FALL 2020

biosupplytrends
QUARTERLY

SPECIAL FOCUS:
**INNOVATION**

# Healthcare's Changing Landscape

*Telehealth Post-Pandemic:*
WILL IT SURVIVE?

BENEFITS AND DRAWBACKS TO THE
*Surge of mHealth*

*How Social Media*
IS INFLUENCING HEALTHCARE

ADVANCES IN THE FIELD OF
*Regenerative Medicine*

*A Growing Argument for Subcutaneous Immune Globulin* p.40

# 8 Critical Steps


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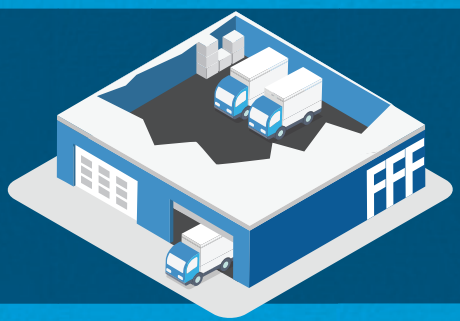



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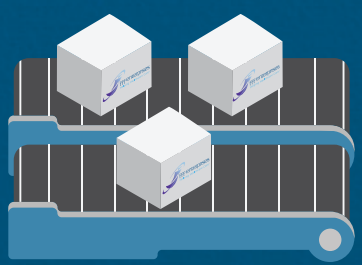

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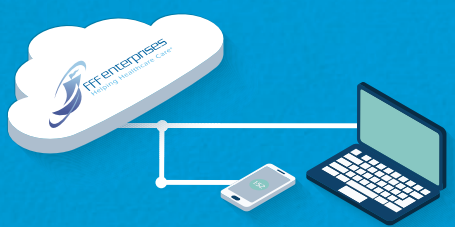

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*BioSupply Trends Quarterly* (ISSN 1948-2620) is a national publication, with quarterly themed issues.

Publisher: FFF Enterprises, Inc., 44000 Winchester Road, Temecula, CA 92590

Subscriptions to *BioSupply Trends Quarterly* are complimentary. Readers may subscribe by calling (800) 843-7477 x1351.





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# The Transformation of Healthcare in a Post-Pandemic Era

**DURING THE** last several years, the American healthcare system has experienced constant change. Most prominent in just this past year are significant alterations in how healthcare is practiced and delivered. And, by the looks of things, these changes are slated to continue. Exactly how they will evolve, though, is up for debate, especially in a post-pandemic era.

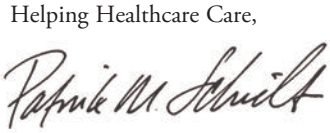
Perhaps the most talked-about shift in healthcare right now is the widespread adoption of telehealth. While the technology is not new, the COVID-19 pandemic hastened its adoptioin in order to protect both patients and providers. Surprisingly, most healthcare consumers have embraced and adapted to this mode of receiving care, resulting in an increase in telehealth use by more than 50 percent over the previous year. But, as we examine in our article "Healthcare Delivery Post-Pandemic" (p.16), the question looms as to whether telehealth is here to stay, despite its relative recent success. The main dilemma is where healthcare is best provided. And, this discussion has moved beyond telehealth to the formation of facilities that would improve healthcare delivery at a more affordable cost such as consolidated care centers. Fortunately, geographic restrictions and reimbursement criteria that previously stymied efforts to provide telehealth have been lifted with federal waivers. Yet, it still remains to be seen whether payers will continue to be on board to achieve long-term positive outcomes.

The need for social distancing while receiving and providing care has also spurred the growth of mHealth apps, wearables and tools. Statistics show the use of mHealth has skyrocketed over the past five years, enabled by 80 percent of Americans owning smartphones. But, as we highlight in our article "The mHealth Revolution: An Alternative to Traditional Healthcare" (p.20), not all mHealth is beneficial. While mHealth has its advantages, including real-time remote communication, paperless documentation, improved treatment compliance and cost savings, among others, federal regulation is needed to ensure quality and safety, especially in terms of privacy and security.

The digital healthcare landscape is also increasingly migrating to social media platforms such as Facebook and Twitter. Referred to as an "extension of the doctor-patient relationship," these platforms are helping providers attract new patients and reach out to existing patients, as we explain in our article "The Doctor Will Tweet You Now" (p.24). What's more, these sites can be used by providers to disseminate accurate health information and share data with other healthcare professionals. But, social media has its risks, which is why the American Medical Association has developed a code of moral ethics to which providers should adhere to ensure HIPAA compliance and to maintain patients' trust.

As always, we hope you enjoy this issue of *BioSupply Trends Quarterly*, and find it both relevant and helpful to your practice.

Helping Healthcare Care,



Patrick M. Schmidt
Publisher

biosupply trends 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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## FDA Implements New Warnings for Cigarette Packages and Advertisements


The U.S. Food and Drug Administration (FDA) issued a final rule to require new health warnings on cigarette packages and in cigarette advertisements, which feature textual statements with photo-realistic color images depicting some of the lesser-known, but serious health risks of cigarette smoking, including impact to fetal growth, cardiac disease, diabetes and more. Beginning June 18, 2021, the new health warnings will be required to appear prominently on cigarette packages and in advertisements, occupying the top 50 percent of the area of the front and rear panels of cigarette packages and at least 20 percent of the area at the top of cigarette advertisements. Once implemented, the new warnings must be randomly and equally displayed and distributed on cigarette packages and rotated quarterly in cigarette advertisements.

The warnings focus on serious health risks less known by the public as being negative health consequences of smoking. For example, current smokers have been found to have almost four times the risk of bladder cancer as never-smokers, and it has been estimated smoking is responsible for 5,000 bladder cancer deaths in the U.S. each year. Yet, research shows the public has limited awareness of bladder cancer as a consequence of smoking.

The set of 11 required warnings are based on the full results of FDA's consumer research studies, the relevant scientific literature, public comments submitted to the proposed rule docket and other legal and policy considerations. The final cigarette health warnings each consist of one of the following textual warning statements paired with an accompanying photo-realistic image depicting the negative health consequences of smoking:

- WARNING: Tobacco smoke can harm your children.
- WARNING: Tobacco smoke causes fatal lung disease in nonsmokers.
- WARNING: Smoking causes head and neck cancer.
- WARNING: Smoking causes bladder cancer, which can lead to bloody urine.
- WARNING: Smoking during pregnancy stunts fetal growth.
- WARNING: Smoking can cause heart disease and strokes by clogging arteries.
- WARNING: Smoking causes COPD, a lung disease that can be fatal.
- WARNING: Smoking reduces blood flow, which can cause erectile dysfunction.
- WARNING: Smoking reduces blood flow to the limbs, which can require amputation.
- WARNING: Smoking causes type 2 diabetes, which raises blood sugar.
- WARNING: Smoking causes cataracts, which can lead to blindness.

In addition, FDA has issued a guidance to accompany the final rule titled "Required Warnings for Cigarette Packages and Advertisements: Small Entity Compliance Guide" for industry to assist small businesses in understanding and complying with the rule. ❖

FDA Requires New Health Warnings for Cigarette Packages and Advertisements. U.S. Food and Drug Administration press release, March 17, 2020. Accessed at www.fda.gov/news-events/press-announcements/fda-requires-new-health-warnings-cigarette-packages-and-advertisements.

## $1.95M Grant Awarded to Study Autoimmune Diseases

The National Institutes of Health (NIH) has awarded a $1.95 million federal grant to researchers investigating the underlying cause (molecular mechanisms) of autoimmune diseases. The five-year study will use mouse models and a new RNA sequencing technology from 10x Genomics to better understand the mechanisms of central and peripheral tolerance.

"The goal of the work is to better understand how the natural limitations of thymic selection predispose us to autoimmunity," said Leszek Ignatowicz, PhD, lead investigator of the study. "This research will provide a better understanding of cellular and molecular mechanisms driving autoimmunity and help to develop therapeutic strategies targeting autoreactive cells that escaped central tolerance." ❖

Melamed D. Researchers Studying Cause of Autoimmune Diseases Awarded $1.95M Grant. *Lambert Eaton News*, June 11, 2020. Accessed at lamberteatonnews.com/2020/06/11/researchers-studying-cause-of-autoimmune-disease-awarded-1-95m-us-federal-grant.

## Judge Rules Against Hospitals' Suit Challenging New Price Transparency Rules

A federal judge ruled against the American Hospital Association and other hospital groups that filed suit in December contesting a finalized rule by the U.S. Department of Health and Human Services (HHS) that requires hospitals to disclose price information, including negotiated prices with insurers. According to the hospitals, the regulation was beyond HHS' authority, a violation of commercial speech and disclosing price information would lead to higher costs. While insurers also pushed back against the regulation, none joined the lawsuit.

But, U.S. District Judge Carl Nichols dismissed the arguments and ruled in favor of HHS. In addition, he dispelled concerns that disclosing negotiated prices could chill negotiations between hospitals and insurers, pointing out patients still see those prices in their explanation of benefits. "Plaintiffs are essentially attacking transparency measures generally, which are intended to enable consumers to make informed decisions; naturally, once consumers have certain information, their purchasing habits may change and suppliers of items and services may have to adapt accordingly," he wrote in his decision. ❖

Reuter E. Judge Rules Against Hospitals in Price Transparency Lawsuit. *MedCity News*, June 23, 2020. Accessed at medcitynews.com/2020/06/court-rules-against-hospital-groups-in-price-transparency-lawsuit.

## HHS Extends COVID-19 Public Health Emergency

At the end of July, the U.S. Department of Health and Human Services (HHS) extended the national public health emergency declared for the COVID-19 pandemic, which grants COVID-19 payment and regulatory flexibilities, for another 90 days. "The Administration will continue its whole-of-America response to ensure Americans can get the care they need throughout the pandemic," said HHS Secretary Alex Azar.

HHS has released a wide range of waivers and regulatory flexibilities during the pandemic to support healthcare providers. These include Medicare payment and billing changes with a goal of closing the funding shortfall experienced by many organizations as a result of COVID-19. For example, Medicare will pay a 20 percent add-on payment for inpatient hospital COVID-19 patients for the duration of the public health emergency. Medicare also released waivers for COVID-19 patients during the emergency period, including the long-term care hospital (LTCH) site-neutral payment policy, the LTCH 50% Rule and the inpatient rehabilitation facility 3-Hour Rule. HHS has also implemented key telehealth payment and coverage flexibilities during the public health emergency, including expanded coverage of telehealth services delivered to Medicare beneficiaries in a wider range of locations. In addition, the department allows for higher reimbursement rates for the newly allowed telehealth services.

HHS is contemplating making some of the waivers and flexibilities granted during the public health emergency permanent. For example, significant adoption of telehealth services during the pandemic has led the Centers for Medicare and Medicaid Services to consider lasting changes to Medicare coverage of telehealth and higher reimbursement for the services. ❖

LaPointe J. HHS Extends Public Health Emergency, COVID-19 Payment Flexibility. Rev Cycle Intelligence, July 27, 2020. Accessed at revcycleintelligence.com/news/hhs-extends-public-health-emergency-covid-19-payment-flexibility.

# Proposed Payment Rules and Court Rulings

By Bonnie Kirschenbaum, MS, FASHP, FCSHP

**SEVERAL PAYMENT** rules, court rulings, executive orders and additional healthcare legislation, some relating to the COVID-19 pandemic, have been implemented, culminating with the delayed 2021 outpatient prospective payment system (OPPS)/ambulatory surgical center (ASC) and physician fee schedule (PFS) rules. Two court rulings and segments of the proposed OPPS/ASC and PFS rules may require action from providers to recover expenses caused by the COVID-19 pandemic. Indeed, to stabilize revenue and cut costs, it will be necessary for providers to work with specialty pharmacies concerning white bagging and negotiate with private insurers.

## Focusing on Site of Care

Site-neutral payment, which reimburses hospital clinic visits at the same rate as physician offices and other ambulatory facilities, resulted in complaints and legal action, and a final decision has now been reached. The controversy began with the 2019 Medicare OPPS final rule by the Centers for Medicare and Medicaid Services (CMS) that made payments for clinic visits site-neutral, reducing the payment rate by 60 percent for evaluation and management services provided at off-campus provider-based departments (PBDs). Since clinic visits are the most common service billed under OPPS, a decreased payment rate for off-campus PBDs at 40 percent of OPPS rates, regardless of whether PBDs were grandfathered under Section 603 of the Bipartisan Budget Act of 2015, was anticipated to save $760 million. At the same time, patients benefited since their co-payments decreased. However, several lawsuits later, the federal appeals court ruled on July 20 that the U.S. Department of Health and Human Services (HHS) has the authority to cut Medicare payments to off-campus clinics to bring them in line with independent physician practices.

The objective behind the rule is to continue to give beneficiaries more affordable choices for where to obtain care to lower out-of-pocket expenses, including those for surgeries. According to CMS, this change allows hospitals and ASCs to operate with better flexibility and patients to have what they need to make informed decisions about where they receive care. The rule eliminates the inpatient-only list over three years to allow services to be provided in the hospital outpatient setting when appropriate and gradually expands the number of procedures Medicare will pay for in the hospital outpatient setting to more than 1,700 additional services, including approximately 300 musculoskeletal services (e.g., joint replacement procedures). Since services in ASCs are paid at a lower rate than hospital outpatient departments, an expanded number of procedures Medicare would pay for when performed in an ASC will give patients more choices about where they receive care and will ensure CMS does not favor one type of care setting over another. In 2021, 11 procedures that Medicare will pay for when provided in an ASC have been added, including total hip arthroplasty. Also in 2021, current restrictions for physician-owned hospitals are loosened.

These site-of-care changes have multiple implications on the supply chain and the provision of pharmacy services, and they become effective at the same time hospitals are trying to regain financial stability. In a descending cost pyramid, hospitals remain at the pinnacle as the most expensive sites, followed by outpatient locations, free-standing clinics and self-administration/treatment/telehealth at home. Due to the COVID-19 pandemic that forced patients away from hospitals, the move to alternate sites of care has become the norm.

## 2021 Proposal for Payment for Non-Opioid Alternatives

The SUPPORT Act requires the HHS Secretary to review payments under the OPPS for opioids and evidence-based non-opioid alternatives for pain management (including drugs and devices,

nerve blocks, surgical injections and neuromodulation) with a goal of ensuring there are not financial incentives to use opioids instead of non-opioid alternatives. Compliant with this, the 2021 proposed OPPS/ASC rule continues the existing policy of paying separately at ASP+6 percent for the cost of non-opioid pain management drugs that function as surgical supplies to perform surgical procedures when they are furnished in the ASC setting. It also continues to package payment for non-opioid pain management drugs that function as surgical supplies to perform surgical procedures in the hospital outpatient department setting for 2021 (with no separate line-item payment).

Decisions concerning how to respond to this continue to require a pairing of the SUPPORT Act, the 2021 payment rules and the site-of-care changes. Therefore, what providers may have chosen to do in a hospital setting may be at odds with these rules.

## Payment Rate Changes for Certain Medicare Part B Drugs Purchased by Hospitals Through 340B

As a continuing commitment to lowering drug prices, CMS is proposing a change that would lower beneficiaries' out-of-pocket drug costs for certain hospital outpatient drugs. This applies to status indicator [SI] K non-pass-through drugs paid for under Medicare Part B; SI G pass-through drugs are not affected. It's important to remember that if a facility's reimbursement decreases, the patient's co-pay decreases by the same percentage.

On July 31, the U.S. Court of Appeals for the District of Columbia Circuit overturned a 2018 district court decision that found HHS exceeded its statutory authority when it reduced 2018 and 2019 Medicare payment rates for many hospitals in the 340B program by almost 30 percent. "We hold that HHS's decision to lower drug reimbursement rates for 340B hospitals rests on a reasonable interpretation of the Medicare statute," Chief Justice Sri Srinivasan said in the opinion for the court. The rationale by HHS to cut the rate for 340B hospitals was to close a payment gap between 340B and Medicare Part B. HHS argued that Medicare should not reimburse hospitals more than they paid to acquire the drugs.

The 2021 proposed OPPS/ASC rules outlined two options being considered for reimbursing drugs purchased under 340B: 1) maintaining the current average sales price (ASP) minus 22.5 percent with conditions and 2) implementing a new rate, based on this year's hospital survey, of ASP minus 34.7 percent plus an overhead payment set at 6 percent of ASP for a net rate of ASP minus 28.7 percent. Exemptions will continue for rural sole community hospitals, certain cancer hospitals and children's hospitals, but they will still be required to report the informational TB modifier.

These OPPS changes apply only to Medicare patients treated in an OPPS setting, and they are not a Health Resources and Services Administration rule change.

## CMS Price Transparency Requirements

An executive order signed June 24, Improving Price and Quality Transparency in American Healthcare to Put Patients First, is designed to increase availability of meaningful price and quality information for patients with the belief that transparency in healthcare pricing is "critical to enabling patients to become active consumers so they can lead the drive toward value." This new rule builds upon a 2015 rule that required hospitals to make public their standard charges upon request and subsequently online in a machine-readable format in 2019. New requirements imposed by the rule are that each hospital operating within the U.S. establish (and update) and make public a yearly list of the hospital's standard charges for items and services provided by the hospital, including for diagnosis-related groups. The rule includes 1) definitions of hospital, standard charges and items and services; 2) requirements for making public a machine-readable file online that includes all standard charges for all hospital items and services; 3) requirements for making public payer-specific negotiated charges for a limited set of "shoppable" services that are displayed and packaged in a consumer-friendly manner; and 4) monitoring for and actions to address hospital noncompliance (including issuing a warning notice, requesting a corrective action plan and imposing civil monetary penalties), and a process for hospitals to appeal these penalties.

The goal of the rule is to create price pressure to lower healthcare costs by enabling consumers to more actively compare prices and proactively shop for care. Rather than perceiving transparency as an unwelcome burden, this rule presents opportunities for healthcare facilities to showcase services they provide and engage patients while meeting its requirements.

Details concerning transparency will be provided in the Winter 2021 issue of *BioSupply Trends Quarterly*. ❖

**BONNIE KIRSCHENBAUM**, MS, FASHP, FCSHP, is a freelance healthcare consultant with senior management experience in both the pharmaceutical industry and the pharmacy section of large corporate healthcare organizations and teaching hospitals. She has an interest in reimbursement issues and in using technology to solve them. Kirschenbaum is a recognized industry leader in forging effective alliances among hospitals, physicians, pharmaceutical companies and distributors and has written and spoken extensively in these areas.

