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QUARTERLY
SPRING 2025 SAFETY

Navigating **Medical Misinformation**

HOW PROVIDERS CAN
Deescalate Patient Fears

Rabies: THE SERIOUSNESS OF RAPID RESPONSE

Infant Botulism:
IMPROVED TREATMENT OPTIONS

MYTHS AND FACTS ABOUT
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BioSupply Trends Quarterly is the definitive source for industry trends, news and information for healthcare professionals in the biopharmaceuticals marketplace.

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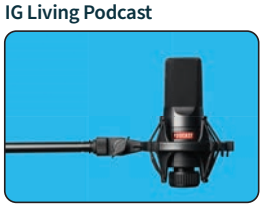

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Honest, Empathetic Rapport Builds Patient Trust

AT ITS CORE, quality care revolves around trust. Patients entrust sensitive health information to providers, and providers rely on patient honesty to guide clinical decisions. Without two-way trust, communication breaks down and outcomes decline. But many things disrupt this crucial component of healthcare, including misinformation and patients' own fears. When patients don't know who or what to believe, they feel unsafe.

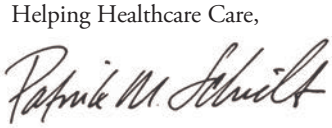
The infodemic of medical misinformation continues to be a problem, and helping patients manuever through it remains a top priority for healthcare professionals. In fact, doctors are best positioned to educate the public and rebuild patient confidence in healthcare. Our article "Navigating the Medical Misinformation Age" (p.22) discusses how misleading, incomplete or incorrect medical information leads people to make dangerous decisions about their health, ultimately putting their lives in jeopardy. We also share best practices for healthcare providers to diplomatically teach patients how to identify false information and how to respond when patients believe something untrue.

With so much conflicting information out there, it's no wonder fear often gets the best of patients. However, as we explore in "Decatastrophizing Patient Fears" (p.26), misinformation is not the only thing that causes patients to experience anxiety. Patients want to know the truth, but they also want healthcare providers to deliver truth in a way that makes patients feel human. When delivered in a cold, detached manner, essential health information and difficult health news can leave patients feeling dehumanized. Ultimately, patients are afraid of losing control and their sense of self, so we share strategies for healthcare professionals to help preserve both with the ultimate goal of making patients feel seen and safe.

Patients entrust healthcare professionals with more than their private health information: They also entrust healthcare facilities with a slew of medical records, personal information, insurance and financial data. Private, protected health information and adminstrative data used in the day-to-day operations of healthcare facilities are valuable — and therefore vulnerable to cyberattacks. Protecting against electronic invasions is crucial for all healthcare facilities, but poses a bigger challenge to small practices. Our Healthcare Management column titled "Creating a Cybersecurity and Incidence Response Strategy for Small Offices" (p.12), discusses cybersecurity and how small offices can and should learn about ways to ensure their digital security needs are met.

As always, we hope you enjoy the additional articles in this issue of *BioSupply Trends Quarterly*, and find them both relevant and helpful to your practice.

Helping Healthcare Care,



Patrick M. Schmidt
Publisher

biosupplytrends QUARTERLY

Our mission is to serve as the industry's leading resource for timely, newsworthy and critical information impacting the biopharmaceuticals marketplace, while providing readers with useful tips, trends, perspectives and leading indicators on the topics pertinent to their business.

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HHS Announces 15 Additional Drugs for Price Negotiations

The Centers for Medicare and Medicaid Services (CMS) has announced the selection of 15 additional drugs covered under Medicare Part D for price negotiations. In accordance with the Inflation Reduction Act, the negotiations with participating drug companies for these 15 drugs will occur in 2025, and any negotiated prices will become effective in 2027. Between November 2023 and October 2024, about 5.3 million people with Medicare Part D coverage used these drugs to treat a variety of conditions, such as cancer, type 2 diabetes and asthma. The selected drugs accounted for about $41 billion in total gross covered prescription drug costs under Medicare Part D, or about 14 percent, during that time period. When combined with the total gross covered prescription

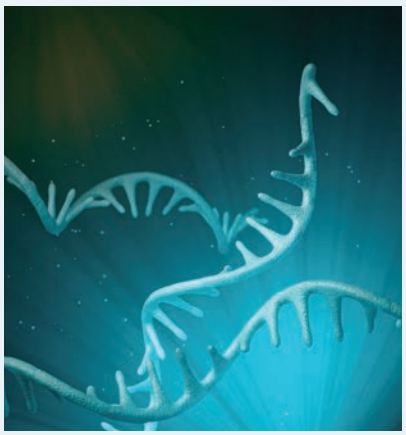
drug costs under Medicare Part D of the 10 drugs selected for the first cycle of negotiations over that same time period, this represents over a third of total gross covered prescription drug costs under Medicare Part D.

The selected drug list for the second cycle of negotiations is: Ozempic, Rybelsus, Wegovy; Trelegy Ellipta; Xtandi; Pomalyst; Ibrance; Ofev; Linzess; Calquence; Austedo, Austedo XR; Breo Ellipta; Tradjenta; Xifaxan; Vraylar; Janumet, Janumet XR; and Otezla.

In negotiating with participating manufacturers, CMS will consider the selected drug's clinical benefit, the extent to which it addresses unmet medical needs, and its impact on specific populations, including people who rely on Medicare, among other considerations such as costs associated with research and development, as well as production and distribution for selected drugs. ❖

HHS Announces 15 Additional Drugs Selected for Medicare Drug Price Negotiations in Continued Effort to Lower Prescription Drug Costs for Seniors. Centers for Medicare and Medicaid Services, Jan. 17, 2025. Accessed at www.cms.gov/newsroom/press-releases/hhs-announces-15-additional-drugs-selected-medicare-drug-price-negotiations-continued-effort-lower.

Grant Awarded to Accelerate Pandemic Influenza mRNA Vaccine Development



The U.S. Department of Health and Human Services (HHS) will provide approximately $590 million to Moderna to accelerate the development of mRNA-based pandemic influenza vaccines and enhance mRNA platform capabilities so the U.S. is better prepared to respond to other emerging infectious diseases. This funding allows Moderna to accelerate development of an H5N1 mRNA influenza vaccine that is well matched to strains currently circulating in cows and birds and expands the clinical data supporting the use of mRNA vaccines that may be needed if other influenza strains emerge with pandemic potential.

Moderna's influenza vaccine candidate uses conventional mRNA technology that was leveraged successfully during the COVID-19 response, resulting in one of the first two FDA-authorized — and ultimately FDA-licensed — COVID-19 vaccines.

In addition, Moderna will design and test an H7N9 mRNA pandemic influenza vaccine in a Phase III clinical study. If successful, this vaccine potentially could become the first licensed for H7N9. Moderna also will design up to four additional novel pandemic influenza vaccines and test preliminary safety and immunogenicity (generating an immune system response) in Phase I clinical studies. This work will create the necessary background data to enable accelerated development of an mRNA vaccine targeted to various influenza virus subtypes of pandemic potential. This approach takes advantage of the versatility of Moderna's mRNA platform, leveraging an existing manufacturing platform capability to support product development across multiple health threats. ❖

HHS Provides $590 Million to Accelerate Pandemic Influenza mRNA-based Vaccine Development, Enhance Platform Capability for Other Emerging Infectious Disease. U.S. Department of Health and Human Services press release, Jan. 17, 2025. Accessed at www.hhs.gov/about/news/2025/01/17/hhs-provides-590-million-accelerate-pandemic-influenza-mrna-based-vaccine-development-enhance-platform-capability-other-emerging-infectious-disease.html.

CMS Releases Proposed 2026 Payment Policy Updates for MA and Part D Programs

The Centers for Medicare and Medicaid Services (CMS) released the 2026 Advance Notice for the Medicare Advantage (MA) and the Medicare Part D Prescription Drug Programs that would update payment policies for these programs. This release complements the 2026 MA and Part D proposed rule that CMS released in November 2024. If finalized, these policies and updates would continue common sense, fiscally responsible technical updates to MA payments. Payments from the government to MA plans are expected to increase on average by 4.33 percent, or over $21 billion, from 2025 to 2026, as proposed.

CMS is concurrently releasing the draft 2026 Part D Redesign Program Instructions that continue to implement the redesign of the Medicare Part D program. The Inflation Reduction Act redesigned Medicare Part D to reduce prescription drug costs and improve benefits for Medicare enrollees, including the first-ever cap on annual out-of-pocket prescription drug costs for all people with Medicare prescription drug coverage that went into effect on Jan. 1, 2025. With the Inflation Reduction Act, annual out-of-pocket costs will be capped at $2,100 in 2026 for people with Medicare Part D, which is the 2025 out-of-pocket cap of $2,000 indexed for inflation. ❖

CMS Releases Proposed 2026 Payment Policy Updates for Medicare Advantage and Part D Programs. Centers for Medicare and Medicaid Services press release, Jan. 10, 2025. Accessed at www.cms.gov/newsroom/press-releases/cms-releases-proposed-2026-payment-policy-updates-medicare-advantage-and-part-d-programs.

Grant Allows UCLA to Launch Autoimmunity Center to Find Cures

The National Institutes of Health (NIH) has awarded a $3.4 million grant to help establish a new Autoimmunity Center of Excellence at the University of California, Los Angeles (UCLA). The center will study the mechanisms that cause autoimmunity, which occurs when the body's defense system turns against tissues in its own body, and identify potential cures. Specifically, it will focus on hormone-related (endocrine) autoimmune disorders such as type 1 diabetes.

"We have medicines for these types of autoimmune conditions, but they fail to address the root of the problem," said microbiology, immunology and molecular genetics professor Maureen Su, MD, who is also a practicing pediatric endocrinologist at UCLA. "For example, we treat type 1 diabetes with insulin in the clinic, but the primary problem is the immune system. Right now, we replace the insulin that is missing, but we don't fix the immune system's constant damage to the insulin-producing tissues. Without these insulin-producing tissues, blood sugars can be very difficult to keep in control, despite treatment with insulin as a medicine. Rather than just Band-Aiding the problem, we aim to fix the actual autoimmune problem."

Seeking targets for cures, the new center will house three main projects, each focused on a particular research question:

1) How is long-term autoimmune disease established? While some autoimmune conditions resolve over time, others establish themselves more firmly. This project will be led by Manish Butte, MD, a UCLA professor of pediatrics and chief in the division of immunology, allergy and rheumatology.

2) How do cancer immunotherapies cause autoimmune disorders? Some immunotherapies used to fight cancer seem to cause autoimmune disorders. How does this happen? Melissa Lechner, MD, a UCLA assistant professor of medicine in the division of endocrinology, diabetes and metabolism, will be leading this project.

3) What are the mechanisms that create sex differences in endocrine autoimmune disorders? This project, funded by the NIH Office of Research on Women's Health, will be led by Su Willy Hugo, PhD, an adjunct assistant professor in the UCLA Department of Medicine, who will lead data analysis for the center. ❖

UCLA Launches Autoimmunity Center To Find Cures. Mirage, Oct. 12, 2024. Accessed at www.miragenews.com/ucla-launches-autoimmunity-center-to-find-cures-1335733.

Payment Complexity Demands Data Integrity

By Bonnie Kirschenbaum, MS, FASHP, FCSHP

ONE OF THE principles of highly reliable organizations is a sensitivity to operations.[1] Without a doubt, this can be applied to the very complex nature of healthcare payment with its myriad of workflows, ever-changing rules, processes and the overlay of technology that can, and often does, lead to workarounds. Staff simply finds a way of avoiding what they see as inefficiencies, annoyances or unwelcome changes, particularly if they don't agree with them.

But, expectations abound when new administrations bring new ideas and policy changes! Just days after the transfer of power, the new Department of Government Efficiency team has focused on the Centers for Medicare and Medicaid Services (CMS). Considering that the Department of Health and Human Services (HHS) controls hundreds of billions of dollars in annual payments to healthcare providers, it's inevitable that any search for fraud, waste or abuse of spend would target agencies such as Medicare and Medicaid. The Government Accountability Office (GAO), a nonpartisan watchdog, has concluded that Medicare and Medicaid represent more than 40 percent of improper payments across the federal government.[2]

"Both Medicare and Medicaid are susceptible to payment errors — over $100 billion worth in 2023," GAO wrote in April 2024.[3] They define improper payments as any payments that should not have been made or that were made in an incorrect amount, including overpayments and underpayments. Modern Healthcare reports that "Improper payments made through programs of [HHS], which ballooned during the COVID-19 pandemic, are on the decline but still amounted to more than five percent of outlays by the agency last year — or about $88.5 billion." Improper payments in Medicaid and Medicare Advantage have decreased since 2021, but problem payments in Medicare fee-for-service have increased, and improper payments in the Medicare prescription drug benefit program have seen a small increase since 2022.[4]

These billions of dollars in payments are the sum total of every transaction that all providers, pharmacies, healthcare facilities and organizations have submitted for payment. As such, following are things healthcare organizations should consider.

An Updated Drug Database

A living, active database of all medications, biologicals and products should be created that will be used in claims. Included should be the drug's name, strength, dosage, national drug code (NDC), healthcare common procedure coding system (HCPCS) code, billing unit and sell price. This data set is known as the charge description master (CDM) that should be linked to the drug dictionary or pharmacy drug master that populates the electronic health record so computerized provider order entries automatically create the charge posted on the claim. The CDM should be kept current by adding new items and deleting obsolete ones.

The NDC code is critical: The first set of numbers identifies the manufacturer, and the remaining numbers identify the drug and strength. It is essential to ensure that the manufacturer identified by the NDC code matches the product being purchased. Codes and billing units may change, as in the example provided in the table. Note that both the HCPCS code changes and the billing/service unit changes. Failure to update the CDM results in losing 90 percent of the revenue for the product! Therefore, these errors should be identified and eliminated:

1) Outdated CDMs. Update CDMs when the manufacturer and the product's NDC change. Keep the CDM in sync with what is being purchased.

2) Use of miscellaneous HCPCS

Table. HCPCS Code and Dose Descriptor/Billing Unit for Nplate

Service Dates	HCPCS Code and Dose Descriptor	Service/Billing Units	Billing Example
New coding effective 1.1.2025	J2802 Injection, romiplostim 1 mcg	1 service/billing unit = 1 mcg Nplate	500 mcg dose = 500 service units billed
Previous coding 12.31.2024 or prior	J2796 Injection, romiplostim 10mcg	1 service/billing unit = 10 mcg Nplate	500 mcg dose = 50 service units billed

codes rather than the drug-specific ones. Miscellaneous HCPCS codes should be reserved only for the very brief time that a drug is used before a HCPCS code has been assigned; it always must be accompanied by the NDC code.

3) Reusing CDM numbers for new products rather than creating new ones. Always create a new CDM for a new product.

Billing for Waste/Discarded Drug

CMS requires compliance with policies for drug waste billing. Therefore, organizations must ensure wasted product was actually wasted and not used in any other manner. CMS bills the manufacturer for the amount submitted in waste billing. Inaccurate descriptions and NDC numbers are subject to audit.

The 340B Program

The growth of the 340B program has outpaced its original provisions and often lacks transparency. Organizations should focus on potential areas of change. Several states have added legislation regulating use of the 340B program. It remains to be seen as to whether or not states can modify a federal program.

Facility Fees

Facility fees are intended to cover costs of maintaining medical facilities, including hospitals, physician offices and clinics, but costs often surprise patients because information is not transparent. The pending Primary Care and Health Workforce Act (S. 2840) is seeking to broadly restrict facility fees by blocking hospitals from charging health plans facility fees for many evaluation, management and telehealth services.

Site-Neutral Policies

Site-neutral payment refers to uniform care reimbursement regardless of care setting. Hospitals are actively opposed to this method, as it would lower their pay. It remains to be seen whether a site-neutral Medicare provision will be included in subsequent major healthcare packages that the Senate Finance Committee propose. However, commercial payers often mandate site of care, so organizations must ensure they know the payer for each patient and what the payers' stipulations are.

Claims Denials

Payers hold the keys to payments, and unfortunately, claim denials are rampant. Payers must appropriately plan and manage benefit coverage for high-investment drugs being used, as well as those in the pipeline. Their tools and tactics include prior authorization, bundled payments, attempting to move drug products from the medical into the pharmacy benefit, mandating treatment pathways or closed formularies, stipulating site of care and even creating risk-sharing collaborations.

It's important to incorporate a facility's agreed-upon payer contract terms into practice and policies. Denials prevention is more efficient than denials management, which often is the fruitless, time-and-resource-consuming quest to overturn denials and collect revenue. Prevention hinges on telling the patient's story completely and accurately with appropriate, codable documentation, including the medical necessity of the service and treatment. ❖

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Creating a Cybersecurity and Incidence Response Strategy for Small Offices

By Amy Scanlin, MS

CYBER ATTACKS cost billions of dollars each year, and small businesses are particularly vulnerable. A complicated and ever-changing array of security infrastructure threats requires dedicated and vigilant awareness of the risks and how-tos of mitigation. Costly investments in IT personnel and training, servers and software, cloud storage and email services, website and domain security can feel daunting. Fortunately, resource-rich, yet no-cost tools can help guide small businesses in developing cybersecurity resilience, helping them develop a detailed cybersecurity plan and create a cyber incidence response, so if an attack happens, corrective actions can minimize damages.

Gaining Cybersecurity Resilience

Cybersecurity resilience begins at the top with the decision to invest in the most effective infrastructure possible and to ensure employees at every level are active participants in protecting the business.

The leading causes of small business data breaches are employees and communication flow. Visiting a malicious website or clicking on an infected link can expose businesses to costly threats and liabilities. As such, a cybersecurity plan must include employee resilience and continuous training to identify and avoid the pitfalls of scammers, phishers and the many types of malware that can infect businesses.

A Department of Homeland Security (DHS)/Carnegie Mellon University partnership offers a self-administered or DHS-conducted, non-technical assessment that helps businesses gauge their own cybersecurity strengths and weaknesses. To access the DHS/Carnegie Mellon tool, visit the Cybersecurity & Infrastructure Security Agency website at cisa.gov, then click on Resources & Tools, Services and Cyber Resilience Review.

The Federal Trade Commission's (FTC) website is also full of resources that help small businesses and their employees understand and identify risks. The site provides training videos such as "Scams and Your Small Business" and quizzes such as "Defending Against Ransomware and Cybersecurity" that use real-world situations that can start discussions and create opportunities to highlight internal challenges, concerns and solutions. To access the FTC training tools, visit FTC.gov, then click on Advice and Guidance, Business Guidance, For Small Business and then Cybersecurity. DHS also provides employee training resources called Stop.Think.Connect., accessible at www.stopthinkconnect.org.

Developing or Strengthening a Cybersecurity Plan

A well-thought-out and detailed cybersecurity plan is a central concern for any business. From protecting employee personal data, patient health information, customer payment methods and so much more, many crucial decision points help to safeguard multiple types of data. So, when developing and implementing a cybersecurity plan, it's time to call in the experts.

Data is most at risk when it is on the move: uploading and downloading from a cloud-based server, when emails and their associated attachments are beaming from one location to another, when patients and employees are logging into portals remotely, etc. All of these entry points are opportunities for hackers to access sensitive business, personal, personnel and medical information.

Common-sense security is layered with up-to-date software, antivirus software, firewalls, passwords, multi-factor

authentication and encryption. But, how should businesses configure networks to ensure maximum protections? The front door of any cybersecurity protection plan is the Internet connection. An internal company network must differ from a public-facing Internet and should employ all the aforementioned layered security mechanisms. It should also be accessible only by specific allowed devices and users while ensuring that business operations can be conducted effectively.

A company server is one of the most vulnerable pieces of a digital footprint. Therefore, cybersecurity professionals recommend using cloud storage and email solutions versus on-site solutions. You may wonder why data is at risk when it is on the move. The reason lies in IT expertise. Wherever data is stored and transmitted, dedicated staff must continually monitor for software updates, vulnerabilities and red flags that company data has been accessed by bad actors. Responding in the event of a cyber incident so that infected areas are contained and malware is prevented from spreading requires skill. Outsourcing IT expertise is one area that is generally more effective from a cost and skill standpoint.

There is a lot to consider when designing and implementing an appropriate cybersecurity plan. The Federal Communication Commission's Small Biz Cyber Planner offers customizable cybersecurity plans that include details on these types of information and topical areas such as privacy and data security, securing mobile devices, credit card payment portals and more at fcc.gov/cyberplanner. This is a great starting point to understanding how to communicate needs and expectations to an IT professional.

A cybersecurity plan must also include an ongoing assessment of cyber hygiene and vulnerability risks. CISA offers a free cyber hygiene vulnerability service that can help. Learn more by visiting cisa.gov, then type "Cyber Hygiene Services" into the search bar.

