An Assessment of Cardiomegaly and Opioid-Related Death

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Outline

- Research questions
- Opioid action, classic autopsy findings, and needles in arms: a tense trio
- Methods
- Present data collected at the Jefferson County OCME
- Discussion of findings

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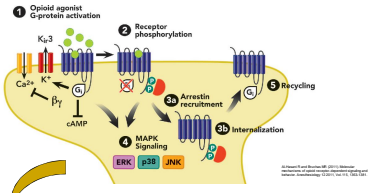
Opioid receptors: Signaling



Neuronal calcium influx, neurotransmitter release

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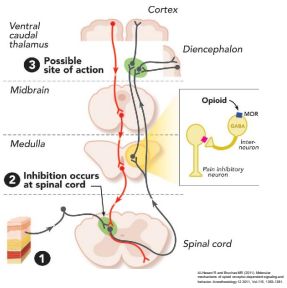
Opioid signaling: Sites of action



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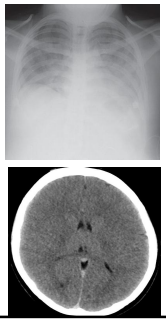
Classic autopsy findings in opioid-related deaths



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Completing the classic triad…

- Opioid-mediated diminished outflow from CNS/spinal cord diminishes micturition reflex → diminished urinary outflow → distended bladder

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JCOCME Experience: Decedents don't always "read the book."

- Many decedents who died an opioid-related death do not show classic autopsy findings just described.
- Next-of-kin, friends, or others present around time of death often do not report the decedent displaying signs of a respiratory-driven death, such as snoring or coughing.
- Some decedents who used heroin are found with a needle in their arm, suggesting a relatively rapid death, such as a cardiac event.

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...But opioid receptor signaling can be cardioprotective

- However, there is evidence that activation of the delta-opioid receptor induces cardiac myocyte hibernation, thereby protecting them from cell damage or death in the event of ischemic events.
- This protection may be even greater when kappa-opioid receptors are simultaneously activated.

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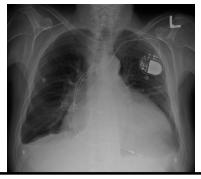
Research questions

- Given the tension among the classic triad, our office's experience, and the putative role of opioid signaling in cardioprotection, do decedents dying opioid-related deaths exhibit cardiomyopathy (e.g. cardiomegaly?)



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Methods

- Queried OCME FileMaker database for deaths
  - Data range: January 1, 2016 – December 31, 2018
  - Deaths due to opioid toxicity vs. control
  - Exclusions:
    - Drugs detected at time of death
    - Deaths due to chronic substance use
    - Age < 20 years
    - BMI < 10 kg/m^2
- Data concerning demographics, BMI, heart weight, body length, body weight were compiled and analyzed using Microsoft Excel

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Results: Demographics

Comparison of Mean Baseline Characteristics			Pr > F
	Opioid (n=537)	Control (n=662)	
Age	39.04	46.03	<0.0001
BMI	27.97	27.89	0.8797
Height (in)	68.82	68.85	0.8878
Weight (lb)	189.20	189.06	0.9708

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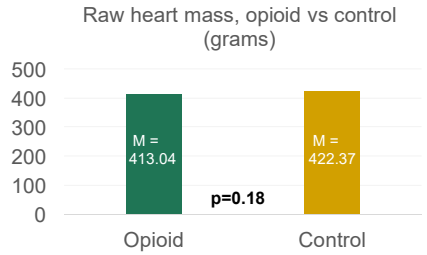
Results: Opioid-related death vs. control heart size 1



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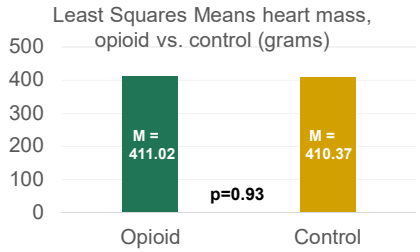
Results: Opioid-related death vs. control heart size 2 -- LSM



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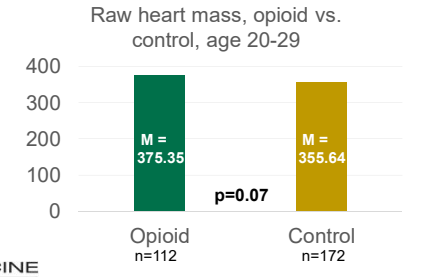

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Conclusions

- Opioid-related deaths have spiked in the past two decades, but the exact pathophysiology underlying the cause of death in many opioid-related deaths remains unclear.
- Some decedents dying of opioid-related deaths do have more massive hearts than previously-published references – as do many controls.
- .There may be underlying cardiac susceptibility in young adults dying of opioid overdose, but its possible significance may be difficult to assess in older populations with comorbid diseases of aging.

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Discussion

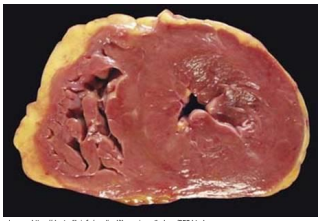

Image: https://doctorlib.info/medical/thoracic-pathology/256.html

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Thank you!

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References

Slide references:

1. Calcaterra S, Glanz J, Binswanger IA. National trends in pharmaceutical opioid related overdose deaths compared to other substance related overdose deaths: 1999–2009. Drug and Alcohol Dependence. 2013;131(3):263–270.
2. Lewis T. The Normal Size of the Heart Muscle Weight.Association for the Publication of the Journal of Internal Medicine 1951.
3. Rudd RA, Seth P, David F, Scholl L. Increases in drug and opioid-involved overdose deaths—United States, 2010–2015. Morbidity and Mortality Weekly Report. 2016;65:1445–1452.

SAMs references:

1. Headrick JP, See Hoe LE, Du Toit EF, et. al. Opioid receptors and cardioprotection- 'opioidergic conditioning' of the heart. *British Journal of Pharmacology* 2015; 172(8): 2026.
2. Pelletier D, Andrew T. Common findings and predictive measures of opioid overdoses. *Academic Forensic Pathology* 2017; 7(1):91.

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CME Question 1

Which of the following represents the classic autopsy findings of an opioid-related death?

a. Cardiomegaly, cerebral edema, distended bladder

b. Pulmonary edema, cerebral edema, distended bladder

c. Pulmonary wedge infarct, cardiomegaly, cerebral edema

d. Abdominal aortic aneurysm, pulmonary edema, distended bladder

e. Cardiomegaly, pulmonary edema, cerebral edema

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CME Question 2

Activation at which of the following opioid receptors induces a cellular hibernation-like state, promoting anti-ischemic effects, thereby partially explaining the cardioprotective mechanism of opioids?

a. Delta

b. Kappa

c. Mu

d. Nociceptin/orphanin FQ

e. Zeta

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CME Question references

1. Pelletier D, Andrew T. Common findings and predictive measures of opioid overdoses. *Academic Forensic Pathology* 2017; 7(1):91.
2. Headrick JP, See Hoe LE, Du Toit EF, et. al. Opioid receptors and cardioprotection- 'opioidergic conditioning' of the heart. *British Journal of Pharmacology* 2015; 172(8): 2026.

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