

NOVEMBER 2021

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

Endocrine news

INTERNATIONAL

The Insulin Century

Endocrine News salutes this lifesaving drug's first century and the work still to be done.

CELEBRATING
100 YEARS OF
INSULIN

- **VITAL CONNECTION:** How the evolution of the patient-provider relationship over the decades has coincided with technological and treatment advances.
- **INSULIN RESISTANCE:** Research from Endocrine Society journals addresses the diagnosis, treatment, and comorbidities of insulin resistance.
- **INSULIN INNOVATIONS:** From smart insulin to insulin that doesn't need refrigeration and more, advances are being developed at a breakneck pace.
- **SPECIAL DELIVERY:** Whether treated at home or in a clinical setting, potential new models of diabetes care could help ease the burden of both patients and providers.

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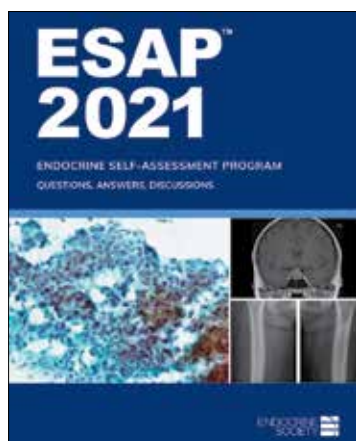
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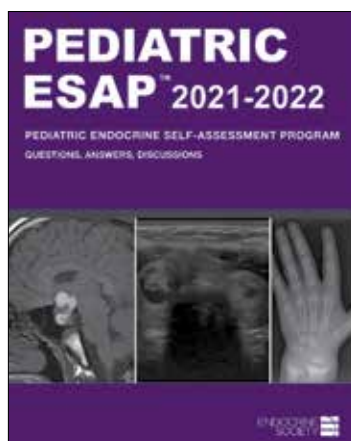
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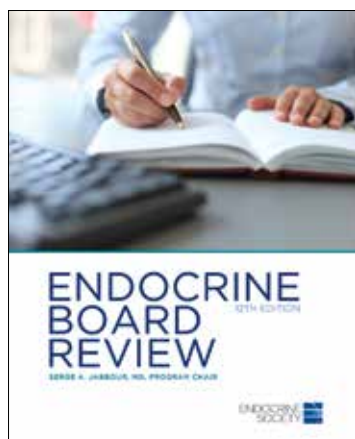
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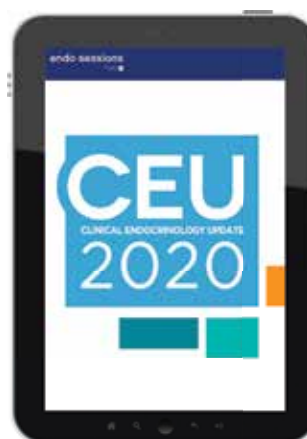
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Smart insulin. Once-a-week insulin. Thermostable insulin. Researchers around the world are working on a variety of insulin innovations, some of which could be available sooner than you think. **BY ERIC SEABORG**

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PATIENCE GOT US THIS FAR ... NOW WE NEED PATIENTS



PATHFNDR-1, our Phase 3 trial of paltusotine for the treatment of acromegaly, is officially open, and we're actively recruiting patients to participate. PATHFNDR-1 is a double-blind, placebo-controlled, nine-month clinical trial to evaluate the safety and efficacy of paltusotine in acromegaly patients. Once-daily, oral paltusotine could prove to be a viable treatment option for patients seeking an alternative to the monthly injections or strict dosing regimens that current options require.



Louis, diagnosed with acromegaly in 2020



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Insulin at 100: How Far We've Come and the Work Still to Be Done

One of the seminal events in the development of modern medicine — and the field of endocrinology — took place 100 years ago. That event, of course, was the discovery of insulin and how it transformed diabetes from a fatal disease to a chronic condition.

As I shared with you in August, we are spending 2021 commemorating this important centennial. Our video interviews with diabetes experts and webinars delving into important issues around insulin and diabetes already have reached more than 900 viewers.

I hope you will join me for our capstone educational event on November 9 — Insulin 2121: The Next 100 Years of Discoveries. This free, half-day event will feature leading researchers and clinicians discussing technologies and therapies that could transform diabetes care over the next 100 years. I am honored to be delivering the introduction for this event. I am particularly interested in this milestone, as I've dedicated the past 35-plus years of my research and clinical career to the management of diabetes, with particular emphasis on the prevention and management of cardiovascular complications in individuals with diabetes.

As we mark Diabetes Awareness Month, it's important to reflect on just how far we've come since 1921, when the first pancreas extracts from duct-ligated dogs were injected into diabetic humans, reversing signs and symptoms of the dreaded disease.

Bloodletting and Tonics

Well into the first decades of the 20th century, doctors and caregivers often would treat their patients with unproven bloodlettings, tonics, potions, and home-remedy concoctions. Hygienic standards were spotty, and penicillin wasn't discovered until 1928.

As a result, many people died of diseases that are easily treated today. Diabetes was one of them.

More than 3,000 years ago, ancient Egyptians described an ailment similar to type 1 diabetes, with excessive urination, thirst, and weight loss.

Fast forward a few millennia. The role of the pancreas in regulating blood sugar levels was discovered in 1889 by German scientists Joseph von Mering and Oskar Minkowski, who found that removing the pancreas from dogs led them to develop diabetes and die shortly afterward.

Several decades later, in 1921, a team at the University of Toronto worked on developing pancreatic extracts from duct-ligated dogs that were then injected into diabetic dogs. The preparations lowered blood glucose in the pancreatectomized dogs but were deemed too toxic for treating humans, according to a history of insulin described in *Endocrine Reviews*.

By January 1922, the Toronto group had decided they could safely begin testing their pancreatic extracts on human subjects.

The first subject was Leonard Thompson, a 13-year-old boy on the brink of death from diabetes in Toronto General Hospital. The results were spectacular. The boy's blood and urinary sugars came down, and his diabetic symptoms were alleviated.

This was the beginning of a new era.

Looking to the Future

Here we are 100 years later. Members of the Endocrine Society are at the forefront of establishing new insulin paradigms, both in basic science and clinical practice. Our members seek to develop new and improved insulin therapies and delivery systems. We advocate for access to affordable insulin products. And we establish better diabetes management practices and guidelines.

I invite you to explore our rich body of resources and programs around insulin and diabetes during Diabetes Awareness Month. These include:

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► Our dedicated web page “100 Years of Insulin.”

Access many curated resources including multipart video essays from Michael B. Davidson, DO, discussing ways to support patients with diabetes and insulin self-management, and Daniel Drucker, MD, discussing the past, present, and future of insulin. (www.endocrine.org/membership/100-years-of-insulin)

► Our Nov. 9 educational event, **Insulin 2121: The Next 100 Years of Discoveries.**


Topics include future treatments around islet cell transplantation; the potential of next-generation glucagon for severe hypoglycemia; and breakthroughs in the artificial pancreas.

► Our diabetes care advocacy information.

Ensuring proper diabetes care and access to affordable insulin are key priorities at the Society. To this end, we recently launched an online advocacy campaign for members to contact lawmakers urging actions to make insulin more affordable.

► The Hormone Health Network (HHN) is raising patient awareness about glucagon and emergency preparedness through its KNOW HYPO campaign.

HHN also will highlight diabetes management, complications, and new therapies and treatment from diabetes experts throughout November.

I look forward to celebrating this important endocrinology milestone with you at our Insulin 2121 event and in our publications and social media channels. 

Carol H. Wysham, MD
President, Endocrine Society

ELECTION LAUNCHED

The election for our president-elect candidates launched in early November. We have two outstanding candidates on the ballot, and I encourage all our voting members to participate in this very important activity. To facilitate the voting process, a link to the electronic ballot is available on the Society's website. Please remember to cast your vote, and remind your colleagues as well. This is your Society, and *your* participation in the election is important! The polls will close on Dec. 15.



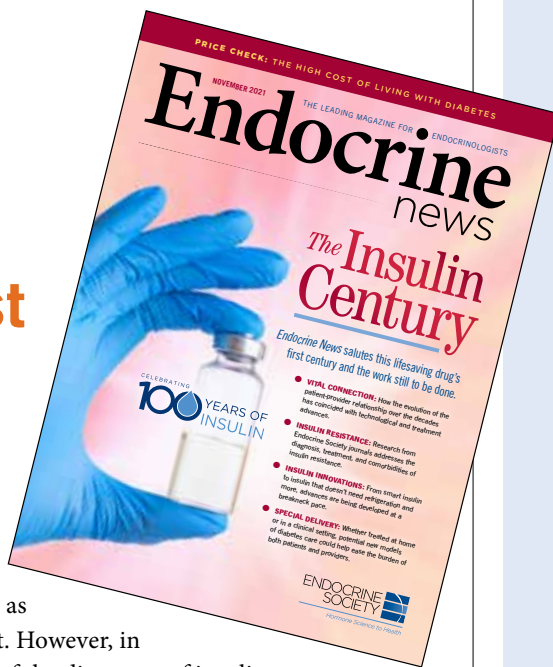
FROM THE **EDITOR**

Endocrine News Celebrates Insulin's First Century

Each November during Diabetes Awareness Month, we typically devote the issue to various diabetes research studies as well as new breakthroughs in treatment. However, in honor of the 100th anniversary of the discovery of insulin, we have skewed our coverage somewhat in this issue of *Endocrine News* to marvel at this Canadian import that has saved lives around the world for the past century.

Instead of a retrospective of insulin's illustrious history — which can be found in great abundance elsewhere and is easily accessed — we've decided to set our sights on what the future of insulin holds for people living with diabetes as well as the providers caring for them. There's also a great deal of enthusiasm for new research and technology surrounding this lifesaving elixir. Just as the doses of insulin that were first administered in the 1920s are different from what is being given today, the insulin of tomorrow will be very different from how it is currently formulated and administered.

Throughout insulin's first century of existence, one condition that has continued to confound researchers, clinicians, and even patients alike is insulin resistance. On page 22, Kelly Horvath addresses this phenomenon with new research from Endocrine Society journals in her article, "Insulin Resistance: New Insights into Development, Diagnosis, and Treatment." Specifically, the new research Horvath discusses concerns the relationship between smoking behavior and insulin resistance with both traditional and e-cigarettes. Horvath also looks at research that discusses a treatment approach for pediatric patients in low- or middle-income countries of diagnosing severe insulin resistance guided by the clinical picture and widely available laboratory tests so patients can avoid severe, disabling consequences. Horvath further looks at research on intestinal flora,



NOVEMBER 2021

Endocrine news

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

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Prepress & Printing: **The Sheridan Group**
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The mission of the Endocrine Society is to advance excellence in endocrinology and promote its essential and integrative role in scientific discovery, medical practice, and human health.

Endocrine News® is published 12 times a year by the Endocrine Society, 2055 L Street, NW, Suite 600, Washington, DC 20036
Phone 202-971-3636 • Fax 202-736-9708
www.endocrine.org

Print ISSN 2157-2089 Online ISSN 2157-2097
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which is a key factor in insulin resistance and contributes to developing polycystic ovary syndrome.

Senior editor Derek Bagley discusses one of the most controversial aspects today concerning insulin: the high price tag in the U.S., in “The Cost of Living (with Diabetes),” on page 16. While healthcare experts, industry leaders, and

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Instead of a retrospective of insulin's illustrious history — which can be found in great abundance elsewhere and is easily accessed — we've decided to set our sights on what the future of insulin holds for people living with diabetes as well as the providers caring for them.

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legislators have taken some steps to address the problem, Bagley reveals that researchers have been studying trends in insulin use that could provide some insights into what drives the cost. However, the experts who spoke to *Endocrine News* agree that it's going to take action on everyone's part before real progress is made. “I think we want to, as individuals, as well as the [Endocrine] Society, advocate to our representatives in Congress and the administration, how important this is for people with diabetes to have effective and affordable insulin,” says Endocrine Society Past-President Robert Vigersky, MD, chief medical officer, Medtronic. “I think the Society and its members need to continue to advocate and pound that message home, and get the individual physicians, the endocrinologists, as well as their patients up in front of their representatives and make the case.”


As part of its “100 Years of Insulin,” the Endocrine Society has been sponsoring a litany of online events and videos

highlighting the drug's history and future, as well as its evolution. One of those webinars, “Building a Strong Patient-Provider Relationship” highlighted the importance of trust between the patient and provider and how that relationship has evolved in the past several decades. On page 28, Horvath delves into the details of this roundtable discussion in “Evolution of Diabetes Management: The Patient-Provider Relationship, Accessing Resources, and Surmounting Obstacles” that weaves a remarkable tale of how patient self-care has changed in the past 50-plus years, as well as the new technology and services available to people living with diabetes.

On page 36, Eric Seaborg heads into a pretty exciting future about the development of new types of insulins in “Coming Attractions: Insulin's Intriguing Future.” From “smart insulin,” once-a-week insulin, and insulin that would no longer need to be refrigerated, researchers around the world are working on a variety of insulin innovations. Some of these new formulations could be available sooner than you might expect, creating yet another step forward for this lifesaving therapy.

The future of delivering that therapy is discussed in Bagley's Practice Resources article, “Special Delivery: A Look at New Modes of Diabetes Care,” on page 44. Here, Bagley discusses how potential new models of diabetes care could help ease the burden of both the patients and the providers, whether treatment takes place at home or in a clinical setting.

By the way, the “Building a Strong Patient-Provider Relationship” webinar and many other videos celebrating the 100 years of insulin are available online at: **www.endocrine.org/membership/100-years-of-insulin** and are highly recommended!

If you would like to share your own stories, please feel free to share your experiences with us. Don't hesitate to contact me at: **mnewman@endocrine.org**. 

— **Mark A. Newman**, Editor, *Endocrine News*



Melmed Named Inaugural Winner of Transatlantic Alliance Award

The Endocrine Society and the European Society of Endocrinology (ESE) have awarded their inaugural joint honor — the Transatlantic Alliance Award — to Shlomo Melmed, MB, ChB, FRCP, MACP.

