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A Rare Public Health Challenge

By Dr. Joni L. Rutter, Director of the National Center for Advancing Translational Sciences

Most public health challenges may seem obvious. The COVID-19 pandemic, for example, swept the globe and in some way touched the lives of everyone. But not all public health challenges are as readily apparent.

Rare diseases are a case in point. While individually each disease is rare, collectively rare diseases are common: More than 10,000 rare diseases affect nearly 400 million people worldwide. In the United States, the prevalence of rare diseases (over 30 million people) rivals or exceeds that of common diseases such as diabetes (37.3 million people), Alzheimer's disease (6.5 million people), and heart failure (6.2 million people).

Shouldering the Burden of Rare Diseases

As with common diseases, the personal and economic burdens of rare diseases are immense. People who live with rare diseases often struggle for years before they receive an accurate diagnosis, with some remaining undiagnosed for a decade or longer. The diagnostic odyssey includes countless doctor visits, unnecessary tests and procedures, and wrong diagnoses. For people in rural and low-income communities, lack of access to care is an additional barrier to an accurate diagnosis. And a diagnosis often doesn't lead to better health — only about 5 percent of rare diseases have U.S. Food and Drug Administration–approved treatments.

Collectively, the personal burdens of those with rare diseases impose a significant economic cost on the nation. When quantifying the health care expenses for people with rare diseases, we found that they have three to five times greater costs than those without rare diseases[1]. In the United States, the total direct medical costs for those with rare diseases is approximately $400 billion annually, a figure validated independently by the EveryLife Foundation for Rare Diseases. The EveryLife study also included indirect and non-medical costs, resulting in a higher total economic burden of nearly $1 trillion annually[2].

What's even starker is that the true scope and impact of rare diseases actually may be greater because rare diseases aren't easily visible in our health care system. Many of the diseases are too rare to have a code that identifies them in the electronic health record (EHR).

NCATS Director Joni L. Rutter, PhD.
Photo courtesy of NIH

Speeding Up the Search for Solutions

Each and every day, NIH's National Center for Advancing Translational Sciences (NCATS) works with patients, advocates, clinicians, and researchers to meet the public health challenge of rare diseases. Driving those conversations are three overarching goals to help people living with rare diseases get the high-quality care they need, faster:

1. Shorten the duration of the diagnostic odyssey by more than half. The diagnostic odyssey for someone with a rare disease takes on average seven years, and there are several ways we can speed the journey. For example, we are designing computational tools to detect rare genetic disorders from EHR data.

More than 10,000 rare diseases affect nearly 400 million people across the globe. Photo courtesy of Christina Loccke, Lindsey Bergstrom and Sarah Theos, and The National Institutes of Health

This work is part of a broader research effort focused on using genetic analysis and machine learning to make it easier for health care providers to diagnose people with rare diseases correctly. Also, connecting patients more quickly with each other and the research community can hasten the search for answers. Check out the resources below to learn about rare diseases, find patient support organizations, and get involved in research efforts.

2. Develop treatments for more than one rare disease at a time. A key strategy is leveraging what rare diseases have in common. Some of our efforts build upon the fact that 80–85 percent of rare diseases are genetic. We can use this knowledge to develop genetic and molecular interventions for groups of rare diseases. Two programs — the Platform Vector Gene Therapy pilot project and the Bespoke Gene Therapy Consortium, which is part of the public-private Accelerating Medicines Partnership® — are streamlining the gene therapy development process. Their ultimate goal is to make gene therapies more accessible to many people with rare diseases. We also have joined in to advance the clinical application of genome editing for rare genetic diseases.

   The NCATS-led Rare Diseases Clinical Research Network, which is supported across NIH, brings scientists together with rare disease organizations and patient advocacy groups to better understand common characteristics, which also might speed clinical research. With this in mind, we are adapting a clinical trial strategy used in cancer research to test a single therapy on multiple rare diseases.

3D rendering of genetic medicine with DNA isolated. Photo credit National Institutes of Health, National Center for Advancing Translational Sciences (xsense/Shutterstock)

Photo courtesy of the California's Stem Cell Agency, University of California San Francisco

3. Make it easier and more efficient for scientists to discover and develop treatments for rare diseases. NCATS develops ways for new treatments to reach people more quickly. Repurposing drugs, for example, is revealing already-approved drugs that may work for rare diseases. Programs such as Therapeutics for Rare and Neglected Diseases and Bridging Interventional Development Gaps move basic research discoveries in the lab closer to becoming new drugs. Ambitious initiatives, such as the Biomedical Data Translator, unite data from biomedical research, clinical trials, and EHRs to find treatments for rare diseases faster.

The COVID-19 pandemic showed us the power of working together to solve public health challenges. Let's now come together to address the public health challenge of rare diseases. If you want to get involved, please join us at Rare Disease Day at NIH 2023 on February 28. You'll hear personal stories, learn about the latest research, and discover helpful resources. I hope to see you there!

References:

1. The IDeaS initiative: pilot study to assess the impact of rare diseases on patients and healthcare systems. Tisdale A, Cutillo CM, Nathan R, Russo P, Laraway B, Haendel M, Nowak D, Hasche C, Chan CH, Griese E, Dawkins H, Shukla O, Pearce DA, Rutter JL, Pariser AR. Orphanet Journal of Rare Diseases. 2021 Oct 22; ;16(1):429.
2. The national economic burden of rare disease in the United States in 2019. Yang G, Cintina I, Pariser A, Oehrlein E, Sullivan J, Kennedy A. Orphanet Journal of Rare Diseases. 2022 Apr 12;17(1):163.

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Percentage of Overdose Deaths Involving Methadone Declined between January 2019 and August 2021

National data indicate COVID-era treatment expansion was not associated with harms, add evidence to support take-home treatment for opioid use disorder.

The percentage of methadone-involved overdose deaths relative to all drug overdose deaths declined from January 2019 to August 2021, according to a new study. Access to methadone, a medication to treat opioid use disorder, was expanded at the start of the COVID-19 pandemic to allow more patients to take home doses, rather than visit a clinic daily. These data indicate that broader access to treatment was not associated with harms. While drug overdose deaths both with and without methadone increased in the month of March 2020, overdose deaths that did not involve methadone continued to increase in the months after the policy changes, while overdose deaths involving methadone held steady.

Published today in *JAMA Psychiatry*, this study was a collaborative effort led by researchers at the National Institute on Drug Abuse (NIDA), part of the National Institutes of Health, and the National Center for Injury Prevention and Control, part of the Centers for Disease Control and Prevention.

In 2021, provisional data from CDC estimate more than 107,000 people died of a drug overdose, with 75% of those deaths involving an opioid. The overall rise in overdose deaths is largely attributable to the proliferation in the drug supply of illicit fentanyl, a highly potent synthetic opioid. A key component of the federal government response to the overdose crisis is expanding access to medications for opioid use disorder. However, only

Christopher Jones, PharmD, DrPH, MPH CAPT, US Public Health Service Acting Director. Photo courtesy of CDC

18% of people with opioid use disorder receive medication as treatment. Though the benefits of providing safe and effective medication for opioid use disorder are well-known, decades of stigma against treating substance use disorders with medication has contributed to minimal reach.

"Treatment is an essential tool to stop the addiction and overdose crises, but it is vastly underused," said NIDA Director and senior author, Nora Volkow, MD. "This evidence adds significant weight to the argument that effective treatment for substance use disorders should be offered in an accessible and practical way that works for people who need it."

In the United States, methadone for the treatment for opioid use disorder can only be provided through federally certified opioid treatment programs, where most patients are required to visit a clinic in-person, on a daily basis, in order to get their medication. For decades, this requirement has been identified as an often-insurmountable barrier to access and retention for this treatment, particularly for people trying to balance employment, childcare, and other needs. The requirement presented unique challenges during the COVID-19 pandemic, as accessing in-person treatment became limited due to concerns about exposure to COVID-19. In order to ensure continuity of care for individuals receiving methadone treatment, on March 16, 2020, the Substance Abuse and Mental Health Services Administration (SAMHSA) allowed states to request exceptions to provide up to 28 days and 14 days of take-home methadone for stable and less stable patients, respectively.

To assess the impact and potential harms of these policy changes, investigators used data from January 2019 through August 2021 from the CDC's National Vital Statistics System, a national mortality database. Researchers calculated monthly drug overdose deaths without methadone, monthly drug overdose deaths involving methadone, and the percentage of overall overdose deaths involving methadone. They then assessed whether there was a shift in outcomes before and after the methadone take-home policy change in March 2020. They did this through interrupted time series analyses, a method of evaluation for large scale public health interventions with well-defined starting points.

Researchers found that non-methadone-involved overdose deaths increased

Photo courtesy of The National Institute of Child Health and Human Development, Image credit Adobe Stock

by an average of 78 more deaths each month before March 2020, increased by 1,078 deaths during March 2020, and then continued to increase by an average of 69 more deaths each month after March 2020. Methadone-involved overdose deaths experienced a similar increase in March 2020 (increased by 94 deaths). However, the trend in number of deaths per month before and after this initial uptick remained stable, and the percentage of overdose deaths involving methadone declined at similar rates before and after the take-home policy change, declining from 4.5% of overdose deaths in January of 2019 to 3.2% in August 2021.

Taken together, these findings indicate that the modest increase in methadone-involved overdose deaths in March 2020 was likely a reflection of the overall spike in overdose deaths driven by illicitly produced fentanyl and not an outcome of the take-home policy change. Mirroring findings from smaller studies, these national data provide evidence that the expanded opioid treatment program take-home methadone policy change established in March 2020 was not associated with increases in methadone-involved overdose deaths, despite marked increases in overall overdose deaths during the study period. Coupled with other studies that have demonstrated positive benefits related to these policies, the authors note that these findings can inform decisions about permanently expanding take-home methadone from opioid treatment programs.

"The goal of health policy should be to promote health and reduce harm, and our goal in conducting studies like this is to ensure that those policies are based on the best available scientific evidence," said lead author Christopher M. Jones, PharmD, DrPH, acting director of the National Center for Injury Prevention and Control at the CDC. "Projects like this also underscore the important findings that can emerge when we collaborate across agencies under a common mission, as we continue to work together to address the overdose crisis."

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Tobacco Smoking Rates are Decreasing in People with Major Depression and Substance Use Disorder

Despite decline, smoking cessation efforts still critical for people with substance use or other psychiatric disorders.

B Han, ND Volkow, C Blanco, D Tipperman, EB Einstein, WM Compton

Significant reductions in cigarette use were found among U.S. adults with major depression, substance use disorder, or both from 2006 to 2019, according to a new analysis of nationally representative survey data published today in *JAMA*. The study was conducted by researchers at the National Institute on Drug Abuse (NIDA), part of the National Institutes of Health, and the Substance Abuse and Mental Health Services Administration (SAMHSA). These findings suggest that groups at higher risk of cigarette smoking can be reached by, and may have benefitted from, tobacco use prevention and cessation efforts that have led to significant declines in tobacco use in the general population. At the same time, the findings highlight remaining disparities, documenting higher smoking rates in people with psychiatric disorders than in those without.

Dr. Wilson Compton, NIDA Deputy Director. Photo courtesy of NIH

"This study shows us that, at a population-level, reductions in tobacco use are achievable for people with psychiatric conditions, and smoking cessation should be prioritized along with treatments for substance use, depression, and other mental health disorders for people who experience them," said Nora Volkow, MD, director of NIDA and co-author of the study. "Therapies to help people stop smoking are safe, effective, and may even enhance the long-term success of concurrent treatments for more severe mental health symptoms in individuals with psychiatric disorders by lowering stress, anxiety, depression, and by improving overall mood and quality of life."

Cigarette smoking, the leading preventable cause of disease, disability and death in the U.S., has been declining. Experts attribute this in part to increases in available treatments, insurance coverage of these treatments, cigarette prices, smoke-free and tobacco-free policies, mass media and educational campaigns and other evidence-based strategies to help people avoid or quit using cigarettes that have been implemented in recent decades.

Quitting cigarette smoking and tobacco use reduces the risk of cancer, heart disease, stroke and lung diseases. Studies have also found that smoking cessation in people with psychiatric disorders can help decrease anxiety, depression and stress; lower likelihood of a new-onset substance use disorder; and improve quality of life.

Past studies have documented that smoking rates remained essentially unchanged in people with substance use disorders, major depression or other psychiatric disorders. Now, analyzing data from more than 558,000 individuals aged 18 and older who participated in the 2006 to 2019 National Surveys on Drug Use and Health (NSDUH), researchers found that while people with major depression, substance use disorder or both were more likely to smoke cigarettes than people without these disorders; improvements in smoking cessation were seen among those with these psychiatric disorders during the 14-year period. The NSDUH, conducted annually by SAMHSA, provides nationally representative data on cigarette smoking, tobacco use, major depressive episode and substance (alcohol or drug) use disorders among the US civilian, non-institutionalized adult population. Among the population studied here, roughly 53% were women, 41% were aged 18 to 25 and 62% were non-Hispanic white.

After controlling for factors such as age, sex, race/ethnicity, education and family income, the researchers found that past-month smoking rates declined by 13.1% from 2006 to 2019 among adults with a past-year major depressive episode and by 8.2% from 2006 to 2019 among adults without. The difference in past-month cigarette smoking among those with versus without past-year major depressive episode significantly narrowed from 11.5% in 2006 to 6.6% in 2019.

Similarly, past-month cigarette smoking declined by 10.9% from 2006 to 2019 among adults with past-year substance use disorder and by 7.8% among adults without. For people with co-occurring substance use disorder and major depression, past-month smoking rates decreased by 13.7% during this 14-year period and by 7.6% among adults without these disorders.

"These declines tell a public health success story," said Wilson Compton, MD, NIDA's Deputy Director and the senior author of the study. "However, there's still a lot of work to be done to ensure tobacco use in patients with substance use disorder, depression, or other psychiatric conditions continue to decrease. It is crucial that healthcare providers treat all the health issues that a patient experiences, not just their depression or drug use disorder at a given point in time. To do this, smoking cessation therapies need to be integrated into existing behavioral health treatments. The result will be longer and healthier lives for all people."

During 2006 to 2019, among adults with past-year major depressive episodes or substance use disorder, past-month cigarette smoking declined significantly across every examined age, sex, and racial and ethnic subgroup, except that among non-Hispanic American Indian or Alaska Native adults smoking rates did not decline. Given that American Indian and Alaska Native communities face the highest smoking and lowest quitting rates among racial and ethnic subgroups in the United States, this highlights the need to channel additional prevention and treatment efforts into these communities.

In future work, the researchers note the need to include data on certain populations at high risk of psychiatric disorders and cigarette smoking, such as institutionalized individuals or those experiencing homelessness without living in a shelter. More work is also needed to continue to monitor national trends in differences in tobacco use and nicotine vaping among adults with or without psychiatric conditions — including substance use disorder — during the COVID-19 pandemic.

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Photo courtesy of NIH/Thinkstock\Nastco

Diagnosing Hidden Hearing Loss

By Sharon Reynolds, Freelance Science Writer to NIH's National Institute on Deafness and Other Communication Disorders

One in eight people nationwide live with hearing loss in both ears. A common cause of hearing loss is damage to the hair cells found in the inner ear. These cells detect sound waves and communicate with the cochlear nerve, which routes sound information to the brain. Loud noise, aging, and some medications can all potentially cause loss of these delicate hair cells.

Standard hearing tests measure how well people detect certain frequencies of sound. Yet some people who have normal results on standard hearing tests may still struggle to follow a conversation in noisy environments. This type of hearing loss is sometimes called "hidden hearing loss" because it isn't readily detected using common tests of hearing.

NIH-funded researchers led by Dr. Stéphane Maison from the Mass Eye and Ear have been studying ways to identify cochlear nerve damage, which could be a cause of hidden hearing loss. In their new study, they examined more than 95,000 word-recognition scores from hearing tests.

Photo courtesy of the National Institutes of Health

Stéphane F. Maison, AuD, PhD, CCC-A, Associate Professor of Otolaryngology–Head and Neck Surgery. Photo courtesy of the Mass Eye and Ear

They included scores from people with a wide range of conditions that cause hearing loss. These included aging, noise overexposure, and conditions known to specifically cause nerve damage.

The team hypothesized that people with cochlear nerve damage would have lower scores on the word-recognition task than predicted by their standard hearing tests. This could happen because, although they could hear certain sounds, the nerve damage would prevent those sounds from being processed correctly by the brain. The results were published on June 23, 2022, in Scientific Reports.

The researchers found that many people had word-recognition scores that were lower than predicted by their standard hearing tests. Age-related cognitive decline wasn't a major factor in such discrepancies. The deficits in word recognition were highest in people with conditions known to significantly damage the cochlear nerve fibers.

The team next combined the data from this study with previous work that examined damage to the cochlear nerve during autopsies in different age groups. They used this information to develop a model that could estimate the amount of nerve, or neural, fiber loss based on the difference between predicted and measured word-recognition scores.

"Now, for the first time, we know how much neural loss has to accumulate before scores on the clinical word-recognition test begin to decline. Further work is needed to improve this model and offer ways to assess neural damage in standard hearing exams," Maison says.

Photo courtesy of the NIH's National Library of Medicine

References: Predicting neural deficits in sensorineural hearing loss from word recognition scores. Grant KJ, Parthasarathy A, Vasilkov V, Caswell-Midwinter B, Freitas ME, de Gruttola V, Polley DB, Liberman MC, Maison SF. Sci Rep. 2022 Jun 23;12(1):8929. doi: 10.1038/s41598-022-13023-5. PMID: 35739134.

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Hearing Impairment in Hispanic/Latino Adults

Hearing impairment is one of the most common chronic conditions affecting adults. It often goes undiagnosed and untreated for years. Having trouble hearing can make it difficult to detect smoke alarms, phones, and doorbells. Hearing loss also can make it hard to have conversations with family and friends, leading to frustration and isolation.

About 15% of American adults report some hearing loss. To determine the prevalence of hearing impairment among U.S. Hispanic/Latino adults and identify associations with potential risk factors, a research team looked at data gathered as part of the Hispanic Community Health Study/Study of Latinos (HCHS/SOL).

HCHS/SOL is the largest U.S. study of Hispanic/Latino health. It's being conducted in 4 cities: the Bronx, Chicago, Miami, and San Diego. Participants include more than 16,000 self-identified Hispanic/Latino adults, ages 18 to 74 at first visit. They represent a wide range of backgrounds, including Central American, Cuban, Dominican, Mexican, Puerto Rican, and South American. The study has been supported in part by NIH's National Institute on Deafness and Other Communication Disorders (NIDCD) and National Heart, Lung, and Blood Institute (NHLBI).

Researchers asked participants to listen to tones at different pitches and then averaged the hearing thresholds in each ear at 4 different pitches. A person was considered to have hearing loss if his or her average hearing threshold was louder than 25 decibels (about as loud as the sound of rustling leaves) in at least one ear. Participants' body mass index, blood pressure, and blood glucose were determined. They completed surveys in English or Spanish regarding education, income, noise exposure, heart disease history, smoking, and other factors that might be associated with hearing impairment. Results appeared online on May 28, 2015, in *JAMA Otolaryngology* — Head & Neck Surgery.

Hearing impairment often goes undiagnosed and untreated for years.
Photo courtesy of the National Institutes of Health, Sezer66/Thinkstock

Photo courtesy of the Substance Abuse and Mental Health Services Administration

The researchers found that 15% of the participants had hearing loss in one ear and that roughly half of these (8%) had hearing loss in both ears. Among different subgroups, Hispanics of Puerto Rican descent had the highest rate of hearing loss, while Mexican-Americans had the lowest.

The prevalence of hearing impairment was higher among participants who had diabetes or prediabetes, males, those 45 years and older, and those exposed to loud noise. Participants were less likely to have hearing loss if they had at least a high school diploma or GED and higher household income. These associations do not prove cause and effect, however. More research will be needed to determine the environmental, cultural, and genetic factors that might be involved.

"Hearing loss can affect a person's overall quality of life and has been linked to depression and dementia in older adults," says former NIDCD Director Dr. James F. Battey, Jr. "This study paints a detailed picture of hearing loss among a large and diverse group of Hispanic/Latino participants, and could help inform the development of intervention strategies to meet the needs of this growing population in the United States."

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How to Promote Ear Health for People with Diabetes

We all have a role to play to help people with diabetes live their best life, and Audiologists play a key role in the early detection and treatment of diabetes-related hearing and balance complications, such as hearing loss and an increased risk of falls. These conditions can be avoided or delayed with annual audiological evaluations and treatment if needed.

By working regularly with audiologists as part of a patient's health care team, primary care providers can help their patients with diabetes reduce the risk of complications that can occur when they don't hear important medical information. They can also help reduce injuries from unnecessary falls, which in turn can limit patients' ability to manage their diabetes.

Key Messages to Share With Your Patients

- Encourage your patients with diabetes to get annual hearing tests, wear ear protection around loud noises, eat a healthy diet, and manage their blood glucose levels.
- Remind your patients not to clean their ears with swabs, pencils, tweezers, or paper clips.
- Encourage your patients to monitor their hearing by paying attention to changes, asking loved ones if they've noticed hearing changes, and using a self-assessment tool like the Hearing Handicap Inventory Screening.
- Tell your patients that:
  - An audiologist can screen them for balance-related problems caused by changes to the vestibular system.
  - People with diabetes may be prescribed ototoxic medications, which can contribute to more severe hearing loss than that caused by aging alone.8
  - People with diabetes-related hearing loss may have a reduced quality of life.
  - Share information from CDC's Take Charge of Your Diabetes: Healthy Ears fact sheet.

Take These 5 Actions to Help Your Patients

1. Know the risks of hearing and balance disorders for people with diabetes.

Illustration courtesy of the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health

People with diabetes are at a higher risk for hearing and balance complications, including hearing loss and risk of falls. However, only about 23% of older adults report having an annual audiological evaluation.[1]

In the United States:

- 96 million adults have prediabetes. Hearing loss is 30% higher in adults with prediabetes than in those without this condition.[1]
- Studies have consistently shown that hearing loss is twice as common in people with diabetes compared to people without diabetes.[2]
- Some studies have found that diabetes has pathological effects on the semicircular canals and otolith organs in the inner ear.[3] These effects contribute to problems with the vestibular system, which manages balance.
- Vestibular dysfunction is 70% higher[4] in people with diabetes than in those without the disease, and the incidence of falls is 39% higher.[5]
- Diabetes has been shown to reduce cerebral microcirculation, including in the auditory centers of the brain.[6] It may also affect cortical auditory processing,[7] and both of these conditions can affect hearing.

2. Understand how diabetes can affect hearing and balance and encourage your patients to monitor their ear health.

   At each health care visit, tell your patients with diabetes about the signs of hearing and balance problems. This will help them be aware of changes when they start. Make sure your patients understand the information by asking them to repeat back what they heard.

3. Ask your patients questions about their ear health at each health care visit.

   For example:

   - Do you have any concerns about your hearing?
   - Do you get a hearing screening, also called an audiological evaluation, every year?
   - Do you know how diabetes can cause hearing loss?
   - Have you fallen recently? Do you have a fear of falling? Do you often feel dizzy or off balance?

   You can refer your patients to an audiologist or ask them if they want more information about recommended ear care for people with diabetes. You can base this action on how your patients answer your questions and any other concerns they share during the visit.

4. Remind your patients to keep their blood glucose, blood pressure, and blood lipids within normal levels for optimum hearing health.

   Use the following discussion points to help you talk with your patients about their self-care habits and their feelings about managing diabetes:

   - Promote the ABCs of diabetes (A1C, blood pressure, cholesterol, and smoking cessation) and a healthy lifestyle.
   - Ensure that patients have access to health coaches, patient navigators, and community health workers when possible.
   - Ask your patients what other health exams they are getting, including regular ear health checkups.
   - Assess symptoms that might require referral to a specialist.

     Follow up with your patients to track how well they are managing their diabetes and connecting with their health care team.
   - Assess socioeconomic factors that can affect health, such as food insecurity, housing insecurity or homelessness, financial barriers, and lack of social support. Use this information when you make treatment decisions.
   - Refer patients to local community resources when available.

5. Refer your patients to diabetes self-management education and support (DSMES) services.

Photo courtesy of the National Institutes of Health

DSMES services help people live well with diabetes. Whether a person has just been diagnosed with diabetes or has had it for years, DSMES services will make it possible for them to:

- Work with a diabetes care and education specialist to set and track goals.
- Practice how to fit diabetes self-care behaviors, like healthy eating and problem-solving, into all parts of their life.
- Learn how to use knowledge, skills, and tools to build confidence and emotional strength to manage diabetes.
- Find ways to get support (in person or online) from family, friends, their community, and their health care team.

Learn more about DSMES at https://www.cdc.gov/diabetes/managing/education.html

Encourage your patients to find a DSMES program that is recognized by the American Diabetes Association or accredited by the Association of Diabetes Care & Education Specialists by visiting http://www.diabeteseducator.org/living-with-diabetes/find-an-education-program

Additional references available at https://www.cdc.gov/diabetes/managing/diabetes-hearing-loss.html

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Cardiovascular-related Deaths in the U.S. Fall, but Disparities Remain

Findings support personalized public health interventions to help close gaps.

Kyalwazi AN, Loccoh EC, Brewer LC, et al. Disparities in cardiovascular mortality between Black and white adults in the United States, 1999 to 2019

Research supported by the National Institutes of Health shows that cardiovascular-related deaths have declined over the past two decades, but disparities remain. Researchers found that inequities are mostly driven by differences in race and ethnicity, geographic location, and access to care, among other factors. The findings were published in Circulation, and the research was partially funded by the National Heart, Lung, and Blood Institute (NHLBI), part of NIH.

In one paper, researchers analyzed data from the Centers for Disease Control and Prevention and found that, after adjusting for age, rates of cardiovascular disease-linked deaths dropped among Black and white adults between 1999 and 2019, as did heart disease-related disparities between the two groups. However, Black adults continue to experience higher death rates than white adults, especially in rural or segregated areas, according to the researchers.

"The persistent disparities observed in our study likely reflect the fact that Black adults disproportionately experience social, economic, and environmental barriers to optimal health due to systemic inequities and structural racism," said Rishi K. Wadhera, MD, a section head of Health Policy and Equity at the Smith Center for Outcomes Research at Beth Israel Deaconess Medical Center and an assistant professor of medicine at Harvard Medical School, Boston.

Wadhera and the researchers found these disparities were most pronounced among younger Black adults. Lack of access to quality maternal health care and mass incarceration could help explain that trend, they wrote. Importantly, what has helped mitigate those effects, they said, are initiatives in Black communities that expand access to cardiovascular disease risk screenings, prevention, and care — for example, blood pressure screenings at barbershops.

In a second paper, researchers with the Multi-Ethnic Study of Atherosclerosis (MESA) described similar associations after partnering with 6,814 U.S. adults. During 15 years of follow-up, Black adults had a 34% greater risk for overall death compared to white adults. The researchers found that common social determinants of health — such as the socioeconomic status of a person's neighborhood, access to health care, income, and education — served as independent predictors for death.

After adjusting for those factors, such as comparing adults with similar household income and financial resources, education, and access to health care, the relative excess risk of death in Black adults fell by about half, to 16%. Similar reductions were noted among Hispanic and Asian Americans compared to white adults.

The study also considered other factors associated with overall and cardiovascular deaths among Black, white, Hispanic, and Asian Americans, including social, lifestyle, and clinical risk factors. After factoring in these variables, Hispanic and Asian Americans had the lowest risk for overall death, which was partially reversed after accounting for immigration history. In this case, less time living

Photo courtesy of the National Heart, Lung, and Blood Institute: Drazen Zigic/Shutterstock

in the United States had a slightly protective effect — which may be due to better baseline health of participants or having less time to adapt to an American lifestyle.

About one in five MESA participants (1,552) died during the 15-year period. Cardiovascular-related events accounted for one-fourth of these deaths, and this proportion was highest in Asian Americans (27.6%), followed by Black (25.4%), Hispanic (25%), and white (20.1%) adults.

"In addition to assessing traditional risk factors for heart disease, such as diabetes, family history, blood pressure, cholesterol, and smoking, this research shows the importance of identifying and accounting for social determinants of health when calculating risk," said Wendy S. Post, MD, MS, a study author and director of cardiovascular research at Johns Hopkins University School of Medicine, Baltimore. "More importantly, we must identify systemic factors in our society that can be altered to improve these longstanding inequities.

A third paper describes an increase in heat-related cardiovascular deaths among U.S. adults during the summer months of 2008-2017.

Using data from the CDC, the authors found older adults, men, and Black adults were most likely to experience cardiovascular-related deaths due to an increase in temperatures where the heat index rose to at least 90 degrees. They also discussed potential solutions to help reverse these outcomes, such as increasing access to shade or cooling centers in communities.

"Multiple factors can independently and synergistically influence cardiovascular health," said Nicole Redmond, MD, PhD, MPH, chief of the Clinical Applications and Prevention Branch in NHLBI's Division of Cardiovascular Sciences. "Further study of the intersection of environmental, social, behavioral, and clinical risk factors and potential interventions are needed to mitigate these risks and close the equity gap."

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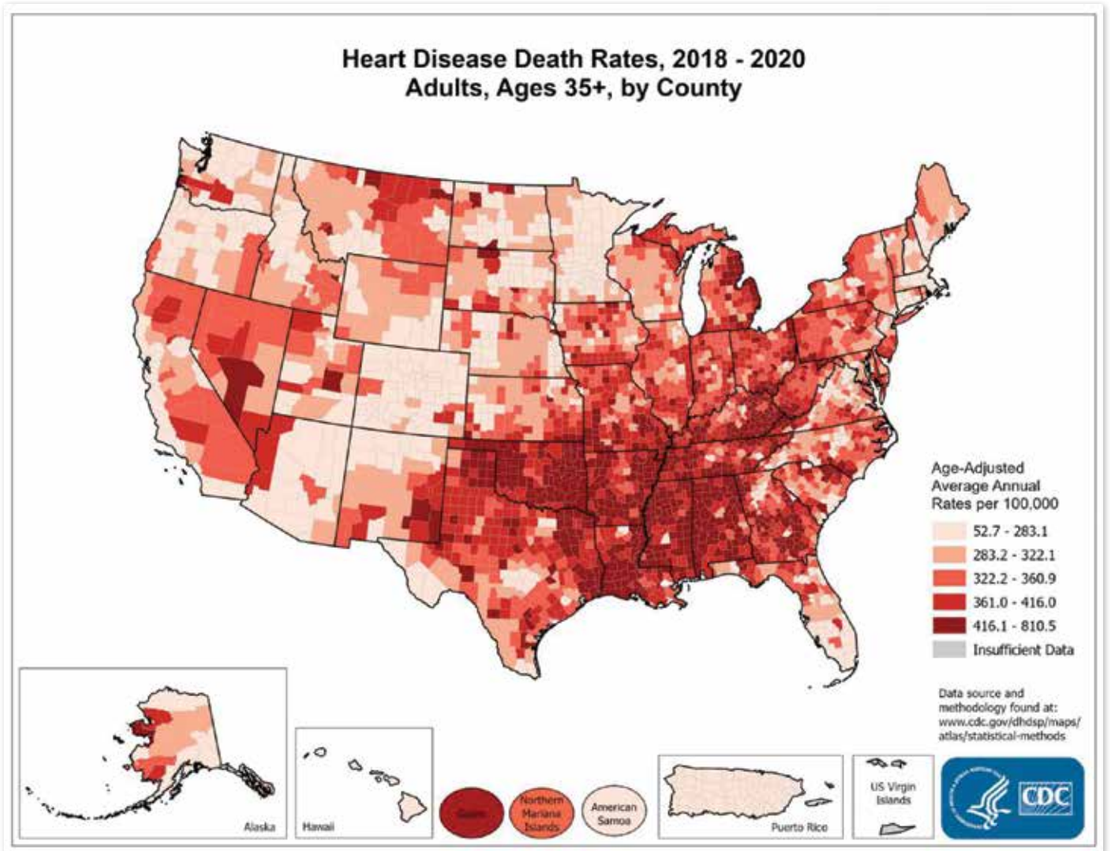


Graphic courtesy of the National Center for Chronic Disease *Prevention and Health Promotion*

Good Hydration May Reduce Long-term Risks for Heart Failure

Serum sodium levels may help identify adults with a greater chance of experiencing heart disease.

By Delong Liu, PhD, Colin O. Wu, PhD, and the Division of Intramural Research at NHLBI

Staying well-hydrated may be associated with a reduced risk for developing heart failure, according to researchers at the National Institutes of Health. Their findings, which appear in the E*uropean Heart Journal*, suggest that consuming sufficient amounts of fluids throughout life not only supports essential body functioning, but may also reduce the risk of severe heart problems in the future.

Heart failure, a chronic condition that develops when the heart does not pump enough blood for the body's needs, affects more than 6.2 million Americans, a little more than 2% of the population. It is also more common among adults ages 65 and older.

"Similar to reducing salt intake, drinking enough water and staying hydrated are ways to support our hearts and may help reduce long-term risks for heart disease," said Natalia Dmitrieva, PhD, the lead study author and a researcher in the Laboratory of Cardiovascular Regenerative Medicine at the National Heart, Lung, and Blood Institute (NHLBI), part of NIH.

After conducting preclinical research that suggested connections between dehydration and cardiac fibrosis, a hardening of the heart muscles, Dmitrieva and researchers looked for similar associations in large-scale population studies. To start, they analyzed data from more than 15,000 adults, ages 45-66, who enrolled in the Atherosclerosis Risk in Communities (ARIC) study between 1987-89 and shared information from medical visits over a 25-year period.

In selecting participants for their retrospective review, the scientists focused on those whose hydration levels were within a normal range and who did not have diabetes, obesity, or heart failure at the start of the study. Approximately 11,814 adults were included in the final analysis, and of those, the researchers found, 1,366 (11.56%) later developed heart failure.

To assess potential links with hydration, the team assessed the hydration status of the participants using several clinical measures. Looking at levels of serum sodium, which increases as the body's fluid levels decrease, was especially useful in helping to identify participants with an increased risk for developing heart failure. It also helped identify older adults with an increased risk for developing both heart failure and left ventricular hypertrophy, an enlargement and thickening of the heart.

For example, adults with serum sodium levels starting at 143 milliequivalents per liter (mEq/L) — a normal range is 135-146 mEq/L — in midlife had a 39% associated increased risk for developing heart failure compared to adults with lower levels. And for every 1 mEq/L increase in serum sodium within the normal range of 135-146 mEq/L, the likelihood of a participant developing heart failure increased by 5%.

In a cohort of about 5,000 adults ages 70-90, those with serum sodium levels of 142.5-143 mEq/L at middle age were 62% more likely to develop left ventricular hypertrophy. Serum sodium levels starting at 143 mEq/L correlated with a 102% increased risk for left ventricular hypertrophy and a 54% increased risk for heart failure.

Based on these data, the authors conclude serum sodium levels above 142 mEq/L in middle age are associated with increased risks for developing left ventricular hypertrophy and heart failure later in life.

