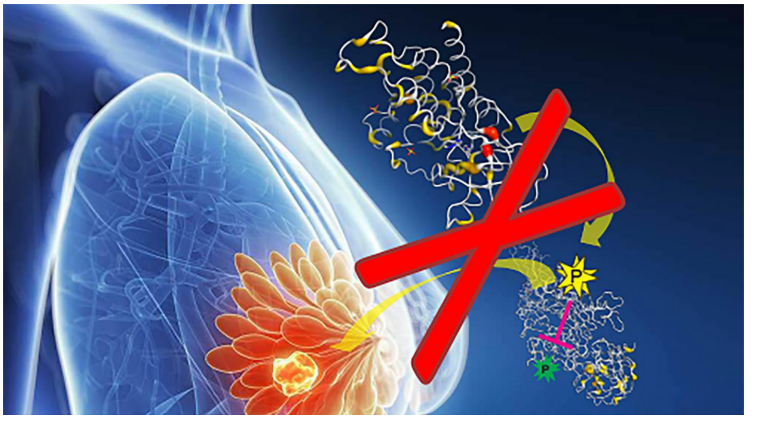
Study Reveals Individuals' Susceptibility to Cancer-Causing Agents

A UK study has suggested new insights into the mechanisms behind how cancer-causing agents in the environment activate genetic recombination in DNA could help to explain some of the effects of exposure as well as predicting which individuals may be more susceptible to developing the disease.



One of the most widely found carcinogens is benzopyrene—a general chemical pollutant found in smoke from stoves such as wood burners, exhaust fumes and barbequed meat and fish. One active ingredient of benzopyrene, BPDE, directly damages the DNA sequence forming what is known as adducts which in turn promote cancer-causing mutations.

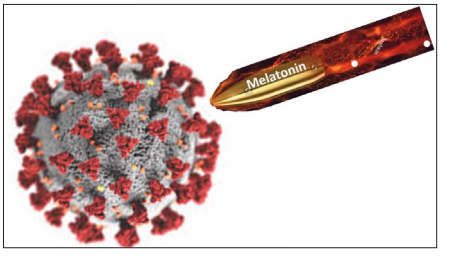
This latest study treated human cell lines with BPDE before using molecular biology methods, such as microscopy, to characterize the homologous recombination pathway in detail. Results have offered new insights showing that HR proceeds by an unusual mechanism at BPDE adducts and the process can be activated even when there are no stalled or collapsed replication forks. Instead, it is activated at single-stranded gaps in the DNA that are generated by the re-priming activity of PrimPol—a protein encoded by the PRIMPOL gene in humans.

The findings also address longstanding questions by showing that at bulky DNA adducts, the exchanges between the sister chromatids (the identical copies formed by the DNA replication of a chromosome), products of HR that have been traditionally connected with replication fork collapse and DSB repair, are associated with the repair of post-replicative gaps. Furthermore, these post-replicative gaps are produced by PrimPol, shedding light on the function of PrimPol during DNA damage tolerance.

The paper "PrimPol-dependent single-stranded gap formation mediates homologous recombination at bulky DNA adducts" is published in *Nature Communications.*

Melatonin's Potential to Treat COVID-19

According to a new study from the Cleveland Clinic, Melatonin could be a possible treatment for those who contract the coronavirus. The findings were published in the journal *PLOS Biology.*



The hormone, which regulates the body's circadian rhythm and sleep-wake cycle, was associated with a 30% reduced likelihood of testing positive for COVID-19. However, additional studies are needed, the researchers said.

The research team analyzed patient data from Cleveland Clinic's COVID-19 registry and saw that melatonin usage was related to a reduced likelihood of testing positive. They specifically looked at the common symptoms and causes of death for severe COVID-19 and other diseases, such as sepsis and respiratory distress syndrome, to see if any current drugs on the market could help with coronavirus cases.

Overall, they determined that autoimmune, lung and neurological diseases were most similar to the disease caused by the coronavirus, and they identified 34 potential drugs that might help. Melatonin was a top contender among them.

"It is very important to note these findings do not suggest people should start to take melatonin without consulting their physician," Feixiong Cheng, the lead author of the study and a researcher in the Cleveland Clinic's Genomic Medicine Institute, said in a statement.

