The Lord is like a strong tower, where the righteous can go and be safe.
Proverbs 18:10

DIYARYO KABITENYO
Nagmamalasakit sa lalawigan

ISSN: 2651-8215
Entered as FIRST CLASS MAIL at Imus Post Office with Business Mail Permit No. IC-19-06-249
Vol. 23 No. 15 | June 1-7, 2020 | P 10.00

Be alert, stand firm in the faith, be brave, be strong.
1 Corinthians 16:13

# Brgy in Carmona placed on total lockdown

CARMONA, Cavite – The municipal government here placed Barangay Cabilang Baybay under total lockdown after seven employees residing in two boarding houses tested positive for the coronavirus disease 2019 (COVID-19) after a rapid diagnostic test (RDT).

According to the Facebook page of Mayor Roy M. Loyola, the patients were employees of a company based in Muntinlupa.

With RDT not confirmatory and not 100 percent reliable, the seven patients will undergo reverse tran-

Turn to page 2

Philippine Navy personnel wear face masks inspired by the colors of the Philippine flag during the flag ceremony celebrating the National Flag Day in Alapan, Imus, Cavite last May 28. The National Flag Day commemorates the first unfurling of the Philippine flag by General Emilio Aguinaldo at the Teatro Caviteño in Cavite City following the Battle of Alapan on May 28, 1898.

DIYARYO KABITENYO
ISSN: 2651-421X
ARNULFO BARCO
Publisher – Editor
GENER BARCO
Operations Manager
DIYARYO KABITENYO is a [illegible] weekly [illegible] throughout the province of Cavite. It has its editorial and business offices at [illegible] Trece Martires City, Cavite. It is registered at the Department of Trade and Industry Region IV-A (CAL) No. 00284. Our telephone number is 2617560813.
Subscription Rate: 1 month – P 40.00; 3 months – 120.00; 6 months – 240.00
Advertising Rate: Commercial – P200.00/col. cm; Legal – 300.00/col. cm.
PAPI
Publishers Association of the Philippines, Inc.

# New drug combination being tested to conquer COVID-19

Montefiore Health System-Albert Einstein College of Medicine have begun the next stage of the Adaptive COVID-19 Treatment Trial (ACTT), to evaluate treatment options for people hospitalized with severe COVID-19 infection. The new iteration of the trial, known as ACTT-2, is sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health.

In March, Montefiore was the first New York location to join the multicenter trial, which evaluated remdesivir, a broad-spectrum antiviral drug given intravenously. Preliminary results from the trial, announced last month and published May 22 in the New England Journal of Medicine, show that patients with COVID-19 who received remdesivir recovered in 11 days on average, compared to 15 days for patients in the placebo group – a statistically significant improvement. Of the 1,063 clinical trial participants, 91 of them, nearly 10%, were from Montefiore and Einstein.

Following up on remdesivir's promising results, the trial is now studying remdesivir in combination with baricitinib or placebo in a double-blind, randomized trial. Baricitinib is marketed for reducing inflammation associated with rheumatoid arthritis.

# New understanding of RNA movements can be used to treat cancer

Research from Karolinska Institutet published May 27, 2020 in Nature shows that an RNA molecule involved in preventing tumour formation can change its structure and thereby control protein production in the cell. The finding can have important clinical implications as it opens for new strategies to treat different types of cancer.

Short RNA molecules in our cells, called microRNAs, are important regulators of messenger RNAs (mRNA) – the molecule that codes for the building blocks of our body, the proteins. The exact mechanism of this regulation remains elusive, but it is known that microRNAs can silence mRNA molecules and thereby prevent protein production. Therefore, they have the potential to be used as tools or targets for drugs.

"It's important to increase our understanding of how microRNA regulates protein production because this process is disturbed in many different types of diseases, including cancer," says Katja Petriold, Associate Professor at the Department of Medical Biochemistry and Biophysics at Karolinska Institutet in Sweden who led the study. "We show for the first time that a microRNA-mRNA complex has a structure that changes and that this movement has an effect on the biological outcome, i.e. the amount of protein produced in the cell."

The researchers studied a microRNA known as miR-34a, which plays an important role in cancer by indirectly regulating the activity of the p53 protein, known as the guardian of the genome for its ability to prevent cancer formation. Changes in the function of p53 are very common in human cancers. miR-34a downregulates the mRNA that codes for Sirt1, a protein that deactivates p53.