A randomized, controlled trial will be necessary to confirm these preliminary findings, the researchers said. However, these early associations suggest good hydration may help prevent or slow the progression of changes within the heart that can lead to heart failure.

"Serum sodium and fluid intake can easily be assessed in clinical exams and help doctors identify patients who may benefit from learning about ways to stay hydrated," said Manfred Boehm, MD, who leads the Laboratory of Cardiovascular Regenerative Medicine.

Fluids are essential for a range of bodily functions, including helping the heart pump blood efficiently, supporting blood vessel function, and in orchestrating circulation. Yet many people take in far less than they need, the researchers said. While fluid guidelines vary based on the body's needs, the researchers recommended a daily fluid intake of 6-8 cups (1.5-2.1 liters) for women and 8-12 cups (2-3 liters) for men. The Centers for Disease Control and Prevention also provides tips to support healthy hydration.

nih.gov

Study Adds to Debate about Screening for Melanoma

By Carmen Phillips

Should people undergo regular checks for skin cancer, particularly the deadliest form, melanoma? That depends on who you ask.

In its most recent recommendations, an influential federal health advisory panel said there isn't enough evidence to recommend for or against routine skin cancer screening. But professional dermatology organizations and skin cancer advocacy groups aren't necessarily on the same page, with at least one recommending that adults have annual skin checks.

With that backdrop come new results from one of the largest skin cancer screening initiatives of its kind conducted in the United States. The NCI-supported observational study involved nearly 600,000 people who went to see their primary care physician for a routine visit.

The findings were not necessarily surprising. They showed that people who were screened for skin cancer during the 5-year study period were more likely to be diagnosed with very early-stage melanoma than those who were not screened, according to results reported April 6 in JAMA Dermatology.

In other words, the suspect moles found, and subsequently removed, by doctors during screening were present only on the top layer of the skin — known as the epidermis — or 1 mm or less below the epidermis. These are called in situ (or stage 0) and stage 1 melanomas, respectively.

Although the study leaders expected that more early-stage melanomas would be found, they didn't necessarily anticipate the extent to which screening would increase the likelihood of being diagnosed with these thin melanomas. In the case of in situ cancers, for example, the difference was more than two-fold.

The findings reinforce an underlying expectation that comes with screening for any cancer, explained the study's lead investigator, Laura Ferris, MD, PhD, professor of dermatology at the University of Pittsburgh School of Medicine. When it comes to cancer screening, Dr. Ferris said, "If you go looking for something, you tend to find more of it, and you tend to find more early-stage disease."

The findings also contribute to an ongoing debate about screening for skin cancer: Does it reduce the number of deaths from melanoma, which is the goal of screening? Or is it simply leading to lots of people being diagnosed with a cancer that would never have caused them any harm, a phenomenon called overdiagnosis?

Isaac Brownell, MD, PhD, Senior Investigator, Chief, Cutaneous Development and Carcinogenesis Section Dermatology Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases.
Photo courtesy of NIAMSD

Identifying so many early-stage melanomas "does raise a concern about overdiagnosis," Dr. Ferris said. But that doesn't mean that some of the melanomas being found aren't potentially deadly. It also doesn't mean that the increase in melanoma incidence over the past several decades should be solely chalked up to overdiagnosis and ignored or dismissed as irrelevant.

"That would be throwing out the baby with the bathwater," she said.

Uncertainty around screening for melanoma

Once a rare form of cancer, melanoma's incidence in the United States has steadily and consistently climbed over the past five decades. It's now the fifth most common cancer — behind breast, lung, prostate, and colon.

As is the case with some of those other common cancers, melanoma's increased incidence has been linked to the fact that doctors are looking for it more than they used to. Routine skin checks, specifically a kind known as total-body skin examinations, have become commonplace among dermatologists in particular, even if a person is coming in for another reason.

When there is a sustained increase in the incidence of a type of cancer that can be found through early detection, but the number of people dying from it stays the same, it automatically raises concerns about overdiagnosis. In other words, if truly life-threatening cancers were being found early enough to be treated successfully, the number of deaths from that cancer should drop.

Thyroid cancer, for example, was once rare. But its incidence in the United States skyrocketed over several decades before stabilizing in the mid-2010s. The increase was driven largely by the incidental discovery of small thyroid tumors, such as during imaging scans of the neck and head for other health problems. Deaths from thyroid cancer, however, have remained unchanged.

Melanoma has followed a similar track, leading some researchers to argue that screening is not saving lives, just leading to more melanoma diagnoses. The federal panel, the US Preventive Services Task Force (USPSTF), issued an "inconclusive" recommendation on skin cancer screening in 2016. The evidence, the panel concluded, wasn't sufficient to show that screening reduces deaths from melanoma.

The American Academy of Dermatology doesn't specifically recommend regular screening. But it does promote skin self-checks and has long operated a program to help others organize free skin cancer screenings.

There are no easy answers to the screening question, said Isaac Brownell, MD, PhD, of the National Institute of Arthritis and Musculoskeletal and Skin Diseases, a skin cancer expert and practicing dermatologist.

Although screening will pick up more early-stage cancers, the true lethal threat posed by in situ and stage 1 tumors isn't known, Dr. Brownell continued. Some smaller studies, however, have suggested that they might present a substantial risk of death.

"There are definitely people with early-stage disease who will later progress and die" if their tumor is not removed, Dr. Brownell said.

USPSTF is in the process of updating its recommendations on skin cancer screening. It's unclear, though, whether there's any new evidence that could lead the panel to recommend routine screening.

Typically, such evidence would come from a randomized clinical trial, the gold standard of medical studies. In such studies, participants are randomly assigned to specific groups — in this case, routine screening or usual care — and their outcomes are compared.

For several reasons, including a likely very large price tag and complicated logistics, there's no expectation that a randomized trial of skin cancer screening will be conducted any time soon, wrote Robert Swerlick, MD, director of the Department of Dermatology at the Emory University School of Medicine, in an editorial in JAMA Dermatology that accompanied the new study results.

"While the need for such a trial has been highlighted repeatedly, very little has been published regarding how such a study could be undertaken and sufficiently powered to detect an effect of screening examinations on melanoma deaths," Dr. Swerlick wrote.

In the absence of evidence from randomized clinical trials and any consensus from medical groups, Dr. Ferris said she and her colleagues had been intrigued by early findings from a large study of skin cancer screening conducted in northern Germany.

Initial data from the German study suggested that screening was leading to fewer deaths from melanoma. So Dr. Ferris and her colleagues decided to launch a similar study that they hoped could inform screening practices in the United States.

Finding many early-stage melanomas

The study ran from 2014 to 2018 in the University of Pittsburgh Medical Center (UPMC) system, a hospital and physician organization with a massive footprint in western Pennsylvania.

It enrolled people aged 35 and older who were seeing their primary care physician for a routine office visit. Participating physicians were not required to ask every patient if they wanted to be screened. They also were invited, but not required, to undergo training on how to perform total-body skin exams.

Of the nearly 600,000 patients who were included in the study, about 24% (144,581) had at least one documented screening during the study period. The study's primary measure of interest was the stage of the melanomas diagnosed in the screened and unscreened groups.

During the 5-year study period, more early-stage melanomas were diagnosed in both groups than thicker, later-stage melanomas. People in the screening group, however, were 160% more likely to be diagnosed with an in situ melanoma, and 80% more likely to be diagnosed with a stage 1 melanoma.

In both the screened and unscreened groups, most melanoma diagnoses occurred more than 2 months after the initial patient visit. These were considered to be "interval melanomas," which,

Photo courtesy of the National Library of Medicine

in practical terms, means they were most likely diagnosed because of another skin screening or because a patient proactively went to their doctor to get a mole checked.

Because of how the study was designed and conducted, it has several limitations, Dr. Ferris and her colleagues explained.

For example, people in the study who underwent screening may be more healthful in general, the quality of the screenings performed may have been variable, and all the relevant information about screening in both groups is likely incomplete. All these factors could have affected the study's results, they noted.

Is all cancer overdiagnosis created equal?

The findings from the UPMC study provide "very strong evidence of overdiagnosis," wrote Dr. Swerlick, who initially raised concerns about screening-induced melanoma overdiagnosis in the mid-1990s. "The purpose of applying increasing amounts of screening intensity is to avoid melanoma death. … Screening skeptics cannot prove a negative, but it should fall on screening advocates to demonstrate that such activities add value to patients' lives."

Concerns about the overdiagnosis of cancer that can result from screening are well founded, wrote Sancy Leachman, MD, PhD, director of the Melanoma Research Program at the Knight Cancer Institute in Portland, Oregon, and several colleagues in another accompanying editorial in *JAMA Dermatology.*

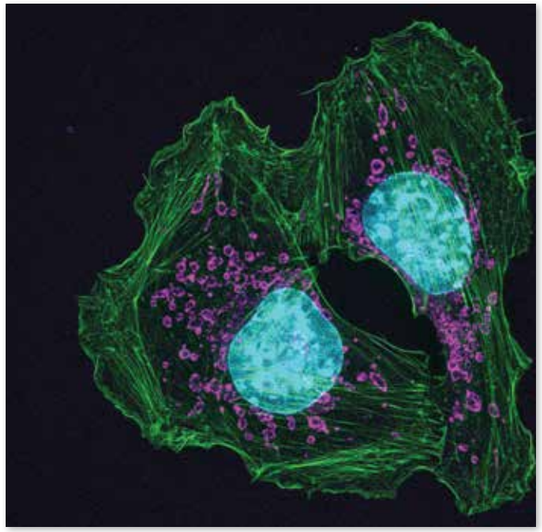
They argued, however, that melanoma is different in many respects from other cancers where overdiagnosis has been a concern.

Melanoma "is more lethal at a smaller volume compared with other cancers," Dr. Leachman and her colleagues explained. Cancer-fueling mutations can quickly build up in melanoma, they continued, "which means that thin melanomas are vulnerable to rapid transformation to thicker more deadly melanomas."

And although there are now a host of proven treatments for later-stage melanomas, they are not uniformly effective, can have significant side effects, and are expensive. All those factors make "early diagnosis particularly important and counterbalance the risk of overdiagnosis," they wrote.

Dr. Ferris agreed, in part. Removing a thin melanoma found because of screening is far less onerous and potentially dangerous than, say, the invasive procedures required to follow up on a lesion identified in the lungs during screening for lung cancer.

"That's a much bigger deal than taking a mole off," she said. But she cautioned that there are potential downsides of melanoma overdiagnosis, both for individual people and society more broadly. For individuals, they now have a cancer diagnosis, which can lead to everything from long-term anxiety to increased health insurance costs and greater difficulty getting life insurance.



Skin cancer cells from a mouse. Photo courtesy of Knight Cancer Institute, Catherine and James Galbraith

There's also a shortage of dermatologists in the United States, particularly in certain areas of the country. The time dermatologists spend on skin checks and the routine follow-up tests that can ensue is likely contributing to the long delays to see a dermatologist in some areas, she said. That can have a trickle-down effect.

"We might be limiting our ability to get others with a higher risk of melanoma in [for an appointment]," she said, potentially delaying the diagnosis of truly life-threatening cancers.

Focusing melanoma screening on those at higher risk?
In the German study on which the UPMC study was partially modeled, the early suggestion that screening reduced the number of deaths from melanoma went away after participants were followed for a longer time.

And with the unlikely prospect of a randomized clinical trial of skin cancer screening, Dr. Ferris said researchers will have to be "open minded" about different ways to evaluate and implement screening. One potential way to mitigate melanoma overdiagnosis, she continued, is to focus screening on those at increased risk of the disease.

There are no widely recognized criteria for classifying whether a person is at increased melanoma risk. But physicians can consider certain factors when deciding whether to conduct full-body skin exams, said Dr. Brownell, who also codirects the Cutaneous Oncology Program at Walter Reed National Military Medical Center's Murtha Cancer Center.

For example, men over age 50 are more likely to have potentially dangerous melanomas, he explained, as are people with fair skin, who have had blistering sun burns, and who have a family or personal history of skin cancer.

Incorporating these sorts of risk factors into physician decision-making "would simultaneously increase the numbers of melanomas detected per individuals screened and reduce the total number of overdiagnoses," Dr. Leachman and her colleagues wrote.

Can new technology help?

In addition to personal factors that can identify those at increased melanoma risk, noninvasive tools are becoming available that can help physicians make more informed choices about whether to remove suspicious moles and potentially reduce overdiagnosis.

For example, dermatologists routinely use dermoscopy, which involves a souped-up magnifying glass that can zoom in on a mole, to look for features that are indicative of those seen in melanoma.

Another imaging-based tool starting to be studied, called in vivo confocal microscopy, provides "a cellular view of the skin," Dr. Brownell explained. It allows physicians to see individual melanocytes — the pigment-producing cells in which melanoma forms. If the clinician sees "funny-looking melanocytes," he said, "they can then biopsy that lesion."

This technology is still being studied, he noted, and is mostly only available at large medical centers.

One noninvasive method that is increasingly being used in everyday practice relies on a special kind of tape that is placed on a mole and then removed, capturing genetic material from melanocytes. That material, Dr. Ferris explained, is then analyzed for the presence of melanoma-related genetic changes.

A newer technology, also available mostly at large cancer centers, is total body photography. Typically used on people at high risk of skin cancer or who previously had skin cancer, the technology can capture high-resolution images of every mole on a person's body in a single short scan. Techniques using artificial intelligence are also being studied as a way to noninvasively identify cancerous moles.

But more research is needed to determine if these technologies can help better identify truly dangerous melanomas and limit overdiagnosis, Dr. Brownell said.

Until then, a screening juggling act is likely to continue.

"As a society, we need to ask if the costs and potential harms [of overdiagnosis] are justified by the number of lives that could be lost to melanoma" without screening, he said. "And we just don't know those answers."

cancer.gov

Natural Disasters, Emergency Wound Management for Healthcare Professionals

The risk for injury during and after a natural disaster is high. Tetanus is a potential health threat for persons who sustain wound injuries. Tetanus is a serious, often fatal, toxic condition, but is virtually 100% preventable with vaccination. Any wound or rash has the potential for becoming infected and should be assessed by a health-care provider as soon as possible.

These principles can assist with wound management and aid in the prevention of amputations. In the wake of a flood disaster resources are limited. Following these basic wound management steps can help prevent further medical problems.

Evaluation

- Ensure that the scene is safe for you to approach the patient, and that if necessary; it is secured by the proper authorities (police, fire, civil defense) prior to patient evaluation.
- Observe universal precautions, when possible, while participating in all aspects of wound care.
- Obtain a focused history from the patient, and perform an appropriate examination to exclude additional injuries.

Treatment

- Apply direct pressure to any bleeding wound, to control hemorrhage. Tourniquets are rarely indicated since they may reduce tissue viability.
- Examine wounds for gross contamination, devitalized tissue, and foreign bodies.
- Remove constricting rings or other jewelry from injured body part.
- Cleanse the wound periphery with soap and sterile water or available solutions, and provide anesthetics and analgesia

Hurricane Ian satellite image from September 29, 2022 at 9:42 AM. Photo courtesy of Beaufort County South Carolina

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whenever possible.

- Irrigate wounds with saline solution using a large bore needle and syringe. If unavailable, bottled water is acceptable.
- Leave contaminated wounds, bites, and punctures open. Wounds that are sutured in an unsterile environment, or are not cleansed, irrigated, and debrided appropriately, are at high risk for infection due to contamination. Wounds that are not closed primarily because of high risk of infection should be considered for delayed primary closure by experienced medical staff using sterile technique.
- Remove devitalized tissue and foreign bodies prior to repair as they may increase the incidence of infection.
- Clip hair close to the wound, if necessary. Shaving of hair is not necessary, and may increase the chance of wound infection.
- Cover wounds with dry dressing; deeper wounds may require packing with saline soaked gauze and subsequent coverage with a dry bulky dressing.
- If wound infections develop, see "Guidance for Management of Wound Infections" (see below).
- Follow tetanus prophylaxis guidelines for all wounded patients found at: https://www.cdc.gov/disasters/disease/tetanus.html
- Follow tetanus prevention guidelines found at: https://www.cdc.gov/tetanus/about/prevention.html

Other Considerations

- Be vigilant for the presence of other injuries in patients with any wounds.
- Ensure adequate referral, follow-ups, and reevaluations whenever possible.
- Dirty water and soil and sand can cause infection. Wounds can become contaminated by even very tiny amounts of dirt.
- Puncture wounds can carry bits of clothing and debris into wound resulting in infection.
- Crush injuries are more susceptible to infection than wounds from shearing forces.

Guidance for Management of Wound Infections

Most wound infections are due to staphylococci and streptococci. This would likely hold true even in the post-hurricane setting.

- For initial antimicrobial treatment of infected wounds, beta-lactam antibiotics with anti-staphylococcal activity (cephalexin, dicloxacillin, ampicillin/sulbactam etc.) and clindamycin are recommended options.
- Of note, recently an increasing number of community associated skin and soft tissue infections appear to be caused by methicillin-resistant Staphylococcus aureus (MRSA).

Photo courtesy of the Town of Fort Myers Beach Florida

Infections caused by this organism will not respond to treatment with beta-lactam antibiotics and should be considered in patients who fail to respond to this therapy. Treatment options for these community MRSA infections include trimethoprim-sulfamethoxazole (oral) or vancomycin (intravenous). Clindamycin is also a potential option, but not all isolates are susceptible.

- Incision and drainage of any subcutaneous collections of pus (abscesses) is also an important component of treating wound infections.

Special Considerations Related to Contamination of Wounds by Water

Contamination of wounds with water (fresh or sea water) can lead to infections caused by waterborne organisms. Though infections with these organisms are uncommon, even after floods, this possibility should be considered in patients who fail to respond to initial therapies described above. Water-borne organisms often implicated in these infections include: Aeromonas spp., non-cholera Vibrio spp. and sometimes Pseudomonas or other Gram-negative rods.

Trimethoprim/sulfamethoxazole, amoxicillin/clavulanate and newer fluoroquinolones (levofloxacin, moxifloxacin, gatifloxacin) will treat Aeromonas and the fluoroquinolones will also treat Pseudomonas and many other Gram-negative pathogens.

Clinicians should consider Vibrio as a possible causative organism of wound infections incurred in coastal waters or from contact with shellfish or marine wildlife. Vibrio vulnificus wound infections may require extensive debridement and mortality can be high. These infections often manifest with bullous lesions that may be hemorrhagic. Persons with underlying hepatic disease or other immunocompromising illness are at highest risk of Vibrio vulnificus infection. When this infection is suspected, the recommendation is that patients be treated with a combination of ceftazidime and doxycycline.

cdc.gov

CPG

HHS Medical Teams Boosting Health Care Services in Florida in Aftermath of Hurricane Ian

By the HHS, Administration for Strategic Preparedness and Response (ASPR)

More than 350 U.S. Department of Health and Human Services (HHS) medical, public health, and disaster response personnel were deployed to support Florida communities as part of the Biden Administration's government-wide response to the devastation caused by Hurricane Ian.

"Hundreds of dedicated medical professionals from HHS are engaged in the disaster response to help residents affected by Hurricane Ian," said HHS Assistant Secretary for Preparedness and Response (ASPR) Dawn O'Connell "We will do everything we can to support the people of Florida as the local healthcare infrastructure comes back online."

Personnel from HHS' National Disaster Medical System (NDMS) currently provided care in Florida's Sarasota, Charlotte, and Lee counties. In Sarasota County, personnel provided surge support in medical tents for the influx of patients arriving at the Sarasota Memorial Hospital Emergency Department. In Charlotte County, personnel operated a stand-alone medical station in tents outside the Charlotte County Cultural Center. Three of five Charlotte County hospitals were closed due to damages sustained from Hurricane Ian; the fourth was operating at partial capacity, leaving only one fully open hospital. In Lee County, teams supported four hospitals — Cape Coral Hospital, Lee Memorial Hospital, HealthPark Medical Center, and Gulf Coast Medical Center — as well as staffing a stand-alone medical station in tents outside the Peace River North Port Rehabilitation Center.

Teams of responders from the National Disaster Medical System working with the staff at the Sarasota Memorial Hospital Emergency Department in Venice, FL to protect health and save lives following Hurricane Ian.
Photo courtesy of ASPR

HHS continued working with federal and state partners to prioritize medical assistance to other areas affected by Hurricane Ian. Additional NDMS teams were alerted to stand ready to support medical missions in the hardest hit areas of Florida.

NDMS teams travel with federal medical equipment and supplies. HHS deployed approximately 60 trucks — 600,000 tons — of equipment and supplies for NDMS teams' use in providing patient care in Florida.

In addition to sending in medical teams, supplies, and equipment, HHS took proactive measures to support the needs of at-risk populations.

- HHS declared a public health emergency for Florida and South Carolina following President Biden's emergency declarations for each state, giving the Centers for Medicare & Medicaid Services (CMS) beneficiaries and their health care providers and suppliers greater flexibility in meeting emergency health needs, including making section 1135 waivers available to help ensure that beneficiaries in impacted areas receive the care they need.
- The HHS emPOWER program provides information on the number of Medicare beneficiaries in impacted zip codes who rely on electricity-dependent durable medical equipment and certain healthcare services, such as dialysis, oxygen tank, or home health, to help the state anticipate, plan for, and respond to the needs of these potentially at-risk citizens.
- The Centers for Disease Control and Prevention (CDC) worked together with state authorities to push out information and resources specific to at-risk populations, including older adults, those with chronic conditions, and people with other functional and access needs. Topics include floodwater safety, carbon monoxide poisoning prevention and other power outage safety; and food and water safety.
- CDC also issued a clinical guidance through the Health Alert Network (HAN) for carbon monoxide poisoning.
- The Substance Abuse and Mental Health Services Administration also made the Disaster Distress Helpline available 24 hours a day, seven days a week. People in impacted areas can call or text 1-800-985-5990 to connect with a trained crisis counselor.

aspr.hhs.gov

Celebrating a Decade of the CDC's Public Health Emergency Management (PHEM) Fellowship Training Program

Established in 2013, CDC's Public Health Emergency Management (PHEM) Fellowship is conducted twice year at CDC in Atlanta, Georgia. The fellowship builds PHEM capacity among members of the international public health community through standardized training, mentorship, and technical assistance. It targets mid-career professionals who work in public health preparedness and response in countries who have signed on to International Health Regulations.

During their four months in Atlanta, fellows receive specialized training in public health emergency management functions and operations, participate in site visits, take part in public health exercises and responses, and receive guidance from federal, state, and local emergency management specialists.

Trained experts who know what to do are critical to building a functioning EOC; more valuable than state-of-the art equipment or supplies is the knowledge emergency management experts can bring to the table. When every second counts, understanding how to coordinate an effective response can save lives.

PHEM and Global Health Security

Monitoring and responding to public health events through an Emergency Operations Center is a cornerstone of both the International Health Regulations (IHR) and the Global Health Security Agenda (GHSA).

These two international agreements are key to the world's effort to better prevent, detect, and respond to public health threats. Having an Emergency Operations Center that can respond within two hours of an emergency is one of the stated goals of the GHSA.

Official presentation of new PHEM Intermediate Participants' Training Manual to Lagos State Director of Surveillance, Epidemiology & Health Security at the training venue, September 2021. Photo courtesy of the CDC

The goals of the Public Health Emergency Management Fellowship Program are to:

- Provide in-depth exposure to public health emergency management frameworks, functions, staff, and program elements.
- Provide in-depth exposure to the functioning of a Public Health Emergency Operations Center (PHEOC).

By the end of the fellowship, Fellows will understand public health emergency management principles and gain a working knowledge of the functioning of an emergency operations center. Furthermore, they will be able to demonstrate the following skills:

- Collect, analyze, and disseminate critical public health information
- Manage an emergency situation effectively
- Have an understanding of emergency operation centers operations, organizational structure, staffing, and schedules
- Interact with staff responsible for carrying out emergency management
- Train relevant professional staff members in their home country

Since the 2013 inaugural class, CDC has graduated 69 Emergency Management Specialists from 28 different countries. Fellows come from diverse cultural and career backgrounds. Fellows must be willing to commit to the four-month program, demonstrate English proficiency, and achieve the necessary CDC security clearance.

FETP resident wearing personal protective equipment (PPE) while investigating COVID-19 in the Amazonas state of Colombia. Photo courtesy of the CDC

PHEM Fellows usually:

- Hold a Master's degree, doctorate or equivalent in public health, epidemiology or a related field
- Have a level of responsibility within their Ministry of Health that reflects leadership of a public health emergency management function and requires coordination with other emergency management functions
- Have a position, or are expected to have a position, that will support their training or influence others upon return to the home country

In 2017, CDC hosted 30 fellows that represented 17 countries. This was the first time Fellows from Bangladesh, Democratic Republic of the Congo, and Indonesia participated in the program. Fellows come from various positions within Ministries of Health. Roles fellows have held prior to joining the Fellowship include:

- Epidemiology/Surveillance
- Emergency Preparedness and Response
- Medicine / Community Health
- Infectious Disease Preparedness
- Information Management and Technology

Facilitators (CDC-N and NCDC) reviewing a session on PHEOC De-Escalation and De-Activation during the training, September 2021. Photo courtesy of the CDC

Post-Fellowship Experiences

Upon completion of PHEM Fellowship, Fellows are asked to apply their learning to develop a personal toolkit: a series of papers, recommendations or projects that can be shared with colleagues in their countries on their return. Alumni of PHEM Fellowship have participated in 13 exercises and 29 real-world public health emergency responses, serving in a variety of roles, including response incident manager, outbreak investigation team lead, operations coordinator, and liaison officer.

Fellows facilitate the expansion of public health emergency management within their countries and have returned to their home countries to assume key roles in public health. Examples of roles fellows have taken on after their training include:

- Director of the Public Health Emergency Center in the China CDC
- Director of the Disaster Risk Management Unit in the Kenya Ministry of Health
- Strategic Health Operations Centre Officer-in-Charge in India's National Centre for Disease Control
- EOC Manager in the Thailand Ministry of Public Health Department of Disease Control

"CDC has been a successful role model for National Public Health Institutes, emphasizing science, service, prevention, and surveillance. Its efforts over the years, including its support of IANPHI's programs, have strengthened public health globally and promoted best practices."

— Jeffrey P. Koplan, MD, MPH
Former Director of CDC and co-founder of IANPHI

For more information contact: Karen Ossorio, Country Support Team Lead, Global Emergency Management Capacity Development Branch (proposed) Division of Emergency Operations, OPHPR, CDC
kcu7@cdc.gov / 404-281-4298

cdc.gov

IHS Invests Nearly $136 million for Special Diabetes Program for Indians

The Indian Health Service is announcing an investment of nearly $136 million in funding for the Fiscal Year 2023 Special Diabetes Program for Indians to provide diabetes treatment and prevention services for American Indian and Alaska Native communities. Individual award amounts for the first budget year are anticipated to be between $12,500 and $7.5 million.

"We are excited about this new round of funding for Indian Country to address diabetes-related health issues in our American Indian and Alaska Native communities," said Acting Director Elizabeth Fowler. "Since its inception in 1997, the Special Diabetes Program for Indians has helped to dramatically increase access to important diabetes treatment and prevention services throughout Indian Country. With this new round of funding, the IHS is committed to continuing its support for diabetes treatment and prevention for IHS, tribal, and urban Indian health programs."

Photo courtesy of Indian Health Service

SDPI program sites have successfully implemented evidence-based and community driven strategies to prevent and treat diabetes within American Indian and Alaska Native communities. Using guidance from tribal leaders, the SDPI has also engendered a national diabetes network for American Indians and Alaska Natives.

SDPI continues to be a key factor in the improvements seen in diabetes-related health problems in American Indian and Alaska Native people, including reductions by at least one-half in the rates of new cases of diabetes-related kidney failure and eye disease. These outcomes show remarkable progress in the treatment and prevention of diabetes in American Indian and Alaska Native people.

The IHS Division of Diabetes Treatment and Prevention provides programmatic leadership for the SDPI overall, as well as extensive training and resources, which are widely used by SDPI sites and clinicians across the country. Under the last competitive SDPI announcement, IHS made awards to 301 tribal, urban, and IHS SDPI program sites in 35 states.

ihs.gov

Photo courtesy of Indian Health Service

Director's Note: Griffin P. Rodgers, MD, MACP

Director, National Institute of Diabetes and Digestive and Kidney Diseases

Dr. Griffin P. Rodgers has served as NIDDK's acting director since March 2006 and served as the Institute's deputy director since January 2001.
Photo courtesy of the NIH's National Institute of Diabetes and Digestive and Kidney Diseases

The potential for discovery lies around every corner, and NIDDK is on an expedition to foster scientific advances on all fronts. We work to strengthen biomedical research through community collaboration and by bringing opportunities across cultures and time zones to reach people where they are.

In this issue, we share about how NIDDK is helping expose students in Guam to the excitement of scientific discovery through our STEP-UP program, which enables students to gain hands-on research experience, one-on-one mentorship, and access to modern laboratory techniques without traveling far from home.

We also highlight new NIDDK funding opportunities across our mission areas that put community engagement at the center of our efforts to reduce health disparities and improve health equity. As NIDDK program director Dr. Shavon Artis Dickerson said, "when it comes to identifying research priorities and activities to improve health equity, the experts are not in academia, they are in the community."

"Somewhere, something incredible is waiting to be known."

— Carl Sagan

In our Getting to Know feature, Dr. Constance Noguchi shares stories about her work and wisdom for people beginning their careers. We also meet NIDDK fellow Dr. Xiaofei Bai and learn about how he finds inspiration for his research from his hometown community in Inner Mongolia, China.

Within our NIDDK community, we continue to build a strong foundation for equity. I'm pleased to share about a new program that provides NIDDK staff with tools and a professional network for advancing equity, diversity, inclusion, and accessibility at NIDDK and beyond.

In our efforts to strengthen the biomedical research workforce, we recognize that, while talent is everywhere, opportunity is not. I invite you to join NIDDK in spreading the word about our programs and opportunities that aim to bridge this gap by subscribing External link to the NIDDK Director's Update, exploring our website and following us on social media @NIDDKgov

We hope by getting out and meeting people where they are, something incredible will be discovered.

On April 8, 1986, the National Institute of Arthritis, Metabolism, and Digestive Diseases was renamed the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases. It's mission is to conduct and supportmedical research and research training and to disseminate science-based information on diabetes and other endocrine and metabolic diseases; digestive diseases, nutritional disorders, and obesity; and kidney, urologic, and hematologic diseases, to improve people's health and quality of life.

niddk.nih.gov

Project Firstline

Year One Overview

Project Firstline is an infection control training and education collaborative that intends to provide equity of understanding for all frontline healthcare workers, nurses, certified-nurse assistants, environmental services technicians, doctors, allied health professionals, and administrative/intake staff. The innovative content is designed so that — regardless of a healthcare worker's previous training or educational background — they can understand and confidently apply the infection control actions necessary to protect themselves and their patients.

In October 2020, CDC launched Project Firstline to provide all US frontline healthcare workers with the infection control education and training they need and deserve to protect themselves, their patients, and their colleagues from infectious disease threats.

During its first year, Project Firstline and its partners:

- Developed more than 130 educational products about infection control, including an Inside Infection Control video series featuring CDC infectious disease expert Dr. Abby Carlson.
- Created and released a facilitator toolkit with guided session plans and role- and setting-speci ic job aids.
- Hosted more than 300 educational events reaching approximately 33,300 healthcare workers in professions ranging from environmental service workers, to nurses, to physicians.

94% of healthcare workers who participated in these educational events reported improved understanding of infection control topics, while 93% stated they would recommend the trainings to others.

LOOKING AHEAD: THE FUTURE OF PROJECT FIRSTLINE

With increases in healthcare-associated infections observed during the COVID-19 pandemic, it's more important than ever to equip healthcare workers with the infection control knowledge they need to keep themselves and their patients safe. Project Firstline aims to become the go-to resource for infection control training and education for all frontline healthcare workers.

To achieve this goal, the Project Firstline team will continue to listen to and learn from the diverse audiences it's trying to reach. These insights and others learned during the past year are

Graphic courtesy of the CDC

helping inform development of a new suite of educational materials designed to help healthcare workers build a foundational knowledge and understanding of infection control that they can apply daily in their work.

For more information about Project Firstline training, visit https://www.cdc.gov/infectioncontrol/projectfirstline/index.html

cdc.gov

How Texas is Addressing the Threat of Rabies through Vaccinating Wildlife

Interview with Dr. Susan Rollo, Texas State Public Health Veterinarian

By Tom Adams, Publisher of Federal Health & Medicine

With rabies always remaining a public health threat, the importance of awareness for its professionals about prevention and access to treatment, as well as other programs that can help reduce the threat, remains as a priority. This is one of those areas where the state of Texas is conducting its annual bait drop program that vaccinates wildlife against rabies to reduce the risk of animal to human transmission. It was my pleasure to speak with the chief of the program Dr. Susan Rollo, Texas State Public Health Veterinarian and recognize her contribution as well as its nearly 30 year history.

Thank you Dr. Rollo for joining me, and as you know our publication reaches many professionals serving rural areas, where animal to human contact and the risk of rabies is greater. And while other states may have similar wildlife vaccination programs, many do not and could benefit from knowing more about the success of yours when considering a future program of their own.

Our program stemmed from when in 1988 a rabid coyote was first detected here in Texas, and along with educating ourselves about some of the things the Canadians were doing with bait drops, we decided in Texas to try this project and started working with the USDA national rabies program in 1995. We still continue working with them today, and they support us with some personnel and provide some of our bait. They also work in 14 other states along the northeastern part of the U.S., all the way from Maine down to Alabama, where they are mostly combating raccoon rabies.

We don't have the raccoon strain of rabies here in Texas, but do have the

Dr. Susan Rollo, Texas State Public Health Veterinarian. Photo courtesy DSHS

skunk strain still. And as we eradicated the coyote canine strain and fox strain, the remaining strains we have in Texas are the skunks and bats. We did try the baits with skunks from 2012 to 2016 and determined the skunks were not able to bite into the baits well enough to get immunized, so we stopped that project in 2016. I was a part of that project as well, working in the Houston office at the time, and we went out to put baits out and then went back to trap the skunks to test them and see if they were immunized, and we found that we really didn't have very good success, so therefore we only have the buffer zone here in Texas now. We've had different time periods over the last almost 30 years of having outbreaks in fox where we kind of adjusted our zones to fit where those outbreaks were, but we've eventually been able to push those strains down to the border so now we're just doing the buffer zones along the Texas Mexico border.

This program has eliminated the threat of those few strains but we still have the skunk strain which spills over to dogs and cats, and other livestock and other animals such as raccoons from that skunk strain, and of course we still have the bats. So for public health departments, the main educational piece for them is always that rabies is here, and it's here to stay. There's no way to eradicate rabies in bats, and that exposure is very concerning. So we make sure we continue our education with local health departments, and that health departments have a presence and works with animal control, serves officers in the cities and that we identify exposures so that we can get those people accessed and treated if they need it. That really is the cornerstone of our program is identifying and addressing any kind of exposures to potential rabies.