Treatment of Benign Prostatic Hyperplasia with Urolift Advanced Tissue Control

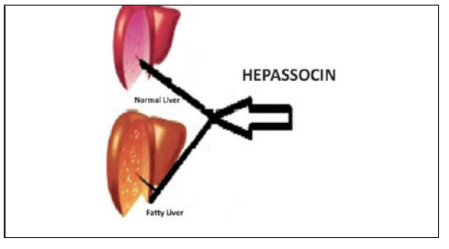
Urolift Advanced Tissue Control system, launched by Teleflex is a product designed to treat patients with benign prostatic hyperplasia (BPH). The system can be used to open the urethra by inserting small implants that hold the lobes of the prostrate in a retracted position. The device is specifically tailored to treat those with challenging prostatic anatomy, including those with large lateral lobes and an obstructive median lobe.

The Urolift system aims to provide a minimally invasive approach to treating the condition, and does not require an incision or destructive enlargement of the urethra. Patients can be treated in an outpatient procedure that takes only about an hour or two. A urologist can advance the device into the urethra under cystoscopic visualization, and then use it to insert small implants around the enlarged prostatic lobes, pushing them aside to create more space.

Tissue control wings that help to hold tissue back during the procedure are included in the new system, helping the urologist to visualize the blockage more easily. The device tip has also been enhanced, making it easier to deliver the implants. Laser-etched indicators on the needle location marker also help to predictably place the implants.

Overexpression of Hepassocin in Diabetic Patients Increases Hepatic Lipid Accumulation

According to a study 'Endocrine, Metabolic & Immune Disorders - Drug Targets Drug Targets', published in 2019, overexpression of hepassocin (HPS) increased the accumulation of hepatic fat and NAFLD activity scores (NAS) in mice. The aim of this study was to investigate the relationship between hepassocin and steatosis of the liver in diabetic patients with or without NAFLD in humans. Insulin resistance is the actual determining factor for both Non-alcoholic fatty liver disease (NAFLD) and diabetes, and can simplify the accumulation of triglycerides in the liver.



The study enrolled 60 patients plus 20 healthy controls that were divided into 4 groups: Group I: included 20 patients who were diagnosed as diabetes mellitus type 2, Group II: included 20 patients who were diagnosed as nonalcoholic fatty liver disease (NAFLD), Group III: included 20 patients who were diagnosed as diabetes type 2 and NAFLD, and Group IV (control group): included 20 healthy person or controls who were matched in age and sex with patients group. All patients and controls were subjected to full history taking, thorough clinical examination, laboratory investigations including measurement of serum hepassocin in peripheral blood by ELISA technique.

There was a significant overexpression of serum hepassocin in patients with type 2 diabetes and NAFLD patients (Group 3) more than diabetic patients (Group 1) and even more than non-alcoholic fatty liver disease (Group 2).

This study provides evidence that increased HPS may facilitate increased hepatic lipid accumulation with NAFLD and type 2 diabetes.

Vaccine Preservation without Refrigeration

Chemical engineers from the United States of America have developed a new way to stabilize vaccines with proteins instead of relying on refrigeration. The scientists, including those from the Michigan Technology University in the US, said vaccines typically require shipping temperatures ranging from 2 to 8 degrees Celsius, and half of them are wasted annually because they aren't kept cold enough.

According to the study, published in the journal *Biomaterials*

Science, the viruses in vaccines, which train our cells to identify and vanquish viral invaders, unfold when it's hot, or when there's space to move around.

In the current study, the researchers developed a way to mimic the body's crowded environment in vaccines without relying on refrigeration.

They used synthetic proteins that have positive or negative charges and stick together and form a separate liquid phase when put in a solution -- a process called

complex coacervation.

According to the researchers, this liquid phase wraps around the outer cover of viruses, holding the inner material together.

"Coacervate materials are something that we actually see all of the time in our daily lives," said Sarah Perry, study co-author from the University of Massachusetts Amherst in the US.

The researchers said this process works for nonenveloped viruses, such as polio the and common cold virus, which have no lipid, or fatty layer, around them.

"We need to understand how different polymers interact with our viruses and how we can use this to create a toolbox that can be applied to future challenges," Perry added.

New Report Suggests *In Utero* SARS-CoV-2 Transmission

A new report of mother-to-fetus transmission of SARS-CoV-2 through umbilical cord blood adds to an evidence that the virus can be transmitted in utero. Further, this case suggests such infections may not be easily detectable in neonates until days after birth.

Isabelle Von Kohorn, MD, PhD, of Holy Cross Health in Silver Spring, Md., and colleagues, described a case of neonatal infection with SARS-CoV-2 in a boy delivered by C-section at 34 weeks to a mother diagnosed with COVID-19 some 14 hours before. The newborn was immediately removed to a neonatal ICU and reunited with his mother a week later, once the mother had recovered. The report is published in the Journal of the *Pediatric Infectious Diseases Society*.

