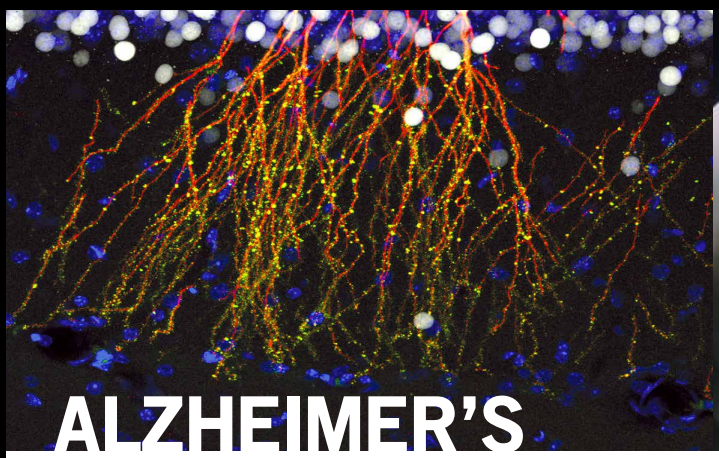
MEDBULLETIN



ALZHEIMER'S

LOWER BRAIN SEROTONIN: A DRIVER OF COGNITIVE DECLINE

SHEILA YU

An estimated 47 million people worldwide have dementia, with the majority of these cases being Alzheimer's Disease (AD).[1] AD is a neurodegenerative disease characterized by the deterioration of specific nerve cells, the formation of neuritic plaques, and the presence of neurofibrillary tangles.[2] Researchers have previously linked the characteristics of AD to severe declines in serotonergic neurons, but until recently, it was not clear whether these reductions were the cause or effect of the disease.[3]

A study published in *Neurobiology of Disease* suggests that lower levels of serotonin transporters (SERT) may precede neurodegeneration. Led by Clifford Workman at the Johns Hopkins School of Medicine, the research team compared 28 participants with mild cognitive impairment (MCI) to 28 controls throughout a series of memory tests, MRI scans, and PET scans. Lower SERT levels were observed in the cortical, limbic, and peri-limbic regions of MCI patients compared to healthy controls. Results from the study reveal a strong correlation between SERT levels and scores on the memory test in participants with MCI, suggesting that serotonin is heavily implicated in the early stages of cognitive decline.[4]

The conclusions from the study can be used to improve current methods of treatment for AD. Drugs such as cholinesterase inhibitors help to mask the symptoms of AD. However, they do not treat the underlying disease or slow its progression.[5] Methods to increase serotonin functioning in the brain provide a promising avenue to slow or stop the progression of AD along with other forms of dementia.[3] Studies are in progress to elucidate the mechanism of serotonin in the transition from MCI to dementia and to relate serotonin degeneration to other aspects of AD neuropathology.[4]

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DEVELOPMENT

ARTIFICIAL WOMBS: A SOLUTION FOR PREMATURE BABIES?

DANIEL DIATLOV

For years, researchers and physicians have been trying to extend the viability of babies that are born prematurely. Babies born under 37 weeks of gestation are considered premature and are at an increased risk for death and disability.[1] These risks increase exponentially the younger the age of the infant; the youngest possible age of viability is roughly 22 weeks.[1] Premature infants are usually placed on life support systems which allow for the maintenance of homeostatic stability. However, this increases their risk of infection, organ damage due to ventilation, and neurological defects.[2]

In recent decades, various researchers have been attempting to create artificial wombs in which a premature baby may continue to develop in a more stable and natural environment. The first successful attempt was in 1997 when Dr. Yoshinori Kuwabara of Juntendo University announced that a 17-week-old goat fetus survived for three weeks in an artificial womb.[3] The fetus was placed in a plastic container of warm amniotic-like fluid and supplied with nutrients through a tube inserted into its umbilical cord.[3]

Recently, in a paper published in June 2017, scientists used a technique called *ex vivo* uterine environment therapy to grow six premature lambs for one week in an artificial womb.[4] Five of the six lambs completed the week-long therapy with no significant physiological changes or defects.[4] The *ex vivo* uterine environment is essentially an amniotic fluid bath equipped with an artificial placenta that can sustain a developing preterm fetus.[4] It is important to note that the artificial womb is not intended to replace the human womb, but rather act as an alternative to current neonatal incubators. With refinement, this technology has the potential to be applied to human fetuses within the next decade, allowing for more successful outcomes in preterm fetuses. However, the ethics of such a therapy are questionable and have yet to be elucidated.