# Tips for Recruiting Healthcare Talent

By Ronale Tucker Rhodes, MS

**LONG BEFORE** the COVID-19 pandemic struck the U.S. at the beginning of this year, the demand for healthcare services was soaring, creating an urgent need for more healthcare workers. For instance, in just the first three months of 2017, the healthcare industry added approximately 60,000 new jobs, including nurses, physicians, allied professionals, leaders and nonclinical positions.[1] And, the U.S. Bureau of Labor Statistics (BLS) projects healthcare occupations will grow 14 percent from 2018 to 2028, much faster than the average for all occupations, adding about 1.9 million new jobs.[2]

The reasons for this immense growth? The greatest driver is an aging population. According to projections from the U.S. Census Bureau, the number of people 65 years and older will grow from 43 million in 2012 to 84 million in 2050, escalating from 14 percent of the population to 21 percent. What's more, this population will need a greater quantity and complexity of healthcare services. According to the Centers for Disease Control and Prevention, people over age 65 experience three times more hospital days than the general public, and those over 75 years experience four times more hospital days.[3]

Another growth driver is the economy. BLS says U.S. employment will rise from 150.5 million in 2014 to 160.3 million in 2024. More people with jobs means more people who have health insurance and money to pay for co-pays and deductibles.[1] (Although, as of this writing, it is not known whether the economy will continue to grow at this rate due to the pandemic.) Add to this equation the Affordable Care Act, which has allowed more people to purchase health insurance.[4]

And, while the growth in jobs is great news for the healthcare industry, it poses a critical problem since there is a major shortage of trained professionals. According to the BLS Job Openings and Labor Turnover Survey (which is conducted every two years), while job openings have traditionally outpaced job hires in healthcare, the gap between openings and hires has been widening rapidly since 2014. Job openings have been rising, while job hires have remained relatively static (Figure 1). Job openings include new jobs, retirements, quits and any other kind of job separation. Another BLS survey projects 1.26 million total healthcare job openings per year for 2016 through 2026. For all practitioners and technical occupations, the projection is 624,000 job openings per year, which includes 204,000 registered nurse job openings per year (Figure 2).[3]

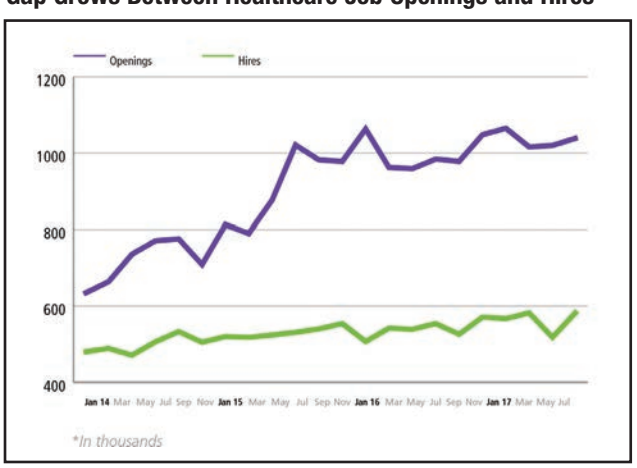
In light of the uber-competitive environment to attract workers, healthcare facilities would be wise to embrace some key recruitment strategies.

## Attracting Talent

With the widening gap in the number of jobs versus the number of workers, it all comes down to supply versus demand. Today's market is a worker's not a seller's market, and that's exactly how facilities need to approach the hiring process.

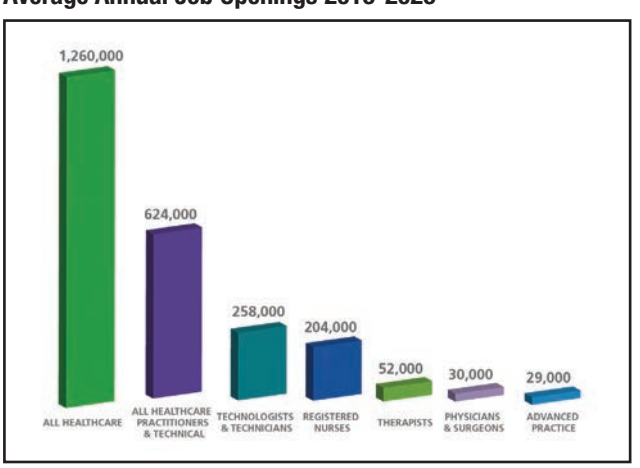
It starts with branding. According to PeopleScout, a recruitment process outsourcing provider, "to increase the number of candidates accepting offer letters, healthcare organizations need to make sure their employment brand is positive." When posting a job, the human resources department should invest time in writing a compelling post that catches candidates' attention and

**Figure 1.**
**Gap Grows Between Healthcare Job Openings and Hires**




Source: Bureau of Labor Statistics

**Figure 2.**
**Average Annual Job Openings 2016-2026**




Source: Bureau of Labor Statistics

convinces them the organization is better than the competition.[4] Candidates will be shopping for their next employer, and they will be drawn to organizations that look like good places to work. Therefore, it's important to get individuals' attention by creating a catchy company profile and promoting the positives of working at the facility the candidate is considering. This means highlighting the company culture by "telling compelling stories about their workplace and employees."

And, it means touting the company's benefits, including compensation, flexible work environments, healthcare and other positives. For instance, organizations can look for ways to implement policies around flextime and telecommuting. They can also offer opportunities beyond the traditional benefit packages. Barkley Davis, senior director of physician recruitment at LifePoint Hospitals, says debt relief is the top priority for nearly all new physicians. Therefore, LifePoint offers some doctors monthly stipends if they accept a job offer while they are still in training.[5]

During the recruitment process, candidates should be provided a top-notch experience from the application and interview to the job offer and onboarding. "Put yourself in the candidate's shoes to ensure your organization is treating candidates with respect and making them feel valued," says Jen Dewar, a human resources marketing consultant. "With the stiff competition for talent, candidate experience could be the difference between a candidate choosing to work for your organization rather than a competitor."[6]

## Growing a Talent Pool

But it isn't enough to just post a job to find the best candidates. When new positions open up, healthcare organizations should already have a source list of candidates. This means continually growing a talent pool. There are a number of ways to do this:

1) Not all candidates, even great ones, who apply for a position will get offered or take the job. Some may not have all the required qualifications, and some may decide to stay in their current position. But, contact with those candidates should be nurtured so when the time is right, they can be tapped.[6]

2) Rather than just relying on resumés received in response to a job posting, a resumé database of candidates who have already expressed an interest in the organization can be a useful and faster recruiting tool. It can also minimize sourcing costs. And, newer databases offer advanced features such as Boolean and semantic search to find the right candidate quickly, as well as to access public web profiles.[4]

3) Employee referral programs can be a great resource for finding talent. These programs can provide monetary rewards, but trips, vouchers and other items can help to better market the program. Even incentives such as time off and gift vouchers are less expensive than cash rewards.[7]

4) Partnering with national and state job boards, public health departments, professional societies, universities, colleges, academies and high schools is another way to develop comprehensive talent pipelines.[5] For instance, individuals typically join professional associations to advance their careers by networking, working toward designations, etc. Posting on these associations' job boards or attending as a guest to networking events can expose the organization to those seeking opportunities.[8]

## Embracing Technology

Healthcare recruiting technology can make recruiting more cost-effective by improving costly time-to-fill metrics, reducing costs and streamlining the hiring process. This technology includes (among others):[9]

- Social media platforms such as LinkedIn, Instagram and Facebook to search for potential candidates, find a good match to fill the skill gap, establish a connection with them and inspire them to apply for the open positions in their organization;
- Direct sourcing platforms that integrate with databases of local talent communities, diversity job boards and different minority associations; and
- Chatbots that talk to candidates via automated messages and interactions, and which also provide general FAQs fed into the chatbots so queries will be automatically addressed.

Other tips include optimizing job ads to achieve higher ranking in search engines so job openings are noticed more quickly by candidates. And, when using a referral program, tapping into referral software allows hiring managers and recruiters to send requests for referrals for particular positions. Referral software can also help employees share open positions with their social network. Too, applicant tracking systems can typically integrate with dedicated referral software services, or offer their own referral tools.[7]

## Analyze Recruiting Activities

It's important for healthcare organizations to focus their resources strategically when it comes to recruiting talent. Analyzing recruitment activities will also provide useful insight into what is working well and what needs improvement. ❖

### References


1. AMN Healthcare. Healthcare Industry Forecast: High Demand Due to Aging, Economy. Accessed at www.amnhealthcare.com/latest-healthcare-news/healthcare-industry-forecast.
2. U.S. Bureau of Labor Statistics. Healthcare Occupations. Accessed at www.bls.gov/ooh/healthcare/home.htm.
3. AMN Healthcare. Future for Healthcare Jobs: Seven Charts Show Intensifying Demand for Services and Workforce. Accessed at www.amnhealthcare.com/latest-healthcare-news/future-for-healthcare-jobs.
4. Auerbach D. Need to Hire Health Care Workers? Get Back to Basics. Career Builder, Sept. 20, 2017. Accessed at resources.careerbuilder.com/health-care/hiring-health-care-worker-basics.
5. PeopleScout. Six Tips for Healthcare Recruiting. Accessed at www.peoplescout.com/insights/six-tips-for-healthcare-recruiting.
6. Dewar J. 6 Healthcare Recruitment Trends for 2018. Healthcare Source. Accessed at education.healthcaresource.com/healthcare-recruitment-trends-2018.
7. Bika N. 6 Ways to Build an Employee Referral Program That Works. Workable. Accessed at resources.workable.com/stories-and-insights/employee-referral-program.
8. Bouley J. 6 Tips for Healthcare Recruiting Success. Hospital Recruiting.com, Oct. 11, 2016. Accessed at www.hospitalrecruiting.com/blog/3532/6-tips-for-healthcare-recruiting-success.
9. Vallikat A. Talent Acquisition and Technology: Redefining Talent Acquisition In 2020. PeopleHum, Dec. 23, 2019. Accessed at www.peoplehum.com/blog/talent-acquisition-and-technology-redefine-talent-acquisition-in-2020.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*Medicines*

## FDA Approves Uplizna to Treat Rare Autoimmune Disease of the CNS

The U.S. Food and Drug Administration (FDA) has approved inebilizumab-cdon (Uplizna) to treat neuromyelitis optica spectrum disorder (NMOSD) in adult patients with the anti-AQP4 antibody. It is only the second therapy approved to treat the rare autoimmune disease of the central nervous system.

Approval was based on results of a clinical study of 230 adult patients, 213 of whom had antibodies against AQP4 (anti-AQPR antibody positive), that evaluated the efficacy and safety of intravenous Uplizna. During the 197-day study, the risk of an NMOSD relapse in the 161 anti-AQPR antibody positive patients who were treated with Uplizna was reduced by 77 percent when compared to the placebo treatment arm. There was no evidence of a benefit in patients who were anti-AQP4 antibody negative.

"Until recently, patients with NMOSD had no FDA-approved treatment options," said Billy Dunn, MD, director of the office of neuroscience in the FDA's Center for Drug Evaluation and Research. "Uplizna now represents the second approved therapy for these patients within the past year. We continue to remain highly committed to the development of additional safe and effective drugs for this rare and devastating disease." ❖

Kohli KK. FDA Approves Ineblizumab for Rare Autoimmune Disease of CNS. Medical Dialogues, June 11, 2020. Accessed at medicaldialogues.in/neurology-neurosurgery/news/fda-approves-ineblizumab-forrare-autoimmune-disease-of-cns-66615.

*Research*

## Studies Show Influenza and Pneumonia Vaccines May Reduce Risk of Developing Alzheimer's

Two studies show the influenza (flu) and pneumonia vaccines lessen the risk of developing Alzheimer's disease (AD) in the future.

The first study examined a large American health record data set of more than 9,000 patients over age 60 years and found having one flu vaccination was associated with a 17 percent reduction in Alzheimer's incidence. Further, those vaccinated more than once over the years saw an additional 13 percent reduction in incidence. The protective association appeared to be strongest for those who received their first vaccine at a younger age, for example at age 60 years versus 70 years.

"There has been a concern in the medical community that many sources of inflammation such as urinary tract infections worsen the course of patients with Alzheimer's disease," said Albert Amran, a fourth-year medical student with McGovern Medical School at The University of Texas Health Science Center at Houston. "Hence, we have been worried that vaccinations, a form of inflammation, could also worsen the course of AD."

The second study, which examined the associations between pneumococcal vaccine with and without an accompanying flu shot and the risk of AD, analyzed more than 5,000 people over 65 years who were participating in the Cardiovascular Health Study, a long-term government funded examination of risk factors for cardiovascular disease. Some participants had a known genetic risk factor for AD: the rs2075650 G allele in the TOMM40 gene, which has also been linked to a higher risk for lifetime depression. The researchers found that getting a pneumococcal vaccine between the ages of 65 years and 75 years reduced risk of developing AD by 25 percent to 30 percent after adjusting for sex, race, birth cohort, education, smoking and genetic risk factors. However, the largest reduction in the risk of AD — up to 40 percent — was seen among people vaccinated against pneumonia who didn't have the risk gene.

"This is an encouraging finding that builds upon prior evidence that vaccination against common infectious diseases — such as the flu — is associated with a reduced risk for Alzheimer's and a delay in disease onset," said neurologist Richard Isaacson, founder of the Alzheimer's Prevention Clinic at NewYork-Presbyterian and Weill Cornell Medical Center. "Regular use of the flu vaccine, especially starting at an early age, may help prevent viral infections that could cause cascading effects on the immune system and inflammatory pathways. These viral infections may trigger Alzheimer's-related cognitive decline." ❖

Kane A and LaMotte S. Flu and Pneumonia Shots May Lower Risk for Alzheimer's, Studies Find. CNN Health, July 27, 2020. Accessed at www.cnn.com/2020/07/27/health/flu-pneumonia-shot-lowers-alzheimers-risk-wellness/index.html.

*Research*

## BCG Vaccine Being Studied as Potential Protection Against COVID-19

Because research has shown the Bacillus Calmette-Guérin (BCG) tuberculosis vaccine boosts production of immune cells, it is currently being trialed in people as potential protection against COVID-19.

Boosting the production of immune cells may help explain why the BCG vaccine can protect newborn babies from dying due to sepsis. In one study conducted in Perth, Australia, blood samples were analyzed from 85 newborns in Gambia, Cuinea-Bissau and Papua New Guinea, half of whom had been vaccinated. The study found newborns who had been vaccinated had about twice as many immune cells, called neutrophils, in their blood. In another study, researchers vaccinated newborn mice with BCG and then infected them with bacteria to induce sepsis. They also infected nonvaccinated mice. And, just like the babies in the other study, the mice that had been vaccinated produced double the number of neutrophils, which then protected them from dying by consuming the bacteria that cause sepsis.

"There is increasingly strong evidence that BCG, a vaccine designed to work against tuberculosis, has advantageous nonspecific effects against a range of pathogens in humans," said Danika Hill at the Babraham Institute in Cambridge, U.K. However, Hill warns, "whether BCG, and any potential effect on neutrophils, could be beneficial against [the coronavirus] is unclear and warrants careful consideration." According to Nelly Amenyogbe at the Telethon Kids Institute in Perth, Australia, who conducted the first study mentioned earlier, because BCG has effects on other parts of the immune system, beyond neutrophils, it is possible that these other effects may provide some benefit against COVID-19. "If vaccines such as BCG are able to provide nonspecific protection against newly emerging pathogens, this could be a game-changer for managing COVID-19 and any further pandemics," says Hill. ❖

Liverpool L. BCG Vaccine Helps Fight Infections by Boosting Immune Cell Production. *New Scientist*, May 6, 2020. Accessed at www.newscientist.com/article/2242866-bcg-vaccine-helps-fight-infections-by-boosting-immune-cell-production/#ixzz6LlX6BOes.

*Research*

## CoVIg-19 Plasma Alliance Expands Membership and Clinical Trial Collaboration

The CoVIg-19 Plasma Alliance, a plasma industry collaboration established to accelerate the development of a plasma-derived hyperimmune globulin therapy for COVID-19, now includes 11 plasma companies, and now also includes global organizations from outside the plasma industry who are providing vital support to encourage more people to donate plasma. In addition to those announced at its inception — Biotest, BPL, CSL Behring, LFB, Octapharma and Takeda — the alliance's new industry members include ADMA Biologics, BioPharma Plasma, GC Pharma, Liminal BioSciences and Sanquin that will contribute specialist advisory expertise, technical guidance and/or in-kind support to contribute to the Alliance goal of accelerating development and distribution of a potential treatment option for COVID-19.

The alliance is also working with the National Institute of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health to test the safety, tolerability and efficacy of the hyperimmune therapy in adult patients with COVID-19. This global study, which started in the summer, will form the foundation for the potential regulatory approval of the hyperimmune therapy.

"Hyperimmune globulin therapy has the potential to be one of the earliest treatment options for COVID-19, and


we look forward to working with NIAID and health authorities to bring this therapy to patients as early as possible," said Bill Mezzanotte, executive vice president and head of research and development at CSL Behring and co-leader of the CoVIg-19 Plasma Alliance. "One of the stated goals of the alliance is to be an effective partner for important institutions such as NIAID and also to help develop coherent regulatory strategies that can give global health authorities the confidence to streamline the approval process of hyperimmune globulin therapy for COVID-19."

Because developing a hyperimmune globulin treatment relies on the collection of convalescent plasma, the alliance has gained support from large organizations outside of the plasma industry such as Microsoft and Uber Health. Microsoft is providing technology support, including the alliance website and the plasmabot for donor recruitment. The plasmabot streamlines the process for a potential donor to quickly gain information about their nearest collection center from across the member network. In parallel, Uber Health donated 25,000 round-trip rides to transport potentially eligible donors to and from plasma collection centers. These rides are coordinated by the plasma collection center directly for individuals with confirmed appointments.

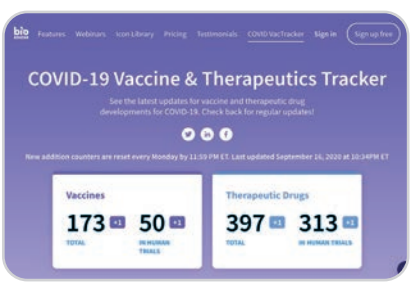
"Partnership and collaboration are critical to the success of the CoVIg-19 program," said Julie Kim, president of plasma-derived therapies business unit at Takeda, and co-leader of the CoVIg-19 Plasma Alliance. "We now have enough plasma to initiate clinical manufacturing, but more is needed to ensure both speed and scale. The growing and active involvement of leading companies from outside the plasma industry who support this alliance, as well as convalescent plasma for transfusion initiatives, demonstrates the potential of convalescent plasma to fight this public health crisis. Together, we all share the same goal — to save lives by using the power of convalescent plasma in different ways." ❖

CoVIg-19 Plasma Alliance Builds Strong Momentum Through Expanded Membership and Clinical Trial Collaboration. CSL Behring press release, May 7, 2020. Accessed at www.prnewswire.com/news-releases/covig-19-plasma-alliance-builds-strong-momentum-through-expanded-membership-and-clinical-trial-collaboration-301054894.html.
The CoVIg-19 Plasma Alliance. The Fight Against COVID-19 Starts with You. Accessed at www.covig-19plasmaalliance.org/en-US#recruitment.

*Research*

## New Site Tracks Vaccines and Drugs/Treatments in Development for COVID-19

BioRender, an online tool for creating scientific figures, has created a robust, interactive COVID VacTracker that is maintained regularly and updated daily. The comprehensive database covers both clinical vaccines and clinical drugs/treatments utilizing data visualization to show development progression of discrete vaccines and drugs. The tracker is also in a sortable format, making it easy to compare, contract and navigate between various vaccines and drugs. It can be accessed at biorender.com/covid-vaccine-tracker.



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# Healthcare Delivery Post-Pandemic

The COVID-19 pandemic has generated a wave of changes in how healthcare is delivered, but what are the long-term benefits and can they be sustained?

By Amy Scanlin, MS

**WITHOUT QUESTION**, the COVID-19 pandemic caused by the SARS-CoV-2 novel virus has resulted in severe financial stress on the healthcare system. During the first several months of the pandemic, facilities were closed except for emergency room visits, in-person management of chronic and life-critical treatments and, of course, patients who were infected with the virus. Indeed, the industry ground to a halt, laying off workers and postponing elective procedures and routine patient care. In fact, the American Hospital Association estimated in a four-month window from March 2020 to June 2020, hospital systems in the U.S. saw more than $200 billion in losses, leading the Congressional Budget Office to project between 40 percent and 50 percent of hospitals could have negative margins by 2025.[1] "It has been a major disruption to the healthcare system," says Ann Greiner, president and CEO of the Primary Care Collaborative (PCC), a not-for-profit multistakeholder membership organization dedicated to advancing an effective and efficient health system.

