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DIARRHEA DIGEST

DIARRHEA DIGEST is an irregular publication of TECHLAB®, Inc. dedicated to the etiology, diagnosis, and therapy of diarrheal diseases and related aspects of intestinal ecology

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Is there a relationship between Norovirus, Influenza and C. difficile Outbreaks?

A recent study by the Centers for Disease Control and Prevention found the number of patients who died from gastrointestinal related infection and disease has nearly doubled from 1999 to 2007; approximately 83% of patients dying from infection were over the age of 65 [1]. The majority of these deaths were attributed to *C. difficile* infection (CDI), with norovirus as the second leading cause of patient mortality. Recent studies have indicated that norovirus outbreaks may be epidemiologically linked to CDI. Investigations have found that approximately 25% of norovirus cases occur in hospitals and long-term care facilities. In such environments, viral infections can be rapidly transmitted due to patient to patient contact, visitors, and interaction with hospital staff [1]. Moreover, if the native intestinal flora has been previously disrupted from norovirus infection, *C. difficile* may have an opportunity to colonize the intestinal epithelium. *C. difficile* associated infection is typically preceded by the administration of broad-spectrum antibiotics. The use of antibiotics can cause significant alterations to the diversity intestinal microorganisms. In a similar manner, infection from norovirus may cause changes to gut microbiota and potentially allow for the invasion of opportunistic pathogens.

Case studies have documented incidences of simultaneous infection involving both norovirus and ribotype ARL 027 *C. difficile* in pediatric patients [2]. In these instances, patients were prescribed metronidazole to alleviate symptoms believed to be caused by *C. difficile*. After a 10-day antibiotic course, *C. difficile* was still cultured from stool samples. From these investigations, it was deduced that norovirus adversely affects the epithelial homeostasis of the intestinal lining and may exacerbate the cytotoxicity from *C. difficile* toxins A and B. An article by Wilcox and Foley et al. reported higher rates of CDI in closed hospital units with simultaneous infection from viral gastroenteritis [3]. However, in a publication from Svraka et al., *C. difficile* was unable to be associated with norovirus outbreaks in a long-term care facility [4]. One possible explanation for this finding may be related to the large number of stool

specimens submitted for testing for *C. difficile* during norovirus outbreaks. During such an event, it is likely that the number of false-positive results (i.e., results showing *C. difficile* to be present but not necessarily causing the symptoms) will increase in parallel with the quantity of samples analyzed. Thus, an apparent outbreak of norovirus may simply reflect increased specimen examination.

Infectivity from both norovirus and *C. difficile* exhibit seasonality as prevalence is much greater during the winter months compared to the rest of the year. As in the case of many gastrointestinal viruses, lower humidity during the winter months tends to support the transmission of viruses from person to person [5]. Additionally, individuals tend to stay indoors during the winter season because of the cold weather. In doing so, transmission from infected individuals and from contaminated surfaces is likely to increase. Recently, Polgreen et al. observed a strong statistical association between *C. difficile* infection and the influenza virus during the winter months [5]. Peak incidence from *C. difficile* was recorded 1-2 months following seasonal influenza. One hypothesis for this correlation is that overprescribed antibiotics can spur an increase in CDI [5]. In the case of the influenza virus, antibiotic prescriptions will have no effect in clearing the virus and will cause disruption to the intestinal microbiota. A subsequent investigation has indicated that a 20% reduction in influenza activity would reduce respiratory fluoroquinolone prescriptions by approximately 8%. Thus, in demonstrating a unique relationship between influenza and CDI, renewed initiative should be taken to promote seasonal influenza vaccination and reduce unnecessary antibiotics.

Krista Williams

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In light of the rising frequency of human/grizzly bear conflicts, the Alaska Department of Fishing and Gaming is advising hikers, hunters, and fishermen to take extra precautions and keep alert of bears while in the field. The department has posted the following notice:
We advise that outdoorsmen wear noisy little bells on their clothing so as not to startle any bears. We also advise outdoorsmen to carry pepper spray with them in case of an encounter with a bear. It is also a good idea to watch out for fresh signs of bear activity. Outdoors men should recognize the difference between black bear and grizzly bear feces. Black bear feces is smaller and contains lots of berries and squirrel fur. Grizzly bear feces has little bells in it and smells like pepper.

source: http://www.jokebuddha.com/Feces#ixzz2OwMMq5Zj

First Medical Description of Irritable Bowel Syndrome: "The bowels are at one time constipated, another lax, in the same person. How the disease has two such different symptoms I do not profess to explain"

Cumming - London Medical Gazette 1849

Blood type and diarrhea

According to the Stanford School of Medicine Blood Center, the percentages of ABO blood types in the American population are as follows: 44% O, 42% A, 10% B and 4% AB. It's surprising that there are a lot more people with blood type A than B. If your blood type is B or AB, consider yourself the lucky minority. And this is why:

You might have heard about the effect of blood type on personalities. There is no scientific evidence on whether or not the B blood type makes you an easygoing and creative person, but several studies suggest that the B antigen protects you from several viral and bacterial infections.

