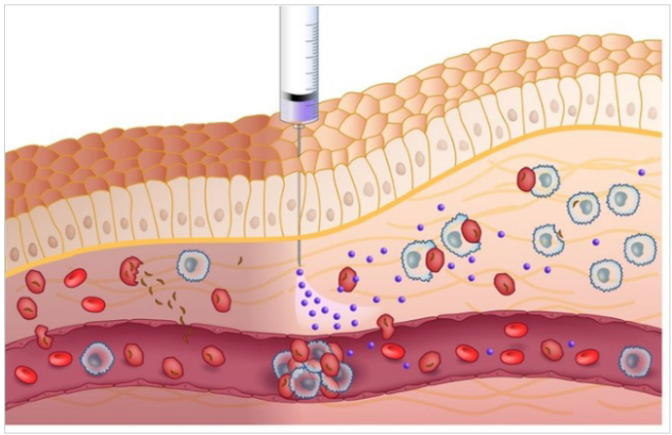
Role Of Interstitial Space in Malaria Recurrence and Treatment

A recent article published in *Nano Research* stated that the vital role of interstitial space in malaria infection and treatment has been neglected in current research efforts.

Here, the authors informed about the reinfection capacity of parasites sequestrated in the interstitial space, which combat the mechanism of recurrence. Malarial parasite-infected mice were treated with artemisinin-loaded liposomes through the interstitial space and exhibited a better therapeutic response. Notably, compared with oral administration, interstitial administration showed an unexpectedly high activation and recruitment of immune cells and resulted in better clearance of parasites from organs, as well as enhanced pathological recovery.



It was inferred that the interstitial route of administration prolongs the blood circulation time of artemisinin and increases its plasma concentration, and may compensate for the inefficiency of oral administration and the nanotoxicity of intravenous administration – providing a potential strategy for infectious disease therapy.

Low Doses Of 'Laughing Gas' Could Be Fast, Effective Treatment for Severe Depression

A new study at the University of Chicago Medicine and Washington University found that a single inhalation session with 25% nitrous oxide gas was nearly as effective as 50% nitrous oxide at rapidly relieving symptoms of treatment-resistant depression, with fewer adverse side effects. The study, published in *Science Translational Medicine,* also found that the effects lasted much longer than previously suspected, with some participants experiencing improvements for upwards of two weeks.

These results bolster the evidence that non-traditional treatments may be a viable option for patients whose depression is not responsive to typical antidepressant medications. It may also provide a rapidly effective treatment option for patients in crisis.

Often called "laughing gas," nitrous oxide is frequently used as an anesthetic that provides short-term pain relief in dentistry and surgery.

In a prior study, the investigators tested the effects of a one-hour inhalation session with 50% nitrous oxide gas in 20 patients, finding that it led to rapid improvements in the patient's depressive symptoms that lasted for at least 24 hours when compared to placebo. However, several patients experienced negative side effects, including nausea, vomiting and headaches.

"This investigation was motivated by observations from the research on ketamine and depression," said Peter Nagele, MD, Chair of Anesthesia and Critical Care at UChicago Medicine. "As nitrous oxide, ketamine is an anesthetic, and there has been promising work using ketamine at a sub-anaesthetic dose for treating depression. We wondered if our past concentration of 50% had been too high. Maybe by lowering the dose, we could find the 'Goldilocks spot' that would maximize clinical benefit and minimize negative side effects."

Relationships Between Serum Electrolyte Concentrations and Ileus

Prolonged postoperative ileus (PPOI) occurs in around 15% of patients after major abdominal surgery, posing a significant clinical and economic burden.

A new article published in *Physiological Reports* evaluated peri-operative electrolyte concentration trends and their association with ileus and predicted the impact on bioelectrical slow waves in interstitial cells of Cajal (ICC) and smooth muscle cells (SMC).

In this joint clinical-theoretical prospective study, data were collected from 327 patients undergoing elective colorectal surgery.