Using Nuclear Magnetic Resonance (NMR) and other biophysical methods, the researchers solved the structure and dynamics of miR-34a binding the mRNA molecule. When they measured these dynamics, they found that the complex exists in two structurally different states, one moderately active with a population of 99 per cent and one with enhanced activity, a population of 1 per cent. These states can interconvert, as they are in equilibrium, and the population of each state can be modified by external factors.

(BRGY... from page 1)

transcription-polymerase chain reaction (RT-PCR) to confirm if they're COVID-19 positive.

Though the patients are now staying in a quarantine facility, Barangay Cabilang Baybay has been placed under lockdown while contact-tracing was being done.

Republic of the Philippines
Province of Cavite
Municipality of Ternate
OFFICE OF THE MUNICIAPAL CIVIL REGISTRAR

RA Form No. 11 (SECRO)

NOTICE FOR PUBLICATION

In Compliance with Section 5 of RA 9048, a notice is hereby served to the public that RODRIGO V. PELAÑA has filed in this office a petition for Change of First Name from "HILARIO JR" to "BUENAVENTURA" in the Certificate of Live Birth of HILARIO PILINA JR. who was born on APRIL 12, 1940 in TERNATE, CAVITE and whose parents are HILARIO PILINA and GREGORIA ICASIANO.

Any person adversely affected by said petition may file his written opposition with this office not later than 8 JUNE 2020.

(Sgd.) MARIETA R. LOZANO
Municipal Civil Registrar

DIYARYO KABITENYO - May 25 and June 1, 2020

Republic of the Philippines
Province of Cavite
Municipality of Ternate
OFFICE OF THE MUNICIPAL CIVIL REGISTRAR

NOTICE TO THE PUBLIC

17 MARCH 2020

CCE-0086-2020RA 10172

In compliance with the publication requirement and pursuant to DCRG Memorandum Circular No. 2013-3 Guidelines in the Implementation of Administrative Order No. 1 Series of 2012 (IRR on R.A. 10172) Notice is hereby served to the public that HARRICAR HERNANDEZ LOZANO-ROLLON has filed with this office, a petition for CORRECTION OF ENTRY in her husband's DATE OF BIRTH from "April 10, 1977" to "April 10, 1973" in the Certificate of Live Birth of ROMMEL VEZCARA ROLLON who was born in Ternate, Cavite and whose parents are ROMEO OSANO ROLLON and PURIFICACION VEZCARA.

Any person adversely affected by said petition may file his written opposition with this office not later than 8 JUNE 2020.

(Sgd.) MARIETA R. LOZANO
Municipal Civil Registrar

DIYARYO KABITENYO - May 25 and June 1, 2020

Republic of the Philippines
OFFICE OF THE MUNICIPAL
CIVIL REGISTRAR
Indang, Cavite

In the matter of Change of First Name in the Certificate of Live Birth (SECPA) of

MARIE ANN H. MATEO

CFN-0003-2020

MARIAN M. RIDDIL
Petitioner

NOTICE OF PUBLICATION

There is a petition filed for the change of first name in Civil Registry Form No. 3 (SECPA) of MARIE ANN H. MATEO from "MARIE ANN" to "MARIAN"

NOTICE IS HEREBY GIVEN that any interested person may file his/her objection with this office not later than 8 JUNE 2020.

Let this NOTICE be published at least once a week for two (2) consecutive weeks in a newspaper of general circulation as required under Section 5 of Republic Act No. 9048.

(Sgd.) MERCYA. CHAVEZ
Officer-in-Charge
Municipal Civil Registrar

DIYARYO KABITENYO - June 1 & 8, 2020

# More effective human antibodies possible with chicken cells

Antibodies for potential use as medicines can be made rapidly in chicken cells grown in laboratories. Researchers refer to their technique as the human ADLib system, short for autonomously diversifying libraries. The technique automatically builds vast numbers, or libraries, of diverse antibodies using chicken immune system cells' natural method for shuffling their genes.

Often shaped like the letter 'Y,' antibodies are produced by the immune system to fight infections and prevent re-infection. Small portions of that Y shape are highly variable. Antibodies use these unique shape to form a perfect molecular tag with specific antigens, molecules on the surface of the cause of an infection. To effectively eliminate an infection, antibodies must recognize, attack and stay attached to an antigen.

