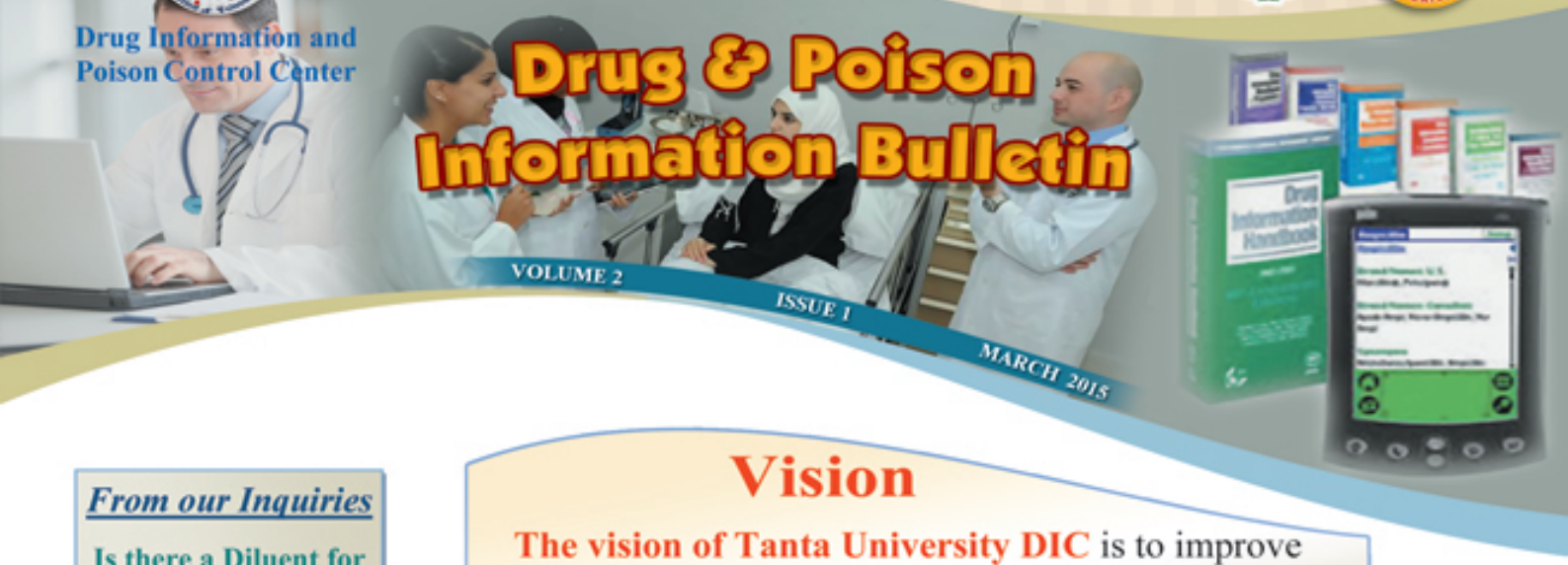
Drug Information and Poison Control Center

Drug & Poison Information Bulletin

VOLUME 2 ISSUE 1 MARCH 2015



Vision

The vision of Tanta University DIC is to improve national healthcare service through provision of evidence-based, unbiased, patient oriented drug information service & adverse drug reporting system.

From our Inquiries

Is there a Diluent for IV Diazepam??

It is recommended not to mix or dilute *diazepam* with other solutions or drugs in syringe or infusion flask. If not feasible to administer directly IV, inject slowly through as possible to the vein insertion.

Sources:
Drug Information Handbook, Handbook on Injectable Drugs.

Inside this issue:

FDA Warns of Cardiac Reactions with sofosbuvir Drug combinations

The U.S. Food and Drug Administration (FDA) is warning that serious symptomatic bradycardia can occur when the antiarrhythmic drug **amiodarone** is taken together with either the hepatitis C drug **Harvoni (ledipasvir/*sofosbuvir*) or with Sovaldi (*sofosbuvir*)** taken in combination with another **direct acting antiviral**, such as the investigational drug Daclatasvir or Olysio (simeprevir) for the treatment of hepatitis C infection.

The reports included the death of one patient due to cardiac arrest and three patients requiring placement of a pacemaker to regulate their heart rhythms. The other patients recovered after discontinuing either the hepatitis C drugs or amiodarone, or both. The cause of these events could not be determined.