As far as threats along the borders, we continue to monitor and do what we can about other strains that we currently don't have here that are moving in our direction. One of them is the Arizona fox strain, which is moving east and is now in New Mexico, really only one county away from the Texas border. We are also looking at potential new raccoon strains coming from the east, but that's a longer distance away and would take longer to get here. And we don't have good data for the Mexico side of things, and we aren't aware of any wildlife surveillance that's occurring down there, so that's why were unsure about what kind of strains we could get from Mexico.

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NOT ALL PROTECTIVE MEASURES ARE WORN ON THE OUTSIDE.

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RabAvert®
Rabies Vaccine

PROTECTING OUR TROOPS FOR 25 YEARS AND COUNTING.

RabAvert® (Rabies Vaccine) is proven effective providing robust protection.[1,2]

The market-leading rabies vaccine in the US.[3]

Worldwide clinical experience, with more than 50 clinical trials since 1983.[1]

INDICATIONS AND USAGE

RabAvert is a vaccine approved for all age groups to help prevent rabies infection both before and after a suspected exposure.

IMPORTANT SAFETY INFORMATION

- People with a history of severe allergic reaction (e.g., anaphylaxis) to RabAvert or any of its ingredients should not receive RabAvert for protection before a potential exposure (PrEP) to the rabies virus. They should receive a different rabies vaccine if a suitable product is available. However, because rabies is almost always fatal if left untreated, the protection provided with RabAvert after a potential exposure (PEP) to the rabies virus outweighs the risks associated with a severe allergic reaction..
- The ingredients of RabAvert, which could in rare cases, cause allergic reactions in some people, include egg and chicken proteins, processed bovine (cow) gelatin and trace amounts of neomycin, chlortetracycline, and amphotericin B. Let your healthcare professional know if you have had any issues, including allergic reactions, with any of these ingredients or with vaccines in general.
- Severe, potentially life-threatening allergic reaction, swelling of the brain and spinal cord; loss of movement or sensation due to nerve damage, such as inflammation of the brain or temporary loss of movement; Guillain-Barré Syndrome; inflammation of spinal cord; inflamed nerves of the eye; and multiple sclerosis have in very rare cases been reported.
- RabAvert should be injected into muscle only. RabAvert injected into a vein may cause a reaction throughout the body, including shock.
- Fainting can occur when injectable vaccines are used, including RabAvert. Your healthcare provider should put procedures in place to avoid falling injury and to restore blood flow to the brain after fainting.
- Patients with a weakened immune system due to illness or the use of certain medications or treatments (such as radiation therapy, antimalarials, and corticosteroids) may have issues developing immunity. If such a patient is receiving RabAvert, then the healthcare professional may measure immune response through blood testing. Vaccination with RabAvert for protection before a potential exposure (PrEP) to the rabies virus should be delayed in anyone who is sick or recovering from an illness.
- RabAvert contains albumin which is a protein found in human blood that carries an extremely remote risk for transmission of viral diseases, including Creutzfeldt-Jakob disease (CJD), a rare brain disorder. No cases of transmission of viral diseases or CJD have ever been identified for albumin.
- Persons who have not been previously vaccinated against rabies will receive Human Rabies Immune Globulin (HRIG). HRIG should not be administered to persons who have been previously vaccinated as it may counteract the effect of the rabies vaccine. Let your healthcare provider know if you were previously vaccinated for rabies as you may not need HRIG.
- Only use RabAvert while pregnant or breastfeeding if clearly needed. RabAvert was not studied in pregnant or lactating women so it is not known if RabAvert can cause any harm to the fetus, have any effect on ability to get pregnant, or whether it is passed through breast milk to infants (but many drugs are excreted in human milk).
- There is no information on how RabAvert works when given at the same time as other vaccines.
- The most common side effects in clinical trials were reactions at the injection site, such as reddening, hardening, and pain; flu-like symptoms, such as lack of energy, tiredness, fever, headache, muscle pain, and feeling of discomfort; joint pain; dizziness; swelling of lymph nodes; upset stomach; and rash.
- Vaccination before a potential exposure (PrEP) to the rabies virus does not remove the need for additional therapy after a suspected or known rabies exposure.
- Seek the advice of a healthcare professional to help assess your specific level of risk if you are traveling to areas of high risk of rabies exposure; in frequent contact with the rabies virus or rabid animals, such as on the job; and/or are active outdoors and could encounter animals with rabies in the wild.
- If you are exposed to a potentially rabid animal, seek medical attention right away before you have symptoms. Once symptoms are present, the rabies infection has spread through the body and survival is unlikely.

Reporting Suspected Adverse Reactions

- Patients should always ask their healthcare professionals for medical advice about the appropriate use of vaccines and adverse events. To report SUSPECTED ADVERSE REACTIONS, contact Bavarian Nordic at 1-844-4BAVARIAN or the US Department of Health and Human Services by either visiting **www.vaers.hhs.gov/reportevent.html** or calling **1-800-822-7967**.

REFERENCES: 1. Giesen A, et al. 30 years of rabies vaccination with Rabipur: a summary of clinical data and global experience. *Expert Rev Vaccines*. 2015;14:351-367. **2.** RabAvert Rabies Vaccine. Prescribing Information. Accessed July, 2022. https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=84b7a672-eeb1-4527-84ac-68196b156be2 **3.** IQVIA. Data on file. 2018 - May 2022. Accessed July 2022.

PRESCRIBING INFORMATION

RabAvert

Rabies Vaccine

Rabies Vaccine for Human Use

DESCRIPTION

RabAvert Rabies Vaccine produced by GlaxoSmithKline GmbH for Bavarian Nordic A/S is a sterile, freeze-dried vaccine obtained by growing the fixed-virus strain Flury Low Egg Passage (LEP) in primary cultures of chicken fibroblasts. The strain Flury LEP was obtained from American Type Culture Collection as the 59th egg passage. The growth medium for propagation of the virus is a synthetic cell culture medium with the addition of human albumin, polygeline (processed bovine gelatin), and antibiotics. The virus is inactivated with β-propiolactone and further processed by zonal centrifugation in a sucrose density gradient. The vaccine is lyophilized after addition of a stabilizer solution that consists of buffered polygeline and potassium glutamate. One dose of reconstituted vaccine contains ≤12 mg polygeline (processed bovine gelatin), ≤0.3 mg human serum albumin, 1 mg potassium glutamate, and 0.3 mg sodium EDTA. Small quantities of bovine serum are used in the cell culture process. Bovine components originate only from the United States, Australia, and New Zealand. Minimal amounts of chicken protein may be present in the final product; ovalbumin content is ≤3 ng/dose (1 mL), based on ELISA. Antibiotics (neomycin, chlortetracycline, amphotericin B) added during cell and virus propagation are largely removed during subsequent steps in the manufacturing process. In the final vaccine, neomycin is present at ≤10 mcg, chlortetracycline at ≤200 ng, and amphotericin B at ≤20 ng per dose. RabAvert is intended for intramuscular (IM) injection. The vaccine contains no preservative and should be used immediately after reconstitution with the supplied Sterile Diluent for RabAvert (Water for Injection). The potency of the final product is determined by the National Institutes of Health (NIH) mouse potency test using the United States (US) reference standard. The potency of 1 dose (1.0 mL) of RabAvert is at least 2.5 IU of rabies antigen. RabAvert is a white, freeze-dried vaccine for reconstitution with the diluent prior to use; the reconstituted vaccine is a clear to slightly opalescent, colorless to slightly pink suspension.

CLINICAL PHARMACOLOGY

Rabies in the United States: Over the last 100 years, the epidemiology of rabies in animals in the US has changed dramatically. More than 90% of all animal rabies cases reported annually to the Centers for Disease Control and Prevention (CDC) now occur in wildlife, whereas before 1960 the majority was in domestic animals. The principal rabies hosts today are wild terrestrial carnivores and bats. Annual human deaths have fallen from more than a hundred at the turn of the century to 1 to 2 per year despite major epizootics of animal rabies in several geographic areas. Within the US, only Hawaii has remained rabies free. Although rabies among humans is rare in the US, every year tens of thousands of people receive rabies vaccine for postexposure prophylaxis.

Rabies is a viral infection transmitted via the saliva of infected mammals. The virus enters the central nervous system of the host, causing an encephalomyelitis that is almost invariably fatal. The incubation period varies between 5 days and several years, but is usually between 20 and 60 days. Clinical rabies presents either in a furious or in a paralytic form. Clinical illness most often starts with prodromal complaints of malaise, anorexia, fatigue, headache, and fever followed by pain or paresthesia at the site of exposure. Anxiety, agitation, and irritability may be prominent during this period, followed by hyperactivity; disorientation; seizures; aerophobia and hydrophobia; hypersalivation; and eventually paralysis, coma, and death.

Modern day prophylaxis has proven nearly 100% successful; most human fatalities now occur in people who fail to seek medical treatment, usually because they do not recognize a risk in the animal contact leading to the infection. Inappropriate postexposure prophylaxis may also result in clinical rabies. Survival after clinical rabies is extremely rare, and is associated with severe brain damage and permanent disability.

RabAvert (in combination with passive immunization with Human Rabies Immune Globulin [HRIG] and local wound treatment) in postexposure treatment against rabies has been shown to protect patients of all age groups from rabies, when the vaccine was administered according to CDC's Advisory Committee on Immunization Practices (ACIP) or World Health Organization (WHO) guidelines and as soon as possible after rabid animal contact. Anti-rabies antibody titers after immunization have been shown to reach levels well above the minimum antibody titer accepted as seroconversion (protective titer) within 14 days after initiating the postexposure treatment series. The minimum antibody titer accepted as seroconversion is a 1:5 titer (complete inhibition in the rapid fluorescent focus inhibition test [RFFIT] at 1:5 dilution) as specified by CDC[1] or ≥0.5 IU/mL as specified by WHO.[2,3]

Clinical Studies:

Preexposure Vaccination: The immunogenicity of RabAvert was demonstrated in clinical trials conducted in different countries such as the US,[4,5] the United Kingdom (UK),[6] Croatia,[7] and Thailand.[8-10] When administered according to the recommended immunization schedule (Days 0, 7, and 21 or 0, 7, and 28), 100% of subjects attained a protective titer. In 2 studies carried out in the US in 101 subjects, antibody titers >0.5 IU/mL were obtained by Day 28 in all subjects. In studies carried out in Thailand in 22 subjects and in Croatia in 25 subjects, antibody titers of >0.5 IU/mL were obtained by Day 14 (injections on Days 0, 7, and 21) in all subjects.

The ability of RabAvert to boost previously immunized subjects was evaluated in 3 clinical trials. In the Thailand study, preexposure booster doses were administered to 10 individuals. Antibody titers of >0.5 IU/mL were present at baseline on Day 0 in all subjects.[9] Titers after a booster dose were enhanced from geometric mean titers (GMTs) of 1.91 to 23.66 IU/mL on Day 30. In an additional booster study, individuals known to have been immunized with Human Diploid Cell Vaccine (HDCV) were boosted with RabAvert. In this study, a booster response was observed on Day 14 for all individuals (22/22).[11] In a trial carried out in the US,[4] an IM booster dose of RabAvert resulted in a significant increase in titers in all subjects (35/35), regardless of whether they had received RabAvert or HDCV as the primary vaccine.

Persistence of antibody after immunization with RabAvert was evaluated. In a trial performed in the UK, neutralizing antibody titers >0.5 IU/mL were present 2 years after immunization in all sera (6/6) tested.

Preexposure Vaccination in Children: Preexposure administration of RabAvert in 11 Thai children aged 2 years and older resulted in antibody levels higher than 0.5 IU/mL on Day 14 in all children.[12]

Postexposure Treatment: RabAvert, when used in the recommended postexposure WHO program of 5 to 6 IM injections of 1 mL (Days 0, 3, 7, 14, and 30 and optionally on Day 90) provided protective titers of neutralizing antibody (>0.5 IU/mL) in 158/160 patients[8,9,13-16] within 14 days and in 215/216 patients by Days 28 to 38.

Of these, 203 were followed for at least 10 months. No case of rabies was observed.[8,9,13-20] Some patients received HRIG, 20 to 30 IU/kg body weight, or Equine Rabies Immune Globulin (ERIG), 40 IU/kg body weight, at the time of the first dose. In most studies,[8,9,13,17] the addition of either HRIG or ERIG caused a slight decrease in GMTs which was neither clinically relevant nor statistically significant. In one study,[16] patients receiving HRIG had significantly lower ($P<0.05$) GMTs on Day 14; however, this was not clinically relevant. After Day 14 there was no statistical significance.

The results of several studies of normal volunteers receiving the postexposure WHO regimen, i.e., "simulated" postexposure, showed that with sampling by Days 28 to 30, 205/208 vaccinees had protective titers >0.5 IU/mL.

No postexposure vaccine failures have occurred in the US since cell culture vaccines have been routinely used.[1] Failures have occurred abroad, almost always after deviation from the recommended postexposure treatment protocol.[21-24] In 2 cases with bites to the face, treatment failed although no deviation from the recommended postexposure treatment protocol appeared to have occurred.[25]

Postexposure Treatment in Children: In a 10-year serosurveillance study, RabAvert was administered to 91 children aged 1 to 5 years and 436 children and adolescents aged 6 to 20 years.[19] The vaccine was effective in both age groups. None of these patients developed rabies.

One newborn received RabAvert on an immunization schedule of Days 0, 3, 7, 14, and 30; the antibody concentration on Day 37 was 2.34 IU/mL. There were no clinically significant adverse events.[26]

INDICATIONS AND USAGE

RabAvert is indicated for preexposure vaccination, in both primary series and booster dose, and for postexposure prophylaxis against rabies in all age groups.

Usually an immunization series is initiated and completed with 1 vaccine product.

No clinical studies have been conducted that document a change in efficacy or the frequency of adverse reactions when the series is completed with a second vaccine product. However, for booster immunization, RabAvert was shown to elicit protective antibody level responses in persons tested who received a primary series with HDCV.[4,11]

Preexposure Vaccination: See Table 1 and DOSAGE AND ADMINISTRATION.

Preexposure vaccination consists of 3 doses of RabAvert 1.0 mL given intramuscularly (deltoid region), 1 each on Days 0, 7, and 21 or 28[1] (see also Table 1 for criteria for preexposure vaccination).

Preexposure vaccination does not eliminate the need for additional therapy after a known rabies exposure (see DOSAGE AND ADMINISTRATION: Postexposure Prophylaxis of Previously Immunized Persons).

Preexposure vaccination should be offered to persons in high-risk groups, such as veterinarians, animal handlers, wildlife officers in areas where animal rabies is enzootic, certain laboratory workers, and persons spending time in foreign countries where rabies is endemic. Persons whose activities bring them into contact with potentially rabid dogs, cats, foxes, skunks, bats, or other species at risk of having rabies should also be considered for preexposure vaccination. International travelers might be candidates for preexposure vaccination if they are likely to come in contact with animals in areas where dog rabies is enzootic and immediate access to appropriate medical care, including biologics, might be limited.[27,28]

Preexposure vaccination is given for several reasons. First, it may provide protection to persons with inapparent exposure to rabies. Second, it may protect persons whose postexposure therapy might be expected to be delayed. Finally, although it does not eliminate the need for prompt therapy after a rabies exposure, it simplifies therapy by eliminating the need for globulin and decreasing the number of doses of vaccine needed. This is of particular importance for persons at high risk of being exposed in countries where the available rabies-immunizing products may carry a higher risk of adverse reactions.

In some instances, booster doses of vaccine should be administered to maintain a serum titer corresponding to at least complete neutralization at a 1:5 serum dilution by the RFFIT (Table 1); each booster immunization consists of a single dose. See CLINICAL PHARMACOLOGY. Serum antibody determinations to decide upon the need for a booster dose is suggested by ACIP and is considered cost effective.

Table 1. Rabies Preexposure Prophylaxis Guide – United States, 1999[a]

Risk Category and Nature of Risk	Typical Populations	Preexposure Prophylaxis Recommendations
Continuous. Virus present continuously, often in high concentrations. Specific exposures likely to go unrecognized. Bite, non-bite, or aerosol exposure.	Rabies research lab workers,[b] rabies biologics production workers.	Primary course. Serologic testing every 6 months; booster vaccination if antibody titer is below acceptable level.[b]
Frequent. Exposure usually episodic, with source recognized, but exposure might be unrecognized. Bite, non-bite, or aerosol exposure.	Rabies diagnostic lab workers,[b] spelunkers, veterinarians and staff, and animal-control and wildlife workers in rabies enzootic areas.	Primary course. Serologic testing every 2 years; booster vaccination if antibody titer is below acceptable level.[c]
Infrequent (greater than population-at-large). Exposure nearly always episodic with source recognized. Bite or non-bite exposure.	Veterinarians and animal-control and wildlife workers in areas with low rabies rates. Veterinary students. Travelers visiting areas where rabies is enzootic and immediate access to appropriate medical care including biologics is limited.	Primary course. No serologic testing or booster vaccination.[c]
Rare (population-at-large). Exposures always episodic with source recognized. Bite or non-bite exposure.	US population-at-large, including persons in rabies-epizootic areas.	No vaccination necessary.

[a]Adapted from the Recommendations of the Advisory Committee on Immunization Practices: Human Rabies Prevention – United States, 1999.[1]

[b]Judgment of relative risk and extra monitoring of vaccination status of laboratory workers is the responsibility of the laboratory supervisor.[29]

[c]Minimum acceptable antibody level is complete virus neutralization at a 1:5 serum dilution by rapid fluorescent focus inhibition test. A booster dose should be administered if the titer falls below this level.

Postexposure Treatment: See Table 2 and DOSAGE AND ADMINISTRATION.

The following recommendations are only a guide. In applying them, take into account the animal species involved, the circumstances of the bite or other exposure, the immunization status of the animal, and presence of rabies in the region (as outlined below). Local or state public health officials should be consulted if questions arise about the need for rabies prophylaxis.[1]

Table 2. Rabies Postexposure Prophylaxis Guide – United States, 1999[a]

Animal Type	Evaluation and Disposition of Animal	Postexposure Prophylaxis Recommendations
Dogs, cats, and ferrets	Healthy and available for 10 days' observation	Should not begin prophylaxis unless animal develops clinical signs of rabies[b]
	Rabid or suspected rabid	Immediately vaccinate
	Unknown (e.g., escaped)	Consult public health officials
Skunks, raccoons, bats, foxes, and most other carnivores	Regarded as rabid unless animal proven negative by laboratory tests[c]	Consider immediate vaccination
Livestock, small rodents, lagomorphs (rabbits and hares), large rodents (woodchucks and beavers), and other mammals	Consider individually	Consult public health officials. Bites of squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, mice, other small rodents, rabbits, and hares almost never require antirabies postexposure prophylaxis.

[a]Adapted from the Recommendations of the Advisory Committee on Immunization Practices: Human Rabies Prevention – United States, 1999.[1]

[b]During the 10-day observation period, begin postexposure prophylaxis at the first sign of rabies in a dog, cat, or ferret that has bitten someone. If the animal exhibits clinical signs of rabies, it should be euthanized immediately and tested.

[c]The animal should be euthanized and tested as soon as possible. Holding for observation is not recommended. Discontinue vaccine if immunofluorescence test results of the animal are negative.

In the US, the following factors should be considered before antirabies treatment is initiated.

Species of Biting Animal: Wild terrestrial animals (especially skunks, raccoons, foxes, and coyotes) and bats are the animals most commonly infected with rabies and are the most important potential source of infection for both humans and domestic animals. Unless a wild animal is tested and shown not to be rabid, postexposure prophylaxis should be initiated upon bite or non-bite exposure to the animals (see definition in "Type of Exposure" below). If treatment has been initiated and subsequent testing in a qualified laboratory shows the exposing animal is not rabid, postexposure prophylaxis can be discontinued.[1]

The likelihood of rabies in a domestic animal varies from region to region; hence, the need for postexposure prophylaxis also varies.[1]

Small rodents (such as squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, and mice) and lagomorphs (including rabbits and hares) are almost never found to be infected with rabies and have not been known to transmit rabies to humans in the US. Bites from large rodents such as woodchucks (including groundhogs) and beavers should be considered as possible rabies exposures, especially in regions where rabies is enzootic in raccoons.[30] In all cases involving rodents, the state or local health department should be consulted before a decision is made to initiate antirabies postexposure prophylaxis.[1]

Circumstances of Biting Incident: An UNPROVOKED attack is more likely than a provoked attack to indicate the animal is rabid. Bites inflicted on a person attempting to feed or handle an apparently healthy animal should generally be regarded as PROVOKED. A currently vaccinated dog, cat, or ferret is unlikely to become infected with rabies.[1]

Type of Exposure: Rabies is transmitted by introducing the virus into open cuts or wounds in skin or via mucous membranes. The likelihood of rabies infection varies with the nature and extent of exposure. Two categories of exposure should be considered:

Bite: Any penetration of the skin by teeth. Bites to highly innervated areas such as the face and hands carry the highest risk, but the site of the bite should not influence the decision to begin treatment. Recent epidemiologic data suggest that even the very limited injury inflicted by a bat bite (compared with lesions caused by terrestrial carnivores) should prompt consideration of postexposure prophylaxis unless the bat is available for testing and is negative for evidence of rabies.[1]

Non-bite: The contamination of open wounds, abrasions, mucous membranes, or theoretically, scratches with saliva or other potentially infectious material (such as neural tissue) from a rabid animal constitutes a non-bite exposure. In all instances of potential human exposures involving bats, and the bat is not available for testing, postexposure prophylaxis might be appropriate even if a bite, scratch, or mucous membrane exposure is not apparent when there is reasonable probability that such exposure might have occurred. Postexposure prophylaxis can be considered for persons who were in the same room as the bat and who might be unaware that a bite or direct contact had occurred (e.g., a sleeping person awakens to find a bat in the room or an adult witnesses a bat in the room with a previously unattended child, mentally disabled person, or intoxicated person) and rabies cannot be ruled out by testing the bat. Other contact by itself, such as petting a rabid animal and contact with blood, urine, or feces (e.g., guano) of a rabid animal, does not constitute an exposure and is not an indication for prophylaxis. Because the rabies virus is inactivated by desiccation and ultraviolet irradiation, in general, if the material containing the virus is dry, the virus can be considered noninfectious. Two cases of rabies have been attributed to probable aerosol exposures in laboratories, and 2 cases of rabies in Texas could possibly have been due to airborne exposures in caves containing millions of bats.[1]

The only documented cases for rabies from human-to-human transmission occurred in 8 patients, including 2 in the US, who received corneas transplanted from persons who died of rabies undiagnosed at the time of death.[1] Stringent guidelines for acceptance of donor corneas have been implemented to reduce this risk.

Bite and non-bite exposure from humans with rabies theoretically could transmit rabies, but no laboratory-diagnosed cases occurring under such situations have been documented. Each potential exposure to human rabies should be carefully evaluated to minimize unnecessary rabies prophylaxis.[1]

Postexposure Treatment Schedule: See also DOSAGE AND ADMINISTRATION.

The essential components of rabies postexposure prophylaxis are prompt local treatment of wounds and administration of both HRIG and vaccine.

A complete course of postexposure treatment for previously unvaccinated adults and children consists of a total of 5 doses of vaccine, each 1.0 mL: one IM injection (deltoid) on each of Days 0, 3, 7, 14, and 28. For previously immunized adults and children, a total of 2 doses of vaccine, each 1.0 mL: one IM injection (deltoid) on each of Days 0 and 3. No HRIG should be administered to previously vaccinated persons as it may blunt their rapid memory response to rabies antigen.

Local Treatment of Wounds: Immediate and thorough washing of all bite wounds and scratches with soap and water is an important measure for preventing rabies. In animal studies, thorough local wound cleansing alone has been shown to reduce markedly the likelihood of rabies. Whenever possible, bite injuries should not be sutured to avoid further and/or deeper contamination. Tetanus prophylaxis and measures to control bacterial infection should be given as indicated.[1]

Postexposure Prophylaxis of Rabies: The regimen for postexposure prophylaxis depends on whether or not the patient has been previously immunized against rabies (see below). For persons who have not previously been immunized against rabies, the schedule consists of an initial IM injection of HRIG exactly 20 IU/kg body weight in total. If anatomically feasible, the FULL DOSE of HRIG should be thoroughly infiltrated in the area around and into the wounds. Any remaining volume of HRIG should be injected intramuscularly at a site distant from rabies vaccine administration. HRIG should never be administered in the same syringe or in the same anatomical site as the rabies vaccine. HRIG is administered only once (for specific instructions for HRIG use, see the product package insert). The HRIG injection is followed by a series of 5 individual injections of RabAvert (1.0 mL each) given intramuscularly on Days 0, 3, 7, 14, and 28. Postexposure rabies prophylaxis should begin the same day exposure occurred or as soon after exposure as possible. The combined use of HRIG and RabAvert is recommended by the CDC for both bite and non-bite exposures, regardless of the interval between exposure and initiation of treatment.

In the event that HRIG is not readily available for the initiation of treatment, it can be given through the seventh day after administration of the first dose of vaccine. HRIG is not indicated beyond the seventh day because an antibody response to RabAvert is presumed to have begun by that time.[1]

The sooner treatment is begun after exposure, the better. However, there have been instances in which the decision to begin treatment was made as late as 6 months or longer after exposure due to delay in recognition that an exposure had occurred. Postexposure antirabies treatment should always include administration of both passive antibody (HRIG) and immunization, with the exception of persons who have previously received complete immunization regimens (preexposure or postexposure) with a cell culture vaccine, or persons who have been immunized with other types of vaccines and have had documented rabies antibody titers. Persons who have previously received rabies immunization should receive 2 IM doses of RabAvert: one on Day 0 and another on Day 3. They should not be given HRIG as this may blunt their rapid memory response to rabies antigen.

Postexposure Prophylaxis Outside the United States: If postexposure treatment is begun outside the US with regimens or biologics that are not used in the US, it may be prudent to provide additional treatment when the patient reaches the US. State or local health departments should be contacted for specific advice in such cases.[1]

CONTRAINDICATIONS

Preexposure Prophylaxis:

Hypersensitivity: History of anaphylaxis to the vaccine or any of the vaccine components constitutes a contraindication to preexposure vaccination with this vaccine.

Postexposure Prophylaxis: In view of the almost invariably fatal outcome of rabies, there is no contraindication to postexposure prophylaxis, including pregnancy.[1]

WARNINGS

Patients considered to be at risk of a severe hypersensitivity reaction to the vaccine or any of the vaccine components should receive an alternative rabies vaccine if a suitable product is available.

Anaphylaxis, meningitis; neuroparalytic events such as encephalitis, transient paralysis; Guillain-Barré Syndrome; myelitis; retrobulbar neuritis; and multiple sclerosis have been reported to be temporally associated with the use of RabAvert. See PRECAUTIONS and ADVERSE REACTIONS. A patient's risk of developing rabies must be carefully considered, however, before deciding to discontinue immunization.

For intramuscular use only. For adults, the deltoid area is the preferred site of immunization; for small children and infants, administration into the anterolateral zone of the thigh is preferred. The use of the gluteal region should be avoided, since administration in this area may result in lower neutralizing antibody titers.[1]

Unintentional intravascular injection may result in systemic reactions, including shock.

Syncope (fainting) can occur in association with administration of injectable vaccines, including RabAvert. Syncope can be accompanied by transient neurological signs such as visual disturbance, paresthesia, and tonic-clonic limb movements. Procedures should be in place to avoid falling injury and to restore cerebral perfusion following syncope. See PRECAUTIONS and ADVERSE REACTIONS.

Development of active immunity after vaccination may be impaired in immune-compromised individuals. Please refer to PRECAUTIONS: Drug Interactions.

This product contains albumin, a derivative of human blood. It is present in RabAvert at concentrations of ≤0.3 mg/dose. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases. A theoretical risk for transmission of Creutzfeld-Jakob disease (CJD) also is considered extremely remote. No cases of transmission of viral diseases or CJD have ever been identified for albumin.

PRECAUTIONS

General: The healthcare provider should question the patient, parent, or guardian about (1) the current health status of the vaccinee and (2) reactions to a previous dose of RabAvert or a similar product. Preexposure vaccination should be postponed in the case of sick and convalescent persons and those considered to be in the incubation stage of an infectious disease. A separate, sterile syringe and needle should be used for each patient. Needles must not be recapped and should be properly disposed of. As with any rabies vaccine, vaccination with RabAvert may not protect 100% of susceptible individuals.

Hypersensitivity: RabAvert contains residues of egg and chicken proteins, such as ovalbumin. In instances where individuals have developed clinical symptoms of anaphylaxis such as generalized urticaria, upper airway (lip, tongue, throat, laryngeal, or epiglottal) edema, laryngeal spasm or bronchospasm, hypotension, or shock, following exposure to egg or chicken protein, the vaccine should only be administered by personnel with the capability and facilities to manage anaphylaxis post vaccination.

Since reconstituted RabAvert contains processed bovine gelatin and trace amounts of neomycin, chlortetracycline, and amphotericin B, the possibility of allergic reactions in individuals hypersensitive to these substances should be considered when administering the vaccine.

Epinephrine injection (1:1,000) must be immediately available should anaphylactic or other allergic reactions occur.

When a person with a history of hypersensitivity must be given RabAvert, antihistamines may be given; epinephrine (1:1,000), volume replacement, corticosteroids, and oxygen should be readily available to counteract anaphylactic reactions.

Drug Interactions: Radiation therapy, antimalarials, corticosteroids, other immunosuppressive agents, and immunosuppressive illnesses can interfere with the development of active immunity after vaccination and may diminish the protective efficacy of the vaccine. Preexposure vaccination should be administered to such persons with the awareness that the immune response may be inadequate. Immunosuppressive agents should not be administered during postexposure therapy unless essential for the treatment of other conditions. When rabies postexposure prophylaxis is administered to persons receiving corticosteroids or other immunosuppressive therapy, or who are immunosuppressed, it is important that a serum sample on Day 14 (the day of the fourth vaccination) be tested for rabies antibody to ensure that an acceptable antibody response has been induced.[1]

HRIG must not be administered at more than the recommended dose, since active immunization to the vaccine may be impaired.

No data are available regarding the concurrent administration of RabAvert with other vaccines.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies with RabAvert have not been conducted to assess the potential for carcinogenesis, mutagenesis, or impairment of fertility.

Use in Pregnancy: Animal reproductive studies have not been conducted with RabAvert. It is also not known whether RabAvert can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. RabAvert should be given to a pregnant woman only if clearly needed. The ACIP has issued recommendations for use of rabies vaccine in pregnant women.[1]

Use in Nursing Mothers: It is not known whether RabAvert is excreted in animal or human milk, but many drugs are excreted in human milk. Although there are no data, because of the potential consequences of inadequately treated rabies exposure, nursing is not considered a contraindication to postexposure prophylaxis. If the risk of exposure to rabies is substantial, preexposure vaccination might also be indicated during nursing.

Pediatric Use: Children and infants receive the same dose of 1 mL, given intramuscularly, as do adults.

Only limited data on the safety and efficacy of RabAvert in the pediatric age group are available. However, in 3 studies some preexposure and postexposure experience has been gained[12,19,26] (see CLINICAL PHARMACOLOGY: Clinical Studies).

Geriatric Use: Clinical studies of RabAvert did not include sufficient numbers of subjects aged 65 and older to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

ADVERSE REACTIONS

In very rare cases, neurological and neuroparalytical events have been reported in temporal association with administration of RabAvert (see WARNINGS). These include cases of hypersensitivity (see CONTRAINDICATIONS, WARNINGS, and PRECAUTIONS).

The most commonly occurring adverse reactions are injection site reactions, such as injection site erythema, induration, and pain; flu-like symptoms, such as asthenia, fatigue, fever, headache, myalgia, and malaise; arthralgia; dizziness; lymphadenopathy; nausea; and rash.

A patient's risk of acquiring rabies must be carefully considered before deciding to discontinue vaccination. Advice and assistance on the management of serious adverse reactions for persons receiving rabies vaccines may be sought from the state health department or CDC (see CONTRAINDICATIONS).

Local reactions such as induration, swelling, and reddening have been reported more often than systemic reactions. In a comparative trial in normal volunteers, Dreesen et al..[4] described their experience with RabAvert compared with an HDCV rabies vaccine. Nineteen subjects received RabAvert and 20 received HDCV. The most commonly reported adverse reaction was pain at the injection site, reported in 45% of the HDCV group and 34% of the group receiving RabAvert. Localized lymphadenopathy was reported in about 15% of each group. The most common systemic reactions were malaise (15% RabAvert vs. 25% HDCV), headache (10% RabAvert vs. 20% HDCV), and dizziness (15% RabAvert vs. 10% HDCV). In a recent study in the US[5], 83 subjects received RabAvert and 82 received HDCV. Again, the most common adverse reaction was pain at the injection site in 80% in the HDCV group and 84% in the group receiving RabAvert. The most common systemic reactions were headache (52% RabAvert vs. 45% HDCV), myalgia (53% RabAvert vs. 38% HDCV), and malaise (20% RabAvert vs. 17% HDCV). None of the adverse events were serious; almost all adverse events were of mild or moderate intensity. Statistically significant differences between vaccination groups were not found. Both vaccines were generally well tolerated.

Uncommonly observed adverse events include temperatures above 38°C (100°F), swollen lymph nodes, pain in limbs, and gastrointestinal complaints. In rare cases, patients have experienced severe headache, fatigue, circulatory reactions, sweating, chills, monoarthritis, and allergic reactions; transient paresthesias and 1 case of suspected urticaria pigmentosa have also been reported.

Observed During Clinical Practice (See WARNINGS and PRECAUTIONS): The following adverse reactions have been identified during post approval use of RabAvert. Because these reactions are reported voluntarily from a population of uncertain size, estimates of frequency cannot be made. These events have been chosen for inclusion due to their seriousness, frequency of reporting, causal connection to RabAvert, or a combination of these factors:

Allergic: Anaphylaxis, Type III hypersensitivity-like reactions, bronchospasm, urticaria, pruritus, edema.

Central Nervous System: Neuroparalysis, encephalitis, meningitis, transient paralysis, Guillain-Barré Syndrome, myelitis, retrobulbar neuritis, multiple sclerosis, presyncope, syncope, vertigo, visual disturbance.

Cardiac: Palpitations, hot flush.

Local: Extensive limb swelling.

Skin and Subcutaneous Tissue Disorders: Angioedema.

The use of corticosteroids to treat life-threatening neuroparalytic reactions may inhibit the development of immunity to rabies (see PRECAUTIONS, Drug Interactions).

Once initiated, rabies prophylaxis should not be interrupted or discontinued because of local or mild systemic adverse reactions to rabies vaccine. Usually such reactions can be successfully managed with anti-inflammatory and antipyretic agents.