Melmed is executive vice president of academic affairs, dean of the medical faculty, and distinguished professor of medicine at Cedars-Sinai, in California. He is an international endocrine leader and receives this award for his pioneering research in pituitary medicine and endocrine tumors.

The Transatlantic Alliance Award, which was launched earlier this year, recognizes an international leader who has made significant advancements in endocrine research on both sides of the Atlantic — in Europe and the U.S.

Melmed exemplifies transatlantic endocrine leadership, as evidenced by his high-quality transnational educational initiatives and professional society leadership. Coupled with his exemplary scholarly contributions in the highest-quality basic and clinical journals, Melmed's achievements reflect a dual combination of outstanding basic and clinical creativity, underscoring his standing as an international research and clinical leader of pituitary medicine. He has made an outstanding and ongoing contribution to the endocrine community's fundamental and clinical understanding of pituitary tumor biology as it is applied to the advancement of transatlantic endocrinology.

Melmed will present his lecture at ESE's 24th European Congress of Endocrinology (ECE) 2022, which will take place May 21 – 24, 2022, in Milan, Italy. Melmed also will speak at the Endocrine Society's annual meeting, **ENDO 2022**, which will be held June 11 – 14, 2022, in Atlanta, Ga. Presentation of the award will alternate between **ENDO** and ECE in future years.

"Dr. Melmed's distinguished career has set a high bar for endocrine researchers on both sides of the Atlantic," says Endocrine Society President Carol Wysham, MD, clinical professor of medicine at the University of Washington. "We and our partners at ESE are proud to be recognizing a worldwide leader who is advancing our field."

ESE President Professor Martin Reincke, says, "The caliber of endocrinologists nominated for the inaugural award was extremely competitive and the contribution that all have made to our discipline has been extraordinary. I congratulate Dr. Melmed as being a highly worthy winner and am very much looking forward to his lecture at our Congress next May."

Nominations for the 2023 Transatlantic Alliance Award will open later this year.

Zilbermint Named to AMA's Prediabetes Measure Development and Testing Project Panel



Mikhail “Misha” Zilbermint, MD, was recently appointed to the Technical Expert Panel (TEP) for the American Medical Association Prediabetes Measure Development and Testing Project.

Zilbermint will represent the Endocrine Society on the TEP, which has been tasked with updating a set of three electronic Clinical Quality Measures (eCQMs) for patients with prediabetes based on the recent U.S. Preventive Services Task Force recommendations. The TEP, which will be made up of 15 members of various clinical experts and patient representatives, will provide input on the technical specifications of the measures and testing results.

“Prediabetes is common among Americans (every third adult has prediabetes). But it is a very big deal as people with prediabetes are at higher risk of developing type 2 diabetes, stroke, and even heart disease,” Zilbermint says. “Importantly, these are some of the top reasons why patients are being hospitalized. Healthcare systems do not invest enough in managing the prediabetes pandemic, and people themselves are ‘not invested.’ I am hoping to help our communities tackle this challenge.”

Zilbermint, an endocrinologist specializing in inpatient diabetes and prediabetes management, is an associate professor of clinical medicine and chief of endocrinology at Suburban Hospital, in Bethesda, Md. He currently serves as the medical co-director of the Baltimore Metropolitan Diabetes Regional Partnership grant focusing on the deployment of diabetes self-management training programs.

Zilbermint also volunteers at an adult community center where he teaches diabetes prevention. A member of the Endocrine Society since 2010, he is a member of the Quality Improvement subcommittee (QISC), as well as on the *Endocrine News* Editorial Advisory Board.

Banting House: Birthplace of a Breakthrough

Photo: Courtesy of Banting House National Historic Site/Diabetes Canada



The Flame of Hope at the Banting House is an “eternal flame” that will burn until there is a cure for diabetes.

At two o'clock in the morning on October 31, 1920, Sir Frederick Banting awoke with the idea that led to the discovery of insulin. The idea changed the world, saving the lives of millions of patients with diabetes across the globe and continues to do so. For years, most people referred to the house as “The Birthplace of Insulin.”

In 1984, the house at 442 Adelaide Street North in London, Ontario, Canada, where Banting was living when he had his fateful idea, became a museum dedicated to Banting's work

“The historical significance of Banting's discovery to people with diabetes and to Canadians has yet to be eclipsed by a cure.”

— CHRISTOPHER RUTTY, PHD, A PROFESSIONAL MEDICAL AND PUBLIC HEALTH HISTORIAN AND ADJUNCT PROFESSOR AT THE DALLA LANA SCHOOL OF PUBLIC HEALTH AT THE UNIVERSITY OF TORONTO

and life. The Banting House National Historic Site of Canada now stands as a source of pride for many Canadians and for those who live with diabetes or take care of someone who does.

“The historical significance of Banting's discovery to people with diabetes and to Canadians has yet to be eclipsed by a cure,” says Christopher Ruddy, PhD, a professional medical and public health historian and adjunct professor at the Dalla Lana School of Public Health at the University of Toronto.

Among its many artifacts and materials, the Banting House features a statue of Banting writing his idea down, as well as the Flame of Hope, which was kindled by Queen Elizabeth, The Queen Mother, in 1989. The gas-powered flame will burn until a cure for diabetes is found. Until then, it burns to remind us that insulin only manages diabetes.

For more information: <https://bantinghousenhs.ca/>



BY DEREK BAGLEY
Senior Editor

Omitting Race from Kidney Function Equations Leads to More Accurate Results

At the end of September, a paper appeared in the *New England Journal of Medicine* that showed omitting race from equations for estimated glomerular filtration rate (eGFR) leads to more accurate results when determining kidney function.

The researchers, led by Lesley Inker, MD, MS, director of the Kidney Function and Evaluation Center at Tufts Medical Center, in Boston, Mass., point out that the current equations that use creatinine or cystatin C incorporate age, sex, and race to estimate kidney function, but the authors write that race in these equations is a social construct and not a biological one. “Inclusion of race in GFR estimating equations, along with other algorithms in medicine, is facing increasing scrutiny because race is a social and not a biologic construct; its inclusion ignores diversity within and among racial groups and may contribute to systemic racism in medicine,” the authors write.

For this study, the researchers developed three new eGFR equations without using race from two development data sets — 10 studies for serum creatinine and 13 studies for both serum creatinine and cystatin C — as well as a validation set of 12 studies. About 14% of participants in the validation set were Black, and the researchers found that the current creatinine equation that incorporates race overestimated GFR in Black patients. “When the adjustment for Black race was omitted from the current eGFR equation, measured GFR in Blacks was underestimated,” the authors write.

The researchers’ new equation using age and sex but not race underestimated GFR in Black participants and overestimated GFR in non-Black participants. New creatinine–cystatin C equations without race were more accurate than new creatinine equations, with smaller differences between race groups, the authors write. “New eGFR equations that incorporate creatinine and cystatin C but omit race are more accurate and led to smaller differences between Black participants

and non-Black participants than new equations without race with either creatinine or cystatin C alone,” they conclude.

The same day the *NEJM* paper was published, the National Kidney Foundation (NKF) and the American Society of Nephrology (ASN) Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Diseases released its final report, which outlines a new race-free approach to diagnose kidney disease. In the report, the NKF-ASN Task Force recommends the adoption of the new eGFR 2021 CKD EPI creatinine equation that estimates kidney function without a race variable. The task force also recommended increased use of cystatin C combined with serum (blood) creatinine, as a confirmatory assessment of GFR or kidney function.

“I am honored to have been a part of the NKF-ASN Task Force. By careful review of the evidence and perspectives shared with us, and listening and learning from each other, we were able to arrive at a recommendation for estimating GFR that does not include race that is based on rigorous science, patient centered, and can be immediately implemented across all clinical laboratories,” Inker says. “We hope that our emphasis on an overall approach to assess kidney function, using initial tests followed by more accurate tests as the clinical situation requires, will increase awareness of the importance of careful consideration of GFR in all patients.”

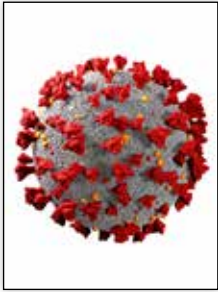
Neil Powe, MD, MPH, MBA, FASN, chief of medicine at the Priscilla Chan and Mark Zuckerberg San Francisco General Hospital and the Constance B. Wofsy Distinguished Professor, vice chair of medicine at the University of California, San Francisco and co-chair of the joint NKF-ASN task force adds, “We hope strong efforts will develop new, more informative, GFR markers and unite all of us in a focus on interventions to eliminate health disparities, thereby improving the quality of care for everyone in the U.S.”



“

Inclusion of race in GFR estimating equations, along with other algorithms in medicine, is facing increasing scrutiny because race is a social and not a biologic construct; its inclusion ignores diversity within and among racial groups and may contribute to systemic racism in medicine.

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The findings also suggest that a class of diabetes drugs called thiazolidinediones, which boost adiponectin production, may be useful in treating COVID-19 when it includes hyperglycemia.

”

COVID-19 May Trigger Hyperglycemia and Worsen Disease by Harming Fat Cells

COVERD-19 may bring high risks of severe disease and death in many patients by disrupting key metabolic signals and thereby triggering hyperglycemia, according to a new study in *Cell Metabolism*.

Researchers led by James C. Lo, MD, PhD, an associate professor of medicine in the Weill Center for Metabolic Health and the Cardiovascular Research Institute at Weill Cornell Medicine and a cardiologist at NewYork-Presbyterian/Weill Cornell Medical Center, found that hyperglycemia is common in hospitalized COVID-19 patients and is strongly associated with worse outcomes. The researchers also found evidence suggesting that SARS-CoV-2 can induce hyperglycemia by disrupting fat cells' production of adiponectin, a hormone that helps regulate blood sugar levels.

To better understand this important but mysterious aspect of COVID-19, Lo and colleagues — including Society member Laura Alonso, MD, chief of the Division of Endocrinology, Diabetes, and Metabolism at Weill Cornell Medicine and NewYork-Presbyterian/Weill Cornell Medical Center and the Herbert J. and Ann L. Siegel Distinguished Professor of Medicine at Weill Cornell Medicine — analyzed the records of 3,854 patients who were hospitalized with COVID-19 at NewYork-Presbyterian/Weill Cornell Medical Center, NewYork-Presbyterian Queens, and NewYork-Presbyterian Lower Manhattan Hospital in the first few months of the pandemic in the U.S.

They found that a remarkably high proportion (49.7%) of these patients presented with hyperglycemia or developed it during their hospital stays.

Hyperglycemia in these COVID-19 patients was also strikingly associated with worse outcomes. Compared to patients with normal blood sugar levels, the patients with hyperglycemia were nine times more likely to develop severe lung dysfunction (acute respiratory distress syndrome, or ARDS), 15 times more likely to be given mechanical ventilation, and three times more likely to die.

Surprisingly, the researchers found that hyperglycemia and the dire risks it brings also occur in other, non-COVID-19 forms of severe lung dysfunction. They found it in the same proportion in ARDS cases associated with COVID-19 and in ARDS cases from non-COVID-19 causes such as severe influenza or bacterial pneumonia. However, hyperglycemia in the latter cases appeared to be caused mostly by the death or dysfunction of beta cells that produce insulin. Further tests revealed that the COVID-19 ARDS patients had severe declines in blood levels of adiponectin.

How SARS-CoV-2 disrupts fat cells' production of adiponectin isn't yet clear. It may do so indirectly, by raising the general level of inflammation, which in turn disrupts fat cells. But the researchers demonstrated that SARS-CoV-2 can infect human and mouse fat cells, hinting at the possibility that the virus disrupts adiponectin production in this direct way in COVID-19 patients. The findings also suggest that a class of diabetes drugs called thiazolidinediones, which boost adiponectin production, may be useful in treating COVID-19 when it includes hyperglycemia. Further research is needed before this becomes clinically actionable.

People Over 40 with Type 1 Diabetes and COVID-19 Are More Likely to be Hospitalized

Adults with type 1 diabetes need to be extra cautious of COVID-19 as they are more likely to be hospitalized and die, according to a new study published in *The Journal of Clinical Endocrinology & Metabolism*.

Researchers led by Carla Demeterco-Berggren, MD, PhD, of the University of California San Diego in San Diego, Calif., point out that people with diabetes are at higher risk for COVID-19-related complications, especially if they are over the age of 40. Children with COVID-19 rarely develop severe respiratory symptoms and often remain asymptomatic. In contrast, adults experience respiratory symptoms of varying severity, with older adults and those with diabetes at higher risk of acute respiratory distress syndrome and death.

“Our study shows people over 40 with type 1 diabetes have worse outcomes from COVID-19 than children and young adults. Children and young adults experienced milder disease and a better prognosis,” Demeterco-Berggren says. “These findings indicate the need for



age-tailored treatments, immunization, and clinical management of individuals affected by type 1 diabetes and COVID-19. Public health recommendations, including wearing masks and getting vaccinated, need to be followed by all to reduce the risk of contracting COVID-19.”

The researchers analyzed data from 767 patients with COVID-19 and type 1 diabetes from 56 diabetes clinics across the U.S. Fifty-four percent were 18 or younger, 32% were 19 – 40 years old, and 14% were over 40. The study found patients over 40 were seven times more likely to be hospitalized with COVID-19 compared to the younger group. No patients from the 18 and under group died, while three died from the over 40 age group and two died from the 19 – 40 age group.

People with diabetes and COVID-19 who were 40 and older were more likely to experience adverse outcomes such as death, diabetic ketoacidosis, or severe hypoglycemia. This group also had a significantly higher prevalence of obesity, hypertension, or cardiovascular disease and chronic kidney disease when compared to the younger groups.

“These data and others indicate that risk for hospitalization for people with type 1 diabetes is age dependent, with the majority of children and young adults being spared from hospitalization and adverse outcomes,” the authors conclude. “Public health recommendations need to be followed by all to reduce risk of contracting COVID-19, and if a person with type 1 diabetes contracts COVID-19, then appropriate sick-day management including contact with the diabetes care team is recommended.”

