Take Home Pearls

Thursday, July 15, 2021

Keynotes 1 & 2

Obesity, CVD, & Metabolic Surgery in Diabetes — Steven Nissen, MD

- NIH Study (16 US centers), randomly assigned 5145 overweight or obese patients with Type 2 diabetes to intensive lifestyle intervention
- Weight loss through decreased caloric intake and increased physical activity vs standard support and education
- Primary outcome: composite of CV death, nonfatal MI, nonfatal stroke, or hospitalization for angina.
- Maximum follow-up of 13.5 years, median 9.6 years (IQR, 8.9-10.3) with <4% lost to follow up

Diabetes Drug Safety Updates — Lisa Yanoff, MD

- FDA updates product labeling with new safety information based on clinical trial and post-marketing data when warranted
- The Prescribing Information has a section in the Highlights called Recent Major Changes, where you can find important changes to the product labeling
- The FDA Adverse Event Reporting System (FAERS) is a database that contains adverse event reports, medication error reports and product quality complaints resulting in adverse events that were submitted to FDA
    - FAERS data is available to the public via the FAERS Public Dashboard: https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-public-dashboard

PLENARY ONE: Diabetes Management

Treatment Guidelines Have Entered the 21st Century — Ralph DeFronzo, MD

- Please refer to slides found on the plenary under "Session Content"

Is the AACE Algorithm More Practical? — George Grunberger, MD

- It's all Patient-Centric
- Try to avoid hypoglycemia and weight gain
- Think of cardio- and renovascular benefits while improving glycemia

PLENARY TWO: Healthcare Policy & Economics

COVID-19 and Health Economics — Sandip Garg, MBA

- Reassess global supply chains for critical medical goods
- Invest in public health infrastructure, from staffing to technology
- Technologically transform the entire patient journey
- Reassess the value of health care needs and "quality" imperatives
- Bridge the gap in social determinants and disparities in access

Lessons from Europe — Chantal Mathieu, MD

- Heath care is a big priority in Europe: regulatory approval of medicines central; reimbursement, market access, and organization of health care per country
- Systems, like the Belgian one, allow monitoring of quality of care delivery: global access for patients with diabetes to drugs and tools for therapy organized by government
- The Commission also assessed that health systems will likely require more than €70 billion in additional public spending per year (pre-COVID estimate was €20 billion) — increase of 0.6% of GDP

PLENARY THREE: Artificial Pancreas Systems

eHCL Systems — Eda Cengiz, MD, MHS

- Diabetes technology is reshaping diabetes management and offers essential tools to improve outcomes.
- HCL System Outcomes: reduction in hypoglycemia, outstanding nighttime blood glucose control, meal-related excursions are as good or better than conventional therapy.
- Technology as an ally to outsmart diabetes:
    - User-friendly systems to improve quality of life, reduce burden, and optimize glycemic control
    - Keeping up with diabetes technology tools for better patient care

Is a Bihormonal AP System a Reality? — Roman Hovorka, PhD

- Insulin-only: suitable for majority of people with Type 1 diabetes including nocturnal glucose control
- Glucagon dual-hormone system: suitable to those particularly prone to hypoclycaemia
- Pramlintide: potential to fully closed loop with ultra-rapid insulin analogues and to improve postprandial glucose
- Longer studies warranted to assess comparative benefits of single and dual-hormone closed-loop system

Advances in Insulin Delivery Systems — Moshe Phillip, MD

- Closed-loop systems pumps and sensors:
  - Nighttime — we are already there!
  - Daytime — still in progress
  - Other "closed-loop-like systems" (DSS) are in development (at least one is already FDA approved)