"Our ADLib system can generate human antibodies against various antigens faster than existing methods," said Hidetaka Seo, a project researcher at the University of Tokyo and first author of the recently published scientific paper.

In standard techniques, individual antibodies are first identified and then produced through a slow, multi-step process involving bacteria, animal cells, or sometimes injecting antibodies from the blood of vaccinated or infected animals, and then modifying these animal antibodies for safe human use.

The first ADLib system was developed in 2005 by some members of the current research team, who at the time were working at the RIKEN research institute outside of Tokyo. The original ADLib system produced chicken antibodies using chicken immune system cells. In the years since, other researchers have generated human antibodies in whole live chickens.

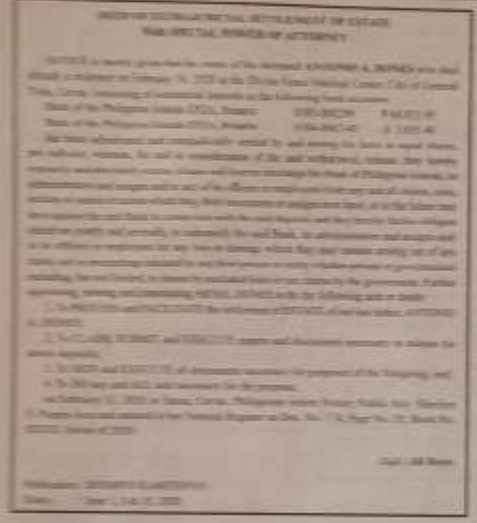
"We had the idea for the human ADLib system at that time, but the technology was very difficult to develop," said Professor Kunihiro Ohta, a co-author of the recent research paper, who led the original ADLib research group at RIKEN and is currently dean of the Graduate School of Arts and Sciences at the University of Tokyo.

"This is the first case of human gene recombination sequences capable of providing practical antibody libraries being developed using avian cells grown in a laboratory," said Seo.

To develop the human ADLib system, researchers first inserted human genes to replace the chicken immune cells' antibody genes and the surrounding suite of DNA known as paratogenes. The cells then grow in a dish and multiply for several weeks generating antibody genes of various new combinations.

This random antibody-generator quality of the ADLib system leads to many useless antibodies, but it also generates more efficient antibodies than the "built-for-purpose" antibodies that a human or animal immune system naturally produces during an infection.

Separately, researchers coat tiny magnetic beads with antigens of interest. Finally, the chicken cells are burst open and the contents are washed over the magnetic beads.



## Beware of false negatives in diagnostic testing of COVID-19

One of the most commonly used diagnostic tools, particularly during this pandemic, is the reverse transcriptase polymerase chain reaction test (RT-PCR), which uses a person's respiratory sample to detect viral particles and determine if the person may have been exposed to a virus.

Laboratory professionals across the U.S. and the globe have used RT-PCR to find out if a person has been infected with SARS-CoV-2, the virus that causes COVID-19. These tests have played a critical role in our nation's response to the pandemic. But, while they are important, researchers at Johns Hopkins have found that the chance of a false negative result — when a virus is not detected in a person who actually is, or recently has been, infected — is greater than 1 in 5 and, at times, far higher.

The researchers caution that the predictive value of these tests may not always yield accurate results, and testing of the test seems to matter greatly as the accuracy.

In the report on the findings published May 13 in the journal Annals of Internal Medicine, the researchers found that the probability of a false negative result decreases from 100% on Day 1 of being infected to 67% on Day 4. The false negative rate decreased to 20% on Day 8 (three days after a person begins experiencing symptoms).

# Taking inventory of which drugs the world is using to treat COVID-19

With doctors and researchers around the world searching for effective treatments for COVID-19, many drugs approved to treat other diseases are being used in hopes that they'll be effective against the virus, a use that's known as "off-label." New research from the Perelman School of Medicine at the University of Pennsylvania catalogued every use documented in medical literature so far and found physicians have reported on the use of more than 100 different off-label and experimental treatments. The effort, called COVID19 Registry of Off-label & New Agents (CORONA), is an attempt to take an inventory of what's being used where, as well as to spot any evidence of treatments that warrant further investigation in a randomized clinical trial.

The findings published in Infectious Diseases and Therapy May 27, 2020.