“The goal of our study is to prevent poor COVID-19 outcomes for adults with type 1 diabetes and to highlight the need to base healthcare decisions on data as the COVID-19 pandemic evolves,” Demeterco-Berggren says. ^{EN}



“

These findings indicate the need for age-tailored treatments, immunization, and clinical management of individuals affected by type 1 diabetes and COVID-19. Public health recommendations, including wearing masks and getting vaccinated, need to be followed by all to reduce the risk of contracting COVID-19.

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ENDO 2022

June 11 – 14, 2022 • Atlanta, Georgia/Virtual Event

ADVANCE REGISTRATION:

Early Bird: January 12, 2022 – March 4, 2022

Advanced: March 5, 2022 – May 18, 2022

Late/Onsite: May 19, 2022 – June 14, 2022

ABSTRACT DEADLINE: January 17, 2022

HOUSING DEADLINE: May 20, 2022

ENDO 2022, taking place June 11 – 14, will be the Society's inaugural hybrid meeting; attendees can participate in Atlanta, online ... or both! This increased flexibility will foster expanded connectivity, community, and knowledge sharing among the diverse, international endocrine community. Each format has intrinsic benefits, and when the time comes, attendees will have the option to select the best format that suits their desires and needs when June 2022 rolls around.

Attendees can expect top-flight education at **ENDO 2022**, as well as a new vibrancy and contemporary conference experience with expanded networking. Learners can expect a range of carefully curated sessions in a variety of delivery formats spanning the endocrinology journey from bench to bedside and back again. **ENDO 2022** attendees will have the opportunity to tailor their learning experience to fit their precise professional and personal development needs. Further, the Society is also ramping up its investment in technology-forward learning enhancements to align the **ENDO** learning experience with the reality of day-to-day life in the 21st century. www.endocrine.org/endo2022



Pulmonary Meet 2021: 9th Annual Congress on Pulmonary and Critical Care November 22 – 23, 2021 (Virtual Event)

The 9th Annual Congress on Pulmonary and Critical Care is scheduled to take place virtually November 22 – 23, 2021. Based on the overall theme of "Advanced Treatment in Pulmonology," the goal of this year's conference is to learn and share innovative ideas and developments on current research by gathering leading international researchers, industry researchers, scholars, decision makers, and other professionals in pulmonology and critical care.

<https://pulmonary-criticalcare.global-summit.com/>

19th Annual World Congress Insulin Resistance, Diabetes, and Cardiovascular Disease Los Angeles, California December 2 – 4, 2021 (Hybrid Event)

The World Congress on Insulin Resistance, Diabetes, and Cardiovascular Disease (WCIRDC) is a unique and exciting multidisciplinary CME conference. Since its inception, the Congress has become the premiere global meeting dedicated to diabetes, obesity, lipids, cardiovascular disease, metabolism, and energy balance. It provides an exclusive opportunity for practicing professionals, clinical and basic scientists, researchers, and other clinicians to collaborate on emerging scientific principles and management strategies. The WCIRDC faculty consists

of distinguished global experts who link research to clinical practice in a bench-to-bedside approach that is unique to this state-of-the-art program.

<https://www.wcir.org/>

Medical Management of the Metabolic-Bariatric Surgery Patient

**February 15, 2022
10:00 a.m. – 5:20 p.m. (ET)
(Webinar)**

Severe obesity and its complications are best managed by an interdisciplinary team including both surgical and medical providers. This webinar will feature presentations by leading experts, panel discussions, and dedicated time for interactive Q&A to cover best practice recommendations for the pre- and post-operative management of patients

undergoing metabolic-bariatric surgery. Topics include optimizing pre-operative care as well as recognizing and developing approaches to the variability in post-operative weight loss and remission rates of obesity-related complications in both adult and pediatric patients. All registrants will receive on-demand access to recordings throughout 2022.

<http://www.obesity.org/meetings-education/webinars/>

BPS 2022: 66th Biophysical Society Annual Meeting

San Francisco, California

February 19 – 22, 2022

The Biophysical Society annual meetings are the largest annual gathering of biophysicists around the world. The meetings include symposia, workshops, 15 subgroup programs, over 500 platform speakers selected from submitted abstracts, the Biophysical Society Lecture, more than 4,000 packed poster presentations, as well as educational exhibits, exhibitor presentations, and career development sessions.

www.biophysics.org/2022meeting#/

AAES 2022

Cleveland, Ohio

May 22 – 24, 2022

(Virtual Event)

May 22 – 24, 2022

As the leading endocrine surgery association in North America, the American Association of Endocrine Surgeons (AAES) Annual Meeting is the premier event to connect with professionals and leaders across the globe in the field of endocrine surgery while receiving high-level education on the latest advancements in science and research. The 2022 Annual Meeting will be a hybrid event taking place in Cleveland, Ohio, but with virtual opportunities. While in-person podium presentations are preferred, exceptions will be made, and the ability to travel to the meeting venue is not a prerequisite for abstract acceptance.

<https://www.endocrinesurgery.org/2022-annual-meeting>

INTERNATIONAL ITINERARY

2021 World Endocrine & Obesity Conference

Bangkok, Thailand

November 19 – 20, 2021

Designed as a hybrid conference with both virtual and in-person platforms, the 2021 WEOC will address the complex nature of critical care cases, including their unique physiology, array of procedures, and potential complications. The latest management strategies for challenging clinical problems will be presented, and current controversies will be discussed utilizing a variety of educational methodologies.

<https://endocrine.episirus.org>

ESA SRB ANZBMS Annual Scientific Meeting

Melbourne, Australia

November 21 – 24, 2021

The ESA/SRB/ANZBMS Annual Scientific Meeting will cover the most recent state-of-the-art advances in the fields of endocrinology, reproduction, and bone and mineral research including awards sessions, oral presentations, and poster abstracts. This is a face-to-face meeting, with virtual/online components and options and a contingency plan to shift online in the event of disruption due to COVID-19.

www.esa-srb-anzbms.org/

2nd Euro Diabetes and Endocrinology Congress

Rome, Italy (Hybrid)

December 6 – 7, 2021

EDE Congress 2021 will combine many aspects of diabetes and endocrinology research, including metabolic disorders, weight management, cardiac risks, and advancement in treatments with a focus on emerging new technologies and a view to generate cross-disciplinary ideas and foster potential early-career researcher collaboration. This two-day event will bring together physicians, surgeons, podiatrists, scientists, scholars, and other nursing staff with a common interest in diabetes and endocrinology treatment. All attendees are expected to actively participate in the Congress, either by giving an oral/poster presentation or as a delegate.

<https://diabetic.plenareno.com/>

BY DEREK BAGLEY

The Cost of Living *(with Diabetes)*

A century after its discovery, insulin's price tag in the U.S. remains alarmingly high for many people living with diabetes. While experts in healthcare and industry have worked with legislators to address the problem, much more needs to be done so that this lifesaving therapy is available to all who need it.



When Leonard Thompson's life was saved by insulin 100 years ago, it changed the world. If diabetes had been the Gordian knot, insulin was and remains the best attempt at forging the blade to cut it. But right out the gate, there were problems. Surgeon Frederick C. Banting and his student Charles Best experimented on dogs, so locals began to claim that the scientists were stealing dogs, which led to some protest. Then there were tensions among the physicians over patents. The first American patient to receive insulin was Elizabeth Hughes, daughter of Secretary of State Charles Evans Hughes. According to Christopher Ruddy, PhD, a professional and public health historian and adjunct professor at the Dalla Lana School of Public Health at the University of Toronto, the key reason Banting accepted Elizabeth as a patient was that she had a private nurse, Blanche Burgess, who had valuable clinical experience.

In the early 1920s, the average person with diabetes had to spend about half their income on insulin. In 100 years, in the U.S. at least, not much has changed. There are many patients who ration their insulin because of cost, who have to decide whether to buy insulin or pay their rent, buy insulin or put food on the table, skimp on their livelihoods to save their lives. After 100 years, after Banting famously refused to put his name on the patent and biochemist J.B. Collip and Best sold the patent for \$1, there are places in the world that can't get access to insulin — a life-saving drug that's been around for a century — at all.

"The paradox is that it's partially the cost of insulin that's preventing the people who need it, to actually get it," says Robert Vigersky, MD, chief medical officer at Medtronic, director emeritus of Diabetes Institute at Walter Reed National Military Medical Center, in Bethesda, Md., and past-president of the Endocrine Society. "And it's really heartbreaking to see in low- and middle-income countries where the cost of insulin is prohibitive and/or the supply is just not there. The flip side is that in the developed countries in the world, there's this huge disparity between cost of insulin in the U.S. versus Canada or Europe. And I think it just highlights that our system needs to be fixed and to make it equitable so that life-threatening conditions, which require a drug like insulin is available without an economic penalty associated with it."

Make no mistake: Physicians, industry leaders, and lawmakers know that there's a problem that needs to be addressed, and to their credit, they've taken some steps to lower costs. Pharmaceutical companies have introduced alternatives like generics and biosimilars that should encourage competition and drive prices down, and legislation has been floating around to lower prescription drug prices across the board.

But for many people living with diabetes or taking care of someone with diabetes, those steps need to pick up the pace. "Insulin is a necessity for people with type 1 diabetes, and for many people with type 2 diabetes," says Rita Kalyani, MD, associate professor and clinical researcher in the Division of



“ Patient-centered, individualized care is a core component in diabetes management. The cost of insulin needs to be a factor in shared decision making with patients; **for some patients, human insulin may be the better option and is also more affordable.**”

— RITA KALYANI, MD, ASSOCIATE PROFESSOR AND CLINICAL RESEARCHER, JOHNS HOPKINS SCHOOL OF MEDICINE, BALTIMORE, MD.

“ It’s really heartbreaking to see in low- and middle-income countries where the cost of insulin is prohibitive and/or the supply is just not there. The flip side is that in the developed countries in the world, there’s this huge disparity between cost of insulin in the U.S. versus Canada or Europe. **And I think it just highlights that our system needs to be fixed and to make it equitable so that life-threatening conditions, which require a drug like insulin is available without an economic penalty associated with it.**”

— ROBERT VIGERSKY, MD, CHIEF MEDICAL OFFICER, MEDTRONIC; DIRECTOR EMERITUS, DIABETES INSTITUTE AT WALTER REED NATIONAL MILITARY MEDICAL CENTER, BETHESDA, MD.; PAST-PRESIDENT, ENDOCRINE SOCIETY

Endocrinology, Diabetes, and Metabolism at Johns Hopkins School of Medicine, in Baltimore, Md. “Cost should not be a barrier to offering the standard of care treatment for any patient. Unfortunately, many patients who can’t afford insulin are being forced to ration their insulin or skip doses altogether until they can afford to pay for their insulin; this clearly impedes optimal diabetes care.”

And after 100 years, there are still those out there who could make a difference who seem to be doing their level best to dull the proverbial blade to cut that knot. “It’s an unintended consequence of our political system,” Vigersky says. “At the moment, there’s a lack of agreement on almost everything.”



But even with all the concern and public scrutiny surrounding insulin costs, not much is known about recent trends in its ambulatory use in the U.S., trends that could give insights into what drives insulin costs and potentially inform health policy.

Analog Impact

In October, *JAMA Network Open* published a paper titled “Trends in Insulin Types and Devices Used by Adults With Type 2 Diabetes in the United States, 2016 to 2020,” by Sudipa Sarkar, MD, MSC, et al., which noted that many have speculated that the trend in increasing insulin costs is due to increasing use of analog insulin but that little is known about the recent trends in insulin use in the U.S.

“There has been increasing use of newer, analog insulins which predominate in the U.S. and have represented more than 80% of total insulin treatment visits over the past five years,” says Kalyani, who is senior author of the paper. “The rising cost of analog insulins has far outpaced the rate of inflation. We need greater transparency to better understand the key drivers of insulin pricing; the continued introduction of biosimilars can also help create competition in the marketplace and help limit future price increases.”

The authors conclude that ambulatory insulin use in the U.S. during the past five years remained dominated by use of insulin analogs and insulin pen delivery devices, with increasing uptake of newer products as they have been brought to market. Insulin glargine represented more than half the insulin visits throughout the study period.

“Though clinical inertia may be a factor, on the other hand, we saw continued uptake of newer insulin products as they were brought to market including the use of biosimilar insulins,” Kalyani says. “Our study also did not investigate which specific insulins, for instance, were included on drug formularies.”

The authors also point out that for patients who can take human insulin, prescribing that could potentially offset the cost of newer insulins for patients who need them, which again speaks to tailored care. Kalyani says that she tries to explore lower-cost alternatives or patient assistance plans to help cover costs for insulin treatment in her practice. “Patient-centered, individualized care is a core component in diabetes management,” Kalyani says. “The cost of insulin needs to be a factor in shared decision making with patients; for some patients, human insulin may be the better option and is also more affordable.”

In their conclusion, the authors write that an in-depth understanding of these recent trends in insulin use may shed light on what’s driving the increasing cost of insulin, as well as knowledge gaps that persist. “Understanding recent trends in the types of insulin that are most commonly used in the U.S. can provide important insights regarding the potential drivers of insulin cost,” Kalyani says. “Other knowledge gaps regarding the clinical use of insulin include a better understanding of the factors that influence the specific insulin product that providers recommend to their patients, or that patients prefer to use when managing their diabetes.”

A Call to Action and Advocacy

Last year, a paper appeared in the *Mayo Clinic Proceedings* that detailed the account of a patient with type 1 diabetes in his mid-20s who worked as a restaurant manager in Minnesota. He couldn’t afford the deductible and monthly premiums of his insurance, and he couldn’t afford to pay for his insulin with cash, so he tried to ration his insulin. He was found dead in his apartment from diabetic ketoacidosis.

The paper, “The High Cost of Insulin in the United States: An Urgent Call to Action,” by S. Vincent Rajkumar, MD, claims that the most common forms of analog insulin cost 10 times more in the U.S. than in any other developed country and points to the fact that some Americans are traveling to Canada and Mexico to purchase more affordable insulin.