PLENARY FOUR: Diabetes + COVID-19

Overview of Morbidity/Mortality from COVID-19 — Irl Hirsch, MD

- Those with T2D have a worse prognosis than those without diabetes
- The impact of pre-infection glucose control in these patients to date is unclear
- The impact of tight glucose control after hospital admission is not clear, yet there is data that IV insulin infusion and improved control may be beneficial
- To date, those with T1D have mixed data with regards to mortality and new diagnosis, yet more DKA is seen with minorities
- To date, DPP4 inhibitors and metformin (data not shown) have interesting retrospective data for pre-infection use, yet RCTs are required. Post-infection SGLT2 inhibitors do not appear to have an effect (complete data needs to be reviewed)

Managing Diabetes Virtually — R. Paul Wadwa, MD

- The role of telemedicine in diabetes care has grown exponentially in the last 16 months
- Telemedicine (in some form) will be a part of future diabetes care
- Stay tuned for changes in state/federal guidelines and reimbursement for telemedicine in the next few years
- Consider how you can use telemedicine as a tool in clinical practice to optimize diabetes care delivery

Telehealth and Virtual Visits — Moshe Phillip, MD

- Digital/virtual diabetes clinic should be developed for all people with diabetes
- Digital clinic aim to empower people with diabetes to self treat their diabetes
- Data ownership should be regulated worldwide — it's for the patients to decide whom to share it with
- Easy, passive transmission of data from all different devices to integrate, interpret, and create a meaningful advice for both HCPs and people with diabetes
- Digital clinic may replace some of the face-to-face appointments and increase interactions between visits

Friday, July 16, 2021

Keynotes 3 & 4

In-Patient CGM Use: Challenges & Regulations — Courtney H. Lias, PhD

- Hospitals should consider whether they have the resources and expertise necessary to adequately implement CGM use in their facility and provide appropriate training to healthcare providers
- The performance of CGMs in an acutely sick population is unknown
- However, depending on the device, some hospitals may determine that the benefits of CGM use in hospitals during the pandemic (reduction in patient/HCP exposure, reduces consumption of personal protective equipment) may outweigh the risk during this emergency

Hope vs. Hype in T1D — Jay Skyler, MD

- Please refer to slides found on the plenary under "Session Content"

PLENARY FIVE: Challenges & Emerging Diabetes Solutions

Appropriate Management of Diabetic Kidney Disease — Daniel Bessesen, MD

- Controlling glucose, weight, and blood pressure are still important
- GLP1 agnoists have some benefits
- SGLT2 inhibitors have moderate benefits in preventing nephropathy
- Mineralocorticoid receptor antagonism may have utility in the future

Hospital "Headaches": Patients on Degludec & Other Non-Formulary Drugs — Irl Hirsch, MD

- With the plethora of new insulins (and more coming), transitioning in the hospital to formulary insulins is a challenge which will only grow. Safety a concern!
- Subtle differences in insulin kinetics (eg: fast-acting aspart compared to aspart and lispro) will have little imparct when insulin is changed in the hospital
- The subtle kinetic changes of U300 glargine and detemir compared to U100 glargine likely have minimal impact when substituted in a hospital setting but studies would be welcomed
- Based on the PK/PD of degludec, transition to U100 glargine appears safest by substituting 50% of t hose dose as glargine on day 1 with all of the dose on day 2. This is likely more critical in T1D but formal studies would be welcomed

PLENARY SIX: CGM, Pumps, & Diabetes

iCGM and Future CGM — George Grunberger, MD

- CGM is accurate enough for insulin dosing
- Future of diabetes technology is interoperability → iCGM
- Indications for use of CGM are expanding

Customizable AP System — Gregory Forlenza, MD

- There are an increasing number of different AP systems with different methods of customizing their function
- There is not a "best" design, but rather different designs which may work better for different individuals
- Understanding how to customize each system remains important for providers and educators

Keynote 5

Update on Islet Replacement — Jay Skyler, MD

- Please refer to slides found on the plenary under "Session Content"

PLENARY SEVEN: Pregnancy and Diabetes

Oral Hypoglycemics in GDM: Quick Fix but Unforeseen Consequences? — Linda Barbour, MD

