasts normally live in and on the body without causing any symptoms. Invasive candidiasis is a fungal infection that can occur when *Candida* yeasts enter the blood stream. In people at risk, invasive candidiasis may occur when a person's own *Candida* yeasts enter their bloodstream, or it can also happen if medical equipment or devices, particularly intravenous (IV) catheters, become contaminated with *Candida*. The presence of *Candida* in the blood is a condition referred to as candidemia.
- *Candida* is one of the most common causes of central-line associated infections in healthcare settings; and although it is rare in people without risk factors, it is the fourth most common cause of hospital-acquired blood stream infections in the United States. Once it's in the bloodstream, the infection may spread and infect various organs.

People at highest risk for developing candidemia include:

- Intensive care unit (ICU) patients
- Surgical patients
- Patients with central venous catheters
- Very low-birth-weight infants

Treatment should also include the prompt removal of catheters.

Prevention

In some high-risk patients, anti-fungal agents may be used prophylactically to prevent infections. Good infection control practice including proper hand hygiene in addition to following the infection prevention guidelines published by the CDC, Health Canada, and professional associations (such as the Society of Healthcare Epidemiology of America (SHEA) and the Infectious Disease Society of America (IDSA) are the best method for preventing of these life-threatening infections.

Patients and their families should ask if a central line is really needed, and if so, they should speak up if the skin around the central line becomes sore or red, or if the dressing becomes wet or dirty.

Cleaning and Disinfection of Environmental Surfaces

Good general health and hygiene are very important for treating candida infections of the skin. Keeping the skin dry and exposed to air is helpful. Drying powders may help prevent fungal infections.

Possible Complications

These complications may occur:

- Infection of the nails may cause the nails to become oddly shaped and may cause an infection around the nail.
- *Candida* skin infections may return.

Cutaneous candidiasis

When an overgrowth of *Candida* develops on the skin, an infection can occur. This condition is known as candidiasis of the skin, or cutaneous candidiasis.

Candidiasis of the skin often causes a red, itchy rash to form, most commonly in the folds of the skin. This rash may also spread to other areas of the body. While the symptoms are often bothersome, they can be treated with improved hygiene and antifungal creams or powders.

High standard of hygiene and good general health are vital in the prevention of an infection by this fungus.

An infection is more likely when a person has other skin problems or has become unhealthy for other reasons.

- Wash regularly and dry the skin carefully afterwards. Overweight people should be careful to dry all skin folds.
- Avoid using other people's towels.
- Wear clothes that are made of cotton or wool. These will allow the skin to breathe and rid itself of surplus moisture. Change clothes and socks regularly so that you are always wearing dry ones.
- Wear sandals or leather shoes instead of trainers.
- Wash the hands very carefully after touching an infected area and after applying an antifungal cream.

A combination study with two biocides (EtOH and H_2O_2) and fluconazole demonstrated that the combination had enhanced efficacy.

- **Antifungal medication.** If you're at high risk for developing invasive candidiasis, your healthcare provider may prescribe

antifungal medication to prevent the infection. This is called "antifungal prophylaxis," and it is typically recommended for:

- Some organ transplant patients
- High-risk ICU patients
- Chemotherapy patients who have neutropenia
- Stem cell transplant patients who have neutropenia

Some doctors may also consider giving antifungal prophylaxis to very low birth weight infants (less than 2.2 pounds) in nurseries with high rates of invasive candidiasis.

- **Be a safe patient.** There are some actions that you can take to help protect yourself from infections, including:
  - Speak up. Patients and caregivers can ask how long a central venous catheter (central line) is needed, and if so, how long it should stay in place. Tell your doctor if the skin around the catheter becomes red or painful.
  - Keep hands clean. Be sure everyone cleans their hands before touching you. Washing hands can prevent the spread of germs.
- **Healthcare providers** can follow CDC-recommended infection control practices every time they work with a central line.

Prevention of Recurrence

The majority of HIV specialists do not recommend secondary prophylaxis (chronic maintenance therapy) of recurrent oropharyngeal or vulvovaginal candidiasis because of the effectiveness of therapy for acute disease, the low mortality associated with mucosal candidiasis, the potential for resistant *Candida* organisms to develop, the possibility of drug interactions, and the cost of prophylaxis (**DIII**). However, if recurrences are frequent or severe, an oral azole, fluconazole (**CI**), or itraconazole solution (**CI**) (or for recurrent vulvovaginal candidiasis, daily prophylaxis with any topical azole [**CII**]) should be considered. Other factors that influence choices related to such therapy include impact of recurrences on the patient's well-being and quality of life need for prophylaxis for other fungal infections, cost, toxicities, drug interactions, nutritional status, and potential to induce drug resistance among *Candida* and other fungi.

