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First Nasal Spray for Anaphylaxis Approved

The approval of Neffy® marks the first epinephrine product for the treatment of anaphylaxis that is not administered by injection.

Anaphylaxis, an acute, life-threatening disorder, involves a multi-systemic allergic reaction. Symptoms range from mild skin flushing to severe respiratory distress. Epinephrine, both a neurotransmitter and a hormone, acts on both alpha- and beta-adrenergic receptors. Through its action on beta-adrenergic receptors, epinephrine causes bronchial smooth muscle relaxation and helps alleviate bronchospasm, wheezing, and dyspnea that may occur during anaphylaxis.

Previously, only injectable epinephrine products were available for treatment, and some people, especially children, may delay or avoid therapy due to a fear of injections. This nasal spray would thus reduce barriers to rapid treatment of anaphylaxis. The approval was based on four studies, consisting of 175 healthy adults without anaphylaxis. They each measured the levels of epinephrine concentrations in the blood following the administration of Neffy® or an approved epinephrine injection. The studies resulted in comparable blood concentrations in both administrations, with similar increases in blood pressure and heart rate, both of which are important effects in epinephrine based anaphylaxis treatment. A complete repeat dosing nasal allergen challenge study and updated nitrosamine testing also showed that no measurable levels of nitrosamines, a carcinogen, were detected.

The recommended dosage of Neffy® is one spray, which contains 2 mg of epinephrine, administered into one nostril. If no improvement is seen or if symptoms worsen after the initial treatment, a second dose of Neffy® can be administered in the same nostril starting 5 minutes after the first dose.

Overall, Neffy® is a needle-free, safe, and effective epinephrine drug solution that provides an unmet need to patients.

Written by: Zeenat Entezar
U.S. Food and Drug Administration 2024

Acetaminophen's Effects on Positive Empathy

Acetaminophen (paracetamol) is one of the most widely used over-the-counter pain relievers in the world, known primarily for treating physical pain. However, new research suggests that its impact extends beyond physical discomfort—acetaminophen can also dampen emotional sensitivity, specifically positive empathy.

In a double-blind, placebo-controlled trial, 114 participants were given either 1,000 mg of acetaminophen or a placebo. Participants were then asked to rate their emotional responses to scenarios depicting positive experiences on a scale of 1 to 10. Results show that the group taking acetaminophen exhibited significantly reduced emotional reactions, such as personal pleasure and other categories of empathy, compared to the placebo group ($p<0.05$). Furthermore, cognitive evaluations of the scenarios were unaffected, as both groups rated the objective positivity of the experiences similarly.

Supporting these findings, a

See Acetaminophen pg 3

Statins: The Unexpected Therapeutic Benefits You Didn't Know About

Statins are well-studied pharmacological agents that are best known for their cholesterol-lowering effect mediated by inhibition of HMG-CoA reductase. However, statins also have therapeutic potential outside cardiovascular health. An important off-target effect of statins is the inhibition of a number of kinases that are involved in driving cancer cell growth and survival.

In cancer cells the up regulation of the cellular pathway blocked by statins makes them an attractive potential therapy for treating cancer in combination with chemotherapeutic agents such as doxorubicin, cyclophosphamide, and pentoxifylline as well as tyrosine kinase inhibitors like sorafenib, vemurafenib, and gefitinib. Higher doses of statins can inhibit this essential cellular pathway decreasing the availability of intermediate molecules which slow the proliferation of cancer cells. Statin research has been done in several types of cancer including breast, brain, liver, and gynecological cancers indicating a large potential field of further research.

Statins can also decrease the production of pro-inflammatory cytokines, which may be beneficial in the treatment of chronic inflammatory diseases such as rheumatoid arthritis, IBD, multiple sclerosis, systemic lupus erythematosus, Hashimoto's, and psoriasis. The differentiation of immune T-helper cells can be influenced by statins to promote the anti-inflammatory Th2 cells while inhibiting inflammatory Th1 cells. Statins can also work to inhibit GTPase prenylation which can help modulate immune cell activity.

While we often think of statins in relation to cholesterol and heart health, the off-target effects of statins have potential benefits in cancer and chronic inflammation. Further research into these areas may elucidate cellular mechanisms that allow future therapies to be developed.

Written by: Kevin Hatley
British Journal of Pharmacology 2024; doi: 10.1111/bph.17309

Is COVID Driving Us Mad? The Mental Toll on the Unvaccinated vs. Vaccinated

As it is understood, immunization against COVID-19 is crucial for both preventing and minimizing the severity of the disease. However, the impact on other COVID side effects, such mental health complications, presents a new frontier to explore.

