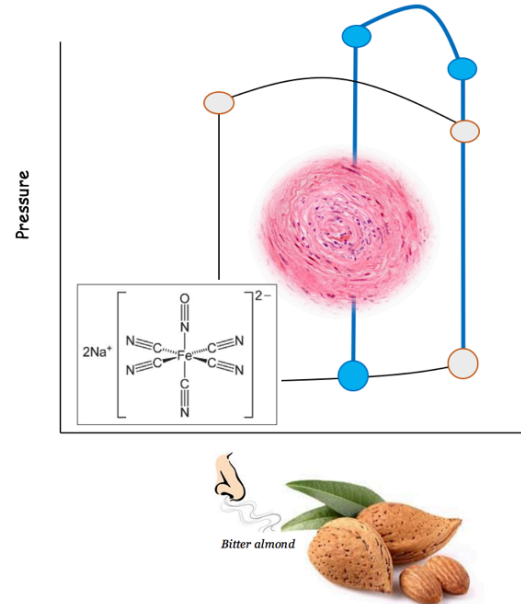
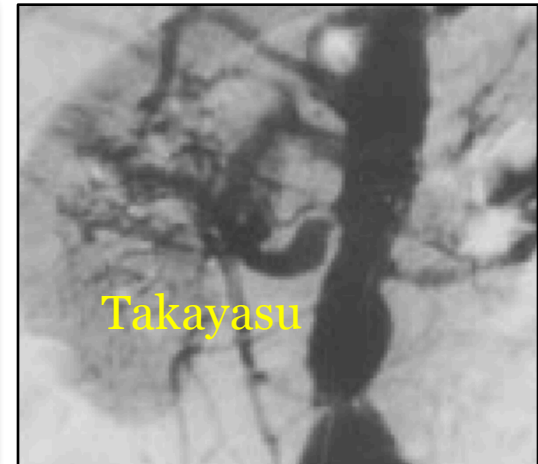
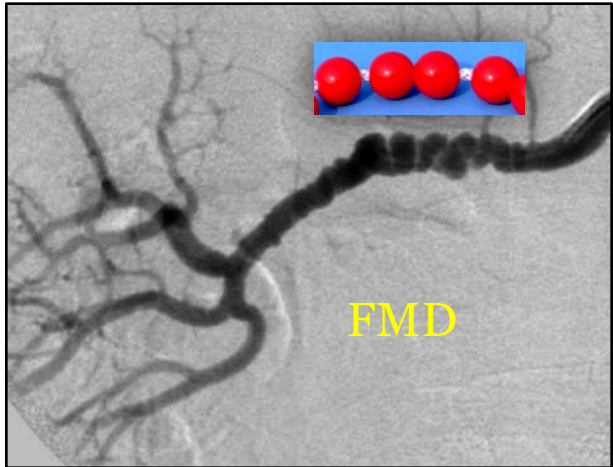


Renovascular Hypertension for the USMLE Step One Exam



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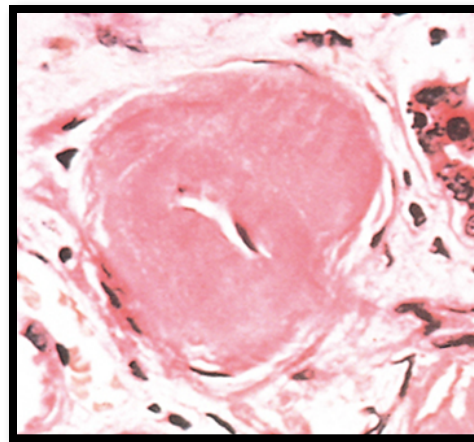
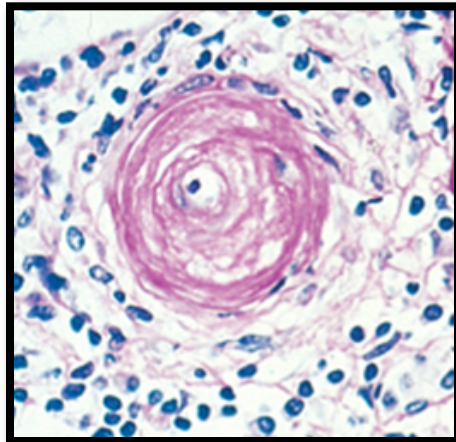