"We can't win this fight if we don't take stock of the tools that are already being used and search for new ones that could be effective. While off-label use is happening all over the world, there's currently no system in place to track it, so we felt like we had to create one," said the study's lead author David C. Fajgenbaum, MD, MBA, MSc, an assistant professor of Translational Medicine & Human Genetics and director of the Center for Cytokine Storm Treatment & Laboratory (CSTL) at Penn.

Fajgenbaum is also the executive director of the Castleman Disease Collaborative Network (CDCN), and a Castleman patient himself. In 2012, after failing to respond to other therapies and having relapsed multiple times after chemo, Fajgenbaum's research suggested a drug approved for other uses may be effective for his condition. Based on his own research and in consultation with his treating physician, Fajgenbaum decided to treat the drug on himself and has been in remission ever since.

"With the world facing its greatest public health crisis in a generation, we decided to take action, using the same approach that helped me and applying it to potentially help find promising leads in the treatment of COVID-19," Fajgenbaum said.

The team reviewed almost 2,700 published papers from all over the world detailing the treatment of COVID-19. From these, they gathered data on 9,152 patients and found doctors had used 115 different drugs.

# How do we disconnect from the environment during sleep and under anesthesia?

During sleep and under anesthesia, we rarely respond to such external stimuli as sounds, even though our brains remain highly active.

Now, a series of new studies by researchers at Tel Aviv University's Sackler Faculty of Medicine and Sagol School of Neuroscience find, among other important discoveries, that noradrenaline, a neurotransmitter secreted in response to stress, lies at the heart of our ability to "shut off" our sensory responses and sleep soundly.

"In these studies, we used different, novel approaches to study the filtering of sensory information during sleep and the brain mechanisms that determine which we awaken in response to external events," explains Prof. Yuval Nir, who led the research for the three studies.

The first study, published in the Journal of Neuroscience on April 1 and led by TAU doctoral student Yaniv Sela, calls into question the commonly accepted idea that the thalamus – an important relay station for sensory signals in the brain – is responsible for blocking the transmission of signals to the cerebral cortex.

"The shutdown of the thalamic gate is not compatible with our findings," says Sela whose study compares how neurons in different brain regions respond to simple and complex sounds while asleep or awake.

Using rat models, he found that the responses of neurons in the auditory cortex were similar when the rodents were awake or asleep. But when he examined the perirhinal cortex, related to complex conscious perception and memory associations, he found that neurons showed much weaker responses during sleep.

"Basic analysis of sound remains during sleep, but the sleeping brain has trouble creating a conscious perception of the stimulus," Sela adds. "Also, while we found that initial and fast responses are preserved in sleep, those that occur later and require communication between different regions in the cortex are greatly disrupted."

The second study, published on April 8 in Science Advances, finds that the locus coeruleus, a tiny region of the brainstem and the main source of noradrenaline neurotransmitter in the brain, plays a central role in our ability to disconnect from the environment during sleep. Led by TAU doctoral student Hanna Hayat at Prof. Nir's lab, the research was conducted in collaboration with Prof. Tony Pickering of Bristol University, Prof. Ofer Yizhar of the Weizmann Institute and Prof. Eric Kremer of the University of Montpellier.

"The ability to disconnect from the environment, in a reversible way, is a central feature of sleep," explains Hayat. "Our findings clearly show that the locus coeruleus-noradrenaline system plays a crucial role in this disconnection by keeping a very low level of activity during sleep."

For the purpose of the research, the scientists used rat models to determine the level of locus coeruleus activity during sleep and which sounds, if any, would be responsible for waking up the rodents.

They found that the rats' varying levels of locus coeruleus activity accurately predict if the animals would awaken in response to sounds. The team then silenced the locus coeruleus activity through optogenetics, which harnesses light to control neuronal activity, and found that the rats did not readily awaken in response to sound.

"When we increased the noradrenaline activity of the locus coeruleus while a sound played in the background, the rats woke up more frequently in response, but when we decreased the activity of the locus coeruleus and played the same sound in the background, the rats only rarely woke up," says Hayat. "So we can say we identified a powerful 'dial' that controls the depth of sleep despite external stimuli.

"Importantly, our findings suggest that hyperarousal in some individuals who sleep lightly, or during periods of stress, may be a result of continued noradrenaline activity during sleep when there should only be minimal activity."

