Diabetes Care
Teenage Life With Type 1 Diabetes
New Advances in Diabetes Care
Diabetic Nephropathy: New Perspectives
The Importance of Fracture Prevention

Features
Thoughts on Medical Education
Annual Meeting 2016
AMA Interim Meeting Report
Liability Risks in Telemedicine
Learn the latest treatments and play an important role in the care of Soldiers and their families. As a physician on the U.S. Army Reserve health care team, you’ll continue to practice in your community and serve when needed. You’ll work with the most advanced technology and distinguish yourself while working with dedicated professionals. You’ll make a difference.

For more information, visit healthcare.goarmy.com/gw69 or contact SFC Glasscock at 913-469-1702.
Editorially SPEAKING

03  Thoughts on Medical Education
   By Charles W. Van Way III, MD

Features

06  Annual Meeting 2016
   MEDICAL SOCIETY MEMBERS AND FRIENDS GATHERED TO CELEBRATE THE ACCOMPLISHMENTS OF THE PAST YEAR
   AND LOOK TO THE YEAR AHEAD

10  Report on the November 2016 AMA Interim Meeting
   BROAD RANGE OF ADVOCACY ISSUES DISCUSSED
   By The Missouri Delegation to the AMA; Submitted by Charles W. Van Way III, MD

36  As Telemedicine Expands, Understand the Liability Risks
   TELEMEDICINE PRACTICE LAWS VARY BY STATE; EVALUATE YOUR "WEBSITE MANNER"
   By Dustin Shaver, NORCAL Mutual Insurance Company

Diabetes Care: SPECIAL SECTION

13  The Burden and Benefits of Teenage Life With Type 1 Diabetes
   BEING ABLE TO MANAGE THE TRIFECTA OF MEDICINE, EXERCISE AND FOOD IS VITALLY IMPORTANT FOR TEENS
   By Amelia G. Cooper and Blake A. Cooper, MD

20  New Advances in Diabetes Care
   MONITORING SYSTEMS AND PUMPS BENEFIT TYPE 1 PATIENTS; ORAL AND INJECTABLE MEDICATIONS HELP THOSE WITH TYPE 2 DIABETES
   By Richard Hellman, MD, FACP, FACE

26  Diabetic Nephropathy: New Perspectives
   DESPITE IMPROVEMENTS IN BOTH GLYCEMIC AND BLOOD PRESSURE CONTROL, DN REMAINS A MAJOR HEALTH PROBLEM
   By Mariana Touza, MD, ASH-SCH

30  Diabetes and Bone: The Importance of Fracture Prevention in Diabetes Management
   By Betty M. Drees, MD, FACP, FACE

34  More Aggressive Treatment Needed to Address Type 2 Diabetes Epidemic
   SPEAKERS AT NOV. 17 FORUM DISCUSS POPULATION HEALTH MANAGEMENT APPROACHES TO DIABETES CARE
   By Jim Braibish

ON THE COVER:
Amelia Cooper of Kansas City with her father Blake Cooper, MD, KCMS member. See Amelia’s article in
this issue on her experience living with type 1 diabetes. (Photo by Mike Curtis)
One of the things we all have in common is our exposure to the medical education system. Now, we’ve had different experiences. Some of us are MDs, some DOs. Some have been educated in foreign schools, either in their home countries, or in international venues. And we all have opinions about our own education, and how we should be educating our successors. In my case, I’ve spent all of my career in teaching hospitals, with both residents and students. I’ve had a lot to do with medical education. Being part of the system has been something of a mixed experience.

It has been more than 100 years since the Flexner Report in 1910 condemned the general quality of medical education. The report held up as an ideal the Johns Hopkins model of university-based post-graduate physician education. Since then, this model has become almost universal in the United States and Canada, with some variations between MD and DO schools. Medicine has become totally integrated into higher education, with all that implies for the quality of medical education. All students mix classroom education with “hands-on” work in hospitals. While the level of responsibility allowed to students has decreased steadily over the past 30-40 years, students still see patients, and participate in their care.

But the model is beginning to show its age. Most obviously, it’s failed to meet society’s demand for physicians. Granted, U.S. schools have been expanding recently, but we’re still not keeping up. We have widespread shortages in nearly all specialties.

One side effect of the shortage has been the development of some 31 “offshore” schools in the Caribbean. These schools are closer to the 19th-century proprietary schools than they are to the Hopkins model. Academic classwork is in the school, instruction is in English, and clinical training usually takes place in U.S. hospitals with considerably less direct supervision than is common in MD and DO schools in the U.S. Whatever one may think about the quality of these schools, they are fully subscribed. Collectively, they turn out several thousand physicians per year.

**STUDENTS BURDENED WITH DEBT, LENGTH OF EDUCATION**

The medical education system doesn’t serve students particularly well. The cost is astronomical. The average student graduates with $200,000 of educational debt. Imagine the burden on students who marry one another. And of course, we underpay residents so badly that the debt simply accumulates. To get through the process, a student must undergo at least three high-stakes selection processes. Undergraduate college, medical school, and then residency. And maybe one or two more for fellowships. Plus, an ever-increasing number of national examinations. Small wonder that the smart kids are going into engineering or computer science.

From the student’s standpoint, the system wastes a lot of time. Four to six years of undergraduate, four years of medical school and then 3 to 10 years of residency and fellowship training. The biggest change since 1910 has, of course, been resident education. Making medicine a four-year post-graduate school was a great idea in 1910. Today, we’re piling on the years. The age of finishing resident education is up to the mid- or late-thirties. The sheer amount of knowledge required of today’s physician makes it difficult to cut much time out of medical school. UMKC manages to cut college plus medical school down to six years, so it can be done. But only one other school in the country is doing that. While other types of accelerated programs are enjoying a small surge of popularity, past surges have died out.

(continued)
SHORTAGE OF RESIDENCY POSITIONS  
(continued)  
To add insult to injury, we’re busily adding medical school capacity to a system without adding residency positions. Right now, there aren’t enough positions for all graduates. Currently, 6% of U.S. medical school graduates go unmatched, as do 50% of foreign graduates, including American graduates of Caribbean schools. Now, only about 600 of the 5,000 acute care hospitals have residency programs. And only about 300 have multiple programs. There are many hospitals which could support residency training but have chosen not to. Why? There are a lot of barriers. Many physicians, perhaps most, are unwilling to commit to the time and effort required to train residents. Patients often have mixed feelings about being cared for by residents. Most new medical schools are being established around hospitals which already have residency programs, so a new school does not mean new residency slots. Hospitals find it expensive, even with federal subsidies for residency training. The federal subsidy is capped. Although there is some room for new programs, it is very hard to expand existing programs. Lastly, accreditation for new programs is fairly difficult, as it should be.

Let’s see. Medical students are poorly served. Residents are overworked and underpaid. There aren’t enough residency slots. Does the system work well for anyone? Well, medical school faculty do well enough. I’ve had a great career as a faculty physician. They’re often overworked, but that’s true for all doctors. They tend to be underpaid relative to other physicians in the same specialty, so that’s sort of a minus. Job security is pretty good, unless you move up to a chair. Deans do very well, often making nearly as much as hospital executives. But their turnover makes mayflies look long-lived, so there’s a lot of insecurity.

Teaching hospitals are clear winners. We have built some of the world’s best hospitals and health systems around our major teaching hospitals. Locally, imagine Kansas City without KUMC, TMC or Saint Luke’s. Whatever we do to fix the system, we should preserve these institutions. Indeed, while the teaching hospital model is too expensive for all hospitals, we would be well-advised to incorporate that model into more of our non-teaching hospitals.

We do not, let me say, need a 21st-century Flexner Report. Our medical education system continues to produce bright and well-trained young physicians. Residency programs do a very good job of training both generalists and specialists. We’re doing something right. No, we’re doing a great deal right. But we need to improve. How?

RECOMMENDATIONS  
We should reduce barriers to medical education. Early commitment to medical school would help. Shortening both undergraduate and medical school would be positive. Further, it is vital to increase the number of residency positions available. Right now, we have 28,000 positions and 42,000 applicants, or one and one-half applicants for each position. There’s a long way to go. Creating more residency slots is absolutely vital. The increased number of medical school graduates isn’t going to do any good if they cannot get trained.

As noted above, the teaching hospital model is extremely strong. But it is also expensive and difficult. Many hospitals simply cannot afford to have residents, and many physicians cannot afford to incorporate teaching activities into their practices. So as we are making up our wish list, we need to address how we can incorporate teaching into more hospitals and more practices.

We should remove harassments. Right now, we require four separate tests of students, three of which are before graduation. The silliest of these is Step 2CS, which requires students to pay $1,000, travel to one of six centers, and talk with “simulated” patients to test whether they can take a history and physical. Really? Our schools are so bad that we need to test the medical equivalent of reading and writing? The pass rate is 96% for U.S. graduates, so it’s not as if the test serves any real purpose. Of course, somebody benefits. The USMLE collects in the neighborhood of $20 million a year from students taking the exam.

We should do something about debt. The national need for physicians is a serious matter. Perhaps we should underwrite medical education to a much greater degree than at present. Universities tend to view medical schools as cash cows, and medical students as captives. Of course, the problem isn’t just medical schools. Cost inflation in higher education is about twice as high as health care cost inflation, which itself is twice as high as everything else. Somehow, we need to get educational costs under control. If education is a national priority, as all politicians say it is, then why do we keep making it more expensive?

What can we do to make residency training more bearable? We’ve cut down somewhat on the workload, but it’s still very high. Pay is pretty much capped because Medicare pays for most
residency training. And of course, no hospital will pay residents more than they get from the Feds. It’s cheap labor, after all. Supply and demand doesn’t work here. It’s a controlled market. But residents still should be paid better. Paying subsistence wages to a 35-year-old professional is not going to motivate young people to follow us into medicine.

The system isn’t broke. But it’s creaking. It’s time to fix it before it DOES break.

LAST WORDS

Beginning with our next issue, Kansas City Medicine will have a new editor-in-chief, Michael O’Dell, MD, MSHA. Dr. O’Dell is past president of the Kansas City Medical Society, chair of the UMKC Department of Community and Family Medicine, and associate chief medical officer for the Truman Medical Centers Lakewood campus. He has been contributing to our journal for the last several years. I’ll let him introduce himself next issue.

I’ve been the editor for 22 years, starting back when it was the Medical Bulletin of Greater Kansas City. It’s time to pass the responsibility. Dr. O’Dell is already planning issues for next year. You’ll be in good hands.

It’s been a great time. Thanks to all of you for allowing me to serve the Medical Society for the last 22 years. You’ll still see my name on the masthead, as “Emeritus Editor.” And I will continue contributing to the journal.

Managing Editor’s Note: On behalf of KCMS, thanks to Dr. Van Way for his 22 years of commitment to providing a quality journal for the members of the Medical Society. He has set a high standard which we will work to maintain moving forward.

Charles W. Van Way, III, MD, is editor of Kansas City Medicine and is emeritus professor of surgery at the University of Missouri-Kansas City, and director of the UMKC Shock Trauma Research Center. He can be reached at cvanway@kc.rr.com.

REFERENCES:

EXCLUSIVE OFFER FOR KCMS MEMBERS

Save Up to 25% on Medical Malpractice Insurance Rates

Kansas City Medical Society has partnered with the Keane Insurance Group to offer members significant discounts up to 25%* on medical malpractice insurance rates. Members can benefit from great rates, with coverage from a national carrier with an A.M. Best “A” (Excellent) rating and access to award-winning risk management CME activities.