Creating a Cyber Incidence Response Plan

Despite the best-laid plans, unfortunately, sometimes the unthinkable happens. Preparing for a cyber incident by putting procedures into place can limit potential damages. Businesses can do the hard work up front using the FCC Small Biz Cyber Planner and CISA's Cyber Guidance for Small Businesses (cisa.gov/cyber-guidance-small-businesses) and then working with an IT professional to develop a plan unique to the business. The plan should be kept in writing, and should be reviewed and practiced often.

As part of the cyber incidence response plan, businesses can connect in advance with applicable law enforcement, including local and FBI representatives. CISA regional offices also provide protective security advisors, cybersecurity advisors, emergency communications division coordinators and others who help companies plan and respond to cyber incidents. It's beneficial to document contact information for these helpful resources upfront and include it in the cyber response plan.

Next, roles and responsibilities should be assigned for the whos and hows of a cyber incidence response. An incident manager should be at the helm of response coordination to handle communication flow and delegate tasks to ensure pieces fall into place. A technical manager (TM) will be the subject matter expert who knows the whats and wheres of sensitive company data. The TM will also work with any outside technical experts to limit data exposure, address vulnerabilities and bring systems back online, including eradication of the unauthorized intrusion and software and data recovery with a clean reinstallation. The communications manager will be the public face of the incidence response, speaking with reporters, stakeholders and other interested parties.

Because responding to a cyber incident is stressful, as much work as possible should be performed ahead of time so the entire focus can be on identifying, stopping and correcting vulnerabilities. Following the incident resolution, the cyber incidence response team should review the response and improve procedures in case a similar incident happens in the future.

Experts Are Out There; Use Them

The resources provided here offer great starting points to learn about cybersecurity and to begin planning for protecting small businesses. By learning more about the complicated world of cybersecurity, business owners will be better able to work with IT professionals to ensure their businesses are understood and their security needs are met.

While these resources are not a substitute for a dedicated IT professional, they do provide the fundamentals of assessing vulnerabilities, designing robust cybersecurity plans and responding to a cyber incident. Together, these important safeguards will provide the best possible chance of staying ahead of the curve. Use these resources and others like them to create the most robust cybersecurity plan for your business. ❖

AMY SCANLIN, MS, is a freelance writer and editor specializing in medical and fitness topics.

Research

RSV Vaccine Prompts Robust Response in Older Recipients

Findings of a Phase III randomized controlled trial showed Pfizer's RSV Prefusion F (RSVpreF) vaccine triggered strong immune responses among people aged 60 years and older during its first two seasons.

The RENOIR (RSV vaccine efficacy study in older adults immunized against RSV disease) study led by a research team at the University of Rochester and RSV vaccine manufacturer Pfizer randomly assigned a subset of participants in the United States and Japan in a 1:1 ratio to receive one dose of the vaccine or a placebo. The vaccine, sold under the brand name Abrysvo, contains molecules called antigens designed to produce an immune response against RSV-A and RSV-B. It is approved for preventing RSV infection in adults aged 60 years and older, those aged 18 to 59 at increased risk for severe illness and infants through maternal vaccination.

The immunogenicity subset was made up of 1,151 participants, and the evaluable immunogenicity population included 1,067. The median participant age was 67 years, 62.6 percent of whom were aged 60 to 69 years, 5.5 percent of whom were aged 80 and older, 51 percent of whom were men, 80 percent of whom were White, 12 percent of whom were Black, 41 percent of whom were Hispanic and 52.3 percent of whom had at least one high-risk chronic condition.

The investigators collected blood samples from participants before and one month after vaccination and before the second RSV season from August 2021 to December 2023. One month after vaccination, the geometric mean fold rise (GMFR) in levels of neutralizing antigens was 12.1 for RSV-A and -B. Geometric mean titers declined at the second preseason visit but stayed substantially higher than baseline (4.7). One month postvaccination, GMFRs for neutralizing responses were 12.0 to 13.0 for subgroups stratified by age group.

In the RSVpreF group, proportions of participants with immune responses were higher one month postvaccination (RSV-A, 84.3 percent; RSV-B, 85.6 percent) than at the preseason-2 visit (59.4 percent and 57.5 percent, respectively) and much higher than placebo (less than 3.0 percent and less than 7.7 percent, respectively, at any timepoint). RSV-A and -B GMFRs in participants with selected chronic conditions were generally comparable to those of their otherwise healthy peers (range, 11.4 to 14.4). The vaccine also showed a favorable safety profile during both seasons, with 6.2 percent of RSVpreF and 6.1 percent of those in the placebo group reporting a serious adverse event.

According to the researchers, these data from the RENOIR study continue to support vaccination of older adults with bivalent RSVpreF to prevent RSV illness from both RSV-A and RSV-B subgroups. ❖

Van Beusekom, M. RSV Vaccine Prompts Robust Immune Response in Older Recipients Over 2 Seasons. University of Minnesota, Feb. 17, 2025. Accessed at www.cidrap.umn.edu/respiratory-syncytial-virus-rsv/rsv-vaccine-prompts-robust-immune-response-older-recipients-over-2.

Vaccines

GSK's Penmenvy Meningococcal Vaccine Approved by FDA

GSK's Penmenvy (meningococcal groups A, B, C, W and Y vaccine) has been approved by the U.S. Food and Drug Administration (FDA) for use in individuals aged 10 through 25 years. The vaccine targets five major serogroups of Neisseria meningitidis, which commonly cause invasive meningococcal disease (IMD). The vaccine combines the antigenic components of GSK's two well-established meningococcal vaccines, Bexsero (meningococcal group B vaccine) and Menveo (meningococcal [groups A, C, Y and W-135] oligosaccharide diphtheria CRM197 conjugate vaccine).

Approval was supported by positive results from two Phase III trials [NCT04502693; NCT04707391] that evaluated the vaccine's safety, tolerability and immune response in more than 4,800 participants aged 10 to 25 years. The safety data demonstrated that the vaccine has a safety profile consistent with GSK's licensed meningococcal vaccines.

"We are excited about the opportunities ahead to help improve meningococcal vaccination coverage in the United States, especially for IMD caused by serogroup B," said Tony Wood, chief scientific officer at GSK. "Building on our global leadership in meningococcal vaccination and our longstanding commitment to address unmet need in disease prevention, we aim to help protect more teens and young adults at a life stage when they are at an increased risk."

According to GSK, integrating GSK's MenABCWY vaccine into healthcare provider practices could simplify meningococcal vaccination delivery and help protect more U.S. adolescents against these five common disease-causing serogroups for which the Centers for Disease Control and Prevention has issued recommendations. ❖

Penmenvy, GSK's 5-in-1 Meningococcal Vaccine, Approved by US FDA to Help Protect Against MenABCWY. GSK press release, Feb. 15, 2025. Accessed at www.gsk.com/en-gb/media/press-releases/penmenvy-gsk-s-5-in-1-meningococcal-vaccine-approved-by-us-fda-to-help-protect-against-menabcwy.

Vaccines

FDA Approves Chikungunya Vaccine

The U.S. Food and Drug Administration (FDA) has approved VIMKUNYA (chikungunya vaccine, recombinant) for injection, the first virus-like particle (VLP) single-dose chikungunya vaccine in the U.S. for persons 12 years of age and older.

Approval was based on results from two Phase III clinical trials that enrolled more than 3,500 healthy individuals 12 years of age and older. The studies met their primary endpoints, with results showing that 21 days after vaccination, the vaccine induced neutralizing antibodies in up to 97.8 percent of the vaccinated individuals and demonstrated a rapid immune response starting to develop within one week. The vaccine was well-tolerated, and vaccine-related adverse events were mainly mild or moderate in nature. VIMKUNYA is a VLP vaccine, which means that it uses virus-like particles designed to mimic the chikungunya virus without the ability to infect cells, replicate or cause disease.

"The approval of our chikungunya vaccine is a testament to our unwavering commitment to addressing unmet medical needs and protecting communities worldwide," said Paul Chaplin, president and CEO of Bavarian Nordic. "As climate change continues to expand the reach of mosquito-borne illnesses like chikungunya, this milestone underscores the importance of cutting-edge solutions to safeguard travelers and vulnerable populations. We are proud to provide the first vaccine specifically approved for the prevention of chikungunya virus in individuals aged 12 and over, offering a critical tool to combat this emerging and growing health challenge."

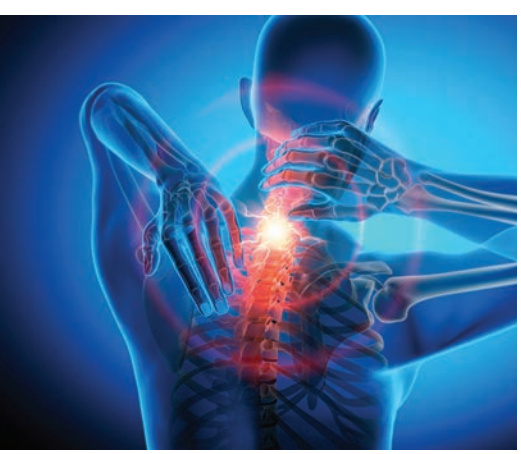
Concurrent with the approval, FDA awarded Bavarian Nordic a priority review voucher under the Tropical Disease PRV program, which the company intends to monetize when appropriate.

Bavarian Nordic aims to provide commercial availability of VIMKUNYA in the U.S. in the first half of 2025. ❖

Bavarian Nordic Receives U.S. FDA Approval of Chikungunya Vaccine for Persons Aged 12 and Older. Bacarian Nordic press release, Feb. 14, 2025. Accessed at www.bavarian-nordic.com/media/media/news.aspx?news=7053.

Medicines

FDA Approves New Medication for Acute Pain



The U.S. Food and Drug Administration (FDA) has approved Vertex Pharmaceuticals' Journavx (suzetrigine), a new type of prescription pain medication for adults to treat moderate to severe acute pain. This first class non-opioid pain medication, which does not have addictive properties (unlike opioids often used for this type of pain) is the first to be approved by FDA in more than 20 years. Journavx works by inhibiting the NaV1.8 pain signal in the peripheral nervous system, a channel that is not expressed in the brain or anywhere else in the central nervous system, which is why it does not have addictive properties like opioids.

Approval was based on two clinical trials that found Journavx to be as similarly effective as hydrocodone, an opioid pain medication, for reducing acute pain, with the added benefit of being a non-opioid and non-addictive drug. One trial that tested the medicine in adults between ages 18 and 80 found it reduced moderate to severe acute pain for adults from baseline by about 50 percent in 48 hours. The average time to meaningful pain relief ranged from two to four hours, compared to eight hours in the placebo group. In another clinical trial, the drug was tested in patients with a broader range of surgical and non-surgical acute pain conditions and was found to be safe and effective, with more than 80 percent of patients rating Journavx as a good, very good or excellent pain medication when investigating multiple acute pain types.

"Today's approval is an important public health milestone in acute pain management," said Jacqueline Corrigan-Curay, JD, MD, acting director of the FDA's Center for Drug Evaluation and Research. "A new non-opioid analgesic therapeutic class for acute pain offers an opportunity to mitigate certain risks associated with using an opioid for pain and provides patients with another treatment option."

The drug cannot be used with certain other drugs that strongly inhibit a certain enzyme in the liver, so some people may not be able to take Journavx, depending on what other medications they are taking. Grapefruit should also be avoided while taking Journavx. ❖

Kobern, J, and Kekatos, M. FDA Approves New Type of Non-Opioid Pain Medication, 1st of Its Kind in More Than 20 Years. Yahoo News, Jan. 30, 2025. Accessed at www.yahoo.com/news/fda-approves-type-non-opioid-232833936.html.

Medicines

New Biosimilar Autoimmune Disease Treatment Approved by FDA

Celltrion's Avtozma (tocilizumab-anoh), a biosimilar to Actemra (tocilizumab), in both intravenous (IV) and subcutaneous (SC) formulations, has been approved by the U.S. Food and Drug Administration. Avtozma, formerly known as CT-P47, is an interleukin-6 receptor antagonist indicated for the treatment of adults with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs; adults with giant cell arteritis; patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis or active systemic juvenile idiopathic arthritis; and hospitalized adult patients with COVID-19 who are receiving systemic corticosteroids and require supplemental oxygen, noninvasive or invasive mechanical ventilation or extracorporeal membrane oxygenation.

Approval was based on a Phase III study that demonstrated the product is highly similar to Actemra. The trial evaluated the efficacy and safety of tocilizumab-anoh with reference tocilizumab (r-TCZ) in 471 patients with moderate to severe active rheumatoid arthritis. Study participants were randomly assigned 1:1 to receive tocilizumab-anoh or r-TCZ intravenously every four weeks through week 20 in the first treatment phase. In the second treatment phase prior to week 24, those who received r-TCZ were re-randomized to either maintain treatment or switch to tocilizumab-anoh until week 48. The coprimary endpoints were the mean change from baseline in disease activity score 28 using erythrocyte sedimentation rate (DAS28-ESR) at week 12 and week 24.

Findings showed the estimated treatment differences in DAS28-ESR were -0.01 and -0.10 at week 12 and 24, respectively. Additionally, comparable pharmacokinetics, safety and immunogenicity were observed between the biosimilar and reference product. There was also sustained efficacy and no safety issues when switching from r-TCZ to tocilizumab-anoh.

"Introducing both IV and SC formulations of Avtozma provides flexibility and a wider range of treatment options," said Thomas Nusbickel, chief commercial officer at Celltrion USA. "This approval represents a strategic addition to our immunology portfolio, further strengthening our commitment to delivering accessible and high-quality treatment options for patients and healthcare providers." ❖

Kang, J. FDA Approves Tocilizumab Biosimilar Avtozma. Medical Professionals Reference, Jan. 31, 2025. Accessed at www.empr.com/news/fda-approves-tocilizumab-biosimilar-avtozma.

Research

Grifols Receives $21M to Study Parkinson's Plasma Samples

Grifols has received $21 million from the Michael J. Fox Foundation to fund a pilot study analyzing the company's repository of longitudinal Parkinson's disease (PD) plasma samples in hopes of developing an early-warning system for the emergence of PD. The pilot program Chronos-PD will cover a period of up to 10 years and is aimed at tracking how distinct plasma proteins evolve over time in people with PD.

"Going back in time to search for the earliest signs of PD, even before symptoms appear, has potential to revolutionize PD management," stated Grifols Chief Scientific Innovation Officer

Jörg Schüttrumpf, MD. "The hope is to accelerate and ultimately develop new diagnostics and disease-modifying therapeutics that could mitigate or even prevent the condition from manifesting itself. Our vision is that this platform continues to grow in terms of knowledge, partnerships and its ability to help society advance in fighting some of the world's most pressing public health challenges."

Operating 390 plasma collection centers in North America and around the world, Grifols has collected more than 100 million biospecimens representing thousands of disease states, including PD. Grifols' subsidiary Alkahest will lead the initiative using artificial intelligence and integrative analysis of multiomics and real-world data. ❖

Grifols Scores $21M for Parkinson's Plasma Sample Analysis. LabPulse, Jan. 14, 2025. Accessed at www.labpulse.com/research-and-development/funding/article/15712038/grifols-scores-21m-for-parkinsons-plasma-sample-analysis.

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Research

Multiple Myeloma Patients Treated with Teclistamab May Benefit from IVIG Supplementation

Results of a recent study show patients with multiple myeloma (MM) undergoing teclistamab therapy may benefit from primary intravenous immune globulin (IVIG) supplementation, which appears to reduce the risk of high-grade infection. Furthermore, IVIG may benefit patients receiving this therapy within the 30 days leading up to data cutoff.

Data from patients who received at least one dose of teclistamab at one of four academic centers in the U.S. were included in the study. The authors distinguished between primary and secondary IVIG; in the former, patients received IVIG within the first 60 days of initiating teclistamab, while in the latter, patients initiated IVIG prior to teclistamab. Patients who developed an infection prior to receiving IVIG, however, were classified as not receiving IVIG prophylaxis.

Overall, data from 168 patients were included. The median age of patients was 70 years, 25 percent of whom were African American, and the median number of prior therapy lines was five. Most (95 percent) patients received at least one prior stem cell transplantation. The median follow-up was 8.5 months. At this point, data showed that the median duration of teclistamab therapy was 4.6 months; the median number of prior therapy doses was five. Analysis showed that 42 percent of patients received IVIG, with 63 of these 71 patients receiving primary IVIG. The most common IVIG dosing schedule was 0.4 mg/kg every four weeks.

Results showed that 181 infections occurred in 92 patients, 53 percent of which were bacterial and 42 percent of which were viral; nine fungal infections were also noted in seven patients. Among the infections, 55 percent were grade 3 or worse and 57 percent required hospitalization. Analysis of data from the overall cohort showed that the three-month cumulative incidence for any infection was 43 percent, and the three-month incidence of grade 3 or worse infection was 23 percent.

Subgroup analysis suggested that patients who did not receive IVIG had a three-month cumulative infection incidence rate of 49 percent, whereas patients who received primary or secondary IVIG had three-month cumulative infection rates of 36 percent and 38 percent, respectively, though the difference was not significant.

Grade 3 or worse infections did, however, occur at a lower rate among patients who received primary IVIG (9.8 percent) than among patients who received secondary IVIG (38 percent) or no IVIG (32 percent).

Univariate analysis suggested, furthermore, that having had a last IVIG dose within the preceding 30 days to data cutoff reduced the risk of infection by approximately 0.59 compared with no IVIG. Other timescales in final dosing did not reach statistical significance.

According to the researchers, future studies are necessary to identify patients at highest risk of infections, allowing for more targeted IVIG therapy adjustments. ❖

Goodman, J. IVIG Supplementation May Reduce Risk of Infection Among Patients with Multiple Myeloma Receiving Teclistamab. Hematology Advisor, Jan. 27, 2025. Accessed at www.hematologyadvisor.com/reports/teclistamab-ivig-supplementation-reduce-risk-infection-treatment-risk.

Medicines

Triglyceride Drug Approved to Treat Adults with FCS

Tryngolza (olezarsen) has been approved by the U.S. Food and Drug Administration to be used with diet to reduce triglycerides (TG) in adults with familial chylomicronemia syndrome (FCS), a rare, genetic disorder that prevents the body from breaking down fats (TG) in the bloodstream. This is a first-in-class approval, meaning Tryngolza uses a new mechanism of action, or works differently in the body, than other therapies currently used to treat FCS. Tryngolza is injected subcutaneously (under the skin) once per month.

The efficacy and safety of Tryngolza were evaluated in a randomized, placebo-controlled, double-blind clinical trial (NCT04568434) in 66 adult patients with FCS and fasting TG levels of at least 880 mg/dL (the average baseline TG level was approximately 2600 mg/dL). The primary endpoint was percent change in fasting TG levels from baseline to month six (average of weeks 23, 25 and 27) compared to placebo.

The average percent change in TG from baseline to month six in the Tryngolza treatment group was -42.5 percent compared to the placebo group. Median percent and absolute changes in TG levels from baseline over time demonstrated a consistent lowering effect during the 12-month treatment period.

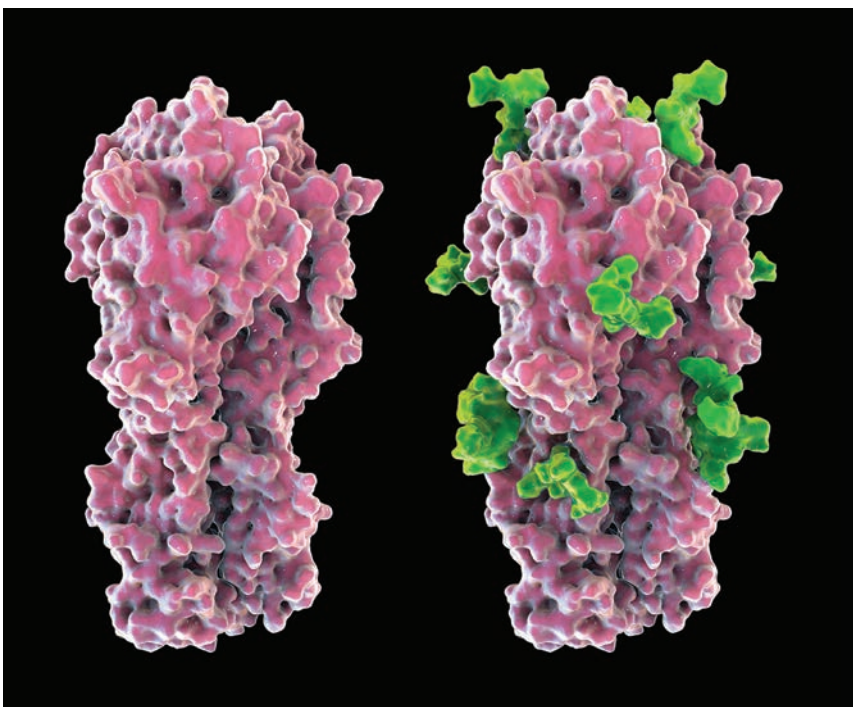
The most common adverse reactions in patients treated with Tryngolza were injection site reactions, decreased platelet count and joint pain or stiffness (arthralgia). ❖

FDA Approves Drug to Reduce Triglycerides in Adult Patients with Familial Chylomicronemia Syndrome. U.S. Food and Drug Administration news release, Dec. 19, 2024. Accessed at www.fda.gov/drugs/news-events-human-drugs/fda-approves-drug-reduce-triglycerides-adult-patients-familial-chylomicronemia-syndrome.