The findings showed that – on the postoperative day (POD) 1 calcium and POD 3 chloride, sodium was lower in the PPOI group and POD3 potassium was higher in the PPOI group. Deficits beyond the reference range in PPOI patients were most notable for sodium. Models demonstrated an 8.6% reduction in slow-wave frequency after the measured reduction in extracellular NaCl on POD5 was associated with

changes in cellular slow-wave morphology and amplitude.

The results suggested that low serum sodium and chloride concentrations are associated with PPOI. Electrolyte abnormalities are unlikely to be a primary mechanism of ileus. However, electrolyte abnormalities may adversely impact motility recovery. Hence, resolution and correction of electrolyte abnormalities in the ileus may be clinically relevant.

Unusual Copper and Iron Found Forming in Brains of Alzheimer's Patients

A team of researchers associated with several institutions in the U.K., Germany and the U.S. has found evidence of an unusual kind of copper and iron in the brains of Alzheimer's patients. In their paper published in the journal *Science Advances*, the group describes their discovery of the metals in two Alzheimer's patients and what it could mean for the study and treatment of the disease.

Alzheimer's is a progressive brain disorder. Brain cells waste away, leaving those afflicted to lose brain function until they eventually die; there is no cure. In this new effort, the researchers have made what they describe as a surprising discovery—small amounts of a certain kind of copper and iron inside of amyloid plaque samples taken from two Alzheimer's patients.

Copper and iron are found throughout the bodies of healthy people, including the brain. The body uses them for a variety of purposes. Also, they can both exist in the body in different oxidation states depending on the compound where they reside. The body also regulates such metals because they can take on harmful forms; harmful types are expelled. In this new effort, the researchers found some of those harmful elemental forms in the amyloid plaque, one of the hallmarks of Alzheimer's.

The work involved collecting brain tissue from two deceased Alzheimer's patients and then using X-ray imaging to learn more about the material inside of the plaque that had formed in the tissue. It was during this study that the team found traces of unusual forms of copper and iron. More specifically, they found nanoparticles of both in the cores of the plaque that had not oxidized—they had not gained or lost any electrons. They note this is the first instance of such nanoparticles being seen in human tissue of any kind. The researchers suggest the metals they found could explain how Alzheimer's harms cells—their surfaces would be highly reactive, which could lead to damage when exposed to brain cells.

Vitamin D Deficiency May Increase the Risk for Addiction to Opioids and UV Rays

Vitamin D deficiency strongly exaggerates the craving for and effects of opioids, potentially increasing the risk for dependence and addiction, according to a new study led by researchers at Massachusetts General Hospital (MGH). These findings, published in *Science Advances*, suggest that addressing the common problem of vitamin D deficiency with inexpensive supplements could play a part in combating the ongoing scourge of opioid addiction.

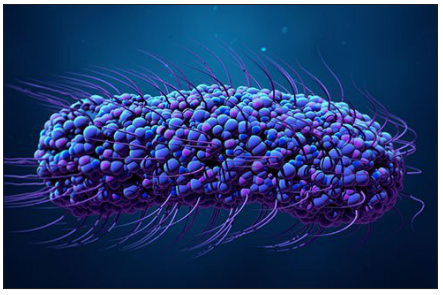
Earlier work by David E. Fisher, MD, PhD, director of the Mass General Cancer Center's Melanoma Program and director of MGH's Cutaneous Biology Research Center (CBRC), laid the foundation for the current study. In 2007, Fisher and his team found something unexpected: Exposure to ultraviolet (UV) rays (specifically the form called UVB), causes the skin to produce the hormone endorphin, which is chemically related to morphine, heroin and other opioids all activate the same receptors in the brain. A subsequent study by Fisher found that UV exposure raises endorphin levels in mice, which then display behavior consistent with opioid addiction.

The theory led Fisher and colleagues to hypothesize that sun-seeking is driven by vitamin D deficiency, to increase the synthesis of the hormone for survival and that vitamin D deficiency might also make the body more sensitive to the effects of opioids, potentially contributing to addiction. "Our goal in this study was to understand the relationship between vitamin D signaling in the body and UV-seeking and opioid-seeking behaviors," says lead author Lajos V. Kemény, MD, PhD, a postdoctoral research fellow in Dermatology at MGH.