Contact Tom McNeill to learn more. 816.474.4473 | tom.mcneill@keanegroup.com

*Program available to physicians in good standing with KCMS. Discounts subject to underwriting approval.
Stephen Salanski, MD, KCMS 2016 president, reviewed highlights of 2016:

• Educational programs included a May 10 seminar on population health management featuring Scott Conard, MD, from Dallas, and a Nov. 17 program on diabetes led by Kevin Pantalone, DO, of the Cleveland Clinic.
• A joint Vaccination Task Force was formed with the Wyandotte-Johnson County Medical Society in summer 2016 which conducted a campaign to promote vaccination against HPV.
• The Medical Society supported Tobacco 21 legislation which (as of the annual meeting) had been passed in 18 communities in the Kansas City area.
• KCMS also passed a resolution supporting formation of a prescription

Clockwise from top left: Victor Smecher, PhD; Stephen Salanski, MD; Angela Bedell; Ravi Johar, MD; Gary Pettett, MD; Jeffrey Burns, MD.

ANNUAL MEETING 2016

Medical Society members and friends gathered to celebrate the accomplishments of the past year and look to the year ahead at the 2016 KCMS annual meeting on Sept. 14 at the National World War I Museum and Memorial
drug monitoring program in Jackson County.

• Improved coordination of MetroCare programs for the uninsured and underinsured in the area has been advanced by KCMS.

• Many legislative advocacy successes were achieved in conjunction with the state medical associations, including Kansas passage of minors’ restrictions on tanning bed access.

• Regular member communications include *Kansas City Medicine*, a weekly e-news, the KCMS website and Facebook page.

  Angela Bedell, CAE, executive director and CEO, noted that Medical Society membership has grown to 3,600 area physicians.

  **Jeffrey Burns, MD**, from The University of Kansas Medical Center, discussed the formation of the KC Memory Strings Alliance to recruit volunteers for Alzheimer’s disease research. The effort is supported by the Global Alzheimer’s Platform (GAP) Foundation.

  Guest speaker **Victor Strecher, PhD, MPH**, from the University of Michigan School of Public Health, shared his research—and life experiences—showing how living with a purpose in life has a profound effect on one’s health, longevity and energy level. He encouraged physicians to think about their purpose and the benefits they give to patients and society.

  Accepting 2016 KCMS awards were:

  • **Gary Pettett, MD, FAAP**, *Lifetime Achievement Award*
  
  • **Glenn R. Hodges, MD**, *Community Service Award*
  
  • **Bridget McCandless, MD, MBA, FACP**, *Patient and Community Advocate Award*
  
  • **Casey Willimann, MD**, *Rising Star Award*

(continued)
2016 KCMS ANNUAL MEETING

Jeffrey Burns, MD; Mark Cohen, MD; Gaye Cohen

Troy Sydzyik; Brian Mahoney, DO; Michelle Haines, MD; Mike Haines; Carole Freiberger-O'Keefe, DO; Patrick O'Keefe, MD

Ellen and John Goheen, MD; Richard Hellman, MD

Stephanie Bush of NORCAL Insurance; Tom McNeill of Keane Insurance Group

Robert Caffrey, MD; Kathy Caffrey; Grace Albano, MD

Thomas Allen, MD; Michael O'Dell, MD; Marc Taormina, MD; Tony Sun, MD
Your Missouri Delegation to the American Medical Association continues to have a strong voice in the AMA, because in our midst is President-Elect David Barbe, MD, of Mountain Grove, Mo. Our neighbor, Richard Warner, MD, of Overland Park, Kan., currently serves as president of the Organization of State Medical Association Presidents (OSMAP). As usual, other members of the delegation have served in various ways. Dr. Van Way, your correspondent, served on the Committee on Rules and Bylaws, which performs several functions at the meeting itself.

The AMA has two meetings each year. This Interim Meeting, held this year in November in Orlando, Fla., is intended to focus on the political and legislative arena. Advocacy is its purpose. The results of the Nov. 8 national election, a week before the meeting, stirred up the House of Delegates (HOD). Few had expected the result.

AMA President Andrew Gurman, MD, and Executive Vice President James Madura both spoke. They expressed relief at the end of the awful election campaign, and optimism going forward. A public statement released by Dr. Gurman committed the AMA to working with the new administration, and to the “core principle” that “any new reform proposal should not cause individuals currently covered to become uninsured.” Disturbingly, there seemed little acknowledgement by the leadership that the Affordable Care Act has failed in many respects, and should be fixed.

A highlight of the meeting was the presentation of the AMA’s highest award, the Meritorious Service Award. This year, it was given to Bennet Omalu, MD, who discovered of the new disease of chronic traumatic encephalopathy. Chronic brain injury (CBI) has changed our views of such disparate subjects as professional football and military casualties. Dr. Omalu was met with opposition from the National Football League, medical experts, sports figures, and even some universities. Dr. Omalu expressed his gratitude for the support of the AMA. His passionate acceptance speech was given a standing ovation.

The Reference Committee on Constitution and Bylaws considered several issues, including end-of-life care, ethical conflicts of employed physicians, and the definition of female genital mutilation (FGM). The Board of Trustees has recommended increasing specialty society representation, and further increasing the relative representation of the larger societies, such as the American College of Physicians and the American College of Surgeons. Shifting the HOD further towards specialty organizations has risks, and is opposed by many. The HOD approved this recommendation, and it will be implemented. Stay tuned.

Reference Committee B considered many legislative and regulatory issues. Physician offices have been classified by the FDA as “compounding facilities,” and are now subject to a whole host of regulations. A resolution was passed to lobby the FDA to change this classification. The AMA is already working on the problem. Falsely adding physicians to the National Data Bank was highlighted. Documentation using the problem-oriented medical record is still not recognized as valid by CMS. Using SOAP may cause denial of payment. And then we have MACRA.

MACRA UPDATE

In 2015, the Medicare Access and CHIP Reauthorization Act (MACRA) eliminated the SGR formula. But it then created new ways for paying physicians: Merit-Based Incentive Payment Systems (MIPS) and Alternative Payment Models (APM). To make things more confusing, MACRA is now re-named QPP, Quality Payment Program. The final rules have just been released and will take effect in January 2017. All that said, pushback from the AMA has softened the blow somewhat. Smaller practices may be able to exempt themselves from the requirements. Required reporting measures have been made simpler. There is more...
Physicians will be able to participate to different degrees in the program next year and will not, at least in the short term, be exposed to losing money. This is a work in progress. MACRA passed Congress with large bipartisan majorities. It is unlikely to go away, although ongoing modifications are very likely in the new political environment.

Unfortunately, many physicians simply don’t realize this is coming. Many have delegated this to practice managers. Others are involved in group, corporate, or employed practices. There was widespread concern that practices will be hurt by their failure to prepare for reporting. Much information is available on the AMA website, https://www.ama-assn.org/practice-management/understanding-medicare-payment-reform-macra, as well as from the CMS website at https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/Value-Based-Programs/MACRA-MIPS-and-APMs/MACRA-MIPS-and-APMs.html.

RESOLUTIONS ON MOC, INTERNATIONAL STUDENTS

One Missouri resolution was considered. This asked for a study of extension of the Family Medical Leave Act to businesses now exempt. The intent clearly was to advocate extension. The resolution was amended to “encourage” study. We may find out in another few months whether or not the AMA thinks this is a good idea.

Committee C considered medical education. Maintenance of Certification (MOC) was again a major concern. Besides several resolutions, there were several presentations about the problems with MOC. One of our colleagues from Oklahoma, Woody Jenkins, MD, presented the successful opposition of physicians to an attempt in the legislature to mandate MOC as a condition of licensing. A strong resolution committed the AMA to promote state legislation and hospital staff bylaws discouraging the use of MOC status in decisions about licensure, hospital privileges, and re-credentialing. Missouri medical students were instrumental in adopting a policy encouraging mental health screening and treatment for medical students and residents.

Committee F considers finance and governance. A resolution was adopted calling for financial oversight and audit of the American Board of Internal Medicine, other medical boards, and the American Board of Medical Specialties. This reflects a profound distrust of the accrediting boards, in part driven by their expansion of MOC.

Committee J considers medical practice issues. There was particular interest in the plight of medical students and residents who are protected from deportation under Deferred Action for Child Arrivals. DACA, enacted by executive action in 2012, has resulted in a number of students entering medical education. There are 31 such individuals in medical schools, and perhaps as many more in residency programs. If DACA is abolished, as seems likely, these students will likely be unable to complete their educations. The HOD voted to advocate for their exemption from any changes in DACA.

Another resolution concerned communication among physicians in the age of compartmentalized EHRs, strongly advocating for improvements in interconnection and transparency. There were resolutions about ensuring equal access to high quality care, in such disparate settings as veterans, same-sex couples, prisons, and breast reconstruction. A very popular resolution called for insurance plans to collect co-pays and deductibles from their plan enrollees, rather than requiring doctors to do it for them. Good luck with that.

Committee K studies issues of science and public health. Probably the most controversial was a resolution that the AMA cease to oppose the legalization of marijuana, as was done in a number of states in the last election. The question was referred to Council. It was said that a report from the National Academies of Science, Engineering, and Medicine will be released in the next few months. Expect further debate at the next Annual Meeting in June 2017.

As usual, a number of resolutions were passed to make small improvements in the practice of medicine and public health. There were brisk discussions on such issues as opioid abuse, early childhood education, neuropathic pain as a new diagnosis, environmental exposures to lead and to polycyclic aromatic hydrocarbons, and youth incarceration in adult prisons. There was concern over the October 17 action by the DEA which mandates a 25% decrease in opioid production. This action is very likely to have unintended adverse effects. Graphic warning levels on tobacco packages were strongly supported, although these have not survived court challenges in the past.

The Physicians Foundation of (continued on next page)
AMA REPORT (continued)
the AMA supports physicians and health care in general. It has been particularly active in the area of costs. A recent book by the late Richard Cooper, MD, Poverty and the Myths of Health Reform, is a must-read for anyone concerned with the continuing rise in health care costs. The Foundation’s biennial physician survey was completed in 2016. Almost two-thirds were pessimistic about the future of medicine. The major sources of dissatisfaction were paperwork and third-party interference with the practice of medicine. The major source of satisfaction was their relationships with their patients. The direction of future AMA advocacy should be obvious.

Firearm-related injuries remain a health concern of the AMA. There were resolutions to further regulate firearms. Perhaps the best of these was a resolution to facilitate studies on firearm injuries and interpersonal trauma. Research in this area has not been funded by the federal government, for a variety of reasons which include political pressure. Current and proposed legislation continues to be guided by untested assumptions. Debates about restrictions and other measures to reduce gun violence are singularly uninformed by data.

Surprisingly little attention was paid to graduate medical education. No one at this meeting appeared to be very concerned that we do not have enough training positions. We cannot accommodate even all U.S. graduates, much less international grads. There is a growing number of young physicians who can neither work nor pursue further training. The lack of training positions has become a barrier to increasing the physician workforce. A report on this issue is forthcoming, and we may expect more action on this issue at the Annual Meeting in June 2017.

Charles W. Van Way, III, MD, is editor of Kansas City Medicine and is emeritus professor of surgery at the University of Missouri-Kansas City, and director of the UMKC Shock Trauma Research Center. He can be reached at cvanway@kc.rr.com.