Research

Coupling HA Molecules from Various Flu Strains Could Make Vaccines More Effective

Seasonal influenza (flu) vaccines, which contain hemagglutinin (HA) molecules from various viral strains, have limited efficacy because most vaccinated people produce antibodies against only one of the vaccine strains. This "subtype bias" occurs either because prior exposure to a particular flu strain primes the immune system to respond to that strain later or variation in people's genes for key immune system components affects the vaccine response. But now, results from a recent study suggest coupling HA molecules from various flu strains could make flu vaccines more effective.



The researchers, who examined the relative contributions of these mechanisms to flu vaccine responses, aimed to use this information to develop a vaccine that could limit the biased response. They began by measuring flu vaccine responses in 39 pairs of identical twins. In most cases, the immune systems of both twins showed the same subtype bias to a seasonal vaccine. Yet they also showed signs of having been exposed to different flu strains in the past.

The researchers also studied the response to seasonal flu vaccine in 15 infants, aged 6 to 12 months, who had never been infected with flu before. Most of the infants still developed a subtype-specific antibody response. Together, these findings suggest that individual genetic variation might exert a larger role than prior virus exposure in driving subtype bias, although initial virus exposure also contributes to such bias.

B cells and T helper (TH) cells coordinate to produce antibodies against a virus. When a B cell finds a molecule, like HA, that it recognizes, it engulfs it and chops it up into fragments called peptides, which are displayed on its surface to activate TH cell support. The peptides are anchored to the cell surface by molecules called MHC-II. Variations in the genes for MHC-II molecules can affect which peptides are displayed. HA from one flu strain may have more peptides that can be displayed on a B cell than other strains, which could lead some B cells to get more TH cell support than others, and hence bias antibody production toward that strain.

To reduce bias in TH activation, the researchers linked together HA molecules from up to four different subtypes before vaccination so a B cell that recognized any one of the individual HAs would engulf all of them. Then, they reasoned, the different B cells would be able to display the same set of peptides and activate TH cell support equally well.

As expected, mice vaccinated with a mixture of unlinked antigens developed a clear subtype bias. But mice vaccinated with the linked HAs produced equal amounts of antibodies against all the subtypes tested. Similar results were obtained in organoids grown from human tonsil tissue — a laboratory model that generates an immune response.

The researchers also tried coupling an avian flu HA with the seasonal flu HA. This construct elicited a stronger immune response in the tonsil organoids than the avian flu HA did on its own.

"Overcoming subtype bias this way can lead to a much more effective influenza vaccine, extending even to strains responsible for bird flu," said Mark Davis, PhD, at Stanford University School of Medicine who led the research. "The bird flu could very likely generate our next viral pandemic." ❖

National Institutes of Health. Building a Better Flu Vaccine, Jan. 14, 2025. Accessed at www.nih.gov/news-events/nih-research-matters/building-better-flu-vaccine.

Diagnostics

Blood Test Can Predict How Long Vaccine Immunity Will Last

A study led by researchers at Stanford Medicine has shown that variation in vaccine durability can, in part, be attributed to a type of blood cell called megakaryocytes, typically implicated in blood clotting. In the study, Bali Pulendran, PhD, a professor of microbiology and immunology, and colleagues, initially studied an experimental H5N1 bird flu vaccine given with an adjuvant — a chemical mixture that enhances the immune response to an antigen but, on its own, does not induce an immune response. The researchers followed 50 healthy volunteers who received either two doses of the bird flu vaccine with the adjuvant or two doses without the adjuvant. They collected blood samples from each volunteer at a dozen time points over the first 100 days after vaccination and carried out in-depth analyses of the genes, proteins and antibodies in each sample. Then, they used a machine-learning program to evaluate — and find patterns within — the resulting dataset.

The program identified a molecular signature in the blood in the days following vaccination that was associated with the strength of a person's antibody response months later. The signature was mostly reflected in tiny bits of RNA within platelets — small cells that form clots in the blood. Platelets are derived from megakaryocytes, cells found in the bone marrow. Platelets, when they break off megakaryocytes and enter the bloodstream, often take small pieces of RNA from the megakaryocytes with them. While researchers can't easily track the activity of megakaryocytes, platelets carrying RNA from megakaryocytes act as proxies. "What we learned was that the platelets are a bellwether for what is happening with megakaryocytes in the bone marrow," Dr. Pulendran said.

To confirm whether megakaryocytes were affecting vaccine durability, Dr. Pulendran's research group simultaneously gave mice the bird flu vaccine and thrombopoetin, a drug that boosts the number of activated megakaryocytes in the bone marrow, which led to a six-fold increase in levels of anti-bird flu antibodies two months later. Further experiments showed that activated megakaryocytes produce key molecules that increase the survival of the bone marrow cells responsible for making antibodies, or plasma cells. When these molecules were blocked, plasma cells survived less in the presence of megakaryocytes. "Our hypothesis is that megakaryocytes are providing this nurturing, pro-survival environment in the bone marrow for plasma cells," Dr. Pulendran said.

The scientists tested whether the trend held true for other vaccine types. They looked at previously collected data on the responses of 244 people to seven different vaccines, including vaccines against seasonal influenza, yellow fever, malaria and COVID-19. The same platelet RNA molecules — signs of megakaryocyte activation — were associated with longer-lasting antibody production for the various vaccines. The molecular signature could predict which vaccines lasted longer, as well as which vaccine recipients would have a longer-lasting response.

Dr. Pulendran and his colleagues plan to conduct studies that probe why some vaccines might spur higher levels of megakaryocyte activation in the first place. Those findings could help researchers develop vaccines that more effectively activate megakaryocytes and lead to more durable antibody responses. In the meantime, the scientists want to develop tests to determine, using their newly discovered molecular signature, how long a vaccine is likely to last. That could help speed up vaccine clinical trials — in which researchers often must follow people for months or years to determine durability — but also could yield personalized vaccine plans. ❖

William, S.C.P. Blood Test Can Predict How Long Vaccine Immunity Will Last, Stanford Medicine-Led Study Shows. Stanford Medicine News Center, Jan. 2, 2025. Accessed at med.stanford.edu/news/all-news/2025/01/test-immunity-last.html.

Research

Common Virus May Cause a Type of Alzheimer's

Researchers have discovered a link between a chronic gut infection caused by a common virus, known as cytomegalovirus (CMV), and the development of Alzheimer's disease in some people. CMV occurs in most people during childhood, but after the initial infection, the virus usually remains dormant in the body for life.

In the study, the researchers had access to a range of donated organ tissues, including the colon, vagus nerve, brain and spinal fluid, from 101 body donors, 66 of whom had Alzheimer's disease. This helped them study how the body's systems interact with Alzheimer's disease, which is often considered through a purely neurological lens. They traced the presence of CMV antibodies from donors' intestines, to their spinal fluid, up to their brains and even discovered the virus itself lurking within the donors' vagus nerves. This means CMV may have found a biological loophole where it can remain active long enough to travel to the gut-brain axis superhighway, known more officially as the vagus nerve. On arriving at the brain, the active virus has the potential to aggravate the immune system and contribute to the development of Alzheimer's disease. The same patterns showed up when they repeated the study in a separate, independent cohort.

Human brain cell models provided further evidence of the virus's involvement by increasing amyloid and phosphorylated tau protein production and contributing to neuron degeneration and death. Importantly, these links were found only in a very small subset of individuals with chronic intestinal CMV infection. Given that almost everyone comes into contact with CMV, simply being exposed to the virus is not always cause for concern.

"We think we found a biologically unique subtype of Alzheimer's that may affect 25 percent to 45 percent of people with this disease," biomedical scientist and lead author Ben Readhead from Arizona State University said. "This subtype of Alzheimer's includes the hallmark amyloid plaques and tau tangles — microscopic brain abnormalities used for diagnosis — and features a distinct biological profile of virus, antibodies and immune cells in the brain."

According to the researchers, this means antiviral drugs might be able to prevent some people from developing Alzheimer's, especially if researchers can develop blood tests to quickly detect active CMV infection in the gut. Readhead and his team are working to develop such a blood test so the CMV infection can be treated with antivirals, and perhaps prevent patients from developing this type of Alzheimer's. ❖

Cockerill, J. Scientists Discover Common Virus Could Be Causing a Type of Alzheimer's. Science Alert, Jan. 6, 2025. Accessed at www.sciencealert.com/scientists-discover-common-virus-could-be-causing-a-type-of-alzheimers.

Medicines

FDA Approves Zepbound to Treat Obstructive Sleep Apnea

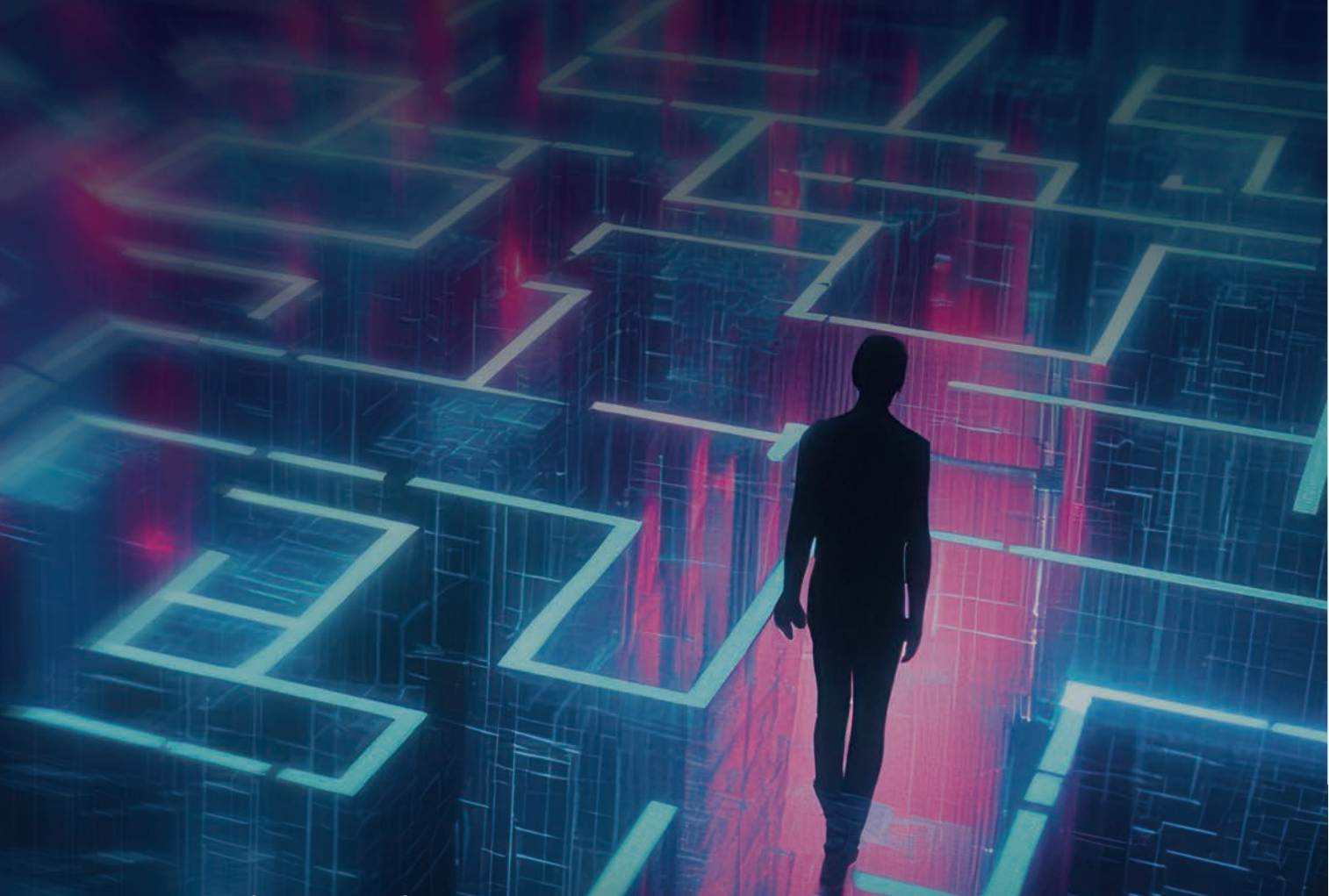
The U.S. Food and Drug Administration (FDA) has authorized the use of Eli Lilly & Co.'s Zepbound for adults with obesity and moderate to severe obstructive sleep apnea (OSA), a common condition in which a person struggles to breathe properly during sleep. It is the first prescription medication approved to treat obstructive sleep apnea.

Approval is based on studies that have shown that by aiding weight loss, Zepbound helps reduce sleep apnea symptoms in some patients. In two studies with adults who had obesity and moderate to severe OSA over a

52-week period, participants who received Zepbound experienced a "statistically significant and clinically meaningful reduction" in episodes of shallow breathing or temporary pauses in breathing while asleep compared to those who received a placebo, according to FDA. That was true for both participants who used a CPAP machine and those who did not.

"This is a major step forward for patients with obstructive sleep apnea," said Sally Seymour, MD, director of the Division of Pulmonology, Allergy and Critical Care in the FDA's Center for Drug Evaluation and Research. ❖

Kim, J. FDA Approves Weight Loss Drug Zepbound to Treat Obstructive Sleep Apnea. NPR, Dec. 21, 2024. Accessed at www.npr.org/2024/12/21/nx-s1-5236098/zepbound-sleep-apnea-approved-fda#.



Navigating the **Medical Misinformation Age**

When it comes to online health information, the Internet is a place where falsehoods flourish. Combating questionable content is no easy task, requiring education, legislation and diligence from stakeholders in the healthcare, scientific and public health communities.

By Trudie Mitschang

IN THE DIGITAL age, access to health-related content has never been easier. From social media platforms and celebrity-endorsed product testimonials to miracle cures sold on slick professional websites, information addressing health concerns can be acquired within seconds. Unfortunately, this vast availability of information comes with a significant drawback: the proliferation of medical misinformation.

Medical misinformation refers to false or misleading health-related content that is typically accessed and spread online. Inaccurate, misleading and blatantly fake information creates confusion, causes mistrust of health professionals and prevents people from getting the healthcare they need. Common topics rife with inaccuracies include inquiries about disease symptoms and treatments, vaccine efficacy and safety, and public health guidelines. Unlike disinformation, which is content that is deliberately false and shared with the intent to deceive, misinformation may be unwittingly accessed and unknowingly shared by individuals who have no malintent — they simply believe it to be true.

A 2023 survey conducted by the Kaiser Family Foundation (KFF)[1] found that when presented with a series of false statements regarding everything from COVID-19 vaccines to reproductive health, roughly half to three-quarters of survey participants were unsure whether each of the claims was true or false, describing many as "probably true." For example, when presented with the false statement: "More people have died from the COVID-19 vaccines than have died from the COVID-19 virus," at least 20 percent of respondents said it was definitely or probably true.

In a 22-page advisory about the dangers of inaccurate online health information,[2] U.S. Surgeon General Vivek Murthy, MD, MBA, warned that it has the potential to thwart public health initiatives. "Health misinformation is a serious threat to public health. It can cause confusion, sow mistrust, harm people's health and undermine public health efforts," he stated. "Limiting the spread of health misinformation is a moral and civic imperative that will require a whole-of-society effort." The advisory urged individuals to take personal responsibility for the spread of misinformation.

Of course, getting your patients to alter their online behavior is no easy task. "Once people start accessing and sharing misinformation online, it can be difficult for them to disengage because of the connections they form," said Deen Freelon, PhD, a computational social scientist and a professor at the University of Pennsylvania's Annenberg School for Communication.[3] "Information transfer is a highly social experience that offers a rush of positive feedback — even well-intended people fall into echo chambers where others reinforce their inaccurate information or harmful beliefs," he said.

The Role of Social Media

About a quarter of KFF survey participants said they used social media at least weekly to "find health information or advice." It's interesting to note that health misinformation differs from other forms of inaccurate online content, such as political opinions, in that health misinformation purveyors often stand to benefit financially by selling a product or service, often through social sites such as TikTok.

Of the people who regularly use the news aggregation and discussion site Reddit, one in six say they "have a lot of trust" in the health and medical information found there. Weekly TikTok, YouTube and X users also expressed a lot of trust in the health information they see on those platforms.[3] From a demographic perspective, young adults tend to be at a higher risk for believing false information accessed via social media. In one Canadian survey,[4] 73 percent of 18- to 25-year-olds reported following at least one social media influencer who promotes anti-science views.

In a 22-page advisory about the dangers of inaccurate online health information, U.S. Surgeon General Vivek Murthy, MD, MBA, warned that it has the potential to thwart public health initiatives.

A recent review of 69 studies of health misinformation on social media sought to identify the main health misinformation topics and their frequency on different social media platforms.[5] The studies surveyed used a variety of research methods, including social network analysis, evaluation of content, evaluation of quality, content/text analysis and sentiment analysis. Researchers concluded that the incidence of health misinformation was highest on X, especially regarding the use of tobacco and other drugs, with some studies citing 87 percent of such posts containing misinformation. Health misinformation about vaccines was also a trending topic, with around 43 percent of posts containing misinformation. It also uncovered that most frequently discussed topics were regarding vaccination and infectious diseases, including Ebola and the Zika virus. Other topics such as nutrition, cancer, water fluoridation and smoking were also prevalent.

Combating this type of activity online is complex. The very nature of social media allows users to self-curate their feeds and content, which means that those who follow anti-vaccine content, for example, are much more likely to be flooded with similar content based on automated algorithms. These algorithms in turn reduce the likelihood that individuals who regularly consume misinformation will be exposed to content that contradicts the prevailing viewpoints of their social media network. Additionally, there is the very human tendency toward confirmation bias — our penchant for believing and sharing information that agrees with our existing beliefs — that makes any attempt at debunking misinformation ineffective and even counterproductive. That's why

online debates about hot topics like vaccine safety quickly escalate into heated debates and arguments.

"Most myths actually don't survive. It's really just a few that get pushed and pushed and pushed that do survive," said Lisa Singh, PhD, a professor of computer science and public policy at Georgetown University and the director of the Massive Data Institute at the McCourt School of Public Policy. "As misinformation circulates, it becomes more familiar and starts to feel 'more real and true.' Moreover, if myths align with people's core beliefs or feelings, or are promoted by sources they trust, there is a greater chance they will be accepted."[6]

illnesses and deaths that could have been prevented.

To address these challenges, Brian Southwell, PhD, adjunct professor in the Department of Medicine at Duke University School of Medicine is engaging with other researchers, medical professionals and organizations to tamp down medical misinformation.[6] "Misinformation itself has become a buzzword. We sometimes use the term without really thinking about what it means, but belief in false claims can lead to real harm if it undermines trust in established medical practices and institutions," he explained.

Incorrect information about health and disease prevention has led people to make dangerous decisions about their treatment and care, engage in harmful practices, avoid beneficial and lifesaving preventions and otherwise put themselves and others at risk.

The Erosion of Trust in Medical Science

The effects of healthcare misinformation can be profound and far-reaching, impacting individuals, families, healthcare institutions and entire communities. Incorrect information about health and disease prevention has led people to make dangerous decisions about their treatment and care, engage in harmful practices, avoid beneficial and lifesaving preventions and otherwise put themselves and others at risk. The results include avoidable clinic and hospital admissions, billions of dollars in additional healthcare costs, needless

Dr. Southwell, along with Nadine Barrett, PhD, associate professor in family medicine and community health, is working with the National Academy of Science, Engineering and Math (NASEM) committee on understanding and addressing misinformation about science. That eventually will result in a consensus report on the scope and consequences of misinformation about science. "As we look across the country, we see a lot of headlines about misinformation in health and medicine," Dr. Southwell added. "We need better engagement and widespread collaboration between many different types of organizations. Duke is helping to provide that."[6]

Trust also plays a central role in health communication, and research shows that formally trained healthcare professionals and scientists do garner ample public trust. According to 2023 data from the Pew Research Center, 77 percent of U.S. adults trust medical scientists to act in the public's best interest — the highest rating given to any group or institution in society. By contrast, elected officials were the least trusted, with just 24 percent of U.S. adults expressing the same degree of confidence.[7]

That said, trust can also be exploited by healthcare professionals who share or recommend false healthcare information. One recent example is when Joseph Ladapo, MD, PhD, the surgeon general of Florida, shared a far right-wing website article claiming that mRNA COVID-19 vaccines have "deadly side effects." The article, which was originally published on a site with a history of promoting false claims and conspiracy theories, cited unverified Vaccine Adverse Event Reporting System data and quoted a controversial writer known for promoting anti-vaccine conspiracies.[8] In the piece, the surgeon general called the Centers for Disease Control and Prevention (CDC) "unethical" for continuing to recommend COVID-19 vaccines. Some responses to the post questioned the credibility of the article and its source, while others thanked Dr. Ladapo for speaking out.