Reporting of Adverse Events: Adverse events should be reported by the healthcare provider or patient to the US Department of Health and Human Services (DHHS) Vaccine Adverse Event Reporting System (VAERS). Report forms and information about reporting requirements or completion of the form can be obtained from VAERS by calling the toll-free number 1-800-822-7967.[1] In the US, such events can be reported to Bavarian Nordic: phone: 1-800-675-9596.

DOSAGE AND ADMINISTRATION

For intramuscular use only. The individual dose for adults, children, and infants is 1 mL.

In adults, administer vaccine by IM injection into the deltoid muscle. In small children and infants, administer vaccine into the anterolateral zone of the thigh. The gluteal area should be avoided for vaccine injections, since administration in this area may result in lower neutralizing antibody titers. Care should be taken to avoid injection into or near blood vessels and nerves. After aspiration, if blood or any suspicious discoloration appears in the syringe, do not inject but discard contents and repeat procedure using a new dose of vaccine at a different site.

Preexposure Dosage:

Primary Immunization: In the US, ACIP recommends 3 injections of 1 mL each: 1 injection on Day 0 and 1 on Day 7, and 1 either on Day 21 or 28 (for criteria for preexposure vaccination, see Table 1).

Booster Immunization: The individual booster dose is 1 mL, given intramuscularly.

Booster immunization is given to persons who have received previous rabies immunization and remain at increased risk of rabies exposure by reasons of occupation or avocation.

Persons who work with live rabies virus in research laboratories or vaccine production facilities (for continuous-risk category, see Table 1) should have a serum sample tested for rabies antibodies every 6 months. The minimum acceptable antibody level is complete virus neutralization at a 1:5 serum dilution by RFFIT. A booster dose should be administered if the titer falls below this level.

The frequent-risk category includes other laboratory workers such as those doing rabies diagnostic testing, spelunkers, veterinarians and staff, and animal-control and wildlife officers in areas where rabies is epizootic. Persons in the frequent-risk category should have a serum sample tested for rabies antibodies every 2 years and if the titer is less than complete neutralization at a 1:5 serum dilution by RFFIT should have a booster dose of vaccine. Alternatively, a booster can be administered in the absence of a titer determination.

The infrequent-risk category, including veterinarians, animal-control and wildlife officers working in areas of low rabies enzooticity (infrequent-exposure group), and international travelers to rabies enzootic areas, do not require routine preexposure booster doses of RabAvert after completion of a full primary preexposure vaccination scheme (Table 1).

Postexposure Dosage: Immunization should begin as soon as possible after exposure. A complete course of immunization consists of a total of 5 injections of 1 mL each: 1 injection on each of Days 0, 3, 7, 14, and 28 in conjunction with the administration of HRIG on Day 0. For children, see PRECAUTIONS: Pediatric Use.

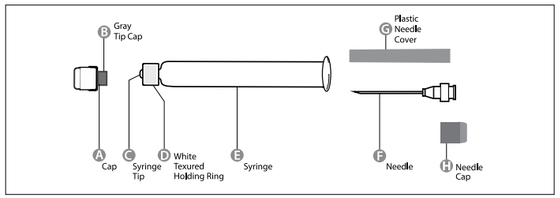
Begin with the administration of HRIG. Give 20 IU/kg body weight.

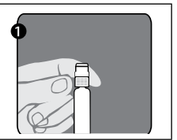
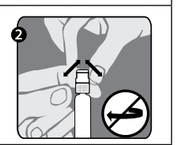
This formula is applicable to all age groups, including infants and children. The recommended dosage of HRIG should not exceed 20 IU/kg body weight because it may otherwise interfere with active antibody production. Since vaccine-induced antibody appears within 1 week, HRIG is not indicated more than 7 days after initiating postexposure prophylaxis with RabAvert. If anatomically feasible, the FULL DOSE of HRIG should be thoroughly infiltrated in the area around and into the wounds. Any remaining volume of HRIG should be injected intramuscularly at a site distant from rabies vaccine administration. HRIG should never be administered in the same syringe or in the same anatomical site as the rabies vaccine.

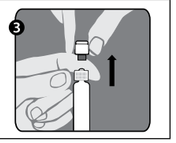
Because the antibody response following the recommended immunization regimen with RabAvert has been satisfactory, routine post-immunization serologic testing is not recommended. Serologic testing is indicated in unusual circumstances, as when the patient is known to be immunosuppressed. Contact the appropriate state health department or CDC for recommendations.

Postexposure Prophylaxis of Previously Immunized Persons: When rabies exposure occurs in a previously vaccinated person, that person should receive 2 IM (deltoid) doses (1 mL each) of RabAvert: one immediately and one 3 days later. HRIG should not be given in these cases. Persons considered to have been immunized previously are those who received a complete preexposure vaccination or postexposure prophylaxis with RabAvert or other tissue culture vaccines or have been documented to have had a protective antibody response to another rabies vaccine. If the immune status of a previously vaccinated person is not known, full postexposure antirabies treatment (HRIG plus 5 doses of vaccine) is recommended. In such cases, if a protective titer can be demonstrated in a serum sample collected before vaccine is given, treatment can be discontinued after at least 2 doses of vaccine.

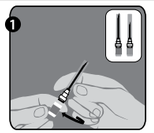
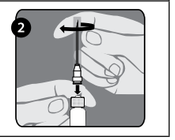
Instructions for Reconstituting RabAvert: Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. If either of these conditions exists, the vaccine should not be administered.



Step 1: With one hand, hold the syringe (E) with the cap pointing upward. Be sure to hold the syringe by the white textured holding ring (D).	
Step 2: With the other hand, grasp the cap (A) and firmly rock it back and forth to break its connection to the white textured holding ring (D). **Do not twist or turn the cap.**	

Step 3: Lift up to remove the cap (A) and the attached gray tip cap (B). Be careful not to touch the sterile syringe tip (C).	

Needle application (these instructions apply to both the green and the orange needles):

Step 1: Twist to remove the cap from the green reconstitution needle. Do not remove the plastic cover (G). This needle is the longer of the two needles.	
Step 2: With one hand, firmly hold syringe (E) by white textured holding ring (D). With your other hand, insert needle (F) and twist clockwise until it locks into place. Once needle is locked, remove its plastic cover (G). The syringe (E) is now ready for use.	

The package contains a vial of freeze-dried vaccine, a syringe containing 1 mL of sterile diluent, a sterile needle for reconstitution, and a sterile needle suitable for IM injection. The longer of the 2 needles supplied is the reconstitution needle. Affix the reconstitution needle to the syringe containing the Sterile Diluent for RabAvert. Insert the needle at a 45° angle and slowly inject the entire contents of the diluent (1 mL) into the vaccine vial. Mix gently to avoid foaming. The white, freeze-dried vaccine dissolves to give a clear to slightly opalescent, colorless to slightly pink suspension. Withdraw the total amount of dissolved vaccine into the syringe and replace the long needle with the smaller needle for IM injection. The reconstituted vaccine should be used immediately.

A separate sterile syringe and needle should be used for each patient. Needles must not be recapped and should be disposed of properly.

The lyophilization of the vaccine is performed under reduced pressure and the subsequent closure of the vials is done under vacuum. If there is no negative pressure in the vial, injection of Sterile Diluent for RabAvert would lead to an excess positive pressure in the vial. After reconstitution of the vaccine, it is recommended to unscrew the syringe from the needle to eliminate the negative pressure. After that, the vaccine can be easily withdrawn from the vial. It is not recommended to induce excess pressure, since over-pressurization may prevent withdrawing the proper amount of the vaccine.

HOW SUPPLIED

RabAvert product presentation is listed in Table 3.

Table 3. RabAvert Product Presentation

Presentation	Carton NDC Number	Components
Single-dose kit	50632-010-01	• 1 vial of freeze-dried vaccine containing a single dose [NDC 50632-013-01] • 1 disposable prefilled syringe of Sterile Diluent for reconstitution (1 mL) [NDC 50632-011-01] • 1 small needle for injection (25 gauge, 1 inch) and 1 long needle for reconstitution (21 gauge, 1 ½ inch)

RabAvert should be stored protected from light at 2°C to 8°C (36°F to 46°F). After reconstitution, the vaccine is to be used immediately. The vaccine may not be used after the expiration date given on package and container.

REFERENCES

1. CDC. Recommendations of the Advisory Committee on Immunization Practices (ACIP). Human Rabies Prevention – United States, 1999. Morbidity and Mortality Weekly Report Recommendations and Report, January 8, 1999, Vol.48, RR-1; 1.1-21.
2. Smith JS, Yager, PA & Baer, GM. A rapid reproducible test for determining rabies neutralizing antibody. *Bull WHO*. 1973; 48: 535-541.
3. Eighth Report of the WHO Expert Committee on Rabies. WHO Technical Report Series, no. 824; 1992.
4. Dreesen DW, et al. Two-year comparative trial on the immunogenicity and adverse effects of purified chick embryo cell rabies vaccine for preexposure immunization. *Vaccine.* 1989; 7: 397-400.
5. Dreesen, DW. Investigation of antibody response to purified chick embryo cell tissue culture vaccine (PCECV) or human diploid cell culture vaccine (HDCV) in healthy volunteers. Study synopsis 7USA401RA, September 1996 – December 1996 (unpublished).
6. Nicholson KG, et al. Preexposure studies with purified chick embryo cell culture rabies vaccine and human diploid cell vaccine: serological and clinical responses in man. *Vaccine.* 1987; 5: 208-210.
7. Vodopija I, et al. An evaluation of second generation tissue culture rabies vaccines for use in man: a four-vaccine comparative immunogenicity study using a preexposure vaccination schedule and an abbreviated 2-1-1 postexposure schedule. *Vaccine.* 1986; 4: 245-248.
8. Wasi C, et al. Purified chick embryo cell rabies vaccine (letter). *Lancet.* 1986; 1: 40.
9. Wasi C. Rabies prophylaxis with purified chick embryo (PCEC) rabies vaccine. Protocol 8T--201RA, 1983 - 1984 (unpublished).
10. Wasi C. Personal communication to Behringwerke AG, 1990.
11. Bijok U, et al. Clinical trials in healthy volunteers with the new purified chick embryo cell rabies vaccine for man. *J Commun Dis.* 1984; 16: 61-69.
12. Lumbiganon P, et al. Preexposure vaccination with purified chick embryo cell rabies vaccines in children. *Asian Pacific J Allergy Immunol.* 1989; 7: 99-101.
13. Vodopija I. Post-exposure rabies prophylaxis with purified chick embryo cell (PCEC) rabies vaccine. Protocol 7YU-201RA, 1983-1985 (unpublished).
14. John J. Evaluation of purified chick embryo cell culture (PCEC) rabies vaccine, 1987 (unpublished).
15. Tanphaichitra D, Siristonpun Y. Study of the efficacy of a purified chick embryo cell vaccine in patients bitten by rabid animals. *Intern Med.* 1987; 3: 158-160.
16. Thongcharoen P, et al. Effectiveness of new economical schedule of rabies postexposure prophylaxis using purified chick embryo cell tissue culture rabies vaccine. Protocol 7T--301IP, 1993 (unpublished).
17. Ljubicic M, et al. Efficacy of PCEC vaccines in post-exposure rabies prophylaxis. In: Vodopija, Nicholson, Smerdel & Bijok (eds.): Improvements in rabies post-exposure treatment (Proceedings of a meeting in Dubrovnik, Yogoslavia). Zagreb Institute of Public Health 1985.17.
18. Madhusudana SN, Tripathi KK. Post exposure studies with human diploid cell rabies vaccine and purified chick embryo cell vaccine: Comparative Serological Responses in Man. Zbl Bakt 1989; 271: 345-350.
19. Sehgal S, et al. Ten year longitudinal study of efficacy and safety of purified chick embryo cell vaccine for pre- and postexposure prophylaxis of rabies in Indian population. *J Commun Dis.* 1995; 27: 36-43.
20. Sehgal S, et al. Clinical evaluation of purified chick embryo cell antirabies vaccine for postexposure treatment. *J Commun Dis.* 1988; 20: 293-300.
21. Fishbein DB, et al. Administration of human diploid-cell rabies vaccine in the gluteal area. *N Engl J Med.* 1988; 318: 124-125.
22. Shill M, et al. Fatal rabies encephalitis despite appropriate postexposure prophylaxis. A case report. *N Engl J Med.* 1987; 316: 1257-1258.
23. Wilde H, et al. Failure of rabies postexposure treatment in Thailand. *Vaccine.* 1989; 7: 49-52.
24. Kuwert EK, et al. postexposure use of human diploid cell culture rabies vaccine. *Dev Biol Stand.* 1977; 37: 273-286.
25. Hemachudha T, et al. Additional reports of failure to respond to treatment after rabies exposure in Thailand. *Clin Infect Dis.* 1999; 28: 143-144.
26. Lumbiganon P, Wasi C. Survival after rabies immunisation in newborn infant of affected mother. *Lancet.* 1990; 336: 319-320.
27. Centers for Disease Control and Prevention. Health Information for International Travel, 2003-2004 (The Yellow Book). Atlanta: US Department of Health and Human Services, Public Health Service, 2003. Internet version at: http://www.cdc.gov/travel/yb
28. World Health Organization. International Travel and Health, 2002. Geneva, Switzerland. Internet version at: http://www.who.int/ith
29. CDC and NIH. Biosafety in microbiological and biomedical laboratories. 3rd. ed. Washington, D.C. HHS Publication no. (CDC) 93-8395, Washington, DC: US Department of Health and Human Services, 1993.
30. Krebs JW, et al. Rabies surveillance in the United States in 2001. *J Am Vet Med Assoc.* 2002; 221: 1690-1701.

BAVARIAN NORDIC

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RAB:6PI
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continued from page 35

Baits are about the size of a ketchup packet. Photo courtesy DSHS

Helicopter pilot Cole May, with USDA Wildlife Services. Photo courtesy DSHS

You mentioned that some animals were more successfully vaccinated than others with the bait drop, namely skunks that were not responding to it and also that bats could not be vaccinated. Would the strains affecting them be more of a priority of awareness for public health professionals, and would that threat come more directly to humans from these animals or indirectly from them infecting domesticated animals such as dogs and cats that would be more apt to interact with humans?

Actually there is a lot of direct exposure between bats and people, simply because bats can get into houses and into cities like here in Houston, under bridges in Austin, so we do see quite a few exposures. Bats can also get into apartment complexes. We've even had them get into hospitals and lots of different places, so there's exposures that happen quite often between bats and humans. There was one person that died from rabies here in Texas as a result of being infected by a bat that was not recognized and treated at the time.

I appreciate you elaborating on that because here is another example of differences from state to state, whereas here in Florida we are used to hearing reports of rabies found in dogs or raccoons, which are so common here that I was not as aware of the threat from bats, but understand that it needs to be addressed as a priority, especially since bats cannot be vaccinated and will always pose this threat to humans. As you mentioned them being under bridges where they could potentially pose a threat to the homeless population in concentrated areas is certainly a high risk as opposed to wildlife far removed from human proximity. Public health is the frontline of care for many of these people in need and would certainly want to be able to recognize and treat in time.

Going back to the subject of bait though with regard to animals it is effective on, can you tell me more about how the USDA is involved with producing and providing it? I would like to highlight this for all of our readers to know more about how they may be able to work with them as well.

The USDA does not actually produce the bait, they work with a company that manufactures it and both USDA and the state of Texas purchase this for distribution within our state. USDA wildlife services supports our program here in Texas because, I think we may be the only state that has a program on the state side verses those 13 other states I mentioned which only have the USDA federal programs to distribute those baits, but don't have their own state program to purchase and distribute them separately. Here is Texas, I think it was in 1995 when after two human deaths then Governor Ann Richards declared rabies a state health emergency and supported this wildlife program with purchasing and distribution of these baits. Ever since then the state of Texas health department has supported this program by purchasing these baits in addition to what the USDA purchases.

As far as specialized awareness programs to public health professionals, we have zoonotic control veterinarians in all of our regions here in Texas, so we actually have departments in each of our regions that deal, probably 70% of their job duties is dealing with rabies exposures. So we have a very strong program here in Texas, and those regional veterinarians and their staff work with local health departments as well as counties that do not have health departments where they serve as the health department for those counties. So there are a lot of interaction between the health departments and our staff.

Considering how many regions you have and how some counties don't have their own health departments but receive assistance from other health departments, how do you conduct testing for rabies overall, or is there a centralized system?

We do have a state laboratory for testing in Austin, but we also have a few others such as one here in the Houston health department, El Paso, and San Antonio that do rabies testing, so we can expedite samples to any of those labs where local health professionals can work with whichever is closer. That direction is also part of our program of awareness and education.

USDA Helicopter used in the operation.
Photo courtesy DSHS

Texas Department of State Health Services
2023 Oral Rabies Vaccination Program (ORVP) At-A-Glance

What:	The 29th annual rabies vaccine bait airdrop to control and prevent domestic dog/coyote variant rabies and gray fox variant rabies
Start Dates:	January 10 in Edinburg January 15 in Del Rio (depending upon weather) January 21 in Alpine (depending upon weather)
Duration:	Entire project expected to be completed in approximately 2 weeks
Where:	South Texas International Airport, Edinburg Del Rio International Airport, Del Rio Alpine-Casparis Municipal Airport, Alpine
Counties:	18 counties total, comprising the Border Maintenance Zone
Vaccine Bait:	Oral rabies vaccine manufactured by Boehringer Ingelheim Animal Health USA Inc., Athens, Georgia. Vaccine is enclosed in a small plastic packet (similar to a fast-food ketchup package) dipped in fish oil and coated with fish-meal crumbles.
Bait Quantity:	813,900 oral rabies vaccine baits at 64-70 baits per square mile
Project Cost:	Approximately $2 million
Funding:	State of Texas and the USDA Animal and Plant Health Inspection Service/Wildlife Services
Aircraft:	Four white with blue and red trim Beechcraft King airplanes from Dynamic Aviation Group, Inc., and a Hughes 500 yellow and black helicopter from Texas Wildlife Services
Air Operations:	8 to 12 flights per day at 500 to 1,000 feet above ground level along half-mile interval lines

Results:

- The first ORVP bait drop took place in 1995 in South Texas to control an outbreak caused by a domestic dog/coyote variant of the rabies virus. The number of animal cases caused by this variant decreased from 122 cases in 1994 – the year before the first vaccine bait drop – to zero by 2000.
- There have been 2 cases due to the domestic dog/coyote rabies virus variant since that time (one in 2001 and one in 2004), each within a mile of the Rio Grande River.
- The first vaccine airdrop in West-Central Texas targeting the Texas fox (or gray fox) rabies virus variant took place in 1996. The number of animal cases caused by this variant decreased from 244 cases in 1995 to zero cases from May 2009 to April 2013.
- In May 2013, a cow infected with the gray fox rabies virus variant was identified in Concho County, and the ORVP contingency response included distribution of vaccine baits in the 2,500 square-mile area around the case in June 2013, January 2014, and January 2015. No additional rabies cases attributed to the gray fox variant have been identified in Texas since then.
- There have been no human cases of rabies attributable to these rabies virus variants since the ORVP began.

I also did want to mention that there is a new strain we have recently become aware of and that is the vampire bat strain which is in Mexico, but they've spotted a vampire bat about 40 miles in from our border, and vampire bats will feed on cattle and can be source of rabies to not only cattle but also people. So that's a new strain we are very concerned with.

Additional facts about the Texas Department of State Health Services 2023 Oral Rabies Vaccination Program (ORVP) are it takes approximately 2 weeks for completion and covers 18 counties total, comprising the Border Maintenance Zone, placing 813,900 oral rabies vaccine baits at 64-70 baits per square mile at a cost of approximately $2 Million. Four white with blue and red trim Beechcraft King airplanes from Dynamic Aviation Group, Inc., and a Hughes 500 yellow and black helicopter from Texas Wildlife Services are used to conduct 8 to 12 flights per day at 500 to 1,000 feet above ground level along half-mile interval lines.

Results from the first ORVP bait drop that took place in 1995 in South Texas to control an outbreak caused by a domestic dog/coyote variant of the rabies virus, showed the number of animal cases caused by this variant decreased from 122 cases in 1994 – the year before the first vaccine bait drop – to zero by 2000. And there have been no human cases of rabies attributable to the rabies virus variants addressed since the ORVP began.

NIH Funds New Tuberculosis Research Advancement Centers

By Lakshmi Ramachandra, PhD, chief, Tuberculosis and Other Mycobacterial Diseases Section, Division of Microbiology and Infectious Diseases, NIAID

The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, announced four new grant awards to establish Tuberculosis Research Advancement Centers (TRACs). The centers will support the development of a next generation of tuberculosis (TB) researchers by providing focused mentoring and funding support for new investigators; opportunities for multidisciplinary and collaborative research; and training in laboratory and clinical settings. The total funding in the first year of these five-year grants is approximately $4.3 million.

TB is a bacterial disease that currently is the second leading cause of death, after COVID-19, from a single infectious agent worldwide. In 2020, as many as 10 million new TB cases were diagnosed and approximately 1.5 million lives were lost to the disease. Alleviating the global burden of TB through research to discover or improve diagnostics, therapeutics and vaccines is a top priority for NIAID, as outlined in the 2018 Strategic Plan for Tuberculosis Research.

Awards have been made to the following institutions:

Texas Biomedical Research Institute, San Antonio
Principal Investigator: Larry Schlesinger, MD
Grant P30AI168439-01

The Interdisciplinary NexGen TB Research Advancement Center (IN-TRAC) will support career development, and provide experiential training in biosafety and biocontainment training, animal models, and animal imaging modalities. Participants will be trained in TB clinical research and TB patient care at the only free-standing TB hospital in the United States (Texas Center for Infectious Disease, San Antonio) and at clinics and field sites along the Texas-Mexico border.

Johns Hopkins University, Baltimore
Principal Investigators: Petros Karakousis, MD, and Richard Chaisson, MD
Grant P30AI18436-01

Working with partners and collaborators at clinical sites in Baltimore and internationally, the Johns Hopkins University (JHU) TRAC will enhance the integration, productivity and impact of JHU's existing TB research programs and foster career development. The JHU TRAC will also support clinical, basic and computational TB research through services provided via four research cores: a clinical core; a microbiology, immunology, animal modeling and imaging core; a pharmacology and pharmacometrics core; and a bioinformatics, modeling and biostatistics core.

Emory University, Atlanta
Principal Investigators: Neel Gandhi, MD, and Jyothi Rengarajan, PhD
Grant P30AI168386-01

The Emory/Georgia TB Research Advancement Center (TRAC) and partner institutions will support career development and provide Center participants with access to study populations in the United States and in countries with a high burden of TB. This TRAC will also provide resources for studies in pathogenesis and host immunity in animal models, including research with non-human primates. It will also offer opportunities to use cutting-edge technologies and integrate systems biology into experimental design.

University of Washington School of Medicine, Seattle
Principal Investigators: Chetan Seshadri, MD, Rhea Coler, Ph.D., and David Sherman, PhD
Grant P30AI168034-01

The Seattle Tuberculosis Research Advancement Center (SEA-TRAC) will catalyze new avenues of research and train new investigators to make a meaningful impact on the TB epidemic. The Development Core will oversee educational, training and grant programs designed to foster career development of junior or senior investigators who are new to TB research. The Clinical and Translational Science Core will lead training and consulting in clinical research methodology and foster collaborative research with international partners. The Basic Science Core will provide training for scientists new to working in the Biosafety Level-3 (BSL-3) environment and will lead training and consulting in advanced microbiology and immunology methods. The Data Sciences Core will leverage strengths in biostatistics, computational biology and modeling to train scientists who are new to data science and will offer consulting services for advanced research questions.

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TB 101 for Health Care Workers

Foreign-born populations in the United States have a higher rate of tuberculosis (TB) than U.S.-born populations. Among countries of origin for foreign-born persons with TB, since 1993 Mexico has contributed almost twice as many new cases as the second highest contributing country. Two-thirds of all foreign-born TB cases occur in the border states of California, Texas, Arizona, and New Mexico.

TB 101 for Health Care Workers is a Web-based course designed to educate health care workers about basic concepts related to TB prevention and control in the United States.

The target audience for the course includes newly hired TB program staff and health care workers in areas related to TB (such as individuals who work in correctional facilities or community health organizations and other health care settings). It is also a great resource for any health care worker to refresh their knowledge of TB.

The course is divided into six sections:

- Lesson 1: Introduction
- Lesson 2: TB Transmission and the Development of TB Disease
- Lesson 3: Testing for TB Infection
- Lesson 4: Diagnosis of TB Disease
- Lesson 5: Treatment of Latent TB Infection
- Lesson 6: Treatment of TB Disease

At the conclusion of the course, the participant will be able to:

- Describe what causes tuberculosis (TB).
- Explain how TB is spread.
- Explain the difference between latent TB infection and TB disease.
- List the methods that can be used to test for TB infection.
- Describe the process of diagnosing tuberculosis disease.
- Explain why latent TB infection (LTBI) is treated.
- Describe treatment regimens for LTBI.
- Describe the preferred treatment regimen for TB disease.
- Describe TB treatment adherence strategies.
- Describe my role, responsibilities, and scope of practice as a team member.

To begin the course, please visit: https://www.cdc.gov/tb/webcourses/tb101/

cdc.gov

Experimental Monoclonal Antibodies Show Promise against Epstein-Barr Virus

By Jeffrey Cohen, MD, chief of NIAID's Laboratory of Infectious Diseases

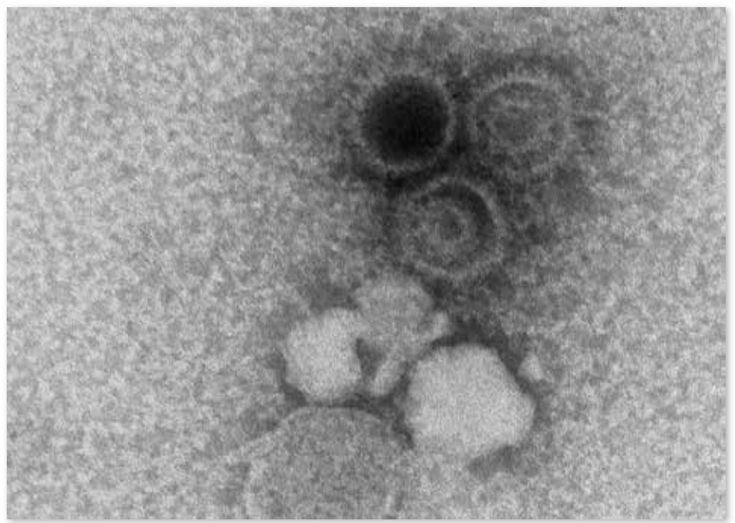
A panel of investigational monoclonal antibodies (mAbs) targeting different sites of the Epstein-Barr virus (EBV) blocked infection when tested in human cells in a laboratory setting. Moreover, one of the experimental mAbs provided nearly complete protection against EBV infection and lymphoma when tested in mice. The results appear online today in the journal Immunity.

Scientists from the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, in collaboration with researchers from Walter Reed Army Institute of Research, led the study.

EBV is one of the most common human viruses. After an EBV infection, the virus becomes dormant in the body but may reactivate in some cases. It is the primary cause of infectious mononucleosis and is associated with certain cancers, including Hodgkin lymphoma, and autoimmune diseases, such as multiple sclerosis.

People with weakened immune systems, such as transplant recipients, are more likely than immunocompetent people to develop severe symptoms and complications from EBV infection. There is no licensed vaccine to protect against the virus.

The researchers developed several investigational mAbs targeting two key proteins — gH and gL — found on EBV's surface. The two proteins are known to facilitate EBV fusion with human cells and cause infection. When tested in the laboratory setting, the investigational mAbs prevented EBV infection of human B cells and epithelial cells, which line the throat at the initial site of EBV infection.



An electron microscopy image showing three Epstein-Barr virions. Photo courtesy of NIAID

Analyzing the structure of the mAbs and their two surface proteins using X-ray crystallography and advanced microscopy, the researchers identified multiple sites of vulnerability on the virus to target. When tested in mice, one of the experimental mAbs, called mAb 769B10, provided almost complete protection against EBV infection when given. The mAb also protected all mice tested from EBV lymphoma.

The findings highlight viable EBV vaccine targets and the potential for the experimental mAbs to be used alone or in combination to prevent or treat EBV infection in immunocompromised patients most susceptible to severe EBV-related disease, according to the researchers. Additional research with mAb 769B10 is planned, the authors note.

References:

WH Chen et al. Epstein-Barr virus gH/gL has multiple sites of vulnerability for virus neutralization and fusion inhibition(link is external). Immunity DOI: 10.1016/j.immuni.2022.10.003 (2022).

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Addressing Syphilis Disparities in the American Indian and Alaska Native Population

An exclusive interview with Indian Health Service National HIV/HCV/STI Consultant, Rick Haverkate

By Tom Adams, Publisher of Federal Health & Medicine

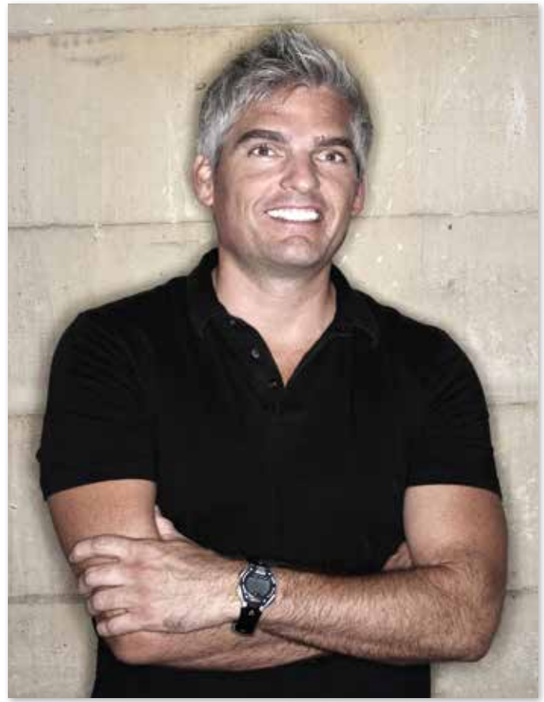
Despite decades of national STI prevention efforts, rising numbers of infections continue across the general population. In particular, spikes within certain minority groups reveal disparities and prompt the call for action to expand efforts of addressing needs in certain segments and removing barriers identified as deterrents for individuals to gain access for awareness, early detection screening, and rapid linkage to care.

In particular, reported cases of syphilis within the American Indian and Alaskan Native populations are much higher than the general population, placing them in the forefront of this epidemic. Insights from what the Indian Health Service is doing that can be used to better understand addressing minority populations of many different cultures presenting similar challenges are important to highlight, which is why I so greatly appreciate the information shared from my interview with Rick Haverkate from the IHS that can benefit all of our public health readers to strengthen their ability within their own communities.

Thank you Rick for joining me and sharing your insights on this epidemic within our nation and the threat it poses to public health.

It is my pleasure and thank you for your interest in this topic — anytime we can help educate our community about the importance of public health, specifically syphilis, it's all the better for every one of us. At IHS, we are working hard at a syndemic approach to STIs, which includes syphilis, HIV, and Hepatitis C. So we know that none of those disorders live in the universe all by themselves. If we are talking to people about things that lead to syphilis, we also need to discuss things like injection drug use, and sex while under the influence of alcohol and drugs that contribute to the rise we are seeing in new HIV and Hepatitis C diagnoses. So we include STIs in the whole big family of this epidemic.

It is imperative that we talk about things like social determinants of health, which include stable housing, employment, education, food and shelter, and mental health and domestic violence issues, so every time we see a patient we really have to look at them in that "whole health" point of view. That is where syphilis has to come in, especially when we look at the prevalence and increases in the rise of syphilis among American Indian and Alaska Native people, which was four times that of whites. In particular, we have seen a huge increase among females. The rate of syphilis in American Indian and Alaska Native females is



Indian Health Service National HIV/HCV/STI Consultant, Rick Haverkate. Photo courtesy of Indian Health Service

seven times higher than males — higher than any other race or ethnicity within the United States. The Centers for Disease Control and Prevention has preliminary 2021 data that show an even steeper increase.

I have seen this "whole health" approach more and more recently with many of the interviews I've had the privilege to conduct for our magazines, especially within the Veterans Health Administration that has cited using its electronic health record system as a tool for gathering a variety of data to help provide that big picture of understanding. How would you define the way this education is geared towards the medical professional as opposed to the individual patient?

We know the syphilis numbers are high, but not because of cultural reasons. It is not because of a person's race or ethnicity – typically being American Indian does not increase your risk of syphilis or other STIs. But many times, access to care is a function or a result of some of the disparities that exist. It is important for people to feel like they have a medical home, to feel like they are included in outreach, and that messaging is targeted towards them, or that folks at that clinic really care about them, and public health approaches really include them as an American Indian or Alaska Native person. So we're trying really hard to implement educational tools for our providers.

The IHS works closely with the University of New Mexico's Project ECHO (Extension for Community Healthcare Outcomes) program. Our tribal partners at the Northwest Portland Area Indian Health Board are doing some fantastic work to help maximize our ECHO coverage area and participation throughout the country. We have an incredible cohort of IHS, tribal, and urban Indian healthcare providers, clinicians, public health nurses, health educators, and social workers who ECHO brings to virtual meetings every month, and the folks from the health board train them on things like screening, follow up, and getting people into care and keeping them there.

So some of those policies that we have at our fingertips at IHS and at the tribal and urban Indian healthcare levels are working. Some of our health sites are in very remote areas of the country, so it can be challenging to recruit. The IHS is short staffed around Indian Country, up to approximately 60% of our facilities are understaffed, so you can imagine the burden a new outbreak like syphilis takes on our already overstretched staffing.

It takes so much work to do things like contact tracing and getting people screened so they know their status. Increasing knowledge of status is one of our main concerns. Getting people to come in for their initial screening is hard enough, but then the staff must follow-up to make sure they get into care. So the clinical and public health staff do their best to notify anyone that might have been exposed to syphilis. There are multiple barriers, but we do our best to ensure folks are receiving really good and appropriate care.

The IHS is trying hard to look at things like, how do we break outside of our bubble of communicating with patients? Whether it is through texting, or messaging with different forms like email. People have telephones, but lots of times they are unable to afford a data plan, live in areas where they do not have good cellular service, or their phone number changes frequently for a variety of reasons. Lots of us are unable to afford to keep a phone in operation consistently 365 days a year, so our phone numbers change. If you write down your phone number on your form, I may not necessarily be able to call you next week because maybe that phone number has expired.