But with disruption comes tremendous learning opportunities for how to better prepare for future challenges. These lessons, including expanding telehealth services, rethinking where care is provided and, potentially, dramatically changing payment systems, have the potential to create a more nimble and responsive healthcare system.

## How Healthcare Is Provided

Although the capability of telehealth services has been growing for years, its use has played second fiddle to in-person provider visits since their inception. That is, until the COVID-19 pandemic struck. Stymied by challenges from payers, restrictions for practicing medicine across state lines, technology infrastructure and mindset, it wasn't until the pandemic nearly shut down the healthcare industry save for essential services that the opportunities telehealth could afford were realized, and that sent providers scrambling to put systems into place. In fact, it is estimated that during the pandemic, telehealth services have increased by 50 percent over their use in 2019.[2] And the U.S. Department of Health and Human Services has responded with a pledge of $15 million to support telehealth services through the duration of the pandemic.[3]

While telehealth services have technically been reimbursable since 1997, geographic restrictions to meet stringent reimbursement criteria mostly prohibited their use. These restrictions required a patient to live far from a service provider, and visits had to take place outside of a patient's home. But the pandemic exposed the urgent need for telehealth, resulting in the Centers for Medicare and Medicaid Services' (CMS) temporary removal of the bureaucratic telehealth reimbursement restrictions, which paved the way for adopters (both providers and patients) to utilize these services. More touchpoints such as telephone and webcam were also enabled, and barriers to care, including transportation and time constraints, were removed. Yet transitioning to telehealth has not been without its unique challenges such as investment in technology, access to high-speed Internet and patients who have difficulty accessing virtual care.

Now, months into the pandemic with increased telehealth use, practices are financially and emotionally stressed with nearly 70 percent reporting they are not ready for reduced or terminated payments for telehealth visits once an end to the national emergency is declared. Fewer than 50 percent of practices report having enough cash on hand to stay open, over one-third have laid off or furloughed staff and 53 percent report patients are not scheduling well visits or chronic care visits despite their availability.[4]

As such, pressure on Congress to continue funding telehealth services and to make permanent changes to the healthcare system is mounting. Even so, use of telehealth services may take some convincing, according to PCC. While more than 70 percent of primary care patients surveyed are comfortable using telehealth during the COVID-19 pandemic, most prefer to return to in-person care when they are able,[5] particularly depending on the type of care sought.

*While telehealth services have technically been reimbursable since 1997, geographic restrictions to meet stringent reimbursement criteria mostly prohibited their use.*

Nevertheless, the technology behind telehealth is advancing, including demands for artificial intelligence (AI) to bring real-time telephone triage consultation services. Additionally, AI can serve emergency rooms, doctor offices, healthcare research and other services through quicker diagnostics that result in faster and potentially more accurate decision-making and care. Questions remain, though, on the regulatory, insurance and usability fronts for how to capture, submit and utilize remote monitoring of

patient health data.

Without a doubt, the trajectory of telehealth opportunity will continue to rise, but there will be important considerations about which services best lend themselves to virtual care and how those services can best be provided. And, as telehealth grows, there is likely to be increased demand for more flexibility in provider licensing by practice region and skillset[6] as the geographic barrier of proximity to care is removed.

*Without a doubt, the trajectory of telehealth opportunity will continue to rise, but there will be important considerations about which services best lend themselves to virtual care and how those services can best be provided.*

## Healthcare Facilities Reenvisioned

The Institute of Medicine (IOM) estimates 44.5 percent of all financial waste in U.S. healthcare comes from inefficient care delivery and unnecessary services.[7] Couple that with the immense financial challenges presented by the pandemic and the urgency to find lasting solutions to improve healthcare, delivery at an affordable cost has never been more greatly needed. In this environment, reenvisioned care access points may be a long-term outcome from this pandemic. This is particularly so while it is determined whether hospitals or clinics are the best place for patients to receive care and rural areas struggle with the high cost of maintaining facilities and the challenges of providing specialty care.

Federal waivers (such as section 1135 [available whenever the president declares a national disaster or emergency] that were used in combination with section 1332 of the Affordable Care Act and section 1115 of the Medicaid Families First Coronavirus Response Act) have paved the way for a more nimble state response to the COVID-19 crisis, and now the pursuit of federally based statutory authority for program waivers is also being encouraged. When considered along with other determinants of health such as social services, housing, nutritional support, etc., there is now conversation about where healthcare is best provided.

One solution in discussion, and in some cases in practice, is the formation of outpatient urgent care centers that can serve a larger number of patients, including those receiving telehealth services, which would enable hospitals to focus attention on critical care services, resources and expertise. These centers — alternatives for patients who would otherwise seek care in the emergency room — could consolidate and improve care through better utilization of resources, increased patient volume and lowered costs.

Consolidated care offers the potential benefit of consolidating critical supplies, thus easing operational costs such as purchasing, staffing and storage, as well as facilitating smoother supply and demand through one or a few central locations. In addition, a healthcare hub model may offer rural locations with miles separating thinly stretched resources, equipment and specialist efficiencies. However, PCC's Greiner cautions these efficiencies don't necessarily equal lowered costs, particularly in regard to primary care.

Additionally, community-based facilities such as workplaces, schools, community and other nonhospital settings provide opportunities for conveniently located supportive care such as nutritional, mind-body and support group services. Making health support more easily accessible by bringing it to the patient could ensure better access to information and support for patients' all-around health. Supportive care services could also be added to the menu of hospital-based offerings, enabling a more holistic approach for both patients and providers.[8]

## The Business of Healthcare

Any discussion about the future of healthcare must consider providers and payers. During the pandemic, CMS began offering advance payments to providers based on lump-sum collection estimates for care instead of fee-for-service payments, which have been the norm. And many private insurers followed suit, which is welcome news for an industry struggling for years with rising insurance costs and confusing reimbursement policies.

The notion of moving away from fee-for-service payments, which some argue incentivizes volume and discourages telehealth services since they are historically reimbursed at a lower rate, has been percolating for some time. This is especially the case since primary care is at the forefront of helping to keep patients healthy and out of hospitals. "Primary care fee-for-service doesn't work well in a pandemic," says Greiner.

Many advocates are calling for lump-sum payments per patient under their care payable by CMS, pointing to the success of some commercial Medicare Advantage programs that already operate under a lump sum reimbursement model that results in better patient outcomes at a lower cost.[9]

A huge challenge to healthcare is the number of uninsured that has only been growing along with the increasing unemployment rate caused by the pandemic. Although Congress passed legislation covering the cost of COVID-19 testing and treatment, the long-term ramifications of the economy and nation's health are likely to significantly and perhaps permanently affect the healthcare industry.

*Any discussion about the future of healthcare must consider providers and payers.*

Of course, there are many challenges to overcoming the historically slow cogs of lasting change. Insurance, multiple federal oversight agencies, and state and federal legislation all will have an impact. From staffing shortages to increasing costs, the challenges sometimes seem to be moving in opposition. Yet, there are glimmers of hope as the industry evolves and adapts, favoring telehealth over traditional brick and mortar in a global pandemic. And the significance of any future change may be directly proportional to the length of time it takes to get an approved COVID-19 vaccine.

One thing is certain, if all parties come to the table with honest discussion and respectful debate, whatever model of healthcare emerges from this crisis has the potential to serve the collective whole — one that addresses the immensity of health disparities, captures the capabilities of technological advances and supports the resilience of the tireless healthcare workers. Opportunity for change is knocking at the healthcare industry's door. However difficult in the short-term, opening the door to embrace change may be the only long-term viable solution. ❖

## References


1. Hospitals and Health Systems Face Unprecedented Financial Pressures Due to COVID-19. American Hospital Association Report, May 2020. Accessed at www.aha.org/guidesreports/2020-05-05-hospitals-and-health-systems-face-unprecedented-financial-pressures-due.
2. Scott D. How the Covid-19 Pandemic Will Leave Its Mark on US Health Care. Vox, April 22, 2020. Accessed at www.vox.com/the-highlight/2020/4/15/21211905/coronavirus-covid-19-pandemic-medical-health-care-hospitals.
3. HHS Awards $15 Million to Support Telehealth Providers During the COVID-19 Pandemic. U.S. Department of Health and Human Services press release, May 13, 2020. Accessed at www.hhs.gov/about/news/2020/05/13/hhs-awards-15-million-to-support-telehealth-providers-during-covid19-pandemic.html.
4. Primary Care Collaborative, July 1, 2020, Week 15 Survey Update. Accessed at www.pcpcc.org/2020/07/01/primary-care-covid-19-week-15-survey.
5. What Do Patients Want from Primary Care — Both During and After COVID-19? Primary Care Collaborative press release, June 4, 2020. Accessed at www.pcpcc.org.
6. Baur A, Georgiey P, Munshi IR, and Marek S. Healthcare Providers: Preparing for the Next Normal After COVID-19. McKinsey blog, May 8, 2020. Accessed at www.mckinsey.com/industries/healthcare-systems-and-services/our-insights/healthcare-providers-preparing-for-the-next-normal-after-covid-19.
7. Pearl R. Radical Solution for Saving America's Hospitals. *Forbes*, March 29, 2019. Accessed at www.forbes.com/sites/robertpearl/2018/03/29/radical-solution-hospitals/#651ad8794808.
8. Butler S. After COVID-19 — Thinking Differently About Running the Health Care System. JAMA Health Forum, April 23, 2020. Accessed at jamanetwork.com/channels/health-forum/fullarticle/2765238.
9. Levy N. Coronavirus Already Changing Medical Care in the U.S. *Los Angeles Times*, April 10, 2020. Accessed at www.latimes.com/politics/story/2020-04-10/coronavirus-lasting-changes-healthcare.



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# The mHealth Revolution:
## An Alternative to Traditional Healthcare

With the growing number of healthcare apps, patients and providers need to be aware of their benefits, as well as their shortfalls that could affect patient care.

By Meredith Whitmore

**BEFORE COVID-19**, few could have imagined the immeasurable effects a pandemic could wreak on the world's health. Due to quarantines and the resulting lack of healthcare availability for many, it is now more important than ever for patients and healthcare providers to have technology to provide access to healthcare information and guidance. Fortunately, mHealth (an abbreviation for mobile health) has been a growing industry for some time, but it is now coming of age and is increasingly more significant. As a MedTech Boston blog notes, "With the reach of mHealth technologies spreading further, it is expected to become one of the most game-changing aspects in the current healthcare scenario."[1]

For those less familiar with mHealth, the World Health Organization's Global Observatory for eHealth defines it as a "medical and public health practice supported by mobile devices such as mobile phones, patient monitoring devices, personal digital assistants (PDAs) and other wireless devices."[2] mHealth is often utilized to educate consumers about preventive healthcare services, and it is also used for disease surveillance, treatment support, epidemic outbreak tracking and chronic disease management.[3]

## The Data

The statistics alone indicate mHealth is and will continue to be a key component for physicians and other healthcare providers. For example:[4]

• More than 318,000 mHealth apps are currently available — nearly double the number in 2015. The wealth of possibilities for health guidance becomes clearer considering more than 80 percent of American adults today have a smartphone, and 95 percent of teens have access to a smartphone, which they report using "almost constantly."

• More than 60 percent of Americans have downloaded an mHealth app within the past six years.

• At least 62 percent of Americans have used their smart devices to gather health-related information, which means mHealth use is more common than online banking, job searches and accessing educational content.

• Two-thirds of the largest U.S. hospitals offer mobile health apps, indicating there is increasing openness to mHealth as apps and technology continue to improve.

• 74 percent of patients say using mobile apps, wearables and other mHealth tools helps them cope with and manage their conditions.

• 85 percent of health insurance companies think mHealth creates value.

• The biggest cost-saving benefit from mHealth apps will be reduced hospital costs by decreasing readmission rates and length of stay, and by assisting with patient compliance to medication plans, according to the majority of respondents (60 percent) in a Research2Guidance report.

• The global mHealth app market is expected to reach $111 billion by 2025. Fitness apps account for the largest portion of the U.S. mHealth app market, which is expected to grow to $50 billion by 2025.

## Benefits of mHealth

Judging from the statistics, it seems mHealth is here to stay. Following are some of its advantages:

*Real-time communication with remote patients.* While an in-person visit is often best — or at least most satisfying for providers and patients in many cases — the perks of telehealth cannot be denied, even when we are not in the midst of a pandemic. mHealth apps and equipment such as TytoHome/TytoCare, KardiaMobile EKG and many other technologies enable healthcare professionals and patients to work together remotely, allowing patients to stay within the safety, comfort and convenience of their own homes while healthcare providers can converse while checking vitals and other important data in real-time.[5] "The new reality is that patients want to seek care in their own environment and on their own schedule online, as opposed to going to the office and waiting for a provider," says Mark Greenwood, MD, a family medicine specialist in Richfield, Utah, who is working with a Humana Medicare Advantage pilot mHealth program.[6]

*Readily accessible and efficient paperless health documentation.* Thanks to mHealth, many of the reports, prescriptions and other documentation that healthcare providers must complete can now be done electronically and then digitized through mHealth apps. And patients can now access their healthcare documentation and providers' instructions via smart devices. More accessibility means fewer documents lost and less confusion for both parties. Even healthcare expense report management companies such as Expensify are now digital, using Cloud storage instead of paper filing.[7,8]

*High patient receptivity and better treatment compliance.* mHealth can make life less stressful for patients who like to be involved in their care, and conversely, it can motivate those who are not typically as diligent. By enabling patients to track and record their prescriptions and set up reminder notifications to help them avoid missing a dosage, for example, mHealth can help patients feel in control and organized. It also allows prescribers and others to answer treatment questions and provide clear, easily accessible information to patients to ensure better treatment compliance. With some apps, providers can also watch as patients track their compliance if patients desire.[5,6 7, 9]

***With more and more mHealth apps being developed by hospitals and other agencies, health coaching is also becoming more available for patients.***

In addition to medication management, other types of treatment progress can be monitored by patients, which often helps them achieve a sense of success and empowerment. Whether it is a workout or physical therapy regimen, a dietary plan, insulin dosage and blood sugar level tracking, heart rhythms or blood pressure, there are mHealth apps for those and more — and they can keep patients involved and providers connected.[6,7,9] A 2018 Accenture Consumer Survey revealed "healthcare consumers continue to show strong use of digital technology for self-service

care — and the numbers are rising each year. In 2018, 75 percent of U.S. consumers surveyed said technology is important to managing their health. Patients are increasingly open to intelligent technologies taking on elements of their care such as medical consultations and monitoring. And they are using self-service digital health tools that go beyond websites.… Nearly half (48 percent) of healthcare consumers are using mobile/tablet apps compared to just 16 percent in 2014."[9]

*Patient coaching.* With more and more mHealth apps being developed by hospitals and other agencies, health coaching is also becoming more available for patients. One online program provided by San Francisco-based Omada Health for patients at risk for diabetes is having positive results. In the year-long pilot, patients were assigned a health coach, as well as private online support and moderated discussions that provided social support and personalization. "You can't just send someone a scale and a step tracker and pray for results," says Omada Chief Executive Sean Duffy. "You have to combine these instruments with high-touch intervention."[6] As clinicians and software developers find increasingly efficient and helpful ways to engage and guide patients in their own healthcare, it is expected there will be more of these hospital programs. Health coaching is already available in less clinical settings through fitness, weight loss and mindfulness apps, among others.[7,8]

*Although there are an ever-increasing number of apps available, many of them are subpar as evidenced by poor functionality, poor follow-through by providers and/or poor user reviews.*

*Cost savings.* Healthcare is expensive and can be a burden for individuals who have inadequate health coverage, including very high insurance deductibles. Because mHealth apps are improving continuously, some predict they will eventually be able to work as de facto healthcare providers as long as they are used in conjunction with primary care physicians or other providers, ensuring people's health needs are regularly met — especially in areas suffering from healthcare shortages.[7]

*Treating chronic disorders.* Apps that help patients manage specific chronic conditions such as asthma, diabetes, high blood pressure and heart disease already exist. These apps seek to improve quality of life by connecting users to others who have the same health challenges, as well as by offering helpful articles, recording/tracking tools and additional resources. Chronic diseases need continuous evaluation, and in addition to tracking their conditions, individuals can schedule appointment reminders and other notifications.[7]

## mHealth Drawbacks

Clearly, mHealth has its benefits. Yet, while the technology is already helpful and increasingly promising, it is definitely not without shortcomings:

*Quantity does not ensure quality, and there is little federal regulation.* Although there are an ever-increasing number of apps available, many of them are subpar as evidenced by poor functionality, poor follow-through by providers and/or poor user reviews. According to Amir Lerman, MD, a cardiologist at the Mayo Clinic whose interests involve digital health, "You can't just build an app in your garage and think it is going to change medical care. You need to have a treatment plan behind it and a health system to care for the patient."[6]

At this point in mHealth's development, it remains the Wild West on some levels. While healthcare providers can do their own research about selecting the most effective apps to recommend to patients, it can be time-consuming and frustrating. And as Dr. Richard Larson, MD, PhD, at the University of New Mexico Health Sciences Center School of Medicine who conducts research on mHealth said, "The rapid growth of mobile health apps has resulted in confusion among healthcare providers and the public about which products rely on evidence-based medicine. Only a small subset of mHealth apps are regulated by the [U.S. Food and Drug Administration] FDA."[10] In fact, FDA has issued few regulatory restrictions for mHealth. According to a recent article in *The Lancet*, "In most countries, medical device regulation applies only to a subset of high-risk health apps that have well-defined medical purposes. However, most health apps available on the market target a wide range of health-related issues, including diet and exercise, pregnancy and mental health, while still being considered nonmedical devices."[11]

On top of this, many apps lack privacy and security. A Business Insider report states, "A recent analysis of mobile health apps found their data-sharing practices to be excessive, which cre-

ates privacy risks that should make providers wary about prescribing mHealth apps to their patients."[9]

*Users could become too reliant.* Despite the lack of federal regulation and privacy/security issues, the majority of people in the United States — and perhaps the world — use mHealth apps today in some form. And experts fear people — whether patients or providers — will become too reliant. Some consumers, for example, are choosing mHealth apps and devices over professional help, which is certainly not the safest option. In fact, a 2015 Harvard Medical School study on symptom-checking websites and apps found "of the top 23 symptom checkers, correct diagnoses were listed first in only 34 percent of standardized patient evaluations." The study also showed the "correct diagnoses were listed by symptom-checking tools within the top 20 possible diagnoses in less than 60 percent of the evaluations."[8] In other words, many people are misusing apps and taking their health into their own hands inappropriately. And, clearly, an inaccurate diagnosis or lack of diagnosis is dangerous. For providers who recommend apps to patients, it is absolutely crucial to stress that proper medical care via a qualified provider, not merely an app, is a key component of good health.

## Future of mHealth

In some ways, healthcare is easier than ever for patients and providers because of mHealth, including its wearables, apps and other devices that allow patients to manage their well-being in groundbreaking new ways. But the technology faces challenges even beyond developing and enforcing regulatory standards. As James Michiel, MPH, previously senior mHealth and informatics analyst at Emory University's Rollins School of Public Health in Atlanta, Ga., and now director of product strategy and innovation at Aetna, states, "The future of mHealth is open — open access, open source, open data and open innovation." And come what may in the future, Michiel adds, "It is imperative … these tools and technologies are used deliberately and efficiently, with an eye toward the end user in a way that ensures long-term sustainability and development."

Simply put, mHealth must find ways to continue to serve its users better by protecting, guiding and serving them through clearer guidelines and increasingly improved functionality for providers and patients.