In response, several U.S. health agencies drafted and published a letter signed by U.S. Food and Drug Administration (FDA) Commissioner Robert Califf, MD, and CDC Director Rochelle Walensky, MD, MPH, stating: "It is the job of public health officials around the country to protect the lives of the populations they serve, particularly the vulnerable. Fueling vaccine hesitancy undermines this effort."[9]

Staying Safe in the Misinformation Age

In today's digital age, discerning fact from fiction is more difficult than ever before, but there are some safeguards that can be used to identify misinformation. When discussing healthcare claims, here are some best practices physicians can recommend to their patients:[10]

Verify the source. Not all websites, social media accounts or publications are credible. When accessing health-related information, be sure to check the credentials of the author or organization. Is the content created by a qualified healthcare professional or a recognized institution? Also, look for websites ending in .gov, .edu or those belonging to well-known health organizations like the World Health Organization (WHO) or CDC. Avoid sources that prioritize sensationalism over evidence.

Look for evidence-based information. Ensure that claims are supported by peer-reviewed studies or data from reputable journals. Also, be wary of anecdotal evidence or unverified testimonials, as they often lack scientific support. It's also a good idea to cross-check information with multiple trusted sources to ensure consistency.

Watch for red flags. Claims of a "miracle cure" or "secret solution" that mainstream medicine is hiding or statements that demonize entire groups of healthcare professionals or organizations are cause for concern. Also, watch for overly emotional language designed to instill fear or urgency.

Exercise caution on social media sites. Avoid sharing content unless you've verified its accuracy. Make it a habit to follow credible accounts of medical professionals and organizations.

Use trusted fact-checking tools. Websites like Snopes, FactCheck.org and HealthFeedback.org can review and debunk misleading claims.

Consult a healthcare professional. When in doubt, consult a doctor or a licensed healthcare provider. They can provide personalized advice and help patients interpret confusing or conflicting information. Patients should also avoid self-diagnosis based on online content, as it may lead to unnecessary anxiety or incorrect treatment.

While efforts to address online healthcare misinformation are underway, the problem is both widespread and persistent. Turning the tide against the onslaught of misleading content will require a multifaceted approach at both the public health and individual consumer levels. As we look to the future, healthcare institutions and public health agencies are tasked with:

- Promoting health literacy: Education campaigns should teach individuals how to critically assess online health information, including recognizing credible sources such as peer-reviewed journals and official health organizations.
- Strengthening platform policies: Social media companies must take responsibility for reducing the spread of false health information. This can include flagging or removing misleading content and amplifying verified information from trusted sources.
- Empowering healthcare professionals: Doctors, nurses and other healthcare workers should be trained to address patients' concerns about misinformation effectively and empathetically.
- Enacting legislation: Governments can enact laws to penalize the deliberate spread of harmful misinformation while balancing freedom of speech concerns.
- Community engagement: Engaging local communities and influencers in spreading accurate health information can increase its reach and acceptance.

Healthcare Professionals Play a Role

Navigating the sea of healthcare information available online can be overwhelming, and the general population's tendency to just "Google" unexpected aches, pains or symptoms has become an ingrained behavior for most. Healthcare professionals can encourage patients to apply critical thinking and use reliable resources to protect themselves from accessing misinformation and encouraging others to do the same. By prioritizing education, regulation and technological innovation, we can all create a safer and better-informed digital healthcare world. ❖

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Decatastrophizing Patient Fears

Your words, tone and body language can escalate patient fears, but they also have the power to ease anxiety and help patients cope.

By Meredith Whitmore

IF WE'RE brutally honest with ourselves, we've all acted like Henny Penny at some point in our lives. Like the frantic bird catastrophizing the end of the world in the classic children's book *Chicken Little*, we imagine the worst possible outcome when faced with something that could fundamentally change our lives. In stressful situations, it's difficult to regulate our emotions — and sometimes we're incapable of regulating them at all.

Unlike Henny Penny's fear, however, patients' fears *are* grounded in reality. Whether facing a routine checkup or major surgery — or even visiting a friend in a hospital setting — clinical environments and the unknown cause significant discomfort. For example, a blood draw *can* hurt, and waiting for a diagnosis or wondering if a treatment will work *is* nerve-wracking. Add to this discomfort a sterile, sometimes cold, tech-ridden environment and being touched by strangers who use "foreign" tools such as blood pressure cuffs, EKG wires, IV needles and betadine and it's no wonder patients struggle to keep their feelings in check. But your demeanor can help them ease their anxiety and move forward more calmly.

Fundamentals of Medical Anxiety

The fear of doctors, or iatrophobia, and "white coat syndrome" are real phenomena. In fact, experts estimate that 15 to 30 percent of patients whose blood pressure appears high in a clinical setting experience white coat syndrome.[1] But what, more specifically, is behind these patients' — and other patients' — fears? Reasons why patients catastrophize their fear are much more nuanced than merely being afraid of pain.

A patient survey by The Empathy Project, a program at New York

University's (NYU's) Langone School of Medicine, found that top patient fears are infection, incompetence, death, cost, medical mix-ups, needles, rude doctors and nurses, germs, diagnosis/prognosis, communication issues and loneliness.[2] The survey undoubtedly found more factors than physical discomfort. Most fundamentally, patient fears can ultimately be reduced to two realms: fear of loss of control (of body and lives) and fear of depersonalization.[2,3] As a provider, how can you help ease these fears?

What *Not* to Do

Looking at examples of what *not* to do is a good place to start. Examples of ways providers behave poorly help highlight ways you may be contributing to patient fears. Here are two patient stories shared with The Empathy Project to consider:

- Alicia Flaum, director of the CBS show "60 Minutes," shared the story of when her doctor informed her of a cancer diagnosis. "I went to my primary care physician, and my blood counts came back. One of them was low. He sent me to a hematologist, and eventually, after going through a couple of hematologists and a little bit of an ordeal, I was diagnosed with myelodysplastic syndrome. I said, 'How long will I be out of work?' And he said, 'Probably about six months. At least six months.' And I said, kind of to myself, but out loud, 'Gee, I hope they'll hold my job for me.' And he said to me, 'Well, I mean you've had a good run, right?'"[2] The doctor's words seemed to dismiss Flaum's understandable concerns.
- Social worker Jordana Schein-Levi experienced a lack of concern from physicians as well. During a crisis situation, several doctors explained what her newborn daughter's serious heart condition entailed and the procedures necessary to address it immediately. When they finished an efficient but cold explanation, the doctors left the room, leaving her feeling lost, apprehensive and incapable of thinking clearly.[2] "I didn't know what to do. I felt like, you know, 'Do I breathe? Do I move? Do I pick up the phone?' I didn't even know what questions to ask. I didn't know what half the words they used meant. And I was really frozen."[2] Schein-Levi's doctors gave her clinical information, but their lack of compassion made a difficult situation harder to deal with.

Put Yourself in Their Shoes

Part of developing a more helpful approach starts with realizing that you have been a patient yourself, or you certainly will be a patient in the future. Supporting your patients involves considering your own need for empathy and recognizing your patients need it too.

Top patient fears are infection, incompetence, death, cost, medical mix-ups, needles, rude doctors and nurses, germs, diagnosis/prognosis, communication issues and loneliness.

"Words matter. Tone matters," says Jon LaPook, MD, chief medical correspondent at CBS News and medical professor at New York University (NYU) School of Medicine.[2] What you say matters, but how you say it matters, too. Your attitude carries as much weight as your attention. As Dr. LaPook explains, "Empathy is when the doctor's not just in the room, but really with you. It should be at the core of everything we do in medicine."[2]

At The Empathy Project, instructors teach medical students to imbue their work with humanity and treat their patients as people, not just a diagnosis. "It's not about teaching empathy directly all the time, but reminding people to bring themselves to the work that they're doing," explains Richard E. Greene, MD, MHPE, medical professor at NYU. "I think the students who you don't always notice empathy in first think that they're going into medicine to be scientists [rather than caring professionals who invest in patients]."[2]

Certainly, learning how to balance empathy with professional distance is part of learning how to relate well to patients. "I think you become a master of being present and connected, but having that monologue in the back of your head that tells you what's appropriate and what's not appropriate," Dr. Greene says.[2] Empathy may not come naturally, but as Dr. LaPook and Dr. Greene explain, learning to be empathetic comes down to being your best self: "Who you are and the person you bring into the room is your most therapeutic tool in your arsenal. To show up and be present and to make eye contact and to listen and to not be afraid of the patient's reactions, of the patient's questions. And don't be afraid to say, 'I don't know.' And don't be afraid to say, 'I'm sorry.' And don't be afraid to be human in the room."[2]

Developing empathy also involves recognizing hidden thoughts and feelings

patients may have about their condition. For example, some patients might feel self-blame and condemnation because their personal habits and behaviors could have contributed to it. It might be difficult to avoid silently (or subconsciously) judging a patient for their poor health management, but your patients need your empathy to help them cope. Recognizing and understanding your thoughts about your patients and their situation can help you set aside your judgments and prioritize their feelings. Look at the situation through their eyes, and treat them the way you would want to be treated.

Patient fears can ultimately be reduced to two realms: fear of loss of control (of body and lives) and fear of depersonalization.

Your Words Have Weight

Schein-Levi's negative encounter caused her to think about what doctors *should* have said, and consider what the best way to deliver bad news to patients and their families might be. "There needs to be an awareness that you as a doctor are about to change someone's life," she says. "And whoever you [the recipient of bad news] were five minutes before those words come out the doctor's mouth, you're no longer that person. [Doctors] have got to have this awareness, that you are at the beginning of a very long journey in someone's life. You're the gatekeeper. The moment you say these words [of diagnosis, procedures and prognosis], you change their life. So you [the professional] gotta work at that."[2]

Schein-Levi described a more positive interaction with a different physician who was treating one of her other daughters that demonstrated an effective, professional and compassionate way of delivering difficult news. Instead of receiving cold, aloof comments that left Schein-Levi bewildered and afraid, this interaction helped her accept the circumstance and move forward with confidence. "So they called in one of the top docs to take a look at her," she explains, "and he came into my room and he said to me, 'You know, this can be OK. Hi. I'm Dr. So-and-So. Let me tell you what I'm doing here, and let me tell you what I think's going on with your daughter.' And I was so struck by the fact that he was willing — and I use this language only because it was my sense that he took a risk that other people weren't willing to. That they thought, somehow, by talking to me in a way that you would talk to a friend or just not start off with the clinical piece, but human to human, and take the risk of saying, 'Hey, this can be OK.' He wasn't promising me that she would be cured, or that my life would be wonderful. He was saying to me: Sometimes in life, even bad things can be OK because you as a human being can deal with it. And I was so struck by that, that he was willing to do that. It didn't in any way diminish his clinical expertise or anything that was going to happen from that moment forward. And he had me. And I trusted him."[2]

Flaum had a more positive experience that helped her move forward as well. After asking doctors many questions, watching her healthcare team seemingly evade questions and finally receiving answers she could not understand, a different doctor extended humility and compassion that comforted her. Flaum explains that this doctor took the time to explain the complex series of tests Flaum would need and why she would need them, and when the doctor saw her struggling to understand, said, "You know what? We don't really understand it either."

"And I loved that," Flaum said. "I thought that was so honest and great, and I've really come to love her."[2]

Putting It All Together

No one wants to face difficult news only to be devalued, ignored or dehumanized, and fear can quickly escalate when patients aren't treated with some measure of compassion when they seek medical care. Engendering a level of deep trust in patients, whether you are a physician, nurse or any other healthcare provider, should always be one of your professional goals. Your support and empathy help patients cope and recover faster. Make the effort to grow in empathy. Adjust your thinking and behavior, if necessary, to reflect who you are — and who you want to be as a professional. You alone have the power to continue to improve your skills accordingly, and it's an exceptionally worthy endeavor. ❖

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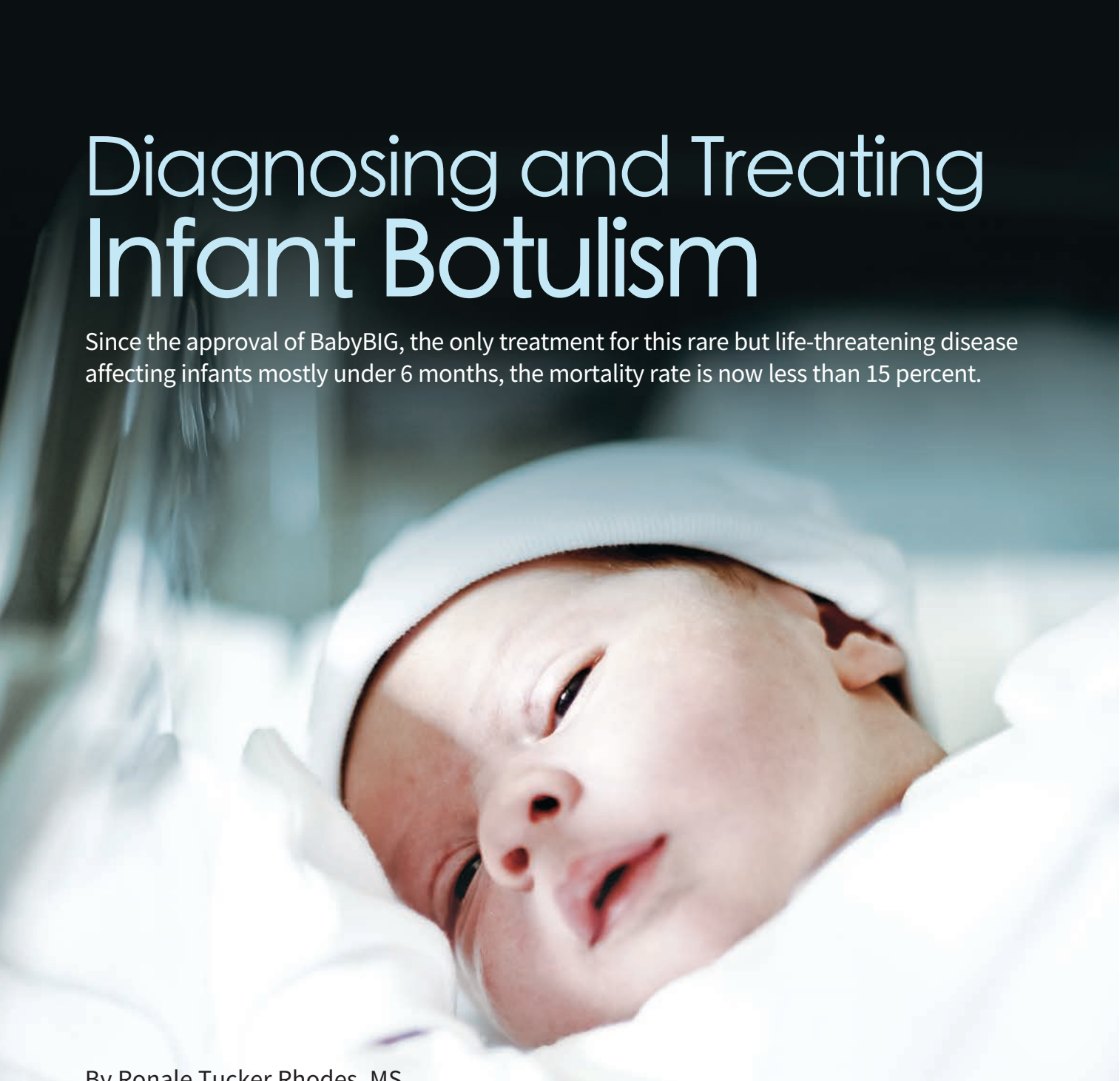
Diagnosing and Treating Infant Botulism

Since the approval of BabyBIG, the only treatment for this rare but life-threatening disease affecting infants mostly under 6 months, the mortality rate is now less than 15 percent.



By Ronale Tucker Rhodes, MS

INFANT BOTULISM occurs globally and is now the most common form of human botulism in the United States.[1] According to a *StatPearls* continuing education activity published in 2023 that reviewed the causes, pathophysiology and presentation of infant botulism, this rare disease is responsible for approximately 70 percent of all new botulism cases a year. In the United States, 1.9 of 100,000 live births yield approximately 77 new cases annually, and there is an equal distribution of males and females. However, Hispanics and Asian families have a higher incidence of infant botulism because of their use of herbal medications and raw honey.[2]

In 2019, the most recent statistics available in the U.S., state and local health departments reported de-identified data about 152 confirmed cases of infant botulism to the Centers for Disease Control and Prevention (CDC) through the National Notifiable Diseases Surveillance System, all of which were laboratory-confirmed. Fortunately, no deaths were reported. The median age of infants was 4 months (range 2 weeks to 10 months), 57 percent (87) of whom were male.[3] Mostly, infant botulism

occurs in babies younger than 6 months.[4]

The disease was first recognized in 1976 by Stephen Soulé Arnon, MD, and colleagues after Dr. Arnon received a call about a paralyzed infant from Salinas, Calif. Through epidemiological and laboratory investigation, they collected the novel evidence that the baby's digestive tract was colonized with Clostridium botulinum (C. botulinum), the bacterium that produces an exceptionally potent neurotoxin. As additional infants with acute weakness in California were detected throughout 1976, Dr. Arnon and his co-discoverers named the condition infant botulism, in contrast to botulism resulting from contaminated food or wounds.[5]

What Is Infant Botulism?

Infant botulism is an intestinal toxemia that results after spores of the bacterium C. botulinum or related species are swallowed and temporarily colonize an infant's large intestine and produce botulinum neurotoxin. The neurotoxin binds to cholinergic nerve (nerves involved in motor control, including the muscles in the face, neck and tongue) terminals that sever intracellular proteins necessary for acetylcholine (a neurotransmitter that plays a role in memory, learning, attention, arousal and involuntary muscle movement) release.[6]

Causes and Prevention of Infant Botulism

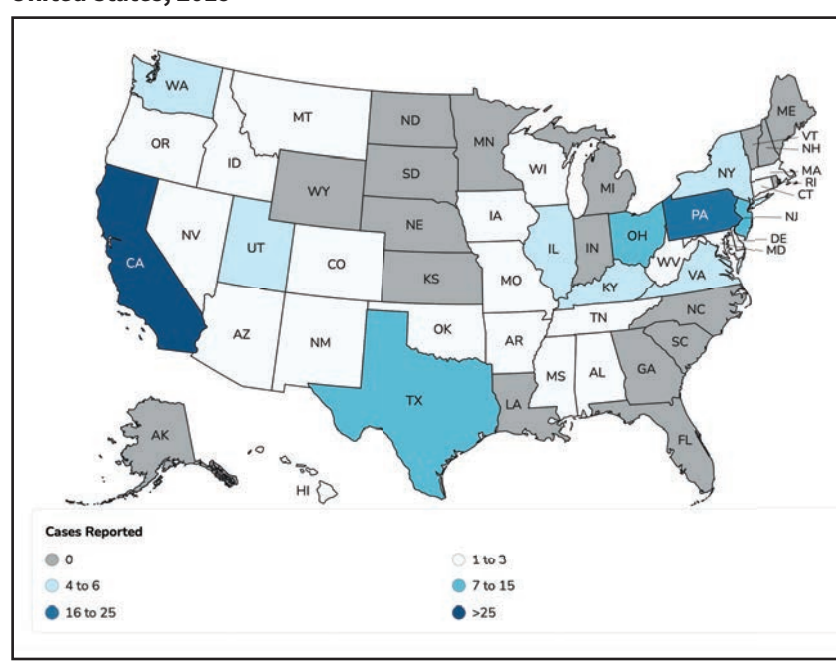
Even though there are multiple ways to contract botulism, only three main serotypes are responsible for all of these infections: type A (predominantly found west of the Mississippi River), type B (predominantly found east of the Mississippi River) and type E (found in the Pacific Northwest with a preponderance in Alaska).[2]

According to an article published in *Current Microbiology* in 2024, "honey has been identified as the only well-known risk factor for infant botulism, despite a multitude of international environmental surveys isolating C. botulinum spores from ground soil, aquatic sediments and commonly available infant foods. Associations of infant botulism cases with confirmed sources of C. botulinum exposure have primarily implicated outdoor soil and indoor dust, as well as commonly ingested foods, including honey, dry cereals and even powdered infant formula. Yet the origin of infection remains unknown for most infant botulism cases."[1]

It was Dr. Arnon who led the discovery that honey can contain spores of C. botulinum, and that exposure to honey is a risk factor for some cases of infant botulism. His efforts to alert the public to avoid feeding honey to infants were joined internationally by pediatric and public health authorities, eventually resulting in voluntary labeling of commercial honey in the U.S.[5] Today, the American Academy of Pediatrics (AAP) recommends that honey should not be given to infants younger than 12 months of age. However, AAP says honey is safe for children 1 year and older.[4]

There is no vaccine available to prevent botulism.[4]

Figure. Confirmed Infant Botulism Cases by State or Territory — United States, 2019



Cases were reported from 32 states, with California (43 cases, 28 percent) and Pennsylvania (17 cases, 11 percent) reporting the most. The toxin types were A (50 cases, 43 percent), B (97 cases, 54 percent), Bf (two cases, 1 percent), Af (one case, <1 percent), Ba (one case, <1 percent) and F (one case, <1 percent). Type Bf infant botulism is very uncommon; only 16 U.S. cases have been previously reported (seven from California, six in Texas, one in Maryland, one in New Jersey and one in New Mexico). The two type Bf cases in 2019 were identified in New York and Texas. Toxin types Af, Ba and Bf indicate bivalent strains, which means one strain can produce two types of toxin. The capital letter indicates the most abundant toxin type. No deaths were reported.

