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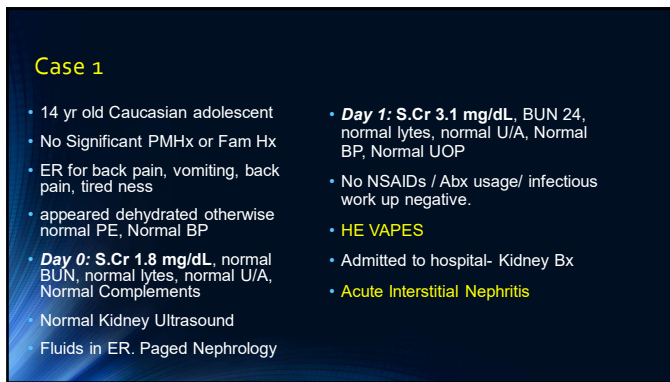
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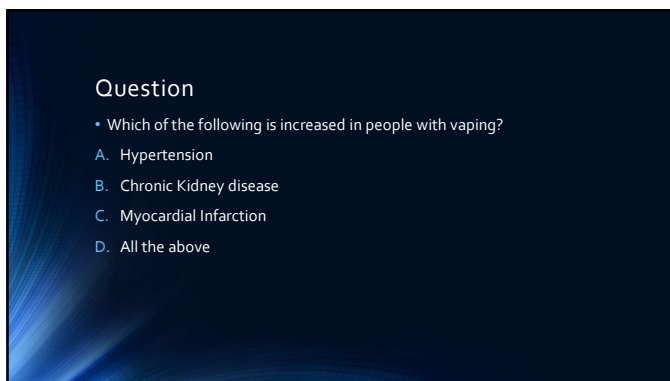
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Update<sup>3</sup> on Spice, Drugs and Rock and Roll –  
is there anything new under the sun?  
Dr. Ryan Redman & Dr. Sudha  
Mannemuddhu

### Nicotine- Cigarettes and Vaping

- Smoking/ Vaping is an independent risk factor for kidney failure
- It is associated with CKD, progression of Diabetic nephropathy or death from end-stage kidney disease (ESKD)
- Mechanism:**
  - Hemodynamic mechanisms (RAAS activation)
  - Non-hemodynamic mechanisms (ROS & nuclear factor-kappa B (NF-κB) production)
  - Nicotine → ROS & NLRP6 inflammasome → mild apoptosis and necrosis

Toxics 2020, 8, 92; doi:10.3390/toxics8040092

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### Implications

- Proteinuria and hematuria** was noted in patients with EVALI (20 patients) Abraham et al
- Animal studies (PMID: 33606584)
  - Vaping and cigarette smoking → impaired endothelium-dependent & endothelium-independent vasodilation, systemic HTN, ↑ systemic vascular resistance (16 weeks) → LVH (32 weeks) → **elevated heart weight and aortic thickness (60 weeks)**
  - earlier and were more severe with higher nicotine exposure
- 1.2X HTN, 2.2X coronary artery disease, 3.8X MI** compared to non-users (PMID: 35899059)
- current-smokers had a 4.0 times, former-smokers had a 3.3 times** higher risk of kidney failure when compared with never-smokers (Hallan 2011, Kidney International)

JASN June 2002, 13 (6) 1663-1672

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### Case 1 Rx and follow-up

- Received 1 g IV Methyl Prednisolone x 3 days → 60 mg of oral Prednisone x 4 weeks, followed by taper over 4-5 weeks
- Followed for 2 more months – normal BP, urinalysis and kidney function tests

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Update on Spice, Drugs and Rock and Roll –  
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**Case 2**

- 17 yr old Caucasian adolescent with Alport syndrome- CKD, HTN, and deafness
- Baseline S.Cr: 1.6 mg/dL No follow-up for 6 months, presented to ER with back pain
- Appeared dehydrated, elevated BP
- **Day 0: S.Cr 3.2 mg/dL**, normal lytes, proteinuria+
- Hx of not taking anti-HTNives
- Fluids in ER. Paged Nephrology
- **Admitted to hospital**
- MIVF, Tylenol for back pain
- No NSAIDs / Abx usage. He **vapes**
- **Day 3: S.Cr 2 mg/dL**, normal lytes, proteinuria+, Elevated BP, Normal UOP
- Agreed to take Lisinopril and follow-up with nephrology. ?Quit Vaping
- **1 year later → S. Cr 2s, BP is better while on Lisinopril, proteinuria+, still vaping**