Von Kohorn and colleagues reported that, while the infant's nasopharyngeal swab test for SARS-CoV-2 was negative at 24 hours after birth, repeat molecular tests (using different assays) from 49 hours on were positive and indicated an increasing viral burden, although the infant never developed symptoms of COVID-19. In addition to being found in the nasopharynx, viral RNA also was detected in cord blood and in urine. No viral RNA was found in the placenta.

The circumstances of the birth, and the care taken to keep mother and her infant at a safe distance along with masking of the mother, made it "extremely unlikely" that the infant acquired his infection by the respiratory route, Von Kohorn and colleagues wrote.

"While we cannot rule out microscopic maternal blood contamination of cord blood in this or any other delivery, cord blood collection procedures are designed to avoid gross contamination with maternal blood. Microscopic contamination would not explain the RNA levels observed in our patient's cord blood," they wrote.

Clinicians should note that a neonate born to a mother with COVID-19 may take time to test positive for SARS-CoV-2 , the investigators argued, though the current recommendation of the American Academy of Pediatrics is to test nasopharyngeal secretions of well newborns at 24 and 48 hours but not again in the absence of symptoms. "This case suggests that some cases of SARS-CoV-2 in newborns may be detectable only after 48 hours of life."

Lung Ultrasound Better than Chest X-Ray for COVID-19 Diagnosis

According to a new research, point-of-care lung ultrasound is better than chest x-ray for diagnosis of COVID-19 pneumonia.

Investigators compared the diagnostic performance of lung ultrasound (LUS) performed with a portable hand-held device with chest x-ray (CXR) in patients at high-risk for COVID-19.

"Lung ultrasound sensitivity outperforms chest x-ray," Kendra Mendez, MD, Temple University Hospital, Philadelphia, Pennsylvania, said in her presentation at the American College of Emergency Physicians (ACEP) 2020 "Unconventional" online congress.

The prospective study was performed over a 2-week period in April 2020 during a surge in COVID-19 cases at Temple University Hospital. A total of 143 patients age 18 and over with signs and symptoms of COVID-19 were enrolled as they came into the emergency department. To enroll, patients had to present with a temperature of 100.4° Fahrenheit (38° Celsius) or higher, a heart rate of 100 bpm or higher, a respiratory rate of 16 rpm or greater, SpO2 less than 94%, and presentation of a combination of cough, dyspnea, myalgia, malaise, ageusia, and anosmia.

"Pregnant patients and those unable to consent were excluded," Mendez noted.

In addition, medical residents or an emergency physician performed an LUS using a portable device, followed by a portable anterior-posterior CXR on all participants.

In the 70 patients with both positive LUS and CXR test results, 58 had a positive NCCT.

In the 42 patients with a positive LUS and a negative CXR, only 23 had a positive NCCT.

In the six patients who had a positive CXR and a negative LUS, there were no positive NCCTs, indicating lung ultrasound was the more reliable indicator.

Researchers performed an NCCT on seven of the 25 remaining patients who had negative LUS and CXR, because they presented with high-risk symptoms including lymphopenia less than 1000/mm3, a temperature higher than 101° Fahrenheit, a heart rate equal to or higher than 110 bpm, a respiratory rate of 20 or more, oxygen levels lower than 92%, systolic blood pressure lower than 100 mmHg, and were considered immunocompromised.

Two out of these seven patients had a positive NCCT result.

"Both had similarly poor specificities," Mendez reported in her talk.

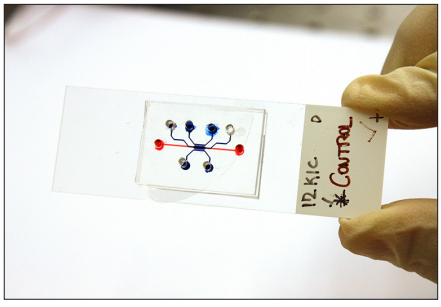
She reported that LUS had a sensitivity of 97.6% (95% confidence interval [CI], 91.6 - 99.7) compared with CXR at 69.9% (95% CI, 58.8 - 79.5). Specificity was 33.3% (95% CI, 16.5 - 54.0) for LUS and 44.4% (95% CI, 25.5 - 64.7) for CXR.