Source: Centers for Disease Control and Prevention. National Botulism Surveillance Summary, 2019, updated May 13, 2024. Accessed at www.cdc.gov/botulism/php/national-botulism-surveillance/2019.html.

Symptoms of Infant Botulism

Symptoms are progressive, with an incubation period ranging from three to 30 days after exposure to the bacteria. Symptoms may range from mild to severe, usually appearing around 3 to 4 months of age. Typically, symptoms begin with constipation, a weakened cry, loss of facial expression, a reduced gag reflex, slow feeding and overall weakness or floppiness. Children may also have blurred or double vision, a dry mouth, drooping eyelids (ptosis), difficulty swallowing and speaking, poor feeding, sluggish pupils and a flattened facial expression. The toxin can also cause paralysis of the trunk, arms, legs and respiratory system and may possibly cause respiratory arrest.[4,6]

In 2020, researchers published an article in the *Hawaii Journal of Health and Social Welfare* that discussed two cases of infant botulism with atypical initial presentations that were diagnosed on Oahu. "Patient A is a 3-month-old male who presented with altered mental status, including inconsolability, who progressed to loss of gag reflex and constipation. Due to early concern for meningitis, Patient A was treated with antibiotics, however further evaluation led to eventual positive testing for botulinum B toxin. Patient B is a 2-month-old female who presented with somnolence and fever after immunizations and progressed to respiratory failure and apparent dehydration. Because she presented shortly after receiving immunizations, metabolic disorders were strongly considered as a potential cause of symptoms, but Patient B had normal metabolic evaluation and eventually tested positive for botulinum A toxin." The researchers noted that altered mental status and fever are unusual presentations for infant botulism; however, they recommended infant botulism be considered in infants with altered mental status when the course of illness includes the development of constipation and weakness, and evaluations are not suggestive of alternative causes, including infection, metabolic diseases and spinal muscular atrophy.[7]

Diagnosing Infant Botulism

Because infant botulism has a broad spectrum of clinical severity, it may be difficult to recognize in its early stage. And, since infants are unable to describe their symptoms, the onset of infant botulism can be detected only by careful observation (see Physical Examination Signs Helpful in the Diagnosis of Infant Botulism). Nevertheless, early diagnosis is essential for prompt intervention and optimal management.[8]

Compared to a century ago when the mortality rate was close to 90 percent for this rare but serious disease, today the mortality rate is less than 15 percent.

A stool culture and direct toxin assay are needed to diagnose infant botulism. A stool culture can be obtained with an enema, but not glycerin suppositories, and a toxin assay can be obtained from stool, serum or gastric contents. Results for the direct toxin specimen are often available the morning after the specimen has been received, while the stool culture results can vary from one week to one month. It should be noted that only 60 percent of stool cultures yield a positive result. According to the authors of the continuing education activity mentioned previously, the best test is the mouse inoculation test performed by CDC. And, today, while polymerase chain reaction (PCR) is available to detect spores and the results are available within 24 to 72 hours, PCR is not readily available in all hospitals.[2]

No imaging is required to make the diagnosis. However, it is recommended that a lumbar puncture be performed to rule out meningitis.[2]

Treating Infant Botulism

BabyBIG is the only known treatment for infant botulism. According to the Infant Botulism Treatment and Prevention Program (IBTPP) created by Dr. Arnon and colleagues, the decision to treat with BabyBIG should be based on clinical presentation and findings and should not be delayed by waiting for results of laboratory confirmatory testing.[9]

BabyBIG (first known as BIG-IV) was developed by Dr. Arnon following the passage of the federal Orphan Drug Act of 1983. Dr. Arnon received funding from the FDA Office of Orphan Products Development to conduct a clinical trial of BIG-IV in California from 1992 through 1997. This was followed by a six-year nationwide open-label study of BIG-IV from 1997 to 2003, culminating in FDA licensure of BIG-IV as BabyBIG on Oct. 23, 2003.[5] BabyBIG is the standard of care for infant botulism and shortens hospital stay by an average of three-and-a-half weeks. It is an expensive treatment,

costing close to $50,000; however, it results in a decrease in hospital stays and, thus, charges.[2]

According to a study published in 2017, since its licensure in 2003, BabyBIG has treated approximately 93 percent of U.S. patients with laboratory-confirmed infant botulism. In the study, medical records and billing information were collected for U.S. patients treated with BabyBIG from 2003 to 2015. Length of hospital stay (LOS) and hospital charge information for treated patients were compared with the BIG-IV Pivotal Clinical Trial Placebo Group to quantify decreases in LOS and hospital charges, with results showing the use of BabyBIG reduced mean LOS from 5.7 to 2.2 weeks, with a mean decrease in hospital charges of $88,900 per patient. For all U.S. patients from 2003 to 2015, total decreases in LOS and hospital charges were 66.9 years and $86.2 million, respectively.[10]

Approximately 50 percent of infantile botulism cases will require intubation and an advanced airway even if they have been treated with BabyBIG; however, those who are not treated may require mechanical ventilation longer. In addition, it is recommended that after resolution, all live-virus vaccinations should be delayed by five months.[2]

Most children recover fully from botulism, although it can take several weeks to months.[4]

IBTPP's Success for Infant Botulism

In 1992, Dr. Arnon established IBTPP, a unit of the California Department of Public Health, which is a public service program that provides clinical consultation and access to the treatment BabyBIG for infants suspected of having infant botulism. The organization aims to improve the treatment of infant botulism and prevent the disease by offering 24/7 consultation to healthcare providers regarding diagnosis and management of suspected cases, particularly focusing on early intervention with BabyBIG.[11]

Compared to a century ago when the mortality rate was close to 90 percent for this rare but serious disease, today the mortality rate is less than 15 percent[2] due to the passage of the Orphan Drug Act and the almost 15 years of clinical research conducted by Dr. Arnon and colleagues that resulted in FDA approval of BabyBIG. As of May 31, 2024, the IBTPP website states that BabyBIG has been administered to more than 2,180 infants in 48 states and Washington, D.C., and has resulted in more than 128 years of avoided hospital stays and more than $174 million of avoided hospital costs. And, on average, infant botulism patients have an approximately 3.6 week reduction in time spent in the hospital, resulting in more than $94,000 in avoided hospital costs (when compared to the pivotal clinical trial placebo group).[9,11] ❖

Physical Examination Signs Helpful in the Diagnosis of Infant Botulism

- Test 1. Take the patient to a dark room. Shine a bright light into the eye; note quickness of pupillary constriction. Remove the light when constriction is maximal; let the pupil dilate. Then immediately repeat, continuing for two to three minutes. Findings: The initially brisk pupillary constriction may become sluggish and unable to constrict maximally. Also, constrictor muscle fatigability may yield a "pseudo" gibbus.
- Test 2. Shine a bright light onto the fovea, keeping it there for one to three minutes even if the infant tries to deviate her/his eyes. Findings: Latent ophthalmoplegia may be elicited, and/or purposeful efforts to avoid the light may diminish, because fatigability with repetitive muscle activity is the clinical hallmark of botulism. Also observe for initial squirming of the extremities that may diminish because of fatigability.
- Test 3. Place a clean fifth finger in the infant's mouth, taking care not to obstruct the airway. Note the strength and duration of the reflex sucking. Findings: The suck is weak and poorly sustained. The gag reflex strength also may be quickly checked (if the infant has not been fed recently).

Source: Infant Botulism Treatment and Prevention Program. Clinical Diagnosis. Accessed at www.infantbotulism.org/physician/clinical.php.

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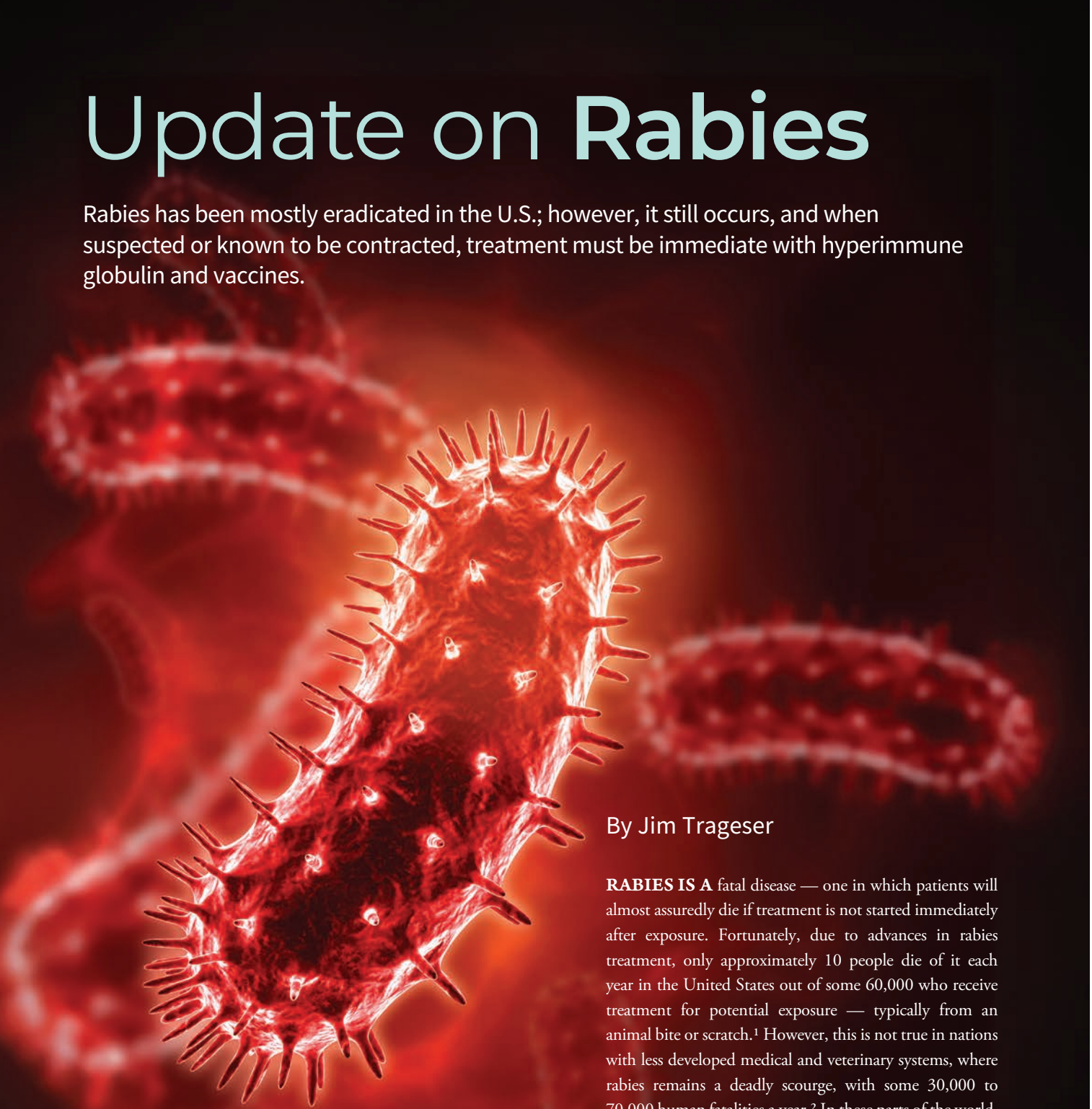
Update on **Rabies**

Rabies has been mostly eradicated in the U.S.; however, it still occurs, and when suspected or known to be contracted, treatment must be immediate with hyperimmune globulin and vaccines.



By Jim Trageser

RABIES IS A fatal disease — one in which patients will almost assuredly die if treatment is not started immediately after exposure. Fortunately, due to advances in rabies treatment, only approximately 10 people die of it each year in the United States out of some 60,000 who receive treatment for potential exposure — typically from an animal bite or scratch.[1] However, this is not true in nations with less developed medical and veterinary systems, where rabies remains a deadly scourge, with some 30,000 to 70,000 human fatalities a year.[2] In these parts of the world, the disease is almost always acquired from a bite by an infected dog.

Rabies has been known and described in both humans and dogs since ancient times, with the Mesopotamian Codex of Eshnunna (roughly 2000 BC) describing the legal obligations of owners of infected dogs.[3] The common name itself is derived from the Latin verb rabere, which translates as "to rage" in reference to the manic delusions that patients of rabies may exhibit, particularly if exposed to water.[4]

Even the scientific name of the genus of viruses that cause rabies, Lyssavirus, is taken from the Greek lyssa, for frenzy or madness.

In 1885, Louis Pasteur successfully tested a rabies vaccine using an attenuated virus. It was used to save a boy's life that same year after he was bitten by a rabid dog.[5] Dogs have historically been and remain the primary vector of rabies in humans in wide swaths of Africa and Asia. However, thanks to widespread veterinary immunization that began in 1908, rabies in domesticated dogs in the United States, Canada and Western Europe is practically eradicated today.[6] Instead, bats are the leading source of rabies infections today in the United States, Canada and Western Europe, although nearly all mammals can be infected by and spread rabies.[7]

What Is Rabies?

Rabies is a viral disease that causes encephalitis in humans. It is almost always fatal once the infection takes hold, with reports of fewer than two dozen people in history surviving a documented case of rabies.[8] (And, of those who did survive, only one has shown much in the way of recovery; the others all suffered from significant damage to the brain.)

The viruses that cause rabies are part of the Lyssavirus genus. While most human cases of rabies are caused by the Rabies lyssavirus (RABV), there are some two dozen species of virus in the Lyssavirus genus, and it is believed all of them can lead to the rabies disease.[9] In Australia, for instance, rabies is caused by Australian bat lyssavirus (ABLV); however, ABLV is very rare, with only three recorded human cases in history.[10]

While rabies is widespread in wild animal populations in the continental United States, including Alaska, it does not exist in Hawaii.[11] But even where it is common, biologists are trying to reduce the natural reservoir of the virus by spreading oral vaccines onto food left for wildlife.

As mentioned, nearly all cases of rabies in the United States are spread by bats, although rabies has been found in wild skunks, raccoons and foxes.[1] It is also thought that an infected human could spread rabies to other humans, but no such case has ever been documented. It's possible to acquire rabies while traveling, particularly to areas of the world where dogs are not routinely vaccinated and remain the primary vector. In fact, some 80 Americans have contracted rabies in this way since 1990.[1]

After the viral infection enters the body through a wound in the skin, typically a bite or a scratch, it then spreads through the peripheral nervous system toward the central nervous system, including the brain stem and brain. Once the virus reaches the brain stem and brain, encephalitis occurs, causing the symptoms usually associated with rabies: hydrophobia and agitation, or conversely, a state near catatonia. Death usually occurs fairly rapidly after encephalitis begins.[2]

Symptoms and Progression of Rabies

The most significant symptom of a potential rabies infection is a bite or scratch from a wild or unknown domesticated animal. Most recent cases of rabies in the United States have occurred after individuals handled a bat, often when trying to remove it from a home or outbuilding.[12]

If the animal that bit or scratched is not captured to be tested for rabies, or if the animal is caught and tests positive, treatment needs to begin immediately. By the time symptoms other than the bite or scratch appear, the disease is untreatable and fatal. Untreated rabies is clinically diagnosed based on presentation of symptoms; there is currently no blood or other test for rabies. A postmortem laboratory test to confirm rabies generally

Facts About Rabies

- In the U.S., approximately 4,000 animal rabies cases are reported each year, with more than 90 percent occurring in wildlife such as bats, raccoons, skunks and foxes.
- The rabies virus is caused by the deadly Lyssavirus.
- Exposure to the rabies virus can occur through a bite, scratch or contact with infected saliva to open wounds or mucous membranes such as the eyes, nose or mouth.
- Only mammals can get rabies.
- There are two types of rabies: furious (where the animal appears agitated, irritable, unpredictable and viciously aggressive) and paralytic (where the animal has an inability to swallow, and presents with excessive salivation, drooping of jaw, stumbling, paralysis and coma).
- The rabies virus attacks the brain and is fatal once symptoms appear.
- Worldwide, 99 percent of human cases of rabies are caused by dog bites.
- Today in the U.S., most cases of rabies are caused by wildlife due to widespread veterinary immunization.
- In 2024, the Centers for Disease Control and Prevention reported wildlife accounted for more than 90 percent of reported animal rabies cases, with bats (33 percent), raccoons (30 percent), skunks (20 percent) and foxes (7 percent) most often exposing Americans to rabies.
- There is no cure for rabies, but it is 100 percent preventable through prompt, appropriate medical care.
- Post-exposure treatment for rabies typically exceeds $8,000 per person.

involves examining brain tissue for the antigen associated with the rabies virus.[13]

As mentioned above, there are two manifestations of rabies: furious rabies and paralytic rabies.[14] Most patients with untreated rabies will develop furious rabies, which is marked by heightened aggression, seizures and delirium. Dogs that develop this form may froth at the mouth, which is where popular culture imagery of rabid dogs comes from. Paralytic rabies leads to weakness and paralysis.

Both of these forms will show up only toward the end of the disease progression, in the third of four stages:

- Incubation phase: This is the period in the days or weeks after infection, before the virus makes its way into the peripheral nervous system. This can last from just over a week to up to two years, although in most cases it is between one and three months.[15] There are no symptoms during this phase.
- Prodromal phase: Once the virus enters the peripheral nervous system, the prodromal phase begins. Tingling or numbness at the wound and flu-like symptoms may be reported.[14] This period usually lasts from two to 10 days.
- Acute neurologic phase: In this phase, the virus has entered the central nervous system, encephalitis has begun and the patient begins to show symptoms of neurological dysfunction. This is when the patient will either exhibit furious or paralytic symptoms. Both may include fever, and toward the end of this phase, breathing may become irregular. Paralytic patients may experience a longer duration of the acute neurologic phase, sometimes up to a month. Furious patients may only last a few days to a week before progression.[14]
- Coma phase. In this phase, the patient will lose consciousness, breathing will grow more irregular and full paralysis may occur. This phase usually lasts only a few days before death.

Preventing Rabies

Due to the low risk of exposure in the United States (60,000 potential exposures per year out of a population of 335 million, or less than two one-hundredths of a percent chance), rabies vaccines are not part of the normal childhood vaccination regimen.[16] However, preventive vaccine exceptions are made for high-risk individuals, including veterinary staff, and those who work with or come in close proximity to wild animals (zoo workers, park rangers, wildlife biologists, etc.). They may also be considered for patients traveling to a part of the world with a high incidence of rabies.

One such vaccine is the purified chick embryo cell vaccine (PCECV), which may be marketed under the brand name RabAvert.

Treating Rabies

Treatment for rabies must begin before a formal diagnosis can take place; the mere possibility of exposure to rabies is enough to begin treatment. And, treatment must be started early in the incubation phase before the virus has entered the nervous system.

The treatment regimen itself hasn't changed much since Pasteur's day: Rabies vaccine is still applied in a series of injections over the course of a few weeks. One advancement (beyond the obvious improvements in quality control and a wider network of trained professionals to administer the treatments) is the addition of human rabies immune globulin (HRIG) to the tool chest available to physicians.