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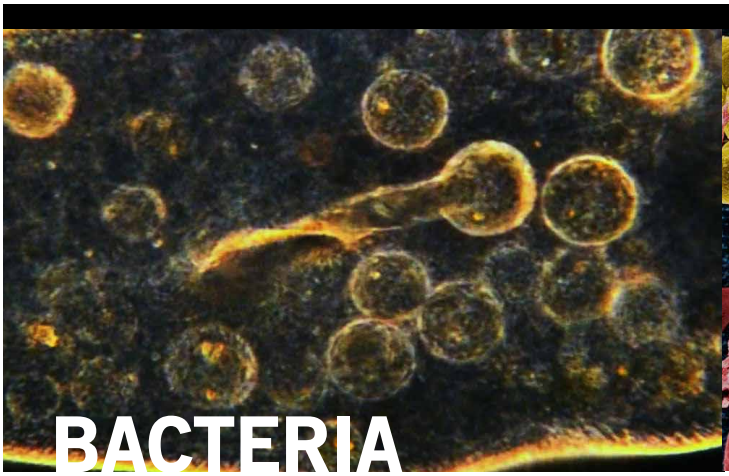

BACTERIA

PARALLELS IN SOCIETAL EVOLUTION BETWEEN MICROBES AND HUMANS

ADAM WADE-VALLANCE

In September of 2016, Mo et al. published an article in *Science* entitled "Spatiotemporal Microbial Evolution on Antibiotic Landscapes".[1] This landmark article describes a novel system for studying bacterial evolution. The findings elucidate the importance of antibiotic gradients in the emergence of antibiotic resistance in microbes and the many genetic pathways through which resistance can be achieved.[1]

Among these findings was one particular observation: evolution is not simply survival of the fittest.[1] The paper studied bacterial evolution using a system in which bacteria were inoculated into a large agar plate full of growth media. However, to move beyond their starting location to access more growth media, the bacteria had to evolve antibiotic resistance. At each stage, the concentration of local antibiotic increased ten-fold.[1] One would imagine that only the most resistant bacteria would able to reach the front of the ever-expanding bacterial population and forge onwards into unexplored territory and greener pastures. However, this was not the case.

The authors observed a unique effect whereby many highly-resistant mutants were trapped behind the progressing bacterial front. By virtue of being first, lesser-resistant bacteria had colonized ahead of highly resistant mutants, physically excluding them from expansion. This led the authors to conclude that the evolution and expansion of a bacterial population is not necessarily driven by its most evolved members.

Human society faces a similar phenomenon. Capitalism has been espoused as "survival of the fittest" for decades, yet this is a flawed truth. Fitness is surely required to survive in a capitalist society, but first-ness is also of great importance. High socioeconomic birth is accepted to predict success. Man, like microbe, is not governed purely by survival of the fittest.

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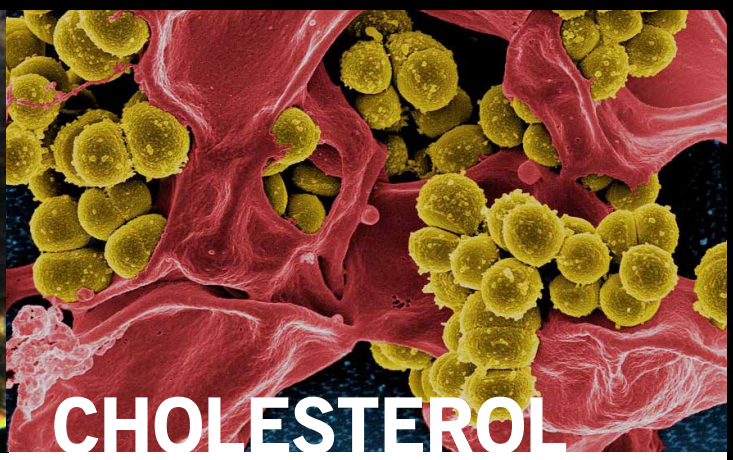

CHOLESTEROL

PCSK9 INHIBITORS FOR FAMILIAL HYPERCHOLESTEROLEMIA

KELVIN NG

Familial Hypercholesterolemia (FH) is a genetic disorder that causes abnormally high levels of low-density lipoprotein cholesterol (LDL-C), a risk factor for early onset cardiovascular diseases such as stroke or heart attack. FH is often caused by dysfunctional LDL-C receptors, preventing effective removal of circulating LDL-C, but may also arise through other mutations.[1]

1 in 500 people are heterozygous, having one allele for FH, while 1 in 1,000,000 people are homozygous, having two alleles.[2] Untreated, most homozygous FH patients develop cardiovascular disease by 20 and die by 30. Heterozygous FH is fortunately less severe, but still dramatically increases the risk of cardiovascular disease.

Clearly, FH requires aggressive cholesterol lowering therapy. Statins, which have traditionally been used to lower LDL-C levels, are often insufficient. In fact, Pijlman et al. found that only 21% of FH patients on statins reach target LDL-C goals set by doctors.[3] In cases where statins are inadequate, patients are forced to combine therapies or undergo invasive procedures.[4] A new class of drugs to enter the market, PCSK9 inhibitors, are much more powerful than statins. PCSK9 breaks down LDL-C receptors, preventing their ability to remove LDL-C from the blood. Thus, PCSK9 inhibitors prolong the lifespan of LDL-C receptors and allow for increased removal of LDL-C. Shown to lower LDL-C by 30-40%, PCSK9 inhibitors are very effective at treating FH patients.[5] PCSK9 inhibitors present an exciting opportunity to improve FH management, and with time may have a significant impact on the pharmaceutical industry at large due to their increased effectiveness compared to statins. Currently, however, PCSK9 inhibitors are not cost effective at the price of $503,000 per quality-adjusted-life-year gained.[6]

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