MSMA Convention in Kansas City March 31-April 2

Take advantage of a host of learning and networking opportunities close to home at the 2017 Missouri State Medical Association annual convention Friday, March 31 through Sunday, April 2 at the Sheraton Kansas City Hotel at Crown Center.

Convention general sessions Friday and Saturday feature educational speakers on pertinent issues. The House of Delegates will vote on resolutions about matters affecting medicine. There will be special section meetings and receptions for young physicians, various medical school alumni groups, international graduates, residents/fellows and more. Social events include the MSMA Foundation fundraising dinner and the MSMA president’s reception.

Registration is open to both MSMA members and non-members. For more information and to register, visit www.msma.org/annual-convention.
THE

burden & benefits of teenage life

WITH TYPE 1 DIABETES

BEING ABLE TO MANAGE THE TRIFECTA OF MEDICINE, EXERCISE AND FOOD IS VITALLY IMPORTANT FOR TEENS

REPRINTED WITH PERMISSION FROM THE SEPTEMBER/OCTOBER MISSOURI MEDICINE

photos by Mike Curtis
Thank you to the editors of *Missouri Medicine* for inviting me to write this article and share my experience as a teenager with type 1 diabetes. By writing about diabetes from a young patient’s perspective, I hope I can bring insight based on my experience with what works, what does not, and how to keep motivated.

Diabetes management is a daily burden. By using the most up-to-date medical devices as well as being proactive with diet and exercise, the disease is manageable. Burnout from this rigorous regimen is common and keeping engaged and upbeat is a big issue—especially for teenagers.

In July 2012 at age 12, I was diagnosed with type 1 diabetes (T1D). That summer was very hot in Missouri, but I was drinking even more water than my friends—several large glasses an hour. Without any family history of this chronic disease, the diagnosis was a complete shock to my family and me. While my friends worry about homework, social events and the latest fashions, I have the added stress of blood-sugar control. Diabetes is unrelenting, yet manageable, and it has altered the shape and trajectory of my adolescence. With tremendous support of friends and family, and by utilizing state-of-the-art technology, I have been able to successfully navigate this stage of my diabetic management. I have also journeyed into scientific research and advocacy with a goal of the betterment of T1D care.

My diagnosis came out of the blue. I was scared and overwhelmed in the hospital during my inpatient stay. While I would not have believed it at the time, I was actually much luckier than most kids in my situation. Kansas City has the nationally famous Children’s Mercy Hospital with superb pediatric endocrinologists. My dad is an ophthalmologist, so the new medical jargon of diabetes was easy for him to understand. Perhaps most significantly, my mom fought for me to get an insulin pump and a continuous glucose monitor (CGM) as soon as possible. Most insurance companies make a patient wait six months to get an insulin pump and a CGM, but I received mine within six weeks.

The insulin pump and CGM allowed me to quickly establish a new, relatively manageable routine and to continue doing well at school. Still, school started only four weeks after my diagnosis, and this was all new, so I had a couple weeks of finger pricks and insulin shots during the school day. While I waited for my CGM and insulin pump, my mom had to check my blood sugar a few times each night and wake me up for correction shots or to drink juice. With an insulin pump and CGM, most of those nightly disturbances are avoided. Having diabetes is exhausting enough without waking up three or four times per night to test and correct a high or low blood sugar!
Also, with the insulin pump, I did not have to endure a shot just to eat a snack with my class. More importantly, the CGM alerted me when my blood sugar started trending up or down, allowing me to adjust my basal rate (hourly dosage of insulin), give myself a correction bolus or eat a piece of candy. The CGM is also vital for my sport, cross-country running. With it, I could plan how much I needed to eat before practice each day and feel confident that I would be alerted to a dangerous low while running. Luckily, my two cross-country coaches were very supportive and interested in helping me do well. They even carried Skittles with them at all times in case I needed a sugar boost.

Particularly in middle school, my teachers and principal were very involved in my diabetes management. Without a school nurse, their willingness to learn about diabetes and the treatment of low and high blood sugar as well as the use of a glucagon pen were particularly important. My dad met with the middle-school administrators and all six of my teachers, and gave them a half-hour lesson on type 1 diabetes and its management. All of my teachers keep glucose tablets in their desks, and my friends and sister carry glucose tab keychains on their backpacks. There are now five kids in my high school (of 400 students) with type 1 diabetes so I can always ask one of them for help as well. We definitely keep an eye out for each other.

Eighth grade students at my school engage in a one-day “internship.” My dad had met people from the blog Diatribe (www.diatribe.org) at an endocrinology conference and was very impressed with their work. Since their offices are in San Francisco, where my grandma lives, my dad and I decided to spend a day with Diatribe. This intelligent group of young professionals is working hard to improve health and education and how it affects diabetics (both type 1 and type 2). Many Diatribe staffers are type 1 diabetics. They are proactive. Only if you have ever experienced a high blood sugar reading followed by the excruciatingly long wait for insulin to take effect, would you understand the “light bulb” moment when I saw someone in the Diatribe office treat his high blood sugar with a quick jog. Diatribe asked me to write for their online publication. I chose “Top Ten Things I Wished My Parents Knew When I Was Diagnosed.” It was so exciting to see my name attached to an article in a professional journal. I began to recognize some upside of living with type 1 diabetes and finding my voice.

By this time, I was realizing that I was better off than some of my peers with diabetes. My mom and the moms of my closest friends have learned to cook low-carb meals. My dad runs with me on the weekends and my mom manages my insulin pump and CGM at night. My sister Lilly never complains about the absence of bread in our house. Being able to manage the trifecta of medicine, exercise and food is vitally important for teens. I decided to volunteer as a junior ski instructor for a type 1 diabetes camp to teach kids (continued on next page)
AMELIA COOPER (continued)

how to juggle these things while skiing. Two of my non-diabetic friends came along for the three-day camp. Together, we checked blood sugars in the cold Wisconsin weather. This experience inspired me to investigate how altitude and cold weather affect glucose management. That same year, during an independent-study week at our school, two of my closest friends and I conducted an experiment that tested the effects of altitude on blood sugar. Our results showed that higher altitudes did affect my blood-sugar levels, while those of my non-diabetic peers were not affected at all. I was surprised to find that at sea level, my blood sugar average was extremely close to that of my friends.

These results gave me hope that with proper management, I can be just as healthy as a non-diabetic person. Our experiment and findings were presented as an abstract at the American Diabetes Association (ADA) annual meeting in June 2015. The success of our first experiment prompted my friends and me to conduct another experiment. This time we examined the relationship between stress (cortisol levels) and blood-sugar levels. We each wore a CGM during the day of a mid-term exam and again during a relaxed day during winter break. Our results showed that while stress did not affect the blood sugars of non-diabetics, stress did elevate my blood sugar considerably. Our stress-cortisol levels were similar during our ski week. This emphasizes the importance of diabetics proactively lowering and managing stress. This second project was selected for a poster presentation at the August 2016 American Academy of Diabetes Educators meeting. (See sidebar.)

I have become active with the Kansas City Juvenile Diabetes Research Foundation (JDRF). When they opened up applications to attend the Biennial JDRF Children’s Congress, I jumped at the chance to apply. When I was selected, I was thrilled for the opportunity to be an advocate for the JDRF in Washington D.C. I was able to experience the intricacies (and frustrations) of government first hand. To prepare for our congressional meetings, the delegates went through a “Hill Blitz” training session. We learned how to thank members of Congress for renewing the Special Diabetes Program, and how to encourage co-sponsorship of certain diabetes bills. On the Hill, I spoke with U.S. Senators Roy Blunt and Claire McCaskill and U.S. Representative Emanuel Cleaver II. I was selected to testify before the Senate Special Committee on Aging to tell my story about the challenges and rewards of young people living with T1D. See my testimony here: http://www.c-span.org/video/?c4544517/amelia-coopers-testimony. This experience invigorated me to stay healthy and advocate for medical research funding.

Unfortunately CGM technology is still not available to Medicare patients. While 95% of private medical insurers cover the costs of CGMs, Medicare lags behind. This is a huge problem for older type 1 diabetics who are at a greater risk of severely low blood sugars. As diabetics age, these low blood-sugar levels are difficult to sense with the normal physical cues (sweating, shaking, disorientation, etc.). I strongly support the necessity of CGMs for short-term and long-term health in diabetic patients. With continued work, I hope the Medicare CGM Act becomes law.

The T1D Exchange Clinic Registry’s mission is to “improve the lives of all people touched by T1D by facilitating better care and accelerating new therapies through a collaborative data collection and sharing network.” In May 2015, the Exchange published in Diabetes Care hemoglobin A1C data from more than 16,000 patients ages 2 to 95. Sadly, my peer group in the registry did the worst. Adolescents
Averaged a 9.0% A1C compared with the 9.5% registered by the same age group two decades ago. The American Diabetes Association recommends that adolescents should have an A1C that is lower than 7.5. Even with all that is available, many teenagers still struggle with managing their diabetes.

I am positive and a hard working optimist. I believe that not only universally available better treatment is in store but eventually a cure for all forms of diabetes.

Blake Cooper, MD

Comments from Amelia’s Father

As a vitreoretinal surgeon, I spent my first decade of practice helping patients with advanced complications from diabetic eye disease. I understood the pathophysiology of how and why patients lost their vision. I was even able to halt the progression or at times reverse the damage of diabetic eye disease. I have been fortunate to practice during a time when anti-VEGF agents and small gauge vitrectomy surgery were developed. This has dramatically improved the outcomes for my diabetic patients.

What I did not understand was what it was like for my patients to live with diabetes and how they got to the point of developing visual loss. I will never fully know this, but over the last few years caring for my child with T1D, I am beginning to have a better understanding. I truly believe that this has made me a better practitioner. As a physician, I want to be able to “fix” my patients. As a parent I want to protect and “fix” the problems my child faces. With this in mind over the last four years, I have realized that “fixing” diabetes means trying to figure out a way to reduce the treatment burden and (continued on page 18)

Diabetic High School Student Conducts and Presents National Research

Amelia Cooper, age 17, a type 1 diabetic and a student at The Pembroke Hill School in Kansas City, is shown with educational posters at the annual meeting of the American Association of Diabetic Educators. She presented three posters highlighting original research done by her, other non-diabetic student collaborators and her father Blake Cooper, MD, a retina specialist.

One poster was entitled, “The Effects of Stress on Glycemic Control in a Type 1 Diabetic Compared to Age-Matched Control Group.” In this study, Amelia and non-diabetic friends measured blood sugars by continuous glucose monitoring (CGM). They measured their salivary cortisol levels and completed a Perceived Stress Scale survey to determine their stress levels. Measurements were taken during the week of mid-term exams and later during winter break when they went skiing. They concluded that diabetic blood sugars were negatively affected by the stress of finals while non-diabetic blood sugars were not.

“Comparative Use of Smart Watches with Continuous Glucose Monitoring During Alpine Skiing” was the second reported study. Skiing is an excellent form of exercise. It comes with challenges especially for a person with diabetes.

The ability to check blood sugar when cold, vasoconstricted and fatigued is difficult. A CGM makes this task easier. Coupling a CGM and smart watch makes blood sugar available at a glance. The high school students compared the usefulness and reliability of the Pebble and Apple Watch to the Dexcom receiver. They found both smart watches gave accurate results. This was their most popular poster.