If individuals are bitten or scratched by an untreated or unknown animal, the bite or scratch should immediately be thoroughly washed with soap and water. This can reduce the risk of general bacterial infections, as well as remove virus-carrying saliva, reducing the viral load entering the body.[17]

There is no antiviral treatment for rabies. Rather, rabies treatment is a post-exposure prophylaxis (PEP). When exposure is even suspected, and the patient has not previously received the RabAvert vaccine, treatment will begin on the first medical visit with:

- A single dose of human rabies immune globulin (HRIG) (brand names Kedrab and HyperRAB) administered near the wound to provide an immediate boost to the immune response; and
- The first dose of a rabies vaccine (which should not be administered near the HRIG injection site) to start a longer-term buildup of the immune system.

Follow-up medical visits are then required on days three, seven and 14 and will include the second, third and fourth doses of the rabies vaccine. These subsequent doses can and should be administered near the wound, unlike the first dose. Patients with a compromised immune system should receive a fifth dose of the vaccine on the 28th day after the initial treatment.[17]

For patients who have been vaccinated previously, treatment will consist of a vaccine dose on days zero and three in the deltoid area in adults or in the thigh in children. HRIG should be avoided in those already vaccinated as it may interfere with the vaccine boosters.

The Centers for Disease Control and Prevention recommends two vaccine types for PEP treatment: the human diploid cell rabies vaccine (HDCV) produced by the Merieux Institute and the PCECV vaccine.

One area of potential worry is that current rabies vaccines may not work against emergent Lyssavirus strains being identified in Europe.[18] However, given that these new strains have only accounted for a few dozen human cases, and that the vaccines seem to offer at least some crossover protection, the risk seems to be low.

Looking Ahead

Various international and national health agencies have set a goal for global eradication of dog-mediated rabies by the year 2030. With poor nations in Africa and Asia incurring the highest incidence of rabies, the goal is to bring assistance to these nations by:[19]

- Increasing access to human rabies vaccines
- Inoculating domestic animals, especially dogs
- Controlling the population of wild dogs
- Equipping and training medical facilities to be able to provide timely PEP

In addition, research continues to find more effective treatments of rabies. There are currently more than 100 recent and ongoing clinical studies about rabies listed on the U.S. Food and Drug Administration's clinicalstudies.gov website. Among them are studies in Asia looking at the efficacy of preventive rabies vaccines in young children in areas where rabies is widespread. Most of the studies listed, however, are investigating improvements to existing vaccines and HRIG versions, modifying dosage schedules and other fine-tuning.

With no apparent leads on a rabies treatment that would be effective after the virus gains access to the nervous system, it seems likely that for the foreseeable future, the only viable treatment for those potentially exposed to rabies will be the current PEP. ❖

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Myths & Facts: GLP-1 Drugs for Weight Loss

While there has been a surge in GLP-1 weight-loss drugs since first being approved a decade ago, misconceptions remain that could lead to many patients failing to achieve their weight-loss goals.

By Ronale Tucker Rhodes, MS

WEIGHT LOSS is one of the most talked-about topics. The reason? The number of obese individuals in the U.S. is growing at an alarming rate. Obesity is defined as a body mass index higher than 30 percent. In 1980, the obesity prevalence was 15 percent. This progressed to an obesity prevalence of 31 percent in 2000 and then 42 percent in 2020. And, while there is no consensus on the cause of this growing obesity rate — reduction in physical activity, increase in dietary fat, increase in sugar and sugary beverages, increase in ultra-processed foods, higher cost of healthier diets — there's no denying that Americans need solutions.

It's no wonder, then, that when talking about weight loss today, discussion is dominated by the new GLP-1 (glucagon-like peptide-1) drugs. But, this "new drug on the block" really isn't so new. Researchers began searching for insulin stimulating factors about 100 years ago. And, that's what GLP-1 drugs are: a type of peptide hormone that can stimulate the pancreas to produce more insulin after meals, as well as slow the movement of food from the stomach into the small intestine to help suppress appetite. Despite years of research, the first discovery of a GLP-1 wasn't until 1984, and upon further research into its applications, a drug was approved by the U.S. Food and Drug Administration (FDA) to treat type 2 diabetes. After that, clinical studies and post-release surveillance observations showed that individuals prescribed the drug were also losing weight. So, pharmaceutical companies started investigating the use of GLP-1s for weight-management purposes, and the first GLP-1 weight-loss drug, Saxenda (liraglutide), was approved by FDA in 2014 (it was previously approved to treat diabetes under the name Victoza).

Today, there are three GLP-1 weight-loss drugs available: Saxenda; Wegovy (semaglutide), which was approved in 2021 (it was previously available for diabetes as Ozempic and in an oral form for diabetes as Rybelsus); and Zepbound (tirzepatide), which was approved in 2023 (it was previously available to treat diabetes under the brand name Mounjaro). Zepbound is the first GLP-1/GIP (gastric inhibitory polypeptide) medication, which is thought to be more potent than GLP-1 alone.

Between 2014 and now, prescriptions for these GLP-1 drugs have increased a whopping 300 percent. Yet, many myths surround who should be prescribed these drugs, how they work and what they can and cannot do.[1]

Separating Myth from Fact

Myth: Anyone can take GLP-1 weight-loss drugs.

Fact: GLP-1 weight-loss drugs are typically prescribed to people with a BMI of 30 or higher.[2] Both Saxenda and Wegovy can be prescribed to individuals 12 years and older, while Zepbound can be prescribed only to adults. However, they are not for everyone. People with a history of medullary thyroid cancer, gallbladder disease or pancreatitis, as well as those with multiple endocrine neoplasia syndrome type 2 should avoid taking these drugs.[2]

GLP-1 weight-loss drugs are typically prescribed to people with a BMI of 30 or higher.

In fact, according to Jaime Almandoz, MD, while more than 70 percent of U.S. adults are overweight or obese, only four percent of these people are prescribed GLP-1 weight-loss medicines due to concerns about safety or effectiveness, lack of healthcare provider training in weight management, excessive costs due to insurance companies refusing coverage and a toxic stigma that portrays obesity as a lack of willpower.[3]

There are also strict guidelines for who qualifies for these medications, and there's a spectrum of little-talked-about weight-loss medications available on the market that aren't GLP-1s.[4]

Myth: All GLP-1 weight-loss drugs are the same.

Fact: No, they are similar, but not the same. Saxenda, Wegovy and Zepbound are all GLP-1 receptor agonists that work by stimulating the GLP-1 receptor in the brain to help people feel full.[5]

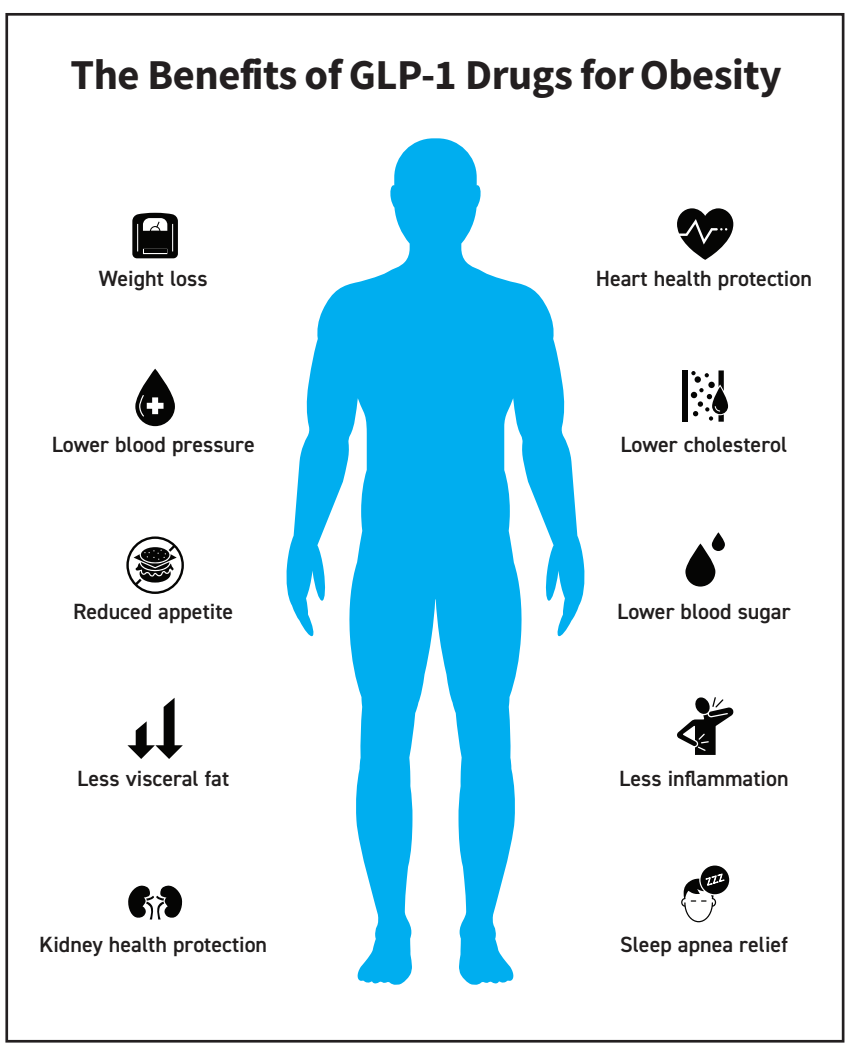
Saxenda (liraglutide) is injected subcutaneously (under the skin) usually once daily, with or without meals. It is started at a lower dose and then gradually increased over the weeks. In a large 56-week clinical trial that evaluated liraglutide in individuals who were overweight or had obesity, as well as had diabetes or prediabetes, participants reported statistically significant weight loss compared with those who took the placebo at the end of the study. Sixty-three percent of the participants lost at least five percent of their body weight and about 33 percent lost at least 10 percent of their body weight.[6] In another study of people without diabetes, Saxenda was more effective for weight loss than lifestyle interventions alone, and weight loss was sustained for more than two years.[7]

Wegovy (semaglutide) is injected under the skin once weekly, at the same time every week, with or without meals. In studies, semaglutide was more

effective at reducing body weight and HbA1c than placebo. When used in addition to lifestyle interventions, 2.4 mg of semaglutide once weekly resulted in an average weight loss of 15 percent. More people who took semaglutide (86 percent) lost at least five percent of their body weight compared with those on placebo (13 percent). And about 70 percent of users lost at least 10 percent of their body weight.[8] Studies have also shown semaglutide to be superior to some other weight-loss agents. Compared with liraglutide, more semaglutide users achieved weight loss greater than five or 10 percent.[9]

Zepbound (terzepatide) is also injected subcutaneously once weekly at a recommended dosage of 5 to 15 mg. Two large 72-week clinical trials that evaluated terzepatide in individuals who were overweight or obese found that by the end of the study, people who also dieted and exercised reported statistically significant weight loss compared to those who took the placebo.[10]

Myth: All GLP-1 agonists work the same for all people.



Adapted from: Sullivan, K. GLP-1 Drugs for Obesity and Weight Loss. Everyday Health, Nov. 18, 2024. Accessed at www.everydayhealth.com/weight-management/glp-1-drugs-for-obesity-and-weight-loss.

Fact: The drugs' efficacy varies from person to person. According to Laura Buford, MD, "factors such as genetics, lifestyle and underlying health conditions all play a role in how an individual responds to these treatments. For example, some people may experience more significant weight loss, while others may see more modest results." What's more, diet, exercise and adherence to the treatment plan affect the outcomes. And, given the individual variability, Dr. Buford says it's necessary for healthcare providers to personalize the plan for each individual such as adjusting the dosage, combining treatments or incorporating lifestyle modifications to optimize results for each person.[11]

Myth: GLP-1 weight-loss drugs are just another diet pill.

Fact: Actually, GLP-1 weight-loss drugs take a completely different approach than diet pills. Diet pills focus on suppressing appetite or increasing metabolism, whereas GLP-1 agonists work by mimicking the action of the GLP-1 hormone that is naturally produced in the body and plays a crucial role in regulating appetite and blood sugar levels. According to Dr. Buford, "by enhancing the effects of GLP-1, these medications help to reduce hunger and increase feelings of fullness, leading to reduced caloric intake without the need for extreme dieting or willpower. This mechanism of action is more aligned with the body's natural processes, making it a more sustainable option for weight loss."[11]

Myth: Using compounded GLP-1 drugs is just as safe as using brand-name GLP-1 medicines.

Fact: According to FDA, "a compounded drug might be appropriate if a patient's medical need cannot be met by an FDA-approved drug, or the FDA-approved drug is not commercially available. However, compounded drugs are not FDA approved," which means

Reduction in Body Weight for GLP-1 Weight-Loss Medications

Brand	Study Duration	Mean Change in Body Weight	Participants with ≥ 10% Weight Loss
Saxenda	56 Weeks	-7.4%	33.9%
Wegovy	68 Weeks	-14.9%	66.1%
Zepbound	72 Weeks	-20.9%	83.5%

Adapted from: Innovative Rx Strategies. Rx Trends: Real-World Data on GLP-1s for Weight Loss. Accessed at innovativerxstrategies.com/real-world-data-on-glp-1s.

FDA does not review them for safety, effectiveness or quality before they are marketed. In fact, FDA has identified some areas of concern for compounded GLP-1 drugs and is working with its state regulatory partners regarding them. Concerns include reports of adverse events, some requiring hospitalization, that may be related to dosing errors or doses beyond what is in the FDA-approved drug label, which means using more product in a single dose, taking doses more frequently or increasing the amount more quickly (titration schedule).[12]

Myth: It's OK to purchase GLP-1 drugs from online or compounding pharmacies that don't require a prescription.

Fact: It's unwise to purchase GLP-1 medications from anywhere other than major retailers who require a prescription, because individuals may actually be getting a counterfeit drug. In fact, counterfeit Ozempic sales are on the rise, and these drugs could contain the wrong ingredients; contain too little, too much or no active ingredient at all or other harmful ingredients; and are illegal.[12]

To spot whether Ozempic is counterfeit, FDA encourages patients and healthcare providers to double-check Ozempic boxes, which might have spelling errors, and the batch number on the box may not match the product strength stated on the same box and pen. The label on a counterfeit pen could also have poorer quality, and it may not stick well to the pen. A genuine Ozempic pen also does not extend in length when you try to set the dose with the dial.[13] In addition, the World Health Organization advises not to distribute, use or sell products labeled with batch numbers listed in its Annex.[14,15]

Myth: The GLP-1 injections are painful.

Fact: In general, the injections aren't painful because the injection pen uses a tiny needle that is inserted just under the skin. These subcutaneous injections are significantly less painful than injections into muscles such as flu shots. One study showed that injections of semaglutide (the active ingredient in Wegovy), which is administered for diabetes or weight loss in the skin of the abdomen, thigh or upper arm, produced little to no injection-site pain.[16]

It's necessary for healthcare providers to personalize the plan for each individual such as adjusting the dosage, combining treatments or incorporating lifestyle modifications to optimize results for each person.

However, there have been reports of injection site discomfort from those new to injecting GLP-1s. But, this side effect can be avoided by following a few best practices before, during and after the injections. These include injecting just under the skin's surface in the stomach, upper arm or thigh, ideally into fat; not injecting into veins or muscles; rotating injection sites and changing the site for each dose to help prevent skin irritation and scar tissue buildup; staying at least two inches away from the belly button when injecting into the stomach; not injecting into areas that are red, bruised or tender; and avoiding injecting into areas with stretch marks or scars.[17]

Myth: People don't have to exercise or eat healthfully when taking GLP-1 drugs.

Fact: According to the labels on these drugs, people *do* have to exercise and eat healthfully while using them. Specifically, the label states these medications should be used in combination with a "reduced calorie diet and increased physical activity." HaVy Ngo-Hamilton, PharmD, pharmacist and clinical consultant for BuzzRx, states that "the amount of diet and exercise will vary among users, leading to various degrees of weight loss. However, consistent physical activity is vital to achieve and maintain the desired weight loss."

Following a balanced diet is important when taking GLP-1 medications because it can help improve the effectiveness of the medication in managing blood sugar levels and weight. "Because these

medications trigger insulin production, slow the emptying of the stomach and cause you to feel full faster and for longer periods of time, eating unhealthy foods or larger portions of food may cause negative gastrointestinal side effects, including abdominal pain, nausea or vomiting," Ngo-Hamilton says.[18]

Myth: GLP-1 drugs are unsafe with numerous side effects.

Following a balanced diet is important when taking GLP-1 medications because it can help improve the effectiveness of the medication in managing blood sugar levels and weight.

Fact: Actually, these drugs are very safe as proven by extensive clinical testing. Results of these trials showed "GLP-1 agonists have a favorable safety profile, with most side effects being mild and temporary. Common side effects include nausea, diarrhea and constipation, which typically subside as the body adjusts to the medication." There are strategies to manage and minimize side effects. For instance, individuals can start with a lower dose that is gradually increased to reduce the severity of side effects. And, taking medication with food or adjusting the timing of doses can help.[11]

Myth: GLP-1 drugs cause suicidal ideation.

Fact: In July 2023, the European Medicines Agency began reviewing reports of patients causing self-harm or having suicidal ideation after taking weight-loss drugs that contain semaglutide. However, a meta-analysis conducted at Case Western University in collaboration with the National Institutes of Health and FDA demonstrated no link between anti-obesity drugs and increased suicidal ideation.[19]

In the study, the researchers used a large electronic health record database to conduct a nationwide retrospective cohort study to assess the association of semaglutide with the incidence and recurrence of suicidal ideation compared with non-GLP1R agonist anti-obesity medications in individuals with overweight or obesity. What's more, they replicated the same analyses in a separate cohort of patients with type 2 diabetes mellitus by comparing semaglutide with non-GLP1R agonist anti-diabetes medications. According to the researchers, "Contrary to reports of increases in suicidal ideation with semaglutide, our analyses revealed a lower risk for both incidence and recurrence of suicidal ideation in patients prescribed semaglutide compared with non-GLP1R agonist anti-obesity and anti-diabetes medications."[20]

"If you look at the study a little bit deeper … there was a decreased risk in [suicidal ideation] in women, men and along every racial group," said Catherine Varney, DO, obesity medicine director for UVA Health and an assistant professor of family medicine at the University of Virginia. "What we're seeing is improvements in mental health and metabolic health. This is really exciting for us to see just further evidence of the benefits of these medications beyond weight loss."[19]

Myth: Losing weight is the biggest benefit of GLP-1 medicines.

Fact: The benefits of weight loss extend far beyond the scale. Researchers report that GLP-1 drugs prescribed for weight loss may improve cognition and lower dementia and cardiovascular disease risk. Scientists at the Washington Universal School of Medicine in St. Louis and the Veterans Affairs St. Louis Health Care System reviewed the health records of two million veterans who were treated for diabetes from October 2017 through December 2023 to determine the GLP-1 medications' effects on the body's organ systems. Some of the veterans took GLP-1 medications, while others were given more traditional drugs sold under brand names such as Jardiance, Glipizide and Januvia. They found widespread associations with the GLP-1 drugs and improvements to cognitive and behavioral health, with benefits including reduced risks of seizures, as well as a lower risk to addiction to substances such as alcohol, cannabis, stimulants and opioids. In addition, the researchers said those taking the GLP-1 drugs also experienced decreased risks of suicidal ideation, self-harm, bulimia and psychotic disorders such as schizophrenia. Their findings also showed a lower risk of neurocognitive disorders such as Alzheimer's and dementia. However, they noted these benefits were a somewhat modest 10 to 20 percent reduction in most risks.[21]

Myth: Taking GLP-1 drugs guarantees weight loss.

Fact: While taking GLP-1 drugs may seem like a guaranteed way to reach weight-loss goals, research shows they don't work for everyone. One clinical trial indicated only about 86 percent of the more than 800 participants achieved "clinically significant" weight loss after taking semaglutide, sold under the brands Ozempic and Wegovy, for 68 weeks, which means a portion of

users did not. "Each person responds differently to medications, and the degree of weight loss achieved with treatment can vary based on personal factors," said Priya Jaisinghani, MD, a clinical assistant professor specializing in obesity medicine at the NYU Grossman School of Medicine.

Of course, there may be factors influencing weight-loss outcomes. First, the dose may not be high enough. A recent study involving 3,390 people taking semaglutide or liraglutide found participants who took high doses of their drug — 1.7 mg, 2.0 mg or 2.4 mg of semaglutide, or 3 mg of liraglutide — lost more weight after a year compared to people taking lower doses. "Increasing the dose of a GLP-1 can sometimes enhance weight loss or maintain consistent weight loss," explained Fatima Cody Stanford, MD, an obesity medicine scientist at Massachusetts General Hospital Digestive Healthcare Center in Boston. "But this is not guaranteed."