This study, involving over 18 million participants across three main cohorts—pre-vaccination, vaccinated, and unvaccinated—tracked individuals for up to two years following a COVID-19 diagnosis to investigate the correlation with successive mental illnesses. Participants were monitored from the day of diagnosis (day 0) and during key periods, including weeks 1-4 and weeks 5-28 post-diagnosis. The study primarily focused on out-comes related to depression and other serious mental health conditions, such as schizophrenia, bipolar disorder, psychosis, PTSD, and more.

The incidence of mental illnesses overall was observed to be higher following COVID-19 infection compared to those who remained uninfected, particularly during the dominance of the Delta variant. Regardless of the specific variant, rates of depression and serious mental illnesses were significantly elevated in the first 1-4 weeks post-COVID diagnosis among pre-vaccinated and unvaccinated individuals (aHR 1.93 and 1.49; aHR 1.79 and 1.45, respectively) compared to vaccinated individuals (aHR 1.16 and 0.91). The adjusted hazard ratio (aHR) indicates that pre-vaccinated and unvaccinated individuals had a substantially higher risk—93% and 79% for depression, and 49% and 45% for serious mental illness. Additionally, the prevalence of mental health issues was higher in those over 60 years of age and more prevalent in males than females.

Individuals who were vaccinated prior to their COVID-19 diagnosis experienced reduced disease severity, likely due to a decrease in systemic inflammation and psychological benefits, such as reduced anxiety about COVID-19 and the ability to maintain social interactions. The results of this study indicate that vaccination provides advantages beyond mere immunity to disease, highlighting the necessity of further investigating these wider implications in order to foster a safer and healthier community.

Written by: Guneet Gill
JAMA Psych 2024; doi: 10.1001/jamapsychiatry.2024.2339

Semaglutide: More Than Meets The Eye

Paraded as an ingenius solution to America's obesity epidemic, semaglutide, a GLP-1 receptor agonist, is an injectable used to manage Type 2 diabetes. Although semaglutide and others like liraglutide and dulaglutide already have been proven to reduce cardiovascular disease, their effects on heart failure are largely unknown.

More common in overweight patients, heart failure (HF) with preserved ejection fraction has had few treatment options until very recently. To address this gap, the SELECT trial, a phase 3 trial spanning 41 countries and 17,604 patients, investigated whether a once-weekly semaglutide 2.4 mg regimen over 16 weeks demonstrated superiority over placebo for cardiovascular outcomes.

From 2018 to 2021, researchers concluded in the analysis that semaglutide reduced major adverse cardiovascular events (MACE; combined outcomes of cardiovascular death, non-fatal stroke, or non-fatal MI) by 20% in patients who had pre-existing ASCVD and were overweight, but did not have diabetes. Among the 4,286 patients who had HF at baseline, semaglutide improved combined outcomes of cardiovascular death or heart failure associated hospitalization showing similar benefits in both reduced (HR: 0.65, CI 95% 0.49-0.87) or preserved ejection fraction (HR: 0.69, CI 95% 0.51-0.91). In addition, age, sex, weight, and glycemic status had no significant effects on MACE, heart failure outcomes, and mortality.

At the time of the study, more patients who had heart failure with reduced ejection fraction were on loop diuretics and mineralocorticoid receptor antagonists. Now recognized as the largest study on GLP-1 agonists, the SELECT trial offers healthcare providers more clinical freedom and assurance that semaglutide, regardless of demographic, reduces adverse events and death from heart failure. Contrary to what the general public may believe, semaglutide, a drug that's flying off shelves is not just for diabetes or weight loss – it offers more than meets the eye.

Written by: Kristie Chau
The Lancet 2024; doi: 10.1016/S0140-6736(24)01498-3

Acetaminophen: continued from pg 2

2024 study published in JAMA explored additional effects of acetaminophen, specifically during pregnancy, and possible neurodevelopmental disorders in children. While the primary focus of this study was on autism, ADHD, and intellectual disabilities, it highlights how acetaminophen can potentially influence neurodevelopmental outcomes, implying a correlation between the drug and altered brain function in children. This further strengthens the possibility that acetaminophen affects emotional and cognitive processes more broadly, including the dampening of empathy in adults.