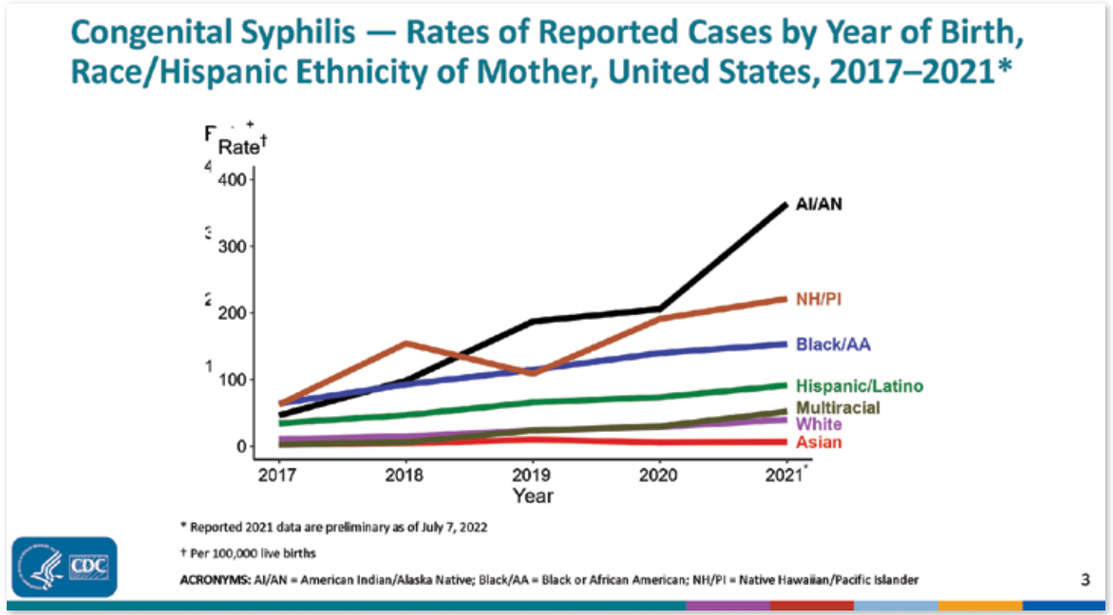
So we are using techniques like contact tracers who know the community and are embedded in the community, who go to parks and community events that can really encourage people to get screened and stay in care. We work with a philosophy known as *treatment as prevention*. That means if we treat people with a relatively painless shot of penicillin, we can cure them of syphilis so that way they are not spreading it to any of their contacts — and that's the prevention part.

Getting out of the facility and into the community is incredibly effective and now more than ever is an essential part of the success for any prevention program. I'm glad to see the cooperation of so many individuals working as a team for this, particularly with the disturbing rise of infection rates. Especially with the unique challenges you mentioned of not always having a way to call, text or email patients for follow up. Having more people involved helps reduce the number of individuals for falling through the cracks of an otherwise successful structure of public health prevention and care. This is exactly what our entire audience of public health professionals can benefit from hearing as they too have similar challenges within their own community. I think it's important to not only recognize the effectiveness of getting out into the community as the first step in prevention programs, but also to recognize the individuals that carry out that role and how essential they are to its success.

I have read that the dangers of syphilis to unborn babies is incredibly high, resulting in a far greater infant mortality rate and risk for birth defects and other health problems that could all be prevented by increasing education among the public to get screened and treated early, how important that is, what a huge difference that can make.

Absolutely, and let me provide an alarming statistic. We talked about the seven fold rate of syphilis among American Indian and Alaska Native women, but we also have the highest rates of congenital syphilis of any race. According to the CDC, the rate of congenital syphilis among American Indian and Alaska Native people increased from 37.7 per 100,000 births in 2016 to 363.7 in 2021. That is a 965% increase. Notably, the 2021 data currently only cover January to July, so when full-year 2021 data become available, the increase from 2016-2021 will be even greater.

We know that in pregnant people with untreated syphilis, up to 40% of their pregnancies will result in spontaneous abortion, stillbirth or perinatal death. Untreated infants, including those asymptomatic at birth, can still go on to develop late manifestations, like damage to their central nervous system, damaged bones and joints, or problems with teeth, eyes, and skin. We have seen a lot of congenital syphilis leading to fetal death, so it is incredibly sad to see that happening. But we're really trying to get out ahead of the syphilis epidemic, so we are working with our maternal child health teams to make sure that pregnant people remain in care. We also make sure that we follow them, and conduct the appropriate kinds of prenatal and perinatal screening.



Statistics courtesy of Indian Health Service

IHS providers work with a pregnant person before they give birth, treating syphilis, and preventing any negative health impacts for the mother and baby. Untreated syphilis is a sad situation and numbers are shocking, but we're still working to combat the outbreak. The IHS has some tools, but again it is just a matter of really getting them implemented into the community, getting people to talk about it, getting clinical staff, community people, and public health folks really involved in messaging.

We offer standardized care to everyone so we are not excluding anyone. You treat me as a whole person, but everyone gets the same appropriate care.

With regard to screening, how do you implement consistency for that with individuals living in remote locations, which pose even more of a challenge to early intervention?

We know that testing is the key, and we know that many folks do not have access to come to a clinic. Some people, including pregnant people, may not want to come into a clinic to be tested for various reasons. Therefore, there is a big barrier there. What we need to keep working on is making it standardized in their clinic, but getting it out from beyond those four walls by using mobile clinics, setting up at community health fairs and events like basketball games, and giving people access to self-testing they can do in the comfort and privacy of wherever they might reside.

So we're looking at expanding the access to self-test kits, where we teach people with a little video or a card that explains how to swab, how to poke your finger to get a small blood sample, what to do with the sample, and where to send it. We are not quite there yet, but the IHS definitely has the tools in mind that once we get approval, we will get those tools into people's hands. The IHS does have the ability to screen and treat in the field lab-based testing that we use in non-clinical settings, and we are working to make the screening a standardized point of care for patients coming into emergency departments.

From there, the IHS is setting up systems for when there is a positive for HIV, Hep C, or syphilis; we then refer them to care with a warm hand-off, not just saying, "Here, call this care provider on Monday when the clinic opens." It is important to do a warm hand-off to keep in contact with the patient and ensure they have followed through with their referral to get into care and treatment.

Isn't that half the challenge in any medical issue is getting the patient to participate and do their own part in making sure they get screening, early intervention, and proper care all the way through? I've seen many other health initiatives that include connections like what you mentioned from individuals that help keep in with the patients and make sure they do everything or help them to do everything they need to for proper care and prevention. Even though you mentioned challenges with some of the electronic forms of communication, do you partner with other government organizations like the CDC to educate the public and how effective are those methods proving to be?

Partnerships are really the key, the IHS has great partnerships with other agencies across the Department of Health and Human Services, such as the CDC, the Health Resources and Services Administration, and the National Institutes of Health, and we worked closely together on the Ending the HIV Epidemic initiative. From there, the IHS participates and collaborates with the Presidential Advisory Council on HIV/AIDS, and the CDC/HRSA Committee on HIV, Viral Hepatitis and STD Prevention and Treatment. Federal folks are always meeting and we bring in official members of community advisory groups to share their priorities and concerns. The IHS then has offline conversations with our federal partners to discuss the needed funding to address the public health issues. The IHS receives a lot of support from the White House and the Health and Human Services Secretary's office, on how we can ensure the IHS funding is working in Indian Country around things like diagnosis, prevention, treatment, and response.

On top of our federal partners, the IHS collaborates with universities and other philanthropic agencies. The IHS has excellent working partnership with our tribal and urban Indian facilities. This is the essential key to success of making programs work in Indian Country. The IHS does not stand-alone, we have to reach out to our urban partners and we do a good job of that. The IHS has found ways to fund them and ways to get a lot of our community some funding to work on this syndemic approach to Hep C, HIV, and STIs. So we're giving the tools around how to write policies, how to train their decision makers, how to implement procedures that get people into screening and into care, including the use of incentives, using new patient contact tracing approaches, and working with maternal child health programs. Partnerships are critical because we are not able to do it all from IHS headquarters. The IHS develops those partnerships, such as with the National Association of County and City Health Officials, an organization that is helping us train providers, and the National Coalition of STD Directors, so there are many great partnerships.

We have a great core group of people around me at IHS who are doing a great job of expanding our capacity-building assistance and technical assistance at IHS, tribal and urban Indian programs.

I'm certainly glad to hear you are multiplying your efforts by adding more members to your team as well as partnerships, and proud to be able to lend our support in promoting awareness for your programs that can help Americans throughout all public health locations. Is there anything else you would like to add or emphasize that we can include in your message?

Just that we cannot do this alone, so I think building those partnerships is one key issue. Encouraging state and county health

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offices to use things like disease intervention specialists to work closely alongside us, maybe to help take some of the burden off of our small IHS and tribal facilities and to conduct contact tracing and field treatment. But I think a barrier may be the ability to share patient data, not necessarily diagnosis data but just something like, "Hey, I saw Mary the other day and she could use a follow up." Something as easy as that, we need to be able to share appropriately with our public health teams to reach out and contact folks to get them into our tribal clinics or be able to refer people to a facility outside of a tribal or IHS healthcare setting for their treatment. Maybe they do not want to come into one of our facilities because of an issue they have had in the past, but we need to get them into care regardless or bring the care to them.

"Preliminary CDC data Jan-July 2021 are 42.2 cases per 100,000, a 57% increase from 2020."

The IHS needs to keep exploring this issue to bring healthcare to the people and make accommodations for them. We have to get beyond the idea that our office hours are Monday through Friday from 9 AM to 5 PM, that if you are not here we are unable to see you. We need to make sure we provide healthcare that meets people where they are.

I think another big issue is helping put temporary staff within the health system. We have talked about shortages of staffing, so maybe we need to start doing some sort of emergency hiring of non-licensed health care workers that are just acting as the staff people that organize testing, counseling, and contract tracing, that prepare mobile clinics, or that advertise the importance of screening. We are so overburdened. IHS clinicians are overworked and we need to consider hiring staff that are non-licensed health care workers. Of course that means they do not have the medical licensing to do some of the direct care, but they can do behind the scenes care coordination and health education that make public health and clinical interventions work.

I recently spoke with the national director for the VA's women's health services for an interview where she told me the VA was doing the exact same thing to ensure women come in for screening and are provided follow up for results and any care needed. The title they use is care coordinators, and they too are non-licensed personnel that can lighten the burden off the licensed clinicians to make sure nobody falls through the cracks.

We know from other areas such as maternal health and HIV that case management works, it works in so many ways. I think any person who walks into any clinic should be assigned a case manager or a patient navigator to make sure they understand how check in works, how to get to the pharmacy, to know what your referral means, to make sure you follow up on your referral and get help answering questions.

Case management at every step of the way is especially important if someone is in a long-term treatment program like HIV care, which is a lifetime commitment, and they need assistance. Not everybody does, but everyone should at least be offered case management and patient navigation. The IHS is working to be able to do that. Some of our clinics, like our Gallup Indian Medical Center in New Mexico, do a really good job of utilizing their patient navigators for people living with HIV or people on pre-exposure prophylaxis (PrEP) to prevent the spread of HIV, and we need the same thing for syphilis.

It is very interesting that syphilis can be prevented, it can be treated, and it can be cured, and education is the key along with early testing to prevent the spread for a person's own protection and others. It there anything else we can share with our readers that may also be helpful in their facility?

Again, the main thing is that we cannot do this alone and our success is determined by a large of group of people working together in Indian Country that are dedicated to being fully committed to this cause. In fact, we just had a leadership meeting with our Chief Medical Officer Dr. Loretta Christensen to discuss implementing an on-demand STI testing program. This would mean that people do not need to have a medical appointment; they can just walk into one of our clinics and say, "I'm here for (blank)." The IHS will give it a name that is not revealing so they can discreetly do the swab and get their screening, given that some people do not want to say that they are there for syphilis testing or STI testing. The IHS is trying to take down barriers to simplify screening for patients.

We are working on that policy now which will require some procedures, but we are trying to come up with a name that means something to the public and to the facilitators and to the clinic. On top of all the other work we are doing, The IHS is always keeping in mind that we need to make this a low burden on everybody, with the ability to get test results and get into treatment quickly.

About the author:

Rick is an enrolled member of the Sault Ste. Marie Tribe of Chippewa Indians. In 1993 he earned an MPH from the University of Hawai'i. His 32-year public health career has been focused entirely on Indigenous peoples of North America. Rick has assumed various roles, including Community Health Educator, Public Health Advisor, and Director of Public Health at the tribal, state, and national levels. He has specialized in the operational management of HIV/AIDS, Maternal and Child Health, Tobacco, Health Promotion/Disease Prevention, and Community Capacity Building. Rick currently works for the Indian Health Service as their National HIV/HCV/STI Program Consultant.

Celebrating Medical Laboratory Professionals Week

Laboratory Heroes Save Lives

Safety and quality in laboratory testing are imperative since doctors and patients rely on laboratories for accurate diagnosis and effective treatment of diseases. Laboratory professionals safeguard patient and public health by reducing diagnostic errors and preparing for disease outbreaks and health threats. These laboratory heroes conduct approximately 14 billion laboratory tests annually, and 70 percent of medical decisions depend on laboratory tests—emphasizing the importance of clinical and public health laboratories in the healthcare system.

CDC's Division of Laboratory Systems (DLS) observes Lab Week each April to recognize clinical and public health laboratory professionals for the contributions they make to the health of our communities, through their work in public health and clinical laboratories, along with family members, friends, and colleagues who are patients in clinical settings.

There is no better time to celebrate the thousands of laboratory professionals working to support the health of patients and communities across America right now! During this year's celebration we will celebrate the United States' critical healthcare workforce and thank you for your service to our country, and the world.

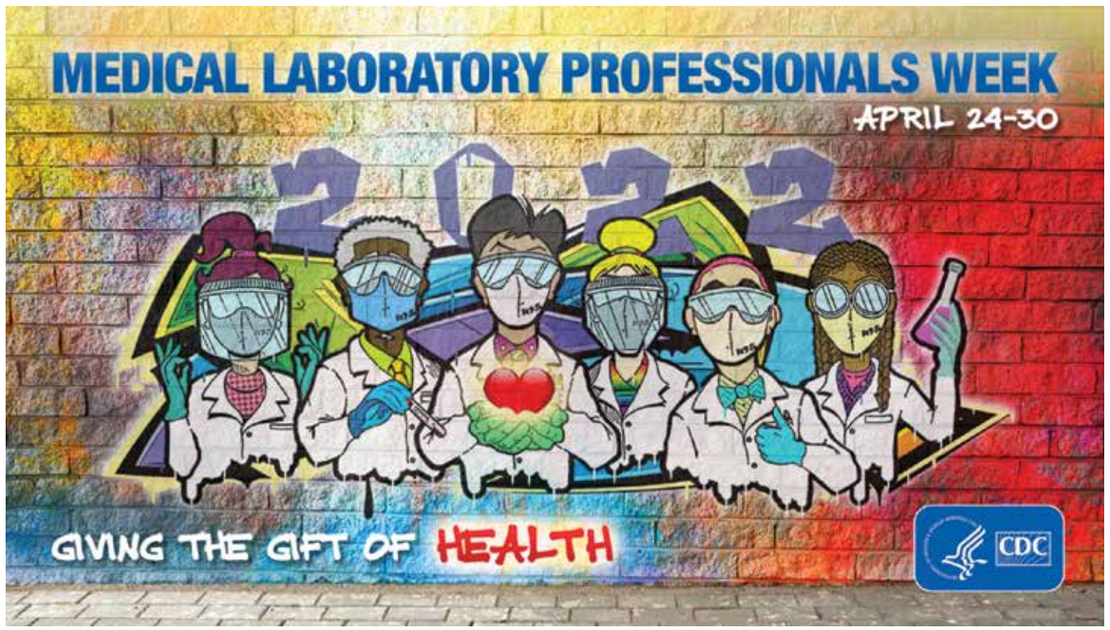
DLS offers a wide range of resources for laboratory professionals, including:

Clinical Laboratory COVID-19 Response Weekly Calls

https://www.cdc.gov/csels/dls/prepared-labs/covid-19-clinical-calls.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fsafelabs%2Fresources-tools%2Fcovid-19-weekly-clinical-calls.html

Downloadable and customizable Laboratory Job Aids, including COVID-19 relevant products

https://www.cdc.gov/labtraining/jobaids.html



Graphic from CDC's 2022 Medical Laboratory Professionals Week celebrates diversity with it's theme, "Giving The Gift Of Health". Courtesy of the CDC

Photo courtesy of the Arizona State Department of Health Services

Laboratory Outreach Communication System messages about COVID-19 and other topics

https://www.cdc.gov/csels/dls/locs/index.html

A wide variety of laboratory training courses, including on-demand learning to meet you where you are now

https://www.cdc.gov/labtraining?Sort= format%3A%3Aasc

Free resources for a Next Generation Sequencing-focused quality management system

https://www.cdc.gov/labquality/qms-tools-and-resources.html

Free educational materials for public health and clinical laboratories

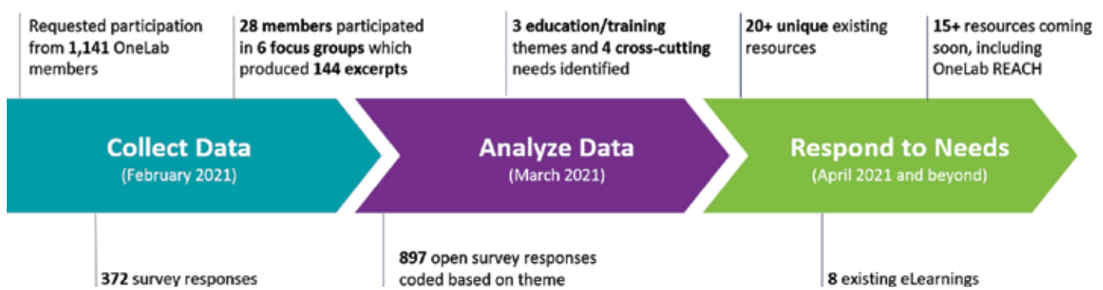
https://www.cdc.gov/csels/dls/educational-materials.html

In February 2021, the CDC launched the OneLab initiative as a collaborative network between laboratory education and training professionals and CDC to meet laboratory learners' most urgent COVID-19 education and training needs and collectively support rapid, large-scale emergency responses.

OneLab's goal is to bridge, train, and sustain a capacity-building community among public health and clinical laboratory professionals to support rapid, large-scale responses to public health emergencies.

Response is to address priority needs, and the OneLab has compiled 100+ free job aids and trainings, with new resources released on a rolling basis. These free job aids are intended to assist clinic and public health laboratory professionals with diagnostic testing, preparedness, core science, informatics, quality, safety, and packing and shipping. These aids were developed to accompany eLearning courses on the CDC Laboratory Training webpage https://www.cdc.gov/labtraining?Sort=format%3A%3Aasc

cdc.gov



Graphic courtesy of the CDC

CDC's Public Health Laboratory Electronic Test Orders and Results Initiative

CDC is collaborating with the nation's public health laboratories (PHLs) and other partners to modernize data systems. CDC and its collaborators are building the technical infrastructure to facilitate the exchange of electronic test orders and results between healthcare facilities and PHLs, an activity abbreviated as "ETOR." This multidirectional platform will streamline channels of data transmission and improve interoperability between partners. This exchange will decrease the use of paper-based test orders and reports, reducing the risk of errors in manual data entry and result reporting, and ensuring that accurate testing information is captured and transmitted to a patient's medical record in a timely manner.

Current examples of ETOR in action include newborn screening and public health emergencies. Approximately four million babies are born in the United States every year, and nearly every one of them is screened at birth for dozens of potentially fatal or disabling health conditions that are treatable if detected as early as possible. Many healthcare providers still submit newborn screening orders through the mail and receive their results by fax. Strengthening ETOR will allow PHLs to plan for and track incoming specimens and immediately report test results with comprehensive data back to the provider, bolstering the peace of mind of new parents and ensuring that thousands of babies receive the prompt care they need.

ETOR connects healthcare facilities and public health laboratories. Graphic courtesy of the CDC

Implementing ETOR will also strengthen public health surveillance and emergency response by linking laboratory data with patient information through standardized data elements included in the test order.

ETOR is a Health Equity Issue. When healthcare facilities in medically underserved areas do not have ETOR systems in place, they may not be able to efficiently exchange laboratory testing data with PHLs. Our initial goal is to ensure that 30% of newly established ETOR connections benefit healthcare systems that serve patients in these communities.

Recent public health emergencies from Zika virus to SARS-COV-2 and monkeypox have demonstrated the urgent need for improved interoperability between PHLs and healthcare facilities. ETOR streamlines the transmission of test orders to allow PHLs to adequately anticipate incoming requests and facilitating a more immediate and comprehensive exchange of data when reporting results.

cdc.gov

Expanding Contraceptive Choices

By Diana W. Bianchi, MD, Director of the Eunice Kennedy Shriver National Institute of Child Health and Human Development

When choosing a contraceptive method, individuals and couples may consider its effectiveness, the side effects it may cause, and whether it is accessible, affordable, and convenient. But while there are many short- and long-acting female contraceptives on the market, options for men are limited to condoms and vasectomies.

A safe, highly effective, reversible method of male contraception would fill an important public health need. Additionally, multipurpose prevention technologies (MPTs) — products that prevent both pregnancy and sexually transmitted infections (STIs) — would increase sexual and reproductive health options for both women and men. NICHD supports a broad range of contraceptive research, including efforts to develop male contraceptives and MPTs.

Male Contraceptives

For example, Nestorone®/Testosterone (NES/T) was developed through a collaboration between NICHD and the Population Council. It is a hormone-based gel that the male partner applies daily to his shoulder blades, reversibly blocking sperm production while maintaining sexual drive and function. NES/T is the first birth control product designed for males that has progressed past early-stage clinical trials.

To date, 112 couples have completed the one-year efficacy stage of an ongoing Phase IIb study evaluating NES/T. Findings from the study, conducted by NICHD's Contraceptive Clinical Trials Network, have been extremely promising so far, with NES/T showing efficacy comparable to that of long-acting reversible female contraceptives — the most effective non-surgical methods currently available for preventing pregnancy. Although the study will take two more years to complete, the investigators intend to perform an interim analysis to begin the process

Diana W. Bianchi, MD. Photo courtesy of The National Institutes of Health

of planning a Phase III clinical trial, the pivotal evaluation required for FDA review and potential approval of NES/T.

NICHD also supports the development of male contraceptives that could be taken as needed shortly before sex. Two such potential on-demand contraceptives target the sperm proteins soluble adenylyl cyclase (sAC) and epididymal protease inhibitor (EPPIN). Researchers at Weill Cornell Medicine found that a single dose of a sAC inhibitor rendered male mice infertile for hours, with normal fertility returning the next day. They are currently developing sAC inhibitor formulations suitable for clinical studies. Separately, investigators at Eppin Pharma, Inc., developed EP055, which reduces sperm motility by binding to EPPIN on the sperm surface. Intravenous EP055 showed promise in a preclinical study, and the company is working to develop oral versions for use in a Phase I clinical trial.

Multipurpose Prevention Technologies

With NICHD support, researchers at Boston University aim to develop an on-demand female MPT product that prevents pregnancy and protects both partners against STIs. They and collaborators created a vaginal film containing an anti-sperm antibody called human contraceptive antibody (HCA). Recent findings from a Phase I study indicate that the film, dubbed ZB06, is safe and shows promise as a contraceptive. Additional data suggest that HCA can trap pathogens in sperm agglutinates — clumps of sperm that form in the presence of the antibody — potentially preventing transmission. The Boston University researchers ultimately plan to combine ZB06 with a vaginal film that delivers antibodies against HIV and herpes simplex virus 2. They also are investigating an HCA-containing penile gel as a candidate for male contraception.

Another NICHD-supported project is evaluating a potential contraceptive vaginal ring that also prevents HIV acquisition. The ring is designed to deliver the antiretroviral medication dapivirine and the hormonal contraceptive levonorgestrel over three months of continuous use. A small Phase I study found that the ring delivered the two drugs at levels predicted to block HIV acquisition and ovulation. However, many participants reported that the ring came out either partially or completely at least once. Researchers made changes to the ring to prevent these expulsions, and enrollment in a Phase I study to evaluate reformulated versions is now underway.

I look forward to continued progress from these and other studies focused on developing innovative contraceptive methods to expand the choices available for individuals and couples. People need safe, effective, and desirable options that fit with their lifestyles.

nichd.nih.gov

HHS Announces Over $20 Million in Awards to Implement Biden-Harris Administration Blueprint for Addressing the Maternal Health Crisis; Reduce Disparities in Maternal and Infant Health

Funding Supports Community-based Doulas, Rural Obstetric Care, New State Task Forces to Tackle Maternal Health Disparities, and Investments in Infant Health Equity

The U.S. Department of Health and Human Services, through the Health Resources and Services Administration (HRSA), announced investments of over $20 million to improve maternal and infant health and implement the White House Blueprint for Addressing the Maternal Health Crisis.

Funding aims to help reduce disparities in maternal and birth outcomes, expand and diversify the workforce caring for pregnant and postpartum individuals, increase access to obstetrics care in rural communities, and support states in tackling inequities in maternal and infant health.

"Today, Black women are three times more likely to die from a pregnancy-related cause in this country than White women. That has to change," said HRSA Administrator Carole Johnson. "To make meaningful change, we need to center our work on the individuals and families we are serving, and that is what today's investments aim to do. The Biden-Harris Administration is committed to prioritizing equity and reducing the unacceptable disparities in maternal and infant health. Through these awards, we are taking additional action to implement the Blueprint that the President and Vice President have laid out for driving impactful solutions and providing our nation's families with the support and resources they need to lead healthy lives."

About 700 people die each year during pregnancy or in the year after. Thousands of women each year have unexpected outcomes of labor and delivery with serious short- or long-term health consequences. Rural populations tend to have worse maternal health outcomes than individuals living in urban areas, and there are disparities experienced by racial and ethnic groups.

HRSA awards include:

- Supporting State-led Maternal Health Innovation: HRSA is awarding $9 million to 9 grantees through its State Maternal Health Innovation Program to create state-led maternal health task forces bringing the voices of key leaders and pregnant and postpartum individuals together and using state-specific maternal health data to develop and use innovative approaches to address the most pressing maternal health needs and address disparities in health outcomes. Innovations cover four categories: provision of direct clinical care, workforce training, maternal health data enhancements, and community engagement.
- Improving Maternal Care in Rural Communities: HRSA is awarding approximately $4 million to 4 awardees through its Rural Maternity and Obstetrics Management Strategies Program to improve maternal care in rural communities by building care networks that coordinate care needs for pregnant individuals; leveraging telehealth and specialty care to better support care needs; and improving financial sustainability of these services in rural communities. Awardees will work to address unmet needs, which may include underlying health risks, health disparities, and other inequities.
- Increasing Access to Community-based Doulas: HRSA is awarding approximately $3 million to 19 Healthy Start programs to increase the availability of doula services in the communities they serve. The Healthy Start program supports community-based strategies to reduce disparities in infant mortality and improve perinatal outcomes for pregnant and postpartum individuals and their children in areas most affected by infant and maternal mortality. This funding will cover training and compensation for doulas, who provide services to women during pregnancy, birth, and post-partum.
- Addressing Infant Mortality: HRSA is awarding $4.5 million to 9 grantees through its Catalyst for Infant Health Equity Program to reduce infant mortality disparities. These funds will support action plans that focus on improving community systems and services that influence health outcomes. Activities include coordination of services to address housing and housing stability management; workforce development and training to address implicit bias; and education and outreach to help community members support maternal and infant health.

HHS is committed to supporting safe pregnancies and childbirth, eliminating pregnancy-related health disparities, and improving health outcomes for parents and infants across our country. As part of this work, HRSA also continues to conduct analysis of the workforce needs to address these critical issues.

hhs.gov

Primary Prevention and Public Health Strategies to Prevent Neonatal Abstinence Syndrome

Neonatal Abstinence Syndrome (NAS) continues to be a growing problem in the United States. NAS occurs when newborn babies experience withdrawal after being exposed to drugs in the womb. NAS can cause low birth weight and other complications leading to prolonged hospitalization. NAS can occur with a variety of both illicit and prescription drugs, including some prescription painkillers. The rates of NAS increased 5 times between the year 2000 and the year 2013. As of 2012, there was an average of one infant born with NAS every 25 minutes in the United States, accounting for an estimated $1.5 billion in healthcare spending that year alone.

Fortunately, NAS is preventable if an expectant mother receives proper care and treatment. One of the most effective prevention strategies is to improve preconception health care, and to educate both patients and providers about appropriate use of prescription drugs during pregnancy. Though there have been some recent initiatives to reduce rates of opioid use, few have included a focus on pregnant women and their babies. Screening of pregnant women can also be an effective prevention strategy by determining who may need additional care or treatment for opioid use.

CDC is working with state and local partners to develop better policies for opioid prescribing among pregnant women by sharing information about how providers and patients can work together to prevent NAS by learning more about the choices that they make, and HRSA offers serveral programs that can be utilized as well.

The Maternal, Infant, and Early Childhood Home Visiting (MIECHV) Program supports pregnant people and parents with young children who live in communities that face greater risks and barriers to achieving positive maternal and child health outcomes. Families choose to participate in home visiting programs, and partner with health, social service, and child development professionals to set and achieve goals that improve their health and well-being. More information and program resources are available at: https://mchb.hrsa.gov/programs-impact/programs/home-visiting

Key Findings: Public Health Reporting of NAS Offers Opportunities for Treatment and Prevention

A new CDC article looked at laws enacted in six states that make health departments or hospitals report all babies born with NAS for public health monitoring. Researchers found that required public health reporting of infants born with NAS enabled states to estimate the number of babies born with NAS. It can also help

Photo courtesy of the Centers for Disease Control

identify opportunities for treatment and prevention for mothers and babies and plan for needed services.

Main Findings

- No national monitoring system currently exists to collect data about NAS in the United States. Researchers identified laws in six states that require public health monitoring of NAS.
- State officials noted that required reporting of infants born with NAS has helped their state
  - — Estimate the number of babies born with NAS in real time.
  - — Locate specific areas more severely impacted by NAS to help target resources.
  - — Identify mothers and babies affected by opioid use disorder who may benefit from local programs and services.
- States that require hospitals to report NAS cases may need additional resources and training for healthcare providers and hospital staff. This can help ensure that high-quality information is collected.
- This report found that states use different criteria and approaches for public health reporting of NAS. States considering implementation of laws requiring NAS case reporting for public health surveillance can benefit from understanding advantages and challenges of the approaches used.

Key Findings Reference

Jilani SM, Frey MT, Pepin D, Jewell T, Jordan M, Miller AM, et al. Evaluation of State-mandated Reporting of Neonatal Abstinence Syndrome – Six States, 2013-2017. MMWR Morb Mortal Wkly Rep. 2019;68:6–10.

cdc.gov

Many Adults with Disabilities Report Frequent Mental Distress

Targeted interventions and programs and policies that ensure receipt of mental health screening, care, and support services could help reduce mental distress among adults with disabilities

Cree RA, Okoro CA, Zack MM, Carbone E (2020). Frequent Mental Distress Among Adults by Disability Status, Disability Type, and Selected Characteristics – United States 2018. Morbidity and Mortality Weekly Report (MMWR).

A study from the Centers for Disease Control and Prevention (CDC) found that adults with disabilities report experiencing more mental distress than those without disabilities. Frequent mental distress, defined as 14 or more self-reported mentally unhealthy days in the past 30 days, is associated with adverse health behaviors, increased use of health services, mental disorders (e.g., diagnosis of major depressive disorder), chronic diseases, and functional limitations (1).

Adults with disabilities more often report depression and anxiety (2), reduced health care access (3), and health-related risk behaviors (4) than do adults without disabilities. CDC analyzed 2018 Behavioral Risk Factor Surveillance System (BRFSS) data to compare the prevalence of frequent mental distress among adults with disabilities with that among adults without disabilities and to identify factors associated with mental distress among those with disabilities. Nationwide, an estimated 17.4 million adults with disabilities reported frequent mental distress; the prevalence of reported mental distress among those with disabilities (32.9%) was 4.6 times that of those without disabilities (7.2%).

Among adults with disabilities, those with both cognitive and mobility disabilities most frequently reported mental distress (55.6%). Adults with disabilities who reported adverse health-related characteristics (e.g., cigarette smoking, physical inactivity, insufficient sleep, obesity, or depressive disorders) or an unmet health care need because of cost also reported experiencing more mental distress than did those with disabilities who did not have these characteristics. Adults living below the federal poverty level reported mental distress 70% more often than did adults in higher income households. Among states, age-adjusted prevalence of mental distress among adults with disabilities ranged from 25.2% (Alaska) to 42.9% (New Hampshire).

Understanding the prevalence of mental distress among adults with disabilities could help health care providers, public health professionals, and policy makers target interventions and inform programs and policies to ensure receipt of mental health screening, care, and support services to reduce mental distress among adults with disabilities.

BRFSS is an annual, landline and cellular telephone–based self-reported survey of noninstitutionalized U.S. adults aged ≥18 years. In 2018, the BRFSS unweighted sample size was 430,949. The combined (landline and cellular telephone) median response rate among the 50 states and the District of Columbia in 2018 was 49.9% (range = 38.8%–67.2%). Adults were considered to have a disability if they reported having one or more of six disability types: hearing, vision, cognition, mobility, self-care, or independent living. Mutually exclusive disability categories were created for each disability type and for adults reporting more than one disability. The latter were further categorized into four groups, based on cognition or mobility, two of the most prevalent disability types: cognition-only, mobility-only, both, or neither.

Adults were considered to have frequent mental distress if they reported 14 or more days in response to the question "Now thinking about your mental health, which includes stress, depression, and problems with emotions, for how many days during the past 30 days was your mental health not good?"

Overall, 26.2% of U.S. adults who responded to questions about disability and mental distress reported having a disability. Nearly one third of adults with disabilities (32.9%) reported experiencing frequent mental distress, compared with 7.2% of adults without disabilities. Frequent mental distress was reported by 55.6% of those with disability in both mobility and cognition, 8.8 times that reported among those without disabilities.

Demographic differences in PRs of mental distress were generally similar among adults with and without disabilities, except for veteran and employment status. Mental distress was more commonly reported among females and persons who were unmarried; unemployed; identified as lesbian or gay, bisexual, or something else; and lived in lower-income households compared with males and those who were married, employed, identified as straight or not gay, and lived in higher-income households.

Persons identifying as non-Hispanic Asian, Hispanic, and middle-aged or older reported mental distress less often than did those who identified as non-Hispanic white, and who were younger. Among adults without disabilities, both veterans and retirees were 20% less likely to report mental distress than were nonveterans and adults who were employed; no differences were found by veteran and employment status for adults with disabilities.

cdc.gov

Save Lives with a Simple Urine or Blood Test: the Importance of Screening People with Type-1 Diabetes for Kidney Disease

By the American Kidney Fund

Kidney disease is the fastest-growing noncontagious disease in the U.S. with 37 million Americans living with chronic kidney disease (CKD). While the rates of kidney disease for the overall U.S. population are concerning, the rates of kidney disease among U.S. veterans are even worse. The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDKD) estimates that the percent of veterans with CKD is 34% higher than the general population. One of the leading causes of kidney disease is diabetes — both type 1 and type 2. In type 2 diabetes, the body continues to create insulin, but does not use it the way it should. Type 1 diabetes, though, is an autoimmune disease in which the body's immune system attacks the cells in the pancreas that make insulin, ultimately meaning the pancreas creates little or no insulin.