## Only Time Will Tell

As with all things, only time will tell how current trends will progress. But mHealth's prognosticators foresee increasingly higher standards and better efficacy in the market. And as more hospitals and healthcare organizations partner together with software developers such as Omada, mHealth's quality and efficiency will surely improve, especially with helpful regulation as FDA recognizes the market's need for increased safety and standards.

The future of mHealth looks bright — at a time when many providers and patients need a bright spot on the horizon. ❖

### References


1. World Health Organization. Frequently Asked Questions on Global Task Force on Digital Health for TB and Its Work. Accessed at www.who.int/tb/areas-of-work/digital-health/faq/en.
2. The Game-Changing Impact of mHealth on Global Healthcare. MedTech Boston, April 3, 2019. Accessed at medtechboston.medstro.com/blog/2019/04/03/the-game-changing-impact-of-mhealth-on-global-healthcare.
3. Tech Target. mHealth. Accessed at searchhealthit.techtarget.com/definition/mHealth.
4. 11 Surprising Mobile Health Statistics. Mobius Tech, March 20, 2019. Accessed at www.mobius.md/blog/2019/03/11-mobile-health-statistics/#:~:text=There%20are%20now%20318%2C000%20mHealth,have%20downloaded%20an%20mHealth%20app.
5. Healthworks Collective. Mobile Medical Apps: A Game Changing Healthcare Innovation. Accessed at www.healthworkscollective.com/mobile-medical-apps-a-game-changing-healthcare-innovation.
6. Landro L. How Apps Can Help Manage Chronic Diseases. *The Wall Street Journal*, June 25, 2017. Accessed at www.wsj.com/articles/how-apps-can-help-manage-chronic-diseases-1498443120.
7. Referral MD. Why mHealth Is Beneficial for Patients. Accessed at getreferralmd.com/2019/04/why-mhealth-is-beneficial-for-patients.
8. Collier J. mHealth: What Is It, and How Can It Help Us? Medical News Today Blog, Sept. 12, 2018. Accessed at www.medicalnewstoday.com/articles/322865#How-can-mHealth-help-us?
9. Resnick R. What Are the Pros and Cons of mHealth? Cureatr, July 17, 2019. Accessed at blog.cureatr.com/pros-and-cons-mhealth.
10. Larson RS. A Path to Better-Quality mHealth Apps. *Journal of Medical Internet Research*, Vol 6, No 7 (2018): July. Accessed at mhealth.jmir.org/2018/7/e10414.
11. Ferretti A, Ronchi E, and Vayena E. From Principles to Practice: Benchmarking Government Guidance on Health Apps. *The Lancet*, June 2019. Accessed at www.thelancet.com/pdfs/journals/landig/PIIS2589-7500(19)30027-5.pdf.



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# The Doctor Will *Tweet* You Now

Social media continues to shape and influence the evolving healthcare landscape.

By Trudie Mitschang

**WHEN YOU THINK** of social media and healthcare, you might not automatically see an obvious connection. While social media is focused on sharing information, many aspects of the healthcare industry are characterized by a need for privacy rules and HIPAA guidelines. But the fact remains: Social media has increasingly influenced and, in some ways, dramatically changed how healthcare is managed. As the world becomes more and more digitally connected, the healthcare industry has had to evolve to meet changing patient preferences and demographics, especially as younger patients who depend on social media become young adults with their own healthcare needs. In 2020 alone, telehealth, once a debated and somewhat fringe idea, went mainstream overnight in the face of a global pandemic. And as more and more people get comfortable with remote access to care, social media healthcare platforms seem poised to become even more prolific.

## Extending the Doctor-Patient Relationship

The *Journal of Medical Internet Research* reports 99 percent of hospitals in the U.S. have an active Facebook page, and the use of other social media platforms like Twitter and Instagram is also on the rise.[1] From a provider perspective, perhaps the biggest benefit of social media in healthcare is information dissemination, which provides physicians and healthcare institutions a platform to share research data, health tips and lifestyle recommendations with patients. Social media can also help build trust between patients and providers; when providers share up-to-date health research and stories on their accounts, patients may feel more confident they are receiving leading-edge care. Not only does this build confidence with existing patients, it also increases the opportunity for patient referrals as people begin reposting information in their own social media feeds.

"Social media is merely an extension of the doctor-patient relationship," says Kevin Campbell, MD, FACC, an internationally

recognized cardiologist who specializes in the diagnosis and treatment of heart rhythm disorders. "When physicians are active on social media sites, it affords them with an additional opportunity to reach patients and impact the daily choices that patients make. Lifestyle changes are much more likely to be implemented with regular reinforcement, and social media is a simple way to reach hundreds of thousands of patients — and it only takes minutes."[2]

Dr. Campbell adds that social media provides patients an opportunity to easily interact with physicians, nurses and other patients, noting that blogging sites offer the opportunity to express opinions and share common experiences. "These often provide patients with a great source of information about a particular physician, hospital or procedure. Twitter is another platform that allows patients to interact and discuss conditions and experiences in real time," he says. "It is a great place for debate, and these discussions lead to better patient engagement."

## Social Media as a Decision Influencer

Millions of people use social media on a daily basis to select a restaurant, find a hair salon or review a travel destination. And, in a similar fashion, people are increasingly turning to social media when it comes to choosing a healthcare provider. A Pew research study showed 83 percent of Internet users have searched for health-related information online, with search topics ranging from mental health and disease management to immunizations. Moreover, the study found 60 percent of social media users trust the information shared by doctors and other health professionals.[3]

According to a PricewaterhouseCoopers (PwC) report, 41 percent of patients interviewed said social media content impacted their choice of hospital or physician.[4] The ability to read reviews from other patients not only offers patients peace of mind, it creates a level of transparency for physicians. In fact, online reviews of individual physicians and group practices can also help to improve the quality of care. If a significant number of individuals leave feedback about poor or unacceptable levels of care, changes are likely to be made to improve them. On the flip side, healthcare providers can also use social media to their advantage by utilizing online polls and surveys to obtain feedback from their patients and then use this data to make changes to improve their services.

The PwC report also noted that by using social media for research and information gathering, patients are able to come more prepared to consultations and may even ask better questions. In addition, social media has become a popular tool for patients to expand their knowledge about their condition and treatment options. For example, 29 percent of patients peruse social media to view other patients' experience with their disease, and 42 percent browse social media platforms to discover health-related consumer reviews, according to the report.[4]

"Social media usage makes patients more inclined to actively communicate with their doctor during the medical consults in the first place," says Kevin Meuret, CEO of Mantality Health, a healthcare practice that performs testosterone replacement therapy on men who qualify. "Growing conversations on social media about 'stigmatized' conditions such as low testosterone levels or psoriasis send a powerful message to other sufferers and encourage their willingness to seek medical attention."[5]

## The Power of Online Patient Communities

The proliferation of self-organized online communities of patients, often focused on a particular disease, is a healthcare trend worth noting. Patient-led sites that serve as virtual support groups are the most well-known platforms and often provide features such as a moderated forum, blogs, advice, support, academic references and a retail page selling relevant products.

These sites provide a sense of connection and community while giving patients an opportunity to share ideas, treatment plans and approaches, and they provide access to others who share similar healthcare experiences. It's these types of connections that can positively influence healthcare outcomes.

Dr. Campbell says when patients are involved in online discussions, they are more aware of their disease process, more likely to make lifestyle changes and more compliant with their medicines. "Twitter chats are a great way to create 'virtual support groups,'" he explains, "and these often breed communities of patients with similar medical problems. These communities are a fantastic way to connect patients (when patients connect, they are able to support one another and hold each other accountable). Just as with an exercise buddy at the gym, this accountability and buddy system works well for improving compliance."[2]

Providers are also using online communities and social media platforms to promote access to care. For example, the Psoriasis Association launched an awareness campaign on Instagram that encourages users to share images of their condition using #getyourskinout and #psoriasiscommunity. Dominic Urmston, digital communications officer at the charity, says, "Users can find people who share similar experiences who they can chat to and support one another. Also, it empowers them so they can share images of their psoriasis and post about their experiences, too. As a result, the condition becomes less stigmatized, and more people are encouraged to weigh in on various treatment options and speak about them with their healthcare providers.[3]

*The proliferation of self-organized online communities of patients, often focused on a particular disease, is a healthcare trend worth noting.*

The *AMA Journal of Ethics* notes that online health communities offer numerous benefits of participation and access to an abundance of information for patients and their caregivers, family members and friends. More than half of members on the popular PatientsLikeMe site said the site was either moderately or very helpful for learning about their symptoms, and it helped them manage symptoms and understand treatments, and almost half said they connected with another member who helped them learn more about a medical treatment.[6]

## Social Media and Public Health

Social media has the advantage of reaching more people worldwide than any other forms of media. This reach is especially useful during a global health crisis, since it provides a platform for sharing important information quickly and in real time. The Zika outbreak in Brazil in 2016 provides an instructive example. The virus, spread through mosquito bites, began to circulate right before thousands of tourists were due to arrive in the country for the Rio Summer Olympics. Using social media, healthcare providers, news outlets and charities were able to disseminate important information about the virus such as how to prevent it from spreading, how to avoid mosquito bites when traveling to the infected area, risks for vulnerable individuals such as pregnant women, and symptoms to look out for. In fact, the Centers for Disease Control and Prevention (CDC) earned a Social Media Campaign award from Ragan Communications for its campaign effectiveness.[7]

Of course, as with any platform that gives communication access to the masses, the opportunity for spreading misinformation increases exponentially as more and more users log on, consume and share social posts. This proliferation of misinformation was displayed widely during the early days of the COVID-19 pandemic, despite efforts by leading social platforms to "control the narrative." For example, Facebook established a COVID-19 information center to share information about the virus from vetted government sources and credible media outlets. Unfortunately, this center was promoted alongside a plethora of other pandemic-related posts, including misleading ones. Other outlets also led the charge to share accurate COVID-19 information with the general public. YouTube started directing people to coronavirus-related videos from official sources like the World Health Organization. And Twitter, Instagram and TikTok took similar approaches. Despite these efforts, one of the identified challenges came from the way people consume information online; inflammatory and misleading headlines are more likely to get attention and clicks than straightforward news bullets from a government-sponsored site.

Even with these drawbacks, in times of crisis, the use of social media offers many benefits, including minute-by-minute real-time information. Through social media, hospitals and other organizations are able to deliver updates on hospital capacity, operation status and emergency room access. Having an active social media presence also allows healthcare professionals to pass along information shared by organizations such as the Red Cross

and CDC or communicate with news outlets.

From a public health perspective, social media can also offer helpful data that might otherwise be challenging to gather. People post about everything online, including their health, and simply tracking something like #flu can reveal when and where a virus is spreading. In their book *Social Monitoring for Public Health*, professors Michael Paul and Mark Dredze explain, "Social media offers advantages over traditional data sources, including real-time data availability, ease of access and reduced cost. Social media allows us to ask and answer questions we never thought possible."[8]

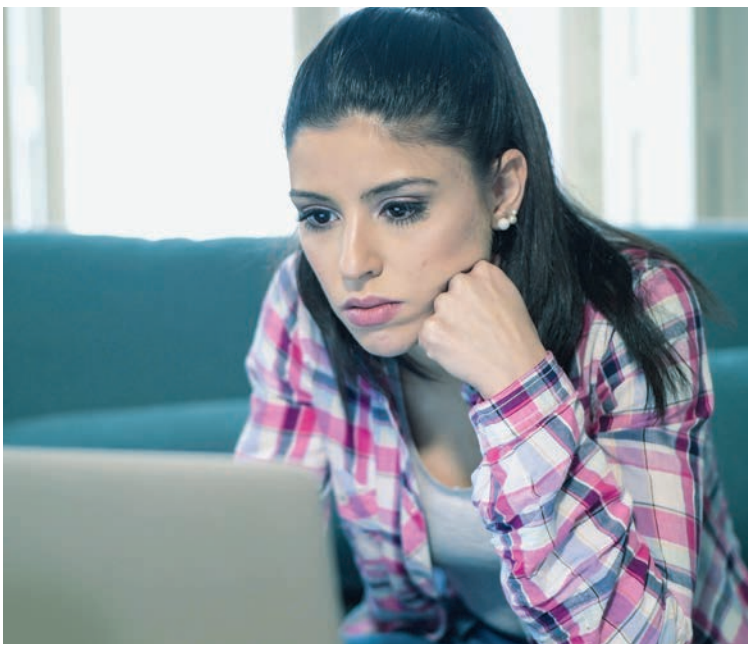
## The Future of Social Media and Healthcare

For providers looking to navigate the numerous potential pitfalls of social media, whether for practice promotion, networking or to connect with patients, ample resources are available to make the prospect less risky. The Association for Healthcare Social Media is a 501(c)(3) nonprofit created to support healthcare providers on social media. The organization provides resources to help physicians who use social media comply with HIPAA concerns, as well as how to disclose conflicts of interest, how to navigate industry relationships and how to cite medical literature so patients and others can easily understand it.[8]

In addition, the American Medical Association (AMA) has developed a code of medical ethics relating to professionalism in social media use.[8] AMA encourages physicians who use social media to:

- Be cognizant of standards of patient privacy and confidentiality, and refrain from posting identifiable patient information online.
- Follow ethics guidance regarding confidentiality, privacy and informed consent.
- Use privacy settings to safeguard personal information when using the Internet for social networking, keeping in mind privacy settings are not absolute.
- Maintain appropriate boundaries of the patient-physician relationship in accordance with professional ethics guidance.
- Consider separating personal and professional content.
- Bring unprofessional content posted by colleagues to their attention, or report the matter to appropriate authorities.
- Recognize that actions online may negatively affect their reputations among patients and colleagues, may have consequences for their medical careers and can undermine public trust in the medical profession.

As social media trends continue to expand and evolve, the healthcare community will undoubtedly have to remain flexible and open to innovation. And, as both younger patients and younger physicians who have grown up with social media



begin to incorporate online platforms into the foundations of their doctor/patient interactions, social media use may become the rule rather than the exception.

The *AMA Journal of Ethics* summarizes it this way: "There are many positive social media uses for healthcare professionals. As technology advances, social media guidelines will be modified, and yet the underlying principles of professionalism will remain. Best practices will emerge and outpace the guidelines, but if they are 'best,' they should maintain — and even enhance — the public's trust in healthcare professionals."[9] ❖

### References


1. Griffis HM, Kilaru AS, Werner RM, et al. Use of Social Media Across U.S. Hospitals: Descriptive Analysis of Adoption and Utilization. *Journal of Medical Internet Research*, Vol 16, No 11 (2014): November. Accessed at www.jmir.org/2014/11/e264.
2. Belbey J. Is Social Media the Future of Healthcare? *Forbes*, Jan. 31, 2016. Accessed at www.forbes.com/sites/joannabelbey/2016/01/31/is-social-media-the-future-of-healthcare/#13cdf1fd522d.
3. Weaver J. More People Search for Their Healthcare Online. NBC News, July 16, 2020. Accessed at www.nbcnews.com/id/3077086/t/more-people-search-health-online/#.Xzhp1hNKgqx.
4. Gamble M. 41% of Consumers Say Social Media Affects Their Hospital Choice. Becker's Hospital Review, April 17, 2012. Accessed at www.beckershospitalreview.com/hospital-management-administration/41-of-consumers-say-social-media-affects-their-hospital-choice.html.
5. Arnold A. How Social Media Usage Affects Doctor to Patient Relationships. *Forbes*, Nov. 7, 2018. Accessed at www.forbes.com/sites/andrewarnold/2018/11/07/how-social-media-usage-affects-doctor-to-patient-relationships/#102d299f5d3c.
6. Wicks P, Massagli M, Frost J, et al. Sharing Health Data for Better Outcomes on PatientsLikeMe. *Journal of Medical Internet Research*, 2010;12(2):e19. Accessed at www.ncbi.nlm.nih.gov/pmc/articles/PMC2956230.
7. CDC's Social Media Campaign Builds Awareness of the Zika Virus. Accessed at www.ragan.com/awards/health-care-pr-and-marketing-awards/2017/winners/social-media-campaign.
8. Newbury C. How to Use Social Media in Healthcare: A Guide for Health Professionals. Hootsuite, March 30, 2020. Accessed at blog.hootsuite.com/social-media-health-care.
9. Kind T. Professional Guidelines for Social Media Use: A Starting Point. *AMA Journal of Ethics*, May 2015. Accessed at journalofethics.ama-assn.org/article/professional-guidelines-social-media-use-starting-point/2015-05.



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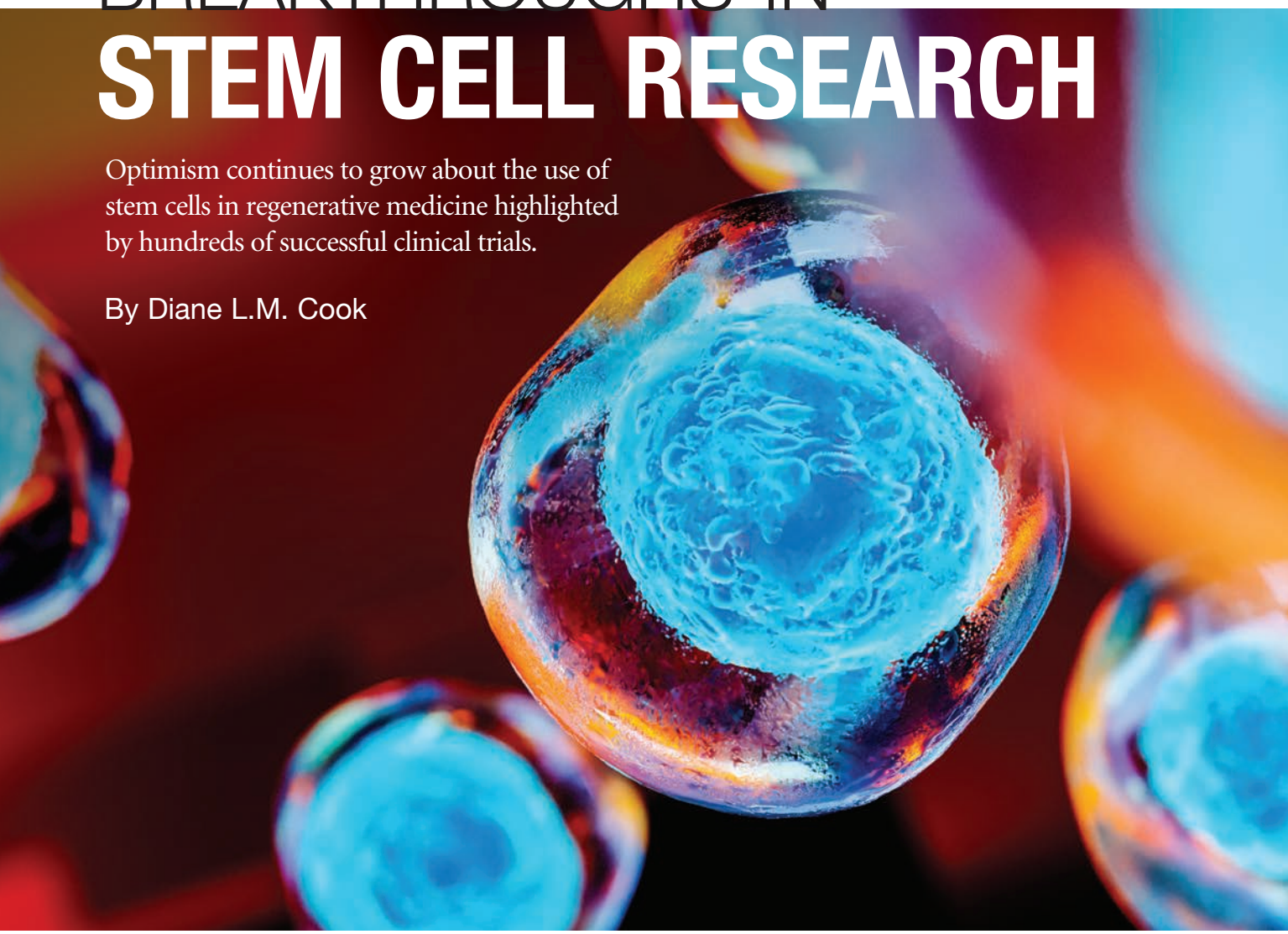
# BREAKTHROUGHS IN STEM CELL RESEARCH



Optimism continues to grow about the use of stem cells in regenerative medicine highlighted by hundreds of successful clinical trials.