Health care professionals should not prescribe either Harvoni or Sovaldi combined with another direct-acting antiviral drug with amiodarone. However, in cases where alternative treatment options are unavailable, ***FDA recommends*** heart monitoring in an inpatient hospital setting for the first 48 hours. Subsequently, monitoring in a doctor's office or self-monitoring of the heart rate should be done every day through at least the first 2 weeks of treatment.

***Source: www.fda.gov* [*Safety Announcement updated on* 24-3-2015]**

New safety information for prescription-strength ibuprofen: Risk of heart attack and stroke at high doses

Health Canada is working with the Canadian manufacturers of prescription oral ibuprofen products to update the safety information regarding the risk of serious cardiovascular side effects (e.g., heart attack and stroke) when these products are used at high doses (at 2400 mg/day). ***This risk increases with dose and duration of use.***

Serious heart and stroke related events are a known risk with all NSAIDs and the prescribing information contains extensive warnings on this risk. The new information is in light of a Health Canada safety review that found that oral ibuprofen taken at high doses **(≥ 2400 mg / day)** increases the risk of heart attack and stroke. The increased risk with high doses of ibuprofen is similar to the risk seen with some other NSAIDs, including COX-2 inhibitors (e.g. celecoxib) and diclofenac. Health Canada recently communicated new prescribing recommendations regarding the cardiovascular safety of diclofenac.

Recommendations:

- Ibuprofen or any NSAID product, prescribed or over-the counter, ***should be used at the lowest effective dose and for the shortest period of time necessary.*** Over-the-counter ibuprofen products should not be taken for more than ***seven days*** unless recommended by a healthcare professional.

- Ibuprofen doses of 2400 mg per day should not be given in patients with ischemic heart disease, cerebrovascular disease, and congestive heart failure or with risk factors for cardiovascular disease. Risk factors include -- but are not limited to -- smoking, diabetes, high blood pressure, high blood cholesterol and strong family history of cardiovascular disease.

- Other management strategies that do **not** include NSAIDs -- particularly COX-2 inhibitors, ibuprofen or diclofenac -- should be considered first for patients with a high risk of a cardiovascular event.

Source: healthycanadians.gc.ca, online.lexi.com

Unsuccessful osteoporosis medication may act as a novel asthma treatment

Researchers at Cardiff University, working with others at King's College, London and the Mayo Clinic in the United States, have discovered that protein molecules called ***calcium-sensing receptors (CaSR)*** play a pivotal role in asthma.

In allergic asthma, there is a link between airways inflammation, which can be caused by environmental triggers - such as allergens, cigarette smoke and car fumes - and airways twitchiness. Researchers show how these triggers release chemicals that activate ***CaSR*** in airway tissue and drive asthma symptoms like airway twitchiness, inflammation, and narrowing.

The research used mouse models of asthma and human airway tissue taken from asthmatic and non-asthmatic people. The researchers found increased numbers of these ***CaSR*** compared with healthy lung tissue. They concluded that this is one of the reasons for the exaggerated inflammatory response that occurs in asthma.

Drugs known to block ***CaSR*** already exist and known as ***calcilytics***. ***Calcilytics*** are not a new drug; they were first developed as a treatment for osteoporosis around 15 years ago but were found generally ineffective in treating this condition.

But while ***calcilytics*** didn't work for osteoporosis patients, they could help millions of asthma patients.

Scientists hope that one day the drug could replace the need for inhalers by stopping asthmatics from ever experiencing any of the symptoms of their condition.

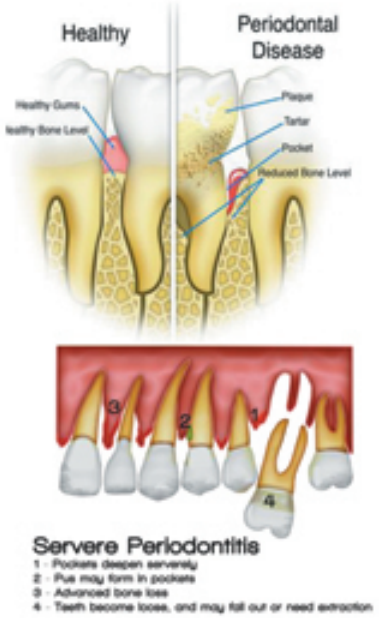
The benefits from the identification of ***CaSR's*** role do not stop at asthma treatment, but the team believes the finding could also lead to potential treatments for other lung conditions, such as chronic obstructive pulmonary disease and chronic bronchitis.