And again, experts are painfully aware of scenarios like these. The Endocrine Society in January published a position statement that maps out some seemingly simple steps



AT A GLANCE

- ▶ Even 100 years since its discovery, insulin costs remain high for many people, leading them to ration or even forego the medication.
- ▶ Healthcare experts, industry leaders, and legislators have taken some steps to address the problem, and researchers have been studying trends in insulin use that may provide some insights into what drives the cost.
- ▶ Insulin pricing remains complex in the U.S., and it will take everyone involved to address the problem.

“

I think we want to, as individuals, as well as the [Endocrine] Society, advocate to our representatives in Congress and the administration, how important this is for people with diabetes to have effective and affordable insulin. I think the Society and its members need to continue to advocate and pound that message home, and get the individual physicians, the endocrinologists, as well as their patients up in front of their representatives and make the case.”

— ROBERT VIGERSKY, MD, CHIEF MEDICAL OFFICER, MEDTRONIC; DIRECTOR EMERITUS, DIABETES INSTITUTE AT WALTER REED NATIONAL MILITARY MEDICAL CENTER, BETHESDA, MD.; PAST-PRESIDENT, ENDOCRINE SOCIETY



to increase insulin affordability, and the Society’s advocacy team has laid out some policy options Congress could take and launched a campaign to encourage members to call on Congress to pass legislation to lower the cost of insulin. But simple doesn’t always mean easy.

Vigersky tells *Endocrine News* that from a policy standpoint, the biggest impact on the industry would come from Medicare allowing open bidding on insulin and be able to purchase insulin from international suppliers, which would set the standard for the rest of the players, whether that’s Medicaid or commercial payers. But he says that would take major legislation, which would affect the entire pharmaceutical industry, which is why such legislation has not been accepted.

For Vigersky, it’s going to take hitting the pavement to get something done. He points to Canada and Medicaid in Minnesota where they’re requiring the biosimilar Admelog to be used in people with type 1 diabetes and anyone else who requires rapid-acting insulin. “That’s additional pressure,” he says. “That’s essentially health ministry and major payer pressure that’s occurring to get the price down.”

“I think we want to, as individuals, as well as the [Endocrine] Society, advocate to our representatives in Congress and the administration, how important this is for people with diabetes to have effective and affordable insulin,” Vigersky continues. “I think the Society and its members need to continue to advocate and pound that message home, and get the individual physicians, the endocrinologists, as well as their patients up in front of their representatives and make the case.”

It’s going to take pressure, and it’s going to take time. That, and everyone coming together to make the effort that by 2121, we won’t have to read stories about 20-year-olds dying from not being able to afford a very old, very essential drug.

“Insulin pricing is complex, and there are many stakeholders in the supply chain,” Kalyani says. “It will require all parties involved including manufacturers, pharmacy benefit managers, healthcare providers, pharmacies, administrators, and employers to come together to address this problem.” **EN**

— BAGLEY IS THE SENIOR EDITOR OF *ENDOCRINE NEWS*. IN THE OCTOBER ISSUE, HE WROTE ABOUT THE UNUSUALLY HIGH RATES OF FATTY LIVER DISEASE IN MEXICAN AMERICAN POPULATIONS COMPARED WITH OTHER HISPANIC AMERICAN POPULATIONS.



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Insulin **RESISTANCE:**

*New Insights into
Development, Diagnosis,
and Treatment*



BY KELLY HORVATH

As we celebrate the centennial of insulin's discovery, recent research from Endocrine Society journals sheds new light on the often-confounding condition of insulin resistance, its comorbidities, and treatment.

This month marks the centennial of what can only be called one of the 20th century's greatest medical breakthroughs: successfully lowering dangerously high blood glucose levels with therapeutic insulin injections. The interdisciplinary medical–research team that included physiologist J.J.R. Macleod, surgeon Frederick C. Banting, Banting's student Charles Best, and biochemist J.B. Collip had thwarted what was until 1922 an automatic death sentence from diabetes-induced hyperglycemia by extracting insulin from cattle.

Although therapy was not discovered until the 20th century, diabetes has been known to physicians for millennia. By the fifth century, ancient doctors in Asia were able to differentiate between types 1 and 2 diabetes, noting that the latter was more common in wealthy individuals (who back then likely ate more and exercised less). This distinction was gradually refined over the next thousand years until Sir Harold Percival Himsworth published research in 1936 describing the phenomenon of insulin resistance. We now classically define it as attenuated sensitivity to insulin-mediated glucose disposal causing such consequences as hyperlipidemia, hypertension, and cardiovascular disease.

While the field of therapeutic insulin development has pushed way past extraction from animal pancreata since the 1980s (with Humulin, a recombinant human insulin formulated in 1978), insulin resistance remains a deeply challenging and complex condition for the hundreds of millions of people globally dealing with it. On the centennial anniversary of the discovery of therapeutic insulin, three recent studies in Endocrine Society journals address this phenomenon in a variety of patients.

Vaping and Insulin Resistance

In “Association Between Smoking Behavior and Insulin Resistance Using Triglyceride-Glucose Index Among South Korean Adults,” published in *The Journal of Clinical*

“While the field of therapeutic insulin development has pushed way past extraction from animal pancreata since the 1980s (with Humulin, a recombinant human insulin formulated in 1978), **insulin resistance remains a deeply challenging and complex condition for the hundreds of millions of people globally dealing with it.**”



“Smoking is believed to contribute to insulin resistance by various proposed pathways. So, not surprisingly, the dual- and single-smoker groups had higher incidences of insulin resistance. **When combined with such co-factors as existing abdominal obesity and unhealthy lifestyle behaviors (e.g., frequent alcohol use, reduced exercise), this association more than doubled when compared to the never-smoker group.**”

Using the triglyceride-glucose index, Korean researchers found an association between smoking traditional cigarettes and e-cigarettes and insulin resistance.

Endocrinology & Metabolism (JCEM) in June, Eun-Cheol Park, MD, PhD, of the Department of Preventive Medicine and Institute of Health Services Research, Yonsei University College of Medicine, in Seoul, Korea, and team take a look at the association between insulin resistance and smoking behavior, including dual smoking of e-cigarettes and traditional cigarettes, a facet so far understudied.

A total of 11,653 participants ages 19 years and older and excluding patients with known high blood glucose levels from the 2016 – 2018 Korea National Health and Nutrition Examination Survey were divided into four groups: dual-smokers (245), single smokers (1,931), previous smokers (2,312), and never smokers (7,408) and tested for insulin resistance using the triglyceride-glucose (TyG) index, a simple blood test that is less expensive than insulin testing and validated by previous studies as a reliable indicator of insulin resistance.

In general, smoking is believed to contribute to insulin resistance by various proposed pathways. So, not surprisingly, the dual- and single-smoker groups had higher incidences of insulin resistance. When combined with such co-factors as existing abdominal obesity and unhealthy lifestyle behaviors (e.g., frequent alcohol use, reduced exercise), this association more than doubled when compared to the never-smoker group.

Other surprises did emerge, however. Primary among them is that dual-smoking had the highest association of all (although a direct link was not found), despite that e-cigarettes were introduced as a healthy alternative to traditional cigarettes. Another surprise is that studies using the homeostasis model assessment of insulin resistance (HOMA-IR) to assess insulin resistance found no association between insulin resistance and smoking behavior, although this is an indirect method, whereas the TyG index is a direct method. The researchers attribute these conflicting results to the difference in measurement tools.

Future studies should be done to consider specifics such as type of e-cigarette and e-cigarette use only to further determine whether an association between vaping and insulin resistance exists.

In the July 2021 JCEM, an international team of researchers proposed a clinical method to close a gap in diagnosing extreme insulin resistance in developing countries.

Diagnosing Severe Insulin Resistance with Limited Resources

From July's JCEM, "Approach to Diagnosing a Pediatric Patient With Severe Insulin Resistance in Low- or Middle-Income Countries," a team of researchers including Abhimanyu Garg MD, of the University of Texas Southwestern Medical Center, Dallas, Texas, and Daniëlle C. M. van der Kaay, MD, PhD, of the Erasmus Medical Center-Sophia Children's Hospital, in Rotterdam, The Netherlands, propose a clinical method to close a gap in diagnosing extreme insulin resistance in children in developing countries, noting that timely diagnosis and treatment are essential in preventing dangerous complications. While comprehensive diagnostic approaches that can address even the rarest underlying disorders are available in developed countries, such resources are commonly unavailable in low- or middle-income countries.

Based on the case of a 15-year-old Surinamese girl presenting with signs of severe insulin resistance such as excessive insulin requirements to lower blood glucose levels, increased muscularity and marked paucity of body fat, and acanthosis nigricans, Garg, van der Kaay, and team developed a systematic approach to a diagnostic work-up that allows investigation of a broad set of differential diagnoses (e.g., insulin resistance syndromes, endocrinopathies, neuroendocrine tumors, anti-insulin autoantibodies, subcutaneous insulin resistance, medications, lipodystrophy syndromes, and other genetic syndromes) through a thorough history and physical examination instead of expensive and possibly hard-to-come-by tests.

Any family history of consanguinity, for example, in a child with diabetes should prompt suspicion for underlying genetic causes of insulin resistance. Likewise, from evaluation of body fat distribution in the physical exam alongside any available lab investigations of liver and kidney function, hormone levels, and so on, other clues can emerge. The researchers have created helpful tables that clinicians can consult to match up assessment data with possible interpretations.

Meanwhile, their Surinamese patient's hyperglycemia persisted four months after admission to the hospital despite several treatment approaches. Ultimately, genetic testing revealed her as having congenital generalized lipodystrophy type 1, also known as Berardinelli-Seip syndrome, that occurs particularly in children with consanguineous parents. The researchers believe, however, that such lipodystrophies can be diagnosed based on the overall clinical picture. At the time of study's publication, their patient was stable, and without disabling visual or renal complications of diabetes.

"We provide a systematic approach to the differential diagnosis and work-up to clinically diagnose a child with insulin-resistant diabetes mellitus," says van der Kaay.



AT A GLANCE

- ▶ Using the triglyceride-glucose index, Korean researchers investigated the relationship between smoking behavior and insulin resistance and found an association between smoking traditional cigarettes as well as smoking both traditional and e-cigarettes and insulin resistance.
- ▶ For pediatric patients in low- or middle-income countries, a team of Dutch, American, and Surinamese researchers has proposed an approach to diagnosing severe insulin resistance that is guided by the clinical picture and widely available laboratory tests so that patients can get timely treatment to attempt to avoid severe, disabling consequences.
- ▶ Also, *Bacteroides* is a key microbial biomarker in PCOS with potential diagnostic value; moreover, gut dysbiosis may underly insulin resistance in PCOS.



Gut Dysbiosis and Insulin Resistance

Finally, from the October issue of *Endocrinology*, “Intestinal Flora is a Key Factor in Insulin Resistance and Contributes to the Development of Polycystic Ovary Syndrome,” by Hong-Wei Zhou, PhD, of the Microbiome Medicine Center, Division of Laboratory Medicine, Zhujiang Hospital, Southern Medical University, in Guangzhou, China, and team examined how dysbiosis might contribute to disordered glucose metabolism in patients with polycystic ovary syndrome (PCOS).

With evidence accumulating that the gut microbiota is involved in the etiology of insulin resistance, they compared the gut microbiome of healthy study participants with that of patients with PCOS. Prior studies demonstrated inconsistent results regarding type of bacterial species in the microbiota of these patients.


Participants included 56 patients with PCOS (according to the Rotterdam criteria) and 31 healthy controls recruited from the gynecology and obstetrics outpatient clinic at the Zhujiang Hospital of Southern Medical University. They provided stool samples, which were then transplanted into mice. Notably, the stool samples from patients with PCOS had high levels of *Bacteroidetes*, a potentially characteristic finding of PCOS intestinal flora that bears further investigation. Compared with mice transplanted with stool from healthy controls, mice transplanted with stool from individuals with PCOS displayed insulin resistance but not disordered glucose metabolism.

PCOS mice given a 35-day antibiotic cocktail treatment improved in terms of both phenotype and insulin resistance, suggesting that the presence of *Bacteroidetes* in the gut microbiome may indeed be a factor in insulin resistance and may promote the pathogenesis of PCOS. These mice also

A new study from the October 2021 issue of *Endocrinology* shows that certain intestinal flora might be a key indicator for insulin resistance, especially in patients with polycystic ovary syndrome (PCOS). Such flora might be a target for therapy in patients with PCOS, ameliorating the insulin resistance that led to the development of PCOS in these patients.

demonstrated decreased serum testosterone and increased cecal farnesoid X receptor levels, which activates the bile acid chenodeoxycholic acid ([CDCA] found in reduced levels in PCOS from *Bacteroidetes* hydrolysis). When the PCOS mice were treated with CDCA, glucose levels improved.

Thus, the intestinal flora might be a target for therapy in patients with PCOS, ameliorating the insulin resistance that led to the development of PCOS in these patients.

As these three studies show, the complexities of insulin resistance continue to emerge, but researchers are discovering new ways to diagnose it and ultimately to treat it. 

For Further Reading

For more information on the research discussed in this article, feel free to check out these studies for a more in-depth look at insulin resistance.

“Association Between Smoking Behavior and Insulin Resistance Using Triglyceride-Glucose Index Among South Korean Adults” —

<https://doi.org/10.1210/clinem/dgab399>

“Approach to Diagnosing a Pediatric Patient With Severe Insulin Resistance in Low- or Middle-Income Countries” — <https://doi.org/10.1210/clinem/dgab549>

“Intestinal Flora is a Key Factor in Insulin Resistance and Contributes to the Development of Polycystic Ovary Syndrome” — <https://doi.org/10.1210/endocr/bqab118>

— HORVATH IS A FREELANCE WRITER BASED IN BALTIMORE, MD. IN THE AUGUST ISSUE, SHE WROTE THE CEU 2021 PREVIEW ARTICLE ABOUT HEALTH DISPARITIES AND THEIR IMPACT ON DELIVERING CARE.