Stenosis Physiology and Related Pathology

The Key Players in *Renovascular* HTN

Vascular Pathology

Hyperplastic arteriolitis



Arteriolar Hyalinosis

Renovascular Disorders (key derivative topics)

- *Malignant HTN (pathophysiology, pathology, pharmacology)*
- Arteriolosclerosis → Nephrosclerosis (pathology)
- Renal Artery Stenosis (physiology and consequences)
 - *Fibromuscular Dysplasia (diagnostics, pathology)*
 - *Takayasu's Arteritis (pathology)*

'Malignant' HTN → Hypertensive Emergency

(...with acute, target organ damage)

- Definition
- Pathology
- Clinical features/Associations
- PharmacRx (Nitroprusside)
 - MOA
 - Pressure-Volume Curves
 - Toxicity

'Malignant' HTN → Hypertensive Emergency

(...with acute, target organ damage)

- Definition: BP elevation with target organ damage (TOD)
 - BP: >200/120
 - Ocular involvement (papilledema/retinal hemorrhage)
 - CNS (confusion/HA)
 - Renal injury (elevated creatinine, hematuria).

It's never subtle...they are going after derivative (pathology, rx)

Papilledema



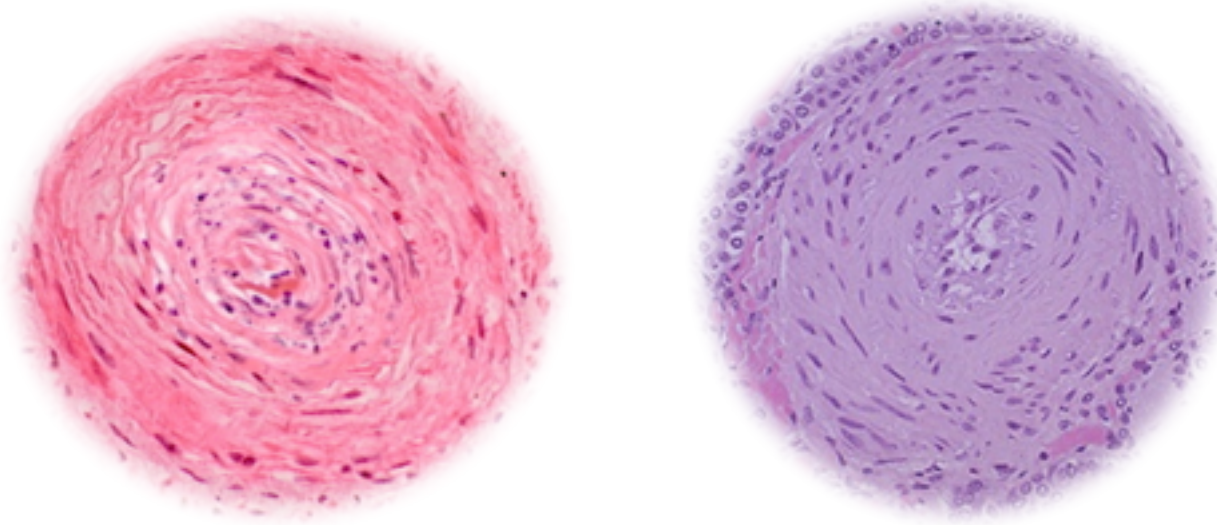
Retinal Hemorrhage



'Malignant' HTN: Pathology

- Pathogenesis
 - Endothelial injury → collagen exposed → platelet deposition
 - Mitogenic factors (PDGF) result in **hyperplasia** of smooth mm

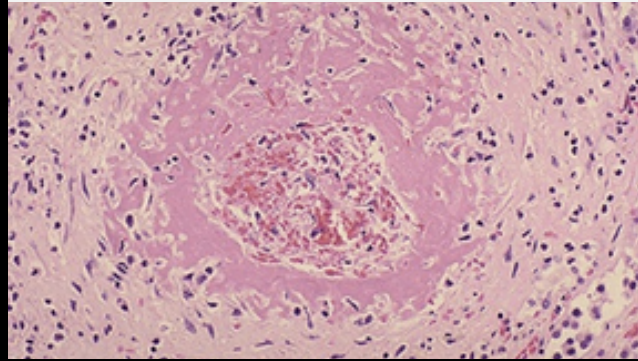
Hyperplasia of smooth muscle → Lumen obliteration



