

# **68 year old female with Hypertensive Emergency**

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# History of past illness:

- 68 y.o. female who was brought to ER by her daughter due to significant functional decline over the month prior to admission:
  - The pt was no longer able to live by herself, not able to ambulate,
  - The pt was very confused and was confusing her relatives,
  - She stopped taking her medications, since she thought they were making her to be this way,
  - She could go several days without eating and lost about 15lbs during a month prior to admission.

# Past medical history:

- DM2,
- COPD,
- depression,
- HTN,
- CKD stage 3,
- mitral valve prolapse,
- CAD, s/p stent in LAD in 2008,
- peripheral vascular disease , s/p stent x 2 to superficial femoral artery in 2008,
- Hyperlipidemia
- Macular degeneration
- Hepatitis C
- Home medications: albuterol, aspirin, bumex, phoslo, plavix, cardizem, gemfibrozil, hydralazine, vicodin, Lantus, lisinopril, multivitamins, zaroxolyn, metoprolol, protonix, lyrica, sodium bicarb, trazodone.
- Family history: dementia in her mother.
- Social history: retired, widowed, hx of smoking of 1PPD for 51 years, quit in 08/2012, no current illegal drug use, however remote hx of IVDA. No alcohol abuse.

# Interval history:

- In the ED she was found to be hypertensive to 200/130s, w/ pulse in mid 90s to low 100s, and was sat`ing normal on room air.
- She received labetalol 20 mg IV x 1, hydralazine 20 mg IV x 1 w/ minimal effect in BP.
- She was started on a nitro gtt and admitted to MICU. She remained on it for 2 days, her home BP meds were reintroduced.
- The pt spent 2 days in MICU and then was transferred to the floor.
- While on the floor the pt became hypertensive again with a BP in 200/130 and hypoxemic with pulse oxygenation 86-88% on RA.
- She was given Bumex IV and then started on Bumex gtt.
- She was transferred back to MICU for further management.
- In MICU bumex gtt was continued, nicardipin gtt and chlorthiazide 500mg BID were added for BP control.
- The pt remained on the gtt for 3 days, diuresed -5L and then eventually weaned from the gtt to Bumex 2mg IV Q8H, isodril 10mg TID, coreg 50mg BID, hydralazine 100mg Q8H and chlorthiazide 500mg BID.
- Due to concern for poorly controlled BP, requiring multiple medications, her random plasma metanephrines and random urine metanephrines were obtained while she was in MICU
- Endocrinology consulted for further management

# Review of systems and physical exam:

- **Not able to obtain review of systems due to AMS.**
- Constitutional: Patient appears well-developed, well-nourished, in no acute distress.
- Eyes: Conjunctivae are not injected. Sclerae anicteric. Pupils are equal, round, and reactive to light. Extraocular movements are intact.
- Neck: Supple. No thyromegaly or nodules palpated. No JVD.
- Cardiovascular: Regular rhythm and rate. No murmurs appreciated. Intact distal pulses.
- Respiratory/Chest: Normal respiratory effort. **Mild crackles bilaterally.**
- Gastrointestinal/Abdomen: Normoactive bowel sounds. Soft, nontender, nondistended.
- Musculoskeletal/extremities: **Edema 1+ bilaterally.**
- Neurological: **AAOx0, does not follow commands.** Normal deep tendon reflexes.
- Vitals: BP 111/56, HR 60, RR 21, height 160 cm, weight 62.8 kg, BMI 24.53.