Physical factors can also play a role. The same study found that people with a higher body mass index lost more weight after a year. Other barriers to weight loss include lifestyle habits, such as not exercising or routinely eating sugary or fatty foods, and medication adherence. According to Dr. Cody Stanford, the drugs are only effective if taken consistently, and people who pause the medication may gain some weight back. GLP-1s can also cause gastrointestinal issues such as nausea and vomiting, which may cause some people to discontinue use due to side effects before achieving their weight-loss goals.[22]

Myth: Insurance will cover the cost of GLP-1 medicines for people who are prime candidates.

Fact: Unfortunately, this is not always the case. Cost is a barrier for some individuals who would like to go on GLP-1 medications since, according to the Kaiser Family Foundation and the Institute for Clinical and Economic Review, they can cost $1,300 or more for a month's supply. And, not all insurance will help cover it. For instance, some employers choose to exclude GLP-1 drugs from employer-sponsored health plans, some insurance plans require prior authorization before approval, and Medicare does not cover GLP-1s for weight loss. It is up to each insurer and its chief medical officer to decide if these medications will be covered. While drug manufacturers sometimes offer discount programs, consumers are often left paying hundreds of dollars out of pocket for their prescriptions.[23]

In addition, a provider may prescribe a GLP-1 off label for obesity when that GLP-1 is covered by insurance only if the person has a type 2 diabetes diagnosis. "Insurance coverage will vary by person and by insurance policy, and recently, more insurance plans have opted not to cover the cost of GLP-1 agonists, particularly those that are being prescribed for off-label use," Ngo-Hamilton says. "For example, when someone doesn't have type 2 diabetes, their healthcare provider prescribes Ozempic as off-label use for weight management."[18]

Dispelling the Myths Now

While not new, GLP-1 drugs have been approved by FDA only in the last decade to treat obesity. However, they are not miracle drugs; diet and exercise are still important factors for sustainable weight loss while taking a GLP-1 medication. In addition, they are costly medications, they are not always covered by insurance, and they generally need to be taken forever. While some individuals don't see results, with a better understanding of the facts about these drugs, physicians can help their patients succeed in their weight-loss goals. ❖

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Infant Botulism:
A Patient's Perspective

By Trudie Mitschang

AS A YOUNG mom, the only thing Susan Dabalos Anderson knew about infant botulism was to avoid feeding her baby honey. When her exclusively breast-fed son became critically ill, she was shocked to learn he had contracted the potentially fatal illness, most likely from airborne spores.

BSTQ: Take us back 18 or so years ago. What were your son's initial symptoms?

Susan: As a chiropractor, my specialty is children, so when our son wasn't lifting his head anymore (which he had been doing since he was 1 month old), I knew something was wrong. He also wasn't nursing properly. He had always been a happy baby, and his demeanor changed suddenly; he became very lethargic.

BSTQ: When did you know something was seriously wrong?

Susan: We took him to see the pediatrician within two days of noticing his symptoms. We were fortunate to see a doctor who had been in practice for over 30 years. Based on his experience and a consultation with another physician, he suspected our son had contracted botulism. That's when they told us we needed to immediately go to Primary Children's Hospital in Salt Lake City.

BSTQ: What happened next?

Susan: Thankfully, our pediatrician had called ahead, so our son was admitted to the hospital as soon as we arrived. During the initial intake, the attending physician discussed the need to give him BabyBIG (botulism immune globulin). The medical team said it was imperative to get him treated as soon as possible, even though they did not yet have a definitive diagnosis because they didn't have a stool sample. Everything was happening quickly, and it was stressful to consider giving our child a medication that we knew nothing about, but within hours we did consent.

BSTQ: You had a scare involving an inexperienced nurse. Tell us about that.

Susan: Due to him having very slow bowel movements, they decided to give him MiraLAX to get a stool sample. The first time he took it, he started throwing up bile. They waited a bit and then gave it to him again, and the same thing happened. We did not allow him to have MiraLAX again because one of the doctors said he was likely allergic to it.

BSTQ: Do you know how your son became infected with botulism?

Susan: Since he was purely breastfed and never given honey, we assume he contracted it from the environment. Salt Lake City had a lot of new housing developments at that time, and we later learned that botulism spores can be present in soil, and when construction disrupts the soil, these spores can become airborne as dust.

BSTQ: Tell us about your son's recovery period. Were there any side effects or developmental issues?

Susan: Our son had a seamless recovery and was out of the hospital in two weeks. He had to drink 60 ccs of breast milk before he was released and, according to the therapist who fed him, he was the first botulism-infected baby she had seen released in fewer than four weeks. We did use suppositories to help him with bowel movements for a few months after he came home. I also started giving him a probiotic whenever he used a binky. The hospital recommended using a binky to help his sucking reflex since that skill can be diminished following a botulism infection. We did not introduce him to solid foods until he was about 8 months old, because I knew breast milk was more important for him, and I wanted to keep breastfeeding as long as possible. We also took him to the pediatrician more often to make sure he was gaining weight appropriately. Thankfully, he caught up with the growth charts at 8 months, and he never had any developmental issues. We were very grateful.

BSTQ: How is your son's health today?

Susan: He is a healthy 21-year-old, 6 feet 3 inches tall and 160 lbs. He lives at home and attends college for mechanical engineering. ❖

Infant Botulism:
A Physician's Perspective

AS THE chief of the Infant Botulism Treatment and Prevention Program (IBTPP) for the California Department of Public Health (CDPH), Steve Arnon, MD, MPH, dedicated 45 years of his career to diagnosing, researching and treating infant botulism, and was credited with saving thousands of lives in California and around the world.

Dr. Arnon's interest in infant botulism was sparked in 1976 when he received a call about a paralyzed infant from Salinas, Calif. Through epidemiological and laboratory investigation, he and colleagues collected evidence that the baby's digestive tract was colonized with Clostridium botulinum, the bacterium that produces an exceptionally potent neurotoxin. As additional infants in California were diagnosed with acute weakness throughout that year, Dr. Arnon and his medical team named the condition infant botulism (in contrast to botulism that results from contaminated food or wounds).

After founding the IBTPP, Dr. Arnon characterized the distinct pathophysiology, epidemiology, clinical features and risk factors of infant botulism (see "Diagnosing and Treating Infant Botulism" on p.30). This eventually led to the discovery that honey can contain spores of C. botulinum, and that exposure to honey is a risk factor for some cases of infant botulism. His efforts to alert the public to avoid feeding honey to infants were joined internationally by pediatric and public health authorities, eventually resulting in voluntary warning labels on commercial honey in the United States.

His paper titled "The Creation and Development of the Public Service Orphan Drug Human Botulism Immune Globulin," described Dr. Arnon's journey of bringing what is now the go-to treatment for infant botulism to market. Following the passage of the federal Orphan Drug Act of 1983, he received funding from the U.S. Food and Drug Administration (FDA) Office of Orphan Products Development to conduct pivotal clinical trials of human botulism immune globulin intravenous (BIG-IV) in California. This was followed by a six-year nationwide open-label study of BIG-IV from 1997-2003, culminating in FDA licensure of BIG-IV as BabyBIG on Oct. 23, 2003. The first and only licensed human botulism immune globulin, BabyBIG is the standard of care for infant botulism and shortens hospital stays by an average of three and a half weeks. Before the development of BIG-IV, the treatment of patients with infant botulism consisted only of meticulous nutritional and respiratory supportive care.[2]

As the longest-standing member of the collaborative Interagency Botulism Research Coordinating Committee, Dr. Arnon has more than 75 peer-reviewed publications to his credit, including textbook chapters about infant botulism, many of which originally helped to describe the disease. He also co-authored the article "Global Occurrence of Infant Botulism, 1976–2006," published by the American Academy of Pediatrics, which offers a comprehensive overview of the disease's worldwide incidence.[3] The data documenting the safety and efficacy of BIG-IV were eventually summarized in the *Journal of Pediatrics*.[4]

Dr. Arnon's work has been highly recognized over the years; he was the recipient of the 1998 FDA Wiley Medal and Commissioner's Special Citation "for commitment and determination to test botulism immune globulin antitoxin for treatment of the life-threatening disease of infant botulism." In 2004, he received the National Organization for Rare Disorders' Therapeutic Achievement Award, and in 2011, he received the CDPH Recognition Lifetime Achievement Award.

Although Dr. Arnon passed away in 2022 at the age of 75, his legacy lives on. In a statement on the IBTPP website, the organization says: "His passion for teaching and mentoring was evident to all who knew him, and he poured his heart and life into the IBTPP. He left an indelible mark on science, medicine, public health, CDPH and infant botulism patients and their families worldwide." ❖

To learn more about the California Department of Public Health's Infant Botulism Treatment and Prevention Program, visit www.infantbotulism.org.

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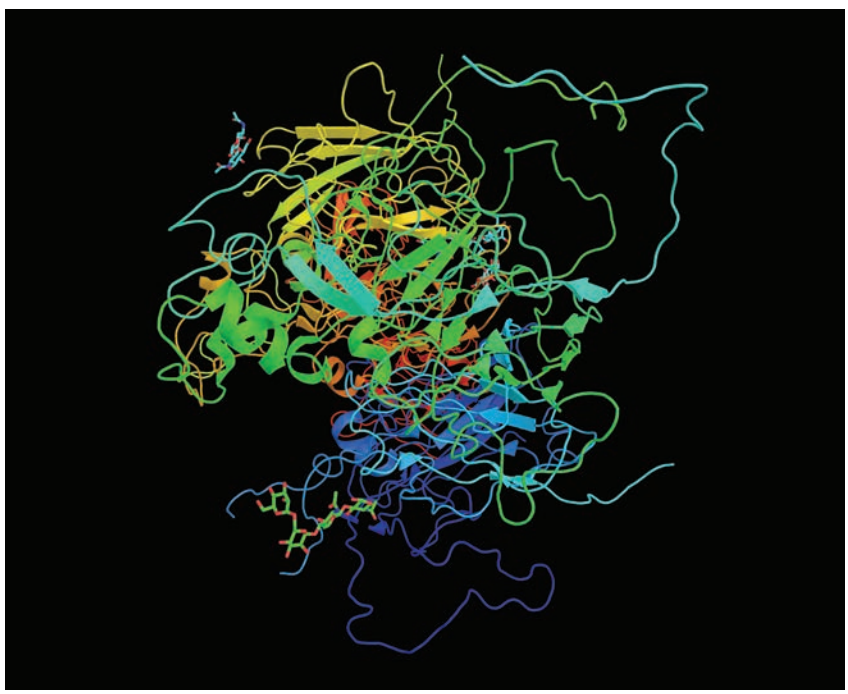
New and Better Hemophilia A Treatment Options Just Keep Coming

By Keith Berman, MPH, MBA



Computer-generated molecular model of human factor VIII

ONE CANNOT name a chronic health disorder whose clinical management has undergone a more dramatic evolution in our lifetimes than hemophilia A. Nor could one imagine a single-disease area of biopharmaceutical development with as many major plot twists, the most surprising of which is playing out as you read these words.

How Far We've Come

Prior to the introduction of the first human factor VIII (FVIII) concentrates in the late 1960s, patients experiencing a painful joint or soft tissue bleed were usually hospitalized and transfused with large volumes of fresh frozen plasma (FFP) in an effort to deliver just enough FVIII to control the bleed. Inevitably, years of joint bleeds would result in worsening hemarthrosis and progressive physical disability. Replacement of FFP by potent FVIII concentrates purified from pooled units of donor plasma both enabled the administration of much more factor and allowed patients to self-infuse at home, dramatically reducing the time from detection of the bleed to treatment.

In response to the 1980s AIDS crisis that infected and killed thousands of hemophilia patients, new generations of heat-treated, chemically-inactivated, monoclonal antibody-purified and nanofiltered human FVIII concentrates essentially eliminated HIV contamination and transmission risk, while additionally conferring protection against hepatitis B and C virus infection. A decade later, approvals of the first synthetic human FVIII concentrates produced by recombinant DNA techniques provided yet more reassurance of safety for physicians, patients and caregivers traumatized by the AIDS crisis.

These advances in the safety and purity of FVIII concentrates coincided with universal adoption of a game-changing advance in clinical management: regular prophylactic infusions of FVIII to help prevent bleeds from occurring in the first place. Then came the approval of Biogen Idec's Eloctate in 2014, heralding a new generation of genetically modified long-acting recombinant FVIII products whose extended intravascular persistence allows for major reductions in self-infusion frequency, translating into improved patient compliance with their prescribed prophylaxis regimens.

Today, physicians and their patients can choose from 16 FVIII products approved for the treatment of hemophilia A, including six recombinant, six long-acting recombinant and four plasma-derived FVIII products.[1]

Beyond FVIII Replacement: Hemlibra, Hympavzi and Alhemo

As transformative as each of these advancements in replacement therapy with FVIII concentrates have been for the management of hemophilia A, perhaps the most surprising new wave of innovations yet arrived in late 2017 with the approval of Hemlibra, an entirely novel non-factor

Table 1. Annualized Treated Bleed Rate with Hemlibra Prophylaxis Versus No Prophylaxis in Patients ≥12 Years of Age Without Factor VIII Inhibitors

Endpoint	Hemlibra 1.5 mg/kg once every week (n = 36)	Hemlibra 3 mg/kg once every two weeks (n = 36)	No prophylaxis (n = 18)
ABR (95% CI)	1.5 (0.9, 2.5)	1.5 (0.9, 2.5)	38.2 (22.9, 63.8)
% reduction in ABR vs. no prophylaxis (95% CI)	96% (0.9, 2.5)	97% (0.9, 2.5)	-
% of patients with zero bleeds (95% CI)	55.6% (38.1, 72.1)	60% (42.1, 76.1)	0% (0, 18.5)
Median ABR (IQR)	0 (0, 3.9)	0 (0, 4)	46.9 (26.1, 73.9)

ABR = annualized bleed rate; CI = confidence interval; IQR = interquartile range

Table 2. Intra-Patient Comparison of Annualized Treated Bleed Rate with Hemlibra Prophylaxis Versus Previous Factor VIII Prophylaxis

Endpoint	Hemlibra 1.5 mg/kg once every week (n = 48)	Previous FVIII prophylaxis (n = 48)
ABR (95% CI)	1.5 (1, 2.3)	4.8 (3.2, 7.1)
% reduction vs. previous FVIII prophylaxis (95% CI)	68% (48.6, 85.8)	
% of patients with zero bleeds (95% CI)	54.2% (39.2, 68.6)	39.6% (25.8, 54.7)
Median ABR (IQR)	0 (0, 2.1)	1.8 (0, 7.6)

ABR = annualized bleed rate; CI = confidence interval; IQR = interquartile range

product developed by Japan's Chugai Pharmaceutical and manufactured by Genentech, a Roche company. Hemlibra (emicizumab-kxwh) is a modified IgG4 bispecific humanized monoclonal antibody (MAb) that binds factor IXa and factor X, bridging these two key elements of the coagulation pathway to restore the function of the missing FVIII normally required for hemostasis.

Approved for hemophilia A patients of any age both with or without FVIII inhibitors, Hemlibra is specifically intended for routine prophylaxis to prevent or reduce the frequency of bleeding episodes. Not unlike subcutaneous human IgG immune globulin preparations, the pharmacokinetics of this uniquely designed MAb allows for subcutaneous self-administration on a weekly, biweekly or potentially even monthly basis. By comparison, the maximum inter-treatment interval for any of the approved long-acting FVIII products is one week or less, and all must be self-administered by intravenous infusion.

But the benefits of Hemlibra go well beyond its superior convenience and ease of administration. The Roche-sponsored HAVEN 3 study, the largest of several interventional trials documenting its efficacy and safety, evaluated Hemlibra in a total of 152 adult and adolescent males previously self-treated prophylactically or on-demand with FVIII concentrates in response to bleeding events. While many more outcome measures were reported (e.g., treated spontaneous bleeds and joint bleeds), tables 1 and 2 summarize 1) the overall performance of weekly or biweekly Hemlibra against concurrent episodic (on-demand) FVIII treatment and 2) weekly Hemlibra against previous FVIII prophylaxis in the same individuals.[2]

Each hemophilia A patient's status and needs are different, and many can continue to be successfully managed with factor therapy. But Hemlibra's strong overall comparative efficacy findings and its simplicity of use have enabled it to capture a very substantial share of the U.S. and EU5* hemophilia A patient market, with well over 20,000 patients treated with Hemlibra worldwide.[3]

Hympavzi (marstacimab-hncq). Last October, a second entirely novel non-factor treatment, Pfizer's Hympavzi, was approved by the U.S. Food and Drug Administration (FDA) for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adults and pediatric patients 12 years of age and older with hemophilia A or B without inhibitors.

This IgG1 antibody targets a specific domain of the tissue factor pathway inhibitor (TFPI), which negatively regulates thrombin generation within the extrinsic coagulation pathway by

* European Union Five (France, Germany, Italy, Spain and the United Kingdom)

inactivating the protease functions of factors Xa, VIIa and the tissue factor complex. Hympavzi's action occurs downstream from FVIII or factor IX, so it is similarly effective in hemophilia B, as well as hemophilia A patients. But like Hemlibra, Hympavzi is easy to self-administer (on a weekly basis only) with a quick subcutaneous injection.

Compared to prior on-demand factor-based therapy, Hympavzi prophylaxis reduced treated bleeds in 33 subjects enrolled in the BASIS study by more than 90 percent, from 38 to just over three bleeds. In a larger cohort of 83 subjects with hemophilia A and B on prior routine factor-based prophylaxis, Hympavzi prophylaxis significantly reduced the annualized bleeding rate (ABR) from nearly eight bleeds to five bleeds.

Alhemo (concizumab-mtci). Last December, just two months after it approved Hympavzi, FDA granted marketing approval for Novo Nordisk's Alhemo, a second proprietary MAb-based TFPI antagonist. Launched in February, Alhemo is specifically indicated as once-daily prophylaxis to prevent or reduce the frequency of bleeding episodes in adults and pediatric patients 12 years of age and older with hemophilia A or B with inhibitors. Alhemo can be dosed subcutaneously by the patient using a prefilled pen and fine gauge needle.

The estimated ABR for hemophilia A and B patients with inhibitors on Alhemo for at least 32 weeks was 1.7 bleeds, a reduction of 86 percent relative to the ABR of 11.8 bleeds for patients whose bleeds were conventionally managed with a bypassing agent (eptacog alfa; NovoSeven).[4]

Alhemo "provides a much-needed alternative to the current standard of care in hemophilia B with inhibitors, while offering patients with hemophilia A with inhibitors more treatment options, ultimately providing more patients with inhibitors the opportunity to personalize their care and address current treatment gaps," said Indiana Hemophilia & Thrombosis Center CEO and co-medical director Amy Shapiro, MD.

Following behind Hemlibra, Hympavzi and Alhemo are several other very promising non-factor treatments, including two in particular that are currently in late-stage clinical development:

Mim8 (Novo Nordisk). This subcutaneously administered factor VIIIa mimetic bispecific antibody bridges factor IXa and X together upon activation, thereby replacing missing FVIII. In clinical trial subjects with hemophilia A aged 12 years and older with or without inhibitors, those given Mim8 once weekly and once monthly, respectively experienced 97 percent and 99 percent reductions in treated bleeds compared to those who received no prophylaxis treatment. Remarkably, 86 percent and 95 percent of subjects, respectively, treated with once-weekly and once-monthly Mim8 experienced no treated bleeds over the 26-week treatment period.

In an intra-patient analysis of subjects previously managed with FVIII prophylaxis, once-weekly and once-monthly Mim8 demonstrated reductions of 48 percent and 43 percent in treated bleeds, respectively; again, roughly two-thirds of these study subjects experienced no treated bleeds.

Fitusiran (ALN-AT3) (Sanofi). This investigational RNA interference (RNAi) agent suppresses the production of antithrombin by targeting the messenger RNA encoded by the SERPINC1 gene that encodes this key regulator of coagulation function. By lowering circulating antithrombin levels, fitusiran administration increases thrombin generation, enhancing hemostasis.[5]

In a multinational Phase III trial of once-monthly prophylactic subcutaneous injections of fitusiran, patients aged 12 years and older with hemophilia A or B with or without inhibitors were crossed over from their routine use of prophylaxis with bypassing agents or clotting factor concentrates (BPAs/CFCs) to fitusiran prophylaxis for seven months. The observed ABRs were 6.5 while on BPA/CFC therapy versus zero during the fitusiran efficacy period. Estimated mean ABRs were reduced with fitusiran treatment by 79.7 percent and 46.4 percent versus BPA and CFC prophylaxis, respectively. Forty-one of 65 study participants (63.1 percent) experienced zero bleeds with fitusiran versus 11 (16.9 percent) with BPAs/CFCs.