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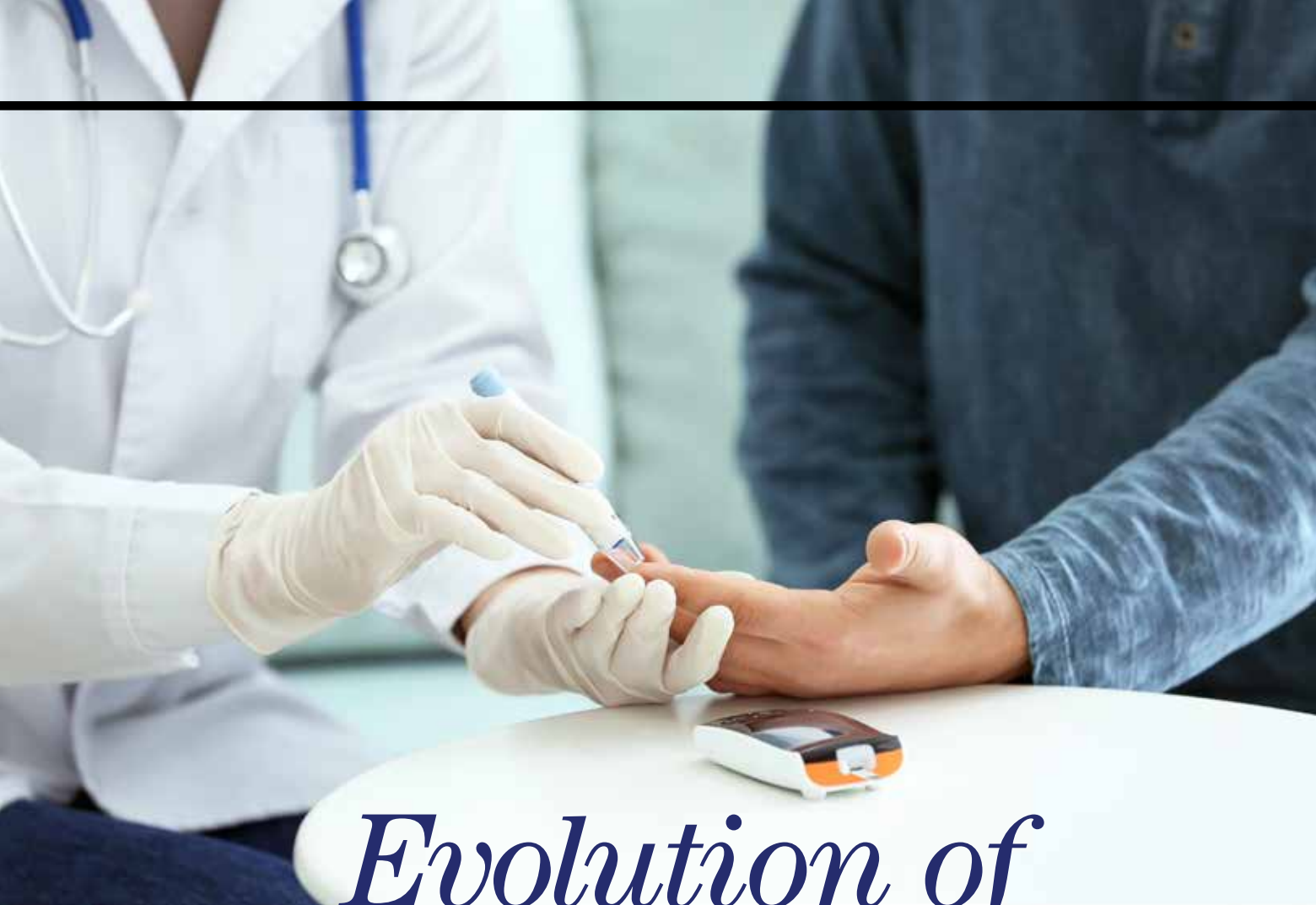


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Evolution of **Diabetes Management**

**The Patient-Provider Relationship,
Accessing Resources, *and*
Surmounting Obstacles**

BY KELLY HORVATH

During insulin's first century, treatments and resources for people with diabetes have steadily progressed. So, too, have relationships between the patient and the provider. A recent Endocrine Society-hosted roundtable highlighted this vital connection and how it has evolved through the decades.

Leonard Thompson was 14 years old in 1922, and he was dying of type 1 diabetes. Mere months earlier, physiologist J.J.R. Macleod, surgeon Frederick C. Banting, and Banting's student Charles Best had successfully extracted insulin from a dog pancreas. When biochemist J.B. Collip joined their team in December 1921, and got a purer extract of insulin from cattle, Thompson became the first human being to receive an insulin injection. The treatment worked, and type 1 diabetes was no longer unsurvivable — for the first time ever.

Fast-forward 100 years, and what was once a death sentence is now a treatable, though chronic, condition. As groundbreaking as the discovery of insulin was, how people with diabetes have adapted to fully living their lives with insulin use is just as remarkable. Another positive to come out of this evolving story is how providers and patients have built collaborative relationships to manage individual cases as effectively as possible. And yet, challenges still abound, from both patient and provider perspectives.

In early August, the Endocrine Society hosted a roundtable entitled “Building a Strong Patient-Provider Relationship” that demonstrates just how critical the patient-provider relationship is as well as spotlights patient resources and identifies persisting gaps. This virtual question-and-answer session included *Endocrine News* editor Mark A. Newman as facilitator and participants Grazia Aleppo, MD, FACE, FACP, Northwestern University; Marguerite Brunner, a patient of Aleppo's; and Evan Strat, a member of the College Diabetes Network.

A Mid-Century Diabetes Diagnosis

Brunner was diagnosed with type 1 diabetes in 1964 at age 12. Back then, the structure of insulin had not yet been discovered, and available options for therapeutic insulin were few. Accordingly, management of her condition was intricate and rigid: “I spent 10 days in Children's Memorial Hospital in Chicago, where I learned to draw up insulin and inject it,” says Brunner. “My mom and I learned the very restrictive diet and to measure everything that I ate on a gram scale.” If Brunner went to a friend's house, her mother prepared food for her to

“ I did all I could to survive and not do too much damage to my body. I thought some about dying early because that had been predicted. I also worried about losing my eyesight. I wanted to have children at some point, but I figured by the time I got to that advanced age I'd either be dead, or there would be a cure.”

— MARGUERITE BRUNNER, CHICAGO, ILL.,
DIAGNOSED WITH TYPE 1 DIABETES IN 1964 AT AGE 12



The participants in the “Building a Strong Patient-Provider Relationship” roundtable included (l to r): *Endocrine News* editor Mark A. Newman as facilitator; participants Grazia Aleppo, MD, FACP; Aleppo’s patient Marguerite Brunner, and Evan Strat, a member of the College Diabetes Network.

take. She had to stick to a three-meal, two-snack-per-day plan with nothing in between except water to maintain blood glucose control. Even diet soda — a brand-new phenomenon in the mid ’60s — was heavily restricted until research was available on how it would affect blood sugar, Brunner explains. She also had to test her urine glucose because home blood tests were not yet on the market. Four times daily she put drops of her urine into a test tube with a clinical test tablet, compared the resulting color changes to a chart, and documented the process.

This was a terribly heavy burden for a child, and it was tinged with awareness of her possible early mortality. “It was all we had, so I did all I could to survive and not do too much damage to my body...” recounts Brunner. “... I thought some about dying early

because that had been predicted. I also worried about losing my eyesight. I wanted to have children at some point, but I figured by the time I got to that advanced age I’d either be dead, or there would be a cure.”

Brunner has now been living with diabetes for 57 years, and she did have those children she had hoped for, due to tremendous advances in diabetes care since 1964, but, she says, “most people have no concept of what it was like then for me.” The first advance to really impact her quality of life was the advent of home blood testing in her adulthood, which she credits with providing her a real sense of what was going on in her body and a better ability to control those processes. As time went on, however, Brunner’s glucose levels became increasingly labile, forcing her to do 15 blood tests a day including overnight. She often had to adjust her life and work around her frequent testing, and she forfeited the career she really wanted to pursue. Diabetes always had to come first. If she got distracted and veered from her schedule, hypoglycemic seizures and other serious consequences were the not infrequent result.

When the insulin pump came along, her quality of life once again saw a boost. She could eat when she was hungry rather than according to an unforgiving schedule. She could sleep a full night through, and it gave her all-around greater control over her body.

But the most important final technological advancement to profoundly improve her life is the continuous glucose monitor (CGM) that works in concert with her pump and adjusts to

Despite the many advances through the years in diabetes care, a good relationship between patient and provider has remained a constant.



“When I was starting college, my biggest concern was how I was going to navigate that transition to being completely independent. A lot of it was the basics, like how I would tell my roommate that I have diabetes or making sure that if something happened and I needed emergency assistance how I would get that.”

— EVAN STRAT, GEORGIA TECH STUDENT, LIVING WITH TYPE 1 DIABETES FOR 11 YEARS

blood sugar fluctuations. Says Brunner: “I think about what my life would have been like if I’d had a CGM a few years earlier. I likely would not have suffered hypoglycemic seizures, and therefore I wouldn’t have fractured two of my vertebrae and injured my shoulder so dramatically that I needed a shoulder replacement. I would have been able to continue the job as a nurse anesthetist I loved and would have been able to teach three-hour literature classes instead of much shorter ones.”

Having lived through the evolution of diabetes technology in a way not many can relate to, Brunner has regrets but remains grateful, above all for her trusted care providers. Her very first pediatric endocrinologist, Matthew Steiner, at Children’s Memorial, brought her books to read to educate herself about her condition, telling her, “[you will] have to manage it’ — he would help me — but it was my disease.” She says it felt like regaining some control over a life she had completely lost control of: “It made a difference and set the pace for me for the rest of my life.” At the Diabetes and Pregnancy Clinic, endocrinologist Richard Phelps is another clinician whose care helped her live her life how she wanted to. “He listened to me very carefully, and he always respected my knowledge of my body and my disease.”

On retiring, Phelps referred Brunner to Aleppo, about whom Brunner says, “She knows the technology like no one. I upload my data, she looks at it for a few minutes, and just like that she comes up with a little tweak that’ll solve whatever issue I’m having,” says Brunner. “I could not do it without her.”

Patient–Provider Partnering

Perhaps the most important advance of all to come out of the evolution of diabetes management is the awareness of the need for providers to partner with their patients for optimal care. Aleppo spoke next, adding the provider perspective to Brunner’s story and offering insight into how to strengthen such relationships.



AT A GLANCE

- ▶ Marguerite Brunner and Evan Strat have type 1 diabetes and have experienced the evolution of diabetes technology firsthand.
- ▶ Endocrinologist Graciela Aleppo believes that diabetes care is optimized when undertaken as a partnership between patient and provider.
- ▶ The Endocrine Society and the Hormone Health Network are a resource hub for patients that makes complex healthcare information comprehensible and keeps them engaged in their diabetes self-management.



Whether younger or more mature, patient buy-in is critical in diabetes self-management. Patients often get more engaged when they can see firsthand what's happening with their glucose levels.

“With new patients with diabetes, I say, ‘OK you sought me out; what can I do for you? ‘What are you trying to get out of this meeting and this relationship?’,” says Aleppo, “because people come to us not as their first doctor usually. So, I try to understand where they’re at and what they need to accomplish.” She says she puts on her detective hat to glean what their primary concern is and whether it’s hypoglycemia, or feeling stuck in a particular regimen, or fear of complications, so she has a base to work with and to build a plan from that includes goal setting. With goals, she says she encourages both short-term and long-term goals and engaging patients throughout the process.

“I always introduce two things: One is education, which can be tricky with somebody like Marguerite, who’s had type 1 diabetes for a long time, because of the huge number of changes in the last 50 years, but some people don’t get the privilege or the chance to actually get to know more about what’s new, and it behooves me to do that. Then I always pitch CGM technology because truly that is the standard of care. [Patients] can really do so much better, prevent hypoglycemia, and really decrease the burden of their disease.”

Even with the CGM technology, new challenges might emerge, such as with very old or very young patients who might need a simplified regimen (e.g., a long-acting insulin injection) or help with administration to keep them safe. Another challenge that tends to occur with type 2 diabetes is hesitancy with starting insulin. “These patients often don’t realize that insulin is hormone-replacement therapy, and they need that physiologic replacement whether it’s with a long-acting insulin, or we go gradually. But it should be a conversation, not an imposition,” Aleppo says. She adds that patient buy-in is critical in diabetes self-management, and being able to demonstrate to patients what’s happening with their glucose levels with CGM often helps to engage them.

“So, it’s very easy to see that this program just doesn’t work one without the other. You have to be in this as a team,” Aleppo says.

Transitioning from Pediatric to Adult Care

Another challenge the patient-provider team faces is how to make the transition from pediatric to adult care and what key aspects should be considered. “First you have to understand that these patients are going through multiple transitions including trying to understand the dynamics of a new practice,” explains Aleppo. “It’s a whole different world.” She says that she tries to get a few minutes alone with transitioning patients whether they come in alone or accompanied by their parents so they can share anything they might hold back on with parents present and to gauge their readiness for self-care including filling prescriptions and scheduling appointments.

A new college student, for example, might be juggling class schedules that change each semester, part-time jobs, and holiday breaks. Diabetes self-management must be re-thought out in each of these scenarios — students must be prepared for anything. “That’s one thing we try to do in our practice,” says Aleppo, “be flexible. We need to accommodate them to keep them safe throughout this time.”

Evan Strat, a student at Georgia Tech who’s had type 1 diabetes for 11 years knows these issues well. “Two of the things that I found really challenging were making sure I was eating healthy and exercising. I noticed that when I cook for myself, I know the carbs in the food, whereas the dining halls were more fast-food oriented and not necessarily offering the best things to eat.” Strat explains. “Similarly, making time in my schedule for exercise helps, but when you have classes and stressful assignments, it feels sometimes like you can’t take 20 minutes out of your day to take a walk or go for a run.”

Strat also described how living with diabetes is difficult in and of itself. “It’s mostly just finding the willpower. Your level of motivation comes and goes, and sometimes diabetes gets really frustrating because your pump sites aren’t working, and you just don’t want to deal with it,” he says.