# Labs:

142	104	78	105
3.3	24	2.7	

Ca 9.0 (8.4-10.2 mg/dL),  
Phos 5.8 (2.5-4.4 mg/dL)  
Mg 2 (1.6-2.5 mg/dL)

## LFTs:

Total Protein 6.3 (6-8.3 g/dL)  
Albumin 3.6 (3.5-6 g/dL)  
Total Bilirubin 0.5 (0.1-1 mg/dL)  
Alk Phos 50 (30-120 U/L)  
AST 38 (8-37 U/L)  
ALT 9 (8-35 U/L)

HA1C 6.1%

TSH 0.58 (0.3-4 mcU/mL)

5.3	7.2	153
	21.9	

Aldosterone <4 (<21 ng/dL)

Renin 2.7 (<=0.6-3.0 ng/mL/h)

## Random plasma metanephrines:

Normetanephrine 1.4 (<0.90 nmol/L)

Metanephrine 0.45 (<0.50 nmol/L)

## Random urine metanephrines:

Metanephrine/Creatinine 973 (29-158 mcg/g )

Normetanephrine/Creatinine 3060 (141-574 mcg/g)

Total Metanephrine/Creatinine 4033 (206-733 mcg/g)

# Labs:

## **Random plasma metanephrines:**

Normetanephrine 2.9 (<0.90 nmol/L)

Metanephrine 0.43 (<0.50 nmol/L)

## **Random urine metanephrines:**

Metanephrine/Creatinine 693 (29-158 mcg/g)

Normetanephrine/Creatinine 2186 (141-574 mcg/g)

Total Metanephrine/Creatinine 2879 (206-733 mcg/g)

## **24hrs urine catecholamines:**

Norepinephrine 11 (5 to 8 mcg/24 h)

Epinephrine 3.9 (0.0 to 20.0 mcg/24 h)

Dopamine 30 (65 to 40 mcg/24 h)

## **24 hrs fractionated metanephrines:**

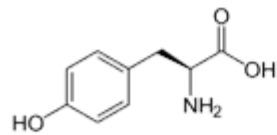
**Metanephrines** 459 (30-180 mcg/24 h  
(Normotensive), <400 mcg/24 h  
(Hypertensive))

**Normetanephrine:** 1835 (138-521 mcg/24 h  
(Normotensive), <900 mcg/24 h  
(Hypertensive))

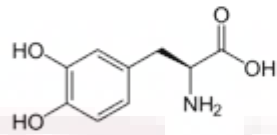
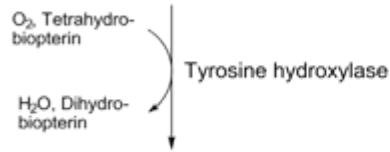
**Metanephrine:** 2294 (171-616 mcg/24 h  
(Normotensive), <1300 mcg/24 h  
(Hypertensive))

- The pt was discharged to rehab on the following regimen: bumex, hydralazine, isodril, coreg and norvasc
- Her BP was in 120-140/60-70 range prior to discharge
- Follow up with endo is scheduled

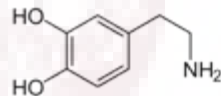
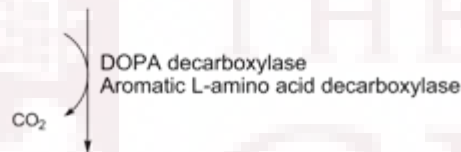
- Does this patient has pheochromocytoma?
- What is the best diagnostic test for pheochromocytoma?
- Can chronic kidney insufficiency affect the results of test and metanephrines measurement?
- What medications might interfere with the test?



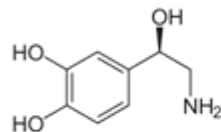
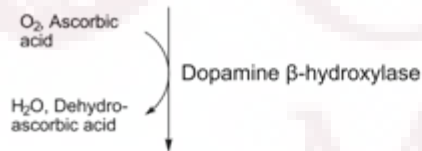
**L-Tyrosine**



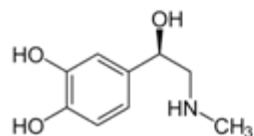
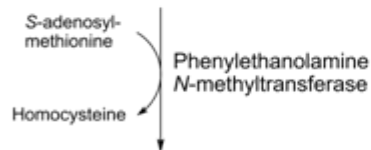
**L-Dihydroxyphenylalanine (L-DOPA)**