The last poster featured research done with her ophthalmologist father. It was titled, “Knowledge Base of a Typical Diabetic Patient Seeking Care in a Vitreoretinal Surgeons Office.” They surveyed 100 consecutive type 1 diabetic patients evaluating their level of diabetic knowledge, then compared their results to their levels of diabetic retinopathy. The results identified the highest level of diabetic knowledge among type 1 diabetics who had the disease for less than five years, showed no active signs of diabetic retinopathy and exercised daily. Higher scores were found in patients with a recent HgA1c between 7-9 than in those who had an HgA1c below 7 or above 9. The survey was also used to direct educational efforts and correct incorrect knowledge in the diabetic survey takers.
AMELIA COOPER (continued)

minimize the complications of hyperglycemia.

To this end I attend several endocrine meetings each year trying to learn as much as possible. I am searching for a cure for my diabetic daughter but also a better understanding of how to help all patients with diabetes. It is truly amazing the progress and change that have occurred since I finished my training. During pharmacology in medical school, I only had three classes of antihyperglycemic agents to learn. Now there are a least 12 different classes of medications with an ever-expanding number of combination drugs. This means better options and outcomes for our patients.

I would love nothing more than to never have to treat another patient with diabetic eye disease. Sadly, that day is not in the near future. I do believe that in the future preventing diabetic eye disease will be possible. The future is promising for patients that are able to access the best care we have to offer. Sadly, only about half of the patients that need care are receiving it. Also many diabetics are not invested with adhering to optimal self-care (e.g. management, nicotine use, exercise, weight, diet, etc.) We can and must do better. The hardest part is getting

Memory Strings Kansas City Alliance Promotes Alzheimer’s Research Participation

The University of Kansas Alzheimer’s Disease Center (KU ADC) and the Global Alzheimer’s Platform (GAP) Foundation are calling on area physicians and community members to support research efforts by recruiting patients for clinical trials. Called the Memory Strings Kansas City Alliance, the effort seeks to raise awareness of the importance of brain health and increase volunteer enrollment in Alzheimer’s disease clinical trials, especially among healthy volunteers.

Physicians are asked to refer patients who would be good candidates for the program, and offer Memory Strings Kansas City Alliance literature in their offices. KU ADC will assess patients for trial participation and provide Alzheimer’s information, classes and resources—regardless of patient volunteer enrollment eligibility. Patients will receive ongoing information about brain and memory health, support services from professionals, and access to health and wellness programs.

With more than five million Americans today living with Alzheimer’s disease—including over 55,000 in the Kansas City area—and the number expected to grow to nearly 14 million by 2050, there remain no cures or disease-altering therapies for this condition. Clinical trials are essential to develop these therapies, and the first patient to have an effective treatment for Alzheimer’s will be a clinical trial volunteer. Ninety percent of what is known about Alzheimer’s has been discovered in the last 15 years, and there are over 100 potential therapies currently in development.

However, the vast majority of Alzheimer’s trials are delayed due to low enrollment, which slows the trial process and increases costs. Surveys show a majority of Americans are willing to consider participating in a clinical trial for Alzheimer’s.

“The Medical Society strongly encourages physicians to support the Memory Strings Alliance,” said Medical Society 2016 President Stephen Salanski, MD. “Only by completing the needed research can we hope to find a cure for Alzheimer’s.”

To learn more and get involved, contact the Memory Strings Kansas City Alliance team at KU ADC by emailing kcmemorystrings@kumc.edu or calling 913-588-0555. Ask for Carroll Oliver or Michelle Cochran.
The boards of directors of the Kansas City Medical Society and the Wyandotte-Johnson County Medical Society are discussing a merger of the two societies. The goal is to create a unified advocacy voice for physicians in the metropolitan Kansas City area, as well as achieve administrative cost savings.

KCMS currently has 3,600 members and covers Jackson, Clay, Cass and Platte counties in Missouri. WyJo has about 600 members in its two Kansas counties. Some physicians are members of both societies.

Planning is underway for a transition that would occur in August 2017. A final determination on the merger is expected by March.

In a related matter, KCMS is conducting a search for new office space in Kansas City to replace the current Country Club Plaza space. The move would take place in 2017.

Ortho Urgent Care Now Open in Leawood

The Kansas City Orthopaedic Institute has opened an Ortho Urgent Care center at its location in Leawood. Open during evenings and weekends, the center provides walk-in access to specialized care for urgent orthopedic injuries.

Conditions treated include fractures, sprains, strains, torn ligaments, muscle contusions and minor lacerations. Center hours are weekday evenings from 5:30 to 9 p.m., Saturdays 9 a.m. to 6 p.m., and Sundays noon to 6 p.m. For concussions and major orthopedic trauma that threatens life or limb, patients should continue to call 911 or go to the nearest emergency room.

“We recognize the need for treatment options beyond traditional urgent care or emergency rooms, where orthopedic specialization may be lacking,” said Charles Rhoades, MD, CEO of the Kansas City Orthopaedic Institute and KCMS member. “Expanding our services to include Ortho Urgent Care allows us to better serve our community’s need for convenient after-hours care while building on our commitment to orthopedic excellence.”

For more information about Ortho Urgent Care, visit kcoi.com/urgentcare or call 913-319-7633.

As the area’s first and only hospital dedicated exclusively to orthopedics, Kansas City Orthopaedic Institute provides comprehensive orthopedic care, from diagnostic imaging to inpatient and outpatient surgery, pain management services, and rehabilitation therapy. Kansas City Orthopaedic Institute is a physician-owned specialty hospital and a joint venture with Saint Luke’s Hospital.
INTRODUCTION

The story of Amelia Cooper highlights the fact that one of the important new advances in diabetes care is the great improvement in access to high-quality diabetes specialty care teams for the pediatric population with diabetes. As a result, many children and adolescents with diabetes have had access to new treatments and technology which have helped them lead healthier and less stressful lives. Kansas City should be very proud that Children’s Mercy Hospital has provided a successful comprehensive program for these patients with both expert medical and behavioral care for the majority of the pediatric diabetes population in this area. This greatly needed support has made a difference, because, as has been shown repeatedly, comprehensive diabetes care, when combined with an intensive approach to glycemic control, reduces complications and deaths in both type 1 and type 2 diabetes.1,2,3,4

From the time the first patient, Leonard Thompson, received the first injection of insulin in 1922, the process of lowering blood glucose has always been complicated by the fact that if we use a highly potent glucose lowering agent—the most powerful being insulin—we may overshoot and cause hypoglycemia. We have always wanted to provide our patients and our providers of care, be it parent, nurse, or physician, with a timely method for measuring glucose, preferably at the point-of-care (POC).

Beginning in the 1970s, POC glucose meters have gradually become more accurate5 and easier to use, but still the methods continued to be painful, intrusive and dependent upon someone having the awareness that a measurement of blood glucose was needed, and taking the time to measure it. For our patients with type 1 diabetes, it became clear that even when checking their capillary blood glucose levels as often as 6-10 times daily and using continuous subcutaneous insulin infusion pumps (CSII), good control was difficult, since when the glucose control became more stringent, hypoglycemia tended to occur more often. It was clear that a new technology was needed to provide real-time, on-demand, nearly continuous information on glucose levels so one could know not just what the glucose level was at a point in time, but what the rate of change was, thereby making a more appropriate response easier and more likely to be successful.6

In 2008, a landmark study from the Juvenile Diabetes Research Foundation showed the power of such continuous glucose monitoring (CGM) systems, showing that if patients used CGM at least 80% of the time, the average glucose levels as measured by HbA1C could be lowered without causing more frequent hypoglycemia.7 These CGM devices have continued to improve since then and have made possible some remarkable advances. One can now make the case that because of the advances of CGM, 2017 may prove to be one of the most pivotal years in diabetes care.8

These CGM devices have continued to improve since then and have made possible some remarkable advances. One can now make the case that because of the advances of CGM, 2017 may prove to be one of the most pivotal years in diabetes care.9

TYPE 1 DIABETES

Many of us have already heard about the research on the so-called “artificial pancreas,” alternatively called

New Advances in Diabetes Care

MONITORING SYSTEMS AND PUMPS BENEFIT TYPE 1 PATIENTS; ORAL AND INJECTABLE MEDICATIONS HELP THOSE WITH TYPE 2 DIABETES

By Richard Hellman, MD, FACP, FACE
the “bionic pump.” The best known study was published in 2014, although it was neither the first nor the only study. In 2014 Edward Damiano and his colleagues published a key study in the New England Journal of Medicine, showing how a wearable bihormonal pump (Tandem Diabetes Care), linked to a subcutaneous CGM device (Dexcom G4), when linked to a hand-held device (Apple iPhone 4s) with software to control the delivery of either insulin or glucagon from the bihormonal pump, was able to keep glucose levels for 20 adults and 32 adolescents in a near-normal range for five days, without any severe hypoglycemia in nearly all the patients they studied.8 This was a personal as well as scientific triumph for Damiano, because one of the adolescents in this study was his son. The pump used in this study was automated for the full five days and the decisions were based on the glucose data received. The insulin or glucagon infusion rates were adjusted every five minutes by the automated control device. This was made possible because each element of this system was communicating wirelessly, in synchrony with each other. It was a remarkable achievement.

Since that study in 2014, his group has extended their work with a large multi-center, multinational study that is measuring the long-term use of their system on patients with type 1 diabetes. This important study should be completed either in 2017 or 2018. However, Damiano’s group is only one of many investigator groups in many countries, but particularly in North America and in Europe, each of whom are working at a feverish pace to prove the value of their alternative solution to better glycemic control for type 1 diabetes.9,10 The problem each of them face is how to get a system to provide near-normal or normal glycemic control without excessive hypoglycemia. The goal is to make it possible for patients with type 1 diabetes to maintain optimal glycemic control so they can go about their lives without having to spend the amount of time and effort currently required to perform the exacting self-care that must be done in order to be successful.

The new CGM systems are so accurate that the FDA approved the application of one manufacturer, Medtronic, to integrate their CGM technology into a hybrid closed loop insulin-only pump which will run automatically overnight without requiring other glucose monitoring.

Although his study has received the most attention, in fact Damiano was hardly the first researcher to have positive results. Several European studies in 2011 used closed loop devices, and another report published in the New England Journal of Medicine in 2013 from Israel showed the utility of an alternative closed loop system, using only insulin, for overnight glycemic control, a so-called hybrid closed loop (insulin only) system.11 Many researchers first chose to not focus on having a pump that would control the glucose levels over the full 24-hour period, but instead chose a simpler task to focus as the Israeli study did on overnight control. Most researchers are using only insulin for their closed loop devices.

The overnight period is of great importance to the person with diabetes, for unrecognized nocturnal hypoglycemia can have devastating consequences. The systems that focused on the overnight period attempted first to prevent nocturnal hypoglycemia, but also to warn the patient if the level became dangerously low. A recent advance in insulin pump technology, termed a “low glucose suspend” feature (LGS), allows subcutaneous insulin pumps to automatically turn off for two hours when the glucose level reaches a certain threshold of hypoglycemia. Pumps with this feature are called sensor-augmented pumps. Although this has been very helpful, the pumps that provide adjustment of insulin delivery downward when the glucose level begins trending down should be even more helpful.

But it is also important to put into perspective that hypoglycemia can be a danger at any time. In fact, whenever the person with diabetes is busy, or distracted, or has hypoglycemic unawareness (a common problem for our patients both young and old, and in both type 1 and type 2 diabetes), then undetected hypoglycemia can cause serious accidents, injury or death.