FDA's decision on Sanofi's pending application for marketing approval was scheduled for March 28 of this year, so as you read this, fitusiran may already be the fourth new non-factor product approved for the treatment of hemophilia A.

The (Current) Fate of Gene Therapy

Over the last four decades, countless commentaries and media stories have touted gene therapy as the holy grail of severe hemophilia A therapy: a potentially curative one-time treatment that could empower the patient's own liver cells to produce sufficient sustained titers of functional FVIII, thus providing extended or even lifelong protection against uncontrolled bleeds.

The once far-off dream of gene therapy to cure hemophilia A began in 1984 when Genentech scientists reported they had fully characterized the massive human FVIII gene and expressed active human FVIII in cultured mammalian cells from recombinant DNA clones encoding the

complete FVIII gene.[6,7]

BioMarin Pharmaceuticals was first to market in mid-2023 with Roctavian, an adeno-associated virus vector-based gene therapy for the treatment of adults with severe hemophilia A. The mean ABR was reduced from 5.4 bleeds at baseline to 2.6 bleeds a median of three years after Roctavian administration. Of 112 clinical trial subjects rolled over from FVIII prophylaxis, just five (four percent) did not respond but 17 (15 percent) lost response to Roctavian treatment over a median period of just over two years. In 22 other subjects followed for a longer period, six (27 percent) lost response to Roctavian treatment over a median of 3.6 years.[8]

But for the large majority of patients who received this one-time gene therapy in clinical trials, it has largely or entirely freed them from the requirement to self-infuse factor or any other treatment to restore normal coagulation function. No instances of thromboembolic events or cancers have been observed in trial subjects or patients given Roctavian since approval.**

Why, then, have only a handful of non-trial hemophilia A patients been dosed with Roctavian as the product approaches two years on the market? And why did Pfizer, which has invested heavily in this space, decide last December to pull out of a late-stage R & D collaboration to develop its own hemophilia A gene therapy (giroctocogene fitelparvovec), and then decide in February of this year to discontinue commercialization of Beqvez, its hemophilia B gene therapy approved just a year ago?

"[Roctavian is] extremely expensive. And I think that it's going to take some time to be able to convince payers to cover this product," said Roctavian clinical study investigator Steven W. Pipe, MD, in an interview last year. "And then secondly… there's a lot of infrastructure that needs to be built out at the institutional level, in order to be a gene therapy infusion center."[9] These patient access-related issues continue to adversely impact usage, and unanswered questions remain concerning the durability and potential long-term side effects of hemophilia gene therapy.

But another consideration cannot be ignored: Prophylaxis treatment options available today have all but eliminated the fear of serious bleeds for many hemophilia A patients, and non-factor treatments in particular have made managing their condition far easier than ever before. "Unlike other genetic disorders for which gene therapy is available, hemophilia A and B each have effective treatment options that have more long-term safety and efficacy data," a team of clinicians at the University of North Carolina at Chapel Hill recently observed. "Given available alternative treatment options…a minority of patients are eager to undergo gene therapy treatment at present, and many are pleased with their current treatment regimen."[10] Put another way, the risk-benefit argument for gene therapy — at least at the moment — doesn't appear to add up for many patients or physicians upon whom they rely for information and advice.

The Dream of a Normal Life with Hemophilia A

Like few other areas of drug development, hemophilia A new product research has married cutting-edge genetic and protein engineering and rigorous clinical science to produce wave after wave of new and better treatment options. The sparse adoption of Roctavian and recent abandonment of clinical-stage gene therapies is obviously disappointing for their developers, but at least in part this reflects the larger success of an astonishing output of new therapies with unprecedented efficacy and convenience.

Thanks to these new products that have and continue to emerge from industry research laboratories, patients and providers today must search their memories or history books to recall that people with severe hemophilia A were once consigned to a lifetime of painful emergent bleeds, severely debilitating joint disease and progressive physical limitations. The dream of a normal life for persons with hemophilia A has arrived. ❖

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** FDA does caution that Roctavian's viral vector-introduced B-domain deleted FVIII gene may still carry the theoretical risk of hepatocellular carcinoma.

Smart Tools for Patient Safety

PATIENT SAFETY remains a nationwide problem. Medication mix-ups, misdiagnoses, surgical errors, sepsis — the list of concerns could go on. The Joint Commission updates its National Safety Goals every year based on the top patient safety risks, and two sources of patient harm consistently appear on the list as top causes of patient harm: patient falls and hospital-acquired infections (HAIs).

Patient falls are the most common adverse events reported in hospitals. Between 700,000 to one million patient falls occur each year, resulting in 250,000 injuries and some 11,000 deaths. Reasons for the falls are as diverse as the patients that experience them: limited mobility; impaired judgment; unfamiliar environments; varying fall prevention strategies.[1] Identifying high fall risk patients and responding quickly when a fall event occurs is easier said than done. High patient volume, staff shortages and burnout make it hard to keep an eye on all patients at all times.

According to the Centers for Disease Control and Prevention (CDC), more than 99,000 deaths each year are related to HAIs, but proper, consistent hand hygiene (washing hands with soap and water, using alcohol-based hand sanitizer and performing surgical hand antisepsis) can reduce this number.[2] In fact, 70 percent of infections could be prevented if healthcare workers followed CDC's recommended protocols. CDC says healthcare workers may need to clean their hands as many as 100 times during a single shift, but adherence to this recommendation is low.[3,4]

What can hospitals do to help lower the burden of falls and improve hand hygiene compliance? Here are two innovative smart tools designed to help.

AvaSure TeleSitter Solution

AvaSure's TeleSitter Solution is an artificial intelligence-powered fall and elopement detection solution that provides automatic alerts to healthcare workers when patients get out of bed. Computer vision and video technology work together to alert workers to potential falls and other high-risk events so clinicians can act fast when patients need them. TeleSitter makes it possible for one observer to monitor 16 patients at once. The high-resolution cameras equipped with 10x optical zoom provide a comprehensive view of hospital rooms, detect potential risk before it happens and, according to AvaSure, reduce adverse events by more than 50 percent. For more information, visit *avasure.com/telesitter*.

Vitalacy Automated Hand Hygiene Monitoring

The most complete solution to monitor and improve hand hygiene habits, Vitalacy's automated hand hygiene monitoring system enforces compliance by tracking how often healthcare workers clean their hands either with soap and water or hand sanitizer. The solution's 24/7 capabilities enable hospitals to meet hand hygiene practice standards while providing budget-friendly and upgradeable hand options, including:

- The SmartBadge, which clips to clothing and can be worn with clinician identification badges.
- The SmartClip, which gives real-time reminders at point-of-care. It can be clipped to a healthcare provider's shirt.
- The SmartBand, which gives real-time reminders at point-of-care and coaches wash duration. It includes silent visual and vibration reminders, works with current dispensers and is easy to integrate into everyday use. It is worn around the wrist.

Each hand hygiene monitoring system comes with the Vitalacy dashboard, which enables easy viewing of all hand hygiene compliance data. Data can be sorted to view reports on individuals, units, departments or the entire building.

For more information and to schedule a demo, visit *vitalacy.com/automated-hand-hygiene-monitoring-technology*.

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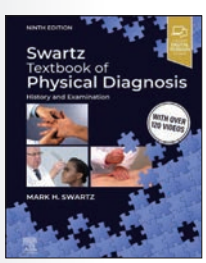
Swartz Textbook of Physical Diagnosis: History and Examination, 9th Edition

Author: Mark H. Swartz, MD, FACP

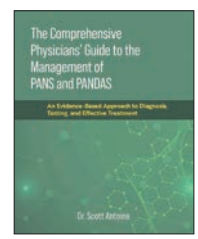
This textbook is written to help medical professionals master each aspect of the art and science of interviewing and physical examination. It teaches how interpersonal awareness is just as crucial during the patient interview and physical exam as skill level, and why clinical competence in this area is essential for physicians, osteopathic physicians, nurse practitioners, physician assistants, nurses and all other members of the healthcare profession. This edition includes fully revised content, three new chapters, hundreds of color images, end-of-chapter review questions and more.

www.amazon.com/Swartz-Textbook-Physical-Diagnosis-Examination/dp/0443235066



The Comprehensive Physicians' Guide to the Management of PANS and PANDAS: An Evidence-Based Approach to Diagnosis, Testing, and Effective Treatment

Author: Scott Antoine, DO



This textbook is written by physicians who care for children with PANS and PANDAS and their families. The material is assembled from peer-reviewed medical literature, in combination with more than 30 years of clinical experience caring for the sickest patients, both in and out of the hospital. Included is conclusive evidence for the existence and pathophysiology of PANS and PANDAS, alongside testing and treatment interventions the author has successfully used in his own practice with hundreds of children. The book concludes with appendices, including commonly used labs, doses of medications and supplements, a sample flare protocol, extensive support for parents, sample intravenous immune globulin orders and more.

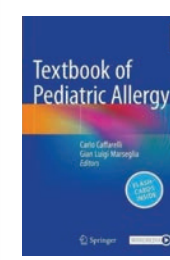
www.amazon.com/Comprehensive-Physicians-Guide-Management-PANDAS/dp/163763269X

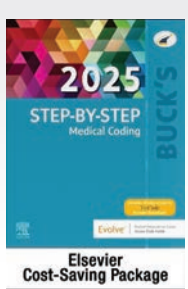
Textbook of Pediatric Allergy

Editors: Carlo Caffarelli and Gian Luigi Marseglia

This textbook provides comprehensive and state-of-the-art coverage of allergic diseases and related cell-based conditions in pediatric patients. Presented are the most common disorders such as allergies to drugs, food (including non IgE-mediated food allergy), asthma, allergens, pollutants and much more, as well as parts on wheezing, daily routine and quality of life in affected children. Flash cards are also included.

www.amazon.com/Textbook-Pediatric-Allergy-Carlo-Caffarelli/dp/303171282X





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Medicare Immune Globulin Reimbursement Rates

Rates are effective April 1, 2025, through June 30, 2025

	Product	Manufacturer	J Codes	ASP + 6% (before sequestration)	ASP + 4.3% (after sequestration)
IVIG	ALYGLO	GC Biopharma	J1599	$276.22	$271.79
	ASCENIV	ADMA Biologics	J1554	$993.37	$977.43
	BIVIGAM	ADMA Biologics	J1556	$154.60	$152.12
	GAMMAGARD SD	Takeda	J1566	$162.02	$159.42
	GAMMAPLEX	BPL	J1557	$114.95	$113.11
	OCTAGAM	Octapharma	J1568	$96.11	$94.57
	PANZYGA	Octapharma/Pfizer	J1576	$140.86	$138.60
	PRIVIGEN	CSL Behring	J1459	$98.36	$96.78
	YIMMUGO	Kedrion	C9399**	•	*
IVIG/SCIG	GAMMAGARD LIQUID	Takeda	J1569	$90.26	$88.81
	GAMMAKED	Kedrion	J1561	$96.69	$95.14
	GAMUNEX-C	Grifols	J1561	$96.69	$95.14
SCIG	CUTAQUIG	Octapharma	J1551	$143.35	$141.05
	CUVITRU	Takeda	J1555	$166.82	$164.14
	HIZENTRA	CSL Behring	J1559	$136.44	$134.25
	HYQVIA	Takeda	J1575	$176.65	$172.83
	XEMBIFY	Grifols	J1558	$142.83	$140.54

* ASP-based Medicare payment rate not yet available; payment rate assigned by your Medicare Administrative Contractor.

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** For other payers, bill YIMMUGO with a HCPCS code or codes as instructed by each payer.

Immune Globulin Reference Table

	Product	Manufacturer	Indication	Size
IVIG	ALYGLO	GC Biopharma	PI	5 g, 10 g, 20 g
	ASCENIV LIQUID, 10%	ADMA Biologics	PI	5 g
	BIVIGAM LIQUID, 10%	ADMA Biologics	PI	5 g, 10 g
	GAMMAGARD S/D Lyophilized, 5% (Low IgA)	Takeda	PI, ITP, B-cell CLL, KD	5 g, 10 g
	GAMMAPLEX Liquid, 5%	BPL	PI, ITP	5 g, 10 g, 20 g
	GAMMAPLEX Liquid, 10%	BPL	PI, ITP	5 g, 10 g, 20 g
	OCTAGAM Liquid, 5%	Octapharma	PI	1 g, 2.5 g, 5 g, 10 g, 25 g
	OCTAGAM Liquid, 10%	Octapharma	ITP, DM	2 g, 5 g, 10 g, 20 g, 30 g
	PANZYGA Liquid, 10%	Octapharma/Pfizer	PI, ITP, CIDP	1 g, 2.5 g, 5 g, 10 g, 20 g, 30 g
	PRIVIGEN Liquid, 10%	CSL Behring	PI, ITP, CIDP	5 g, 10 g, 20 g, 40 g
	YIMMUGO, 10%	Kedrion	PI	5 g, 10 g, 20 g
IVIG/SCIG	GAMMAGARD Liquid, 10%	Takeda	IVIG: PI, MMN, CIDP	1 g, 2.5 g, 5 g, 10 g, 20 g, 30 g
			SCIG: PI	
	GAMMAKED Liquid, 10%	Kedrion	IVIG: PI, ITP, CIDP	1 g, 2.5 g, 5 g, 10 g, 20 g
			SCIG: PI	
	GAMUNEX-C Liquid, 10%	Grifols	IVIG: PI, ITP, CIDP	1 g, 2.5 g, 5 g, 10 g, 20 g, 40 g
			SCIG: PI	
SCIG	CUTAQUIG Liquid, 16.5%	Octapharma	PI	1 g, 1.65 g, 2 g, 3.3 g, 4 g, 8 g
	CUVITRU Liquid, 20%	Takeda	PI	1 g, 2 g, 4 g, 8 g, 10 g
	HIZENTRA Liquid, 20%	CSL Behring	PI, CIDP	1 g PFS, 2 g PFS, 4 g PFS, 10 g PFS
	HYQVIA Liquid, 10%	Takeda	PI, CIDP	2.5 g, 5 g, 10 g, 20 g, 30 g
	XEMBIFY Liquid, 20%	Grifols	PI	1 g, 2 g, 4 g, 10 g

CIDP Chronic inflammatory demyelinating polyneuropathy
CLL Chronic lymphocytic leukemia
DM Dermatomyositis
ITP Immune thrombocytopenic purpura
KD Kawasaki disease
MMN Multifocal motor neuropathy
PI Primary immune deficiency disease
PFS Prefilled syringes

2024-2025/2025-2026 Influenza Vaccines

Administration Codes: G0008 (Medicare plans)
Diagnosis Code: V04.81

Product	Manufacturer	Presentation	Age Group	2024-2025 Code	2025-2026 Code
Trivalent					
AFLURIA (IIV4)	CSL Seqirus	0.5 mL PFS 10-bx	3 years and older	90685	90656
AFLURIA (IIV4)	CSL Seqirus	5 mL MDV	6 months and older	90685	90657
FLUAD (IIV4)	CSL Seqirus	0.5 mL PFS 10-bx	65 years and older	90694	90653
FLUARIX (IIV4)	GSK	0.5 mL PFS 10-bx	6 months and older	90686	90656
FLUBLOK (ccIIV4)	Sanofi	0.5 mL PFS 10-bx	18 years and older	90682	90673
FLUCELVAX (ccIIV4)	CSL Seqirus	0.5 mL PFS 10-bx	6 months and older	90674	90661
FLUCELVAX (ccIIV4)	CSL Seqirus	5 mL MDV	6 months and older	90756*	90661
FLULAVAL (IIV4)	GSK	0.5 mL PFS 10-bx	6 months and older	90686	90656
FLUMIST (LAIV4)	Astrazeneca	0.2 mL nasal spray 10-bx	2-49 years	90672	90672
FLUZONE (IIV4)	Sanofi	0.5 mL PFS 10-bx	6 months and older	90686	90658
FLUZONE (IIV4)	Sanofi	5 mL MDV	6 months and older	90685	90658
FLUZONE HIGH-DOSE (IIV4)	Sanofi	0.7 mL PFS 10-bx	65 years and older	90662	90662

ccIIV4 Cell culture-based trivalent inactivated injectable
IIV4 Egg-based trivalent inactivated injectable
LAIV4 Egg-based live attenuated trivalent nasal spray

* Providers should check with their respective payers to verify which code they are recognizing for Flucelvax Trivalent 5 mL MDV product reimbursement for this season.

2024-2025/2025-2026 COVID-19 Vaccines

Product	Manufacturer	Presentation	Age Group	2024-2025 Code	2025-2026 Code
SPIKEVAX COVID-19 Vaccine, mRNA	Moderna	0.5 mL SDV 10-pk	12 years and older	91322	91322
MODERNA COVID-19 Vaccine, mRNA	Moderna	0.25 mL SDV 10-pk	6 months to 11 years	91321	91321
NOVAVAX COVID-19 Vaccine, Adjuvanted	Novavax	0.5 mL SDV 10-pk	12 years and older	91304	91304
COMIRNATY COVID-19 Vaccine, mRNA	Pfizer-BioNTech	0.3 mL PFS 10-bx	12 years and older	91320	91320

2024-2025/2025-2026 Respiratory Syncytical Virus (RSV) Products

Product	Manufacturer	Presentation	Age Group	2024-2025 Code	2025-2026 Code
ABRYSVO	Pfizer	0.5 mL Kit 1-ctn	60 years and older	90678	90678
ABRYSVO	Pfizer	0.5 mL Kit 5-ctn	60 years and older	90678	90678
ABRYSVO	Pfizer	0.5 mL PFS and Act-O vials 10-ctn	60 years and older and pregnant individuals 32-34 weeks gestation	90678	90678
AREXVY	Pfizer	0.5 mL SDV 10-bx	60 years and older	90679	90679
BEYFORTUS	Sanofi	0.5 mL PFS 5-bx	children up to 24 months	90380	N/A
BEYFORTUS	Sanofi	1 mL PFS 5-bx	children up to 24 months	90381	N/A
mRESVIA	Moderna	0.5 mL PFS 10-bx	60 years and older	90683	90683

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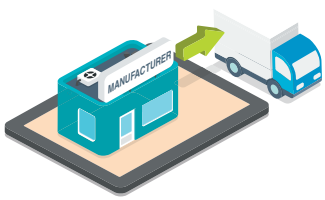
8 Critical Steps

STEP 1

Purchasing

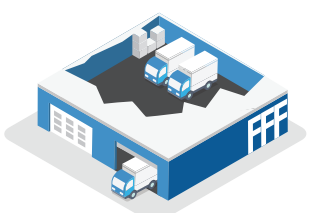
At FFF, we only purchase product from the manufacturer–never from another distributor or source–so the integrity of our products is never in question.



STEP 2

Storage

The healthcare products we store and transport are sensitive to temperature variations. Our state-of-the-art warehouse is temperature-controlled, monitored 24/7, and supported with backup generators in the event of power loss.



STEP 3

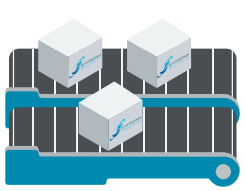
Specialty Packaging

At FFF, we use only certified, qualified, environmentally-friendly packaging, taking extra precautions for frozen and refrigerated products.

STEP 4

Interactive Allocation

FFF's unique capability of interactive allocation allows us to do that through our field sales team's close relationship with our customers. Our team understands customers' ongoing requirements, responds to their immediate crises, and allocates product in real-time to meet patients' needs.



Our commitment to a secure pharmaceutical supply chain is demonstrated by our flawless safety record. The 8 Critical Steps to Guaranteed Channel Integrity have resulted in more than 11,600 counterfeit-free days of safe product distribution.

800.843.7477 | Emergency Ordering 24/7

STEP 5

Delivery

Our delivery guidelines are in compliance with the State Board of Pharmacy requirements. Products we deliver must only be transported to facilities with a state-issued license, and only to the address on the license. We make no exceptions. And we will not ship to customers known to have a distributor's license.

STEP 6

Methods of Delivery

We monitor for extreme weather conditions, and when the need arises, we ship overnight to maintain product efficacy. We also track patient need during life-threatening storms to make sure products are delivered when and where patients need them most.

STEP 7

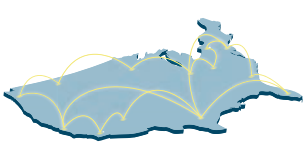
Verification

In compliance with U.S. Drug Supply Chain Security Act (DSCSA) requirements, every product shipped from FFF is accompanied by a packing slip that includes information regarding the manufacturer and presentation, as well as the three T's: Transaction Information, Transaction History, and Transaction Statement.

STEP 8

Tracking

To meet DSCSA requirements, FFF provides product traceability information on all packing slips. In addition, Lot-Track® electronically captures and permanently stores each product lot number, matched to customer information, for every vial of drug we supply.



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