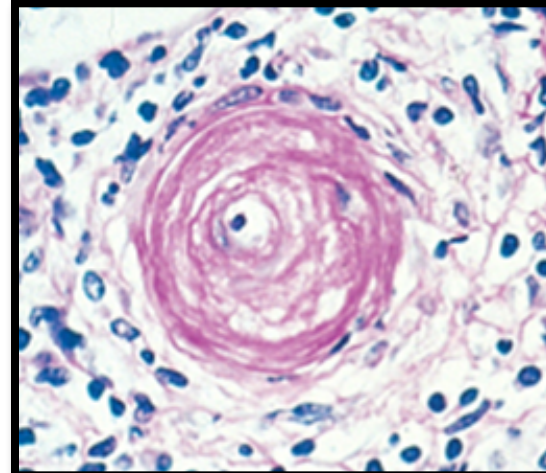
Sheer force injury → Duplication of basement membrane

'Malignant' HTN: Pathology

Loss of cytologic detail



Smudgy (fibrinoid) appearance of necrotic vessel

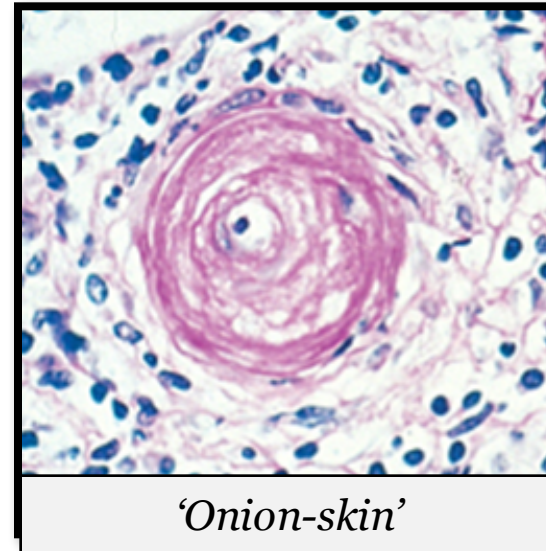
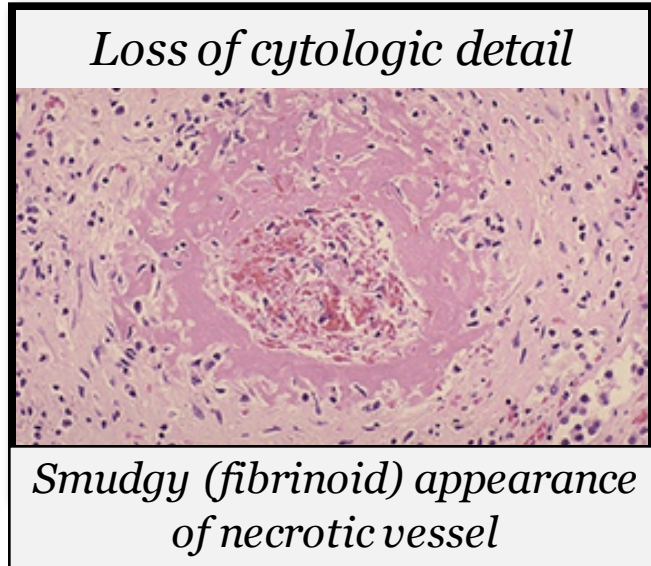


'Onion-skin'

- **Fibrinoid necrosis** (*necrotizing arteriolitis*): fibrinoid deposits and vessel wall necrosis with loss of cytologic detail and 'smudgy' eosinophilic appearance.

Note: PAN is characterized by fibrinoid necrosis (*necrotizing vasculitis*) BUT transmural inflammation is also present

'Malignant' HTN: Pathology



- **Fibrinoid necrosis** (*necrotizing arteriolitis*): fibrinoid deposits and vessel wall necrosis with loss of cytologic detail and 'smudgy' eosinophilic appearance.
- **Hyperplastic** arteriolitis (*arteriolar sclerosis*): concentric proliferation of smooth mm cells with *duplication of BM* (correlates with renal failure).