According to a study published in the American Diabetes Association's (ADA) journal, *Diabetes Care*, the lifetime risk of kidney disease in type 1 diabetes (T1D) has traditionally been estimated at approximately 50% but it may exceed 70%.

Kidney disease is not reversible, but it is treatable — especially when caught and treated early. Unfortunately, CKD often has no signs or symptoms until the disease has progressed to late-stage or end-stage renal disease (ESRD or kidney failure). The only treatments available for ESRD are dialysis or a kidney transplant. To combat the rising rates of kidney disease and prevent more people from "crashing into dialysis," particularly in the veteran population, it is imperative that patients with diabetes be regularly screened for kidney disease with blood and urine tests.

Photo courtesy of the American Kidney Fund

A complete bloodwork count (CBC) panel performed at a routine physical will usually include the patient's blood urea nitrogen (BUN) levels, and if those levels are elevated, it could be an indicator of kidney disease. The CBC also tests a patient's creatinine levels, a waste product from muscles that healthy kidneys filter out of the blood. Again, elevated levels of creatinine can be a sign that the patients' kidneys are not working properly. A urine test can also reveal if a patient has kidney disease. Using a dipstick test, a doctor can see if there is any protein in the patient's urine, which may indicate a kidney problem. Doctors may also use a urine albumin to creatinine ratio (uACR) test, which measures the level of albumin (protein) to creatinine in the urine. The uACR is a good way to detect the earliest stages of kidney disease, and although it is relatively simple to perform, it is not used as often as it should be in routine physicals. If a patient has diabetes, a urine test to screen for kidney disease should be part of their regular care.

ADA publishes its Standards of Medical Care in Diabetes guidelines for the care and management of diabetes. In 2022, the Standards of Care added a section specifically for kidney disease risk management. The guidelines recommend that people who have had a diagnosis of T1D for five or more years be screened at least annually with a urine albumin and estimated glomerular filtration rate (eGFR) blood test.

The American Kidney Fund (AKF), though, recommends that anyone with diabetes be screened for kidney disease annually as soon as they have been diagnosed. The sooner signs of kidney damage are caught, the sooner patients can work with their doctors to slow or stop the progression of the disease, increasing both their life expectancy and quality of life. Furthermore, it reduces the risks for patients developing additional chronic conditions, including cardiovascular disease.

Patients with diabetes who have been diagnosed with earlier stages of kidney disease have several options available to them to help prevent the disease from progressing further. Controlling

Graphic courtesy of the American Kidney Fund

blood sugar levels, controlling blood pressure and managing cholesterol levels are all key to preventing or slowing diabetic kidney disease. Certain medications can also help, including glucose cotransporter 2 (SGLT2) inhibitors and glucagon like peptide 1 (GLP1) receptor agonist. The ADA's 2023 Standards of Care guidelines also added mineralocorticoid receptor antagonists and other cardiovascular and kidney protective medications (previously, these medications were only recommended when alternative treatments were not effective). The new guidelines also recommend referring patients with diabetes to a nephrologist:

- When there is uncertainty about the cause of kidney disease
- For difficult management issues including anemia, secondary hyperparathyroidism, significant increases in albuminuria in spite of good blood pressure control, metabolic bone disease, resistant hypertension, or electrolyte disturbances
- For continuously increasing urine albumin-to-creatinine ratio and/or for continuously decreasing estimated glomerular filtration rate
- When there is advanced kidney disease (eGFR ≥20 mL/min/1.73 m2 and urinary albumin ≥200 mg/g creatinine) requiring discussion of renal replacement therapy for ESRD. AKF has advocated in a letter to the United States Preventative Services Task Force that the threshold for a nephrologist referral be raised to an eGFR of ≥30 mL/min/1.73 m2 as 20 is very low and a person won't have much change of stopping further progression once their labs have reached that level.

Kidney disease is often called the "silent killer" because of its lack of signs and symptoms. Early detection is the best way to slow or stop the progression and, ultimately, to saves lives. That is why AKF launched its Know Your Kidneys™ campaign, which encourages Americans to know the central role of the kidneys in their overall health, and ties that to their ability to experience life's possibilities and milestones. The campaign has a simple, positive message: by knowing the state of your kidneys, you can ultimately know a longer, healthier life. This is just as true — if not more so — for patients living with diabetes, who are even more at risk for developing kidney disease.

For more information about the connection between kidney disease and diabetes, explore AKF's numerous resources including webpages dedicated to the topic as well as video explainers, talk-to-your-doctor guides and archive of webinars at KidneyFund.org/Resources. You can also find recordings of sessions from AKF's annual Kidney Action Week (KAW), a week-long, virtual event aiming to connect patients, caregivers and healthcare providers in AKF's on-going efforts to bring patient-centered kidney-related education to the public.

Our most recent KAW featured the following sessions on the connection between diabetes and kidney disease: "Stage 3 CKD – Diabetes and Kidney Disease" and "Veterans, Kidney Disease and Diabetes: The Mounting Mental Health Burdens of Managing Chronic Diseases," which you can watch on our AKF YouTube channel: https://www.youtube.com/@kidneyfund/

Fact Sheet courtesy of the American Kidney Fund

NIH-funded Study Finds Personalized Kidney Screening for people with Type 1 Diabetes Could Reduce Costs, Detect Disease Earlier

By Ellen Leschek, MD, Program Director, Division of Diabetes, Endocrinology, & Metabolic Diseases, National Institute of Diabetes and Digestive and Kidney Diseases

Taking a personalized approach to kidney disease screening for people with type 1 diabetes (T1D) may reduce the time that chronic kidney disease (CKD) goes undetected, according to a new analysis performed by the Epidemiology of Diabetes Interventions and Complications study group, which is funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), part of the National Institutes of Health.

The finding, published in *Diabetes Care*, provides the basis for the first evidence-based kidney screening model for people with T1D.

Photo courtesy of NIH, NIDDK

Current CKD screening recommendations include annual urinary albumin excretion rate (AER) testing for anyone who has had T1D for at least five years. Albumin is a protein found in the blood and having too much albumin in the urine is a sign of kidney disease. The new findings suggest that AER screening could be personalized to optimize testing frequency and early detection of CKD. Specifically, people with T1D who are at low risk of developing CKD could be tested for AER less frequently to reduce burden and cost, and those at high risk for CKD could be tested more frequently to facilitate earlier CKD detection.

People with T1D have an estimated 50% risk of developing CKD over their lifetime. CKD can progress to kidney failure, requiring dialysis or a kidney transplant. Using more than 30 years of participant data of AER and HbA1c (an integrated measure of blood glucose) from 1,334 participants in the NIDDK-funded Diabetes Control and Complications Trial (DCCT) and the observational follow-up Epidemiology of Diabetes Interventions and Complications (EDIC) study, the study group identified three levels of CKD risk that were associated with a later CKD diagnosis. They then developed a model to estimate the optimal screening intervals for people with T1D to detect CKD at its earliest stages.

According to the model's findings:

- People with AER of 21-30 mg per 24 hours and a HbA1c of at least 9% are at high risk for developing CKD and could be screened for urine albumin every six months. This screening frequency could reduce time with undetected kidney disease so that appropriate interventions can be instituted as early as possible.
- Those with AER ≤ 10 mg per 24 hours and a HbA1c ≤ 8% are at lower risk for developing CKD and could be screened every two years. This change reduces patient burden and potentially saves millions of dollars compared to annual screening.
- All others with T1D ≥ 5 years could continue to be screened annually.

The DCCT, which took place from 1983 to 1993, found that, for people with T1D, keeping blood glucose levels close to normal greatly reduced the chances of developing eye, kidney, and nerve disease. Its follow-up study, EDIC, began in 1994 to explore how diabetes affects the body over time and the long-term benefits of early and intensive blood glucose control in the development of later diabetes complications.

nih.gov

Celebrating the 25th Anniversary of the NINDS Morris K. Udall Centers of Excellence for Parkinson's Disease Research

Interview with Beth-Anne Sieber, PhD, program director at the National Institute of Neurological Disorders and Stroke (NINDS) at the National Institutes of Health (NIH)

By Tom Adams, Publisher of Federal Health & Medicine.

Parkinson's disease (PD) is a chronic, progressive neurodegenerative disorder that affects the lives of between 500,000 and 1,000,000 Americans. It is the second most common neurodegenerative disease after Alzheimer's disease. Recent evidence cited by the Parkinson's Foundation suggests that PD may affect more people than previously estimated, with nearly 90,000 cases annually. Notably, age is the primary risk factor for PD, which is expected to increase as the U.S. population ages.

The National Institutes of Health (NIH) funded an estimated $263 million in research in FY2022. The National Institute of Neurological Disorders and Stroke (NINDS), part of NIH, is the lead federal institute for PD research funding. One of the key components of PD research supported by NINDS is the Morris K. Udall Centers of Excellence program.

It is my pleasure to speak with NINDS program director Beth-Anne Sieber, PhD, about these centers and recognize the program's 25-year anniversary. Research from the centers has advanced our understanding of PD and helped to improve diagnosis and treatment.

Thank you Dr. Sieber for joining me and sharing your insights on the NINDS Udall Centers and how our readers may benefit from the research and resources that these centers provide.

Former Congressman Morris ("Mo") Udall of Arizona, pictured here in a portrait by artist Ray Kinstler, was diagnosed with Parkinson's disease in 1979. The Morris K. Udall Centers of Excellence in Parkinson's Disease Research, funded by the National Institute of Neurological Disorders and Stroke (NINDS), were established in his honor. Illustration courtesy of the United States Congress

Thank you for this opportunity to highlight the NINDS Udall Centers program as we approach its 25th anniversary: on November 13, 1997, the President of the United States signed the Morris K. Udall Parkinson's Disease Research Act of 1997 into law (P.L. 105-78). This legislation was developed in honor of former Congressman Morris ("Mo") Udall of Arizona, who was elected to the U.S. House of Representatives in 1961. Representative Udall was diagnosed with PD in 1979 and remained active in Congress until his retirement in 1991.

The first NINDS Udall Centers were funded in 1998. The Udall Centers utilize a team-based, interdisciplinary research approach to elucidate the fundamental causes of PD, and, in doing so, contribute to improved diagnosis and treatment of persons with Parkinson's and related neurodegenerative conditions. The scope of research in Udall Centers includes both laboratory research in model systems and clinical research with volunteers. An important point is that Udall Center research is investigator-initiated, which means that the researchers themselves identify and pursue a key question in PD research. These questions, and the Centers, evolve over time as we learn more about PD. For example, Udall Centers have provided information on genetics of Parkinson's, studied the role of the environment, characterized PD-related changes in brain cells and the connections between them, and identified potential therapeutic targets. While the Udall Centers are primarily research-focused and serve as national leaders in PD research, as Centers of Excellence their mission includes developing the next generation of PD researchers and clinicians, as well as providing outreach to the local (and often regional) patient/advocacy community. Active Centers convene annually to discuss the latest research advances and identify areas for collaboration.

James H. Shannon Building (Building One), NIH campus, Bethesda MD
Photo credit Lydia Polimeni, National Institutes of Health

In 2015, the NINDS established a related "Exploratory Grants" program, which convenes new teams and supports two years of research leading directly to a Udall Centers application. This initiative has provided a means for several new research teams to transition to a full Center of Excellence programs, providing a pipeline for new ideas and approaches.

At the NINDS, Udall Centers are one complementary component of larger efforts in PD research under the leadership of NINDS Director Walter J. Koroshetz, MD, including the Parkinson's Disease Biomarkers Program (PDBP) and the Accelerating Medicines Partnership for Parkinson's Disease (AMP PD). Udall Center investigators, past and present, participate in these and other PD research efforts at the NINDS and beyond.

Walter J. Koroshetz, NINDS. Photo courtesy of the National Institutes of Health

What are current research areas of interest at the Centers?

Several of the current NINDS Udall centers are focusing on how specific brain circuits, or connections among brain regions, are changed in PD. Studies include understanding why falls may occur more often in PD, as well as how to prevent them; how cognition or mood might change in PD; and also how deep brain stimulation (DBS) therapy works and might be improved. Another area of emergent interest is the role of inflammation and the immune system in PD: does the immune system play a role in the start and progression of PD and, if so, how might that be countered? Finally, another Center is using mathematical and computer modeling to understand how PD progresses, as well as tracking PD-related clinical changes with novel technologies.

Are there opportunities for researchers to collaborate with Udall Centers?

As national leaders in PD research, an important charge to each Center is to share knowledge and resources with the research community. Udall Center investigators are encouraged to collaborate within and beyond the immediate Udall Centers institutions. Each Center maintains a public website, with contact information for interested researchers, as well as for persons with Parkinson's who would like to learn more about the Udall Centers.

How might persons with Parkinson's learn about and participate in Udall Center research? With regard to the patient/advocacy community having a voice within Udall centers, I think it is great to keep that human connection to the research of the disease, and never losing touch of that by incorporating them into the communication both inside the Udall centers and out within the community.

Thank you for asking that important question. Persons living with Parkinson's, like Representative Udall, are the driving force behind the Udall Centers program. While these are primarily research-focused Centers of Excellence, that research enables and inspires the Centers to make strong connections to the patient/advocacy community. There are a number of ways that the patient and advocacy community can interact with Udall Centers.

One is to volunteer for research studies ongoing at the Center: each of the current Udall Centers supports clinical research specific to that Center. If the Udall Center study is not the best match, there are other studies ongoing at Udall Center institutions in which the investigators also participate.

Another is to follow the activities of Udall Centers, either in-person or virtually. Udall Centers provide periodic outreach to the local patient/advocacy communities, in an informational symposium in which the results of Udall Center research are presented. Udall investigators are pro-active in outreach to local and regional PD support groups, and frequently participate in community events such as walks. For those who may not live close to a Udall Center, virtual meetings may be available.

Finally, each Udall Center is required to include a PwP advocate on its external advisory committee. These advocates provide guidance on Center research progress and direction, and also participate in the annual Udall Centers meeting convened by the NINDS.

Beth-Anne Sieber, NINDS Photo courtesy of the National Institutes of Health

I can speak personally about someone I know that was not aware he had a movement disorder because it was so minor, but when he was seen for a routine checkup by his primary who noticed it and asked, "how long have you had these tremors?" he was referred to a movement disorder specialist just like you described that could immediately begin to address the condition, and his was a case that advanced rapidly so earliest intervention was definitely more helpful than addressing it later after symptoms were far worse. He was very fortunate to have a highly observant primary care professional who was aware to notice it, but with so many different things a patient can have that may not be related to what they are coming in for, it's difficult to spot them all without help or education so they can realize it, especially in this day and age of being overwhelmed from COVID, overworked and understaffed. These are real issues that can affect the opportunity for identification and early intervention.

That is an interesting and not uncommon story — a doctor, a significant other, a friend may notice physical change. Because there is currently no blood, imaging or other test to definitively diagnose PD, diagnosis is primarily reliant on astute clinical observation. Understanding how to reliably detect PD in its earliest stages (optimally, before it starts) and understand and treat the underlying biological changes before the condition progresses is, in a way, the "holy grail" of PD research. Research at Udall Centers, as across the NINDS, NIH, and beyond, is actively addressing this issue.

Are there systems available to our readers in the way of testing or screening for early detection that they can use now, or even things you would like to mention that can help in early detection?

As we discussed, there are no lab tests to diagnose PD, no current means to look into the brain for an absolute diagnosis. Researchers are currently developing promising lab tests that may be able to detect subtle changes in biological fluid, such as blood, or saliva, or cerebrospinal fluid; these tests are being developed for clinical application. Complementary efforts are developing ways to image changes in proteins in the brain itself, to track the start and progression of PD.

Other efforts seek to better understand genetic risk and environmental exposures (like chemicals, air pollution or even personal) that might lead to PD. A recent and significant area of interest is the influence of the microbiome, i.e., the collection of microorganisms (such as bacteria, fungi) in our bodies.

Researchers understanding the combination of clinical symptoms that might be exhibited by someone who could develop Parkinson's. Some of those symptoms include changes in sleep patterns, digestion, changes in voice, decreased sense of smell. A number of innovative technologies are also under development, including in the Udall Centers program, that are seeking to identify and track a constellation of physiological changes that may predict PD. There is a wealth of knowledge to be gained from technology, and what that technology will reveal about the physical changes underlying PD.

Photo courtesy of the National Institutes of Health

Why is the 25th anniversary notable and what does the future hold for the Udall Centers?

For 25 years, the Udall Centers have supported research to better understand PD and improve the lives of persons living with Parkinson's. Advances from the centers have helped make strides toward better diagnosis and new treatment strategies. The centers have also played an essential role in training the next generation of leaders in Parkinson's research. As we recognize the 25th anniversary, we look toward the future as the Udall Centers continue to set the standard for scientific excellence in PD research. For more information about Parkinson's disease and the Udall Centers, visit: Focus on Parkinson's Research at https://www.ninds.nih.gov/

A Decade of Alzheimer's and Related Dementias Research Progress

By Richard J. Hodes, Director of the National Institute on Aging (NIA) at the National Institutes of Health (NIH)

As we mark the 10-year anniversary of the National Plan to Address Alzheimer's Disease, which arose from the National Alzheimer's Project Act (NAPA), it's striking to pause for a moment and consider how far we have come. Thanks to increased congressional funding, NIH spending on Alzheimer's and related dementias research advanced nearly 4.5-fold between fiscal years 2015 and 2020, reaching $2.87 billion. This momentum has enabled NIA-funded science to take significant strides forward.

Some of the many major accomplishments that the NAPA has made possible include:

- Illuminating genetics: Ten years ago, we knew of just 10 genes associated with Alzheimer's disease, and 20 years ago, we knew of only four. Today, researchers have identified more than 70 associated genetic areas, opening multiple new foci for potential prevention and treatments.
- Improving Alzheimer's disease models: It is extraordinarily difficult to mimic the brain's complexity in standard lab models. Improving these models will help us better understand brain-related diseases and test existing and novel drugs as potential therapies. Thanks to NIH research, we now have the "Alzheimer's in a dish" model, the first to contain the amyloid and tau hallmarks of the disease. In recent years, scientists built two additional "disease-in-a-dish" models and have developed more than 50 new mouse models including one that produces a form of the human beta-amyloid protein.
- Expanding biomarkers: Before biomarker tests were developed in the early 2000s, the only sure way to know whether a person had Alzheimer's was via autopsy. Researchers can now use brain imaging methods or lab tests to diagnose people living with the disease. NIA-funded scientists continue to explore novel blood biomarkers for various forms of amyloid, tau, and other promising targets. As one result, NIA small business innovation research funding helped validate and commercialize the PrecivityAD™ test, a more affordable and less invasive alternative to traditional Alzheimer's tests like spinal taps or brain scans. This blood biomarker-based test is now widely available to doctors and researchers across the United States.
- Identifying novel drug targets and therapies: The Accelerating Medicines Partnership® Program for Alzheimer's Disease has aided discovery of more than 550 novel candidate therapeutic targets and is now exploring a precision medicine approach to therapy development. In a parallel effort, the Drug Repurposing for Effective Alzheimer's Medicines (DREAM) study, investigators found that use of certain rheumatoid arthritis drugs is associated with a lower incidence of Alzheimer's and related dementias in people with cardiovascular disease.
- Increasing clinical trials, targets, recruitment, and retention: Today, NIA supports more than 400 clinical trials for Alzheimer's and related dementias, compared to just 38 in 2015. These prevention and intervention trials reflect diverse drug and mechanistic targets, across different stages of disease. To enhance clinical trial diversity, recruitment, and retention, NIA developed the National Strategy for Recruitment and Participation in Alzheimer's and Related Dementias Clinical Research and continues to invest in initiatives like the Alzheimer's and Dementia Outreach, Recruitment, and Engagement repository. To enhance diversity in clinical trials, NIA developed the Clinical Research Operations and Management System (CROMS), which will provide real-time tracking of clinical trial enrollment and retention data. Our institution also launched OutreachPro, which enables researchers to create tailored and tested clinical trial recruitment materials to better reach underrepresented populations.
- Paving the way for prevention: Scientists are learning more about risk factors and potential lifestyle changes that may help prevent dementia. In 2019, a randomized clinical trial showed that intensive high blood pressure control may significantly reduce the buildup of brain white matter lesions and the occurrence of mild cognitive impairment. In addition, a 2020 study found that individuals who made multiple healthy lifestyle choices may have a much lower risk for Alzheimer's.
- Building research infrastructure: Targeted strategic investments are helping to expand the research infrastructure for Alzheimer's and related dementias including the Alzheimer's Clinical Trials Consortium, the NIA Impact Collaboratory, and the NIH Intramural Center for Alzheimer's and Related Dementias (CARD), which launched in 2020. These initiatives will expand studies for therapies, enhance recruitment of underrepresented participants, spur innovation around complex care management, and boost basic, translational, and clinical research.

As we take stock of this remarkable decade of discovery, we are inspired by the scientists, clinical trial participants, caregivers, and many other stakeholders whose hard work and dedication are helping to tackle this devastating disease. We hope you will join us as we continue moving forward! To kick things off, we invite you to watch our video series featuring stories of progress from the field at: https://www.youtube.com/playlist?list=PLmk21KJuZUM5en04l9gF08T74EMmFSkY5

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Some Arthritis Drugs May Reduce Alzheimer's and Related Dementias Risk in those with Heart Disease

New findings from the ongoing Drug Repurposing for Effective Alzheimer's Medicines (DREAM) study suggest that certain rheumatoid arthritis drugs may lower incidence of Alzheimer's disease and related dementias in people with cardiovascular disease. While the findings do not support broad use of these drugs for treating Alzheimer's and related dementias, the results may point to a promising precision-medicine approach in specific groups of people at risk for developing these diseases. The research was published in JAMA Network Open and led by scientists at the National Institutes of Health's National Institute on Aging in collaboration with researchers at Harvard Medical School, Boston; Rutgers University, New Brunswick, New Jersey; and Johns Hopkins University School of Medicine, Baltimore.

Discovering new drug targets in Alzheimer's and related dementias is crucial for meeting the enormous public health challenge of these diseases. Prior studies on whether approved rheumatoid arthritis drugs lower the risk of developing dementia have produced mixed results. In this study, researchers analyzed data in Medicare claims from more than 22,000 people, looking at whether those with rheumatoid arthritis who took one of three different classes of arthritis drugs were protected from dementia. There were no statistically significant associations with lowered dementia risk except among those with cardiovascular disease who were treated with one class of arthritis drugs called TNF inhibitors. These inhibitors suppress the immune system by blocking the activity of TNF, which is a substance in the body that can cause inflammation and lead to immune-system diseases, including rheumatoid arthritis.

The NIA DREAM study previously identified several U.S. Food and Drug Administration-approved drugs that are being tested as candidate treatments for Alzheimer's and related dementias.

Who

NIA experts are available for interviews to discuss specific findings of this paper and/or the broad view of the state of Alzheimer's and related dementias research. NIA is the lead U.S. federal agency for research on these diseases. NIA scientists and funded research teams are exploring drugs aimed at multiple different disease pathways, considering combinations of treatments, and working to repurpose existing drugs to treat Alzheimer's and related dementias.

Photo courtesy of NIH: zhanglianxun/Shutterstock

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Broader Perspectives:

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The research was funded in part by the NIA Intramural Research Program project 1ZIAAG000436-01.

NIA leads NIH's systematic planning, development, and implementation of research milestones to achieve the goal of effectively treating and preventing Alzheimer's and related dementias. These activities relate to NIA's AD+ADRD Milestone 7.B, "Initiate research programs for translational bioinformatics and network pharmacology to support rational drug repositioning and combination therapy from discovery through clinical development."

Reference

Desai R, et al. Comparative Risk of Alzheimer Disease and Related Dementia Among Medicare Beneficiaries With Rheumatoid Arthritis Treated With Targeted Diseases-Modifying Antirheumatic Agents. JAMA Open. doi:10.1001/jamanetworkopen.2022.6567

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Study Suggests Epstein-Barr Virus May Cause Multiple Sclerosis

By Brian Doctrow, PhD

Multiple sclerosis (MS) is an autoimmune disease that affects the central nervous system. In people with MS, the body's immune system attacks the insulating layer that surrounds nerve cells, often killing the cells.

The underlying cause of MS remains unknown. One possibility is that it's triggered by a viral infection. Epstein-Barr virus (EBV) has been among the top suspects. EBV is a herpes virus that often causes no symptoms. However, it can cause infectious mononucleosis, or mono, in some people. After an EBV infection, the virus remains in a latent state within cells and, in some cases, may reactivate. EBV eventually infects about 95% of adults, but very few will develop MS.

To explore whether there is a link between MS and EBV, a team of researchers studied more than 10 million active duty US military personnel between 1993 and 2013. Dr. Alberto Ascherio from the Harvard T.H. Chan School of Public Health led the study. NIH's National Institute of Neurological Disorders and Stroke (NINDS) partly supported the work. The results appeared in Science on January 13, 2022.

Active-duty soldiers have blood samples taken every two years as part of routine medical screenings. The Department of Defense Serum Repository contains serum left over from these screenings. From these samples, the researchers determined whether — and when — donors were infected with EBV. They tested samples from 801 people who developed MS. They then compared these to samples from more than 1,500 matched controls (people with similar characteristics who did not develop MS).

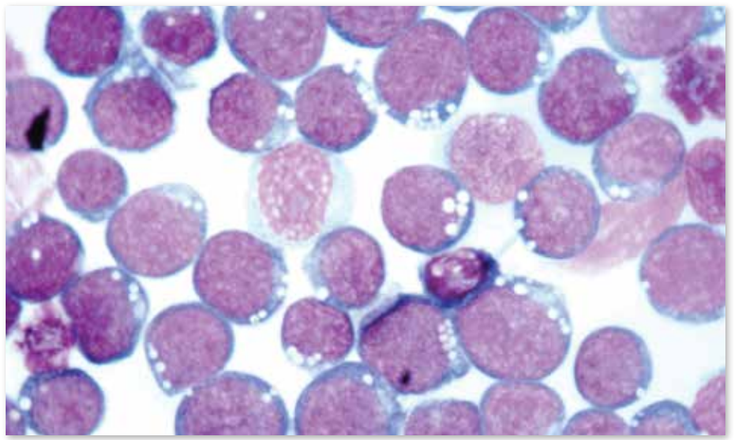
The team found a much higher rate of EBV infection among people who developed MS than among controls. Out of the 801 MS cases, only one person tested negative for EBV in their last sample collected before MS onset. The team calculated that people infected with EBV were 32 times as likely to develop MS as uninfected people.

The researchers found no such association between MS and any other human viruses. This included cytomegalovirus, a virus distantly related to EBV that is transmitted similarly.

The team also measured blood levels of neurofilament light chain (NfL), a biomarker for nerve degeneration. NfL levels increased in people who developed MS compared to those who did not. The increase occurred only after EBV infection and usually before MS diagnosis. This finding shows that the nerve degeneration that accompanied MS did not start before infection with EBV.

The researchers say that the association between EBV and MS risk was too strong to be explained by any other known MS risk factors. The findings strongly suggest that EBV is part of the chain of events that leads to most cases of MS. However, EBV in itself is not sufficient to trigger MS. Other unknown factors certainly play a role.

"The hypothesis that EBV causes MS has been investigated by our group and others for several years, but this is the first study providing compelling evidence of causality," Ascherio says. "This is a big step because it suggests that most MS cases could be prevented by stopping EBV infection."



Epstein-Barr Virus (EBV) Stained with Hematoxylin and eosin (HE), is of the Epstein-Barr virus (EBV). Photo courtesy of the National Cancer Institute

nih.gov

Celebrating 30 Years of the CDC's National Breast and Cervical Cancer Early Detection Program

Exclusive interview with Captain Jacqueline Miller, MD, FACS

By Tom Adams, Publisher of Federal Health & Medicine

The success rate of curing cancer is greater today than ever, mostly because of screening that allows clinicians the advantage of early intervention. Great strides have been made particularly with breast and cervical cancer, and leading the way for the past 30 years has been one of our nation's greatest programs that addresses early intervention for all women that removes barriers such as insurance or an ability to pay for care. It is my great pleasure to speak with the leader of the CDC's National Breast and Cervical Cancer Early Detection Program, Captain Jacqueline Miller, MD, FACS, in recognizing this live saving program and continuing to promote it to the family of caregivers that are essential to it's success.

Thank you Captain Miller for joining me today and thank you for your leadership of such a wonderful program we are proud to be honoring with your interview today. Please share with us how our public health and tribal care readers can utilize your program to the advantage of their patients.

One of the biggest things about our program is that it is not always known and utilized, almost like the best kept secret where people just don't always know it's there. So the big thing is making sure that your readers are aware that the National Breast and Cervical Cancer Early Detection Program is actually in every state across the entire country. Each program is run through the state public health department. If they look on their state health department website, every program is listed there so they can get a direct contact to the program to help determine how they can actually get services.

The focus of the program is to provide screenings to individuals who are low income, in general it's under 250% of the federal poverty level but that can vary from state to state, and for individuals who don't have insurance. Now there are individuals that we call underinsured, meaning they may be able to get the screening test covered, but if they need some follow up tests done, their follow up tests might not be completely covered and if they are low income they may not be able to afford the cost for those additional tests. So that also is an avenue for the individuals to be able to get those tests done with assistance through the National Breast and Cervical Cancer Early Detection Program within their state.

We do fund screening services for people of recommended

Captain Jacqueline Miller, MD, FACS. Photo courtesy of the CDC

screening ages, but we also provide services for people that are outside of the screening ages when they are high risk or what we call symptomatic, for instance if you have a breast lump but you are 35 and younger than the screening age, you can still get taken care of through our program. So we want people to know that the program is there to help, the whole idea is that we want to be able to provide services to find cancers early when they are most treatable, before they become advanced stage, and this can help save lives. This program focuses on people who are medically underserved and might not otherwise be able to get the services they need. So we really want people to understand that about our program.

Another important thing is, we do fund 13 tribal organizations; that specifically focus on the tribal members within their locations. We really are trying to be culturally sensitive and look at whatever we need to consider, geographical location for example, because there are other things besides income that may factor into who can be at increased risk for not having access to care.

A 3D rendering of human papillomavirus. Image credit Donny Bliss, Office of Communications and Public Liaison. Courtesy of the National Library of Medicine

In addition to providing the screening we do provide additional services such as patient navigation. Because we understand there are other barriers that can interfere. Even simple things like childcare can be a problem. Transportation as well, so within our program we can help with that so individuals can get to an appointment, and we can also help them find an appointment. We not only pay for the clinical services to get done but also help people to get access to those services. And finding an appointment that is convenient for you, in your own community can be an issue.

Sometimes people are faced with not having a lot of money for gas and it can be very difficult for them to drive a long distance, they can't really afford to do that. So we can give them gas cards to help when needed.

There's a lot of ways that we have to look at what are barriers where we need to assist, so that it doesn't become an impediment for someone to get the service they need, screening or follow up. If you get screened, it's almost useless if you are not able to get a follow up if you have abnormal results. So we need to make sure that individuals who get screening are also able to get any follow up they need.

Another great thing about this program is that it has a direct connection with the Medicaid program, so individuals who are diagnosed with cancer through the program can be treated. There is a Medicaid waiver program that is available due to a law that Congress passed which allows those individuals to get all their cancer treatments covered through the Medicaid insurance program without them having to pay for any of the treatments themselves. So the nice thing is having that connection, we can help you get to the diagnosis to see if you do or do not have cancer, and if you do then we have a way to refer you to another program where you can get your cancer treatment done.

It's no good to go through all the testing to get diagnosed with cancer if you will not get the treatment for it. So the nice thing is that we take you of you from beginning to the end, you can come in and get your screening test, we can cover any additional testing that you need, and send you to treatment services if you are diagnosed with cancer. That's the biggest thing about our program, and we want to try and find these cancers early.

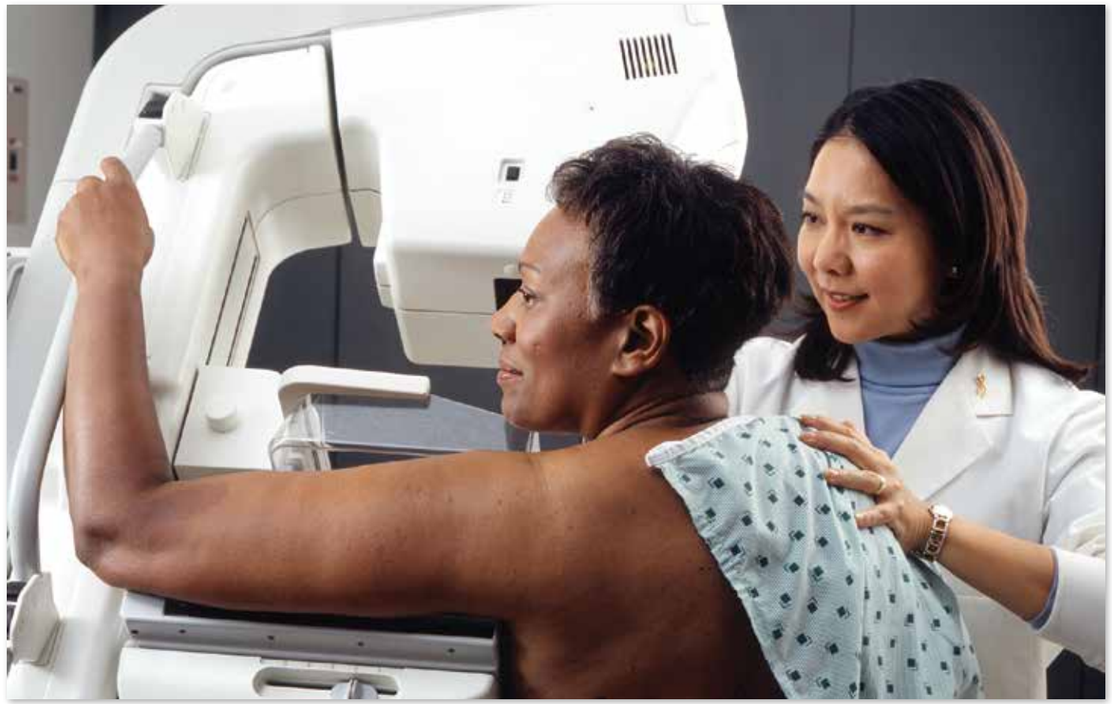
Cervical cancer screening is really prevention because you can find these early changes that are not quite cancer yet, and you can really prevent someone from developing cervical cancer. When we look at the data right now, 60% of those with cervical cancer have never been screened before. So just think, if we can prevent that many people from getting cancer just by providing the screening and potentially finding these early pre-cancerous changes, then we can save lives.