In a norovirus challenge study done on human volunteers, 65% people with O blood type and 67% people with A blood type presented symptoms while none of the people with B or AB blood types got sick [1]. Similar associations between ABO blood type and susceptibility to other enteric pathogens have been reported. People with O blood type are more susceptible to *Vibrio cholerae* and present with more severe symptoms when infected [2]. B blood type also offers some protection against *Escherichia coli* O157:H7 [3].

What's the protective mechanism of the B antigen? The ABO blood types are determined by the presence or absence of carbohydrate antigens on glycolipids and glycoproteins on the surface of mucosal epithelia and red blood cells. A and B antigens are made by enzymatic addition of N-acetyl-D-galactosamine or D-galactose to an H antigen precursor, respectively. The A and B antigens are highly expressed on the villi in the duodenum and jejunum. The binding of certain viral particles to the H antigen on human red blood cells suggests that the H antigen might be the docking site for certain pathogens, and the terminal D-galactose on the B antigen might interfere with the adhesion of pathogens to human cells. Therefore, the blood type may have an impact on colonization by certain intestinal microbes.

More and more studies support the idea that the ABO antigens affect the colonization by intestinal microbes. For example, when the intestinal microbiota from people with different ABO blood type were compared, the microbiota from individuals harboring the B antigen (blood type B or AB) showed higher diversity of certain groups of bacteria, such as the *Clostridium coccoides* group, in comparison with other blood groups [4]. *Helicobacter pylori* utilize ABO blood group antigens as adhesion receptors. Increased density of colonization by *H. pylori* was observed in individuals with type O antigen and people with blood type O are more likely to get duodenal ulcers [5].

With all of the benefits of having the B antigen on our cells, only 14% of the population have blood type B or AB --- congratulations to the lucky minority!

Manli Davis

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Update on C. difficile ribotypes

- Fluoroquinolone resistance is a major reason why ribotype 027 has established itself and continues to spread as the preeminent ribotype, at least here in the U.S. where 027 rates of 30 to 40% are fairly typical.
- The selective advantage of fluoroquinolone resistance is not restricted to 027; it is spreading to other ribotypes. We have found at least six other ribotypes that exhibit this property, which occurs following a single nucleotide substitution in the gyrase A or B genes.
- We are surprised that the mutational rate leading to fluoroquinolone resistance isn't higher among *C. difficile* ribotypes, considering that it occurs via a single nucleotide substitution.
- Ribotype 244 is becoming more common in Australia. This ribotype seems to have selective advantages similar to those carried by 027, suggesting that it may have the ability to spread, much like 027 has done in Europe, Canada, and the U.S.
- Looking at reports coming out of Europe, 078 appears to be increasing in locations where 027 is noticeably absent. Some 078 isolates are fluoroquinolone-resistant, others are sensitive.
- In our own area (southwestern part of Virginia), 078 is basically nonexistent. We still see high rates of 027, most of which are fluoroquinolone-resistant. And we continue to see ribotype 053, of which 100% are resistant to fluoroquinolones. We've looked at more than 50 isolates, all from different patients, and all exhibit high level resistance.
- Fluoroquinolone resistance seems to be a predominating factor in allowing a strain to gain a "foothold" in a hospital. Even so, historically predominant strains that are sensitive to fluoroquinolones continue to persist.

Speaking of ribotypes --- TechLab offers Clostridium difficile Ribotyping

Ribotyping is a PCR based method for classifying *C. difficile* strains. With the emergence of the epidemic strain, ribotype 027, many hospitals and other facilities want to know if this strain is present in their facility. Identifying not only ribotype 027, but other ribotypes as well, is important for understanding *C. difficile* disease and its epidemiology. The cost is $50 per isolate for ribotype 027 analysis only or $75 per isolate beyond ribotype 027 identification. Only unlinked and anonymous *C. difficile* isolates will be accepted- no fecal samples. Contact Bob Carman (rjcarman@techlab.com) or Kimberly Wickham (kwickham@techlab.com) with any questions or to request a submission form.