By Diane L.M. Cook

**THE SCIENTIFIC** and medical communities are optimistic about recent breakthroughs in stem cell research that position them much closer to realizing the benefits of regenerative medicine. Regenerative medicine includes gene therapies, cell therapies and tissue-engineered products intended to augment, repair, replace or regenerate organs, tissues, cells, genes and metabolic processes in the body. It aims to alter the current practice of medicine by treating the root causes of disease and disorders.[1]

During the last 40 years, there have been three major breakthroughs in stem cell research. In 1981, Sir Martin Evans, then-chancellor of Cardiff University in Wales, was the first to identify embryonic stem cells (ESCs) in mice. In 1998, James Thomson, a biologist at the University of Wisconsin, and John Gearhart, PhD, of Johns Hopkins University isolated human ESCs and grew them in a lab. And in 2006, Shinya Yamanaka, PhD, at Kyoto University in Japan revealed a way of making embryonic-like cells from adult stem cells, avoiding the need to destroy an embryo. Dr. Yamanaka's team reprogrammed ordinary adult stem cells by inserting four key genes forming induced pluripotent stem cells (iPSCs).[2]

Since then, scientists have been studying how to use iPSCs for cell-based therapies in regenerative medicine, to screen new drugs and to study disease modeling. They hope this understanding will give them insight into the normal growth of a human body and identify the causes of birth defects so stem cells can be used as a renewable source of replacement cells, tissues and organs to treat myriad diseases and disorders.

## The Promise of Stem Cell Research

The Alliance for Regenerative Medicine (ARM) is a U.S.-based international advocate for regenerative medicine that fosters investment research and development and the successful commercialization of safe, effective and transformational therapies for patients around the world. According to ARM's Director of Science and Industry Affairs Michael Lehmicke, "Stem cells have extraordinary potential to durably treat a number of serious diseases and disorders, including neurodegenerative disorders, cardiovascular disease, diabetes, macular degeneration and other prevalent and orphan indications. As of the end of 2019, ARM is tracking 169 clinical trials worldwide utilizing stem cells, including 25 in Phase III. More recently, we've seen a number of therapeutic developers establish clinical and preclinical programs to investigate the therapeutic potential of stem cells to treat acute respiratory distress syndrome associated with COVID-19."

Kevin McCormack, senior director of public communications at the California Institute for Regenerative Medicine (CIRM), says the potential results of research involving the transplant of stem cells, drug discovery and diagnostics are nothing short of revolutionary: "These treatments are reshaping the way we see disease and the way we treat disease. Instead of using conventional therapies that were good at trying to keep the condition under control, stem cell therapies have the potential to rewind the clock and restore function to diseased or damaged organs and tissues. Transplanting cells can help repair and replace tissues damaged by disease. One day, we hope they will be able to help organs regenerate so that patients won't need to get a transplant; instead, they will be able to regrow a damaged organ."

## Current Stem Cell Research

*CIRM.* Although there are approved marketed regenerative medicine products in specific regions/countries for specific indications that are listed on ARM's website, stem cell research is ongoing in the United States and around the world. For instance, CIRM, which funds clinical trials that test promising stem cell-based treatments for currently incurable diseases or disorders, has funded 63 clinical trials, and another 25 projects in clinical trials have received crucial early support from the institute. In addition to working on stem cell research for blindness, blood cancers, blood disorders, diabetes and sickle cell disease, CIRM is studying how to use stem cells to treat neurodegenerative diseases such as Parkinson's disease (including one in a clinical trial) and amyotrophic lateral sclerosis or Lou Gehrig's disease (two of which are in clinical trials).

To deliver stem cell treatments to patients, CIRM developed the Alpha Stem Cell Clinics Network (ASCCN), an infrastructure comprised of six world-class medical facilities that have the expertise to deliver proven stem cell treatments and U.S. Food and Drug Association (FDA)-sanctioned clinical trial therapies to patients. To date, ASCCN has supported more than 130 clinical trials, targeting more than 40 different diseases and enrolling more than 750 patients.

*Although there are approved marketed regenerative medicine products in specific regions/countries for specific indications that are listed on ARM's website, stem cell research is ongoing in the United States and around the world.*

CIRM also created the iPSC Repository, the world's largest induced pluripotent stem cell bank established to harness the power of iPSCs as tools for disease modeling and drug discovery. The iPSC Repository houses a collection of stem cells from thousands of individuals, some of which are healthy but others that have heart, lung, liver or other diseases or disorders.[3]

In 2017, FDA created the Regenerative Medicine Advanced Therapy (RMAT) designation to fast-track therapeutic tissue-engineered products, cell therapies, human cell and tissue products

or any combination product that may save people from serious or life-threatening conditions or diseases that would otherwise be incurable. Of the 25 RMAT programs to date, six are funded by CIRM.

*The first in-human Parkinson's disease clinical trials using iPSC-derived dopamine-producing cells began in Japan in August 2018, and trials in the U.S. using ESC are underway.*

*International Society for Stem Cell Research (ISSCR).* An independent, nonprofit organization that provides a global forum for stem cell research and regenerative medicine, ISSCR provides information about how stem cells are being used to understand several diseases and conditions. Here's what ISSCR has found:

• Diabetes. Insulin-producing cells derived from ESCs and iPSCs can reverse diabetes in experimental animals. Therefore, the research community is encouraged that cells derived from stem cells may succeed as beta cell replacement therapy and thus essentially cure type 1 diabetes.[4]

• Heart disease. Research is ongoing to test cellular therapies to treat heart attacks by combining different types of stem cells, repeating transplantations or improving stem cell patches. Clinical trials using these improved methods are targeted to begin in 2020.[5]

• Macular degeneration. Stem cell research is helping scientists understand how the different cell types in the retina function together, which has led to exploring ways to replace both rods and cones and the supporting retinal pigment epithelium (RPE) cells. Researchers are making great progress to replace the RPE layer, which they believe will halt or even reverse the vision loss associated with age-related macular degeneration. Some researchers are using iPSCs to grow rods and cones or RPE cells. Other researchers are using ESCs, while others are exploring RPE-specific stem cells that can be grown from the adult RPE (for example, from eyes donated to eye banks). A main goal is to determine the optimal maturation for these cells.

Researchers are also exploring different methods to deliver stem cells to the eye, including creating patches of RPE cells in the lab. Another method showing promise is a suspension of cells, which is injected into the eye under the retina. The cells, derived from iPSCs, RPEs or ESCs, are grown and differentiated in the lab, then placed in a harmless fluid to be injected. For both approaches, a critical question is whether these cells will integrate well with the patient's own RPE stem cells and perform their job of supporting the rods and cones over the long term.[6]

• Multiple sclerosis (MS). The use of glial progenitor cells, which give rise to new myelin-producing oligodendrocytes, is under development as a potential treatment for MS. The goal is to stabilize disease by preventing further neuronal loss and restoring function by remyelinating the demyelinated neurons. The potential use of stem cell-derived glial cells as cellular therapies for treating progressive MS is under review by FDA. Pending acceptable preclinical safety data and FDA approval, clinical trials are scheduled to begin soon.[7]

• Osteoarthritis (OA). Due to a lack of clear support from high-quality studies, as well as a lack of consensus in the scientific and medical communities concerning many aspects of using cell therapies to treat OA (such as when stem cells should be used, the ideal source of stem cells and how they should be prepared, defined or delivered), the effects and effectiveness of cell therapies for treating OA remain unproven, and the scientific community does not currently recommend them.[8]

• Parkinson's disease. The first in-human Parkinson's disease clinical trials using iPSC-derived dopamine-producing cells began in Japan in August 2018, and trials in the U.S. using ESC are underway. In Europe, similar human trials are likely to begin for the first time in 2021. Trials in Australia using a non-ESC source began in 2016, but issues relating to aspects of the trial have been raised, including the origin of the cells, the type of cells transplanted and the availability and transparency of preclinical data.[9]

*Harvard Stem Cell Institute (HSCI).* Through collaborative research, HSCI seeks to stimulate healing in patients by harnessing the potential of stem cells; create targeted treatments by combining new gene- and cell-based therapies with traditional medicines; and accelerate drug discovery by developing novel stem cell-based tools. HSCI's research focuses on the following disease areas: blood, cancer, cardiovascular, diabetes, kidney, musculoskeletal, nervous system (including ALS, Alzheimer's disease, eye diseases, hearing loss, MS and Parkinson's disease) and skin. HSCI also tackles research areas that span across individual diseases and organ systems, such as aging and fibrosis.

Breakthroughs in the HSCI's research include:

• Demonstrating gene-editing machinery can be delivered straight to stem cells where they live rather than in a petri dish.

The findings have major implications for biotechnology research and the development of therapeutics for genetic diseases.[10]

• Discovering how to make beta cells, the cells in the pancreas that measure glucose levels and squirt out insulin as needed.[11]

• Integrating microfluidics and human insulin-producing beta cells in an islet-on-a-chip. The new device makes it easier for scientists to screen insulin-producing cells before transplanting them into a patient, test insulin-stimulating compounds and study the fundamental biology of diabetes. This automated miniature device gives results in real time, which can speed up clinical decision-making. And, it makes it easier to screen drugs that stimulate insulin secretion, test stem-cell-derived beta cells and study the fundamental biology of islets.[12]

• Identifying a stem cell defect as a possible cause of the chronic skin disease psoriasis.[13]

• Discovering that fatty acids influence skeletal stem cell development, which led to the discovery that stem cells can repair bone fractures. This study shows for the first time that specific nutrients can inform stem cells of the type of cell they should become, which is an important step forward in stem cell research.[14]

*The Stanley Center for Psychiatric Research.* The Stanley Center at the Broad Institute of MIT and Harvard is focused on better understanding neuropsychiatric disorders using stem cells and related models as one of many research tools into these disorders rather than using stem cells as treatments. Seeking to reduce serious mental illness, the center's major focus is to clarify the molecular causes of schizophrenia, bipolar disorder and other severe mental illnesses, namely autism and attention deficit hyperactivity disorder, and to translate that knowledge into new therapies and biomarkers for patients.

To study these disorders, the Stanley Center is using human pluripotent stem cells acquired and reprogrammed through a large number of international collaborations, the most notable one the CIRM's iPSC Repository. The Broad Institute has embarked on whole genome sequencing of hundreds of stem cell lines from the iPSC Repository to identify genes associated with neurological disorders, including autism spectrum disorder, and to use this information as a starting point to find cures.

The Stem Cell groups at the Stanley Center are developing stem cell-derived neuronal models and using genome engineering in iPSCs to investigate in-vitro phenotypes associated with genetic variants underlying psychiatric disease. Specifically, these groups are focused on the following projects: Human EnCELLopedia, stem cell genome engineering, human brain organoid models, neuronal spheroids for screening and therapeutic target studies, the brain interaction network, a human stem cell genome project, and massively mosaic experimental systems.

A unique feature of the stem cell collection efforts at the Stanley Center is its focus on developing a cellular and genetic resource of iPSC lines from patients with a spectrum of psychiatric conditions, as well as from ancestrally matched controls. This is critical for fueling downstream studies that aim to link disease-associated human genetic variation to defined cellular phenotypes.[15]

***The combination of stem cell and gene therapy has the potential to become a game-changer in the field of regenerative medicine.***

*Clustered regularly interspaced short palindromic repeats (CRISPR).* The combination of stem cell and gene therapy has the potential to become a game-changer in the field of regenerative medicine. A number of researchers are using CRISPR-Cas9, one of several genome editing techniques that lets scientists rewrite DNA sequences in any cell that could potentially cure genetic disorders and diseases. Genome editing is a technique in which DNA is inserted, replaced or removed at particular locations in the human genome to correct mutations that cause disorders and diseases.[16]

According to Kevin Doxzen, PhD, science communication specialist at the Innovative Genomics Institute (IGI) at the University of California (UC) Berkeley, CRISPR "represents a fascinating bacterial immune system that helps microbes defend themselves against viral attack. There are many different types of CRISPR immune systems, and through the process of studying the arms race between bacteria and viruses, scientists realized that some of the CRISPR proteins, known as Cas (CRISPR-associated) proteins, could be used as programmable molecular scissors. CRISPR-Cas9, the most popular Cas protein, uses small molecules of RNA that search and bind with matching sequences of DNA. This simple act allows Cas proteins to find a specific sequence of DNA among the six billion letters of the human genome. Once a matching DNA sequence is located, the DNA double helix is unwound, and Cas9 cuts both strands of DNA, allowing researchers to alter the DNA in a variety of ways. Many of the foundational CRISPR advancements were done on UC Berkeley's campus."

In just a few years, scientists at UC Berkeley and across the world have integrated CRISPR technology into their research. Many of these researchers are using genome editing for basic researcher questions such as understanding the molecular mechanisms behind wing pattern development in butterflies or brain function in squid. In addition to fundamental research questions, researchers at UC Berkeley are interested in addressing real-world issues using CRISPR technology. IGI, a research partnership between UC Berkeley and UC San Francisco, is leading this front. "Research teams at the IGI are working to develop CRISPR cures for sickle cell disease, autoimmune diseases and other genetic ailments. In addition to biomedical applications, the IGI is advancing the deployment of CRISPR technology agriculture, including to engineer drought-tolerance, disease-resistance and higher nutrition in a range of crops," says Dr. Doxzen.

*There are several major challenges to address before stem cells can be used as cell therapies to treat a wider range of diseases.*

Dr. Doxzen also says CRISPR is already revolutionizing drug discovery and diagnostics: "In the midst of the COVID-19 pandemic, researchers are using genome editing to study the effect of viral infection on human cells and to design new drug treatments. Scientists are also using CRISPR-Cas proteins as a way to detect the presence of COVID-19 in patient samples."

In the next few years, Dr. Doxzen says preliminary results will be seen of a wide range of CRISPR clinical trials aimed at curing genetic diseases, including sickle cell disease, genetic forms of blindness, muscular dystrophy and many more. "At the IGI, we are working to ensure that CRISPR therapies are affordable and accessible, especially for those who could most benefit from these innovative cures," he explains. "As well, in the coming years, society will most likely have the option of buying CRISPR-edited food in their local supermarkets."

CRISPR Therapeutics is a leading gene-editing company focused on developing transformative gene-based medicines for serious diseases using its proprietary CRISPR/Cas9 platform. The company is pursuing gene-editing approaches to allow allogeneic use of stem cell-derived therapies by enabling immune evasion, improving existing cell function and directing cell fate using CRISPR/Cas9. Its first major effort in this area, together with partner ViaCyte, is with diabetes.[17]

## Remaining Challenges

According to ISSCR's report "Stem Cell Facts," there are several major challenges to address before stem cells can be used as cell therapies to treat a wider range of diseases. "First, we need to identify an abundant source of stem cells. Identifying, isolating and growing the right kind of stem cell, particularly in the case of rare adult stem cells, are painstaking and difficult processes. Pluripotent stem cells such as ESCs can be grown indefinitely in the lab and have the advantage of having the potential to become any cell in the body, but these processes are again very complex and must be tightly controlled. iPS cells, while promising, are also limited by these concerns. In both cases, considerable work remains to be done to ensure that these cells can be isolated and used safely and routinely.

"Second, as with organ transplants, it is very important to have a close match between the donor tissue and the recipient; the more closely the tissue matches the recipient, the lower the risk of rejection. Being able to avoid the lifelong use of immunosuppressants would also be preferable. The discovery of iPS cells has opened the door to developing patient-specific pluripotent stem cell lines that can later be developed into a needed cell type without the problems of rejection and immunosuppression that occur from transplants from unrelated donors.

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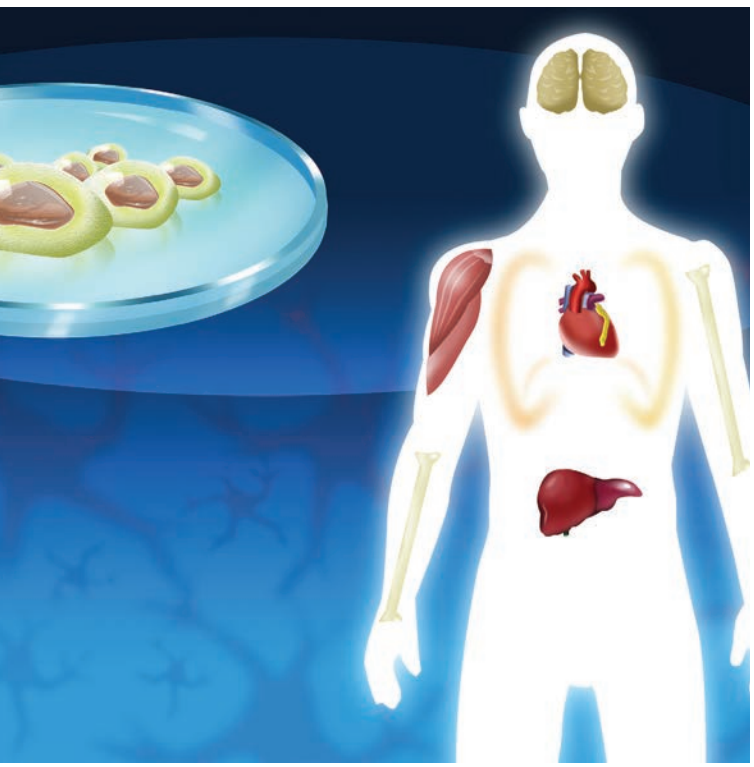

"Third, a system for delivering the cells to the right part of the body must be developed. Once in the right location, the new cells must then be encouraged to integrate and function together with the body's other cells."[18]

## Future of Stem Cell Research

According to CIRM's McCormack, the future of stem cell research is very bright: "The last decade has been one of developing a deeper understanding of the science behind stem cells — how to harness their ability to renew and replicate themselves, how to be more effective in turning them into the kinds of cells we want them to be and creating the kind of changes we need. We believe the next decade will see that basic understanding of how the cells grow and help us become ever more effective at using these cells as therapies. Combined with the increased sophistication of our ability to use gene editing, we feel that this 'one-two punch' will greatly increase our ability to help patients who are suffering from previously incurable conditions."

ARM's Lehmicke agrees: "We expect that stem cell research will continue to grow over the next few years. Sector stakeholders are collaborating to establish best practices that will help to streamline the development and manufacture of these therapies. Additionally, we expect that iPSCs, which are just beginning to enter the clinic, will play a growing role in this area. In particular, we're seeing a growing interest in utilizing iPSCs to create allogeneic or 'off-the-shelf' cell-based immunotherapies to treat cancer. This method may help to alleviate issues of immunogenicity and allow for easier scale up compared to highly personalized autologous therapies, which utilize the patient's own cells and must be manufactured on a patient-by-patient basis."