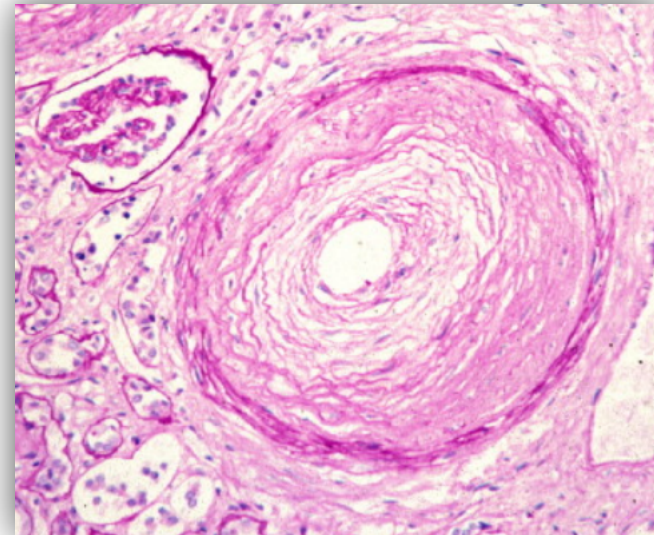
Hypertensive Emergency: *Key Associations*

- Causes ↔ Consequences (TOD)
 - CNS injury ↔ Hypertensive encephalopathy
 - Aortic dissection (renal arteries) ↔ Aortic dissection
 - Cause
 - Drugs (*e.g. MAO-inhibitor, cocaine*), withdrawal (*e.g. clonidine*)
 - Endocrinopathy (*e.g. pheochromocytoma*)
- Consequence
 - Cardiac: ischemia/CHF
 - Renal: AKI

Hypertensive Emergency: *Key Associations*

- Causes ↔ Consequences (TOD)
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 - Endocrinopathy (*e.g. pheochromocytoma*)
 - Consequence
 - Cardiac: ischemia/CHF
 - Renal: AKI
- *Diffuse Systemic Sclerosis*
 - *Obliterative arteriopathy*

*Concentric proliferation of smooth
mm cells with duplication of BM*



Hypertensive Emergency: *Key Associations*

- Causes ↔ Consequences (TOD)

