Text
It’s 9 PM Tuesday. Welcome to #NephJC
My name is Joel Topf, co-founder of #NephJC & self-described salt whisperer.
This is my first time hosting with 280 characters so if i start to ramble, just block me. #NephJC #Withoutlimits
While we get set up, please introduce yourselves and reveal any relevent conflicts of interest (COI) #NephJC
Even if you are just lurking, please introduce yourself! We promise not to bite! #NephJC
I am a clinical nephrologist @OUWB and am only one of 22 people they follow. So proud. #NephJC
Remember to add #NephJC to every tweet you want to be part of the discussion and recorded in the journal club archive.
We recommend using tchat.io or tweetchat.com. They filter out everything but the hashtag and add #NephJC to every tweet, unfortunatly they don't support 280 characters.
So it looks like you are on your own and will need to add "#NephJC" on your own or just limit yourself to 140 characters. I've been using TweetDeck recently and have really enjoyed it. Tweetdeck.com
#NephJC is a great way to build your personal learning network, so hit that follow button early and often!
Tonights #NephJC article is currently available full text at JCI so come and get it! https://www.jci.org/articles/view/89812
Don't miss the excellent #NephJC summary written by Joshua Rein, DO (@ThepHunClub). You can read here: http://www.nephjc.com/news/thiazide
Topic Zero. Tell about the nastiest case of thiazide induced hyponatremia you have ever seen. #NephJC
Topic Zero. What do you think of the abbreviation TIH for Thiazide induced hyponatremia
Topic One: Phenotypical analysis
T1 the authors started with two cohorts. Cohort 1 was 48 patients with TIH (Na <130) and 80 matched controls (normal Na on HCTZ) #NephJC PICTURE
T1 Cohort 2 was 109 cases of TIH and two sets of matched controls: one with normal Na on HCTZ and another with normal Na not on HCTZ. #NephJC
T1 Both cohorts had pretty extensive serum and urine testing, but cohort two had 24-hr urine testing and they went back 2 months re-tested patients. #NephJC
T1 The paper says the patients all had symptmatic hyponatremia but I couldn't find a description of the patient's symptoms anywhere. #NephJC
T1 Table One PICTURE #NephJC
T1 How many of you are frequent users of bendroflumethiazide? Never used it in my life. #NephJC
T1 The patients on thiazides with hyponatremia had a number of mild differences in their electrolytes. This is summarized in the PICTURE. Anyone surprised by any of this? #NephJC
T1 Post-publication peer review alert! Page 3368 says thiazide users had a lower glucose, they had a higher glucose. #NephJC does the copy editing so you don't have to! PICTURE
T1 On the 24-hour urine analysis, urine volume and osmolality were lower in the hyponatremic patients. These patients made less urine but it was more watery. Supplement Figure 3 PICTURE #NephJC
T1 The HIT patients had persistently low chloride and zinc levels 2 months after stopping the thiazides. Spooky Chloride? All other electrolytes normalized. #NephJC
T1 then they looked at free water reabsorption and showed that HIT patients had an eagerated increase inresponse to thiazide exposure compared to people who did not get hyponatremiac. #NephJC
T1 this was new to me. HIT had always been explained as situational rather than having signifigant host factors. #NephJC
T1 I understood HIT as volume depletion leading to ADH paired with increased (or steady) water intake. #NephJC
T1 Another part of my "knowledge" of HIT was that these patients had hypovolemia and increased serum uric acid. Well take a look at this Figure. #NephJC
T1 How do you square low urine uric acid and low serum uric acid? And to add to the weirdness elevated Fractional Excretion of Uric Acid. Picture7 and 8 #NephJC
T1 but the one that really baked my noodle was plasma ADH. So the low osmolality is surpressing the ADH in these hypoosmotic patients but they are still making urine with an osmolality of 366 (plasma osmolality is 255) #NephJC PICTURE

T1 Anybody else wish they included a copeptin assay to confirm these totally wacked findings? https://www.ncbi.nlm.nih.gov/pubmed/16269513 #NephJC PICTURE

TOPIC TWO: GENETIC ANALYSIS #NephJC

T2: They did GWAS of cohort 1 and compared them to a 1958 British Cohort. #NephJC

T2 suggestive associateions with a P< 10^-5 resulted in half a million SNPs from there they narrowed it down to 17. #NephJC PICTURE SNP 1 and 2

T2 Here are the 14 SNPs (yes I know I said 17 in the previous tweet.) #NephJC PICTURE SNP3

T2 They then did a deep dive on the SNPs close to the gene SLCO2A1. One SNP in particular had an OR of 2.58 for HIT

T2 there is a lot of genetics I don't understand but this genetic variant in SLCO2A1 that tracked with an increased risk of HIT was foundin both Cohort 1 and Cohort 2. #NephJC

T2 SLCO2A1 codes for a prostaglandin transporter PGT. This transporter is expressed in lots of places in the kidney. But not in the thick ascending limb. FOund in gloms, capillaries and medullary collecting tubules. #NephJC

T2 then they went and looked at urinary prostaglandin levels by SLCO2A1 status. If they had the HIT mutation they had increased urinary PGE levels. #NephJC PICTURE

T2 after that there is a section that I have no idea what is going on. "In vitro assessment of SLCO2A1 396 Ala/Thr/Glu variants" I'm going to skip it unless anyone has a clue. #NephJC

TOPIC THREE DISCUSSION #NephJC

T3 They discuss how urinary prostaglandins can increase permeability of the medullary collecting duct by 10-15 fold even in the absence of ADH! #NephJC

T3 refernces for that claim: https://www.ncbi.nlm.nih.gov/pubmed/7611450 and https://www.ncbi.nlm.nih.gov/pubmed/7653600