Deepak Srivastava, president of ISSCR and Gladstone Institutes, says, "The stem cell field continues to advance rapidly in both mechanistic understanding of disease and the translation of discovery into new therapies for so many devastating yet unsolved human diseases. Basic science discoveries in this area have matured to gain significant commercial investment in the last year for diabetes, Parkinson's disease, heart failure, muscular dystrophies and cancer, to name a few. Rigorous clinical and preclinical trials are advancing based on transplanting stem cells, reprogramming resident cells, discovering new drugs using stem cells, and delivering missing genes or gene-editing machinery through novel gene therapy vectors."[19] ❖

### References


1. Alliance for Regenerative Medicine, Technologies. Accessed at alliancerm.org/technologies.
2. Coghlan A. Stem Cell Timeline: The History of a Medical Sensation. *New Scientist*, Jan. 30, 2014. Accessed at www.newscientist.com/article/dn24970-stem-cell-timeline-the-history-of-a-medical-sensation.
3. California Institute for Regenerative Medicine. Something Better Than Hope: Annual Report 2018, page 14. Accessed at www.cirm.ca.gov/sites/default/files/files/about_cirm/CIRM%202018%20Annual%20Report.pdf.
4. International Society for Stem Cell Research. A Closer Look at Stem Cells: Diabetes Disease Fact Sheet. Accessed at www.closerlookatstemcells.org/stem-cells-medicine/diabetes.
5. International Society for Stem Cell Research. A Closer Look at Stem Cells: Heart Disease Fact Sheet. Accessed at www.closerlookatstemcells.org/stem-cells-medicine/heart-disease.
6. International Society for Stem Cell Research. A Closer Look at Stem Cells: Macular Degeneration Fact Sheet. Accessed at www.closerlookatstemcells.org/stem-cells-medicine/macular-degeneration.
7. International Society for Stem Cell Research. A Closer Look at Stem Cells: Multiple Sclerosis Fact Sheet. Accessed at www.closerlookatstemcells.org/stem-cells-medicine/multiple-sclerosis.
8. International Society for Stem Cell Research. A Closer Look at Stem Cells: Osteoarthritis Disease Fact Sheet. Accessed at www.closerlookatstemcells.org/stem-cells-medicine/osteoarthritis.
9. International Society for Stem Cell Research. A Closer Look at Stem Cells: Parkinson's Disease Fact Sheet. Accessed at www.closerlookatstemcells.org/stem-cells-medicine/parkinsons-disease.
10. Harvard Stem Cell Institute. Editing Genes at the Source: Breakthrough Research Shows That Stem Cell Genes Can Be Edited in Living Systems, June 5, 2019. Accessed at hsci.harvard.edu/news/editing-genes-source.
11. Weintraub K. The Quest to Cure Diabetes: From Insulin to the Body's Own Cells. WBUR.org, CommonHealth, June 27, 2019. Accessed at www.wbur.org/commonhealth/2019/06/27/future-innovation-diabetes-drugs.
12. Bergman MT. Pancreas on a Chip: HSCI Scientists Have Combined Organ-on-a-Chip and Stem-Cell Technologies to Make a Powerful Tool for Diabetes Research and Beta-Cell Transplantation. Harvard Stem Cell Institute, Aug. 29, 2019. Accessed at hsci.harvard.edu/news/pancreas-chip.
13. Harvard Stem Cell Institute, A Potential New Treatment Target for Psoriasis: HSCI Scientists Identify Stem Cell Defect as a Possible Cause of Chronic Skin Disease, Dec. 16, 2019. Accessed at hsci.harvard.edu/news/potential-new-treatment-target-psoriasis.
14. Harvard Stem Cell Institute. Bone or Cartilage: How Stem Cells Repair Bone Fractures, Feb. 27, 2020. Accessed at hsci.harvard.edu/news/bone-cartilage-van-gastel-2020.
15. Broad Institute. Cellular Neurobiology. Accessed at www.broadinstitute.org/stanley-center-psychiatric-research/cellular-neurobiology.
16. Alliance for Regenerative Medicine. Genome Editing. Accessed at alliancerm.org/bioethics.
17. CRISPR Therapeutics. Regenerative Medicine. Accessed at www.crisprtx.com/programs/regenerative-medicine.
18. International Society for Stem Cell Research. Stem Cell Facts. Accessed at www.closerlookatstemcells.org/wp-content/uploads/2018/10/stem-cell-facts.pdf.
19. International Society for Stem Cell Research. Creating Opportunities to Advance Stem Cell Science, 2019-2020 Year in Review, June 9, 2020. Accessed at www.isscr.org/news-publicationsss/isscr-news-articles/article-listing/2020/06/09/creating-opportunities-to-advance-stem-cell-science-2019-2020-year-in-review.



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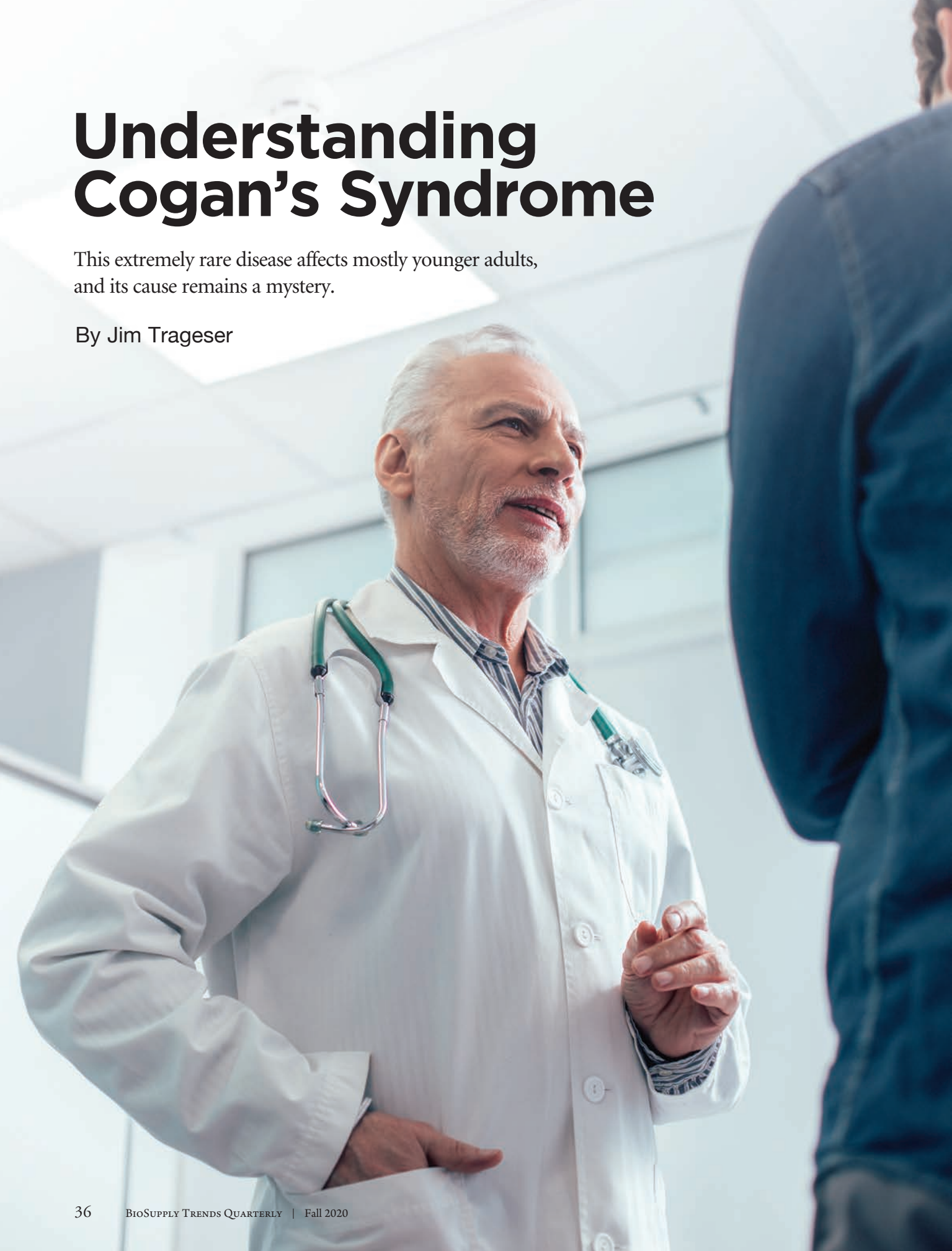
# Understanding Cogan's Syndrome

This extremely rare disease affects mostly younger adults, and its cause remains a mystery.

By Jim Trageser



**COGAN'S SYNDROME** is an extremely rare condition with no single test to identify it and with symptoms that mimic those of many far more common diseases. Its cause remains unknown, as do its specific triggers. But if not diagnosed and treated quickly, it can lead to significant (and sometimes permanent) loss of hearing and degraded vision. It can also manifest with vasculitis, and in extremely severe cases, it can be fatal if the aorta is affected.

Due to its rarity, the actual number of cases is difficult to confirm. The portal for rare diseases and orphan drugs, Orpha.net, reports only approximately 300 cases identified worldwide since the disease was first formally described in 1945, and that was the highest number found (other sources report between 100 cases and 250 cases).[1]

## What Is Cogan's Syndrome?

While most diseases are identified by their underlying cause, Cogan's syndrome is entirely defined by its symptoms: sudden onset of hearing loss, vertigo and inflammation of the eyes with or without vasculitis that cannot be explained by any other possible cause.[2]

The syndrome is named after ophthalmologist David G. Cogan, a faculty member at Harvard who described the condition in 1945[3] as nonsyphilitic "interstitial keratitis associated with vertigo, tinnitus and usually profound deafness."[4] However, it is believed the disease was described in a paper written by R.F. Morgan and C.J. Baumgartner in 1934.[5]

Cogan's syndrome is thought to be an autoimmune disease, possibly even a subset of vasculitis, but disagreement over classification remains. What is known is it is chronic with no cure, although symptoms can often be controlled with treatment, and the severity of symptoms can wane over time.

Interestingly, for a disease that affects so few people, there are two subsets of Cogan's: Cogan's syndrome type I as described in this article and atypical Cogan's syndrome in which either only some symptoms manifest, different symptoms also present or the disease progresses more slowly — over a matter of years rather than months.

The eye inflammation caused by Cogan's generally presents as bilateral interstitial keratitis or other similar corneal stromal keratitis, but it can also take the form of episcleritis, scleritis, uveitis, papillitis, vitritis or choroiditis.[5] The hearing issues arise from inflammation and calcification of the canals, the vestibule or the cochlea.[6]

## Causes of Cogan's Syndrome

Although little is presently understood about the causes of Cogan's syndrome, National Institutes of Health's (NIH) Genetic and Rare Diseases Information Center reports that current research suggests an unknown autoimmune response causes the body to attack tissues of the eye and ear.[7] Indeed, the discovery of autoantigen peptides in the eye and ear tissue of patients with Cogan's strongly suggests an autoimmune response.[6]

Some researchers believe onset of Cogan's syndrome may be a reaction to a previous infection, but this has yet to be established.[3] In fact, currently, no definitive cause or trigger has been identified. And, no genetic cause for Cogan's has been identified, nor does it seem to run in families.

The disease typically affects younger adults between 20 years and 40 years, and sometimes children.[1] Men and women seem equally likely to develop it,[8] as well as individuals of all ethnicities.[2]

## Symptoms and Progression of Cogan's Syndrome

Cogan's syndrome progresses rapidly, with symptoms worsening in a matter of weeks, often before a firm diagnosis has been made. It generally initially presents as hearing loss, inflammation of the eyes or vertigo: 38 percent of patients present with ocular inflammation and 46 percent with auditory symptoms, while just 15 percent have both symptoms at first examination.[5] However, within five months of an initial exam, 75 percent of patients experience both vision and hearing degradation.

*Cogan's syndrome is thought to be an autoimmune disease, possibly even a subset of vasculitis, but disagreement over classification remains.*

Some portion of hearing loss is almost always permanent, and in two-thirds of patients, the loss is severe.[2] In fact, a significant percentage of Cogan's patients permanently lose 100 percent of their hearing. In most patients, both vision and hearing issues affect both sides. In rare cases, only one ear or one eye will be affected at first, but this almost always progresses to both sides being affected.[6]

According to the American Autoimmune Related Diseases Association, other less-common symptoms that may indicate

Cogan's syndrome are fever, nausea, unexplained weight loss, enlarged lymph nodes or photo sensitivity.

Vasculitis can also occur in Cogan's syndrome patients and, in severe cases, can include aortitis. But even when the aorta is not involved, significant organ damage can result from the onset of vasculitis, particularly to the kidneys.[6]

*If a patient presents with red and inflamed eyes and hearing problems, as well as vasculitis, Cogan's syndrome can be considered as a possible diagnosis early on.*

## Diagnosing and Treating Cogan's Syndrome

Since there is no diagnostic test for Cogan's syndrome, a diagnosis is made through a process of elimination. As symptoms and damage can progress quickly, this analysis should be accelerated as much as possible.

If a patient presents with red and inflamed eyes and hearing problems, as well as vasculitis, Cogan's syndrome can be considered as a possible diagnosis early on. But if a patient presents with only vision or auditory issues, other potential causes will need to be considered initially.

Loren Bartels, MD, FACS, director of the Tampa Bay Hearing and Balance Center and an otolaryngology professor at the University of South Florida who has treated patients with Cogan's, says due to the quick progression of the disease, it makes sense to reach out to specialists immediately. The best course "is to share the care with an ophthalmic immunologist, as at least three different conditions can present in a similar fashion: Cogan's, Vogt-Koyanagi-Harada disease and Susac's syndrome," explains Dr. Bartels.

The auditory symptoms of Cogan's are nearly identical to those of Meniere's disease and are also similar to those of syphilis, Lyme disease and Epstein-Barr virus. Consequently, when a patient presents with these symptoms, these other possible causes should be considered. Syphilis and Lyme disease are both bacterial diseases, and they can be diagnosed (or eliminated) through a blood draw and lab test; syphilis with the rapid plasma reagin test or venereal disease research laboratory test; and Lyme disease with a two-part lab test. Epstein-Barr virus is also diagnosed with a blood test that looks for antibodies made in response to the infection.

While the cause of Meniere's disease is not fully understood, it is far more common than Cogan's and, thus, should be eliminated from consideration before making a final diagnosis of Cogan's. Vision-motion tests such as the video head impulse test are used to test for Meniere's disease.

Any differences in blood pressure or pulse on the right side versus the left side may indicate vasculitis, as might a noticeable heart murmur. An MRI can help eliminate the possibility of a tumor or other growth, particularly in the ear canals.[6]

Once a diagnosis has been made, the typical treatment is topical and systemic corticosteroids to reduce the inflammation

causing the damage in the ears, eyes and circulatory system. The Merck Manual recommends topical prednisolone acetate 1% for treatment of keratitis, episcleritis and anterior uveitis. If the front of the eye is affected, mydriatics (a type of medicine that make the pupil of the eye dilate) may be used to prevent the iris from becoming stuck to the cornea.[2]

For inflammation causing auditory issues, the recommended treatment is prednisone 1 mg/kg orally daily for at least two months.[5]

For cases that don't respond to initial treatment or show diminishing response, immunosuppressant drugs may be prescribed to temper the autoimmune response. Infliximab (Remicade, Inflectra) has shown promise for reducing ear damage and also assists with weaning patients from corticosteroids with their long-term side effects.[1]

Dr. Bartels points out that while high-dose steroids are commonly prescribed, "it is unclear whether that changes the long-term progression to severe or profound sensory hearing loss."

He also says that "possibly helpful are immunosuppressive drugs such as methotrexate, cyclophosphamide, cyclosporine or azathioprine, but these would generally be started only if the hearing loss was steroid-responsive." He notes, however, that these drugs have a significant side-effect risk, which is especially pertinent since this disorder commonly occurs in relatively young individuals of child-bearing age.

When damage to the ear causes permanent hearing loss, cochlear implants have proved effective at restoring some auditory function.[1] "These patients uniformly do well with cochlear implants, but a surgical challenge is common," Dr. Bartels explains. "The inferior lateral basal turn of the cochlea is commonly ossified (has obstructive new bone formation that plugs the surgical entry area into the inner ear fluid spaces) and requires delicate drilling to get past. Once past that, the cochlear implant typically slides into the inner ear, the cochlear scala tympani, without difficulty. Caution is needed to avoid insertion through the bony spiral lamina and basilar membrane into the cochlear duct or scala vestibuli."

If one or both corneas are irreversibly damaged, corneal transplants can be considered.

Outside of permanent hearing loss, the gravest risk is from vasculitis, so that needs to be monitored over time — often with liver function tests to track damage. In severe cases, valve implants may be needed in the aorta.

## Ongoing Research

With such a small population affected by Cogan's syndrome, research into its cause and treatments is minimal. Any advances are likely to come via research into other related autoimmune diseases or increases in knowledge about autoimmune disease in general.

One recently canceled study (since not enough subjects volunteered) would have looked at the use of Cacicol20 in promoting the healing of corneal wounds.[9] And, a 2019 study used intravenous immune globulin to treat a Cogan's syndrome patient with repeated severe flare-ups through three successful pregnancies.[10]

*Since a variety of underlying causes can trigger chronic inflammation, there is no one way to prevent its onset.*

## Looking Ahead

While several papers point out that Cogan's syndrome is likely underdiagnosed and thus underreported, even if the true number of cases were 10 times greater, it would remain a statistical anomaly — one most physicians will never encounter over the course of their careers. Nevertheless, a quick diagnosis and aggressive treatment can have tremendous positive impact on a patient's quality of life. Given the high probability of permanent hearing loss for any patient who exhibits Cogan's syndrome, moving rapidly to ascertain the cause of such symptoms should be prioritized so treatment can begin. ❖

### References


1. Cogan Syndrome. Orpha.net, August 2019. Accessed at www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=en&Expert=1467.
2. Vasculitis Foundation. Cogan's Syndrome. Accessed at www.vasculitisfoundation.org/mcm_article/cogans-syndrome.
3. Greco A, Gallo A, Fusconi M, et al. Cogan's Syndrome: An Autoimmune Inner Ear Disease. *Autoimmunity Reviews*, January 2013. Accessed at www.sciencedirect.com/science/article/pii/S1568997212001486.
4. Cogan DG. Syndrome of Nonsyphilitic Interstitial Keratitis and Vestibuloauditory Symptoms. *Archives of Ophthalmology*, February 1945. Accessed at jamanetwork.com/journals/jamaophthalmology/article-abstract/618187.
5. Roat MI. Cogan Syndrome. Merck Manual, May 2020. Accessed at www.merckmanuals.com/professional/eye-disorders/corneal-disorders/cogan-syndrome.
6. Iliescu DA, Timaru CM, Batras M, et al. Cogan's Syndrome. *Romanian Journal of Ophthalmology*, v.59(1); Jan-Mar 2015. Accessed at www.ncbi.nlm.nih.gov/pmc/articles/PMC5729811.
7. Genetic and Rare Diseases Information Center. Cogan's Syndrome. Accessed at rarediseases.info.nih.gov/diseases/1421/cogans-syndrome.
8. Healthline. Cogan Syndrome. Accessed at www.healthline.com/health/cogans-syndrome.
9. Cacicol20 in Corneal Wound Healing and Nerve Regeneration After Phototherapeutic Keratectomy. ClinicalTrials.gov, last updated March 11, 2020. Accessed at www.clinicaltrials.gov/ct2/show/NCT02373397.
10. Scherg F, Haag F, and Krieger T. Off-Label Application of Intravenous Immunoglobulin (IVIG) for Treatment of Cogan's Syndrome During Pregnancy. *BMJ Case Reports*, Oct. 10, 2019. Accessed at pubmed.ncbi.nlm.nih.gov/31604714.