And then when we look at breast cancer, while we can't necessarily prevent it, it makes a huge difference if we can diagnose it early. So if we can diagnose you at a stage 0 or a stage 1, your life expectancy over the next 5 years is anywhere from about 98-100% in general versus when you might go down to a 30% with a stage 4 or something.
Cancer treatments are not benign; cancer treatments can lead to further complications long term. But when we can find the cancer early, you need less treatment. So finding cancer early makes

CDC supports screening for breast, cervical, colorectal (colon), and lung cancers as recommended by the U.S. Preventive Services Task Force (USPSTF). The USPSTF recommends screening for cervical cancer every 3 years with cervical cytology alone in women aged 21 to 29 years. For women aged 30 to 65 years, the USPSTF recommends screening every 3 years with cervical cytology alone, every 5 years with high-risk human papillomavirus (hrHPV) testing alone, or every 5 years with hrHPV testing in combination with cytology (cotesting). Photo credit RossHelen, Getty Images/iStockphoto. Courtesy of the National Cancer Institute

a huge difference not only for living, or not dying from the cancer, but also having less invasive treatment and having less long-term complications related to the treatment.

There are two very important reasons to get the word out, which we are certainly pleased to help do. And I can only imagine the technology advances over the past 30 years that absolutely make this program more effective. Can you tell us more about how public health departments connect people within their own communities for this? Do they provide screening directly as well as working with partnerships?



An Asian female technician positions an African-American woman at an imaging machine to receive a mammogram. Photo credit Rhoda Baer. Courtesy of the National Cancer Institute

Yes, this can vary from program to program, but the public health departments that we fund contract with local doctors and clinics in their state. Some of them will have you call the state health department where they will enroll you and direct you to a local provider's office. While others have enrollment done through their provider's offices. So if a person goes to a clinic to get services done, and the provider says that breast and cervical cancer screening is needed, if they don't have insurance they can enroll you in the program at that time so the program will cover the cost.

Then some states have regional offices, because some states are broken up into health regions, where you might get referred to the health office in your region and depending on how they have it set up they either will refer to someone or make your appointment directly. All of the services are done through regular doctor's offices in the community, so it's not a special clinic you have to go to. The program will connect you with the right health care provider in your area, or vise versa. The health care provider may refer you to your local health department to get you enrolled into the program.

People will quite often come in for something else, like if they have a migraine headache, and the doctor may realize that they need to have these screenings because they haven't had them done or it's been a long time since they were done. So this is an opportunity for the connection to the program to happen. There has to be a verification that you meet the eligibility requirement, so if someone wants to find out information, the easiest way is to go online to find a number to their health department breast and cervical cancer screening program which will give them information on what to do and how to connect.

There's lots of different work within their community. Some work with community organizations to give people vouchers to go in and get screened, for example they will give them a voucher to get a mammogram and tell them to go to a certain facility with this voucher and it will be taken care of. Some work with organizations that will refer people to the program. We try to reach people in many different ways, because there's no one right way to reach everybody. We try to figure out how to meet individuals where they are.

I love the connection with the community providers that public health has. That really keeps information about resources available to everyone in need, regardless of where they are as you said and builds a tremendous alliance between them. Particularly over the past two years as the pandemic brought the need for closer alliance for combating the spread of COVID. In fact I read where during that time it really became an issue for lots of people to be able to come in and get screenings or even routine checkups because of the challenges presented by lockdown restrictions, but I thought I saw where mobile clinics were introduced into your program to go out into the community and rural areas to bring screenings to the people. Can you tell me more about those?

We have some mobile clinics routinely, so there are several programs that use them like tribal clinics where people live in very remote areas. So mobile units are something that clinics may have out there and we will contract with those clinics to also cover services that are done through them for breast and cervical cancer screening and diagnostic services. Whenever there are mobile clinics in areas, as long as it can work and function, then anyone receiving those services in connection with our program will be covered. The only problem was that mobile clinics weren't really any different from other clinics as far as the number of patients coming in. Everyone was affected by COVID. People had to be spread out so screenings could not always done back-to-back. There had to be more in depth cleaning, staff had to practice infection control so everything took a hit. Mobile clinic staffs that were doing breast and cervical cancer screenings were being used to help focus on COVID. A lot of the work that went for routine care went on the back burner and the care that was being provided was COVID care, especially in 2020 and some of 2021 before routine care restarted. So our services had to be toned down because the whole country shut down basically when any services going on was either COVID care or life threatening emergencies. Because we don't operate separate clinics and work with the healthcare system that is in the community, if a community clinic isn't screening we can't pay for a screening. We don't have separate health care clinics from what's available throughout the community because we rely on the healthcare that's being provided in the community to provide our services.

There were numerous reports during and after that time showing people were not getting regular exams and screening and it unfortunately resulting in a rise of cancers that possibly could have been prevented if early detection was available. I'm glad to see much of the resources and funding now being redirected back to their intended use like early detections, where it is so very important for all of the reasons you mentioned.

I would like to say that with the recovery from COVID, it's not really just getting back to baseline but we really have to make up what was missed. We need to get a little bit above baseline because of all the people who have had to delay their care and screenings during the pandemic, so we really need to get them back in along with the people who are coming up to their time for their re-screening. There are two categories of people, those who it is time for them to be screened, and then the people who are overdue because their screening was delayed. So we really need to get those people back in and make sure that anyone who was delayed gets in and gets their screening services.

I certainly respect that you care about all people and want to make sure none are left behind when it comes to early detection. Again, what a wonderful program that addresses the needs of all Americans at every level from early screening detection and then follow through with care. Can you tell me a little bit about your background and what led you into serving and now in leadership role?

My background is general surgery. I was in private practice, and that was back in the days before we had all this specialty surgery services. So I really ended up doing a lot of breast cancer work, because I was one of the few female surgeons in my area at the time. And so, when primary care doctors referred patients to our practice, basically all of the women were sent to me. This was mostly because women felt more comfortable talking with another woman about their issues. So it kind of developed into where I was doing a lot of work with breast cancer patients. I got introduced to public health when we noticed that we had a lot of young people coming in with cancer who either had family history or some other symptoms that were never addressed. So we kept saying, why are we now seeing this at such a late stage that could have been addressed much earlier? Even just staying healthy, there are so many things like a family history, a strong family history of breast cancer or colorectal cancer but nobody is talking to the family saying you are at a high risk until they are coming in with cancer. And so I kept saying, we are missing something here in the community. We need to do something to keep people from getting to this level. We can save more lives and do a better job if we work on the prevention as much as possible.

A radiologist studies 2-D and 3-D digital mammography for finding breast cancers. Photo credit Frans Rombout, Getty Images/iStockphoto. Courtesy of the National Institutes of Health

We started working with people in the community, like local churches, and doing things on our own just trying to get people to focus on their own health and get care. When I was talking with friends they mentioned this program, which I didn't even know existed. So when I heard that the CDC was doing this work I wanted to find out more. I eventually came to CDC through one of their training programs, and with time

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Mobile Mammography reaches the community with partnerships from organizations including the Stony Brook University Cancer Center and support from New York State Department of Health.
Photo courtesy of New York State and Senator Mario R. Mattera

and people knowing my history and personal interest in cancer prevention, I almost fell into the program like it was destined for me. I felt like where I can take care of 15 people in the office in one day, I can help take care of hundreds of people in a day working with this program.

So that interest is how I ended up working with this program. It has a larger reach to address lots of issues, provide communication, and making sure people understand what they need and what is available. All those things make a difference. You can't just say it's here and hope people find it. There's more to it and we have to look at what people need and we have to look at the reality in how people live and how our healthcare system functions. If we don't take that into consideration, we can say all day long what people should be getting done. We have to look at the realities in the real world setting to make sure people can get what they need. That's where clinical care and public health must intersect which is what I have been focusing on. Without that intersection, it's not going to benefit people.

I have to say too that providers also need help. There's a lot on their plate when a patient comes in. People have a lot of body systems that need attention, so just simple things like having that help list with checking the records to make sure that all the screenings are up to date and providing information on what's missing so they can address that with their patient. A provider can't discuss every health in that typical 20-minute visit. So providing that assistance can help. Sometimes even when education needs to happen when a patient comes in about why they need to go get a mammogram or Pap test, this can be done by the nurses or other health affiliates to help.

So that's why it needs to be a team that works together, not just one person responsible for making sure everything gets done. That's just not an efficient way of working.

This program is certainly a great example of teamwork, and I'm glad to see it's stronger than ever and able to help more people now then it's probably ever been able to before, with a potential for getting bigger and better all the time because it works. So we are pleased to not only recognize it, but also the entire team of people involved that make it successful and promote it as much as possible to our subscribers throughout all U.S. public and tribal health facilities. How do people know what screening test to ask for?

It's not really a matter of what's asked for, but what are the recommended screenings that a person should get. When it comes to breast cancer, the recommendation is a mammogram. For those who are high risk for breast cancer like having a strong family history, then the recommendation is that they have a mammogram and breast MRI each year. We provide the test that is recommended by the national bodies like the U.S. Preventive Services Task Force. For cervical cancer screenings there are three different test options that depends on age including a Pap test alone, a Pap test with an HPV test, or an HPV test alone.

When it comes to options between different tests, that decision would come from the provider talking with the patient. Some clinics also have their own policies. We will reimburse whatever appropriate test is ordered by the provider based on the recommendations. We also cover the different types of tests that are available as technology advances. Years ago it was just a regular film mammography, then we added digital mammography, and now we also cover 3D mammography. What we like to really emphasize is that our focus is to reach as many women as possible, and to make sure that everyone is able to get the right screening at the right time.

Jacqueline Miller, MD, FACS, is a board-certified general surgeon and a Captain with the U.S. Public Health Service. She did her undergraduate education at Spelman College in Atlanta, Georgia, and earned her medical degree from Washington University School of Medicine in St. Louis, Missouri. She then completed an internship and residency in general surgery at the University of Mississippi Medical Center in Jackson, Mississippi. After completing her training, she practiced general surgery for eight years in Atlanta with a special interest in breast cancer. She later joined the Centers for Disease Control and Prevention as an Epidemic Intelligence Service Officer in the Division of Adult and Community Health.

Currently, she is the Medical Director for CDC's National Breast and Cervical Cancer Early Detection Program in the Division of Cancer Prevention and Control. She has authored or co-authored more than 90 publications and mentors fellows training in epidemiology. She still provides clinical care in an outpatient clinic setting.

For more information please visit:

National Breast and Cervical Cancer Early Detection Program | CDC
https://www.cdc.gov/cancer/nbccedp/

Cancer Screening Tests | CDC
https://www.cdc.gov/cancer/dcpc/prevention/screening.htm

Find a Screening Program Near You | NBCCEDP | CDC
https://www.cdc.gov/cancer/nbccedp/screenings.htm

Increasing the Proportion of Adults Who Get Screened for Lung Cancer

Healthy People 2030 Objective

Lung cancer screening can help prevent deaths from lung cancer in people at high risk — mostly current and former smokers. But screening rates in this population remain very low. Increasing knowledge about screening recommendations — among both health care providers and people at risk for lung cancer — can help prevent deaths. Increasing knowledge about tobacco initiation and cessation can also help prevent lung cancer deaths.

Lung cancer is the leading cause of cancer death in both men and in women in the United States and is the third most common type of non-skin cancer. The only recommended screening test for lung cancer is low-dose computed tomography (also called a low-dose CT scan, or LDCT).

U.S. Preventive Services Task Force (USPSTF) recommends yearly lung cancer screening with LDCT for people who:

- Have a 20 pack-year or more smoking history, and
- Smoke now or have quit within the past 15 years, and
- Are between 50 and 80 years old.

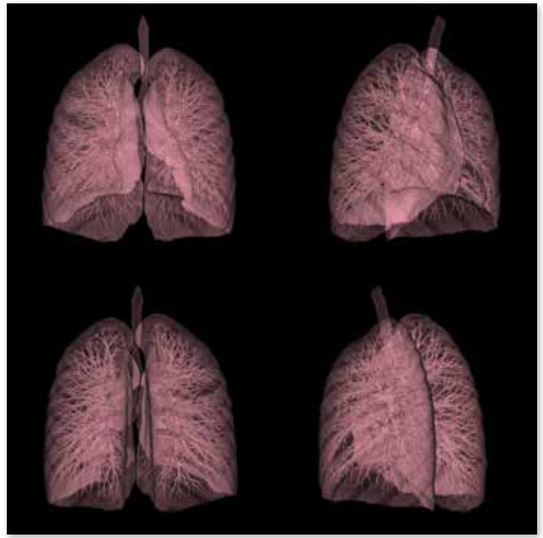


Image courtesy of the National Institutes of Health

A pack-year is smoking an average of one pack of cigarettes per day for one year. For example, a person could have a 20 pack-year history by smoking one pack a day for 20 years or two packs a day for 10 years.

Radiation from repeated LDCT tests can cause cancer in otherwise healthy people, which is why lung cancer screening is recommended only for adults who are at high risk for developing the disease because of their smoking history and age, and who do not have a health problem that substantially limits their life expectancy or their ability or willingness to have lung surgery, if needed.

Screening with LDCT scans has been shown to decrease the risk of dying from lung cancer in heavy smokers.

The National Lung Screening Trial studied people aged 55 years to 74 years who had smoked at least 1 pack of cigarettes per day for 30 years or more. Participants were either current smokers or former smokers who had quit within the last 15 years. The trial used chest x-rays or LDCT scans to check for signs of lung cancer.

Screening with LDCT once a year for three years was better than chest x-rays at finding early-stage lung cancer and decreased the risk of dying from lung cancer in current and former heavy smokers.

Current smokers whose LDCT scan result shows possible signs of cancer may be more likely to quit smoking.

The Task Force recommends that yearly lung cancer screening stop when the person being screened:

- Turns 81 years old, or
- Has not smoked in 15 or more years, or
- Develops a health problem that makes him or her unwilling or unable to have surgery if lung cancer is found.

cdc.gov

CPG

Celebrating the 30th Anniversary of the National Program of Cancer Registries

Exclusive interview with Vicki Benard, PhD, Chief of the Cancer Surveillance Branch

By Tom Adams, Publisher of Federal Health & Medicine

Understanding the complexity of cancer has been a top priority for the medical community of our nation for more than thirty years. CDC's National Program of Cancer Registries collects high-quality data on cancer occurrence, initial treatment, and outcomes. Tremendous advances have come from it with prevention care and cure.

Almost every one of us knows someone in our life that did not survive their battle with cancer, which was the overwhelming prevalence in decades past. However this wonderful program has helped change that outcome by bringing real answers to the questions, and misunderstandings about cancer.

It is an honor for us to recognize this program's history and 30th anniversary, as well it's leader Vicki Benard, PhD, Chief of the Cancer Surveillance Branch who has devoted her full effort to helping bring forth these life saving changes. Thank you for joining me today and for this interview and sharing information that our readers may benefit from knowing more about this program.

Thank you for helping us present the work we are doing. It all began back in graduate school for me. I was a research assistant and worked with the Charleston Heart Study cohort, which started back in the 1960s and followed for decades to look at risk factors for heart disease. I was able to do my dissertation work at the Medical University of South Carolina surrounded by large hospitals. I was able to go into the hospital and show my badge and get medical records, make copies of death certificates, and get any information that was relevant to my study, and then I was able to contact the cohort or their family members if they were deceased and conduct the study. It was just so interesting to me how to make these connections between the disease and potential risk factors.

When I first came to CDC, I worked with the National Breast and Cervical Cancer program and was able to do site visits with the program's affiliates to understand the program and learn as much as I could. I spent most of my years working with cervical cancer and understanding why women continue to get this disease that's largely preventable. It was a great opportunity for me to get to know the program, get to know the division, and then almost six years ago I was given the opportunity to move into a leadership role with the cancer surveillance branch.

This has been a huge learning curve for me to understand the really complex dynamics of the surveillance system. I was a big user of the cancer data in my work, but I just thought the data magically appeared where now I have such an appreciation of all that's involved to ensure that we get complete high quality and timely cancer data and really the importance of being able to measure this over time.

It's incredible how you've been able to collect that data over 30 years, because the technology was not the same then as it is now. But the spirit of those involved in this hasn't changed and now tremendous technology advances can be used to understand more about this disease than every before. Even as someone on the outside, I can see amazing advances when it comes to survivorship of cancer. When I was a child, my father passed away from cancer, but back then there was hardly any way of knowing he was at risk for the type of cancer he had and there wasn't even MRI technology available to see exactly where the cancer was and what areas it was affecting. I was amazed that technicians could even see cancer in an X-ray to identify it, but just look at the quality of tools and education we have available today. I'm sure you would agree it is just as amazing as it is useful.

Vicki Benard, PhD, Chief of the Cancer Surveillance Branch. Photo courtesy of the CDC

Yes, and with the national data we are able to do so much more. We are able to measure and look at opportunities to make a difference in cancer control.

Graphic courtesy of the CDC

How has HIPPA and other medical data restrictions affected this surveillance, and is there anything our readers could benefit from knowing about reporting so they can contribute as much as possible to NPCR and help it's cause?

The interesting thing about cancer is that, it is mandated by law to be reported. When you use the word surveillance system, many may not fully understand what that means. So, if you take it all the way back to when a person first hears the diagnosis that they have cancer, as you know that changes your life forever. But each of these cancer data points represents a person with a unique story. With this national coverage of cancer data, through our National Cancer Registries Program, we can identify ways to prevent and treat cancer.

All healthcare providers and facilities like hospitals are required to report cancer cases to their state's central registry. So they don't have to deal with HIPPA laws. These registries receive this information from multiple sources, because for one case of cancer you may get a report from a pathologist, or from a doctor's office, or from a radiologist, but all of that is consolidated into one cancer case. Then the final data report is sent to the CDC to disseminate into national reports to be shared with you and other audiences. Many people are not aware that reporting of cancer is mandatory by law, which is similar to measles or hepatitis, so that's been the key factor of why we can collect all of this data because that law went into effect 30 years ago.

And I think it's interesting about how this law came about, because before NPCR was established we had 10 states that did not have a registry, and most of the registries really lacked the resources and legislative support to get complete data as we talked about, when they came up with these laws. And at that time, Vermont had one of the highest death rates for breast cancer in the country, but they were also one of those 10 states that did not have a cancer registry program. There was no way to tell, how many women in Vermont were diagnosed with breast cancer that year, where the breast cancers were at, and how to go in and intervene.

In 1992, the Cancer Registries Amendment Act (Public Law 102-15), was the first bill proposed by now Senator Bernie Sanders to become law. And this ensured that basic data on cancer like incidence, stage, treatment, survival, is all collected consistently in every state. I think this was a huge turning point for cancer surveillance and why we are able to support 50 different cancer registries today.

I think it's great to recognize this teamwork and acknowledge how it has made so much of a difference in every aspect of the disease for advancement. How does your agency work together with other cancer agencies like the National Cancer Institute for example?

Our lens through the CDC's NPCR is really about national data, and it's about having every state have a registry. For the National Cancer Institute's SEER program (Surveillance, Epidemiology, and End Results), their lens is more on research. NPCR supports 50 central registries in 46 states, the District of Columbia, and 3 territories. When we combine our data with the SEER program that

creates the official United States cancer statistics. This provides data on all new cancer cases and deaths for the entire U.S. population. So we work together, we collect all this data so that the entire nation is represented.

I see where this complete understanding helps NCI to know where to focus it's research, what types of cancer and who is most at risk, to determine the best use of it's resources could not happen without this data collection. Even going back to breast and cervical cancer and understanding the benefits of early detection are keys to the success of programs like the CDC's National Breast and Cervical Cancer Early Detection Program, that are so much more effective from having this knowledge. In addition to the federal law to report cancers, is there any additional funding to encourage it or bring more awareness to it?

Yes, we provide funds to all of our cancer registries and our funds support infrastructure. Without our funds the states would not be able to have a cancer registry. We provide funds so that they have the systems in place and the laws in place so they can collect the data, which comes to us.

This support obviously encourages the collaboration you mentioned between all areas of medicine, not just oncology professionals but other specialties and even primary care practitioners, but would you say there's a certain area you focus on the most?

What we've seen is that patients used to be diagnosed strictly in hospitals, but now we're seeing that people are often diagnosed within a doctor's office. I think it's around 95% of cancers that are diagnosed with a biopsy and pathology report. That is why we so we're working with laboratories to try and get that data in much earlier. It takes a lot of time to get this data to CDC. That's why we've been focusing on how we can improve the timeliness of the data collected.

Each year the registry collects data for approximately 2 million new cancer cases, and each case has about 200 data elements collected to help provide all of the information related to the case. We are getting data from the path lab, oncologists, the doctor, vital statistics, so there's a lot of information that comes from the medical records that a Certified Tumor Registrar will pull in order to get a complete case.

Graphic ourtesy of SEER.cancer.gov

It currently takes between 24 to 36 months for all this data on new cancer diagnosis to be fully processed and then submitted for national publication to CDC and then released to the public. This timeframe is really too long, and the reason for that is because data collection still relies on very manual tasks. As you've said, we've been around for 30 years and some of the systems are 30 years old. Over the years we've definitely been improving on how we get data in and relying on electronic submission, but we still have systems that are old and need more efficiency. Our goal over the last 5 years has been to help cancer registries get real-time data faster. This means decreasing the time of providing national data so that we can publish 12 months data. And this is very much in line with the CDC's data modernization initiative, where we're developing a cloud-based computing platform, to leverage all the electronic reporting from laboratories and health records, and make the data more timely to help improve faster reporting of cancer incidents and help us make informed decisions about where resources need to be allocated.

There are so many different types of cancers, and it's not always clear to know exactly what factors put people at risk for different types of cancer. Do you feel this data helps identify more risk factors?

Yes, and we've actually been able to create a data visualization tool (www.cdc.gov/cancer/dataviz) that lets you go in and identify cancers by site and risk factors. And the biggest thing for us, especially at CDC is cancers that are largely preventable, and cancers that have screening. So we can go in and look to see where are the cancers that have increased incidence, and then where are those states and counties where the screening rates are low. This allows us to intervene for those cancers that do have a screening program in place.

That's definitely an advancement, early intervention for areas like lung cancer, which used to have a very low chance of survival, which now has improved dramatically. Has this or any other type of cancer improved the most as a result of your program?

Actually, if you go on our website we have a map that you can hit play, and it starts in 1990 and you can see, if for instance you pull up lung cancer, you can watch the entire United States go from a very dark color where lung cancers were very high, to where it goes down over time and you can watch the decrease that's primarily from our efforts to reduce tobacco use. We can see how that risk factor of tobacco use has gone down and so have lung cancer rates with it.

That leads to me to ask about advances in specific treatments for different types of cancers within different individuals, precision oncology as it's called. Has this data collection been an important tool for the development of precision treatment as well?

Absolutely, because we can measure where, if we know the literature is saying that we've seen this then we can go in and look at our data to determine if we've seen decreases overall, where we've seen those decreases, like are we seeing decreases across different age ranges, different races, and regions. So yes, we can use our data to really pinpoint where we are seeing the trend.

This is what I believe the Moonshot initiative is using to accelerate scientific discovery in cancer, foster greater collaboration, and improve the sharing of cancer data to reduce the cancer death rate by half within 25 years and improve the lives of people with cancer and cancer survivors. What has that initiative done for NPCR, or what has NPCR done for it?

To be able to say, we want to decrease cancer by this percent in this year has given us all a goal to work together across the cancer surveillance community. Where NCI is working more in research, we're working more in making sure our states have the capacity and funds to be able to collect high quality and timely cancer data. I think what the Moonshot Initiative has done is help us work better together so that we're all using our resources and our skills and talents to be able to help with a goal of no person getting cancer, and reduce the amount of deaths from cancer.

How did the pandemic affect NPCR?

It definitely affected us because, CDC as a whole was in the spotlight. We had to get that COVID data in faster, and figure it out because people wanted to know how many deaths we were seeing, and what was the rate of COVID everyday. And so, through those mechanisms they were able to get reporting directly to the health department and directly to CDC. We are able to use all of those tools now to be able to get cancer data from the hospitals to the central registries and to the CDC faster. Even though COVID was horrible we've been able to use the good parts of that in getting data in faster.

A lot of our readers are in smaller facilities and serve rural health areas. Is there anything you would want to say about your program that could be helpful for them to know, or helpful for them to be able to contribute more data for NPCR?

I think that the NCI's SEER program has been around since the 1970s, and a lot of people think of that when it comes to cancer registries. So, over the last 30 years, we've really tried to make it known that the National Program of Cancer Registries is the organization that is collecting this data, especially from smaller doctor's offices and smaller clinics.

Some of these clinics had to send a PDF or an Excel file of their cancer statistics because they didn't have the tools to be able to send them any other way. Our role in NPCR has been in getting the software to these smaller doctor's offices, so that they can report easier to the state registry As well as provide many online training opportunities to assist the less experienced abstractor that might typically be a in smaller facilities with high turnover.

We've also been working on building the infrastructure to collect childhood cancers more timely, and that is directly with the laboratories with the emphasis on the smaller hospitals and offices to be able to get that data in a much more timely fashion. So we've created a tool that allows labs to directly report to the central registry.

Can you tell me about what you would like to see in the future of NPCR or what advancements you would like to see the program move towards?

I think the future really is all about data modernization, and how we can make these systems more effective to get the data in quicker, so we can make real-time decisions with real-time data. So really it's using cancer data to drive action now, and it's only with this national data with all of the cancer cases reported that we can measure progress and then target our actions.

Something else we are continuing to work on is addressing equity among health services. Cancer registries are making data available for cancer prevention and control planners to be actionable, especially around health equity. And definitely with our American Indian and Alaskan Native population. The registry data relies heavily on the medical narrative, so whatever the doctor writes as far as race or ethnicity is what's recorded, and we saw that there was a lot of race misclassification, which was a main barrier in collecting the information about American Indian and Alaskan Natives.

In 2008 or 2009 we began to link all of our data directly to the Indian Health Service enrollment data. So this helped to ensure that the data of American Indian and Alaskan Natives are accurate, rather than relying on self reports. This has really improved the accuracy, and we are able to use this analysis that is restricted to areas with healthcare services that are provided directly from the Indian Health Services.

One of our epidemiologists that is part of our branch lives in New Mexico and has been there for about 20 years, so that's very important for us to be able to make sure we capture that community in rural and remote areas as well.

For more information please visit:

National Program of Cancer Registries (NPCR) | CDC. https://www.cdc.gov/cancer/npcr/

United States Cancer Statistics | Cancer | CDC https://www.cdc.gov/cancer/uscs/

USCS Data Visualizations - CDC https://www.cdc.gov/Cancer/dataviz

Accurate Cancer Data on American Indian and Alaska Native People Can Help Expand Services | CDC https://www.cdc.gov/cancer/npcr/american-indian-alaska-native-data.htm

Preventing Liver Cancer in Native Communities by Promoting Vaccination and Screening Among Opioid Users

Among American Indians and Alaska Natives, chronic liver disease is a leading cause of death. While the cause is not always known, some cases can be initiated by conditions such as chronic alcoholism, obesity, and exposure to hepatitis B and C viruses.

The opioid epidemic has increased the number of people who inject drugs in the United States, which may lead to an increased risk of HCV and HBV transmission through use of shared equipment.[1] These factors may contribute to the increase in liver cancer in the United States.[2]

Although the risk of developing liver cancer is low, surviving liver cancer is very difficult. For every 100,000 people, 8 new liver and intrahepatic bile duct cancer cases are reported, and 7 people die of these diseases, according to 2019 data from United States Cancer Statistics.[3]

From 1999 to 2015, American Indian and Alaska Native (AI/AN) people had the highest drug overdose death rates — 22.1 per 100,000 in metropolitan areas and 19.8 per 100,000 in non-metropolitan areas.[4] The HCV-related death rate among AI/AN people in the Northwest is three times higher than the rate among non-Hispanic White people (19.6 versus 5.9 per 100,000).[5] The liver cancer incidence rate among AI/AN people is two times higher than that of non-Hispanic Whites (11.9 versus 5.5 per 100,000).[6]

Demonstration Projects Help Promote Vaccination and Screening Among Opioid Users

CDC provides funding, guidance, and technical assistance to its National Comprehensive Cancer Control Program (NCCCP) recipients to create, carry out, and evaluate plans to prevent and control cancer. In 2019, CDC started a 3-year demonstration project, working with four NCCCP recipients to build sustainable partnerships with local organizations to improve knowledge and awareness of the link between injecting drugs and getting hepatitis and liver cancer.

Native Communities Take Action to Prevent Liver Cancer

The American Indian Cancer Foundation participated in a CDC demonstration project to put promising or proven liver cancer prevention strategies into action. The goal was to reduce the incidence of HBV and HCV infections and opioid overdose and decrease liver cancer rates among people who inject drugs.

Photo courtesy of the CDC and Indian Health Service

For More Information, Contact:
Lindsey Petras, Cancer Program Manager
American Indian Cancer Foundation / Office: 612-314-4848

References:

1. Centers for Disease Control and Prevention, Division of Viral Hepatitis. People Who Use or Inject Drugs and Viral Hepatitis. Last reviewed August 24, 2020.
2. National Academies of Sciences, Engineering, and Medicine. A national strategy for the elimination of hepatitis B and C: phase two report. The National Academies Press; 2017. DOI: 10.17226/24731.
3. Cancer Statistics at a Glance. U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool, based on 2021 submission data (1999-2019): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute. June 2022. Accessed June 30, 2022.
4. Mack KA, Jones CM, Ballesteros MF. Illicit drug use, illicit drug use disorders, and drug overdose deaths in metropolitan and nonmetropolitan areas—United States. MMWR Surveillance Summaries 2017;66(SS-19):1–12. DOI: 10.15585/mmwr.ss6619a1.
5. Hatcher SM, Joshi S, Robinson BF, Weiser T. Hepatitis C-related mortality among American Indian/Alaska Native persons in the northwestern United States, 2006–2012. Public Health Reports 2020;135(1):66–73. DOI: 10.1177/0033354919887748.
6. Islami F, Goding Sauer A, Miller KD, Siegel RL, Fedewa SA, Jacobs EJ, McCullough ML, Patel AV, Ma J, Soerjomataram I, Flanders WD, Brawley OW, Gapstur SM, Jemal A. Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. CA: A Cancer Journal for Clinicians 2018;68(1):31–54. DOI: 10.3322/caac.21440.

cdc.gov

Welcoming Monica Bertagnolli as the 16th Director of the National Cancer Institute

As the first woman to hold the position of NCI director, Dr. Bertagnolli joins NCI from Harvard Medical School where she served as the Richard E. Wilson Professor of Surgery in the field of surgical oncology at Brigham and Women's Hospital in Boston. She also was a surgeon at Brigham and Women's Hospital and a member of the Gastrointestinal Cancer Treatment and Sarcoma Centers at Dana-Farber Cancer Institute in Boston.

In addition to treating gastrointestinal cancers and soft tissue sarcomas, Dr. Bertagnolli is a highly regarded cancer researcher. Her leadership in the NCI-funded Cooperative Groups Program (now NCI's National Clinical Trials Network) has led to the integration of tumor-specific biomarkers in clinical trial protocols. More recently, her research on the APC gene and the role of inflammation in influencing its activity has transformed our understanding of how colorectal cancer develops. Her experience as a physician-scientist inspired Dr. Bertagnolli to become an advocate for increasing the diversity of patients in clinical trials. She has championed and advanced patient-focused programs in rural and remote communities.

"I am thrilled to begin my work at NCI, in partnership with the cancer community," said Dr. Bertagnolli. "I think of the patients I've lost in 37 years as a doctor and how much more we can do for people today. That progress drives me to do more — to do everything we can to save more lives.

"I see our work as aimed at three broad goals: understanding how cancer arises and what biological processes it disrupts; developing and testing new prevention and therapy approaches; and partnering with patients to develop ways for all people to receive the care that best meets their needs and, if they wish, to participate in research," she continued. "With the passion and commitment of the President and his administration to the Cancer Moonshot, I believe the opportunities before us to improve the outlook for cancer patients are unprecedented."

Dr. Monica Bertagnolli. Photo courtesy of the National Cancer Institute

cancer.gov

Recognizing National Children's Eye Health and Safety

Nearsightedness is a Public Health Crisis

By Pamela Saulsby, Florida Department of Health Public Information Officer

Nearsightedness has risen dramatically over the last 50 years. If nothing is done to help slow the increase, half the world's population may be nearsighted by the year 2050. That means much more than a lot of people in glasses. It means a lot of children today are at risk of developing vision-threatening eye conditions tomorrow.

That's why the Florida Department of Health in Leon County (DOH Leon) and the American Academy of Ophthalmology (AAO) are recognizing National Children's Eye Health and Safety Month in August, by sharing information about myopia among children and its progression.

People who have myopia, also known as nearsightedness, can see close-up objects clearly, but objects farther away are blurry. Myopia that begins in early childhood often worsens as the child grows. If these changes are too extreme, it can be hard to correct the blurriness with glasses or contact lenses and the risk of potentially blinding eye conditions rises, including retinal detachment, glaucoma, early cataracts and myopic maculopathy, a leading cause of blindness world-wide.

The socioeconomic impact is also devastating. Studies estimate that the global impact of uncorrected myopia results in a $244 billion annual productivity loss, while blindness from myopic macular degeneration results in a $6 billion annual productivity loss.

While more research is required to understand why myopia is on the rise, new treatment options are available to slow the disease in children so the most devastating consequences of high myopia can be avoided. Check out these resources, including a downloadable poster, infographics and videos, for more information about myopia and preventing its progression.

At DOH Leon we believe it's perfect timing to observe Children's Eye Health and Safety Month as Leon County students return to the classroom. Healthy vision contributes to children's school readiness, ability to learn, overall healthy development. Be sure to set your child up for success by scheduling regular vision screenings.

For more information on eye health, visit www.eyesmart.org

For parents or guardians interested in learning how to protect their children's eye health, the U.S. Department of Health and Human Services Department has online resources on getting your child's vision checked.

Photo courtesy of the Florida Department of Health

About the American Academy of Ophthalmology

The American Academy of Ophthalmology is the world's largest association of eye physicians and surgeons. A global community of 32,000 medical doctors, we protect sight and empower lives by setting the standards for ophthalmic education and advocating for our patients and the public. We innovate to advance our profession and to ensure the delivery of the highest-quality eye care. Our EyeSmart® program provides the public with the most trusted information about eye health. For more information, visit aao.org

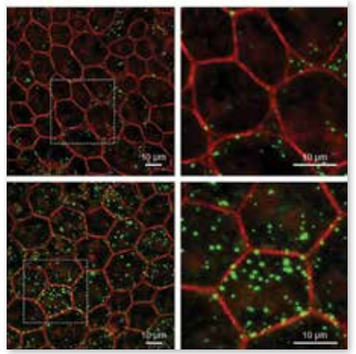
leon.floridahealth.gov

NIH Study Finds Loss of 'Youth' Protein May Drive Aging in the Eye

Loss of the protein pigment epithelium-derived factor (PEDF), which protects retinal support cells, may drive age-related changes in the retina, according to a new study in mice from the National Eye Institute (NEI). The retina is the light-sensitive tissue at the back of the eye, and aging-associated diseases of the retina, like age-related macular degeneration (AMD), can lead to blindness. This new finding could lead to therapies to prevent AMD and other aging conditions of the retina. The study was published in the International Journal of Molecular Sciences. NEI is part of the National Institutes of Health.

