



## Viral Infection Disrupts Neural Development in Offspring: Increasing Risk of Autism

Activating a mother's immune system during pregnancy disrupts the development of neural cells in the brain of her offspring and damages the cells' ability to transmit signals and communicate with one another, researchers have found. The finding suggests how maternal viral infection might increase the risk of having a child with autism spectrum disorder or schizophrenia. The research, published in the *Journal of Neuroscience*. "This is the first evidence that neurons in the developing brain of newborn offspring are altered by maternal immune activation," the researcher said. The study was conducted in mice and rats and compared the brains of the offspring of rodents whose immune systems had been activated and those of animals whose immune systems had not been activated. The pups of animals that were exposed to viral infection had much higher brain levels of immune molecules known as the major histocompatibility complex I (MHCI) molecules. The researchers found that the high MHCI levels impaired the ability of the neurons from the newborn mice's brains to form synapses. Earlier research has suggested that ASD and schizophrenia may be caused by changes in the development of connections in the brain, especially the cerebral cortex. The researchers experimentally reduced MHCI to normal



levels in neurons from offspring following maternal immune activation. "Remarkably, synapse density returned to normal levels in those neurons," the researcher said. These results indicate that maternal immune activation does indeed alter connectivity during prenatal development, causing a profound deficit in the ability of cortical neurons to form synapses that is caused by changes in levels of MHCI on the neurons. In a series of experiments, the researchers determined that MHCI did not work alone to limit the development of synapses, but it interacted with calcineurin and myocyte enhancer factor-2 (Mef2), a protein that is a critical determinant of neuronal specialization. Calcineurin, MHCI, and

Mef2 form a biological signaling pathway that had not been previously identified. In the offspring of the maternal immune activation mothers, this novel signaling pathway was much more active than it was in the offspring of non-MIA animals. This finding provides a potential mechanism linking maternal immune activation to disease-linked behaviors. It also is a mechanism that may help the researchers to develop diagnostic tests and eventually therapies to improve the lives of individuals with these neurodevelopmental disorders.

## Estrogen - A New Weapon Against UTI in Postmenopausal Women



Estrogen stimulates the production of the body's own antibiotic and strengthens the cells in the urinary tract, according to a new study in Sweden. The results, published in the journal *Science Translational Medicine*, show that estrogen supplements may help menopausal women to ward off recurrent urinary tract infections. Urinary tract infections are among the most common

diseases, affecting over half of all women. Menopausal women have an increased risk of recurrent urinary tract infections, which has been associated with low estrogen levels. Infecting bacteria first come in contact with the inside of the urinary bladder. The bladder lumen is covered with epithelial cells, acting as a fence protecting the vulnerable tissue as well as producing antimicrobial peptides- the body's self-made antibiotic. These peptides act as rapid front line soldiers fighting infecting microorganisms. By the early action of the antimicrobial peptides, the number of bacteria can be reduced before they have a chance to multiply. In the postmenopausal woman, however, the epithelium is fragile and often damaged with occasional gaps between cells, which in turn affect the ability to resist infection. In the current study, the researchers treated post-menopausal women with estrogen for 14 days, and then analyzed cells excreted in the urine. They found that estrogen acts on the epithelium in a way that the gaps between the cells lining the bladder lumen are healed, and estrogen is gluing them together. This makes it more difficult for bacteria to break this protecting shield and reach the underlying cells. By treating postmenopausal women locally with estrogen, the cells lining the bladder are strengthened and the body's own defense against infection is improved, making women better suited to fight infections.

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"The anaerobic ones are just sitting there, but the aerobic bacteria are doing jumping jacks, sit-ups, leg lifts ...."