- Metformin associated with low birth weight: less likely to control BGs; insulin often added
- Insulin more likely to control glucose, TG/FFAs; pricey, more difficult
- Consider metformin; if high risk for maternal hypoglycemia, mild GDM; limited ability to use insulin. Avoid in placental insufficiency, normal weight, first trimester okay
- Consider glyburide: if postprandial hyperglycemia; unable to use multiple insulin injections; dose 1 hr before meal, do not use at night for high finger blood glucose; consider combining with NPH at night
- Individualize: insulin secretion vs insulin resistance ? Question LADA/MODY in normal weight "GDM" counsel on unknown long-term safety of both
- MiTY RCT T2D and all RCTs: need longterm follo-up kids

CGM in Pregnancy — Carol Levy, MD

- CGM use has demonstrated benefits for pregnant women with diabetes and reduces patient burden
- Accuracy studies to date show encouraging results
- The frequency of SMBG by pregnant women wearing CGM is not clearly defined and needs further evaluation
- Further studies are needed to further determine the role of SMBG, optimize outcomes, and limit the burdens of self care

Hybrid Closed-Loop in Pregnancy — Sarit Polsky, MD, MPH

- Hybrid closed-loop (HCL) therapy in pregnancies associated with diabetes is still off-label and investigational
- Published, completed clinical trials are small, limited in scope, and have short comparator durations, but show promise
- Case reports of HCL use in T1D pregnancies are emerging in the literature
- They are new clinical trials underway both with investigational and approved HCL systems

PLENARY EIGHT: Prevention & Acute Complications

Current State of CVOT — Jay Skyler, MD

- Please refer to slides found on the plenary under "Session Content"

Lifestyle Challenges During COVID-19 — Daniel Bessesen, MD

- Different people respond to stress differently
- COVID resulted in lower diet quality for many
- COVID led to reduced physical activity for many
- Lifestyle counseling for diet, physical activity, sleep, and stress should be tailored to the individual

Practical Tips for DKA Management — Arleta Rewers, MD, PhD

- Please refer to slides found on the plenary under "Session Content"

Saturday, July 17, 2021

PLENARY NINE: Practical Aspects in Managing Diabetes

Innovation & FDA's Role — Courtney H. Lias, PhD

- FDA's mission includes promotion of public health in addition to protection of public health
- Many programs and initiatives are available to spur innovation
- Together we can advance the availability of innovative new products for patients

Strategies to Prevent Hypoglycemia in Children — Eda Cengiz, MD, MHS

- Hypoglycemia is the most common complication of T1D and a major source of parental stress
- Traditional methods enhanced by new generation diabetes technology tools are essential for hypoglycemia prevention
- Future advances in diabetes technology will provide more tools to prevent and eliminate hypoglycemia in children with T1D
- It is vital for clinicians to familiarize themselves with new diabetes technology systems and incorporate diabetes technology tools into their practice to provide the best care for their patients

Is There a Future for HbA1c? — Irl Hirsch, MD

- Discordance between A1c and glucose management index is common
- Time-in-Range (TIR) has been shown to be associated with diabetic retinopathy both in T1D and T2D
- For those with T2D who perform little if any home glucose monitoring, occasional professional CGM should allow us to understand diabetes control in our "A1c-centric" environment
- Anecdotally, patients seem to be the most prepared to accept TIR as a key diabetes metric

Diurnal Variability of Insulin Requirements — Roman Hovorka, PhD

- ~~Hypoglycemia is a limiting factor diabetes management~~
- Variability in insulin requirements is limiting factor of diabetes management

Treatment of Early Diagnosed T1D — Brigitte Frohnert, MD, PhD

- Early-stage T1D is characterized by blunted first-phase insulin response
- CGM has advantages for education and guidance of therapy in early-diagnosed individuals (currently not approved for use in Stage 2)
- Strategies for using long- vs short-acting insulin should be customized to patient needs and glycemic patterns
- Management of early-diagnosed T1D presents opportunities for early lifestyle counseling

Maintaining an Exercise Program — Daniel Bessesen, MD

- Ask about physical activity
- Any increase is helpful
- Find something enjoyable
- Tailor the plan to the individual

PLENARY TEN: Drug Approval, Initiating T2D Treatment, & Technology

Process for FDA Drug Approval — Mahtab Niyyati, MD

- An Investigational New Drug (IND) application is required for clinical investigation of not only a new drug or biologic, but also if there is a change to an existing approved drug or biologic.
- The Agency strongly recommends that sponsors seek FDA's guidance in drug development.
- The FDA's various guidance for industry providers recommendations on how to interpret the regulatory requirements.