Cryptosporidium Outbreaks

A 2012 Cryptosporidium outbreak in the United Kingdom and Scotland sickened about 300 people. The outbreak was believed to occur following ingestion of prebagged salad products labeled as ready-to-eat. Mild to moderate intestinal disease was reported but no one died from the infection.

Over the past several months, cases of cryptosporidiosis have increased four-fold in parts of Australia, primarily around Melbourne and Victoria. The increase has been blamed on contaminated swimming pools. Chlorine in swimming pools is not sufficient to kill Cryptosporidium oocysts, and efforts are still underway to learn more about the source(s) of the rise in reported cases.

The first fecal transplant

Dr. Ben Eiseman was an innovative surgeon who lived in Denver and practiced at the Denver General Hospital. He later became Head of Surgery at the University of Kentucky, but eventually moved back to Denver because of his love of the outdoors. Colorado has more mountain peaks higher than 14,000 feet than any state in the contiguous U.S., and he climbed all of them. In fact, there is a mountain hut for hikers, the Eiseman Hut, located outside of Vail at 11,180 feet that was funded by Dr. Eiseman and others. Interestingly, the Gore family of Gore-Tex fame --- Gore-Tex is a waterproof breathable fabric made of a chemical component of Teflon --- regularly took ski trips to Vail. In the early 1970s, Dr. Eiseman was on one of the vacation trips when Bob Gore, the son of the founder W. L. Gore & Associates, and one of the inventors of Gore-Tex pulled out a fragment of the material. He told Dr. Eiseman about Gore-Tex, which he described as being highly inert. Dr. Eiseman was excited to hear this because physicians were on the lookout for materials that could be used in the human body for repair but which the body wouldn't reject. Eiseman took the material and implanted it into a pig, showing that Gore-Tex wasn't rejected. This discovery basically led to the first use of Teflon for artery and ligament repairs.

But let's go back even further in Dr. Eiseman's career. In 1958, he performed probably the first fecal transplants ever done for pseudomembranous colitis. His findings were presented in an article entitled "Fecal enema as an adjunct in the treatment of pseudomembranous enterocolitis" (Surgery 44:854-859). Dr. Eiseman and his three co-authors noted that the mortality rate from pseudomembranous eneterocolitis was very high despite antibiotics. They therefore made an attempt to re-establish the intestinal flora in four patients who had undergone surgery, were treated with antibiotics, and who developed life-threatening pseudo-membranous enterocolitis. Three were basically on their deathbeds.

Donor feces was obtained from a normal subject who had not received antibiotics. The donor feces was mixed with saline and administered as an enema in each patient. The low tech method Dr. Eiseman and his team used to prepare the fecal enema -- collect a fecal specimen, dilute it with buffer, and place it in the intestine --- is the same approach being used today to prepare fecal transplants for treating severe *C. difficile* disease. Today's success rate in *C. difficile* patients treated with fecal transplants is >90% --- probably pushing 95%. In this 1958 report, all four patients recovered within days --- 100% success rate. If you look at literature on cases of pseudomembranous colitis prior to the discovery of *C. difficile*, you will see that *Staphylococcus* was isolated in pure culture from some of these cases, although today we

know that *C. difficile* is by far, the primary cause. The article by Dr. Eiseman and co-authors is one of these reports on *Staphylococcus* and pseudomembranous colitis. Fecal samples from all four patients were strongly positive for hemolytic, coagulase positive *Staphylococcus aureus*.

STOOL NOTES

Toilet themes in today's society

You may have heard about the Modern Toilet, which is a bathroom theme-based restaurant chain in Taiwan and other parts of Asia. You can imagine what the restaurant looks like --- you sit on toilets, which fortunately are not actual working toilets, and you receive your food in small bowls that look like miniature toilets. Whether the restaurant creates an atmosphere, so to speak, with this type of décor is not clear, but perhaps it cuts down on the amount of food that is ordered. The chain is successful so the food must be pretty good.

Now, Suwon, South Korea offers the world's first toilet themed park. The inspiration for the park came from the former mayor, who was born in his grandmother's toilet --- yes, strange but true --- and he wanted people to realize that toilets are an important part of life. No arguments there. In the park, there is a statue of Auguste Rodin's "The Thinker" and yes, you guessed it. He's sitting on a toilet.