Source: - www.medicaldaily.com, www.ncbi.nlm.nih.gov

- Science Translational Medicine. 2015 Apr 22; 7(284):284ra60.

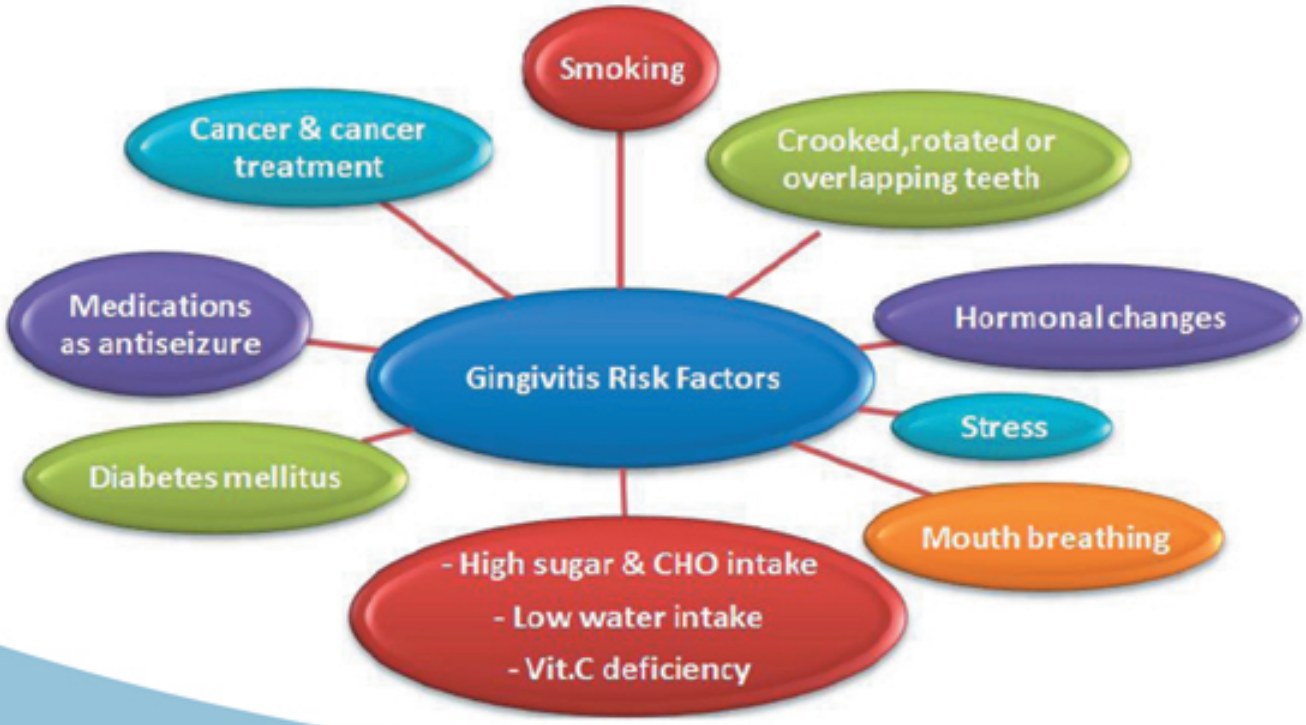
New target for gum disease treatment

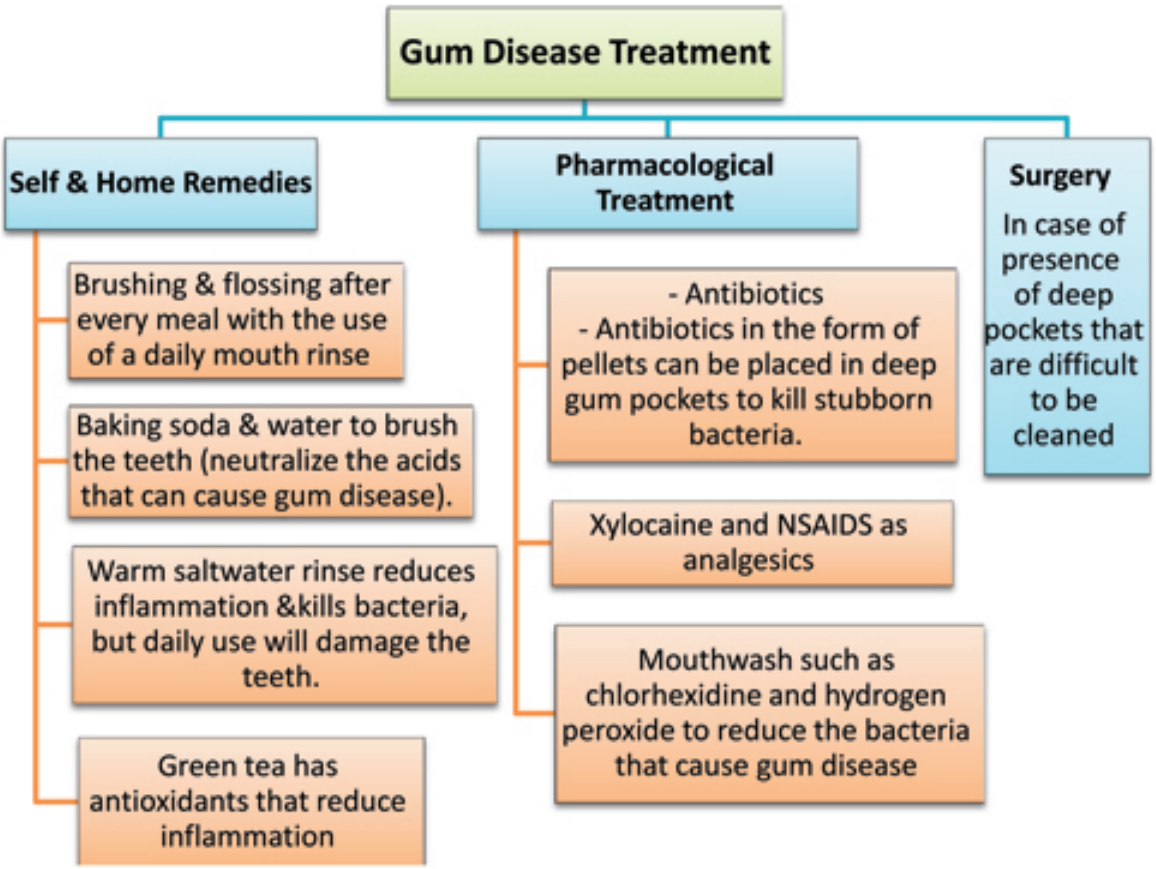
Background:
Gingivitis & Periodontal Disease



Gingivitis is an inflammation of the gums around the teeth and is most commonly a result of poor dental hygiene. It is characterized by red, swollen gums that bleed easily when teeth are brushed or flossed. It starts as food debris mixes with saliva and bacteria-forming plaque that sticks on the surfaces of teeth. If dental plaque isn't removed by brushing with toothpaste and flossing, it can become mineralized and form tartar, or calculus which will begin to irritate the gums and cause gingivitis. If left untreated, gingivitis will extend from the gums to the bone and lead to periodontitis.

Periodontal disease occurs when the bone below the gums gets inflamed or infected. When the underlying bone gets infected, it will start to recede away from the teeth and form deep gum pockets. These pockets collect plaque and bacteria as they are very difficult to keep clean, and more bone loss occurs. As periodontal disease progresses into later stages and more bone tissue is lost, the teeth may eventually become loose and fall out.





Promising new target for gum disease treatment identified

Researchers at the University of Pennsylvania have found a promising new target for treating gum disease. They discovered that complement (C3), a component of the immune system, plays a large role in inhibiting the body's ability to fight gum disease. Targeted therapy experiments which blocked C3 in mice indicated the P. gingivalis bacteria which cause periodontal disease are unable to thrive in its absence. To confirm the finding, researchers administered a C3 inhibitor named Cp40 to monkeys. The result showed that complement's inactivity in monkeys helped prevent the development of gum disease, while reducing inflammation and bone loss in previously infected subjects.

Sources:

- ***J Immunol. 2014 Jun 15; 192(12):6020-7.***
- ***www.medicinenet.com***

New FDA Approved Drugs

Corlanor (ivabradine)

Approval Status: Approved April 2015
Specific Treatments: Chronic heart failure

Corlanor (*ivabradine*) is a hyperpolarization-activated cyclic nucleotide-gated channel blocker. This channel is responsible for the cardiac pacemaker I_f current, which regulates heart rate.