Here again, the newer technology is helpful, he says, because it provides a constant layer of assistance to prevent hypoglycemic episodes. And, although he uses data analysis tools like the Dexcom CLARITY app and the Tandem t:connect, these applications do not “talk” to each other and do not integrate with

“ I always introduce two things: One is education, which can be tricky with somebody ... who’s had type 1 diabetes for a long time, because of the huge amount of changes in the last 50 years, but some people don’t get the privilege or the chance to actually get to know more about what’s new, and it behooves me to do that. **Then I always pitch CGM technology because truly that is the standard of care. [Patients] can really do so much better, prevent hypoglycemia, and really decrease the burden of their disease.**”

— GRAZIA ALEPPO, MD, FACE, FACP, ASSOCIATE PROFESSOR OF MEDICINE – ENDOCRINOLOGY, NORTHWESTERN UNIVERSITY, CHICAGO, ILL.

his pump data. He is hopeful that something will come along to combine all the data he needs in one place.

In the meantime, some low-tech resources like the College Diabetes Network (CDN) and other support groups have helped Strat self-manage his diabetes and live a healthy life. “When I was starting college, my biggest concern was how I was going to navigate that transition to being completely independent. A lot of it was the basics, like how I would tell my roommate that I have diabetes or making sure that if something happened and I needed emergency assistance how I would get that,” he says.

The CDN’s mission is to help young adults with diabetes handle these very situations and thrive. Strat says the Georgia Tech

From weighing food to the development of CGMs, the evolution of diabetes self-management tools has been remarkable.

CDN chapter hosted many helpful events, such as “Diabetes 101” and outreach-advocacy-combined events. “We worked with the dining hall staff to get better nutritional information as well as with the student health center so that people with diabetes could come and drop off their used sharps,” Strat says. “I’ve also been fortunate to be a part of CDN’s Next Gen Fellows program, which is to jumpstart the passion for going into diabetes as a field through professional development workshops and providing the opportunity to go to one of the major diabetes conferences.”

Patient Resources: Connecting the Dots

As upbeat and proactive about their diabetes as Brunner and Strat are, it’s clear that on top of the burden of living with a serious chronic condition, they have also had to continuously adapt to new technologies and new approaches to management over the years, which must have contributed to their load even while the advances themselves intended to lighten it.

The Endocrine Society and the Hormone Health Network ([Hormone.org](https://www.hormone.org)) have created a hub that makes staying on top of available resources easier and more efficient. Aleppo herself helped create a CGM pocket guide to introduce the technology to users, both patients and their caregivers, available for free download in English and Spanish to anyone (https://www.hormone.org/-/media/hormone/files/diseases-and-conditions/diabetes/cgm-guide_eng_final_webspreads.pdf).

“We also have something called the Diabetes Technology Roadmap that tells you what each tool is from a glucose meter



to an insulin pump to an insulin pen to a CGM to explain what these tools do and what might be something you would be interested in,” Aleppo says. (The roadmap is available at: https://www.hormone.org/-/media/hormone/files/infographics/hhn_diabetes_technology_roadmap.pdf.)

But explaining the tools and types of insulin available is only half the battle. Connecting patients to affordable prescription options for them has been an Endocrine Society mission for some time. In “Addressing Insulin Access and Affordability: An Endocrine Society Position Statement,” published in *The Journal of Clinical Endocrinology & Metabolism* in January, the Endocrine Society advocates for ensuring access to affordable insulin. “It points out specific things to stakeholders such as they need to make sure that they are more transparent in how and why insulin costs are so high,” Aleppo explains. It also outlines policies such as limiting cost sharing to a copayment of no more than \$35 and capping costs at no more than \$100 per month. “They also are recommending that the market support more bioavailable and biosimilar insulin preparations and, finally, making significant changes to the payment system for Medicare Part D and Part B, which affects our older patients who may be on a fixed income. It’s really hard to see people crying in your office because they can afford to either buy food or insulin, but not both, so I applaud the Society for being at the forefront of this important mission,” Aleppo says.

While the Society advocates tirelessly to reduce the cost of insulin, an interim resource she recommends is **getinsulin.org** from the nonprofit organization Beyond Type 1 that allows patients to enter their ZIP code and any insurance information. “It tells you with simple prompts what can you do to lower your costs, whether it’s a voucher, special assistant programs, or a combination,” Aleppo says. ^{EN}

SEE FOR YOURSELF

To view the “Building a Strong Patient-Provider Relationship” webinar, along with other videos and webinars celebrating “100 Years of Insulin,” go to: www.endocrine.org/membership/100-years-of-insulin/100-years-videos.

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Hormone Science to Health

A hand in a white glove holds a small, clear vial with a red cap, containing a pink liquid. The background is a solid blue color.

Coming **ATTRACTIONS:** INSULIN'S INTRIGUING FUTURE

BY ERIC SEABORG

Smart insulin.
Once-a-
week insulin.
Thermostable
insulin.
Researchers
around the world
are working on a
variety of insulin
innovations,
some of which could
be available
sooner than you
think.

In a world where everything is becoming smart — phones, speakers, cars, watches, and even doorbells — will it soon be insulin's turn?

The answer is yes, according to Michael Weiss, MD, PhD, chair of the Department of Biochemistry and Molecular Biology at the Indiana University School of Medicine, in Indianapolis. Smart, glucose-responsive insulin that is more active in the presence of glucose and less active in the absence is one of the innovations on the horizon.

As we look ahead during celebrations of the centennial of the discovery of insulin, it's hard to know what the next 100 years will bring. But in addition to a smarter molecule, the potential breakthroughs in the next few years include tissue-specific, once-a-week, and nonrefrigerated formulations.

Insulin analogs have made important strides in recent years, but it is remarkable how little insulin delivery has changed. “Essentially the same substance is being given by the same rather primitive route as it was 100 years ago,” according to Philip Home, MA, DPhil, DM, professor emeritus at the Translational and Clinical Research Institute at Newcastle University in the U.K. Glycemic control remains “suboptimal, although it is a lot better than it used to be. The tools we have available with the insulin analogs, pumps, and glucose sensors have made a difference.”

“**Essentially the same substance is being given by the same rather primitive route as it was 100 years ago.” Glycemic control remains “suboptimal, although it is a lot better than it used to be. The tools we have available with the insulin analogs, pumps, and glucose sensors have made a difference.”**

— PHILIP HOME, MA, DPHIL, DM, PROFESSOR EMERITUS AT THE
TRANSLATIONAL AND CLINICAL RESEARCH INSTITUTE AT
NEWCASTLE UNIVERSITY IN THE U.K



Weight gain is a side consequence of insulin therapy, and that creates a vicious cycle where people are mildly obese, and they get diabetes and they go on insulin, then they are likely to experience weight gain But insulin action in the brain actually promotes satiety and weight loss. The insulin receptor in the brain has a different glycoform than the insulin receptor in the periphery. So, in principle, there is a way of targeting the brain insulin circuitry.”

— MICHAEL WEISS, MD, PHD, CHAIR, DEPARTMENT OF BIOCHEMISTRY AND MOLECULAR BIOLOGY, INDIANA UNIVERSITY SCHOOL OF MEDICINE, INDIANAPOLIS, IND.

Smart Insulin



Despite these advances, current science is not able to mimic the human body's complex subtleties in the interaction of insulin and glucose metabolism. Smart insulin would be a step in this direction. At least two

proof-of-concept papers on glucose-responsive insulin were published recently.

Weiss and colleagues published a report in *PNAS* earlier this year on inserting an artificial ligand-dependent switch into the insulin molecule to this end.

“Insulin changes shape when it binds to the receptor,” Weiss tells *Endocrine News*. “We were part of an international team that figured out a way to make the change in shape inhibitive in the absence of glucose. Our formulation requires glucose to change shape. So, it is the world's smallest glucose-responsive insulin system because it doesn't require a copolymer or something.” The process is reversible, so the insulin would be activated in the presence of glucose and inactivated in its absence in cycles even in the blood stream.

The paper reported successful use of a fructose-specific model in human liver-derived cells, and Weiss says that the team has begun testing a glucose-responsive version in rats.

A team of researchers from UCLA, MIT, and the University of North Carolina at Chapel Hill reported on another glucose-responsive system last year in *Nature Biomedical Engineering*. The researchers created a transdermal patch filled with

microneedles loaded with insulin and a glucose-responsive polymer matrix.

The microneedles penetrate the skin and can sense blood glucose levels, delivering insulin in response to higher glucose and holding back in the absence of glucose. The patches are the size of a quarter and succeeded in controlling glucose levels in minipigs with type 1 diabetes for about 20 hours. The researchers have applied to the U.S. Food and Drug Administration for approval to conduct human clinical trials on a planned once-a-day patch.

Weiss thinks a smart insulin could make it to the market in five years or so, although Home thinks of it more as a “dark horse.”

Tissue- or Organ-Specific Insulin

Weiss says that “tissue-specific or organ-specific insulins have been a holy grail for 30 to 40 years” because insulin action is different in different parts of the body.

“Weight gain is a side consequence of insulin therapy, and that creates a vicious cycle where people are mildly obese, and they get diabetes and they go on insulin, then they are likely to experience weight gain” that exacerbates the problem, Weiss says. “But insulin action in the brain actually promotes satiety and weight loss. The insulin receptor in the brain has a different glycoform than the insulin receptor in the periphery. So, in principle, there is a way of targeting the brain insulin circuitry.”

In addition, subcutaneous insulin administration tends to lead to too much insulin in the periphery and not enough in the liver, compared with endogenous secretion from the beta cells, so researchers are also working on “hepato-selective” insulin.

“There is lots of basic science going into that, and it will eventually get solved,” but it is farther away than some of the other likely innovations, Weiss says, especially in comparison to longer-lasting formulations and thermostable formats.

Once-a-Week Insulin

WEEK: _____

| | | | | |
|----------|---------|--------------|----------|--------|
| MONDAY | TUESDAY | WEDNESDAY | THURSDAY | FRIDAY |
| | | | X | |
| SATURDAY | SUNDAY | NOTES: _____ | | |

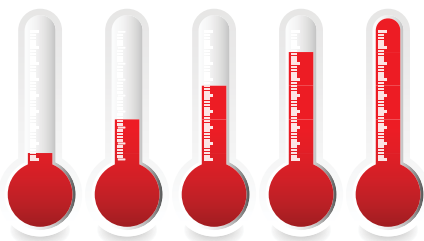
“Once-weekly insulins will most likely be the next addition to the insulin armamentarium,” writes Tim Heise in an article in *Diabetes Research and Clinical Practice*. “To date, clinical data of two once-weekly insulins in development have been published.”

One of these is insulin icodec, an analogue that Novo Nordisk has in Phase 3 clinical trials. The molecule has amino acid substitutions and a fatty diacid attached via a hydrophilic linker, modifications that “lead to strong albumin binding, reduced enzymatic degradation, and attenuated insulin receptor binding and clearance,” Heise writes.

Eli Lilly has a product in Phase 1 and 2 clinical trials called basal insulin Fc, which Home describes as “an Fc-coupled insulin in development for people with type 2 diabetes. This insulin has an apparent half-life of more than 10 days.”

Home agrees that weekly insulin analogues are the most likely to see the market next of these advances, and “could be used in combination with GLP-1 receptor analogues in type 2 diabetes.”

Thermostable Insulin



Weiss thinks that the advance that might come the most quickly relates to “ultrastable insulins to circumvent the need for a cold chain. Now we need to keep insulin from getting exposed even transiently to temperatures above 30 or 35 degrees centigrade. Insulin that does not require the cost and complexity of the present system of

distribution that is a barrier to treating the pandemic of diabetes in the developing world would enable international global delivery of insulin.”

Whichever advance comes to market first, the experts agree that with all the resources and research advancing it, patients will soon experience improvements in insulin therapy. “Glucose-responsive insulins would minimize the risk of hypoglycemia and make people feel comfortable with being more aggressive in their glycemic targets,” Weiss says. ^{EN}



AT A GLANCE

- ▶ Innovations on the close and farther horizons include smart, tissue-specific, weekly, and thermostable forms of insulin.
- ▶ Forms of smart insulin — which can activate or inactivate itself in response to high or low glucose levels — are already being tested in animals.
- ▶ Once-a-week insulin could be the next big advance to hit the market, some experts say.

— SEABORG IS A FREELANCE WRITER BASED IN CHARLOTTESVILLE, VA. IN THE OCTOBER ISSUE, HE WROTE ABOUT HOW UNDERSERVED POPULATIONS WERE BEING REACHED VIA BOOKLETS WRITTEN IN THEIR NATIVE LANGUAGES TO HELP THEM EASILY UNDERSTAND DEVELOPING DIABETES TECHNOLOGY.

Head of the Class:



BY GLENDA FAUNTLEROY SHAW

Q&A with Ashley Herdman

***Endocrine News* spotlights the Endocrine Society's Research Experiences for Graduate and Medical Students summer program by chatting with Ashley Herdman, a 2021 awardee about her experiences in the program, her research projects, and the importance of forging new professional relationships.**

For medical and graduate students with a keen career interest in endocrine research, the Endocrine Society's Research Experiences for Graduate and Medical Students (REGMS) summer program has proven to be a worthy benefit — offering invaluable lab experiences, networking connections, and mentorships that last well beyond the summer months.

Endocrine News caught up with one of the 14 REGMS awardees in 2021, Ashley Herdman, to learn more about her experiences. Herdman is a second-year PhD student at the University of Arkansas for Medical Sciences and is enrolled in the Neuroscience Track of the Graduate Program

in Interdisciplinary Biomedical Sciences. She used the 8-10-week REGMS program to forge new professional relationships and future opportunities as she continues her research in gonadotrope cellular networks.

Endocrine News: How did you become involved with the REGMS program, and what have you found most beneficial from participating?