"People have called PEDF the 'youth' protein, because it is abundant in young retinas, but it declines during aging," said Patricia Becerra, PhD, chief of NEI's Section of Protein Structure and Function and senior author of the study. "This study showed for the first time that just removing PEDF leads to a host of gene changes that mimic aging in the retina."

The retina is composed of layers of cells that function together to detect and process light signals, which the brain uses to generate vision. The retina's light-sensing photoreceptors sit above the retinal pigment epithelium (RPE), a layer of support cells. The RPE nourishes photoreceptors and recycles pieces of the photoreceptor cells called "outer segments," which get used up and their tips shed each time photoreceptors detect light. If the RPE cannot provide recycled components of older outer segment tips back to photoreceptors, these cells lose their ability to make new segments, and eventually become unable to sense light. And without nutrients supplied by the RPE, photoreceptors die. In people with AMD or certain types of retinal dystrophies, senescence (aging) or death of RPE cells in the retina leads to vision loss.



RPE from mice without Serpin1 accumulate more lipids than wild-type mice. Super-resolution confocal microscopy of RPE tissue from wild-type (upper) and Serpin1-null (lower) mice. Detailed images on the right are magnified regions of the RPE tissue imaged on the left (dotted square area). RPE cell boundaries are stained in red, and accumulated lipids are stained in green. Photo credit Ivan Rebustini, NEI

Previous work from Becerra's lab and others has shown that PEDF protects retinal cells, preventing both damage to the cells and abnormal growth of blood vessels in the retina. RPE cells produce and secrete the PEDF protein. The protein then binds to its receptor, PEDF-R, which is also expressed by RPE cells. Binding by PEDF stimulates PEDF-R to break down lipid molecules, key components of the cell membranes that enclose photoreceptor outer segments and other cellular compartments. This breakdown step is a key part of the outer segment recycling process. And while researchers have known that PEDF levels drop in the retina during the aging process, it was not clear whether this loss of PEDF was causing, or merely correlated with, age-related changes in the retina.

To examine the retinal role of PEDF, Becerra and colleagues studied a mouse model that lacks the PEDF gene (Serpin1). The researchers examined the cellular structure of the retina in the mouse model, finding that the RPE cell nuclei were enlarged, which may indicate changes in how the cells' DNA is packed. The RPE cells also had turned on four genes associated with aging and cellular senescence, and levels of the PEDF receptor were significantly below normal. Finally, unprocessed lipids and other photoreceptor outer segment components had accumulated in the RPE layer of the retina. Similar changes in gene expression and defects in RPE metabolism are found in the aging retina.

"One of the most striking things was this reduction in the PEDF receptor on the surface of the RPE cells in the mouse lacking the PEDF protein," said the study's lead author, Ivan Rebustini, PhD, a staff scientist in Becerra's lab. "It seems there's some sort of feedback-loop involving PEDF that maintains the levels of PEDF-R and lipid metabolism in the RPE."

While at first glance, the retinas of these PEDF-negative mice appear normal, these new findings suggest that PEDF is playing a protective role that helps the retina weather trauma and aging-related wear and tear.

"We always wondered if loss of PEDF was driven by aging, or was driving aging," said Becerra. "This study, especially with the clear link to altered lipid metabolism and gene expression, indicates the loss of PEDF is a driver of aging-related changes in the retina."

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NIH, HHS Leaders Call for Research and Policy Changes to Address Oral Health Inequities

Americans' oral health has improved over the last two decades, but disparities in oral health have stubbornly persisted and pose a major global public health threat, write National Institute of Dental and Craniofacial Research (NIDCR) Director Rena N. D'Souza, DDS, PhD, Acting Science Advisor to the President and former National Institutes of Health Director Francis S. Collins, MD, PhD, and U.S. Surgeon General Vivek H. Murthy, MD, MBA, in a new perspective published in The New England Journal of Medicine.

Oral health is intrinsic to overall health and well-being, yet nearly half of adults over age 30 have periodontal (gum) disease, and 90% have caries, or tooth decay, according to the Centers for Disease Control and Prevention. These and other oral diseases disproportionately burden people who are from marginalized and underserved groups.

Drawing on findings and recommendations from NIH's comprehensive report on the nation's oral health, Oral Health in America: Advances and Challenges, the authors write that equalizing oral health and access to care will require research and policy initiatives that make oral health care more affordable, accessible, and responsive to communities.

The COVID-19 pandemic, which has disproportionately impacted the same groups that experience oral health inequities, highlights the effects of social and systemic factors on health and well-being, as well as the interconnectedness of overall health, mental health, and oral health, write the authors. Patients who lack access to dental care and seek treatment for dental problems in hospital emergency departments are commonly prescribed opioids. Misuse of and addiction to opioids and other substances, which have been exacerbated by the pandemic, threaten oral health.

In a similar vein, people with certain mental illnesses have particularly high rates of oral disease. Fully addressing oral health disparities will require research on the environmental, psychosocial, and behavioral factors at the intersection of oral and mental health.

Finally, the authors call for several policy changes to improve access to oral health care. These include integrating oral, medical, and behavioral health care in traditional and non-traditional health care settings, such as schools and community health centers, as well as including communities in the planning, design, and execution of oral health care systems.

Dr. Rena D'Souza, Director of the NIH's National Institute of Dental and Craniofacial Research. Photo courtesy of the National Institutes of Health

Efforts are also needed to diversify the composition of oral health professionals, address education and training costs, and build a strong oral health research enterprise. Harnessing these policy changes and fully integrating oral health into a new era of discovery with a greater emphasis on prevention can disrupt inequities and improve the overall health of individuals, families, and communities.

nih.gov

Report Details 20 Years of Advances and Challenges of Americans' Oral Health

By Jeff Ventura, U.S. Department of Health and Human Services Communications

Despite important advances in the understanding and treatment of oral diseases and conditions, many people in the U.S. still have chronic oral health problems and lack of access to care, according to a report by the National Institutes of Health. Oral Health in America: Advances and Challenges, is a follow-up to the seminal 2000 Oral Health in America: A Report of the Surgeon General.

The new report, which is intended to provide a road map on how to improve the nation's oral health, draws primarily on information from public research and evidence-based practices and was compiled and reviewed by NIH's National Institute of Dental and Craniofacial Research (NIDCR) and a large, diverse, multi-disciplinary team of more than 400 experts.

The report updates the findings of the 2000 publication and highlights the national importance of oral health and its relationship to overall health. It also focuses on new scientific and technological knowledge — as well as innovations in health care delivery — that offer promising new directions for improving oral health care and creating greater equity in oral health across communities.

Achieving that equity is an ongoing challenge for many who struggle to obtain dental insurance and access to affordable care.

"This is a very significant report," said NIH Acting Director Lawrence A. Tabak, DDS, PhD. "It is the most comprehensive assessment of oral health currently available in the United States and it shows, unequivocally, that oral health plays a central role in overall health. Yet millions of Americans still do not have access to routine and preventative oral care."

NIH's new report, Oral Health in America: Advances and Challenges, provides a road map on how to improve the nation's oral health. Graphic courtesy of the National Institute of Dental and Craniofacial Research

The report focuses on new scientific and technological knowledge — as well as innovations in health care delivery — that offer promising new directions for improving oral health care and creating greater equity in oral health across communities.

The newly issued report provides a comprehensive snapshot of oral health in America, including an examination of oral health across the lifespan and a look at the impact the issue has on communities and the economy. Major take-aways from the report include:

- Healthy behaviors can improve and maintain an individual's oral health, but these behaviors are also shaped by social and economic conditions.
- Oral and medical conditions often share common risk factors, and just as medical conditions and their treatments can influence oral health, so can oral conditions and their treatments affect other health issues.
- Substance misuse and mental health conditions negatively affect the oral health of many.
- Group disparities around oral health, identified 20 years ago, have not been adequately addressed, and greater efforts are needed to tackle both the social and commercial determinants that create these inequities and the systemic biases that perpetuate them.

"This is an in-depth review of the scientific knowledge surrounding oral health that has accumulated over the last two decades," said Rena D'Souza DDS, PhD, director of NIDCR, which oversaw and funded the project's three-year research program. "It provides an important window into how many societal factors intersect to create advantages and disadvantages with respect to oral health, and, critically, overall health."

The COVID-19 pandemic emerged while the report was being written. The science around SARS-CoV-2 continues to come into focus in real-time, and, although data were only starting to surface about the oral implications of the disease, the authors included a preliminary analysis of it to assess initial impacts.

The authors make several recommendations to improve oral health in America, which include the need for health care professionals to work together to provide integrated oral, medical, and behavioral health care in schools, community health centers, nursing homes, and medical care settings, as well as dental clinics.

Rena N. D'Souza, DDS, MS, PhD, Director of NIH's National Institute of Dental and Craniofacial Research (NIDCR). Photo courtesy of NIH and the University of Utah

Lawrence A. Tabak, DDS, PhD, Acting Director of the National Institutes of Health. Photo courtesy of the NIH

They also identify the need to improve access to care by developing a more diverse oral health care workforce, addressing the rising cost of dental education, expanding insurance coverage, and improving the overall affordability of care.

"Although there are challenges ahead, the report gives us a starting point and some clear goals that offer reasons to be hopeful, despite those challenges," added D'Souza. "It imagines a future, as I do, in which systemic inequities that affect oral health and access to care are more fully addressed, and one in which dental and medical professionals work together to provide integrated care for all."

Scientists and public health professionals will use the report to identify areas of scientific inquiry and research as well as develop and implement programs that ultimately will improve the oral health of individuals, communities, and the nation.

nih.gov

Study Funded by NIH Supports Optimal Threshold for Diagnosing COPD

A recent study funded by the National Heart, Lung, and Blood Institute (NHLBI) provides evidence to support a simple measurement for diagnosing clinically significant airflow obstruction, the key characteristic of chronic obstructive pulmonary disease (COPD), the fourth leading cause of death in the United States. The study found that a 70% ratio of two indicators of lung function proved as or more accurate than other thresholds for predicting COPD-related hospitalizations and deaths.

Its findings were published online today in the Journal of the American Medical Association. Approximately 16 million Americans have COPD, and it is estimated that millions more have the disease and do not know it.

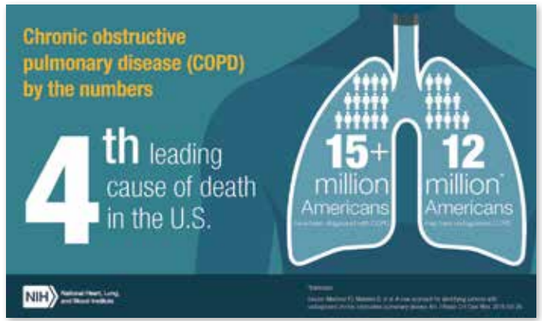
The research, which draws on a wide range of multi-ethnic studies, validates current guidelines from major respiratory societies and contributes to identify a fixed threshold of disease severity. This approach has led to great strides in early detection and treatment of other conditions such as hypertension and diabetes.

"Diagnosis of airflow obstruction remains a major hurdle to improving care for patients with COPD," said James Kiley, PhD, director of the NHLBI Division of Lung Diseases. "This validation of a fixed threshold confirms the usefulness of a simple approach for assessment of the disease.

As we celebrate the 50th anniversary of the Division of Lung Diseases, this rigorous analysis of populations-based, multi-ethnic studies is yet another example of research we fund that improves clinical practice, public health, and patient care."

To monitor lung function and gauge the severity of a lung disease, doctors use spirometry, a test that measures several indicators. Those include the ratio of forced expiratory volume in one second (FEV1) — that is, the amount of air exhaled forcefully in one second — over forced vital capacity (FVC) — or the full amount of air that can be forcefully exhaled in a complete breath. The two values are usually proportional; and lower ratios are seen in individuals with obstructive lung diseases, such as asthma or COPD.

The researchers aimed to determine how accurate various thresholds were in predicting COPD-related hospitalizations and mortality. For that, the NHLBI Pooled Cohorts Study analyzed data from four U.S. population-based studies that collected spirometry results and followed up participants for COPD-related clinical events. The study included 24,207 adult participants, of which 54% were women, 69% white, and 24% black.



Graphic courtesy of the NIH's National Heart, Lung, and Blood Institute

"The selection of a threshold for defining airflow obstruction has major implications for patient care and public health, as the prevalence of the condition could vary by more than a third depending on the metric used," said study author Elizabeth C. Oelsner, MD, MPH, the Herbert Irving Assistant Professor of Medicine at Columbia University, New York City. "Defining 'normal' lung function is very challenging in diverse and changing populations, and certain approaches might interpret low levels of lung function as normal in women, non-whites, or the elderly. We were able to show that a simple fixed threshold worked well in our study's very diverse sample, which improves the generalizability of our results."

The researchers said establishing a diagnostic threshold that is easy to use not only is critical to improving the adoption of spirometry in primary care; it may also result in earlier detection and treatment for patients.

nhlbi.nih.gov

Exercise Energizes Patients with Autoimmune Disease

IRP Study Points to the Biological Roots of Physical Activity's Benefits

By Brandon Levy, Health Communications Specialist for the NIH's Intramural Research Program

British science fiction writer Arthur C. Clarke once wrote that, "Any sufficiently advanced technology is indistinguishable from magic." While not exactly a "technology," exercise has such wide-ranging health benefits that it could understandably be mistaken for magic. Still, scientists persist in investigating precisely why physical activity is so good for us. Recently, a small IRP study showed that exercise training can help reduce the debilitating fatigue that often accompanies the autoimmune disease known as lupus, and also illuminated some of the underlying mechanisms that may lead to those benefits.[1]

Like other autoimmune diseases, lupus occurs when a person's own immune system attacks his or her body. This immune assault causes a variety of symptoms, including fatigue so severe that it prevents patients from pursuing activities that healthy people can do without a second thought.

Sarfaraz Hasni, MD, Staff Clinician, Chief, Lupus Clinical Trials Unit, Director, Lupus Clinical Research Program. Photo courtesy of the NIH's National Institute of Arthritis and Musculoskeletal and Skin Diseases

"Fatigue is a major concern and quality of life issue for patients with lupus," says IRP staff clinician Sarfaraz Hasni, M.D., the new study's first author. "It's an overwhelming feeling of fatigue to the extent that they're not able to do normal activities of daily living. It's a topic of great research interest because nobody understands what causes this extreme amount of fatigue not just in lupus but also in other autoimmune diseases."

"It's a feedback loop," adds IRP staff scientist Lisa Chin, PhD, the study's senior author. "You don't do much activity because you don't feel good, and that leads to further deconditioning in an endless cycle of fatigue that's hard to get out of."

While numerous past studies showed that exercise can help break that cycle, the biological reasons why it does so remained largely unexplored. In the new study, an interdisciplinary group of researchers from across the IRP worked together to shed some light on how exercise affects lupus patients' bodies, including their genes and the energy-generating mitochondria that power their cells.

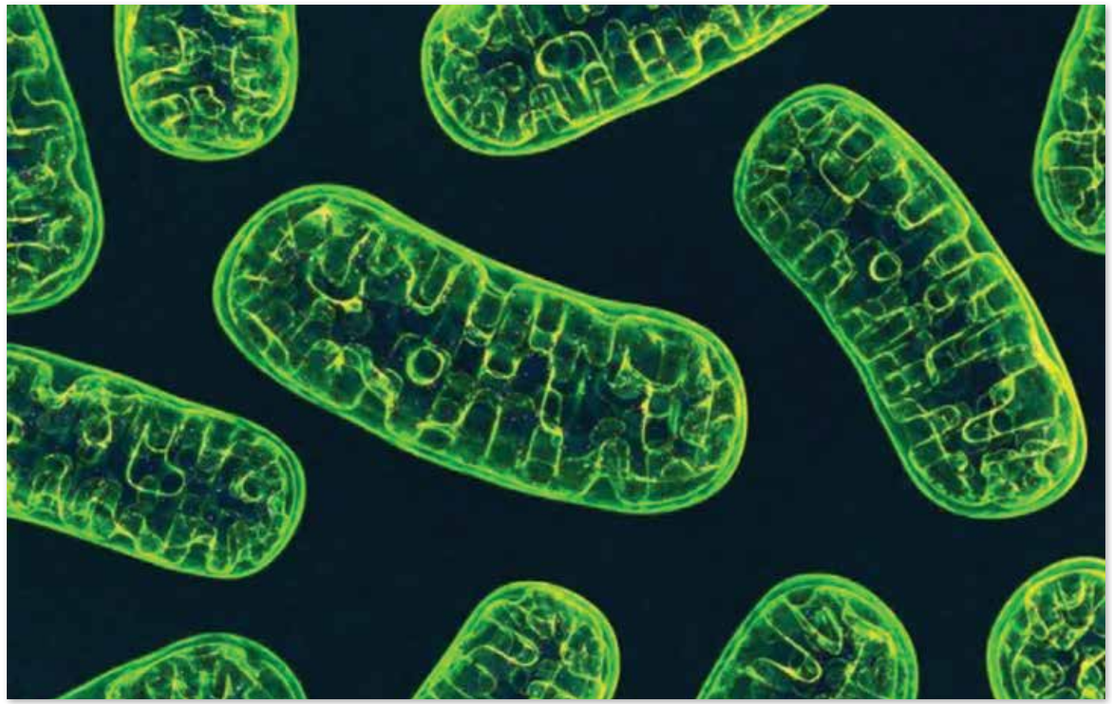
As part of the study, 16 women with lupus came to the NIH Clinical Center three times per week for 12 weeks to do 30 minutes of intense treadmill walking. At the end of the study, patients reported that they were experiencing significantly less fatigue in their everyday lives than they had before, along with improved mental health and sleep.

However, the study did not rely solely on subjective self-reports that could be influenced by the placebo effect. The IRP team also measured changes in the participants' 'anaerobic threshold,' which indicates when the body begins to rely on different energy sources during exercise. Initially, our cells keep us moving by using processes that require plenty of oxygen, but sustained, vigorous physical activity eventually causes them to switch over to 'anaerobic' methods that don't need much oxygen. This change occurs near the point at which exercisers begin to feel worn out, and the study showed that 12 weeks of exercise training markedly lengthened the time it took for participants to reach the anaerobic threshold during a progressively more challenging exercise test.

"Think of it as an indication for when fatigue is imminent," Dr. Chin explains. "If you can delay the time it takes to hit this anaerobic threshold, it means you've delayed fatigue."

"Patients don't know where this threshold is," she continues. "It's a very objective marker because it's assessed after the exercise test and is not based on input from the patient."

Lisa Chin, PhD. Photo courtesy of the NIH's Intramural Research Program



Cellular energy factories called mitochondria (pictured here) were a main focus of the IRP study. Photo courtesy of the NIH's Intramural Research Program

Interestingly, the IRP team found evidence suggesting that exercise reduces lupus patients' fatigue in part by improving the energy output of their cells' mitochondria. The more that a participant's mitochondria ramped up energy production after the 12 weeks of exercise training, the greater that person's reduction in fatigue symptoms tended to be.

Another potential reason that exercise reduced the participants' fatigue may have been by decreasing the amount of a substance called interferon in their bodies. Interferon is known to be a major driver of lupus, but it is hard to measure its concentration in the blood. However, when its levels increase, it boosts the activity of a set of genes called interferon-stimulated genes (ISGs), so examining the behavior of those genes can provide a proxy measurement for interferon levels in the body. When the IRP researchers looked at how the activity of ISGs changed in their participants over the course of the study, they found that slightly more than half of the participants not only had increased mitochondrial energy output but also a marked reduction in the activity of their ISGs.

"If the ISGs are high at the beginning, it means there's a lot of interferon driving the disease, and then later on if it goes down, it means the disease is possibly not as severe," Dr. Hasni explains.

Dr. Hasni and Dr. Chin caution that because the IRP study was small, additional research will be needed to determine with more certainty the biological roots of exercise's benefits for lupus patients. It also remains unclear what type and amount of exercise is required to produce those effects. Nevertheless, the IRP study provided important clues that scientists can pursue further to figure out the best ways to reduce fatigue in individuals with lupus. Those interventions could include exercise, a medication that boosts mitochondrial function, or — most likely — a combination of approaches.

"With exercise, it's a systemic change that you're making, so it's hard to pinpoint exactly what it does, but this study points to mitochondrial dysfunction as contributing to the fatigue," Dr. Chin says. "It's definitely something to look more into with larger trials."

References:

1. Hasni S, Feng LR, Chapman M, Gupta S, Ahmad A, Munday A, Mazhar MA, Li X, Lu S, Tsai ML, Gadina M, Davis M, Chu J, Manna Z, Nakabo S, Kaplan MJ, Saligan L, Keyser R, Chan L, Chin LMK. Changes in cardiorespiratory function and fatigue following 12 weeks of exercise training in women with systemic lupus erythematosus: a pilot study.(external link) Lupus Sci Med. 2022 Oct;9(1):e000778. doi: 10.1136/lupus-2022-000778.

irp.nih.gov

Referring Patients to a Rheumatologist

A primary health care provider can often provide basic care for a patient with arthritis, especially osteoarthritis, but sometimes it is necessary to refer a patient to a rheumatologist. A primary health care provider can often partner with a rheumatologist to provide the best care.

Primary health care providers should consider referring patients to a rheumatologist if:

- You diagnose or suspect an inflammatory type of arthritis (e.g., rheumatoid arthritis, lupus, psoriatic arthritis), or to confirm a diagnosis.
- A patient needs a management plan for a type of inflammatory arthritis.
- A patient has unexpected complications such as unexplained fever, abnormal laboratory findings, or onset of unexplained symptoms (fatigue, rash, anemia, etc.).

To learn more about when to refer a patient, read the American College of Rheumatology's Referral Guidelines at https://www.rheumatology.org/Portals/0/Files/Referral%20Guidelines.pdf

Find rheumatologists near your patient in ACR's Find a Rheumatologist database
https://www.rheumatology.org/Directories/Find-a-Rheumatologist

Telemedicine Resources:

Telemedicine is the remote diagnosis and treatment of patients using technology like video chat. It is a small but rapidly growing part of health care in the United States. Telemedicine is especially important in areas where there are few health care providers or specialists like rheumatologists, such as rural areas or underserved populations. Telemedicine for the diagnosis and management of rheumatic disease is called telerheumatology.

Learn more about telerheumatology:

Telemedicine Bridges Gaps in Patient Access to Rheumatologists
https://www.rheumatologyadvisor.com/rheumatoid-arthritis/telemedicine-bridges-gaps-in-patient-access-to-rheumatologists/article/577033/2/

Telerheumatology: A Systematic Review
https://www.ncbi.nlm.nih.gov/pubmed/27863164

cdc.gov

Photo courtesy of CDC/iStock

Indian Health Service Further Expands Telehealth Services to Meet Patient Needs

Indian Health Service is announcing an expansion of telehealth across IHS federal facilities to meet the needs of American Indian and Alaska Native patients.

In July 2021, IHS awarded a clinical video telehealth contract to AA RingMD, a secure, cloud-based solution that enables patient-to-provider and provider-to-provider telehealth meetings. IHS has been working with AA RingMD staff and engineers to prepare for implementation. Beginning today, IHS clinicians and support staff at federal facilities can use the secure system.

"This expansion of telehealth will increase access to care, patient safety, continuity of care, quality of care, and ultimately patient satisfaction," said IHS Director Roselyn Tso. "We look forward to being able to reach even more of our American Indian and Alaska Native patients across Indian Country."

This platform will be available across multiple devices and allows for expanded televideo visits in settings such as homes or schools with low broadband availability. AA RingMD is the first telehealth-focused platform that IHS has deployed and will complement Webex, the existing IHS telehealth solution, giving IHS two secure options to use when providing telehealth care, both now and when the public health emergency ends.

AA RingMD is a secure system that encrypts audio and video communications. The cybersecurity of IHS's telehealth system is critical to patients' safety, health, privacy, and the integrity of patients' data. IHS recognizes the importance of protecting the personally identifiable information and protected health information entrusted to us and has built a robust program to safeguard this information and ensure that privacy rights are upheld. A plan is in place to adequately address all system vulnerabilities.

IHS Western Oregon Service Unit Director of Nursing Michelle Livingston, RN in 2016, demonstrates the new telehealth system at the Chemawa Health Center in Salem, Ore. Livingston, a veteran, has worked with the Department of Veterans Affairs to develop protocols and implement the new telehealth service.
Photo courtesy of Indian Health Service

Pre-existing rules for the IHS workforce's use of telehealth continue, and health care providers must obtain the patient's verbal consent to meet via telehealth. Health care providers must also verify the patient's identity at the beginning of each encounter and are not authorized to record the session.

The IHS has a long history of using telehealth to meet its mission and the needs of its patients, dating back to the mid-1970s when IHS partnered with NASA and Lockheed Martin to provide telehealth to the Tohono O'odham Nation in Arizona.

In 2020, IHS significantly expanded the use of telemedicine, rapidly ramping up virtual care services from a pre-COVID average of under 1,300 per month to a peak of nearly 42,000 per month at the height of the initial pandemic surge. For the first time, IHS clinicians could provide services into patients' homes. This allowed continued access to care while protecting patients and health care workers. The current average is approximately 11,000 per month.

The Indian Health Service finds telemedicine to be one of the best ways to get health care services to the people and places where they are needed most. IHS collaborates with tribal leaders to deploy telemedicine services that respond to patient and community need. Telehealth service availability varies by location, but may include specialty services such as behavioral health, dermatology, endocrinology, wound management, and rheumatology. IHS facilities in the Great Plains Area and Billings Area also use telehealth in the emergency department to support on-site health care providers.

Currently, IHS has two national telehealth programs and numerous regional telehealth programs. The IHS-Joslin Vision Network Teleophthalmology Program is dedicated to preventing diabetes-related blindness.

The mission of the IHS Telebehavioral Health Center of Excellence (TBHCE) Telebehavioral Health Program is to provide, promote, and support the delivery of high-quality, culturally sensitive telebehavioral health services to American Indian/Alaska Native people. The IHS, an agency in the U.S. Department of Health and Human Services, provides a comprehensive health service delivery system for approximately 2.7 million American Indians and Alaska Natives who belong to 574 federally recognized tribes in 37 states.

ihs.gov

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Discussing Bone, Muscle, Skin, & Autoimmune Diseases: Info for American Indians, Alaska Natives Spotlight on Research

A conversation between Dr. David R. Wilson, director of the NIH Tribal Health Research Office, and Dr. Lindsey A. Criswell, director of NIAMS, about information and resources for American Indians and Alaska Natives related to bone, muscle, skin, and autoimmune diseases.

Dave Wilson: Hello, my name is Dr. Dave Wilson. I am a member of the Navajo Nation, and I am also the Director of the Tribal Health Research Office, also known as THRO, here at the National Institutes of Health. Today I am joined by my colleague Dr. Lindsay Criswell, who is the Director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases, or NIAMS for short, which is also a part of the NIH. Dr. Criswell is a board-certified rheumatologist and was recently elected to the Association of American Physicians, an honor extended to physicians with outstanding credentials in biomedical research. Welcome, Dr. Criswell.

Lindsay Criswell: Thank you, Dr. Wilson. It's a pleasure to be here today to discuss NIAMS' efforts to support tribal health.

Dave Wilson: Almost every household in America, including those in tribal communities, is affected by diseases of the bones, joints, muscles and skin. In fact, American Indians and Alaska Natives are often disproportionately affected by certain diseases like rheumatoid arthritis, for example, and NIAMS works to understand and to treat those diseases and conditions through research. So, Dr. Criswell, my first question, or actually acknowledgement, is I really want to acknowledge NIAMS' history of dedication to tribal health communications. Long before the Tribal Health Research Office was established in 2015, NIAMS led NIH-wide efforts to communicate relevant health information and research advances with tribal communities. Can you discuss a little bit more about NIAMS past and current efforts to support resource development and information sharing with tribal communities?

David R. Wilson, PhD, Director, Tribal Health Research Office (THRO), NIH. Photo courtesy of the National Institutes of Health

Lindsey A. Criswell, MD, MPH, DSc, Director of NIH's National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). Photo courtesy of the National Institutes of Health

Lindsay Criswell: One of the earlier NIAMS-led efforts was the 2005 formation of the NIH American Indian and Alaska Native Health Communications and Information Work Group, which provided a forum for health education and communications staff from across the NIH. This group met regularly to share strategies for effective communication approaches to disseminate reliable health information to tribal communities and hosted workshops to educate NIH staff on socially and culturally conscious methods to reach these communities.

The primary output of this work was the Honoring Health e-newsletter, featuring NIH health topics, resources, events, training and funding opportunities for American Indians and Alaska Natives. This newsletter was formed in collaboration with the Indian Health Service,

Photo courtesy of the Office on Women's Health

also known as IHS, and the Administration for Community Living Administration on Aging, showcasing NIH's ability to work across federal lines to provide quality resources for tribal communities. Many NIH Institutes, Centers and Offices contributed content over the years. In 2020, as you know, NIAMS worked with your office to transition the leadership of the work group and development of the newsletter to THRO, where it now functions as a subcommittee of THRO's Tribal Health Research Coordinating Committee.

NIAMS is proud to have hosted and grown these initiatives for many years, and we're excited that they can now thrive under THRO's leadership. We will continue to support THRO in these efforts and look forward to future opportunities for collaboratively sharing information. NIAMS also collaborates with other Institutes in hosting activities designed to benefit tribal communities. For example, in late 2020, NIAMS worked with the Child Health Institute to plan and implement a two-day workshop that addressed building an indigenous evaluation framework with the Urban Indian Health Institute. This workshop included more than 40 staff from NIH and other federal agencies. They were trained on ways to recognize research, data, and evaluation principles that are aligned with indigenous values and how to ensure the data is used for the benefit of Indigenous people. We recognize the importance of educating NIH staff on how we can better support tribal health. I appreciate the informative NIH-wide lectures that THRO facilitates to educate the research community, such as the recent 2021 lecture on interconnectedness of culture and science.

Dave Wilson: Thank you so much. There is just a tremendous amount of resources available through NIAMS, and we really appreciate that. There are a number of diseases and conditions that NIAMS studies that adversely impact Native people, including systemic lupus erythematosus, or SLE or lupus, arthritis, scleroderma, and Sjögren's syndrome. Can you please tell us a little more about these diseases and why Native American people could be at risk for some of these conditions?

Lindsay Criswell: Yes, it's true that many diseases within the NIAMS mission areas significantly impact or even disproportionately impact Native people. For example, tribal communities have some of the highest rates of arthritis, including rheumatoid arthritis, which is a disease that causes inflammation in the joints and throughout the body. As compared with the general population, Alaska Natives also have higher rates of juvenile idiopathic arthritis, which is the most common form of arthritis in children. And with regard to osteoarthritis, or OA, lifestyle factors such as body weight may play an important role in increasing OA risk in AI/AN communities. Autoimmune diseases, in which the immune cells target the body's own healthy tissues by mistake, also significantly impact tribal communities. These include, as you mentioned, systemic lupus erythematosus, or lupus, which is an autoimmune disease that causes inflammation in multiple organs throughout the body. Another autoimmune condition that disproportionately affects Native communities is Sjögren's disease. Sjögren's causes dry eyes and mouth and inflammation in other parts of the body. Scleroderma, or systemic sclerosis, is an autoimmune disease that causes inflammation in the skin, as well as other areas of the body.

The Choctaw American Indians of Oklahoma have among the highest rates of scleroderma in the country. I should also point out the two forms of arthritis that I mentioned earlier, rheumatoid arthritis and most forms of juvenile idiopathic arthritis are also autoimmune in nature. Although it's not entirely clear why some tribes are more significantly impacted by these diseases when compared with the general population, we suspect that a combination of genetic, immune and environmental factors, or social determinants, all play important roles.

In addition to higher rates of some rheumatic and skin diseases, American Indian and Alaska Native women are at increased risk for osteoporosis, which is a disease that makes the bones weak and prone to fracture. There may be a number of factors at play here. Osteoporosis risk may be particularly tied to an increased prevalence of type 2 diabetes among Native communities.

Dave Wilson: Great, thank you so much. And what you've highlighted is the importance of research and how much we still have to learn about autoimmune diseases and the roles they play in tribal communities. To further expand upon this topic, are there any research areas that you would like to highlight that would be relevant for tribal communities?

Lindsay Criswell: Thank you. So yes, what are we doing to address these disproportionate disease risks among Native communities? Our Oklahoma Rheumatic Disease Research Cores Center has focused on patient-oriented investigation, specifically in American Indian and other communities. The Center has enhanced our understanding of the underlying mechanisms of rheumatic disease in tribal communities, particularly with regards to autoantibody profiles in Native Americans with autoimmune disease.

NIAMS is one of three NIH Institutes that support the Cherokee Nation Native American Research Center for Health, or NARCH, which conducts community-engaged research and scientific workforce enhancement projects keyed to the major health issues affecting American Indians in northeastern Oklahoma. The Center is researching the molecular underpinnings of autoimmunity among tribal members, and key personnel mentor and train American Indian students for careers in academia, medicine and tribal service.

We also supported the Navajo Bone Health Study, which was one of the first initiatives keyed to bone health and osteoporosis in tribal communities. The study helped to characterize osteoporosis risk factors in AI/AN individuals. And NIAMS continues to participate in NIH-wide funding opportunities that are focused on research to improve tribal health.

Dave Wilson: Outstanding. One of the goals for the NIH Strategic Plan for Tribal Health Research is to build research capacity in tribal communities and create opportunities for the next generation of American Indian and Alaska Native researchers. Are there specific training opportunities that you would like to highlight?

Lindsay Criswell: Thank you. So, I've already mentioned the NIAMS-supported NARCH training and mentoring program for American Indian students. NIAMS has also developed a Diversity Supplement Scholars Program that provides funding opportunities for researchers from groups that have been historically underrepresented in science. Through this program, we established an annual cohort of diversity supplement scholars and mentors, with the goal of providing support and resources aimed to foster the scholar's career trajectory towards an independent research career.

The NIAMS Intramural Research Program, or IRP, also participates in the American Indian Science and Engineering Society national and regional meetings to increase the exposure of the NIAMS IRP and recruitment participation efforts for AI/AN communities. The NIAMS IRP has also co-hosted NIH campus tours for students from the National Native American Youth Initiative. NIAMS recognizes the importance of diversity in research, and the value of integrating traditional healing approaches in patient care. We are committed to supporting research that reflects the diversity of our nation and to keeping a diverse scientific workforce pipeline. We look forward to our continued partnership with the NIH Tribal Health Research Office.

Dave Wilson: Dr. Criswell, I want to thank you so much for being here today. It's been a pleasure speaking with you and learning so much more about NIAMS and their long-standing commitment to tribal health research, and its engagement opportunities and resources related to improving the health of American Indian and Alaskan Natives. For everybody out there, thank you so much for listening. We appreciate it.

Lindsay Criswell: Thank you.

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