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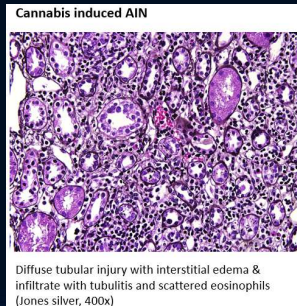
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**Case 3**

- 15 yr old Caucasian adolescent with obesity
- No Significant PMHx or Fam Hx
- Local urgent care persistent vomiting, decreased UOP → Zofran → 4 days later persistent symptoms, malaise, fatigue → PCP
- **Day 0 Labs: BUN 48 mg/dL, S. Cr 4.5 mg/dL**
- Advised to go to ER
- Hx of smoking **Cannabis joints & synthetic cannabis**



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**Question**

- Which of the following statements is true regarding synthetic and natural cannabis?
- A. Synthetic is more potent than natural cannabis
- B. Synthetic is less potent than natural cannabis
- C. Both are equally potent

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### Cannabis

- Cannabis/Marijuana
- Use described as
- categorized as a
- **Research Labs:**
- The first cannabis
- Another major ca
- This led to the dis
- Currently, two syn
- approved by the F

...abaceae family

...ed in 1964, in Israel

...inoid system

...e (schedule II), are

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### Endocannabinoid System

- Has been found to play a beneficial role in renal homeostasis and improvement of tubular cell survival
- Overexpression of CB1 → proteinuria, glomerular pathology, increased urine and sodium output (vascular and tubular control)
- Associated with faster decline in eGFR in patients with CKD compared to non users
- 60 noted cannabinoids in non-synthetic cannabis & >180 different types of synthetic cannabinoids (do not show up in a standard urine drug screen)
- Synthetic cannabinoids stimulate the same receptors, but are much more potent (up to 800x) than THC

Park et al. Am J Physiol Renal Physiol. 2017 Nov 1;313(5):F1124-F1132. PMID:292153.  
 Kozlov A. Clin Kidney J. 2013 Jun;6(2):130-3. PMID:2400490.

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### Case 2 Rx and follow-up

- Received 1 g IV Methyl Prednisolone x 3 days → 60 mg of oral Prednisone x 4 weeks, followed by taper over 6 weeks
- Received Magnesium, Potassium and bicarbonate supplementation for about a month
- Vitamin D def was corrected
- 1 month after completing steroids, he developed Iridocyclitis → TINUS syndrome
- Treated with topical steroids.
- 1.5 year follow-up → Normal Kidney function. He continues to have tubular proteinuria (Not albuminuria), On RAASI

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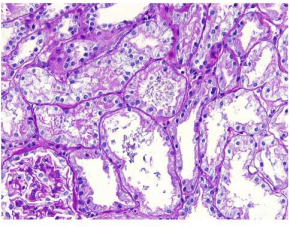
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Update<sup>12</sup> on Spice, Drugs and Rock and Roll –  
 is there anything new under the sun?  
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 Mannemuddhu

**Case 4**

- 16 yr old Caucasian adolescent admitted with seizures and altered sensorium
- Partying- + for alcohol and Cannabis
- HTN, AKI
- S. Cr 1.7 → peaked at 5.4 mg/dL
- Urinalysis 2+ Blood, 2+ protein
- Oliguria
- Isoechoic kidneys (11 and 12 cms)

**Cannabis induced toxic ATI**



Diffuse tubular injury with loss of brush border (PAS, 400x)

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**Take Home Message**

- Smoking/ Vaping is an independent risk factor for kidney failure and is associated with CKD, diabetic kidney disease
- It also increases the odds of HTN, MI, CAD etc
- Endocannabinoid system and balance between CB1 and CB2 activity are essential
- Excessive stimulation can cause AKI, which is worse with synthetic cannabis
- Medicinal value of CBD for CKD/ AKI is still in nascent stages

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**THANK YOU!**  
 QUESTIONS???

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Update<sup>15</sup> on Spice, Drugs and Rock and Roll –  
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