Herdman: I applied for the REGMS program after hearing about it from my mentor, Dr. Angela Odle. We submitted our proposal outlining

“ I hope to go on to a post-doctoral fellowship and continue studying endocrinology. I am so fascinated by the cellular mechanisms of the endocrine system and have had so many good experiences in the field already! **I’m really interested in getting experience teaching or assisting in undergraduate courses throughout a fellowship as well.**”

— ASHLEY HERDMAN, SECOND-YEAR PHD STUDENT,
UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES, LITTLE ROCK, ARK.

our mentorship plan and summer research project and were selected as awardees in March. The most helpful part of the program has been the career-building and networking opportunities. I graduated college and began graduate school during the pandemic, which has made forming professional connections difficult.



Ashley Herdman

2021 REGMS Recipients

Taylor Baker

Case Western Reserve University

Kathryn Bartholomay

University of Colorado Anschutz

Shruti Bendre

University of Illinois

Angie Chen

Northwestern University

Annapurna Chitnavis

Arizona State University

Pratyusa Das

Southern Illinois University School Medical

Ethiopia Getachew

Harvard Medical School

Ashley Herdman

University of Arkansas for Medical Sciences

Steven Hobbs

University of Illinois

Nimisha Nandankar

Rutgers, The State University of New Jersey

Angela Olvera

The University of Wisconsin-Madison

Parleen Pandher

University of Northern British Columbia

Tanya Pierre

University of Alabama at Birmingham

Samuel Plaska

University of Michigan

Look for all of the 2021 REGMS recipients to be featured in the January 2022 issue of *Endocrine News*.

The Endocrine Society scientists and physicians who worked with us over the summer went out of their way to help us navigate scientific communication and networking in the virtual age. In one of our weekly seminars, I mentioned being interested in becoming an undergraduate professor and principal investigator. After hearing this, Matt Sikora, PhD, from the University of Colorado Anschutz, personally took the time to introduce me to professors at undergraduate institutions. I was then able to set up informal interviews with them and learn about their work and how to pursue this type of career. This provided me with new insight and direction, and really speaks to the commitment those in our field have for mentoring young scientists.

EN: Briefly describe your current research goals.

Herdman: I'm currently studying gonadotrope cellular networks and the potential role of leptin in facilitating these connections. We have a new model that allows us to use calcium imaging to observe and analyze the effect of different drugs, including leptin, on gonadotrope activity both individually and at the population level. We plan to use this technique to study the developmental regulation of this network and define some of the pathways involved.

EN: Where do you set your sights after completing your studies at the University of Arkansas?

Interested in REGMS?

Full-time first-year medical students and first- or second-year graduate students who are considering a career in endocrine research are encouraged to apply to the Research Experiences for Graduate and Medical Students (REGMS) program. Awardees participate in an 8-to-10-week summer research project in a lab under the guidance of an Endocrine Society member and receive a \$2,500 honorarium to help with costs incurred during the summer research period.

Read the full eligibility and application requirements at: <https://www.endocrine.org/awards/research-experiences-for-graduate-and-medical-students/application-requirements>.

“ I graduated college and began graduate school during the pandemic, which has made forming professional connections difficult. The Endocrine Society scientists and physicians who worked with us over the summer went out of their way to help us navigate scientific communication and networking in the virtual age.”

— ASHLEY HERDMAN, SECOND-YEAR PHD STUDENT,
UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES, LITTLE ROCK, ARK.

Herdman: When I graduate, I hope to go on to a post-doctoral fellowship and continue studying endocrinology. I am so fascinated by the cellular mechanisms of the endocrine system and have had so many good experiences in the field already! I'm really interested in getting experience teaching or assisting in undergraduate courses throughout a fellowship as well.

EN: Any words of wisdom to share for students who may be considering applying for REGMS?

Herdman: I would encourage everyone who is interested in endocrinology to apply. This program has been very supportive of student research and really helped each of the awardees take steps towards achieving their academic and professional goals. Our seminars and activities will continue during the year, so by being a part of the program we are receiving guidance and encouragement not only for the summer, but throughout our early careers. **EN**

— FAUNTLEROY SHAW IS A FREELANCE WRITER BASED IN CARMEL, IND.
SHE IS A REGULAR CONTRIBUTOR TO *ENDOCRINE NEWS*.



SUPPORTING NEW LEADERS IN CLINICAL CARE

PHYSICIAN LEADERSHIP IS THE FUTURE OF HEALTHCARE

The Excellence in Clinical Endocrinology Leadership (ExCEL) program offers comprehensive leadership training and mentorship to early career physicians of communities underrepresented in medicine and science. Whether you are just beginning as an endocrine fellow or navigating the next steps in your career beyond fellowship, the ExCEL program will help you build leadership skills, explore opportunities for advancement, and expand your network of peers and colleagues.

ExCEL PROGRAM COMPONENTS

LEADERSHIP SKILLS BUILDING:

ExCEL awardees will participate in developing key leadership competencies and management training through a multi-day Clinical Endocrine Career and Leadership Workshop.

BUILDING PARTNERSHIPS AND EXPANDING NETWORKS:

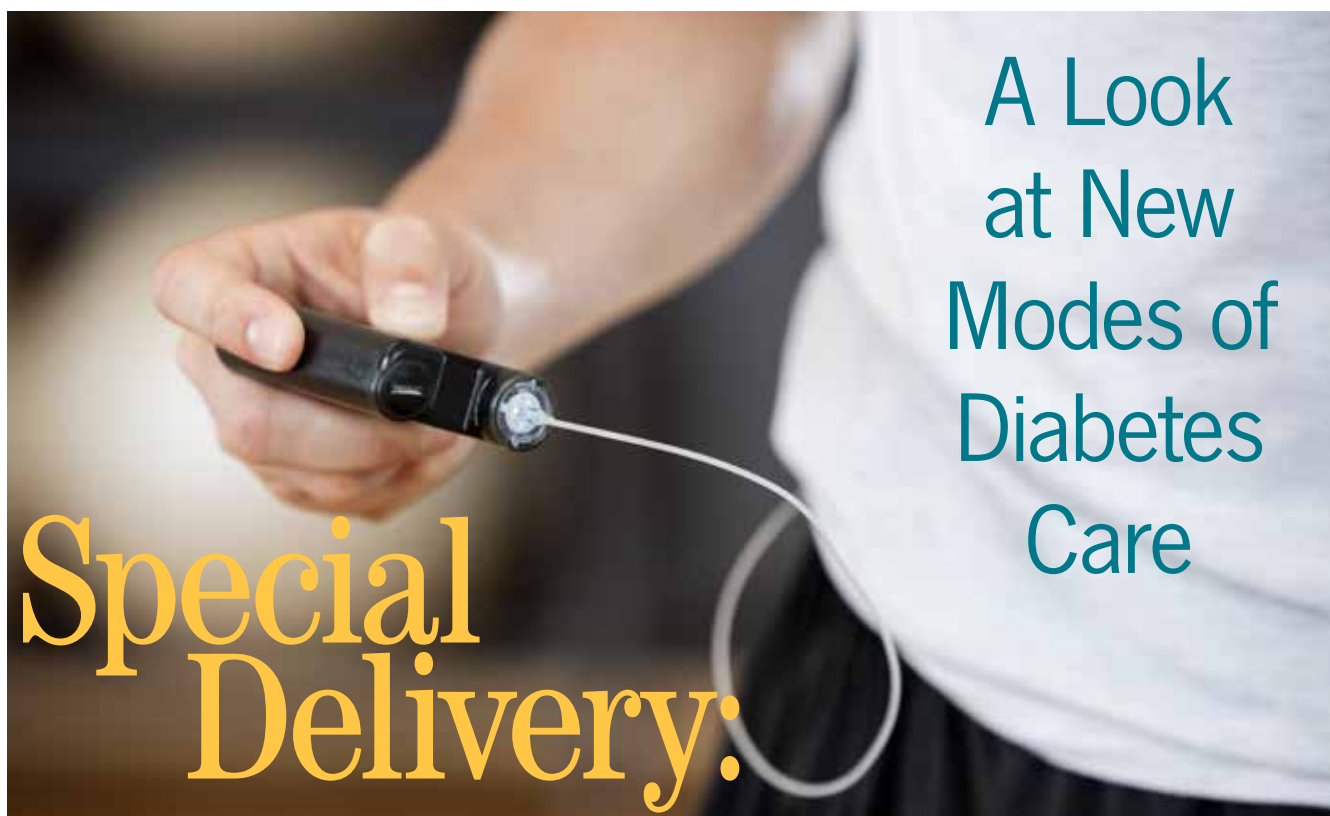
ExCEL's mentoring network will connect fellows with a core team of mentors, provide quarterly virtual check-ins, and deliver continued training through seminars intended to continue skills development and community building.

LEADERSHIP SKILLS IN PRACTICE:

We will assist ExCEL awardees in enhancing their professional credentials through opportunities to volunteer within the Endocrine Society, travel awards to attend and network at the annual meeting, ENDO, and enhance speaking abilities and near-peer mentoring through a Visiting Physician Faculty series.

We are accepting applications for 2022 program until December 10, 2021.
PLEASE VISIT [ENDOCRINE.ORG/EXCEL](https://endocrine.org/excel) TO APPLY.

Thanks to insulin's discovery a century ago, diabetes is no longer the death sentence it once was. However, providing care can often be complicated for both in- and outpatient treatment regimens. Potential new models of diabetes care could help ease the burden of both the patients and the providers, whether treatment takes place at home, in the office, or in a hospital setting.



A Look at New Modes of Diabetes Care

Special Delivery:

When Jim Malone, MD, was treating patients with diabetes, he would have 15-minute appointments, and he'd have to spend 10 of those minutes looking at the patient's handwritten logbook and then trying to decipher any patterns that might point to a need for adjustments in the treatment regimen. That would only leave five minutes for a physical exam — feet, eyes, etc. — and then finally ask the patients how they're doing. "I didn't have time to cover everything," he says.

It has been 100 years now since insulin turned diabetes from a death sentence to a manageable

condition, when Sir Frederick Banting wrote down his idea that would change the world. A little under 70 years after his discovery, the Flame of Hope was completed near Banting's house — now a museum in London, Ontario, Canada — and kindled by Queen Elizabeth. The gas-powered eternal flame is dedicated to all who have been affected by diabetes and will be extinguished the day a cure is discovered.

Still, diabetes care can be complicated, from expensive medications and devices to a lack of understanding what's expected for optimal care, whether that's on the provider or the patient. Pumps and artificial pancreas systems are great

BY DEREK BAGLEY

technology but can often be difficult to operate. So, until a cure is found, diabetologists and endocrinologists are innovating and shifting to new models of diabetes care, models that begin with making sure the clinicians have the time to cover everything and helping to make sure the patients understand how to best care for themselves, so that maybe diabetes fades into the background of these patients' lives. Until managing this disease becomes second nature, which can seem like a cure to many patients with diabetes.

Here, we'll take a look at two new models of diabetes care — one industry-driven, one policy-driven — that should benefit patients and their physicians in both outpatient and inpatient settings.

Easing the Patient's Burden

Malone, after spending 12 years in practice and then more than 20 years as a clinical researcher at Eli Lilly, is now chief medical officer at Bigfoot Biomedical, in Milpitas, Calif., a medtech company dedicated to easing the burden of living with insulin-requiring diabetes. Malone and his team have developed the Bigfoot Unity™ Diabetes Management Program, featuring innovative technologies and proactive, remote-care solutions designed to support clinicians and their population of patients with type 1 or type 2 diabetes on multiple daily injections (MDI) of insulin.

Bigfoot Biomedical co-founder and chief executive officer Jeffrey Brewer tells *Endocrine News* that he was drawn to insulin research and how to use the drug safely when his son was diagnosed with type 1 diabetes in 2002. Prior to that, Brewer was a dot-com entrepreneur, but he says in the 19 years since his son was diagnosed, he has spent the majority of his time thinking about and working on how to live safely with insulin. (His son ended up in the intensive care unit twice, each time after mistakes with doses.)

Brewer got involved with JDRF where he helped establish the Artificial Pancreas Project, an effort to use sensors, data, and algorithms to assist people with dosing their insulin. "The challenge with insulin is it is a very unique drug in that you have to determine the dose, and that requires a big obligation on the part of the person with diabetes and frankly it's just too hard," he says.

Here's how Bigfoot Unity works: When a clinic contracts with Bigfoot, they can begin prescribing the FDA-cleared Bigfoot

“The challenge with insulin is it is a very unique drug in that you have to determine the dose, and that requires a big obligation on the part of the person with diabetes **and frankly it's just too hard.**”

— JEFFREY BREWER, CO-FOUNDER AND CHIEF EXECUTIVE OFFICER, BIGFOOT BIOMEDICAL, MILPITAS, CALIF.



Bigfoot Unity's Smart Pens, which can help patients make sure they're taking the proper doses.



Unity™ System, which features connected smart caps for the patient's long- and rapid-acting disposable insulin pens that integrate with Abbott's FreeStyle® Libre 2 CGM sensor. The system is designed to help the patient follow their prescribed insulin therapy regimen. During use, there's no data entry required of the patient. The patient simply scans the sensor with the pen cap, presses a button, and gets on-demand insulin dose recommendations based upon the patient's current CGM data and their clinician's instructions.

For the clinician, the Bigfoot Unity Program provides secure, cloud-based tools to access its Bigfoot Unity patient data to remotely review therapy adherence. Data from patients are passively captured and automatically uploaded to the Bigfoot Clinic Hub™. Patient reports with integrated glucose and insulin data enable clinics to track patients at the population level, identify key patterns and triage, for example, by patients frequently experiencing low or high glucose values. "What we're doing is working to transform a primarily reactive, episodic therapy for MDI patients into a continuous, proactive approach," Brewer says. "Bigfoot Unity makes it possible for clinicians to make informed, timely therapy adjustment decisions between office visits with a goal of helping them minimize potential issues."

The company also provides Certified Diabetes Care and Education Specialists who provide patient onboarding and training for these technologies, including those patients new to CGM or to multiple daily injection therapy itself.

Patients new to CGM and other diabetes technology can often benefit greatly from some form of an "onboarding" process.