"This study supports portable bedside ultrasound in addition to chest x-ray as a possible screening modality for patients with suspected COVID-19 pneumonia," Bret Nicks, MD, Wake Forest University, Winston-Salem, North Carolina, who was not involved in the study, told *Medscape Medical News* in an email interview. This will help determine a diagnosis, he said, as "patients presenting to the emergency department with COVID-19 can have a broad constellation of signs and symptoms."

Mendez added that LUS can be an especially valuable triage screening modality in resource-limited settings.

Researchers Develop Microfluidic Device to Test Pancreatic Cancer Drugs

Researchers at Purdue University have developed a unique microfluidic device that can be used to test a cancer drug on multiple tumor cells subtypes. Using this technology, the researchers believe that new drug therapies can be discovered and existing medicines used more effectively.



The new microfluidic device features specially designed collagen channels that function as the pancreatic duct on a very small scale. Within, a mix of cancer cells can grow and proliferate and various therapies can be delivered into the channels. In the past, similar devices have been used to work with late-stage tumor cells, but the new technology is intended to be used with earlier cell lines that have not yet mutated. This may help to find out which therapies are most effective at preventing mutations from happening.

Treatment of Glaucoma with New Technique to Regenerate Optic Nerve

Scientists have used gene therapy to regenerate damaged nerve fibres in the eye, in a discovery that could aid the development of new treatments for glaucoma, one of the leading causes of blindness worldwide.

In a study published today in *Nature Communications*, scientists tested whether the gene responsible for the production of a protein known as Protrudin could stimulate the regeneration of nerve cells and protect them from cell death after an injury.

The team, led by Dr. Richard Eva, Professor Keith Martin and Professor James Fawcett from the John van Geest Centre for Brain Repair at the University of Cambridge, used a cell culture system to grow brain cells in a dish. They then injured their axons using a laser and analysed the response to this injury using live-cell microscopy. The researchers found that increasing the amount or activity of Protrudin in these nerve cells vastly increased their ability to regenerate.

Nerve cells in the retina, known as retinal ganglion cells, extend their axons from the eye to the brain through the optic nerve in order to relay and process visual information. To investigate whether Protrudin might stimulate repair in the injured CNS in an intact organism, the researchers used a gene therapy technique to increase the amount and activity of Protrudin in the eye and optic nerve. When they measured the amount of regeneration a few weeks after a crush injury to the optic nerve, the team found that Protrudin had enabled the axons to regenerate over large distances. They also found that the retinal ganglion cells were protected from cell death.

The researchers showed that this technique may help protect against glaucoma, a common eye condition. In glaucoma, the optic nerve that connects the eye to the brain is progressively damaged, often in association with elevated pressure inside the eye. If not diagnosed early enough, glaucoma can lead to loss of vision. In the UK, round one in 50 people over the age of 40, and one in ten people over the age of 75 is affected by glaucoma.

To demonstrate this protective effect of Protrudin against glaucoma, the researchers used a whole retina from a mouse eye and grew it in a cell-culture dish. Usually around a half of retinal neurons die within three days of retinal removal, but the researchers found that increasing or activating Protrudin led to almost complete protection of retinal neurons.

Dr. Veselina Petrova from the Department of Clinical Neurosciences at the University of Cambridge, the study's first author, said, "Our strategy relies on using gene therapy—an approach already in clinical use—to deliver Protrudin into the eye. It's possible our treat-

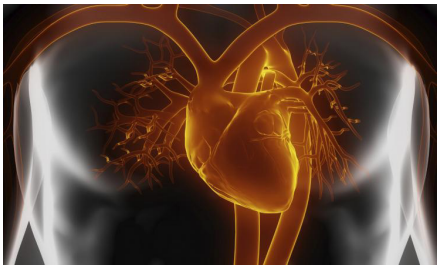
ment could be further developed as a way of protecting retinal neurons from death, as well as stimulating their axons to regrow. It's important to point out that these findings would need further research to see if they could be developed into effective treatments for humans."

Protrudin normally resides within the endoplasmic reticulum, tiny structures within our cells. In this study, the team showed that the endoplasmic reticulum found in axons appears to provide materials and other cellular structures important for growth and survival in order to support the process of regeneration after injury. Protrudin stimulates transport of these materials to the site of injury.

Bone Hormone can Play Role in New Treatment for Cardiac Rhythm Disorder

According to researchers, a hormone that helps regulate bone mass is also produced by the heart and could be used to treat people with a dangerous heart rhythm disorder.