Prolonged use of systemically absorbed azoles, specifically among patients with low CD4+ T lymphocyte counts (i.e., <100 cells/μL) increases the risk for developing azole resistance. Adults or adolescents who have a history of one or more episodes of documented esophageal candidiasis should be considered candidates for secondary prophylaxis. Fluconazole 100-200 mg daily is appropriate (**BI**). However, potential azole resistance should be considered when long-term azoles are considered.

Preventing Oral *Candidiasis*

Keep your mouth clean. Rinse your mouth frequently. Brush your teeth at least twice a day and floss daily or as often as your dentist recommends. If you have to use a corticosteroid inhaler, be sure to rinse your mouth with water or brush your teeth after taking your medication. If you are undergoing treatment for cancer, some studies suggest that using a chlorhexidine (CHX) mouthwash can help to prevent thrush.[9]

- If you have dentures, clean them daily. Ask your dentist for the best way to clean your type of dentures.

See your dentist regularly. If you have diabetes, wear dentures, or have had oral *Candidiasis* before, you may need to visit more frequently. Ask your dentist how often you should come in. Ask your dentist if you need to change your diet or oral hygiene routine.[10]

Eat more yogurts and less sugar. The bacteria in yoghurt may help you maintain a healthy bacteria balance in your mouth. It also might help to cut down on sweets and breads. It is possible that sugar and yeast encourage *Candida* overgrowth. Maintain good blood sugar control if you have diabetes. Well-controlled blood sugar can reduce the amount of sugar in your saliva, discouraging the growth of *Candida*.

Protect infants from thrush. Small children are at risk for oral *Candidiasis*. Clean pacifiers and bottle nipples with hot water after each use. Store milk and prepared bottles in the fridge to prevent yeast from growing. If you are nursing and have red or sore nipples, you may be passing a yeast infection back and forth with your child. Talk to your doctor about obtaining an antifungal ointment for your nipples.

Preventing Invasive *Candidiasis*

Know when you're at risk. Invasive *Candidiasis* occurs when excess *Candida* enters the bloodstream and causes an infection. Invasive *Candidiasis* is most likely to happen in hospital patients or residents of nursing homes. If you are in an intensive care unit or are using a catheter, you are at risk of invasive *Candidiasis*. Having a weakened immune system, low neutrophil, or diabetes can also put you at risk.

You may be at risk if you have taken broad-spectrum antibiotics, experienced kidney failure, or had surgery, especially gastrointestinal surgery.

Take an antifungal medication. To prevent invasive *Candidiasis*, your doctor may prescribe an antifungal prophylaxis. If you have had an organ transplant or a stem cell transplant, you might be prescribed this. Ask about it as well if you are a high-risk ICU patient or a chemotherapy patient. If you have had an infant born at less than 2.2 pounds, ask about the rates of invasive *Candidiasis* at the hospital.

Your doctor may recommend that your infant be given an antifungal medication if the rates of infection are high.

Keep an eye on hospital hygiene. Medical equipment can carry traces of *Candida*. Workers in hospitals might carry traces of it on their hands. While staying in a hospital, make sure your hands are clean, and ask anyone who touches you to wash their hands first. If you are wearing a catheter, ask how long it should stay in, and speak up if it isn't changed on time. If the skin around the catheter becomes swollen, red, sensitive, or painful, tell a healthcare worker immediately.

References:

http://www.wikihow.com/Prevent-Candida-Overgrowth
http://solutionsdesignedforhealthcare.com/candida-albicans
http://www.thebody.com/content/art17163.html#candidiasis
http://www.thebody.com/content/art5867.html
http://www.netdoctor.co.uk/conditions/skin-and-hair/a3621/infection-of-the-skin-by-candida-albicans-cutaneous-candidiasis/
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2533490/
http://www.cdc.gov/fungal/diseases/candidiasis/invasive/risk-prevention.html
https://medlineplus.gov/ency/article/000880.htm

Highlights of the coming issue

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