Department of Pharmacy

BRAC UNIVERSITY
Inspiring Excellence

PHARMA HIGHLIGHTS

ISSUE 47 | AUGUST 2018

The Major Health Risks Posed by Ciprofloxacin

Ciprofloxacin is a broad-spectrum antibiotic that is generally well-tolerated and widely used in clinical practice to treat various forms of infection. It is active against both gram-positive and gram negative bacteria. The most commonly reported drug-related adverse events related to ciprofloxacin are nausea, diarrhea, abnormal liver function tests, vomiting, and rash. Unfortunately, ciprofloxacin poses other health risks as well, mainly affecting the connective tissues, thereby causing retinal detachment, tendonitis, and tendon rupture. This instigated the FDA to issue a warning for the drug and also prompted scientists to investigate if ciprofloxacin affected any other body parts.

The Aorta is the main artery in the human body and it also contains connective tissues. Weakness of this connective tissue can result in aortic aneurysm, heart valve disease, and aortic dissection. To investigate the effect of ciprofloxacin exposure on Aortic connective tissue LeMaire et. al. used a mouse model of aortic aneurysms and dissections (ADD) and found that ciprofloxacin exposure in moderately stressed mouse aortas resulted in the disease progressing more rapidly and more severely. Interestingly they also found that cell death pathways were also more active, LOX levels were low, and there

was an increase in a degradative enzyme (MMP). The MMP and LOX results were then confirmed in a human cell model.

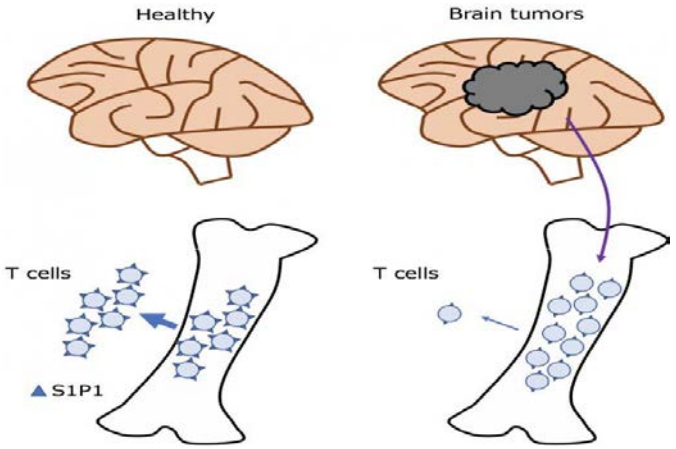
They concluded that ciprofloxacin and other antibiotics of the same class should be used with caution in patients with aortic dilatation. LeMaire is also hopeful that her findings will bring about a change in guidelines to include the warning for both patients with aneurysm and those who are at risk of getting an aneurysm.

Source: AAAS/Eurekalert! Via Baylor College of Medicine, FDA, Jama Surgery

T Cells Trapped by Brain Cancer

Metastatic brain tumors are affecting thousands of people worldwide. A 2018 survey revealed that, 23,880 people in USA alone were diagnosed with brain cancer. Nature Medicine recently published a study which unveiled an underlying cause behind poor brain cancer detection by the human immune system. The study also suggested means of improving the effects of immunotherapy treatments. Researchers from Osaka University in collaboration with other institutions examined the blood levels of T cells in brain cancer patients. The patients showed lowered T cell levels, but their spleens showed no sign of T cell sequestration. Mice models exhibited similar symptoms. But when the bone marrow of the mice models was tested, a remarkable increase in T cell levels was observed.

When the bone marrows of the human patients were evaluated almost identical results were obtained. This happened due to T cell entrapment inside the bone marrow, reducing its concentrations in blood. The study also revealed that T-cell surface protein S1P1 (Sphingosine-1-phosphate receptor 1) levels and bone marrow T cells levels were inversely proportional. The role of protein S1P1 is to assist efflux of T cells from bone marrow. The researchers found that the protein S1P1 level



dropped in patients with brain cancer which prevented the escape of T cells from the bone marrow. They suggested that by preventing internalization of protein S1P1, T cell sequestration in the bone marrow could be inhibited; resulting in the release of T cells from the bone marrow. The study concluded that T cell activation might enhance the efficacy of immunotherapeutic treatments for brain cancers, since the activated T cells will then be adequately available to detect and destroy brain and spine carcinomas.