The third study, published on May 12 in the Proceedings of the National Academy of Sciences (PNAS), led jointly by TAU doctoral student Dr. Aaron Krom of Hadassah Hebrew University Medical Center and TAU doctoral student Anat Marmelshtein, focuses on our response to awakenings and finds that the most significant effect of loss-of-consciousness is the disruption of communication between different cortical regions.

# Optimal time to treat Huntington's disease identified

The earliest brain changes due to Huntington's disease can be detected 24 years before clinical symptoms show, according to a new UCL-led study.

The researchers say their findings, published in The Lancet Neurology, could help with clinical trials by pinpointing the optimal time to begin treating the disease.

There is currently no cure for Huntington's, a hereditary neurodegenerative disease, but recent advances in genetic therapies hold great promise.

Researchers would ultimately like to treat people before the genetic mutation has caused any functional impairment. However, until now, it was unknown when the first signs of damage emerge — but as there is a genetic test for Huntington's susceptibility, researchers have a unique opportunity to study the disease before symptoms appear.

Professor Sarah Tabrizi (UCL Huntington's Disease Centre, UCL Queen Square Institute of Neurology), the study lead, said: "Ultimately, our goal is to deliver the right drug at the right time to effectively treat this disease – ideally we would like to delay or prevent neurodegeneration while function is still intact, giving gene carriers many more years of life without impairment.

"As the field makes great strides with the drug development, these findings provide vital new insights informing the best time to initiate treatments in the future, and represent a significant advance in our understanding of early Huntington's."

The Wellcome-funded study, led by UCL researchers in collaboration with colleagues from the University of Cambridge and University of Iowa, investigated a large cohort of Huntington's mutation carriers at a much younger age than previously examined in detail. 64 people with the mutation took part alongside 67 others without the mutation who served as control subjects for comparison.

The study involved the most extensive testing of Huntington's ever performed, including tests of thinking, behaviour, brain scans and proteins in spinal fluid.

The mutation carriers were, on average, 24 years ahead of the predicted disease onset, based on their age and a genetic test. They exhibited no changes in thinking, behaviour or involuntary movements commonly found in the disease, and there was very little evidence of brain scan changes.

But researchers did detect a subtle increase in the spinal fluid of a neuronal protein called neurofilament light (NfL), which is often the product of nerve cell damage.

Just under half (47%) of the mutation carriers had NfL values in their spinal fluid above the range of values found in the control group, at 24 years before disease onset, suggesting the authors have identified a crucial point at which brain changes first start occurring. NfL values correlated with predicted time to disease onset. The finding was supported by using the data to model predicted trajectories.

Co-first author of the study, Dr Paul Zeun (UCL Huntington's Disease Research Centre) said: "We have found what could be the earliest Huntington's-related changes, in a measure which could be used to monitor and gauge effectiveness of future treatments in gene carriers without symptoms."

Co-first author of the study, Dr Rachael Scahill (UCL Huntington's Disease Research Centre) added: "Other studies have found that subtle cognitive, motor and neuropsychiatric impairments can appear 10-15 years before disease onset. We suspect that initiating treatment even earlier, just before any changes begin in the brain, could be ideal, but there may be a complex trade-off between the benefits of slowing the disease at that point and any negative effects of long-term treatment."

# Ear infections discovered in remains of humans living in Levant 15,000 years ago

Researchers at Tel Aviv University have discovered evidence of ear infections in the skull remains of humans living in the Levant some 15,000 years ago.

"Our research seeks to determine the impact of our environment on illnesses in different periods," says lead author Dr. Hila May of the Department of Anatomy and Anthropology at TAU's Sackler Faculty of Medicine and the Dan David Center for Human Evolution and Biohistory Research at the Faculty of Medicine, located at the Steinhardt Museum of Natural History. "Using advanced radiological and antigen methods developed in our labs, we have been able to detect signs of prolonged inflammation in the middle ear."

Dr. Katrina Fliss-Isakov of the Dan David Center and Sackler Faculty of Medicine and Dr. Dan Kirzen of the Sackler Faculty of Medicine also contributed to the study, which was published on March 25 in the International Journal of Osteoarchaeology.

The researchers found a decline in morbidity as a result of ear infections following the transition from hunting and gathering to farming because of changes in living conditions. But a peak in morbidity was observed in a sedentary population living about 4,000 years ago, in the Chalcolithic period.