Underpinning the advances of the more sophisticated insulin pumps and the closed loop, or bionic pumps, are the great advances made in glucose
monitoring, particularly the CGM. Without CGM technology, no closed loop systems could be feasible. In the last six years, CGM has been shown to be of enormous value in preventing both nocturnal hypoglycemia as well as hypoglycemic events throughout the day. As a result, interest in CGM and related technologies has increased greatly. Many patients now use subcutaneous insulin pumps which are capable of receiving and displaying CGM data, but do not have, unlike sensor-augmented pumps, an LGS feature. These pumps are termed sensor-integrated insulin pumps.

The new CGM systems are so accurate that on Sept. 28, 2016, the Food and Drug Administration (FDA) approved the application of one manufacturer, Medtronic, to integrate their CGM technology into a hybrid closed loop insulin-only pump which will run automatically overnight without requiring other glucose monitoring. This pump (Medtronic Minimed 670G), which is due to be marketed in the United States in March 2017 for use in patients 14 years of age or older, will adjust the insulin dose so as to keep the glucose levels in the near normal range without hypoglycemia overnight, when the patient is most vulnerable.

During the day, however, the pump will not be in an automatic mode, functioning instead in the current mode of a sensor-augmented pump. During waking hours, the patient manually orders and initiates meal and correction insulin doses and monitors their glucose levels using the display module on their pump. With the exception of the LGS function, it remains the patient’s responsibility to respond correctly to the glycemic values they see. It is likely that both Dexcom and Abbott, two rival companies, will also receive similar approval for their CGM devices from the FDA in the coming months, and others are expected to follow soon.

In the next year or two we expect to see a number of closed loop systems reach the market. It is likely that there will be hybrid closed loop pumps (using insulin only), fully automatic closed loop pumps (using insulin only), as well as fully automatic bihormonal pumps which use both insulin and glucagon, and are in the automatic mode 24 hours daily.\cite{12,13,14} But all of these closed loop devices are made possible by the high performance of the improved CGM devices which now have an accuracy of plus or minus 9% when compared to a laboratory reference standard for glucose measurement.

Yet there are still many barriers to be hurdled before all patients with type 1 diabetes will have fully automatic pumps linked to CGM devices that can make insulin decisions for them without them having to intervene. One very large barrier is the cost. Many of the pumps cost more than $4,000, with supplies often more than $1,200 annually, a cost which is prohibitive for most patients unless it is covered by insurance, and often the co-pays and deductibles become overwhelming. We expect that these new pumps will be even more expensive. The cost of a separate CGM system is about $3,000 annually as well.

Another barrier is that the scientific and technical challenges are daunting and not yet resolved. One of many thorny issues is the difficulty in having the pump controller make changes in a timely enough manner so the pump delivers the insulin or glucagon quickly and accurately enough to yield normal glucose levels. Since changes in interstitial glucose levels lag behind changes in blood glucose levels, particularly when patients are getting hypoglycemic or after meals—a 10-15 minute lag is common—and this time lag makes the dosing decisions of a pump much more difficult. Also, the insulin that is given to lower glucose levels needs to diffuse into the subcutaneous tissues, be absorbed into the blood stream, and then attach to a receptor at the cellular level before acting, and that constitutes another delay, which must be factored into the algorithm.

Another problem still will remain, for once the insulin diffuses towards the cell surface and attaches to the receptors, it may continue to stimulate glucose utilization when the glucose level no longer needs to be lowered, leading the glucose lowering effect to overshoot the mark. These considerations have led to device designers trying to make sure their algorithms are safe and conservative, yet responsive and timely, a difficult task. Some researchers are trying to make insulin
and diffusion than those in current use.

Although the use of a bihormonal pump that has one hormone (insulin) to lower glucose and one (glucagon) to raise the glucose would seem to be the superior solution, there are disadvantages for this option, since glucagon is not stable for more than 24 hours in solution and currently must be changed daily in the pump. Also, there are no long-term studies on the safety of extended glucagon infusions in our patients. And finally, these pumps are more complex and more expensive, and may not be as durable.

But those caveats notwithstanding, the science of closed loop systems and CGM appears to be marching on. The number of patents that have been filed in the area of CGM, closed loop devices and controlling software is growing very fast. In 2017, Europe will be the site of the launch of an implantable CGM device that their developers insist will be stable subcutaneously for many months. Also, both Dexcom and Medtronic are putting out more sophisticated and more accurate CGM models; and Abbott Laboratories, which has been very active with CGM in Europe, is now entering the U.S. market with a related device to CGM, the Flash Glucose Monitor. This provides a less expensive technology, which—although it does not provide alarms to the patient—can provide very frequent glucose levels with a factory-calibrated transcutaneous patch and retrospective look at the patient’s glucose trends.\(^{15}\)

It is not clear at this time as to which models of closed loop devices will be most successful. It is likely that the hybrid models, which seek to solve a simpler problem, will be the first to become more widely used, but by 2020, they may not be the best option for our patients. In any case, it appears that 2017 will be the beginning of a new era in providing real-time feedback for our diabetic patients regarding their glucose levels.

While the closed loop insulin pumps will almost certainly be primarily used for patients with type 1 diabetes, it is likely that patients with type 2 diabetes, who have become severely insulin deficient or have recurrent nocturnal hypoglycemia, may be candidates for either the hybrid closed loop insulin pump systems, or even the totally automatic 24-hour duration closed loop pumps. However, what is more likely to occur much sooner is the use of CGM for patients with type 2 diabetes who either have hypoglycemic unresponsiveness or having difficulty with recurrent hypoglycemia, especially at night. As patients age, the risk for hypoglycemia in all diabetic patients has been shown to increase, and even a CGM system as a standalone may be life-saving for these patients.

At the same time these new technologies are moving ahead, the basic scientists, immunologists and engineers are also making progress on islet cell transplantation. There is a consortium of researchers at Harvard and MIT who have recently reported some important progress in animal models of protecting islet cells for up to six months in vivo. Also coming out of this consortium have been advances in growing islet cells from stem cell populations. Many of us, who have been watching the islet cell transplantation field since Dr. Paul Lacy in 1989 announced his successful but unfortunatley very transiently effective, islet cell transplants, have been aware of the enormous challenges in obtaining cells that are suitable to grow human islet cells and the extreme difficulty in keeping them alive and functional in vivo.

We hope that the many teams stretched across the globe will have more success than before, for it is not beyond hope that a breakthrough may lead to long-term success in islet cell transplantation, which potentially could be a permanent cure for type 1 diabetes. Also, in a parallel fashion, researchers are engaged in a number of trials to find the key to turning off the immune process which causes not only type 1 diabetes, but also the adult onset immunological version, latent autoimmune diabetes of adults (LADA), a condition which may affect more people worldwide than does type 1 diabetes, and leads to insulin-dependent diabetes in adulthood.

**TYPE 2 DIABETES, PREDIABETES AND INSULIN RESISTANCE**

From a population health point of view, type 2 diabetes is our biggest problem. The statistics are sobering. By 2040 it is estimated that 642 million people will have type 2 diabetes,\(^{16}\) and it is becoming an enormous burden, both in human suffering and in health care costs, primarily because of the complications.

As a result of years of research, both clinical and basic science, we are now better at understanding that type 2 diabetes is part of a continuum that begins with insulin resistance, of which about 50% is genetically determined and much more likely to occur in many ethnic groups, particularly Latino and Native American...
populations, but in Asian and African American populations as well. Many of these people do not have the phenotype of the metabolic syndrome. Severe levels of insulin resistance may be present in up to 25% of our adult population and increase with obesity and with inactivity. This severe insulin resistance appears to be the forerunner of diabetes as well as lowering their risk for the other complications.

**COMPLICATIONS OF DIABETES**

For a patient with diabetes, in addition to the microvascular complications of diabetic retinopathy, nephropathy and diabetic neuropathy, which are leading causes of blindness, severe levels of insulin resistance may be present in up to 25% of our adult population and increase with obesity and with inactivity. This severe insulin resistance appears to be the forerunner of prediabetes, either impaired fasting glucose or impaired glucose tolerance, and the latter may often be present in the face of normal HbA1C levels and normal fasting glucose levels.

We now know that many of those with prediabetes and those with severe insulin resistance, who do not yet have diabetes, are already at risk for other complications such as hypertension, sleep apnea, nonalcoholic fatty liver disease (NAFLD), early diabetic nephropathy, neuropathy, as well as diabetic retinopathy and at least a two-fold risk of occult coronary heart disease and even early signs of cardiomyopathy.

We now know that many of those with prediabetes and those with severe insulin resistance, who do not yet have diabetes, are already at risk for other complications such as hypertension, sleep apnea, nonalcoholic fatty liver disease (NAFLD), early diabetic nephropathy, neuropathy, as well as diabetic retinopathy and at least a two-fold risk of occult coronary heart disease, and normal fasting glucose levels.

We now know that many of those with prediabetes and those with severe insulin resistance, who do not yet have diabetes, are already at risk for other complications such as hypertension, sleep apnea, nonalcoholic fatty liver disease (NAFLD), early diabetic nephropathy, neuropathy, as well as diabetic retinopathy and at least a two-fold risk of occult coronary heart disease and even early signs of cardiomyopathy. Yet, few programs are in place to help our patients make the lifestyle changes that will lower their risks for kidney failure and amputations, there are both macrovascular complications and a wide variety of other serious issues that frequently cause morbidity, human suffering and mortality.

For example, we now know that our diabetic patients have an increased risk of fractures not just due to problems of balance, weakness and visual loss, but also because of adverse effects of diabetes and its complications on bones, a topic discussed by Betty Drees, MD, starting on page 30 in this *Kansas City Medicine*.

NAFLD is also much more closely associated with type 2 diabetes, and is the precursor to more advanced liver disease such as nonalcoholic steatohepatitis (NASH) and cirrhosis. Cirrhosis due to NAFLD is estimated in the next years to become the leading cause of liver failure in the U.S.

It is evident that our patients with type 2 diabetes are not only at a greatly increased risk for hypertension, coronary artery disease, peripheral and cerebrovascular disease, but also for a diabetic cardiomyopathy. For multiple reasons, they are much more prone to diastolic heart failure, which, unlike the better known systolic heart failure, is very difficult to treat. Almost every cardiac event that occurs in diabetic patients carries a higher morbidity and mortality rate than patients without diabetes.

Both type 1 and type 2 diabetes also have a bidirectional relationship with depression, leading to poorer diabetes control and a higher risk of complications and death. Much more attention still needs to be paid to the emotional stress due to diabetes and the complications of diabetes. There are numerous studies showing that programs which provide an integrated approach to the total needs of the diabetic patient are more successful. We now know that both cognitive dysfunction and dementia are occurring much more often in diabetes. The dementia appears to be clearly linked to insulin resistance in the brain as well as vascular injury due to diabetes and its complications. In fact, unrecognized cognitive dysfunction is a common cause of worsening of diabetes control and the beginning of downhill path for the patient.