Post-Operative Intensive Care Unit Care and Outcome of Typhoid Perforation

Typhoid perforation ileitis is a serious complication of typhoid fever. The purpose of a recent study published in the African Journal of *Pediatric Surgery* was to deduce the rate of post-operative Intensive Care Unit (ICU) admission in patients with typhoid perforation who underwent surgical correction.

This was a prospective observational study in which 67 consecutive patients who had exploratory laparotomy for typhoid perforation in the University College Hospital, Ibadan, were studied.



It was found that overall, 37.3% required critical care. Reasons for admission included poor respiratory effort, hypotension, septic shock and delayed recovery from anesthesia. While 84% of patients required mechanical ventilation with a duration range of 1-5 days. Fourteen patients required ionotropic support and the length of ICU stay ranged from 1-15 days. Meanwhile, 76% of patients were successfully managed and discharged to the ward; however, a mortality rate of 24% was recorded.

The results depicted a high rate of postoperative ICU admission in patients with typhoid perforation, with a high demand for critical care involving mechanical ventilation and ionotropic support. Therefore, in centers that manage patients presenting with typhoid ileitis and perforation, postoperative critical care should be available.

People With HIV Are at Higher Risk of Ageing-Related Genetic Changes

We don't know enough about biological processes in people who are aging with HIV—a new study sheds light on the matter.

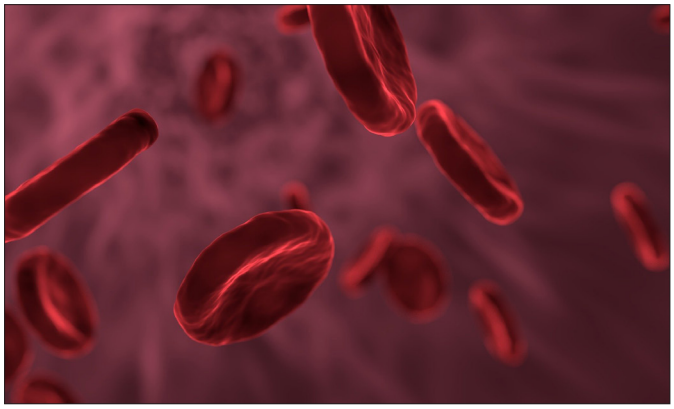
Forty years after the first diagnosis of HIV/AIDS, Australian scientists from the Kirby Institute at UNSW Sydney and the Peter MacCallum Cancer Center have uncovered a vital link in the relationship between HIV and aging. The results were published today in the journal *Nature Medicine.*

In this world-leading study, the research team

evaluated age-related genetic changes in over 400 participants from nine sites at hospitals and community practices. Half of the participants had HIV, and half did not.

The study found that people living with HIV had a higher rate of clonal haematopoiesis (CH) - a common condition among older people caused by a genetic mutation in a small number of blood stem cells.

"One in ten older people in the general population have these mutations in their blood cells, but our study found that one in five people with HIV has these mutations," says Dr Nila Dharan from the Kirby Institute, co-lead author on the paper.



Severe Hyponatremia in Infants with Urinary Tract Infection

Although secondary pseudohypoaldosteronism (PHA) is rare in UTI, it is a known association. Features include hyponatremia and concomitant hyperkalemia.

The goal of a new article published in *Frontiers in Pediatrics* was to highlight uncommon sequelae in UTI to avoid incorrect diagnosis and unnecessary investigations.

This study used clinical data of patients admitted and referred to a pediatric nephrologist at the University Malaya Medical Center from 2019-2020.