Dr. May says the reason for this is twofold: social and environmental. "We know from archaeological excavations of this period, similar to preceding periods, that people lived in a communal area where all activities, from cooking to raising livestock, took place. As a result, the population density in the 'home' was high, hygiene was poor and they suffered from indoor air pollution. Two other factors known about this period – dietary change, the advent of dairy consumption; and climate change, a dip in temperature and a rise in rainfall – also contributed to the prevalence of ear infections."

Until the advent of antibiotics in the 20th century, ear infections developed into chronic conditions. They could also lead to permanent loss of hearing or even death.

"Ear infections are still a very common childhood ailment, with over 50 percent of young children today still suffering from an ear infection at one point or another," explains Dr. May. "The tubes that channel fluid from the middle ear to the pharynx are underdeveloped in young children, so fluids that accumulate in the ear ultimately cause inflammation."

"A prolonged ear infection would cause permanent damage to the bony wall of the middle ear, which is preserved into adulthood. So when we sought to investigate changes in communal health over time in our region, we chose to focus on ear infections, developing a special method for doing so," she adds.

Scientists insert, at a videoscope, a tiny camera mounted at the end of a flexible tube, through the skull's ear canal to the middle ear to observe its bony walls. In addition, they scanned skull remains with a high-resolution micro-CT and examined the middle ear's bony wall using a light microscope.

As living conditions improved, morbidity as a result of ear infections dropped, according to the study. "Houses were larger and featured several rooms, including separate areas for specific activities, i.e. the kitchen was set up in a separate room, or outside, and livestock were kept in a separate area," Dr. May says. "The change in lifestyle and climate is reflected in a decline in morbidity."

"Our study deals with the impact of the environment and social behavior on morbidity rates. To explore this, we examined a common disease that has accompanied humanity since inception – the ear infection," Dr. May continues. "Understanding how diseases appear, spread and disappear throughout human history can help prevent and find solutions to contemporary illnesses. The study clearly points out risk factors and shows how lifestyle changes can affect the incidence of the disease.

"In both our wars and COVID-19, social distancing and adherence to hygiene reduced the spread of infection, while close quarters and unhygienic living conditions saw infections spike," Dr. May concludes.

DIYARYO KABITENYO
Pagmamalasakit sa lalawigan
Vol. 13 No. 10 June 1-7, 2020 P 10.00

# Mouse model mimics SARS-CoV-2 infection in humans

A mouse model of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reproduces features observed in human patients, researchers report May 29 in the journal Cell Host & Microbe. Using CRISPR/Cas9 gene-editing technology, the researchers generated mice that produce human angiotensin-converting enzyme II (hACE2)—the receptor that SARS-CoV-2 binds to and uses to enter host cells.

"A small animal model that reproduces the clinical course and pathology observed in COVID-19 patients is highly needed," says co-senior study author Yuan-Chun Wang of the National Institutes for Food and Drug Control (NIFDC) in Beijing, China. "The animal model described here provides a useful tool for studying SARS-CoV-2 infection and transmission."

Wang and his collaborators used CRISPR/Cas9 to generate a mouse model that could express hACE2. According to the authors, their mouse model has several advantages as compared with other genetically engineered mice that express hACE2 for modeling SARS-CoV-2 infection. Instead of being randomly inserted, hACE2 is inserted precisely into a specific site on the X chromosome and it completely replaces the mouse version of the protein. In addition, this is a genetically stable model, with few differences among individuals. Moreover, the viral RNA loads in the lung are much higher, and the resulting distribution of hACE2 in various tissues better matches that observed in humans.

## Female Gulf War combat veterans have persistent symptoms more than 25 years later

More than a quarter century after the Gulf War, female veterans who saw combat have nearly a twofold risk of reporting more than 20 total medical symptoms, like cognition and respiratory troubles, than their fellow female veterans who were not deployed, investigators report.

A sizeable percentage of the female combat veterans still report neurological symptoms: about two-thirds report difficulty remembering new information and trouble concentrating, investigators report in the Journal of Women's Health.

An association with more headaches among the combat veterans also was reported and there were "strong associations" between deployment status and respiratory symptoms with 39% of combat veterans still reporting difficulty breathing or shortness of breath. More than half also report a low tolerance for heat and cold.

"It's been over 25 years since the war ended and there are very persistent health outcomes," says Dr. Sonya S. Coughlin, interim chief of the Division of Epidemiology in the Medical College of Georgia Department of Population Health Sciences.