When patients with diabetes are hospitalized, that's often when the risk of hypoglycemia and hyperglycemia should come into sharper focus, but that is not always the case. In-house diabetes educators would be a big help.

One of the early patients to be prescribed the program was on a fixed-dose mealtime insulin regimen and one dose of long-acting insulin. "She got trained on the Bigfoot Unity system, was taught about correction doses, which are displayed on the pen cap," Malone says. "She doesn't need to think about her dose. Once she scans her sensor, the CGM glucose is displayed on the pen cap, and then the correction dose pops up right on the pen cap, along with her mealtime dose."

Malone goes on to say that within two weeks, this patient's average CGM reading dropped about 100 mg/dl. "Obviously not all patients are like that, but that really showed us that the system is doing what we designed it to do; help people manage their diabetes."

Supply and Demand: Endocrine Hospitalists

Of course, patients with diabetes still can find themselves in the hospital from time to time, unfortunately. When that happens, the risk of hyperglycemia and hypoglycemia should come into sharper focus, but managing patients' blood sugars and reporting on glycemic metrics has been a blind spot for many hospitals. For instance, according to the recent Centers for Medicare and Medicaid Services (CMS) report, "Although there are many occurrences of hypoglycemia in hospital settings and many such events are preventable, there is currently no measure in a CMS quality program that quantifies how often hypoglycemic events happen to patients while in inpatient acute care."



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“Patients with diabetes still can find themselves in the hospital from time to time, unfortunately. When that happens, the risk of hyperglycemia and hypoglycemia should come into sharper focus, **but managing patients’ blood sugars and reporting on glycemic metrics has been a blind spot for many hospitals.**”

In August, the CMS updated its Hospital Inpatient Quality-Reporting program, measures aimed at tracking and improving practices of appropriate glycemic control and medication management of patients, as well as avoiding patient harm leading to increased risk of mortality and disability. Hospitals have from now until January 1, 2023, to pick from 11 different Electronic Clinical Quality Measures (eCQMs) on which to report. (Two of the 11 measures are for hypoglycemia and hyperglycemia.)

Physicians and industry leaders alike seem to be amenable to and even excited about the changes. Jordan Messler, MD, SFHM, FACP, chief medical officer at Glytec, an insulin management software company that helps providers improve the quality and cost of care, in Waltham, Mass., sees these new measures improving care across the board. Even though reporting these eCQMs will initially be elective, Messler sees them as the extrinsic motivator, the regulation that will drive change and make hospital administrators aware of the fact that endocrinologists and glycemic management teams need more resources, like diabetes educators. “It’s going to get us metrics,” Messler says. “That’ll be consistent once these eventually get reported in 2024. [From the hospitals that decide to report] we’ll have some metrics here that are national benchmarks. We don’t really have that in the glycemic space. It’ll raise awareness from now on as long as metrics exist.”

“I’m thrilled,” says Mihail “Misha” Zilbermint, MD, FACE, associate professor of clinical medicine at Johns Hopkins School of Medicine and endocrine hospitalist at Suburban Hospital in Bethesda, Md. “I know that inpatient glycemic management has not been recognized.”

Zilbermint had already been the point person for reporting and coming up with action plans at Suburban, and he and his colleagues had already implemented their own Glucose Steering Committee and Inpatient Diabetes Management

Service, which saw reduced rates of hypoglycemia and hyperglycemia, as well as length of stay and hospital costs (see the June 2021 issue of *Endocrine News*). So, while the team at Suburban may be ahead of the curve, that doesn’t mean they can rest on their laurels here. Six years ago, Suburban Hospital had one of the highest rates of hypoglycemia in the entire Johns Hopkins health system. They’ve since improved, due in large part to the aforementioned steps. Zilbermint says the biggest challenge for hospitals now with these new CMS rules will be the “nitty gritty implementation on the ground.”

According to Zilbermint, for some hospitals, it may play out this way: The hospital will report the metrics, the hospital brass will see something that needs to be addressed or corrected and call the community endocrinologist in only for the endocrinologist to say, “Yeah, I’ve been telling you this for 10 years.”

Told-you-so situation or not, Zilbermint says these new measures will mean more resources for patient education, and he sees hospitals incorporating endocrine hospitalists and creating more positions in the endocrine and diabetes care spaces, which could mean big things for the specialty of endocrinology as a whole. Until now, hospitals hadn’t recognized the importance of endocrine hospitalists, assuming diabetes care can be done in an outpatient setting. A problem of supply and demand. “I think that the endocrinology fellowship will invest more in training the future generation focused on inpatient glycemic management,” he says. “So, we will increase the supply.”

This process may take years, and Zilbermint says that won’t be an easy process, and there might not be immediate results, but he hopes providers won’t get discouraged. “If you take small steps going the right direction,” he says, “I think you’re going to win big in those metrics, but also ultimately help the patients.” ^{EN}

— BAGLEY IS THE SENIOR EDITOR OF *ENDOCRINE NEWS*. IN THE OCTOBER ISSUE, HE WROTE ABOUT THE UNUSUALLY HIGH RATES OF FATTY LIVER DISEASE IN MEXICAN AMERICAN POPULATIONS COMPARED WITH OTHER HISPANIC AMERICAN POPULATIONS.

Endocrine Society Leads Insulin Affordability Advocacy in 2021

This year marks the 100th anniversary of the discovery of insulin, and despite this important milestone, the price of insulin remains too high for those who rely on it.

In 2021, the Endocrine Society has been the leading voice in the diabetes community in urging Congress to address this ongoing crisis. While our work on this issue is not finished, we have made important progress in advancing policies that would make insulin more affordable for millions of Americans living with diabetes. Our message and position have been heard by the Biden administration and Congress. Here are some of the highlights of our efforts over the past year:

- **Insulin Affordability Position Statement:** The Society published an updated position statement with recommendations to policy makers on addressing insulin access and affordability. The Biden administration incorporated our recommendations into President Biden's plan to lower the cost of prescription drugs.
- **Submitted Statement During Key Congressional Hearing:** In May, the House Energy and Commerce Health subcommittee held a hearing on legislation to lower the cost of prescription drugs. We submitted a statement to the subcommittee thanking them for holding the hearing and calling on Congress to pass legislation to make prescription drugs more affordable.



- **Clinician Hill Day:** In addition to ongoing meetings with congressional leadership by Endocrine Society staff, this past summer the Society hosted a virtual Hill Day for our clinician members to meet with their representatives and senators in Congress. During these visits, Society members urged Congress to pass legislation to lower the cost of insulin.
- **Physician and Provider Group Letter:** In September, we led a letter to congressional leadership signed by several physician and provider organizations calling on Congress to pass legislation to make insulin affordable as soon as possible.



► **Patient Stories:** We asked Society members to share stories concerning their patients' lack of access to affordable insulin. We shared a sample of the stories we collected with congressional offices to help them understand the urgency of this issue.

The Society has been successful in increasing the visibility of the issue of affordable access to insulin and influencing many policy makers that action needs to be taken this year to lower the cost of insulin. However, congressional action on drug pricing is tied to a much larger piece of legislation to advance domestic policy priorities that faces several political hurdles in both the House of Representatives and the Senate.

We will continue to raise awareness of this during Diabetes Awareness Month in November. The Society is planning to host a virtual congressional briefing in late November focusing on "100 Years of Insulin." The briefing will highlight the success of insulin over the past century but also look at the future of insulin, diabetes research, and diabetes care. Please stay tuned for more information about the briefing. Finally, we have launched an online advocacy campaign for Society members to contact your legislators directly about this important issue. Please take action today so we can keep this issue on Congress's priority list by visiting: www.endocrine.org/takeaction.



Photo: Postmodern Studio/Shutterstock.com

Member Advocacy Needed: Join Endocrine Society Advocacy Campaign to Increase NIH Funding

The Endocrine Society needs your help to urge your representative and senators to increase funding for biomedical research and pass a spending bill that delivers at least \$46.4 billion for the National Institutes of Health (NIH) in this fiscal year. The federal government is currently operating under a continuing resolution that expires on December 3, which only provides flat funding based on the previous year's allocation and prevents the NIH and other research funding agencies from starting new programs and fully funding research grants.

Join our campaign at: www.endocrine.org/takeaction to speak up for endocrine research!

KNOW HYPO

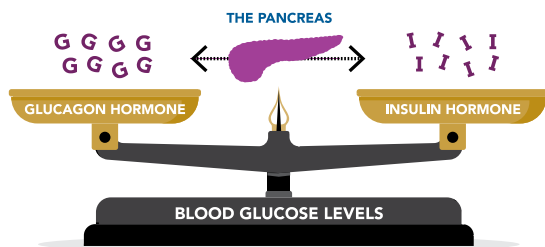
ALL ABOUT GLUCAGON

BEING PREPARED TO USE EMERGENCY GLUCAGON MAY SAVE A LIFE

GLUCAGON HORMONE

The pancreas produces a hormone called glucagon, which keeps blood glucose from **dropping too low**, while insulin is produced to keep blood glucose from **rising too high**. The two hormones counterbalance each other to stabilize blood glucose.

When someone with diabetes experiences hypoglycemia (low blood glucose), administration of glucagon can raise the person's blood glucose quickly.



SIGNS OF SEVERE HYPOGLYCEMIA

When blood glucose drops and is not addressed promptly with a fast-acting sugar source, it can lead to severe hypoglycemia.

Signs include:



CONFUSION



LOSS OF CONSCIOUSNESS

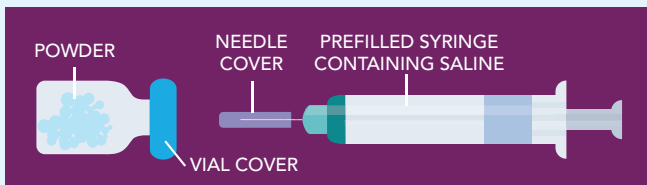


SEIZURE

When these symptoms occur, using emergency glucagon can be life-saving.

ADMINISTERING GLUCAGON

INJECTION KIT:



1. Remove the covers from the powder vial and syringe in the kit.
2. Empty the saline from the syringe into the powder vial.
3. Dissolve the powder in the saline.
4. Draw the solution back into the syringe.
5. Inject the solution into the thigh or arm of the person with severe hypoglycemia.

AUTOINJECTOR PEN:

This comes filled with a premixed form of glucagon.



1. Remove the cap and press the autoinjector against the person's skin. A dose of glucagon is automatically injected.

DRY NASAL SPRAY:

1. Insert the tip of the device into one nostril of the person experiencing hypoglycemia.
2. Push the plunger.



SCAN HERE
TO LEARN
MORE

Patients Have Questions. We Have Answers.

Hormone Health Network is your trusted source for endocrine patient education. Our free, online resources are available at hormone.org

PATIENT EDUCATION RESOURCES

EMERGENCY GLUCAGON FOR KIDS

Severe low blood sugar is a medical emergency, which is why it is important to be prepared with emergency glucagon. A pediatrician can help recommend an emergency glucagon option. The glucagon autoinjector pen is approved for use in children ages two and older. Nasal glucagon is approved for children ages four and older.

Anyone with contact to a child with diabetes should know how to spot signs of hypoglycemia, and should be ready to give emergency glucagon if needed.

These people include:



FAMILY MEMBERS



DAY CARE PROVIDERS



TEACHERS



COACHES



OTHER CAREGIVERS

CARE PROVIDER TIPS:

1



Act quickly and look for the person's glucagon medication. Call **911** if glucagon is unavailable.

2

Follow the instructions on the medicine.



3



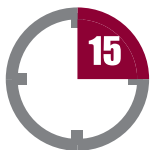
Turn the person on their side after giving glucagon. Vomiting is common, so this prevents choking.

4

Do not hesitate. People cannot overdose on glucagon, so don't worry about giving too much.



5



Call **911** if the person is **still unconscious after 15 minutes** of receiving glucagon or if they're **awake but still confused**.

CONVERSATIONS WITH YOUR HEALTHCARE PROVIDER

Do I need a glucagon prescription? If so, which product is best for my needs?

What can I do to increase my awareness of low blood glucose?

How can I treat mild hypoglycemia to help keep it from becoming severe?

What should be my or my child's target blood glucose range?



THINGS TO KEEP IN MIND



Before buying a glucagon product, make sure the expiration date is at least a year away.



Replenish used glucagon as soon as possible.



Wear a medical ID bracelet or necklace to let others know you use insulin and/or have diabetes.

PROMOTING THE ADVANCEMENT OF EARLY CAREER INVESTIGATORS

FLARE PREPARES PROMISING GRADUATE STUDENTS, POSTDOCTORAL FELLOWS, CLINICAL FELLOWS, AND JUNIOR FACULTY FROM UNDERREPRESENTED MINORITY GROUPS FOR LEADERSHIP ROLES AS INDEPENDENT BIOMEDICAL RESEARCHERS.

FLARE WORKSHOP

The FLARE Workshop is a two-day program that teaches the “business of research,” providing leadership training that addresses the unique challenges faced by early career researchers. It provides trainees and junior faculty with the skills they need to successfully market themselves for employment, transition into full-time research positions, and sustain and advance their careers.

WORKSHOP HIGHLIGHTS

- Create Your Own Individual Development Plan (IDP)
- Craft A Strong Grant Proposal
- Build Your Lab and Research Team
- Networking and Collaborations

OTHER FLARE COMPONENTS

The **FLARE Internship** provides a year of service on one of the Endocrine Society’s governance committees. Interns gain exposure to the Society’s leadership and help shape the Society’s programs.

The **FLARE Mentoring Network** offers a way to identify, connect with and build lasting relationships with accomplished scientists.

The **Early Career Reviewer Program** connects FLARE fellows interested in honing their skills as journal peer reviewers with seasoned reviewers and editorial board members to co-review journal articles.

100% of FLARE participants say they’d recommend this program to their peers and colleagues.

We are accepting applications for our 2022 workshop until December 10, 2021.

PLEASE APPLY ONLINE AT [ENDOCRINE.ORG/FLARE](https://endocrine.org/flare).

FLARE IS FUNDED BY A GRANT FROM THE NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES.

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