**ORAL AND INJECTABLE MEDICATIONS AND TREATMENT**

Together with this information and a deeper understanding of the central importance of insulin resistance, have
come a variety of new therapies and strategies. In the last two decades there have been a number of new classes of both oral and injectable hypoglycemic agents. There are many excellent reviews of both oral hypoglycemic agents as well as insulins and insulin analogues, including an excellent review by Malham and Herrick, just published in Missouri Medicine. Currently we have a wide variety of choices, including injectable medications such as the GLP-1 receptor agonists, which appear to have both central effects to reduce food intake as well as gastrointestinal effects to delay gastric emptying, thereby increasing satiety and suppressing glucagon levels while lowering the glucose levels modestly.

Liraglutide, one of the agents of this class, has recently been shown in a three-year study to be associated with a modest reduction of cardiac events. This is an important milestone, since apart from the SGLT2 inhibitor, empagliflozin, which in a recent trial has also shown evidence of some beneficial effect on cardiac outcomes, none of the other recently developed medications have similar and unequivocal benefits in improvement of cardiac outcomes. And some, such as those in the thiazolidinedione class or in the DPP4 class, are associated with a slight or even moderate increase in the risk of heart failure, so patient selection must be done carefully.

Each of the oral agents and the GLP-1 receptor agonists should be carefully chosen for the particular needs of the patients. It is interesting that, despite the profusion of new medications in the past two decades, only metformin has shown consistently better cardiovascular outcomes when it is a part of the regimen for type 2 diabetes therapy. That is one of the many reasons why lowly metformin is still the first-line drug for those with type 2 diabetes who are not severely insulin deficient or in renal failure.

A number of new insulin and insulin analogues have reached the market and, while I am very pleased with the new choices, some of the costs of these products is staggering. Nevertheless, there is some promise that the new biosimilar insulins may provide at least some reduction in price so that more patients will be able to afford the new insulin analogues and also be able to afford to use the newer and better designed insulin pens that are so helpful for those with poor vision and limited dexterity.

NASAL INSULIN AS THERAPY FOR DEMENTIA

Researchers have discovered that insulin resistance occurs in the brain, and that administration of insulin directly into the brain slows the development of the characteristic changes found in Alzheimer’s. Intranasal insulin leads to increased levels of insulin in the cerebrospinal fluid and subsequently increases brain insulin levels. Perhaps the most exciting finding relating to the problem of dementia and diabetes is the observation that, in patients with insulin resistance and dementia, including those with diabetes, intranasal insulin appears to have a beneficial effect in improving cognition, and functional MRI studies are demonstrating where the effect appears to be found. Also, it appears that some forms of insulin are better than others. Intranasal insulin may become a treatment that is useful for dementia, as well as providing important insights into the etiology of diabetes-associated dementia.

CONCLUSION

In many ways, 2017 may be a very special year for diabetes care. The new tools will be spectacular, and probably none more far-reaching than the new CGM systems. Following these advances will be the closed loop systems and hybrid closed loop systems, made possible by the better CGM devices. The new choices of medications will be helpful, but the challenge of early recognition of who is at risk for diabetes and its complications is still not close to being met. Also, the increased complexity of care often leads to a higher risk of medical errors, by both patients and providers.

Much of our understanding of some of the complications of type 2 diabetes has illustrated how important early recognition is of those who are vulnerable to insulin resistance or have early evidence of visceral obesity, and the importance of making changes at a societal level to make it easier for our population to become leaner and fitter, and practice safer lifestyle behaviors. We certainly have done a remarkable job regarding tobacco, but obesity is proving a much more difficult challenge.

Other barriers remain. We still do not have enough access to adequate preventive measures for our patients, either for primary prevention of diabetes or secondary prevention of the complications. It is unfortunate, for example, that some hospitals appear to be more interested in new pancreas/renal transplant programs than in providing the public education programs that would, in a decade or two, reduce... (continued on page 29)
Type 1 and type 2 diabetes are disorders associated with increased mortality, primarily as a result of renal and cardiovascular disease.

The prevalence of chronic kidney disease (CKD) in the United States comprises 13% of the general population. Among them, Diabetic Nephropathy (DN) is the leading cause of end-stage renal disease. This complication is one of the most important problems among diabetic patients, affecting 30% of this population.

Diabetic nephropathy is a clinical syndrome characterized by glomerular hyperfiltration and albuminuria with activation of the renin-angiotensin-aldosterone system, followed by proteinuria and decline in glomerular filtration rate (GFR).

Recognized risk factors for DN are hyperglycemia, hypertension, dyslipidemia, smoking, obesity and genetic predisposition.

**PATHOPHYSIOLOGY OF DN**

Three basic steps have been described in the progression of DN; 1) glomerular hypertrophy and hyperfiltration, 2) inflammation of the glomeruli and tubulointerstitial area, and 3) apoptosis of cells and accumulation of extracellular matrix.

Several decades ago, studies in animal models demonstrated that glomerular hyperfiltration accompanied by glomerular capillary hypertension is the pathophysiological mechanism for initiation and progression of renal disease in DN. The two most important mechanisms leading to renal hyperfiltration in diabetes are glomerular hemodynamic abnormalities due to neurohormonal activation and tubular factors.

The hemodynamic/neurohormonal hypothesis is based on changes in afferent and efferent arteriolar tone with activation of RAAS resulting in glomerular hyperfiltration.

The tubular hypothesis is based on the fact that hyperglycemia causes increased filtered load of glucose in the proximal tubule. This results in over-activity of SGLT-2 and SGLT-1 receptors and increased tubular reabsorption of glucose and sodium. This will cause downstream activation of the tubuloglomerular feedback system.

The increase in proximal sodium reabsorption leads to decrease sodium delivery in the macula densa, with reduction in adenosine production. Adenosine is a vasoconstrictor, and its reduction causes vasodilation of the afferent arteriole with increase in intraglomerular pressure and subsequent hyperfiltration. Abnormalities in the tubuloglomerular feedback system have been demonstrated in experimental models of diabetes and also in patients with type 1 and 2 diabetes.

The hyperglycemia of diabetes also contributes to micro-inflammatory changes, oxidative stress and extracellular matrix expansion.

The most important change occurs in the glomeruli with expansion of the mesangium, thickening of the glomerular basement membrane (GBM) and hyalinosis of afferent and efferent arterioles. There is also loss of integrity of the filtration barrier and podocyte injury with effacement of foot process and loss of podocytes that play important roles in the development of progressive sclerosis and proteinuria.

However, there are also important changes in tubules and interstitium with tubular atrophy and interstitial fibrosis and inflammation. In high glucose conditions, the cells increase the secretion of inflammatory molecules and profibrotic cytokines. Transforming growth factor beta plays a key role stimulating fibrosis. The increase in glucose trafficking through the proximal tubular cells with a subsequent increased transport of glucose by SGLT2 can also promote inflammation and fibrosis.

**PREVENTING END-STAGE RENAL DISEASE**

Microalbuminuria is an important intermediary endpoint that correlates strongly with future advanced renal disease, retinopathy and mortality. Evidence indicates that achieving optimal glycemic and blood pressure control reduces the risk of an increase in urinary albumin excretion. Angiotensin-converting enzyme (ACE) inhibitors are effective in reducing microalbuminuria, relatively independent of the effect on the blood pressure control.

Data from The Diabetes Control...
...and Complications Trial (DCCT) and The United Kingdom Prospective Study (UKPDS) have molded the understanding and management of diabetes and the risk reduction of cardiovascular disease and kidney disease. In the UKPDS over 10 years, the patient assigned to intensive treatment protocols (hemoglobin A1C 7%) had decreased risk of microvascular complications and decreased progression of albuminuria. The DCCT also showed beneficial effects of intensive versus conventional glycemic control on kidney function, showing delay of onset and slowing of the progression of diabetic nephropathy. The ADVANCE study (Action in Diabetes and Vascular Disease: Preterex and DiaMicon Modified Release Controlled Evaluation) also showed significant reduction in the incidence of nephropathy with intensive glycemic control.

There is ample data to support blood pressure control in type 2 diabetes, because this control reduces proteinuria and progression of DN. The UKPDS suggests the potential microvascular benefits of blood pressure control. Fewer patients in the tight control group (mean blood pressure of 144/82) had urine albumin concentration greater than 50 mg/L at six years. Data from the ADVANCE trial suggest that tight blood pressure control (<120/70) in the context of diabetes and proteinuria improves kidney-specific outcomes. The risk for progression to end-stage renal disease is increased up to seven-fold in patients with diabetes type 2 and hypertension.

Available data suggest that pharmacologic strategies with interruption of renin angiotensin system (RAS) with ACE inhibitors or ARBs are a primary risk-reduction strategy. Data from the study that compared the renoprotective effects of telmisartan and enalapril suggest that ARBs and ACE inhibitors are equally effective in renoprotective effect. The ONTARGET (Ongoing Telmisartan Alone and in combination with Ramipril Global EndPoint Trial) suggests that combined treatment with an ACE inhibitor and ARB was more effective in reducing proteinuria, but was associated with faster decline in GFR.

NEW PERSPECTIVES

Despite current therapies to prevent DN and slow its progression, based on blood glucose, blood pressure and RAAs blockade, there is still a substantial risk of developing end-stage renal disease. This creates a need for new therapeutic approaches.

Sodium glucose cotransporter 2 (SGLT2) inhibition has the potential effect of nephroprotection through lowering of HbA1C, systolic BP and weight in patients with type 2 diabetes, and also has direct renal effects, reducing renal hyperfiltration, proposing decreased intraglomerular hypertension.

The SGLT-2 is localized in the proximal tubule and is responsible for 90% of the glucose reabsorption that is filtered in the kidneys. In type 2 diabetes, as a result of the increase filtered load of glucose, there is an increased expression of SGLT-2 and an increased reabsorption of glucose. This maladaptive mechanism contributes to hyperglycemia.

SGLT-2 inhibition produces glycosuria and reduction in fasting and postprandial blood sugar without the risk of hypoglycemia. The efficacy of SGLT-2 inhibition in reducing plasma glucose is decreased with decreasing renal function. These drugs should not be started in patients with GFR < 60 ml/min/1.73m2 and should be stopped when GFR is < 45 ml/min/1.73m2.

In diabetes, there is evidence of overactivity of SGLT-2 and SGLT-1 resulting in increased tubular reabsorption of glucose and sodium. SGLT-2 inhibition should result in increased delivery of sodium to the macula densa, causing increased adenosine release resulting in vasoconstriction of the afferent arteriole, leading to a reduction in renal plasma flow and GFR.

In clinical studies, the changes in renal function are typically characterized by a decline in GFR during the first weeks of treatment, followed by a progressive recovery. In addition to the effects on GFR, additional data support the concept that SGLT-2 inhibition reduces albuminuria. Overall, the studies consistently demonstrate significant reduction in urine albumin creatinine ratio (UACR) during SGLT-2 inhibition. The recently published study, EMPA-REG OUTCOME, showed that worsening nephropathy occurred in 12% in the SGLT-2 inhibitor group vs. 18% in the placebo group. Doubling of the serum creatinine level occurred in 1.5% in the SGLT-2 inhibitors vs. 2.6% in the placebo group, a significant relative risk reduction of 44%.