## What Is New?

**BEXIMCO PHARMA**



### Infection During Newborn's First Week of Life Associated with Bacterial Infection in Mother

Early-onset neonatal infection (infection in the first 7 days of life), is associated with maternal infection and colonization, a systematic review and meta-analysis published in *PLOS Medicine*. Newborns of mothers with colonization had an odds ratio of 9.4 (95%CI 3.1-28.5) of laboratory-confirmed infection compared with newborns of non-colonized mothers. Furthermore, newborns of mothers with risk factors for infection (pre-mature rupture of membranes, preterm <37 weeks, and prolonged rupture of membranes) had an odds ratio of infection of 2.3 (95%CI 1.0-5.4) compared with newborns of mothers without risk factors. The researchers identified 448 full-text articles of which 83 studies met the criteria to be included in their study and 67 were able to be combined in meta-analyses. The authors specifically excluded studies of nonbacterial infections, tetanus infections,



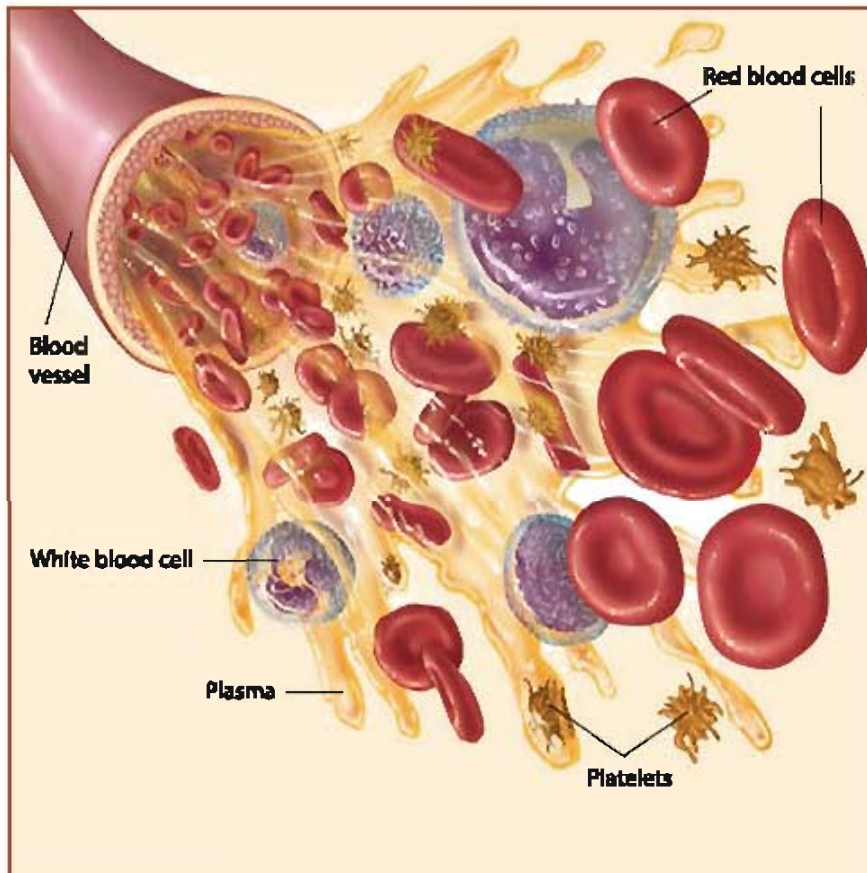
sexually transmitted infections such as chlamydia or other TORCH (Toxoplasmosis, Rubella, Cytomegalovirus, Herpes simplex, Syphilis) infections, because they have different mechanisms of transmission. Discussing the study's implications, the authors state, "The risk of early neonatal infection among women with maternal infections is high and presumably even higher in low-resource settings where most women deliver at home without access to health care. Intra-partum antibiotic prophylaxis could reduce the incidence of maternally acquired early-onset neonatal infections. Development of a

simple algorithm that combines clinical signs and risk factors to diagnose maternal infections would be useful in settings where lab facilities (culture or colonization) are not available."

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### Treatment for Chronic Infections Could Lie in Patient's Blood !