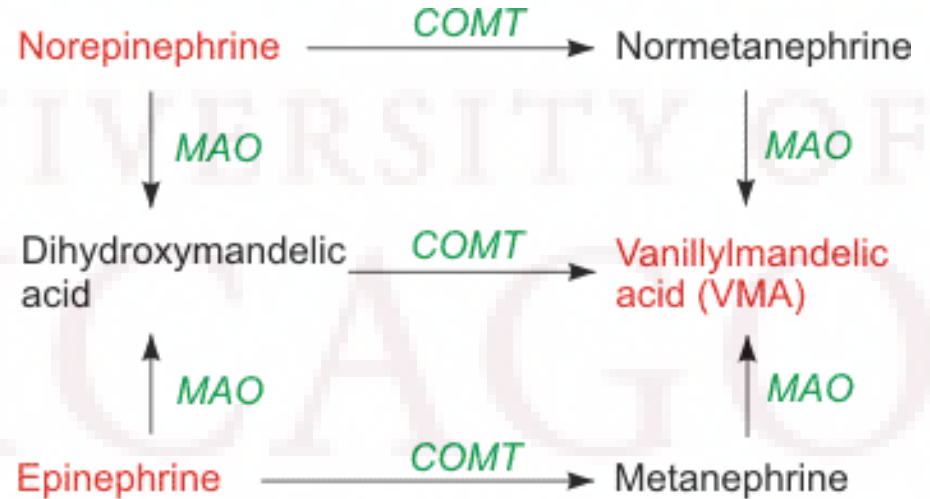
**Dopamine**



**Norepinephrine**



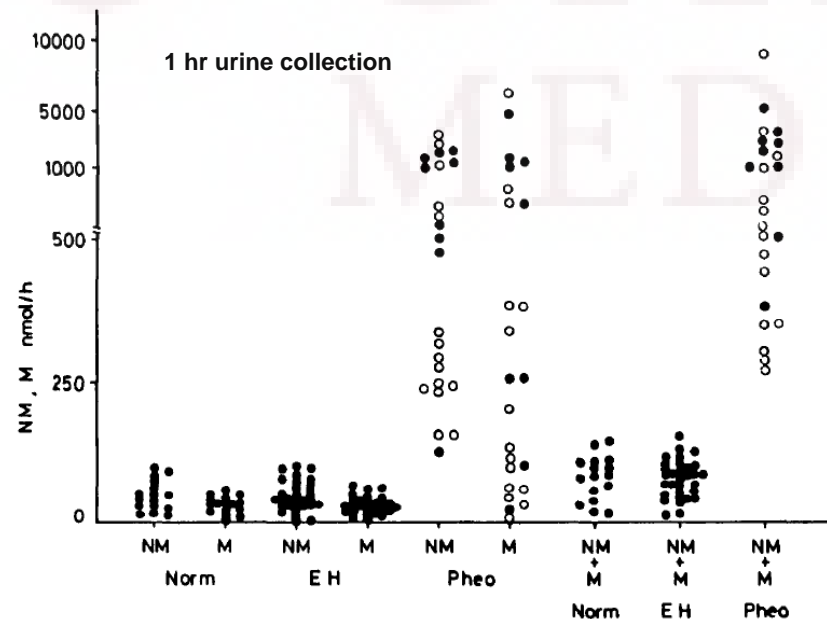
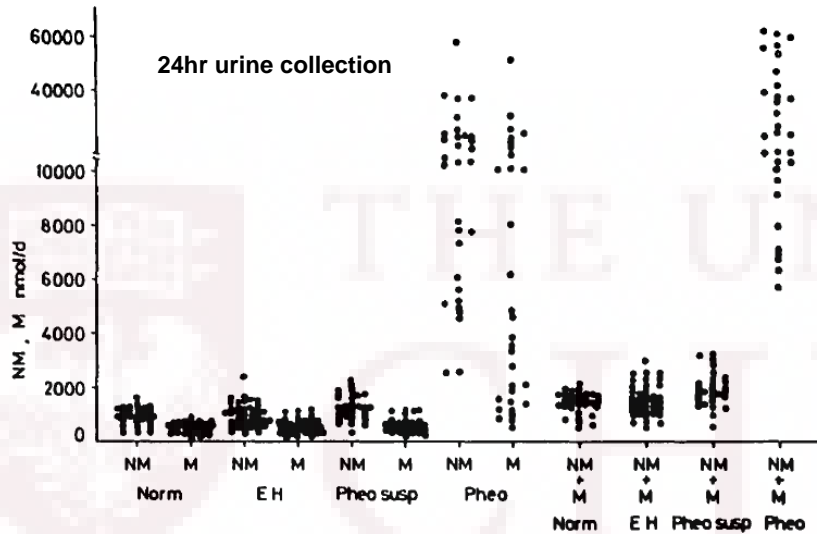
**Epinephrine**



