Ragnar Hanas

Suggest adding: "When metformin is added to insulin therapy, insulin doses must be deceased considerably (ie by 30-50%) to avoid hypoglycemia." This is mentioned on p. 17.

Response: This is already included in the text as written: Transition onto metformin can usually be achieved over 2-6 weeks by decreasing the insulin dose 30-50% each time the metformin is increased.

HbA1c target: ADA suggests 6.5% [48 mmol/mol] for adults with type 2 diabetes treated with lifestyle or metformin only. Young people will have an even longer diabetes duration than adults, and should therefore in my opinion have the same targets as adults.

Response: I (Phil Zeitler) completely agree with you, but the writing group was unwilling to go this far from the recommendations for kids with type 1. Our compromise was to indicate that 6.5% should be considered in some situations. I have modified the text to carry through 6.5% as an alternate target throughout the text.

p. 24: Albuminuria levels are given in mg/g, while the 2014 complications chapter uses mg/mmol for albumin/creatinine ratio. Needs alignment.

Response: thanks for noticing this. SI units added.

p. 25 The use of statins in sexually active adolescent females must be carefully considered and the risks explicitly discussed, as these drugs are teratogenic and not approved in pregnancy.

Response: further emphasized.

I am missing text on acanthosis nigricans. In the clinical context of new-onset diabetes in a country with a low incidence of T2D, AN is a good marker for suspecting T2D and beginning with metformin early, ie before results of autoantibody testing has been received.

Response: I respectfully disagree. AN is a poor discriminator for type 2 diabetes. It is only a marker of insulin resistance, but an obese Hispanic or African kid with type 1 diabetes may very well have AN and relying on this poor discriminator could lead away from the correct diagnosis. While it's possible that AN might be useful in a European country with low reT2D incidence, there are many more places where it would be a mistake to use AN. Therefore, I don't think it adds enough in a few places to include it where it might be misinterpreted.

Joe Wolfsdorf

Page 4 bullet 3

Highlight that this should be a FASTING lipid profile? 3aii (1) states fasting

Response: thanks for pointing this out. This is actually a little complicated. According to the ADA and AHA, and now the AAP, the initial sample doesn't need to be fasting, whereas
we would recommend that the repeat on which treatment decision will be made probably should be. I've tried to clarify. I've also fixed the bullets – the recommendation for repeat fasting sample should have been 3aiii, not a subheading of 3ai.

Page 7 2nd line from bottom of page: typo ethnic/racial

Response: fixed

Page 8 so as not to offend our Canadian colleagues, include Canadian First Nation youth in the list of high risk populations

Response: oh my. That was a bad oversight and not sure how it didn't get picked up before this!

Page 9 3rd line from bottom of page typo: autoimmune-mediated T1D

Response: aren't we medicating people with autoimmune drugs? 😊 fixed

Page 9 The most recent report from SEARCH for Diabetes in Youth study indicated that in youth with T2D, DKA at presentation decreased from 11.7% 2002-2003 to 5.7% in 2008-2010. Dabelea, D et al Pediatrics 2014;133(4):e938-45

Response: I have updated the reference. Since the text only referred to a significant number, I didn't change it. It could be variable in different places and we want people to be aware of the concept that DKA doesn't exclude type 2.

Page 10 Because measurement of diabetes autoantibodies may not be available or cost may be prohibitive, one us has to rely on clinical criteria. The article by Julia von Oettingen in Pediatric Diabetes 2016;17(6):416-425 provides a simple clinical scoring system (weight Z-score, age and race) that may be useful in these circumstances (low resource settings).

Response: As much as this paper had a stellar set of authors, the population studied had very little in common with the typical population faced by a clinician seeing a minority kid with new onset diabetes. This paper looked at the ability to identify type 1, which was strongly driven by young age and white ethnicity. That's very different from picking out type 2 from a minority obese population with new onset diabetes. I've not seen a similar analysis of predictors of type 2 in a group of kids with phenotypic type 2 diabetes, which is what the bullet on page 10 is referring to. Georgeanna did it in the TODAY kids, but there was so much overlap between them that discrimination by characteristics is poor.

Page 11 … as the insulin resistance of puberty wanes

Response: fixed

Page 24 Indicate whether the goals levels refer to fasting or non-fasting samples… or does it matter? Fasting samples more difficult to obtain in clinical practice. May require patient returning to clinic on another day and this adds to the patient’s burden (inconvenient, cost of travel, time off work, missed school, etc.).

Response: addressed as above. non-fasting initially, fasting on return (but that can be prearranged).