Another important trial is the LEADER (Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome). This trial showed that liraglutide, a glucagon like peptide-1 (GLP-1) receptor inhibitor, reduced the risk of renal complications by 22%. The renal microvascular endpoint was a composite of several measures: new onset persistent macroalbu-
minuria, persistent doubling of serum creatinine, end-stage renal disease, or death from renal failure. The study showed 23% decrease in the chance of new-onset macroalbuminuria. There was no significance between group difference in any of the other renal end points.31

CONCLUSION

During the last decades, multiple clinical trials indicate that better glycemic and blood pressure control can delay the onset and slow the progression of kidney disease in diabetes. Despite improvements in both glycemic and blood pressure control, DN remains a major health problem. SGLT-2 inhibition as well as DPP-4 inhibitors could be an important tool preventing the development and progression of DN. It is important to remember that these two medications are relatively new and we still have to understand all the potential side effects and mode of action. Further clinical research is needed to confirm the findings of these trials and be able to clarify whether SGLT-2 inhibitors and DPP-4 inhibitors might have significant nephroprotective effects.

Mariana Touza, MD, is an endocrinologist with Hellman & Rosen Endocrine Associates. Board certified in internal medicine and endocrinology, she most recently was an assistant professor in endocrinology at the University of Missouri-Columbia School of Medicine and associate program director in endocrinology. Dr. Touza is certified as an ASH Specialist in Clinical Hypertension by the American Society of Hypertension Specialist Board. She can be reached at 816-421-3700.

REFERENCES

ADVANCES IN DIABETES
(continued from page 25)

the number of those needing the transplants. We still have a shortage of experts in diabetes care, not only physician diabetes specialists, but also nurses, dietitians and other allied health professionals specializing in diabetes, and too few opportunities for diabetes educators. Our hospitals are still not providing optimal care of glycemia by diabetes educators. Our hospitals are still not providing optimal care of glycemia in the hospital setting and even the best universities are struggling to educate their staff and students in the basic principles of modern diabetes care. Yet, I think that 2017 may be a watershed moment in diabetes care. There is an opportunity to make a very large improvement in outcomes for diabetes, saving money and lives in the process. I hope we will make the best decisions for our patients and ultimately for our society.

Richard Hellman, MD, FACP, FACE, is partner in Hellman & Rosen Endocrine Associates in North Kansas City. He is a clinical professor of medicine at the University of Missouri-Kansas City School of Medicine, and a past president of KCMS and the American Association of Clinical Endocrinologists. Dr. Hellman has achieved recognition by the National Committee for Quality Assurance Diabetes Recognition Program, and has been named a Distinguished Reviewer for the journal Diabetes Care. He can be reached at rhellman@nkcedo.com, or 816-421-3700.

REFERENCES:
BACKGROUND
Diabetes mellitus is associated with an increased risk of fracture, and there is increasing recognition that the skeleton is a target organ system for complications of diabetes. As care of individuals with type 1 diabetes (T1D) and type 2 diabetes (T2D) improves, as the prevalence of (T2D) increases globally, and as the population ages in general, there is a need to understand the underlying mechanisms that increase risk of fractures in patients with diabetes in order to develop interventions to reduce fractures with all of the associated attendant mortality, morbidity and cost.

Epidemiology
The younger age of onset of T1D potentially results in more years of exposure to skeletal risk factors associated with diabetes, as well as risk factors starting when the skeleton is still immature. The increased risk in T1D for any type of fracture is approximately three times that for individuals without diabetes. Although large, prospective epidemiologic studies are lacking, current evidence indicates that the increased risk in T1D starts in childhood and increases with age, is more likely to affect the lower extremities (hip, lower leg, foot), and increases with poorer glycemic control and longer duration of disease. The relative risk of hip fractures is four to five times higher, especially in older populations. Skeletal risk factors may include other co-morbid autoimmune conditions with potential impact on fracture risk, such as celiac disease. Bone mineral density (BMD) is generally reported as decreased in T1D compared to individuals without diabetes or with T2D. The potential effect of race and ethnicity on risk fractures are unknown in T1D.

In older populations, osteoporosis and T2D are both very common and potentially additive in increasing fracture risk. The epidemiology of fractures in T2D diabetes was reviewed last year by Schwartz. The assessment of fracture risk in T2D is complicated by frequent prevalence of obesity in this population since higher BMD is associated with increased body mass index (BMI). Most, but not all, studies report increased fracture risk in T2D, but also increased BMD. There is more data on hip fractures than other types of fractures, with approximately 40% higher risk in T2D compared to individuals without diabetes. The risk of fracture at any given BMD is higher in diabetes than for individuals without diabetes, and thus the WHO Fracture Risk Assessment Tool (FRAX) underestimates fracture risk. This underestimation of fracture risk in T2D has important health policy implications for screening for osteoporosis, as well as for standards of care for individuals with diabetes.

The effect of T2D on fracture risk is higher in younger populations, and approximately twice as high in African-American or Mexican-American populations compared to whites. Individuals with microvascular complications from diabetes have a higher risk of fracture, but this finding is most likely due to the fact that these individuals have a longer duration or severity of disease, rather than a direct impact of the complication itself on the skeleton. Observational studies support increased fracture risk with poorer glycemic control, but no reduction in fracture risk with implementation of tight control. Although a specific glycemic target is not defined for fracture risk, the current evidence from observational studies suggests that glycated hemoglobin levels of less than 8% are associated with reduced risk. Prediabetes is not associated with an increased risk of fracture.

PATHOPHYSIOLOGY
Fractures result when the degree of mechanical stress is sufficient to overcome bone strength. Osteoporosis is a condition of skeletal fragility in which decreases in BMD and changes in microarchitecture contribute to reduce the mechanical strength of bone, such that fractures occur with lower levels of trauma. In diabetes, multiple factors may increase fractures, including de-
Increased BMD, changes in microarchitecture, and increased risk of falls. In T1D, bone density is decreased, and in T2D, it may be decreased, normal, or increased. In both T1D and T2D, bone turnover is decreased and there are changes in bone microarchitecture. However, since T2D is associated with obesity and changes in both glucose and fat metabolism, there are differences in pathophysiology between the two that will likely prove to have differing impacts on bone. Proposed pathologic mechanisms include advanced glycosylation end products in bone collagen, inflammatory mediators generated by visceral fat, altered insulin signaling on bone cells, direct toxic effects of hyperglycemia, diabetes medications, and others. There is emerging evidence that bone cells and adipocytes interact with the central nervous system in complex systems of energy balance and body composition. Patients with T2D have reduced cortical bone porosity and altered mechanical properties that contribute to bone fragility for any given BMD.

Falls increase risk of fractures, and T2D is associated with a higher risk of falls, especially in those treated with insulin, which likely is a marker for greater severity or duration of diabetes. The risk of falls in older insulin-treated T2D may be 2-3 times those without diabetes. The increased risk of falls includes complications of diabetes, such as peripheral neuropathy, and also non-diabetes related conditions, such as pain and low performance status. Even controlled for falls, diabetes is still associated with a higher risk of fracture. Therefore, falls do not account for all of the increased risk of fracture, and the underlying changes in bone strength are thought to be the major pathophysiologic cause.

**EFFECT OF DIABETES DRUGS ON BONE**

Since diabetes is a chronic disease with decades of exposure to drugs for glycemic control, the issue of diabetes drug effects on bone is very important clinically. This is especially true in T2D where there are choices of drugs aside from insulin. (The effects of insulin on bone are complex and not covered in this review.) The following paragraphs summarize the effects of common T2D drugs on bone, but choice of drug therapy for glycemic control should be personalized and made in consideration of all co-morbidities and overall goals.

**Metformin** has direct, anabolic effects on bone cells, but clinical studies have not yet proven a reduction in fractures in humans. Metformin is considered safe from a bone perspective, which is important since it is the first-line therapy in T2D.

**Thiazolidinediones (TZDs)** are currently marketed in the U.S. as rosiglitazone and pioglitazone. They act through PPARγ regulation. PPARγ is also expressed in bone and activation is a drug class effect that results bone loss, especially in older individuals, in women, and with longer duration of exposure.

**Sulfonylureas**—glimepiride, glipizide, and glyburide—have limited data on fracture available from clinical studies. In most of the studies, sulfonylureas were used in the control groups for development of newer diabetes medications, and thus there is little data of sulfonylureas alone. However, there is no evidence that they increase fractures.

The two classes of drugs currently marketed that act through the incretin system are the glucagon-like peptide-1 (GLP-1) receptor agonists (e.g. liraglutide, exenatide) and the inactivating enzyme dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. saxagliptin, sitagliptin, vildagliptin). There are GLP-1 receptors in bone, generating interest in GLP-1 agonists and DPP-4 inhibitors as bone protectors. There are few clinical trials to date with fracture outcomes, and further study is needed, but at this time, these drugs as a class do not appear to increase fracture risk.

**Sodium glucose co-transporters 2 (SGLT2) inhibitors** lower glucose through reabsorption of glucose in the kidney and are currently marketed as canagliflozin and dapagliflozin. They may alter calcium and phosphate balance, but it is too early to know the full impact on bone and fracture risk, or if any effects are a class effect. The FDA in September 2015 issued revised labeling on canagliflozin to reflect data on reduced BMD and increased fractures. These drugs should be used with awareness of potential increased fracture risk pending further studies and longer-term outcomes.

**EFFECTIVENESS OF OSTEOPOROSIS DRUGS IN DIABETES**

Since diabetes leads to decreased bone turnover in T1D and T2D, concern has been raised about the effectiveness of anti-resorptive therapies for osteoporosis, which could further reduce bone turnover. The osteoporosis clinical trials included too few subjects with T1D to draw conclusions on effectiveness of osteoporosis medications in this population. For T2D, post-hoc analysis of raloxifene, a selective estrogen receptor modifier (SERM), indicates similar effectiveness in reducing vertebral fractures com-
pared to non-diabetic women. Observational studies of bisphosphonates in T2D support effectiveness in diabetic patients in preventing fractures. Subjects with T2D in these studies were included based on the same BMD and fracture criteria as those without diabetes. It is not known if anti-resorptive osteoporosis therapy will reduce fractures in diabetes with microarchitecture changes despite normal BMDs. No studies of effectiveness of denosumab in diabetes are yet available. Overall, current evidence supports use of raloxifene and bisphosphonates in patients with osteoporosis and diabetes as effective therapy.

In view of the chronic nature of osteoporosis and extended drug treatment, the question has also been asked whether osteoporosis drugs increase risk of development of diabetes. To date, there is no evidence of increased risk of T1D or T2D with osteoporosis drugs, and there is some evidence for reduced risk of development of T2D with anti-resorptive drugs.

CONCLUSIONS (See Table)
The skeleton is another target of diabetes complications, and thus as the population ages, and as care of patients with diabetes continues to improve, osteoporosis and fracture prevention will become an increasingly important component of diabetes management. Although all of the underlying mechanisms of increased fracture risk are not yet understood, BMD is decreased in T1D, and both T1D and T2D have defects in bone quality leading to increased risk of fracture. Although lower BMD is predictive of fracture risk in diabetes, the risk starts at a higher BMD than those without diabetes. These patients have other risk factors for osteoporosis and fractures as they age, including falls, and side effects of some diabetes medications. Consideration of risk of osteoporosis should be included in decisions on drug therapy for diabetes. If drug therapy for osteoporosis is indicated, anti-resorptive therapies appear as safe and effective as in those without diabetes. Treatment of osteoporosis for patients with diabetes should include fall prevention strategies. Further research is needed to fully understand the mechanisms of decreased bone strength in diabetes, and in order to improve clinical evidence for fracture prevention and provide guidance for personalized care, including recommendations for screening for osteoporosis in individuals with diabetes.

RESOURCE TOOL PLANNED
Dr. Drees is leading a KCMS effort to engage regional physicians in reducing the burden of diabetes in the Kansas City area. To get involved with this project, contact Dr. Drees at dreesb@umkc.edu or 816-218-2582.