MAO = monoamine oxidase  
 COMT = catechol-O-methyltransferase

- What test is the best?

# Random urine metanephrines vs 24hr urine metanephrines:



There were significant correlations of urinary NE, E, NE plus E, NM, M, and TM levels between random 24-h and 1-h urine collections in 24 patients with pheochromocytoma

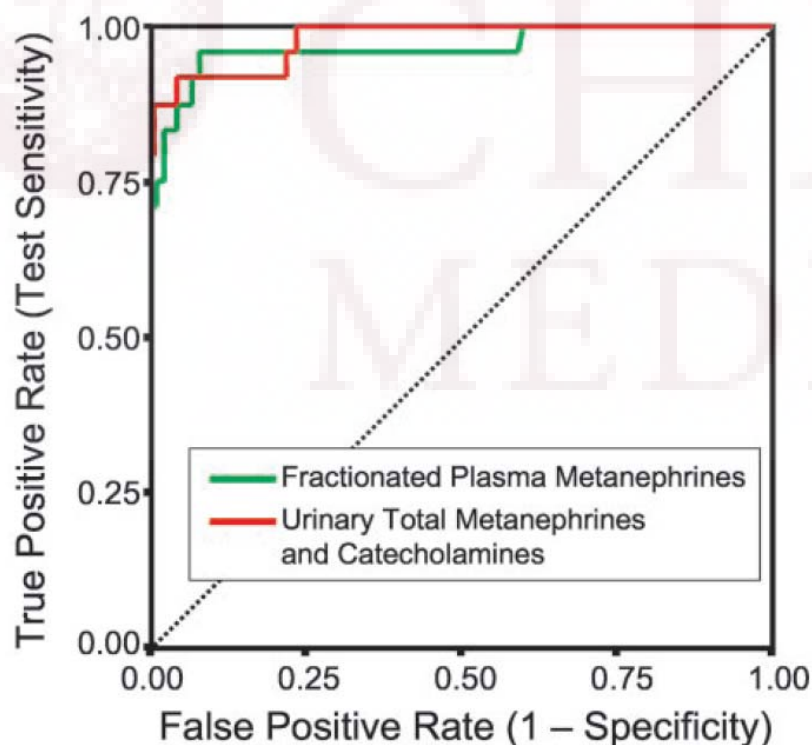
(NE,  $r = 0.79$ ; E,  $r = 0.90$ ; NE plus E,  $r = 0.81$ ; NM,  $r = 0.65$ ; M,  $r = 0.73$ ; TM,  $r = 0.63$ ;  $P < 0.001$ ).

Oishi S, Sasaki M, Ohno M, Sato T. Urinary normetanephrine and metanephrine measured by radioimmunoassay for the diagnosis of pheochromocytoma: utility of 24-hour and random 1-hour urine determinations. J Clin Endocrinol Metab. 1988 Sep;67(3):614-8.