Researchers at the University of Oxford also found that the hormone plays a vital role in reducing atrial scarring. Such scarring makes it harder for electrical impulses to travel smoothly through the atria and can cause them to beat in a chaotic manner, known as atrial fibrillation (AF).



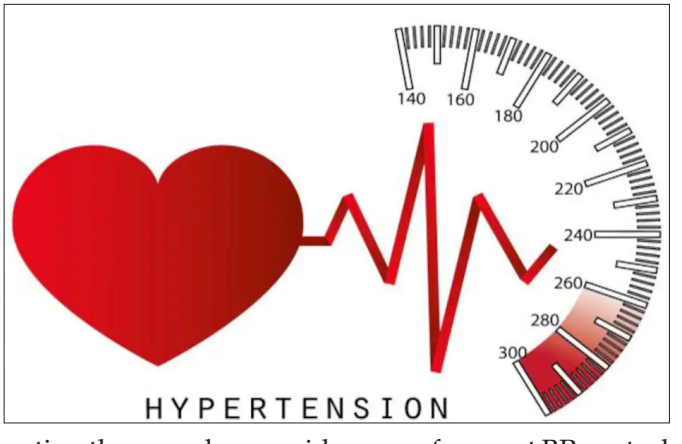
Until now, the hormone calcitonin was only thought to be produced by the thyroid gland, with no known effects on the heart. Research published in *Nature* has revealed that cells in the upper chambers of the heart, known as the atria, produce approximately 16 times more calcitonin than cells in the thyroid.

The researchers studied muscle cells from atrial biopsies taken from people undergoing heart surgery and found that they released calcitonin. Interestingly, cells from biopsies of patients with severe AF produced six times less calcitonin.

Looking further, they saw that the calcitonin receptor was present in atrial cells responsible for producing collagen, a major component of scar tissue. When the team treated these cell called fibroblasts with calcitonin, the cells produced 46 percent less collagen.

2-Drug Combination Treatment for Hypertension

Recent evidence has confirmed the protective effects of 2-drug combination therapy. The hypertension guidelines from European Society of Cardiology (ESC) and the European Society of Hypertension (ESH 2018) and International Society of Hypertension (2020)4, taking these aspects into account, thus mandate the initial use of 2-drug combinations as the first-step of antihypertensive therapy for specific patients with hypertension. Preferred combinations for therapy include calcium channel blocker (CCB)/diuretic + angiotensin receptor blocker (ARB)/ angiotensin-converting enzyme inhibitor (ACEI) due to their complementary effects.



Two-drug treatment enhances hypertension management in several ways. It results in greater BP reduction compared to monotherapy with a steeper correlation between the dose and the BP response. The BP reduction achieved is swift and shows lesser variation in response across patients. Moreover, this BP-lowering is accompanied by a complete lack of or only a slight increase in hypotensive episodes. Combination therapy also provides more frequent BP control along with better adherence to drug treatment and decreased therapeutic inertia.

These advantages were ably supported with clinical data. The National Health and Nutrition Examination Survey showed that compared with monotherapy, patients administered with either free/single-pill combinations (SPC) of antihypertensive agents pre-

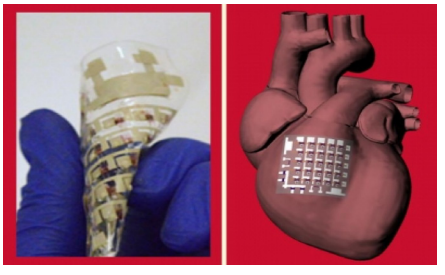
sented with a greater and more frequent BP control (BP <140/90 mmHg) after 1 year. Another study, involving ~4,40,000 patients, showed that drug combinations decreased the rate of therapy discontinuation vs monotherapy, irrespective of the form in which the 2-drug combinations were given (separate pills or SPC). This is significant since increased adherence to anti-hypertensive treatment has been clinically correlated with incidence and risk of CV events. In fact, evidence showed that compared to a <25% adherence rate, a >75% adherence to antihypertensive drugs resulted in a progressive reduction in the risk of hospitalization for cerebrovascular disease, ischemic heart disease and heart failure, across patient subgroups.

Both ESC/ESH and ISH guidelines recommend the use of 2-drug SPCs for antihypertensive therapy. Though SPCs may make it inconvenient to uptitrate treatment effectively if required, several studies have shown that decreasing the number of pills consumed daily have uniformly helped enhance treatment adherence, in spite of variation in baseline patient criteria like CV risk, duration of therapy, age and comorbidity status. SPCs have also proved to be an economical option for therapy with the added advantage of favourable tolerability due to the lower doses of individual drugs. Thus, therapy with a SPC can improve the speed, efficacy and reliability of BP control.