Treatment Initiation for T2D — Chantal Mathieu, MD

- Guidelines still promote sequential therapy in Type 2 diabetes
- Early combination therapy could alter the course of disease in Type 2 diabetes
- Should metformin stay first line?

Advancing Treatment for T2D — Carol Levy, MD

- Advancement of treatment for people with T2D can follow many different trajectories based on available treatment algorithms
- Considerations of health status, treatment goals, and co-morbidities need to be considered when revising treatment regimens

Keynote 6

Pre-Prediabetes: Prelude to Cardiovascular Disease — Ralph DeFronzo, MD

- Please refer to slides found on the plenary under "Session Content"

PLENARY ELEVEN: New Onset Education & Implementing Technology

Initiation of Insulin & Dosing Considerations — Kimber Simmons, MD

- Total daily dose (TDD) of insulin is variable but generally ~0.5–1 IU/kg/day when initiating insulin in Type 1 diabetes
- Adjust TDD based on patient factors. Age, HbA1c at diagnosis, DKA status at diagnosis, and gender effect TDD the most
- Long-acting insulin should be ~50% of TDD
- Toddlers need significantly more insulin for carbs and are more sensitive to insulin
- When initiating insulin pump dosing from MDI, total basal may need decreased, and ICR may need increased

Empowering Patients with Tools & Technology — Liz Beck, RD

- Consider patient lifestyle, occupation, preference
- Ask how you can address their biggest concern
- Not a one-size-fits-all approach
- Meet the patient where they're at

Challenges with AP Technology — Laurel H. Messer, PhD

- Challenges with artificial pancreas systems are related to user burden: hassle, time, wearing devices
- Clinicians can help with careful device selection
- Clinicians can help with setting realistic expectations of AP use
- Reinforce DSM (blousing, high glucose correction, treating lows) — these are still imperative behaviors with artificial pancreas systems

Managing Special Circumstances in T1D — Rachel Garcetti, PA-C

- Exercise and T1D
  - Exercising regularly with T1D is possible and provides many health benefits
  - BG needs to be in a reasonable range prior to exercise to ensure the best performance—exercise type, intensity, and duration key factors here
  - Advanced diabetes technologies can help overcome some of the barriers to regular exercise
  - Exercise guidelines need to be individualized—trial and error is the only way to figure out what works best for any one individual
- Hyperglycemia (steroids)
  - Steroids >> Insulin Resistance
    - Temporary increases to basal rates, increasing basal insulin if on MDI, more aggressive meal/correction doses
  - Caffeine >> Hyperglycemia
    - Black coffee or any carb-free caffeinated beverage can raise BGs, more aggressive boluses or increase basals to compensate
  - Menstrual Cycle >> Luteal phase hyperglycemia
    - Can use temporary basals during the luteal phase, or create a separate basal pattern
    - Increasing basal insulin if on MDI can help
    - May need to dose more aggressively for meals/corrections as well
- Practical Take Home "Pearls"
  - Incidence of DKA hospitalizations continues to increase in the US, but the mortality rate from DKA has decreased
  - DKA is a life-threatening but preventable complication of diabetes
  - Pump patients should have a low threshold to change infusion set and vial of insulin, and/or give insulin via an injection
  - Remember for insulin pump users >> WHEN IN DOUBT, CHANGE IT OUT!