# Fractionated plasma metanephrines vs 24hrs urinary metanephrines and catecholamines:

Biochemical test	Sensitivity <sup>a</sup>	Specificity <sup>a</sup>
Fractionated plasma metanephrines	30/31 (97)	221/261 (85)
24-h urinary total metanephrines and catecholamines (either test positive)	28/31 (90)	257/261 (98)

<sup>a</sup> Data represent number of patients (percentage).



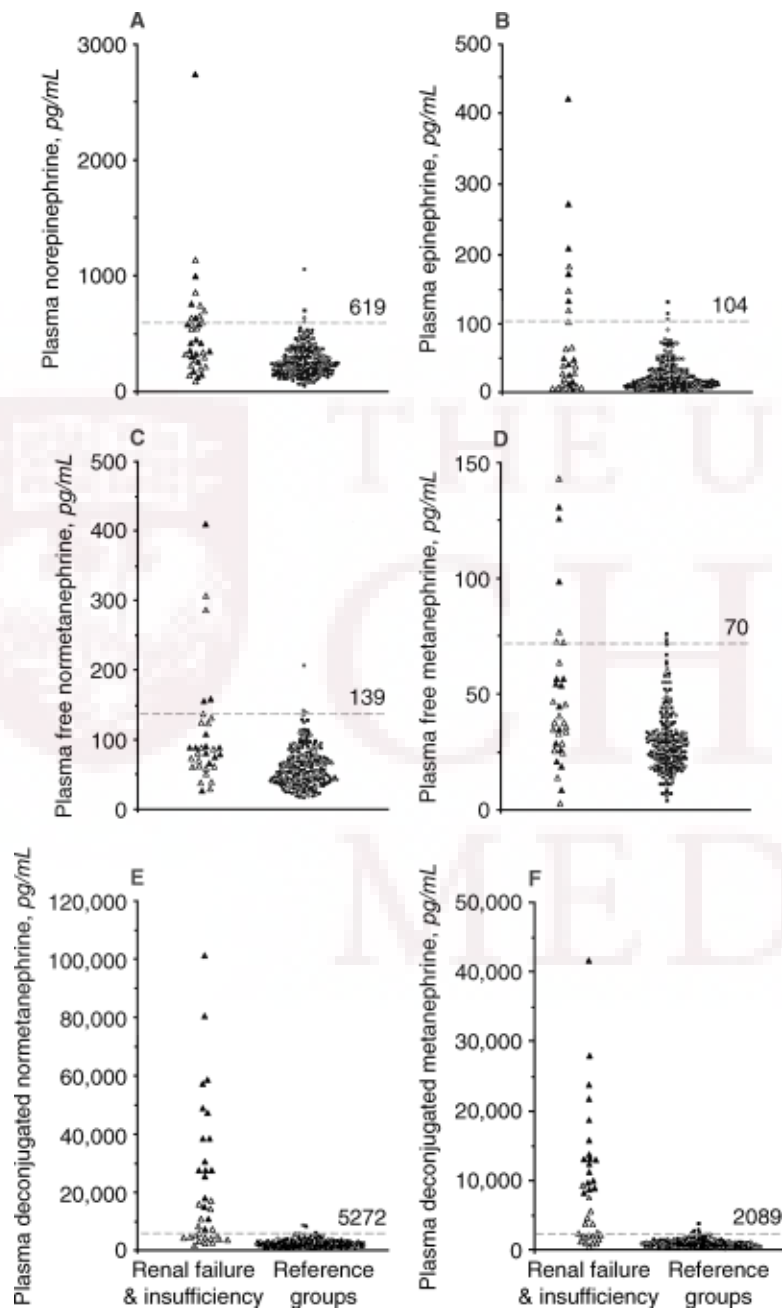
Sawka AM, Jaeschke R, Singh RJ, Young WF Jr. A comparison of biochemical tests for pheochromocytoma: measurement of fractionated plasma metanephrines compared with the combination of 24-hour urinary metanephrines and catecholamines. J Clin Endocrinol Metab. 2003 Feb;88(2):553-8.