A recent discovery provides hope for a new personalized treatment strategy that could use a patient's own blood to treat the infection. This could help treat millions of people living with chronic infections such as HIV, Hepatitis B or Hepatitis C. These findings were published in *The Journal of Clinical Investigation*. Patients suffering from chronic infections often have to undergo long periods of anti-viral drug therapy to control the virus. Anti-viral drugs are not fully effective against viruses such as Hepatitis B and Hepatitis C. Vaccines are a potentially effective means to treat chronic viral infections such as this because they can eliminate the virus naturally. However, vaccines for patients with chronic infections are often difficult to produce since these patients already have weak immune responses or the vaccine is not effective due to genetic diversity amongst viruses. The researchers has discovered that monocytes which can activate an immune response, are also able to capture the virus in chronically-infected patients and use the captured virus to boost the patient's own immune response. By using the viral antigen already present in the blood of the patient suffering from a chronic illness, this strategy redefines therapeutic vaccines by cutting down on time and resources; as there is no need to specially isolate the viral proteins from patients and then inactivate it to create a vaccine. All the proteins present within the virus can be used to create a personalized vaccine for each individual. This also means that many of the complex issues associated with current vaccine therapy against chronic infections can be overcome, such as that of genetic diversity of viruses. One of the greatest beneficiaries of this discovery would be chronically-infected patient populations in lower socio-economic strata. By tailoring vaccines to be more specific to each virus and each patient, vaccine production can be simplified and thus less costly. Vaccines produced via this discovery could improve the accessibility of such treatments. "This excellent discovery is a milestone in vaccine therapy for chronic infections. I believe that these findings will go a long way in improving future therapeutic treatments for chronic infections"-the researchers concluded.

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### Pulmonary Puzzle : Clinical Presentation

**Case :** A 46-year-old man was referred to ear nose throat clinic for the right nasal obstruction, purulent nasal discharge, mid-facial swelling and upper right gingival retraction since 6 months. He had previously received antibiotic therapy with temporary relief. Nasal endoscopy showed medialisation of the right uncinate process, while the oral examination revealed a swelling of the upper right alveolar arch. The head CT (figure) showed an expansive mass occupying the right maxillary sinus.



**Figure:** Coronal CT scan of the paranasal sinuses showing an expansive mass of the right maxillary sinus. The mass erodes the inferior, medial and lateral walls of the sinus and an ethmoidal involvement was observed.

The suspicion of neoplastic disease led to perform an MRI with contrast medium. Despite the high suspicion of fungal disease after MRI, which showed a fungal-like central signal void, the patient

underwent an explorative endoscopic procedure to rule out a neoplastic condition. The intraoperative examination excluded malignancies and the procedure was completed with a wide middle anastomy that allowed toileting the mixed necrotic and fungal-like material occupying the sinus. The known odontogenic cyst—the likely odontogenic focus—was also removed endoscopically. Histopathological examination was done.

**Outcome:** The patient recovered after long-term antibiotic therapy (intravenous ceftriaxone 2 gm 6 hourly daily for 1 month, followed by oral amoxicillin clavulanate 1 gm three times daily for 3 months). There was no relapse during the 1-year follow-up.

### New Strategy to Disarm the Dengue Virus Brings New Hope for a Universal Dengue Vaccine

A new strategy that cripples the ability of the dengue virus to escape the host immune system- has been discovered by *A STAR's Singapore Immunology Network (SiGn)*. This breakthrough strategy opens a door of hope to what may become the world's first universal dengue vaccine candidate that can give full protection from all four serotypes of the dreadful virus. This research published in the *PLOS Pathogens* journal. Early studies have shown that a sufficiently weakened virus is still strong enough to generate protective immune response offers the best hope for an effective vaccine and the path to finding a virus of appropriate strength is fraught with challenges. This hurdle is compounded by the complexity of the dengue virus. Even though there are only four different serotypes, the fairly high rates of mutation means the virus evolve constantly, and this contributes to the great diversity of the dengue viruses circulating globally. Furthermore, in some cases, the immune response developed following infection by one of the four dengue viruses appears to increase the risk of severe dengue when the same individual is infected with any of the remaining three viruses. The new strategy uncovered in this study overcomes the prevailing challenges of vaccine development by tackling the virus' ability to 'hide' from the