Source: Nature Medicine, Mayo Clinic, American Cancer Society

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Is Your Hand Sanitizer Really Saving You from Germs? Think Again.

Antibiotic-resistant microbes are expected to pose a significant threat to public health in the coming decades, and it seems that these microbes are now gaining resistance to hand sanitizers. New research by scientists at the Peter Doherty Institute for Infection and Immunity and Austin Health has shown that certain strains of a microbe called *Enterococcus faecium*, which causes many infections in hospitalized patients, has become ten times more resistant to alcohol-based hand sanitizers compared to older strains. This work also suggested that hand sanitizers may have helped contribute to the rise in resistance.

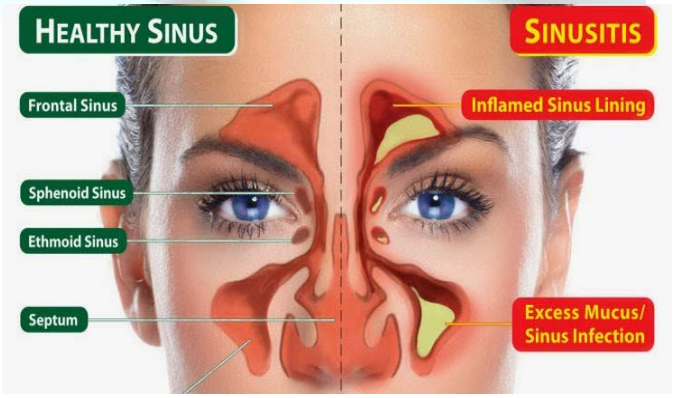
E. faecium is becoming more problematic and are causing more tenacious infections. *Enterococci* bacteria that develop resistance to vancomycin, considered an antibiotic of last resort, are particularly problematic; they are called *vancomycin-resistant enterococci (VRE)*. Patients that take antibiotics or get therapeutics like chemo are especially vulnerable to *VRE* infection. After exposing 139 *E. faecium* strains to an alcohol solution, the team found that the new isolates were more tolerant to alcohol exposure than the older isolates.

Alcohol use in hospitals has gone up significantly due to use of alcohol-based disinfectants. Anywhere we repeat a procedure over and over again, whether it's in a hospital or at home or anywhere else, that gives the bacteria an opportunity to adapt, because that helps them mutate. The ones that survive the new environment better then go on to thrive. That risk also increases when guidelines are ignored. Although WHO recommends the use of hand sanitizer, one cannot rely solely on alcohol-based disinfectants, especially for some bacteria like *VRE*. Additional procedures and policies are highly recommended. For hospitals, this could be super-cleaning regimens like disinfectants which are chlorine-based and an extra level of infection control that does not rely on alcohol-based disinfectants only.

Source: Pursuit at University of Melbourne, Science Translational Medicine

Did You Know That Chronic Allergies Can Change Cells?

Chronic rhinosinusitis leads to serious inflammation and swelling in the sinuses that can last for years. This condition leads to difficulty in breathing and an abnormal tissue growth called polyps, which usually needs to be removed surgically. Polyps grow from the cells that line the respiratory tract. Researchers at MIT have learned more about the cellular processes that underlie chronic rhinosinusitis by creating a map of gene activity in barrier tissues when inflammation occurs. This may have implications for other inflammatory disorders that are seen in barrier tissues, like eczema, inflammatory bowel disease, and asthma. The research team utilized a tool they created called Seq-Well to determine what was happening on the molecular level in individual cells. There were large differences between patients with and without polyps in basal epithelial cells. Genes called IL-4 and IL-13, which are known to promote inflammation from allergies were found at excessive levels in polyps patients. These genes also generate other respiratory tract cells, and may in turn influence how genes are expressed in those cells as well. It is important that factors other than immune cells are considered when studying chronic allergies. Examining the tissue as a whole, rather than biasing the study toward one specific cell type or another leads to finding other components of the tissue that may be irreversibly impacted by inflammation. This work could help researchers aiming to treat chronic allergies. An antibody that blocks IL-4 and IL-13 has already been approved for the treatment of eczema.



Source: MIT, Nature

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