Visitors to the park can get their pictures taken on different types of toilets --- new ideas for greeting cards and postcards. How would you like to receive a "missing you" and "thinking about you" themed card from friends who are sitting on toilets. Then again, it could send a not-so-subtle message for other reasons. And when leaving the park, kids can buy plastic feces as souvenirs. Maybe for show-and-tell at school?

Word Origins --- True or false?

Back in the sixteenth century when manure was transported by ship, dry manure needed to be stored above deck to avoid hydration. When wet, the manure started to ferment and produced methane gas that caused occasional explosion. So "Ship High In Transit" or S.H.I.T was stamped on the crates manure was stored in to make sure that these crates were stored above deck. Then when the ships were passing by, people were wondering "what is that smell"? And that's where the saying "it smells like s_ _ _" came from.

The word crap was probably of middle English origin, likely derived from the Dutch word *krappen*, to cut off or separate, and the Old French word *crappe*, which means waste or rejected material. If you said the first story was false and the second was true, you know your sh _t!

Persimmon bezoars

Many folks from outside of our region (the southeast U.S.) have not heard of persimmons or tasted them. Persimmons are one of those fruits --- actually they are in the "berry family"--- that you have to have been raised with in order to like them --- kind of like rhubarb. Either you like them or you don't. There really isn't an in-between stage. For persons who don't like them, you persimmon-haters should know that they are considered healthy --- they lower athlerosclerosis, improve lipid metabolism, and have antitumor substances. Sounds like an infomercial in which you're not quite convinced that you want to try them.

People who have been raised eating persimmons know that the fruit has to get ripe in order to eat them. Rotten persimmons are no good, but unripe persimmons are worse and will cause you to "pucker up" because of astringent tannins in the fruit. Eating unripe persimmons can lead to the development of phytobezoars, which are insoluble foodballs that develop when the tannins mix with stomach acid. It ends up being kind of like a gooey round ball that binds other foods that you eat.

Bezoars can be caused by many different things. In the case of persimmon bezoars, also referred to as diospyrobezoars, they are hard and almost woody, basically undigestible and difficult to move through the intestine. Apparently you can treat diospyro-bezoars by drinking Coca Cola. The acid in Coca Cola is strong enough to help dissolve the bezoar, although it's still weaker than stomach acid. There's not too much you can say that's good about bezoars in today's world. However, in the middle ages, animal bezoars carried a hefty market price because they were believed to have magical healing powers and would neutralize poisons.

EcoFaeBrick – get a load of these

EcoFaeBrick, a company in Indonesia takes cow droppings and uses them to make bricks. The bricks are as strong as clay bricks, lighter, and they are fired by biogas instead of wood fires, making it a clean system for producing the bricks. The system is healthier for the environment too because the land is not being torn up to collect the clay. It also is helping with the local economy. The company has won awards for their novel approach, and to answer everyone's first question, the bricks have no smell. They cost the same as a clay brick. Milk cows are graded by the amount of milk they produce. Now, maybe we'll have to start grading cows by the amount of feces they produce.

Bug sniffing

Cliff the beagle has been in the news because of his ability to sniff out patients who have *C. difficile* disease. Now dogs are being used to track down bedbug contamination in hotels. They can even determine if a single bedbug is present. Amazing! But apparently hotels are reluctant to bring in bedbug sniffing dogs. Seems it upsets guests to see dogs sniffing around their room.

Interested in throwing cow pies?
Each April, cow patty tossing takes place at the World Cow Chip Throwing Contest in Beaver, Oklahoma is an annual event. The record? >180 feet!

Martian Poop

A married couple will be lifting off the ground in a couple of years on a trip to Mars --- together for close to two years in very tight quarters, so you can see why married couples are being considered. Or at least persons who can get along with each other for a couple of years. The project is aimed at recycling basically everything, including feces. The feces will be recycled to obtain the water, dried and sanitized, and then guess what? It will be placed in bags along the wall to help protect against solar radiation. Apparently food and feces do a good job of absorbing radiation without becoming radioactive.

Upcoming Conferences

American Society for Microbiology, May 18-21, 2013, Denver, CO

Digestive Disease Week, May 18-21, Orlando, FL

Interscience Conference on Antimicrobial Agents and Chemotherapy, Sept 10-13, Denver, CO

CLOSTPATH 2013, Oct 22-26, Palm Cove, Queensland, Australia