host immune system. Dengue virus requires the enzyme called MTase (also known as 2'-O-methyltransferase) to chemically modify its genetic material to escape detection. The researchers discovered that by introducing a genetic mutation to deactivate the MTase enzyme of the virus, initial cells infected by the weakened MTase mutant virus is immediately recognized as foreign. As a result, the desired outcome of a strong protective immune response is triggered yet at the same time the mutant virus hardly has a chance to spread in the host. Animal models immunized with the weakened MTase mutant virus were fully protected from a challenge with the normal dengue virus. The

researchers went on to demonstrate that the MTase mutant dengue virus cannot infect *Aedes* mosquitoes. This means that the mutated virus is unable to replicate in the mosquito, and will not be able to spread through mosquitoes into natural environment. The results confirmed that MTase mutant dengue virus is potentially a safe vaccine approach for developing a universal dengue vaccine that protects from all four serotypes. Dengue is a major public health problem in many of the tropical countries. This study have made a promising step towards a cost-effective and safe dengue vaccine to combat the growing threat of dengue worldwide.

### Red Grapes, Blueberries Enhance Immune Function



Researchers discovered two compounds, the resveratrol found in red grapes and pterostilbene from blueberries. Both of these compounds are called stilbenoids, worked in synergy with vitamin D and had a significant impact in raising the expression of the human cathelicidin antimicrobial peptide, or CAMP gene, that is involved in immune function. The research was published in *Molecular Nutrition and Food Research*, in studies supported by the *National Institutes of Health*. "Out of a study of hundreds of compounds, just these two popped right out," said the researchers. "Their synergy with vitamin D to increase CAMP gene expression was significant and intriguing. It's a pretty interesting interaction"-they added. Resveratrol has been the subject of dozens of studies for a range of possible benefits, from improving cardiovascular health to fighting cancer and reducing inflammation.

The CAMP gene itself has been shown to play a key role in the "innate" immune system, or the body's first line of defense and ability to combat bacterial infection. A strong link has been established between adequate vitamin D levels and the function of the CAMP gene, and the new research suggests that certain other compounds may play a role as well. Stilbenoids are compounds which fight infections, and in human appear to affect some of the signaling pathways that allow vitamin D to do its job. It appears that combining these compounds with vitamin D has considerably more biological impact than any of them would separately. Despite the interest in compounds such as resveratrol and pterostilbene, their bioavailability remains a question. Some applications that may evolve could be with topical use to improve barrier defense in wounds or infections.

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## Coconut Oil Offers Promise for Antibiotic Resistant Germs

Some of the most promising research in recent years shows that, lauric acid or monolaurin, both derived from coconut oil, is effective in treatments for antibiotic resistant super germs. One of the most serious and intractable medical problems is that of antibiotic-resistant infectious microorganisms, the so-called "superbugs." These are- *Methicillin-Resistant Staphylococcus aureus (MRSA)*, *Bacillus anthracis Sterne*, virulent *Escherichia coli*, *Klebsiella pneumoniae*, *Helicobacter pylori*, *Mycobacterium terrae*, viruses with lipid membranes, and a number of invasive fungi. This problem has led to interest in researching the use of natural products to enhance the treatment of infectious disease, such as coconut oil and other oils rich in lauric acid as well as herbal remedies, substances traditionally recognized for decades for their healing properties. Lauric acid and its derivative monolaurin from coconut oil have shown promise in these studies, published in *Toxicology* journals. Lauric acid, forms monolaurin in the animal body which can inhibit the growth of many pathogenic microorganisms. *In vitro* studies were performed on two strains of *S. aureus* and this was followed by *in vivo* studies in mice. The effects of monolaurin and originum, when used in combination were better than the most potent antibiotic and these safe antimicrobial agents could be useful for prevention and therapy of *S. aureus* and numerous other infections. One study done in the Philippines in 2008 found that, virgin coconut oil added to antibiotic therapy, help relieve the symptoms of community-acquired pneumonia in children faster than antibiotic therapy alone. The study included 40 children from 3 months to 5 years old, suffering from community-acquired pneumonia and were treated with intravenous ampicillin. Half of the group was randomized to also receive oral virgin coconut oil in a daily dose of 2 ml/kg body weight for three days. The researchers found that the respiratory rate normalized in 32.6 hours for the virgin coconut oil group vs 48.2 hours for the control group. After three days, 60 % of the controls still had crackles compared to 25% of the coconut oil group. The coconut oil group also had fevers for a shorter time, had normal oxygen saturation faster, and had shorter hospital stays. The researchers concluded: "coconut oil may boost ampicillin's effectiveness because it contains lauric acid, which is known to have antimicrobial properties". Antibiotics are not effective in treating viruses, but the lauric acid and monolaurin derived from coconut oil has been known to destroy viruses. There was an instance in the US in which an infant tested HIV positive had become HIV negative. The infant was fed a high coconut oil content with an infant formula. The action attributed to Monolaurin, which solubilize the lipids-in the envelope of the virus, causing the disintegration of the virus envelope. From 1999 – 2000 another study was done at Manila and the results shows - lauric acid did bring down the viral load of HIV patients. A study published in *Skin Pharmacology and Physiology*