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# No Place Like Home: The Growing Acceptance of Subcutaneous Immune Globulin

By Keith Berman, MPH, MBA


**PRIOR TO THE** approval of the first licensed intravenous immune globulin (IVIG) product in 1981, IgG replacement therapy for patients with primary humoral immunodeficiency disorders (PI) was a painful and wholly inadequate ordeal. Patients had to bear frequent small intramuscular injections of 16.5% immune serum globulin (IMIG), a product whose IgG clumps and fragments caused severe anaphylactic reactions if given by the intravenous route. Poor tolerability to these repeated injections typically limited IMIG dosage, which translated into subprotective steady-state serum IgG levels and often serious recurrent bacterial infections.

Shortly before IVIG was introduced, clinicians at the National Institutes of Health (NIH) reported on their experience with yet a third approach — subcutaneous infusion of IMIG — to treat a 24-year-old woman hospitalized with cellulitis, fever and a history of sinusitis, otitis media, sepsis and pneumonia. Multiple IMIG injections to the woman's tolerable limit had brought her serum IgG level up to only 270 mg/dL, well below the protective range. The NIH team decided to train her to self-administer small volumes of IMIG subcutaneously on a daily basis, and her sepsis and sinopulmonary infection entirely resolved. She continued her daily self-infusions through a normal full-term pregnancy, even boosting her dose without incident to maintain a protective IgG level.[1] Other patients were started on subcutaneous replacement therapy with IMIG.

The new intravenous preparations enabled patients to receive their IG replacement therapy with a single clinic visit every three weeks to four weeks, ending interest in experimentation with subcutaneous IMIG delivery. But experience has revealed that IVIG treatment can come with its own downsides:

- *Systemic adverse reactions.* These most commonly include headache, chills, flu-like symptoms, low-grade fever, urticaria, fatigue, nausea, lightheadedness, myalgia and arthralgia. Rarely, IVIG administration can result in serious adverse events that include thrombosis, renal dysfunction or failure, anaphylaxis, aseptic meningitis and hemolytic anemia.
- *Low IgG trough levels.* While a function of dose and serum half-life, IgG trough levels in the days leading up to the next scheduled IVIG infusion can potentially drop below the fully protective range.
- *Vascular access challenges.* In a small percentage of children and older adults in particular, reliably obtaining venous access for the infusion is problematic, necessitating placement of an infusion port. Unfortunately use of these devices is accompanied by risks of infection and thrombus formation.
- *Lost school/work days.* Depending on infusion time, each scheduled infusion visit requires the patient to be absent from school or work for a half day or longer.

**Table. Polyvalent Immune Globulin Products Approved for Subcutaneous Administration**

| Product | Delivery form(s)[1] | Indication(s)[2] |
|---|---|---|
| Hizentra Immune Globulin Subcutaneous (Human), 20% Liquid | SC | PI, CIDP |
| HyQvia Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase | SC | PI |
| CUVITRU Immune Globulin Subcutaneous (Human), 20% Solution | SC | PI |
| CUTAQUIG Immune Globulin Subcutaneous (Human), 16.5% Solution | SC | PI |
| XEMBIFY Immune Globulin Subcutaneous (Human), 20% Solution | SC | PI |
| GAMMAGARD LIQUID Immune Globulin Infusion (Human), 10% | IV | PI[3] |
| | SC | |
| GAMUNEX-C Immune Globulin Injection (Human), 10% | IV | PI, CIDP[4] |
| | SC | |

1. SC: subcutaneous; IV: intravenous
2. PI: primary immunodeficiency disorders; CIDP: chronic inflammatory demyelinating polyneuropathy
3. Gammagard Liquid is additionally indicated for multifocal motor neuropathy (MMN), but only when administered intravenously
4. Gamunex-C is additionally indicated for idiopathic thrombocytopenic purpura (ITP), but only when administered intravenously

In addition, many PI patients who will require IVIG replacement therapy over their lifetimes voice an entirely different kind of concern: the loss of autonomy or the "medicalization" of their disorder that arises from the need, every few weeks, to undergo an hours-long, nurse-supervised drug infusion procedure.

As early as the 1980s and 1990s, European investigators began to experiment with switching PI patients from IVIG to subcutaneous IG delivery.[2,3,4] Most documented strong patient preference for SCIG, with many citing flexibility of treatment timing and independence from the need to take time away for visits to the infusion clinic. Insulin-dependent diabetics safely self-administer their drug by subcutaneous injection or through an insulin pump. Could chronic IG therapy similarly be self-infused by patients or caregivers at home? For both adults and children with PI, the answer turned out to be "yes."

In 2006, the first IG product specifically formulated for subcutaneous administration — CSL Behring's 16% Vivaglobin — was approved in the U.S. A few years later, Vivaglobin was replaced by Hizentra, whose 20% concentration translated into a modestly lower infused volume requirement. Over the ensuing decade, a number of other subcutaneous immune globulin (SCIG) products have followed (Table).* Using a mechanical or electrically-powered syringe pump, patients can now skip the regular infusion clinic visits and instead self-infuse their product at home biweekly, weekly or multiple times per week, working together with their home infusion provider to customize their regimen to adapt to their individual needs and preferences.

Numerous IVIG-to-SCIG crossover studies have reported that the large majority of adult and pediatric PI patients elect to make a permanent switch to SCIG.[5,6] These are some of the most commonly cited reasons:

- "I can schedule my SCIG treatments at my own convenience."
- "With SCIG, I don't experience as many unpleasant reactions."
- "I don't have to miss work (or my child doesn't have to miss school)."
- "I'm not reminded on a regular basis anymore that I have this genetic disease."

Some patients on IVIG replacement therapy report a sense of malaise over the days leading up to their next infusion as the serum IgG level approaches its deepest trough level. But because smaller doses of SCIG are infused more frequently, IgG serum levels remain more stable, and trough levels don't drop nearly as low as occurs with IVIG. Patients who experience these "rebound" symptoms prior to receiving their next monthly IVIG dose report this problem usually disappears when they switch to SCIG therapy.

But PI patients who participated in crossover studies aren't necessarily a representative sample of the entire population on IG therapy. After all, each agreed to switch their IG therapy to SCIG in the first place, and to respond multiple times to a battery of questions about their comparative treatment experience. Is SCIG

** Among these is Takeda's HyQvia, an innovative "facilitated" SCIG (fSCIG) product that incorporates pre-administered recombinant hyaluronidase to increase tissue permeability, permit very large volumes to be infused into just one or two sites, and reduce dosing to once every three or four weeks. In addition, two 10% IVIG products, Gamunex-C (Grifols) and Gammagard Liquid (Takeda), are also approved for subcutaneous administration to treat PI.*

really well accepted by most patients either previously treated with IVIG or just starting out on IG therapy?

I posed this question to Leslie Vaughan, RPh, chief operations officer at Nufactor, a Specialty Pharmacy. Vaughan brings a perspective shaped by her nearly 30 years of experience in IG home infusion therapy. "Many patients, or parents of young children, understandably have some trepidation at the beginning," she said. "They wonder, 'Am I going to be able to do this?' But we've consistently found that with education, training and support, most do fine and quickly become very comfortable with self-infusion."

**Numerous IVIG-to-SCIG crossover studies have reported that the large majority of adult and pediatric PI patients elect to make a permanent switch to SCIG.**

"Most patients or caregivers can become independent with SCIG administration within three visits," added Nufactor Clinical Nurse Educator Candy Finley, RN, IgCN. "On the first training visit, the nurse completes the infusion while explaining each step," Finley explained. "The patient or caregiver completes each step on the second visit, with nurse assistance as necessary. Usually by the third visit, the nurse can observe and confirm that the patient is performing all steps correctly."

Still, Vaughan pointed out that SCIG therapy is not for everyone: "Adults with very little body fat may not be good candidates. And for some patients with vision or dexterity issues, managing procedure set-up and needle insertion steps can be a problem."

"For any patient starting or trialing SCIG therapy," she added, "it's important to individualize treatment. One patient may prefer to self-administer relatively large volumes of SCIG in each of a number of infusion sites in order to reduce the number of infusion sessions per week or month. Another patient may be more comfortable with placing a single needle and infusing less into that single site." In other words, the flexibility of SCIG dosing strategy permits customization to accommodate each patient's preferences and limitations, while still delivering the prescribed monthly gram dose of IgG.

## The Benefits of Divided SCIG Dosing

For patients on maintenance IG therapy, IVIG administration every three weeks to four weeks results in immediate (within six hours) or delayed systemic adverse reactions in 5 percent to 15 percent of infusions, affecting as many as 20 percent to 40 percent of all patients.[7] Prehydration, premedication, slowing the infusion rate and switching to a different IVIG brand are all employed to try to avoid or at least minimize the acuity of these unpleasant systemic reactions, but the very high IgG serum concentration peak within minutes of direct IV infusion of IgG makes them all but inevitable for some patients.

By contrast, regular subcutaneous administration of IG acts in not one but two ways to moderate the peak serum level and minimize risk of nonserious systemic reactions, as well as potentially serious systemic complications, including renal insufficiency, hemolysis and, in rare instances, thrombosis and anaphylactoid reactions:[8]

- SCIG therapy delivers a similar quantity of IgG as IVIG over a specified time period, but in smaller (or as desired much smaller) divided doses; for example, common once- or twice-weekly SCIG infusion schedules respectively split a monthly IVIG dose into three or six much smaller doses.
- Following infusion, large IgG proteins slowly transit through the lymphatic system, so the serum IgG level peaks (at a far lower concentration than with IV infusion) between two days and four days later.

SCIG administration, with its slow delivery of IgG into the circulation in small divided doses, predictably results in very low systemic reaction rates. Across five published case series evaluating SCIG therapy in PI patients, reported rates of systemic adverse reactions ranged between zero and less than 1 percent.[9] In the largest of these studies, which monitored more than 33,000 SCIG infusions in 158 patients, the systemic adverse reaction rate was just 0.3 percent, including 100 mild and six moderate adverse events in 28 patients, with no anaphylactoid or other severe systemic reactions.[10]

Unsurprisingly, most patients who self-infuse SCIG don't require premedication to limit systemic side effects. But there is a trade-off: more local injection site reactions, which tend to moderate or largely resolve over time.

## SCIG Usage for Autoimmune Neuromuscular Disorders Skyrockets

Over the last several years, Nufactor's home infusion therapy program has seen well over 15 percent annual growth in numbers of PI patients self-administering SCIG. But the story of successful patient adoption of SCIG doesn't stop there. Beginning in the 1990s, numerous patient case series, as well as placebo-controlled trials, have established the efficacy and safety of IVIG for several autoimmune neuromuscular disorders, in particular chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy (MMN) and myasthenia gravis (MG).[11,12,13] Collectively, these three conditions now account for well over one-third of U.S. demand for polyclonal IG products. This is partly because many CIDP, MMN and MG patients who respond to IG require ongoing maintenance IG therapy, and partly because that maintenance dose (typically 1 g/kg every three weeks to four weeks) exceeds the average PI dose by more than two-fold.

But while newly diagnosed hypogammaglobulinemic PI patients and their physicians can elect to start right away with SCIG replacement therapy in lieu of IVIG, this is not the case for patients prescribed IG therapy for their autoimmune neuropathy. CIDP is a good example. Because only roughly one-half of patients adequately respond to IG therapy,[14] clinicians start with a trial of IVIG to determine whether it results in improvement in their disability score. If it does, and ongoing maintenance treatment is required to sustain the therapeutic benefit, SCIG may be considered as an option for patients who qualify.

Similar to the experience with PI, small divided SCIG doses and slow lymphatic transit also appears to sharply reduce both the number and severity of the systemic reactions in patients with inflammatory neuropathies on high-dose IG therapy. Two of its most common side effects — headache and nausea — were examined by Danish investigators in 59 patients with CIDP, MMN or post-polio syndrome treated with IVIG, and 27 CIDP and MMN patients treated with SCIG. In the SCIG group, headache reached a median peak value of just 1 (range 0 to 13 on a 0-to-100 visual analog scale) on day 6, versus a median peak value of 11 (range 0 to 96) in the IVIG group on day 4. A similar dichotomy was seen with reported nausea, again favoring SCIG. Just as importantly, the peak severity experienced by any patient was also far lower in the SCIG group.[15]

The same advantages that have made SCIG so popular within the PI patient community equally apply for patients prescribed maintenance IG therapy for their neurological disorder. Between 2015 and 2019, Nufactor's neurological disease patient population on maintenance SCIG therapy has climbed 70 percent annually. The company appears to be on track for similar growth in 2020.

## An Option to Consider Amid the COVID-19 Pandemic

As the COVID-19 pandemic continues, patients with risk factors for severe COVID-19 disease are, in particular, being encouraged to minimize their exposure to others in the community. PI patients obviously qualify, as do many autoimmune neurological patients on IG therapy because of age, comorbid conditions or concomitant immune suppressive medications such as rituximab, azathioprine or methotrexate.

Home SCIG therapy thus offers yet one more very real advantage over regular clinic visits for an IVIG infusion: a means to minimize risk of COVID-19 exposure risk. As some infectious disease epidemiologists are now suggesting that it may be years before the COVID-19 outbreak is completely behind us, there may be no better time for clinicians who prescribe maintenance IG to take a fresh look at which of their patients might be appropriate for SCIG therapy. ❖

### References


1. Berger M, Cupps TR and Fauci AS. High-dose immunoglobulin replacement therapy by slow subcutaneous infusion during pregnancy. *JAMA* 1982 May 28;247(20):2842-5.
2. Roord JJ, an der Meer JW, Kuis W, et al. Home treatment in patients with antibody deficiency by slow subcutaneous infusion of gammaglobulin. *Lancet* 1982 Mar 20;1(8273):689-90.
3. Abrahamsen TG, Andersen H and Bustnes A. Home therapy with subcutaneous immunoglobulin infusions in children with congenital immunodeficiencies. *Pediatrics* 1996;98:1127-31.
4. Gardulf A, Hammarström L and Smith CIE. Home treatment of hypogammaglobulinemia with subcutaneous gammaglobulin by rapid infusion. *Lancet* 1991;338:162-66.
5. Meckley LM, Wu Y, Ito D, et al. Patient experience with subcutaneous immunoglobulin 20%, Ig20Gly, for primary immunodeficiency disease; a prespecified post hoc analysis of combined data from 2 pivotal trials. *BMC Immunol* 2020 May 4;21(1):24.
6. Mallick R, Jolles S, Kanegane H, et al. Treatment satisfaction with subcutaneous immunoglobulin replacement therapy in patients with primary immunodeficiency: a pooled analysis of six Hizentra studies. *J Clin Immunol* 2018 Nov;38(8):886-97.
7. Stiehm ER. Adverse effects of human immunoglobulin therapy. *Transfus Med Rev* 2013 Jul;27(3):171-8.
8. Kobrynski L. Subcutaneous immunoglobulin therapy: a new option for patients with primary immunodeficiency diseases. *Biologics* 2012;6:277-87.
9. Berger M. Subcutaneous immunoglobulin replacement in primary immunodeficiencies. *Clin Immunol* 2004;112:1-7.
10. Gardulf A, Andersen V, Bjorkander J, et al. Subcutaneous immunoglobulin replacement in patients with primary antibody deficiencies: safety and costs. *Lancet* 1995 Feb;345:365-9.
11. Merkies ISJ, van Schaik IN, Léger J, et al. Efficacy and safety of IVIG in CIDP: combined data of the PRIMA and PATH studies. *J Peripher Nerv Syst* 2019 Mar;24(1):48-55.
12. Sala TP, Crave J, Duracinsky M, et al. Efficacy and patient satisfaction in the use of subcutaneous immunoglobulin immunotherapy for the treatment of auto-immune neuromuscular diseases. *Autoimmun Rev* 2018 Sep;17(9):873-81.
13. Adiao KJB, Espiritu AI, Roque VLA, et al. Efficacy and tolerability of subcutaneously administered immunoglobulin in myasthenia gravis: a systematic review. *J Clin Neurosci* 2020 Feb;72:316-21.
14. Hughes RAC, Donofrio P, Bril V, et al. Intravenous immune globulin (1% caprylate-chromatography purified) for the treatment of chronic inflammatory demyelinating polyradiculoneuropathy (ICE study): a randomised placebo-controlled trial. *Lancet* 2008 Feb;7:136-44.
15. Markvardsen LH, ChristiansenI, Andersen H, et al. Headache and nausea after treatment with high-dose subcutaneous versus intravenous immunoglobulin. *Basic Clin Pharmacol Toxicol* 2015 Jun 12;117:409-12.


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*Dr. Arthur Kleinman cared for his wife, Joan, for 10 years after her Alzheimer's diagnosis, which he chronicled in his book* The Soul of Care: The Moral Education of a Husband and a Doctor.

# Alzheimer's Disease: *A Patient's Perspective*

By Trudie Mitschang

**AN ACCOMPLISHED** physician and professor of psychiatry and medical anthropology at Harvard Medical School, Dr. Arthur Kleinman discovered his impressive credentials left him ill-prepared when his beloved wife, Joan, was diagnosed with a rare form of Alzheimer's at age 59. He chronicles his and Joan's journey in *The Soul of Care: The Moral Education of a Husband and a Doctor*, a memoir that details the rewards and heartbreaks of caring for a loved one in the throes of dementia. During his decade of caregiving until Joan's death in 2011, Dr. Kleinman learned no one emerges from this experience unchanged.

**BSTQ:** Why did you write about your experience caring for Joan?

**Dr. Kleinman:** I started writing when she was just starting on her 10-year course of Alzheimer's disease. She had a very particular kind of Alzheimer's that affects only 5 percent of people, and it began in her occipital lobes, which meant she became blind first. To be both blind and have dementia is very trying, particularly for the person who has it, but also for the caregiver.

**BSTQ:** After her diagnosis, did you and Joan discuss long-term care?

**Dr. Kleinman:** On that first night after the diagnosis, she said in an unemotional, very direct way: "I will not linger with this disease. You will find a way of helping me end it so I do not lose respect or dignity." And of course, I was not about to help her end her life at any point, just because I couldn't conceive of that. But right from the beginning, that was her concern, that she would lose her dignity, and she was an enormously dignified person.

**BSTQ:** Tell us about your early years of caring for Joan.

**Dr. Kleinman:** I remember feeling happy cooking dinner and doing the dishes. Joan's denial of how severe her medical condition was also made it easier for me. We pretended we could cope, that the losses were not so great that we needed to make a fundamental alteration in how we lived. But that's all it ever was: pretending.

**BSTQ:** When and how did things begin to change?

**Dr. Kleinman:** One of the few truisms about illness and caregiving is the only constant is change. In our case, we had only just settled into a manageable caregiving routine when personality and behavioral changes surfaced. There were sudden outbursts of anger, periods when she became silent and withdrawn, frustration with the limitations on what she could get done and, very occasionally, panic. These episodes first colored and then transformed how Joan related to me, making it more difficult to collaborate on her care.

**BSTQ:** You mention in your book that your primary care physicians were a source of strength and encouragement. In what way?

**Dr. Kleinman:** They were an ongoing source of support for us both, engaging deeply with the minutiae of daily living, with how home care was going and with our psychological and social well-being. Their uplifting and enduring presence provided us with something approaching a sense of security as we went through this wretched experience, knowing they would be with us until the end no matter how bad it got, no matter what was required of them.

**BSTQ:** You felt the neurology professionals you worked with failed you. How so?

**Dr. Kleinman:** Neither the young neurologist who followed the progression of Joan's disease every six months, nor any of the other neurological specialists we needed as her disease worsened, showed interest in the necessities of family caregiving. None offered advice about the value of a home health aide. No one told us how we might modify our home to make it more appropriate for Joan's disabilities. None speculated about how a physical therapist or a visiting nurse might help us. Nor did they deem it helpful to refer us to a social worker or therapist. We might have hoped at least for a team-based approach to patients and their families, where we could be referred to other health and welfare professionals in one neurological group for their advice and expertise.