Corlanor is specifically indicated to reduce the risk of hospitalization for worsening heart failure in patients with stable, symptomatic chronic heart failure with left ventricular ejection fraction ≤ 35%, who are in sinus rhythm with resting heart rate ≥ 70 beats per minute and either are on maximally tolerated doses of beta blockers or have a contraindication to beta-blocker use.

Corlanor is supplied as tablets for oral administration. The recommended starting dose is 5 mg twice daily. After 2 weeks of treatment, the dose should be adjusted based on heart rate. The maximum dose is 7.5 mg twice daily. In patients with conduction defects or in whom bradycardia could lead to hemodynamic compromise, initiate dosing at 2.5 mg twice daily.

Source: www.centerwatch.com

Cholbam (cholic acid)

Approval Status: Approved March 2015
Specific Treatments: bile acid synthesis and peroxisomal disorders

Cholbam (cholic acid) is a primary bile acid synthesized from cholesterol in the liver. Patients with bile acid synthesis disorders due to single enzyme defects with peroxisomal disorders (including Zellweger spectrum disorders) lack the enzymes needed to synthesize cholic acid, a primary bile acid normally produced in the liver from cholesterol. The absence of cholic acid in these patients leads to reduced bile flow, accumulation of potentially toxic bile acid intermediates in the liver (cholestasis), and malabsorption of fats and fat-soluble vitamins in the diet.

Cholbam is the first FDA approved treatment for pediatric and adult patients with bile acid synthesis disorders due to single enzyme defects, and for patients with peroxisomal disorders (including Zellweger spectrum disorders) who exhibit manifestations of liver disease, steatorrhea or complications from decreased fat soluble vitamin absorption. Cholbam is approved for use in children aged three weeks and older, and adults.

Cholbam is supplied as a capsule for oral administration. The recommended dosage is 10 to 15 mg/kg administered orally once daily, or in two divided doses, in pediatric patients and in adults.

Source: www.centerwatch.com

New class of cholesterol busters

The proprotein convertase subtilisin kexin 9 **(PCSK9) inhibitors** are a new class of drugs that have been shown to dramatically lower LDL cholesterol levels. They are monoclonal antibodies (MABs) that inactivate PCSK9 protein in the liver.

PCSK9 itself inactivates the needed receptors on the liver cell surface that transport LDL into the liver for break down. Without these receptors, more LDL remains in the blood. So, by inactivating PCSK9 via inhibition, more receptors are available to capture LDL for metabolism and clear from the blood.

Who Needs a PCSK9 Inhibitor: Patients who cannot tolerate statins or cannot achieve their goals using their prescribed statin dose.

Clinical Studies for PCSK9 Inhibitors

Several PCSK9 studies were published in the *New England Journal of Medicine* (NEJM) in March 2015. The studies show that two of these investigational agents, **Evolocumab** or **Alirocumab**, when combined with statins, lower cholesterol better than the statin alone. After one year, those patients who were taking both the PCSK9 inhibitor and the statin together had LDL levels that were at least **60 % lower** than the group taking only statins. Larger studies are ongoing to evaluate PCSK9 inhibitors on the ability to lower outcomes like heart attack, but early results suggest cardiovascular events could be lowered by half.

In studies, PCSK9 inhibitors are given by subcutaneous injection once or twice monthly. In general, PCSK9 inhibitors have been well-tolerated, but neurocognitive side effects, like confusion, and infusion reactions have been seen.
In the **YUKAWA-2** study with **evolocumab**, LDL cholesterol levels were lowered by over 70 % at 12 weeks in patients taking statins who needed additional LDL lowering.

Other phase 3 **PROFICIO studies** enrolling 35,000 patients are ongoing. These include intolerance to statins, monotherapy treatment, patients with familial hypercholesterolemia, studies looking at long-term safety, and cardiovascular outcome studies. Early studies show reduction of events like death, heart attack, stroke and heart failure. **Bococizumab** is another PCSK9 inhibitor which shows positive results. Phase 3 studies are evaluating LDL-lowering in a broad range of patients, including high-risk patients.

Source: www.drugs.com

Editorial Board

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