Betty M. Drees, MD, FACP, FACE, is professor of medicine in the Department of Internal Medicine and the Department of Biomedical and Health Informatics, and Dean Emerita of the University of Missouri–Kansas City School of Medicine. She can be reached at 816-218-2582. dreesb@umkc.edu.

REFERENCES:
9. Lucka-Czernik B, Rosen CJ. Energy Excess, glucose utilization,


DIABETES BY THE NUMBERS

PREVALENCE
- In 2012, 29.1 million Americans, or 9.3% of the population, had diabetes. - Approximately 1.25 million American children and adults have type 1 diabetes.

UNDIAGNOSED
- Of the 29.1 million, 21.0 million were diagnosed, and 8.1 million were undiagnosed.

PREVALENCE IN SENIORS
- The percentage of Americans age 65 and older remains high, at 25.9%, or 11.8 million seniors (diagnosed and undiagnosed).

NEW CASES
- 1.4 million Americans are diagnosed with diabetes every year.

PREDIABETES
- In 2012, 86 million Americans age 20 and older had prediabetes; this is up from 79 million in 2010.

Source: American Diabetes Association
More Aggressive Treatment Needed to Address Type 2 Diabetes Epidemic

SPEAKERS AT NOV. 17 FORUM DISCUSS POPULATION HEALTH MANAGEMENT APPROACHES TO DIABETES CARE

By Jim Braibish, Kansas City Medicine

Physicians must become more aggressive in treating type 2 diabetes at all stages from prediabetes to advanced, according to endocrinologist Kevin Pantalone, DO, of the Cleveland Clinic. He noted how new payment models can help provide for more frequent oversight of diabetes patients.

Dr. Pantalone was the keynote speaker at the Nov. 17 KCMS program on diabetes and population health management which was attended by about 80 KCMS members and guests. He is the director of clinical research in the Department of Endocrinology at the Cleveland Clinic.

The problem of diabetes is getting bigger, he said, citing data showing how the incidence of diabetes has more than doubled since 1980, with 9% of adults now having the disease and another 35% having prediabetes.

“We must do a better job of managing people with type 2 diabetes,” Dr. Pantalone said. “Only one in two patients with type 2 diabetes has an A1C within target. Studies have reported that less than 30% of patients are compliant with one follow-up A1C test over a one-year time frame.”

“If the patient has an elevated A1C, you have to act,” he said, pointing out that complications increase and the disease becomes more difficult to treat as it advances. “We should be aggressive early in the disease course.”

The quality of diabetes care can improve with care coordination and accountability provided in such models as the accountable care organization and the patient-centered medical home, according to Dr. Pantalone.

“The ACO and PCMH allow for more frequent contact with the patient. This is critical to allowing us to get to goal,” he said. “The physician may see the patient four times a year for 20 minutes. The PCMH staff can follow up with the patient much more frequently. The more contact with the patient, the better job we do.”

Also important is earlier referral to endocrinologists of the more serious cases. He suggested that patients with an A1C of over 9 for more than six months should be referred to an endocrinologist. After the patient achieves the A1C goal, he returns the case back to the primary care physician. About 90% of type 2 diabetes cases continue
to be managed by primary care physicians, he said.

**POPULATION HEALTH TOOLS ACHIEVE IMPROVED OUTCOMES**

Qiana Thomason, vice president of clinical operations for Blue Cross Blue Shield Kansas City, described how they are achieving improved outcomes through population health management programs. Initiatives include the Blue KC Medical Home Advanced Primary Care programs and the Comprehensive Primary Care Plus program, the latter a Centers for Medicare and Medicaid Services effort for which Kansas City was chosen as one of only 14 sites nationwide.

Among diabetic patients in 2015, almost 74% of those in patient-centered medical homes had blood pressure under 140/90 compared to 63% for non-medical home patients, she said. A1C levels were under 7.0 for 39% of the PCMH group compared to 37% of the others. Medical home patients also receive more frequent preventive screenings.

In working to continue to improve these population health tools, “It is important that we partner with you to collaboratively plan strategies that will work in your health system. The key is partnership, partnership.”

**DIABETES MEASURES IN MEDICARE QUALITY PAYMENT PROGRAM**

Patricia Meier, MD, regional chief medical officer of the Centers for Medicare and Medicaid Services, opened with a review of the new payment models taking effect in 2017 under the Quality Payment Program. These are set forth in the Medicare Access and CHIP Reauthorization Act (MACRA).

The goal of the Quality Payment Program is to streamline previous multiple quality reporting programs, and to promote practice transformation, she said. Most physicians will use the Merit-based Incentive Payment System (MIPS) in the first year.

There are approximately 300 quality measures from which physicians can choose, she said, and these can be specialty-specific. A number of diabetes measures are available, including in the areas of diabetes foot exam, diabetes eye exam, hemoglobin A1C control and more. Physicians can learn about these and other measures on the Quality Payment Program website, https://qpp.cms.gov.

**DIABETES EDUCATION UNDERUTILIZED**

The Cray Diabetes Self-Management Center at The University of Kansas Medical Center is one of 10 programs in the Kansas City area certified by the American Diabetes Association. Three educators from the center spoke to the session.

Catherine Parkhurst, a 20-year veteran certified diabetes educator, said less than 10% of newly diagnosed patients go to education. Among the barriers to education she noted are patients relying on family or friends or the Internet for information, providers not following up with patients, or people with a family history of diabetes thinking they already know what they need to know. In addition, not all private insurance covers diabetes education while Medicare does.

Education is advisable not just when a patient is first diagnosed, but at other intervals. She said these include after an annual assessment of treatment progress, when new complications arise, or when transitions in care occur such as changing doctors.

Amy Huelle, MPH, RD, CDE, Cray program director, said studies show that patients with education are more likely to take their medications; control their glucose, blood pressure and cholesterol; and use primary care and prevention. They have lower health care costs as well.

Emily Newbold MS, RD, CDE, discussed hypoglycemia awareness recognition and education. Cray offers a Hypoglycemia unawareness class.
As Telemedicine Expands, Understand the Liability Risks

TELEMEDICINE PRACTICE LAWS VARY BY STATE; EVALUATE YOUR “WEBSIDE MANNER”

By Dustin Shaver, NORCAL Mutual Insurance Company

The use of telemedicine continues to grow at an impressive rate. According to the FAIR Health database (the largest repository of private health care claims), telemedicine use in the U.S. nearly doubled between 2007 and 2015. Over half of all U.S. hospitals now use some form of telemedicine, according to the American Telemedicine Association. Telemedicine is widely credited with improving patient access, cost efficiencies and quality of care. This and increasingly favorable state and federal telemedicine legislation may explain the rapid increase in its utilization.

Despite the advantages, telemedicine has liability risks, such as privacy, security, patient confidentiality, credentialing and misdiagnosis due to a lack of continuity of care. Additionally, the soft skills that may come naturally in a personal patient encounter may need to be adjusted for electronic encounters. Telemedicine providers should evaluate their “webside manner.” For example, equipment needs to be positioned to simulate direct eye contact; active listening cues may need to be exaggerated; posture and facial expressions may need adjustment; and sessions must be started and ended appropriately. Seemingly minor electronic communication strategies can significantly affect the success of a telemedicine encounter.

Physicians who adopt telemedicine also have administrative considerations that may pose a challenge and liability risk. For instance, professional licensure portability and individual state mandated practice standards present major challenges. There are significant differences among state telemedicine laws and the laws are constantly changing. In the 2016 legislative session, for example, over 150 telemedicine-related bills were introduced by 44 states. The issues addressed by these bills ranged from informed consent requirements to online prescribing parameters to Medicaid reimbursement. Physicians should be aware of the telemedicine laws in their own state and in the state of every patient in their telemedicine practice.

Understanding the laws is paramount to understanding the medical liability risks that may be involved in the various stages of providing telemedicine.

Medical professionals providing virtual visits must work harder to reduce practice liability exposures. To help enhance patient safety and reduce risk:

• Understand that individual state telemedicine practice laws vary from state to state.

• Consult with your health care business attorney as needed.

• Check your professional licensure portability to ensure that you are licensed to practice in the jurisdiction where the patient resides.
Insights

• Consult with your medical practice liability insurance company to ensure that your policy covers all jurisdictions where you plan to provide services.

• Be aware of online prescribing regulations that vary across jurisdictions.

• Comply with all applicable privacy and security standards for the secure transmission of protected health information between patient, provider and payers.

• Standardize telemedicine patient visits to help minimize the potential for error and to support good communication practices.

• Take care to ensure that the primary care physician and patient relationship is not fractured with ongoing use of telemedicine consultation.

Telemedicine is an emerging form of practice, and the rising rate of adoption by both physicians and patients is an indication of its value. As with all advancement in the field of medicine, the advantages of adopting a new way of practice should be considered carefully and risks assessed. It is important to consult with your medical professional liability insurance provider on your individual policy to ensure you are adequately covered for the scope of practice, and consult with your business attorney as needed.

NORCAL Mutual has a team of risk management specialists available to consult and assist policyholders with the assessment of their practice and to help identify and address risk exposures. To learn more about managing telemedicine risk exposure, NORCAL policyholders can access the September 2016 Claims Rx entitled “Telemedicine Risk Management,” which is available through MyACCOUNT on the new MyNORCAL® mobile app.

Dustin Shaver is vice president of risk management at NORCAL Mutual Insurance Co., overseeing patient safety and ACCME accredited Continuing Medical Education (CME) programs. He can be reached at 844-466-7225. NORCAL Mutual is represented by Keane Insurance Group, a Kansas City Medical Society partner.

Research Points to Orb2 as a Physical Substrate for Memory Strength, Retention

Using molecular tools to manipulate a prion-like protein in fruit flies, researchers at the Stowers Institute for Medical Research have discovered evidence for specific molecular changes necessary for the formation, storage, and retrieval of memories.

In a study published in the Dec. 5 issue of Current Biology, researchers report that the protein Orb2 appears to be part of a memory stamp in the brain produced by a particular experience. The researchers also discovered that another protein, JJ2, assists Orb2 in the formation of long-term memory. This work provides insight on how memories are made and retained in the fruit fly brain. Humans have a protein counterpart to Orb2 called CPEB, which suggests similar mechanisms may be involved in human memory.

Lead researcher Kausik Si, PhD, and colleagues performed a detailed examination of Orb2, a protein previously implicated in long-term memory formation in fruit flies, at different stages of memory. A key characteristic of Orb2 is its prion-like ability to transform from one physical state to another and form clusters, or aggregates, under certain conditions.

Using tools that allow rapid and reversible inactivation of Orb2 protein in neurons, the researchers found that Orb2 can act as a physical substrate for encoding memory and serve as a molecular signature for long-term memory. They also discovered that a DnaJ family chaperone, JJ2, assists Orb2 aggregation and enhances the formation of long-term memory.
For your next patient, prescribe hope.

For over 5 million Americans now living with Alzheimer’s, hope means research — the only way to advance treatment of this disease.

A community dedicated to advancing research for Alzheimer’s disease, the Alliance offers more options for your patients — including free memory screenings, ongoing education and local opportunities to volunteer for research studies.

Turn a routine visit into a referral for a brighter future. Learn how you can join the Alliance now, by emailing kcmemorystrings@kumc.edu or call (913) 588-0555.