Three infants had hyponatremia and hyperkalemia during UTI episodes. Two of these were known to have a posterior urethral valve (PUV) before the onset of UTI and one had UTI, which led to investigations confirming the diagnosis of bladder vaginal fistula. It was noted

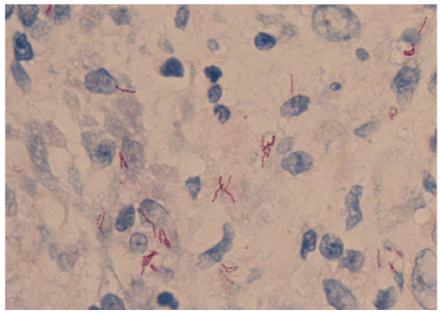
that the electrolyte derangements were temporary and resolved within 48-72 hours of treatment with i.v. fluid and appropriate antibiotic therapy. PHA was confirmed in only one. Reduced aldosterone activity could be due to an absolute reduction in aldosterone titer or a lack of aldosterone responsiveness at the tissue level. In cases with reduced responsiveness, the aldosterone titer is elevated. The infant who had PHA had the mentioned electrolyte abnormalities with a markedly elevated aldosterone titer. This signified the defective action of the hormone at the level of the mineralocorticoid receptor. Although the remaining two infants had no confirmatory hormonal study, all of them recovered within 48 hours of hospital admission, after receiving appropriate treatment for UTI. Moreover, there was a slower recovery of hyponatremia in relation to hyperkalemia, but none of these infants required salt replacement upon discharge.

It was recommended that infants with severe UTI and deranged electrolytes should be screened for structural abnormality and vice versa. Infants who require prolonged salt replacement or show involvement of other systems may require further evaluation, such as hormonal screening.

Physiology Of Cough in Elderly Women with Non-Tuberculous Mycobacterial Lung Infections

Women who are elderly white, thin and non-smoking seem to be more vulnerable to lung infections with Mycobacterium avium complex and few other non-tuberculous mycobacteria (NTM). It has been assumed that such disease in these women is mostly related to the suppression of their cough.

A study has hypothesized that patients with pulmonary NTM (pNTM) infections might have altered cough physiology as compared to the unaffected control participants. Cough was induced by a small dose of capsaicin to assess the cough reflex in pNTM subjects. Almost 8 elderly white women with stable chronic pNTM



infections and 6 unaffected age-matched control participants were enrolled. No significant difference was seen between groups in capsaicin-elicited cough motor response, cough frequency or airflow pattern. The urge-to-cough (UTC) score at the lowest capsaicin concentration was suggestively lower in pNTM as compared to the control participants ($P < 0.05$).

No significant differences were seen in the UTC score between pNTM and control participants at >50 μM capsaicin. The results suggested the lower UTC sensitivity to the lowest capsaicin concentration in pNTM as compared to the control participants. This means that the pNTM participants do not sense a UTC when the stimulus is comparatively small.

The study published in *PubMed* has evaluated the cough sensitivity and cough motor response in patients with nontuberculous mycobacteria (NTM) infection. These study findings are important to recognize the pathophysiological mechanisms that resulted in NTM disease in elderly white women and the syndrome that was developing in elderly white female NTM patients.

Early Lung Cancer Co-Opts Immune Cell into Helping Tumors Invade the Lungs

Immune cells that normally repair tissues in the body can be fooled by tumors when cancer starts forming in the lungs and instead help the tumor become invasive, according to a surprising discovery reported by Mount Sinai scientists in *Nature*.

The researchers found that early-stage lung cancer tumors co-opt the immune cells, known as tissue-resident macrophages, to help invade lung tissue. They also mapped out the process, or program, of how the macrophages allow a tumor to hurt the tissues the macrophage normally repairs. This process allows the tumor to hide from the immune system and proliferate into later, deadly stages of cancer.

Macrophages play a key role in shaping the tumor microenvironment, the ecosystem that surrounds tumors in the body. By investigating this microenvironment, researchers can find key players that drive tumor growth that can be tested as targets for immunotherapy. But modifying macrophages therapeutically has proven difficult.

In this study, scientists studied tissue samples from lung cancer tumors and surrounding lung tissue in 35 patients to see the role of macrophages in the development of the tumors.

Researchers identified the macrophages at play in the early development of lung cancer, identifying a potential target for future drug development. They also found that the process that allows the macrophages to help tumors invade lung tissues is present in mice as well, which will allow them to manipulate the macrophages in future mouse models knowing that the manipulation is relevant to humans.

Half of all early-stage lung cancers relapse, and once they do and reach later stages, it is deadly and irreversible. Knowing how to attack the cancer at an early stage could have huge impacts on the number of patients relapsing and their overall survival.