**BSTQ:** How do you define the "soul of care?"

**Dr. Kleinman:** I think what lies at the soul of care is a form of love. You will do everything you can for another because they mean so much to you. It is also problematic because we all have complex relationships and we've got other things going on in our lives.

**BSTQ:** How did caregiving change you?

**Dr. Kleinman:** Those 10 years changed me almost entirely and made me realize how crucial the human aspect was. I was always good with patients and students, but I wasn't like that generally, and taking care of Joan and seeing how sad and frustrating it was, made me a different person, a better person. ❖

*Dr. Galasko is an associate director at the University of California San Diego Shiley-Marcos Alzheimer's Disease Research Center, which is working to improve current practices in AD.*

# Alzheimer's Disease: *A Physician's Perspective*

**DOUGLAS GALASKO**, MD, is a neurology specialist in San Diego, Calif, who has more than 41 years of experience in the medical field and is currently affiliated with the University of California San Diego Medical Center. He has a special interest in clinical and basic research on Alzheimer's disease (AD) and other neurodegenerative disorders. In particular, he has focused on biological markers and genes related to AD.

**BSTQ:** How do you differentiate between the first warning signs of AD and normal forgetfulness associated with aging?

**Dr. Galasko:** Our brains and cognitive abilities change as we grow older, but not in a way that limits our ability to function. A person with AD has difficulty forming and retaining new memories — for example, richly detailed memories of conversations and events. In the earliest stages, this may occur inconsistently such as only when someone tries to recall a more complex or novel event or a highly detailed conversation or set of instructions. Over time, the memory lapses become more consistent and pervasive. Often, the person with AD does not notice or appreciate the extent of his or her memory changes, and a spouse or relative will report the problems.

**BSTQ:** When should someone be tested for memory loss?

**Dr. Galasko:** Troubling and progressive memory disorders are a problem primarily among people aged 65 years or older, although sometimes they can develop at a younger age. About two years ago, Medicare recommended general physicians include screening for significant memory problems during an annual wellness evaluation for everyone 65 years and older. However, there is no quick, easy and accurate way to do so, and false-positive screening can cause unnecessary distress and concern. A more focused approach is for someone with persistent memory lapses or cognitive changes to be screened and undergo medical evaluation if appropriate.

**BSTQ:** Is dementia preventable?

**Dr. Galasko:** We don't know whether dementia would be inevitable if we all lived to, say, 120 years old or longer. Although the risk rises exponentially with age, and studies have shown about 50 percent or more of people in their 90s have significant cognitive impairment, there are well-documented instances of people with excellent cognitive function at age 100 years or even older.

Studies of the brains of people who underwent detailed testing during life and died in their late 80s or older show that dementia is often related to mixed pathology. AD pathology and vascular changes may interact. Also, based on pathology studies and on recent advances in brain imaging and testing that can identify AD changes in the brain, we know AD and other brain pathology builds up and precedes the onset of memory loss and dementia by a decade or longer. These findings raise hopes for prevention.

**BSTQ:** What approaches are used to prevent AD?

**Dr. Galasko:** An important approach is to address vascular risk factors. Changes in lifestyle, including eating a heart-healthy diet, maintaining regular physical activity and appropriately using medications to control blood pressure and diabetes, may all be helpful. Although the benefits of vascular health interventions may be the greatest when started as early as 50 years old, addressing vascular risk is appropriate at any age. Another approach specific for AD prevention is to intervene against early AD brain pathology as early as possible. Many novel treatments are being developed and tested with the goal of decreasing the extent of AD pathology in the brain. In the past, treatments have been studied in people with symptomatic AD. However, very early treatment may have the greatest benefit — before enough structural damage to the brain has occurred to cause impairment of memory and other cognitive processes.

**BSTQ:** Are there advances in screening and evaluation options?

**Dr. Galasko:** The University of California San Diego Shiley-Marcos Alzheimer's Disease Research Center is playing a prominent role in two efforts to improve current practices. First, as part of the San Diego County Alzheimer's Project, we have spearheaded the development of guidelines and tools to help doctors or other care providers to screen people with memory complaints. Second, with recently approved funding from the state of California, a group of AD centers at academic medical centers across California is developing guidelines and materials to support screening and evaluation of memory problems, which will include tools and information to help physicians make early and accurate diagnoses. And, we are exploring how tests can be used through apps or computerized testing. In terms of what's in the pipeline, we're also learning it is now possible to detect hallmarks of AD in the blood. This is being explored in promising research studies but is not yet available as a clinical test. ❖

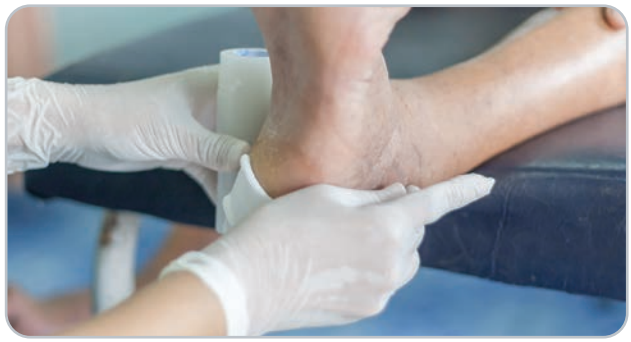
**TRUDIE MITSCHANG** is a contributing writer for *BioSupply Trends Quarterly* magazine.

# High-Dose IVIG Effective in Painful Diabetic Polyneuropathy Resistant to Conventional Treatments

Italian investigators at eight participating sites conducted a randomized, double-blind, placebo-controlled trial to assess the safety and efficacy of intravenous immune globulin (IVIG) in treatment-resistant painful diabetic polyneuropathy (DPN). Eight participating sites enrolled 26 diabetic patients with DPN who reported baseline pain severity greater than 60 units (mm) on a visual analog scale (VAS) at enrollment, and were resistant to antidepressants and antiepileptic drugs. Twenty-three of these patients were randomized (11 in the IVIG arm and 12 in the placebo arm), 21 of whom had a diagnosis of type II diabetes.

IVIG at a dose of 0.4 g/kg per day was administered for five consecutive days. Pain intensity reported using a VAS and quality-of-life assessments were performed at the baseline visit, at the start of therapy one week later, at the end of therapy five days thereafter, and at four- and eight-week follow-up.

The study achieved its prespecified primary end point of greater than or equal to 50 percent pain reduction at four weeks after IVIG administration, achieved in seven of 11 patients (63.6 percent) in the IVIG group versus zero of 12 in the placebo group (P = 0.0013). Only two adverse events were reported during the study: one patient

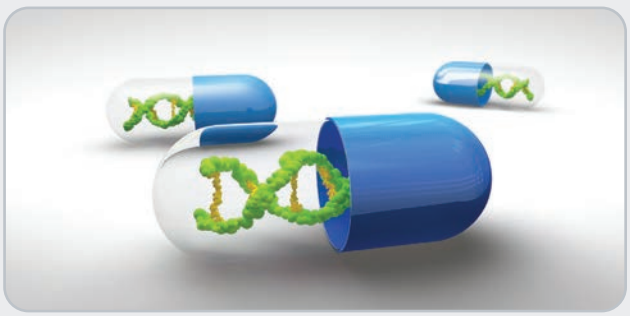


in the treatment arm with a mild dermatitis psoriasiform, and one patient in the placebo arm with a mild influenza.

The investigators concluded treatment with high-dose IVIG appears to be efficacious and safe for patients with DPN resistant to standard therapies.

*Stefano J, Fazio R, Cocito D, et al. High-dose intravenous immunoglobulin is effective in painful diabetic polyneuropathy resistant to conventional treatments. Results of a double-blind, randomized, placebo-controlled, multicenter trial.* Pain Med *2020 Mar 1;21(3):576-85.*

# Stable and Durable Factor VIII Expression in Subjects Dosed with Investigational Hemophilia A Gene Therapy

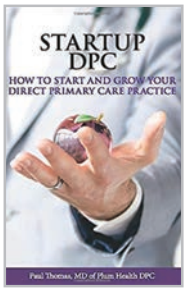


More than two years after receiving Spark Therapeutics' investigational adeno-associated virus (AAV)-mediated gene therapy (SPK-8011), five adult subjects with hemophilia A exhibited stable factor VIII (FVIII) expression, with no evidence of FVIII inhibitors or a cellular immune response.

Two subjects who received the lower-dose of 5 x $10^{11}$ g/kg cohort maintained steady-state FVIII:C levels of 6.9 percent to 8.4 percent, while three subjects in the higher-dose 1 x $10^{12}$ vg/kg cohort had FVIII:C levels ranging between 5.2 percent and 19.8 percent. Two of the three subjects in the 1 x $10^{12}$ vg/kg cohort were treated with steroids for about seven weeks in response to declining FVIII levels in the absence of alanine aminotransferase (ALT) elevation or positive IFN-g ELISPOTs to capsid-derived peptides. Once steady-state FVIII expression was achieved by eight to 12 weeks, and no meaningful change in FVIII:C was seen in any of the five subjects.

Over the 106- to 142-week observation period, there was an overall 95 percent reduction in the annualized exogenous FVIII infusion rate, and a 91 percent reduction in the annualized bleeding rate (ABR). Post-gene therapy administration ABRs for the five subjects were 0.4, 0.0, 0.4, 3.6 and 0.5. "Our data represent the longest stable expression of FVIII following gene transfer and support the ability of AAV-mediated hepatocyte-directed gene transfer to achieve durable FVIII expression for the potential treatment of hemophilia A," the investigators concluded.

*George L, Eyster E, Ragni M, et al. Phase I/II Trial of SPK-8011: Stable and Durable FVIII Expression for >2 Years with Significant ABR Improvements in Initial Dose Cohorts Following AAV-Mediated FVIII Gene Transfer for Hemophilia A [abstract].* Res Pract Thromb Haemost *2020; 4 (Suppl 1).*




### Startup DPC: How To Start And Grow Your Direct Primary Care Practice

*Author: Paul Thomas, MD*

Dr. Paul Thomas, a board-certified family medicine doctor who launched his own direct primary care practice (DPC) straight out of residency with more than $100,000 in student loan debt and whose practice now has more than 700 patients, shares his knowledge about starting a successful DPC practice. Topics included in the book are how to have the right mindset to be successful in the DPC journey; what a typical day looks like for a DPC doctor; how to finance a DPC startup; how to raise money for a DPC practice; how to overcome a lack of business training in medical school and residency; how to construct the perfect timeline for starting a DPC practice; how to write a business plan for a DPC clinic; how to convert an existing fee-for-service clinic to a DPC practice while remaining profitable; what's the difference between DPC and concierge medicine; how to hire a second doctor for a DPC practice; how to find a profitable location for a DPC practice; how to negotiate a lease deal for the medical practice; how to attract patients to a DPC practice; how to brand the practice to stand out in the marketplace; how to build a personal brand to grow a DPC practice; and more.

**www.amazon.com/Startup-DPC-Direct-Primary-Practice/dp/173240383X**

### How Coronavirus Pandemic Will Impact Recombinant Plasma Protein Therapeutics Market Global Analysis and 2019-2024 Forecast Report

*Author: Market Research Reports Search Engine*

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This report, which provides an understanding of the various factors likely to influence the prospects of the recombinant plasma protein therapeutics market in the forecast period, takes into account the historical and current market trends to predict the course of the market in the upcoming years. Further, the growth opportunities, drivers and major challenges faced by market players are discussed in detail. Included is a regional outlook, competitive outlook and product adoption analysis.

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### STAT's Guide to Interpreting Clinical Trial Results

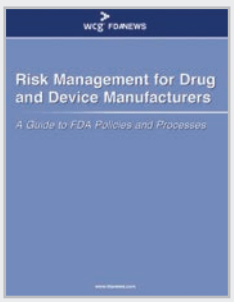

*Author: STAT Reports*

STAT senior writers Sharon Begley and Adam Feuerstein provide basic tools to help researchers read clinical trial results with an appropriately skeptical (or at least critical) eye. They also examine specific examples of spin, noting the sections of papers reporting the results of clinical trials where they appear and why that matters. Highlights include a definition of spin in clinical trials supported by real-life examples; four key questions to ask when evaluating clinical trial results; an overview of additional tools needed to read results more critically; and analysis of the red flags to look for in clinical trial design, execution and reporting of results.

**reports.statnews.com/products/stat-guide-interpreting-clinical-trial-results?variant=32071781318759**

### Risk Management for Drug and Device Manufacturers: A Guide to FDA Policies and Processes

*Author: U.S. Food and Drug Administration*




This guide includes more than 400 pages of FDA requirements and 20 specific documents that include guidances, statements and policies, including assessing requirements for risk evaluation and mitigation strategies (REMS); the format and content of a REMS submission; using a drug master file for shared-system REMS submissions; benefit-risk counseling of patients using a drug with a REMS; determining how to develop a risk minimization action plan; identifying how to conduct a health hazard evaluation; evaluating premarketing risk; meeting FDA-adopted international standards; ISO 10993 on biological evaluation of medical devices; ICH Q9 on quality risk management; and ICH Q10 on pharmaceutical quality systems.

**www.fdanews.com/products/59607-risk-management-for-drug-and-device-manufacturers-a-guide-to-fda-policies-and-processes**

# Medicare Immune Globulin Reimbursement Rates

Rates are effective Oct. 1, 2020, through Dec. 31, 2020

| | Product | Manufacturer | J Codes | ASP + 6% (before sequestration) | ASP + 4.3%* (after sequestration) |
|---|---|---|---|---|---|
| IVIG | FLEBOGAMMA | Grifols | J1572 | $80.77 | $79.47 |
| | GAMMAGARD SD | Takeda | J1566 | $136.61 | $134.42 |
| | GAMMAPLEX | BPL | J1557 | $107.32 | $105.60 |
| | OCTAGAM | Octapharma | J1568 | $82.46 | $81.14 |
| | PANZYGA | Pfizer | 90283/J1599 | ** | ** |
| | PRIVIGEN | CSL Behring | J1459 | $83.01 | $81.67 |
| IVIG/SCIG | GAMMAGARD LIQUID | Takeda | J1569 | $86.40 | $85.02 |
| | GAMMAKED | Kedrion | J1561 | $84.37 | $83.02 |
| | GAMUNEX-C | Grifols | J1561 | $84.37 | $83.02 |
| SCIG | CUTAQUIG | Octapharma/Pfizer | 90284/J3590 | ** | ** |
| | CUVITRU | Takeda | J1555 | $140.22 | $137.97 |
| | HIZENTRA | CSL Behring | J1559 | $108.55 | $106.81 |
| | HYQVIA | Takeda | J1575 | $144.86 | $142.54 |
| | XEMBIFY | Grifols | J1558 | $142.23 | $139.95 |

* Reflects 2% sequestration reduction applied to 80% Medicare payment portion as required under the Budget Control Act of 2011.

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

# Immune Globulin Reference Table

| | Product | Manufacturer | Indication | Size |
|---|---|---|---|---|
| IVIG | FLEBOGAMMA 5% DIF Liquid | Grifols | PI | 2.5 g, 5 g |
| | FLEBOGAMMA 10% DIF Liquid | Grifols | PI, ITP | 5 g, 10 g, 20 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 |
| | OCTAGAM Liquid, 10% | Octapharma | ITP | 2 g, 5 g, 10 g, 20 g, 30 g |
| | PANZYGA Liquid, 10% | Pfizer | PI, ITP | 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 |
| IVIG/SCIG | GAMMAGARD Liquid, 10% | Takeda | IVIG: PI, MMN<br>SCIG: PI | 1 g, 2.5 g, 5 g, 10 g, 20 g, 30 g |
| | GAMMAKED Liquid, 10% | Kedrion | IVIG: PI, ITP, CIDP<br>SCIG: PI | 5 g, 10 g, 20 g |
| | GAMUNEX-C Liquid, 10% | Grifols | IVIG: PI, ITP, CIDP<br>SCIG: PI | 1 g, 2.5 g, 5 g, 10 g, 20 g, 40 g |
| SCIG | CUTAQUIG Liquid, 16.5% | Octapharma/Pfizer | PI | 1 g, 2 g, 4 g, 8 g |
| | CUVITRU Liquid, 20% | Takeda | PI | 1 g, 2 g, 4 g, 8 g |
| | HIZENTRA Liquid, 20% | CSL Behring | PI, CIDP | 1 g, 2 g, 4 g, 10 g<br>1 g PFS, 2 g PFS, 4 g PFS |
| | HYQVIA Liquid, 10% | Takeda | PI | 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
**ITP** Immune thrombocytopenic purpura
**KD** Kawasaki disease
**MMN** Multifocal motor neuropathy
**PI** Primary immune deficiency disease
**PFS** Prefilled syringes

# 2020-2021 Influenza Vaccine

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

| Product | Manufacturer | Presentation | Age Group | Code |
|---|---|---|---|---|
| **Trivalent** | | | | |
| FLUAD (aIIV3) | SEQIRUS | 0.5 mL PFS 10-BX | 65 years and older | 90653 |
| **Quadrivalent** | | | | |
| AFLURIA (IIV4) | SEQIRUS | 0.5 mL PFS 10-BX | 3 years and older | 90686 |
| AFLURIA (IIV4) | SEQIRUS | 5 mL MDV | 6 months and older | 90688 |
| AFLURIA PEDIATRIC (IIV4) | SEQIRUS | 0.25 mL PFS 10-BX | 6-35 months | 90685 |
| FLUAD (IIV4) | SEQIRUS | 0.5 mL PFS 10-BX | 65 years and older | 90694 |
| FLUARIX (IIV4) | GSK | 0.5 mL PFS 10-BX | 6 months and older | 90686 |
| FLUBLOK (ccIIV4) | SANOFI PASTEUR | 0.5 mL PFS 10-BX | 18 years and older | 90682 |
| FLUCELVAX (ccIIV4) | SEQIRUS | 0.5 mL PFS 10-BX | 4 years and older | 90674 |
| FLUCELVAX (ccIIV4) | SEQIRUS | 5 mL MDV | 4 years and older | 90756* |
| FLULAVAL (IIV4) | GSK | 0.5 mL PFS 10-BX | 6 months and older | 90686 |
| FLUMIST (LAIV4) | ASTRAZENECA | 0.2 mL nasal spray 10-BX | 2-49 years | 90672 |
| FLUZONE (IIV4) | SANOFI PASTEUR | 0.5 mL PFS 10-BX | 6 months and older | 90686 |
| FLUZONE (IIV4) | SANOFI PASTEUR | 0.5 mL SDV 10-BX | 6 months and older | 90686 |
| FLUZONE (IIV4) | SANOFI PASTEUR | 5 mL MDV | 6 months and older | 90688 |
| FLUZONE HIGH-DOSE (IIV4) | SANOFI PASTEUR | 0.7 mL PFS 10-BX | 65 years and older | 90662 |

**aIIV3** MF59-adjuvanted trivalent inactivated injectable
**ccIIV4** Cell culture-based quadrivalent inactivated injectable
**IIV4** Egg-based quadrivalent inactivated injectable
**LAIV4** Egg-based live attenuated quadrivalent nasal spray

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

FFF enterprises

# VERIFIED

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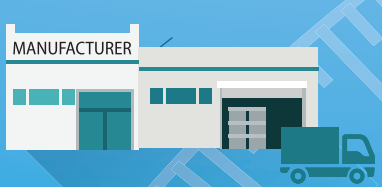


PRODUCT SAFETY

# The VERIFIED

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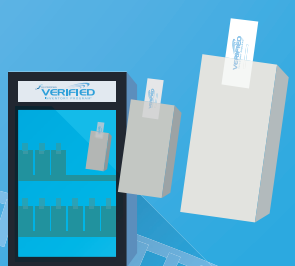


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