# Fractionated plasma metanephrines and catecholamins vs urinary metanephrines and catecholamines:

**Table 3.** Sensitivities and Specificities of Biochemical Tests for Diagnosis of Hereditary and Sporadic Pheochromocytoma\*

	Sensitivity, %†		Specificity, %‡	
	Hereditary	Sporadic	Hereditary	Sporadic
Plasma				
Free metanephrines	97 (74/76)	99 (137/138)	96 (326/339)	82 (249/305)
Catecholamines	69 (52/75)	92 (126/137)	89 (303/339)	72 (220/304)
Urine				
Fractionated metanephrines	96 (26/27)	97 (76/78)	82 (237/288)	45 (73/164)
Catecholamines	79 (54/68)	91 (97/107)	96 (312/324)	75 (159/211)
Total metanephrines	60 (27/45)	88 (61/69)	97 (91/94)	89 (79/89)
Vanillylmandelic acid	46 (30/65)	77 (66/86)	99 (310/312)	86 (132/153)

Lenders JW, Pacak K, Walther MM, Linehan WM, Mannelli M, Friberg P, Keiser HR, Goldstein DS, Eisenhofer G. Biochemical diagnosis of pheochromocytoma: which test is best? JAMA. 2002 Mar 20;287(11):1427-34.



Patients with renal failure had up to two-fold higher plasma concentrations of catecholamines and free metanephrines, and more than 12-fold higher plasma concentrations of deconjugated metanephrines than comparison groups.

Eisenhofer G, Huysmans F, Pacak K, Walther MM, Sweep FC, Lenders JW. Plasma metanephrines in renal failure. *Kidney Int.* 2005 Feb;67(2):668-77.

## Medications that may increase measured levels of catecholamines and metanephrines

Tricyclic antidepressants
Levodopa
Drugs containing adrenergic receptor agonists (eg, decongestants)
Amphetamines
Buspirone and most psychoactive agents
Prochlorperazine
Reserpine
Withdrawal from clonidine and other drugs
Ethanol
Acetaminophen (may increase measured levels of fractionated plasma metanephrines in some assays)

# Take home points:

- When choosing the diagnostic test for the patient, the probability of having pheochromocytoma should be considered:
  - In high-risk patients plasma fractionated metanephrines should be used initially.
  - Negative test will exclude the disease.
  - Mildly positive test could be a false positive and should be followed by 24-urinary fractionated metanephrines, catecholamines, and imaging.
- Kidney dysfunction and medication interfere with measurements of catecholamines and metanephrines and can lead to increased levels of them.

# References:

- Oishi S, Sasaki M, Ohno M, Sato T. Urinary normetanephrine and metanephrine measured by radioimmunoassay for the diagnosis of pheochromocytoma: utility of 24-hour and random 1-hour urine determinations. J Clin Endocrinol Metab. 1988 Sep;67(3):614-8.
- Sawka AM, Jaeschke R, Singh RJ, Young WF Jr. A comparison of biochemical tests for pheochromocytoma: measurement of fractionated plasma metanephrines compared with the combination of 24-hour urinary metanephrines and catecholamines. J Clin Endocrinol Metab. 2003 Feb;88(2):553-8.
- Lenders JW, Pacak K, Walther MM, Linehan WM, Mannelli M, Friberg P, Keiser HR, Goldstein DS, Eisenhofer G. Biochemical diagnosis of pheochromocytoma: which test is best? JAMA. 2002 Mar 20;287(11):1427-34.
- Eisenhofer G, Huysmans F, Pacak K, Walther MM, Sweep FC, Lenders JW. Plasma metanephrines in renal failure. Kidney Int. 2005 Feb;67(2):668-77.