Given acetaminophen's widespread use, it is important to understand how these findings can alter its impact and accessibility on everyday social interactions and emotional well-being. More research is needed to better understand how even the most common analgesics can affect interpersonal relationships and future patient care.

Written by: Amy Huynh
Front. Psychol. 2019; doi: 10.3389/fpsyg.2019.00538

RSV: Complications and New Therapies

RSV (Respiratory Syncytial Virus) is a major cause of lower respiratory tract diseases such as pneumonia and bronchitis in infants, children, and elderly individuals. It is responsible for many hospitalizations and deaths of children and immunocompromised elderly patients. The spread of RSV is seasonal, occurring from the fall to the winter. Like the common cold and flu, it is transmitted through direct contact with respiratory droplets.

RSV predisposes the lung to bacterial coinfection and triggers an overreaction of neutrophils. The overreaction triggers the production of reactive oxygen species which create neutrophil extracellular traps (NETs), resulting in cell death. During the Post-RSV stage, reduced accumulation of neutrophils and the impairment of alveolar macrophages decrease the ability to eliminate bacteria in the lungs. The reduction of immune defense promotes MRSA bacterial growth in the lungs. The ability of RSV to impair the host defenses also highlights its impact on patients with chronic lung diseases such as asthma and COPD.

The study investigated the impact of the USA300 MRSA/RSV coinfection using an MRSA strain that mimics the human response in mice and a clinical isolate of MRSA. RSV impaired the USA300 MRSA clearance during a specific window of susceptibility of 4 and 7 days. The effects of RSV on antibacterial defense are unique from those induced by Influenza, so it is important to categorize the source of bacterial infection to implement the appropriate therapy.

Over recent years, many vaccines have been developed to combat the rise of RSV. Beyfortus (Nirsevimab) is a monoclonal antibody recently approved in the United States and Europe to protect against RSV in infants during their first RSV season. According to the FDA, one dose of Beyfortus (Nirsevimab) is administered as a single intramuscular injection before or during the RSV season. Another vaccine, RSVpreF - Abrysvo, approved for use during pregnancy to protect infants from lower respiratory infections. The vaccine is administered during the third trimester of pregnancy around September to January.

Written by: Munachimso Aghasili
Infection and Immunity 2024; doi: 10.1128/iai.00304-24

Contribution of Calcium Channel Blockers and Selective Serotonin Reuptake Inhibitors to the Risk of Fractures

Elderly patients prescribed calcium channel blockers (CCBs) may be at risk of fracture due to orthostatic hypotension. This may be due to changes in gait and balance, which can contribute to falls and fractures. Selective serotonin reuptake inhibitors (SSRIs), when taken with CCBs can also potentiate this due to CYP3A4 interactions. In the study population receiving antihypertensive medications, 1 out of 4 were concomitantly taking an SSRI. It is well documented that the long-term use of SSRIs, one year or greater, increases the risk of fractures. This paper aimed to collect evidence of this and whether this can be reflected with short term use of SSRIs in younger and older populations.

A retrospective cohort study was conducted to assess the risk of fracture in individuals taking CCBs and SSRIs together compared to those only taking CCBs. Deidentified data was collected from a database representative of the US population covered by employer-sponsored health insurance. Adults, 18 years or older, taking CCBs between January 2008 and December 2019 were included. From this population, those taking an SSRI in addition to a CCB were considered as the comparison group. Patients with a diagnosis of chronic kidney disease (CKD) or a history of fractures were excluded. 191,352 concomitant CCB-SSRI users and 956,760 CCB-only users were identified and evaluated in this study.

The results exhibited crude incidence rates of fracture of 13.9 and 4.7 per 1000 person-years for CCB-SSRI users and CCB-only users respectively. CCB-SSRI users therefore had a 43% increased risk of fractures (HR: 1.43; 95% CI: 1.22-1.66) compared to CCB-only users. These results are independent of whether the taken SSRIs inhibit CYP3A4 or not. This finding demonstrates that concomitant use of CCBs and SSRIs increases the likelihood of fractures in both younger and older populations. These effects can be seen with short-term use of SSRIs, which is unique in this study. Future studies will be needed to support the mechanisms by which the CCB and SSRI drug classes each contribute to the risk of falls and fracture since the inhibition of CYP3A4 hasn't been shown to be a significant contributor to this. This study can now be found as reference in drug databases analyzing drug-drug interactions, such as Lexicomp or UpToDate.

Written by: Harnoor Gill
Annals of Pharmacotherapy 2024; doi: 10.1177/10600280231218286

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