Novel Rubbery Patch for Monitoring and Treating Cardiac Disease

Researchers led by a mechanical engineer from the University of Houston have developed a patch made from fully rubbery electronics that can be placed directly on the heart to collect electrophysiological activity, temperature, heartbeat and other indicators; all at the same time.

The novel device marks the first time bioelectronics have been developed based on fully rubbery electronic materials that are compatible with heart tissue, allowing the device to solve the limitations of previous cardiac implants, which



are mainly made out of rigid electronic materials.

In addition to the ability to simultaneously collect information from multiple locations on the heart, the device can harvest energy from the heart beating, allowing it to perform without an external power source. That allows it to not just track data for diagnostics and monitoring but to also offer therapeutic benefits such as electrical pacing and thermal ablation, the researchers reported in a paper published in the journal *Nature Electronics.*

The epicardial bioelectronics patch builds upon that with a material with mechanical properties that mimic cardiac tissue, allowing for a closer interface and reducing the risk that the implant could damage the heart muscle.

Rapid Malaria Detection with Microneedle Bandage

Researchers at Rice University have developed a microneedle patch that can rapidly detect the presence of malaria in interstitial fluid. Users can apply the patch to their skin, as you would a bandage, and then obtain a result in as little as 20 minutes. The technology is low-cost and requires no expertise to utilize.

Containing a 4 x 4 array of hollow microneedles, the patch gently penetrates the skin when applied and draws interstitial fluid inside itself, where an antibody-based lateral-flow test strip detects protein biomarkers of malaria. The device provides an easy to read visual result in the form of colored strips, similar to a pregnancy test, in about 20 minutes.

At only 375 microns wide, the microneedles are truly tiny, and do not cause significant pain on insertion. They are hydrophilic, and so easily draw interstitial fluid into the device. Interestingly, the bandage may also be useful in detecting other diseases, including COVID-19.

Study Reveals Link Between Prenatal Exposure to Heavy Metals and Risk of Atopic Diseases in Early Childhood

In a recent prospective study, children from the EDEN birth-cohort were followed-up using parental questionnaires with validated questions on asthma, allergic rhinitis, eczema and food allergy symptoms. The questionnaires were administered every four months during the children's first year, and then every year until the age of five, with a final survey at the age of eight years. Serum concentrations of lead (Pb), cadmium (Cd) and manganese (Mn) were assessed in maternal blood samples, collected during mid-pregnancy and in cord blood of 651 mother-children pairs.

The findings showed that levels of Cd in cord blood were associated with greater risk of asthma, eczema and food allergy while Mn levels in maternal serum were associated with eczema. These associations were similar in males and females and were confirmed using log-concentrations of metals as exposures.

The study is published in *Pediatric Allergy and Immunology*.

These results supported the hypothesis that fetal exposure to heavy metals may affect the development of asthma, eczema and food allergy in childhood. Furthermore, the timing of in utero exposure may have a role in these associations.

New Cause of Inflammation in HIV Patients

Researchers from Boston University have identified the important factors which could be contributing to the chronic inflammation in people living with HIV.

While current antiretroviral treatments for HIV are highly effective, data has shown that people living with HIV appear to experience accelerated aging and have shorter lifespans, by up to five to 10 years, compared to people without HIV.

These outcomes have been associated with chronic inflammation, which could lead to the earlier onset of age-associated diseases, such as atherosclerosis, cancers, or neurocognitive decline.

Published in *The Journal of Infectious Diseases*, the results underscore the need to develop new treatments targeting the persistent inflammation in people living with HIV in order to improve outcomes.

According to the study, after infection, HIV becomes a part of an infected person's DNA forever, and in most cases, infected cells are silent and do not replicate the virus.

Occasionally, however, RNA is produced from this HIV DNA, which is a first step towards virus replication.

Anti-retroviral treatments help prevent HIV and AIDS-related complications, but they do not prevent the chronic inflammation that is common among people with HIV and is associated with mortality.

For this study, researchers had a cohort of 57 individuals with HIV who were treated with antiretroviral therapy. They compared inflammation in the blood and various virus measurements among younger (age less than 35 years) and older (age greater than 50 years) people living with HIV.

They also compared the ability of the inflammation present in the blood to activate HIV production from the silent cells with the HIV genome.

Their results suggest that an inability to control HIV RNA production even with anti-retroviral drugs correlates with inflammation.