PLENARY TWELVE: Lipid & Diabetes Cure

How Low Should We Go with Lipids? — Robert Eckel, MD

- Based on absolute risk reduction, LDL-C levels of <55mg/dL provide maximum benefit for CVD risk reduction; lower levels do not appear to be harmful
  - Are studies of lipid lowering therapy ethical in patients with T1D?
- Triglyceride elevations are strongly associated with ASCVD but are not etiologic and the amount of reduction in triglycerides by fibrates or omega-3 fatty acids does not relate to reduced CVD
  - Data suggest that EPA levels achieved reduce CVD by alternative mechanisms
- In patients with severe hypertriglyceridemia, triglycerides should be reduced to <500mg/dL to reduce the risk of acute pancreatitis

Management Differences for Children — R. Paul Wadwa, MD

- Lipids screening and management are important for youth with diabetes
- Adequate management requires discussions with patients/families regarding diet, exercise, and in some cases initiation of medication
- Access to dietitians who can council adolescents with diabetes regarding dietary choices and impact on lipid levels is very important
- Statins and fibrates (and other medications in the future) have an important role for youth with diabetes over age 10 years requiring pharmacological intervention

Omega-3 Fatty Acids for TG Reduction — Steven Nissen, MD

- Weak evidence that eating fish reduces CV events
- Multiple large fish oil trials show neutral results
- A single trial (REDUCE-IT) shows benefits, but a parallel trial (STRENGTH) does not
- REDUCE-IT used a "placebo" with significant adverse effects (mineral oil)
- Both trials show a >50% increase in atrial fibrillation
- Forget about fish oil, just use olive oil (PREDIMED)

Sunday, July 18, 2021

PLENARY THIRTEEN: Emerging Topics

Lipoprotein (a): an Emerging Area — Steven Nissen, MD

- Please refer to slides found on the plenary under "Session Content"

Early Detection (ASK) & Biomarkers (TEDDY) — Marian Rewers, MD, PhD

- Type 1 diabetes begins long before clinical symptoms
- Persons with multiple and single high-affinity autoantibodies have the disease, not just an increased risk
- Home BG testing is the best method to detect dysglycemia, although CGM may have additional advantages
- Screening for autoantibodies and monitoring can prevent DKA, help preserve insulin secretion, and improve long-term HbA1c

Glucagon Formulations for Hypoglycemia — Eda Cengiz, MD, MHS

- Glucagon has been an important hypoglycemia rescue medication with limited use for hypoglycemia prevention
- Next generation glucagon formulations resolve hypoglycemia fast and effectively, and without the need to mix dry powder and liquid
- Future use: prevention, treatment of mild hypoglycemia, and rescue medication
- Liquid stable formulations of glucagon will enable large-scale development and commercialization of bi-hormonal automated insulin delivery systems
- Novel non-diabetic uses for glucagon in conditions of hyperinsulinism, alimentary hypoglycemia

European Perspective of T1D Adjunctive Treatment — Chantal Mathieu, MD

- Hypoglycemia, weight gain, and glucose variability weigh on quality of life of people with T1D
- Novel glucose measuring tools contribute to less risk of severe hypoglycemia and quality of life
- GLP1 RA and SGLT inhibitors are promising adjunct therapies in T1D, but advantages and safety concerns need to be balanced in each individual patient

Update on Basal and Prandial Insulins — George Grunberger, MD

- Goal: to mimic human physiology
- Basal insulins: longer acting, less variability
- Prandial insulins: faster acting
- Getting there but not quite there yet

Decision Support Systems for MDI Patients — Roman Hovorka, PhD

- Day-to-day variability of insulin requirements limits glucose management particularly in non-closed-loop therapy settings
- Decision support systems have the potential to assist in diabetes management
- Necessary pre-requisites includes low-burden data collection and integrated systems/devices
- Potential benefits (to be demonstrated)
    - Replacing (lack of) expertise — non-inferiority claim
    - Improving outcomes — superiority claim
    - Quality of life
- Challenges include clinical inertia