shows that Virgin Coconut Oil-treated wounds healed much faster, by a decreased time of complete epithelialization and higher levels of various skin components. Another study published in the *Journal of investigative dermatology* found that the lauric acid had the potential to be more effective antibiotics in treating acne vulgaris. Research done in the Philippines found monolaurin from virgin coconut oil is more effective, in fighting *M. tuberculosis* as antibiotic drugs streptomycin, isoniazid, rifampicin, and ethambutol. A doctor in Florida saw excellent results from using coconut oil in treating *H. Pyloric* in the gut in his patients. The patients took one teaspoon of virgin coconut oil three times a day, and the results was good or better than taking antibiotics. So, as super germs continue to develop and antibiotics lose their effectiveness, coconut oil can be a possible alternative.

## 'Super Honey' with Amazing Power to Treat Wounds and Kill Superbug Infections

'Super honey': A known honey has produced amazing results treating wounds and infections. Honey has been used for its healing powers for thousands of years, although doctors favor penicillin and antibiotics. However, Surgihoney, which is stored in 10g sachets, can kill bacteria, parasites and fungal infections while also encouraging wounds to heal. The bio-engineered product Surgihoney was tested on babies, new mothers, cancer patients and the elderly for over a year in Hampshire hospitals.



Wounds and ulcers, including those infected with the superbug *Methicillin-Resistant Staphylococcus aureus (MRSA)*, healed within days, while the number of women who suffered infections after giving birth by Caesarean section has halved. It has also healed the wounds of soldiers returning from Afghanistan, and been used to treat acne and to protect the skin of cancer patients fitted with a catheter for chemotherapy. The

researchers said "It will revolutionise wound care around the world." Dr Dryden said: 'I have conducted numerous laboratory tests and compared it with honeys from around the world. 'I found Surgihoney better for treating every type of bug. So for the past year I have been using it on patients and the results have been amazing. There are plenty of products that can kill bacteria but they often don't help heal tissue.' 'Honey is a fantastic natural medicine. The important extra is that it kills the bugs

but doesn't damage the tissue.' The honey has also helped patients suffering from *MRSA*. Surgihoney is being developed by Ian Staples, a businessman who once owned the Halfords motor accessories chain. He bought an organic farm in Southern Chile, set up beehives then funded scientific researchers in Ireland to identify the unique health elements.

## Diagnosis & Follow-up

The Histopathological examination resulted in Actinomycosis and the patient recovered after long-term antibiotic therapy (intravenous ceftriaxone 2 gm four times a day for 1 month, followed by oral amoxicillin clavulanate 1 gm three times a day for 3 months). There was no relapse during the 1-year follow-up. Actinomycosis is a rare condition with frequent cervicofacial involvement caused by Actinomyces. In case of sinonasal involvement, the unresponsiveness to antibiotic therapy alone requires thorough surgical debridement. As for all odontogenic sinonasal conditions presenting no signs of orofacial fistulae, this case was treated according to the literature with nasal endoscopy and long-term antibiotics.



The turbocharged cephalosporin, all the way