- *CNS injury ↔ Hypertensive encephalopathy*

- *Aortic dissection (renal arteries) ↔*

- *Cause*

- *Drugs (e.g. MAO-inhibitor, cocaine), v*

- *Endocrinopathy (e.g. pheochromocytoma)*

- *Consequence*

- *Cardiac: ischemia/CHF*

- *Renal: AKI*

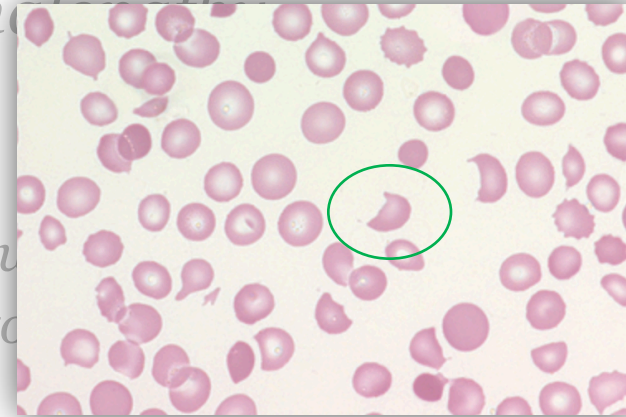
- *Diffuse Systemic Sclerosis*

- ***HELLP Syndrome (preeclampsia)***

- *MHA*

- *Elevated liver chems*

- *Low platelets*



Microangiopathic hemolytic anemia



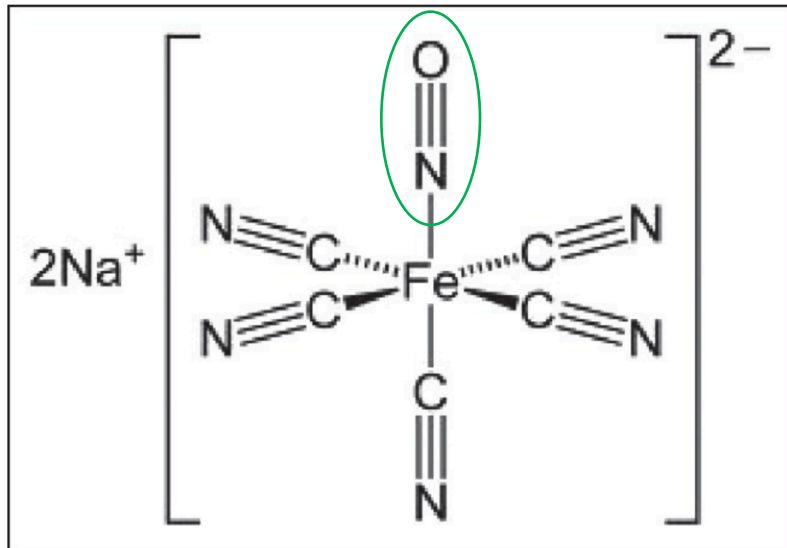
Schistocytes

'Malignant' HTN → Hypertensive Emergency

(...with acute, target organ damage)

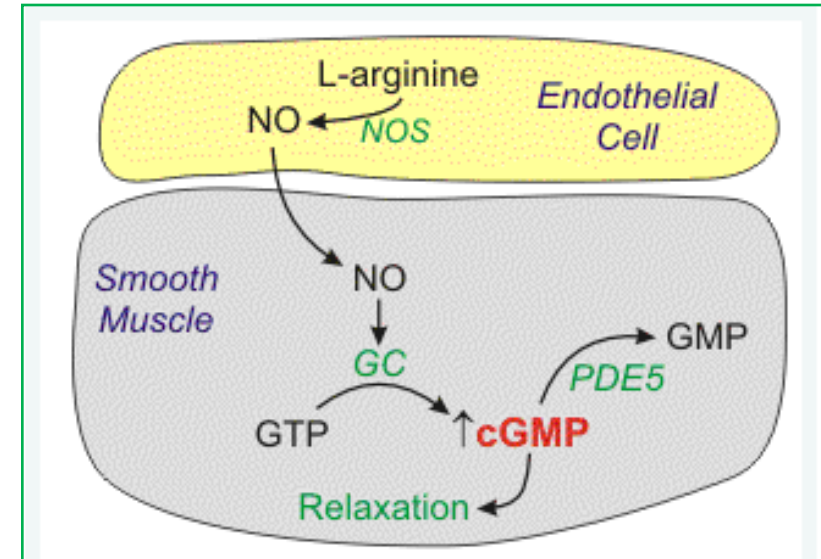
- *Definition*
- *Pathology*
- *Clinical features/Associations*
- *PharmacRx (Nitroprusside)*
 - MOA
 - Pressure-Volume Curves
 - Toxicity

Malignant Hypertension: *Nitroprusside*



Nitric oxide: *vascular smooth mm relaxation*

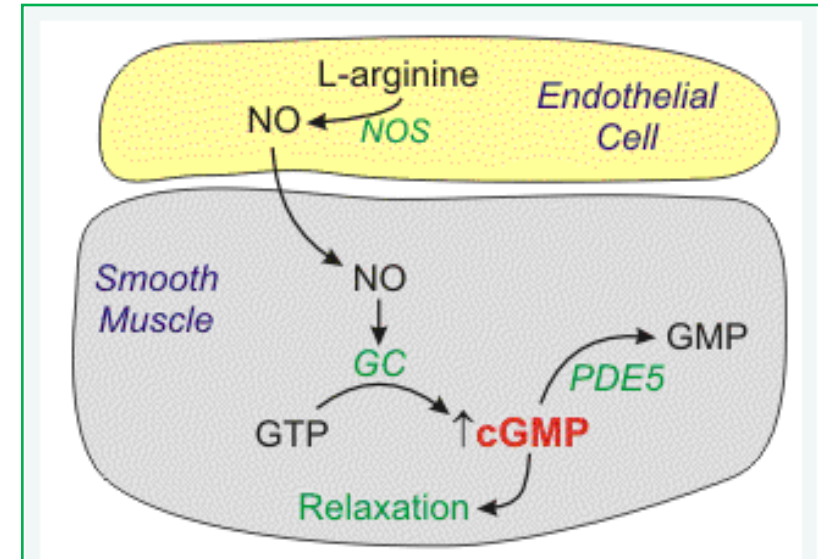
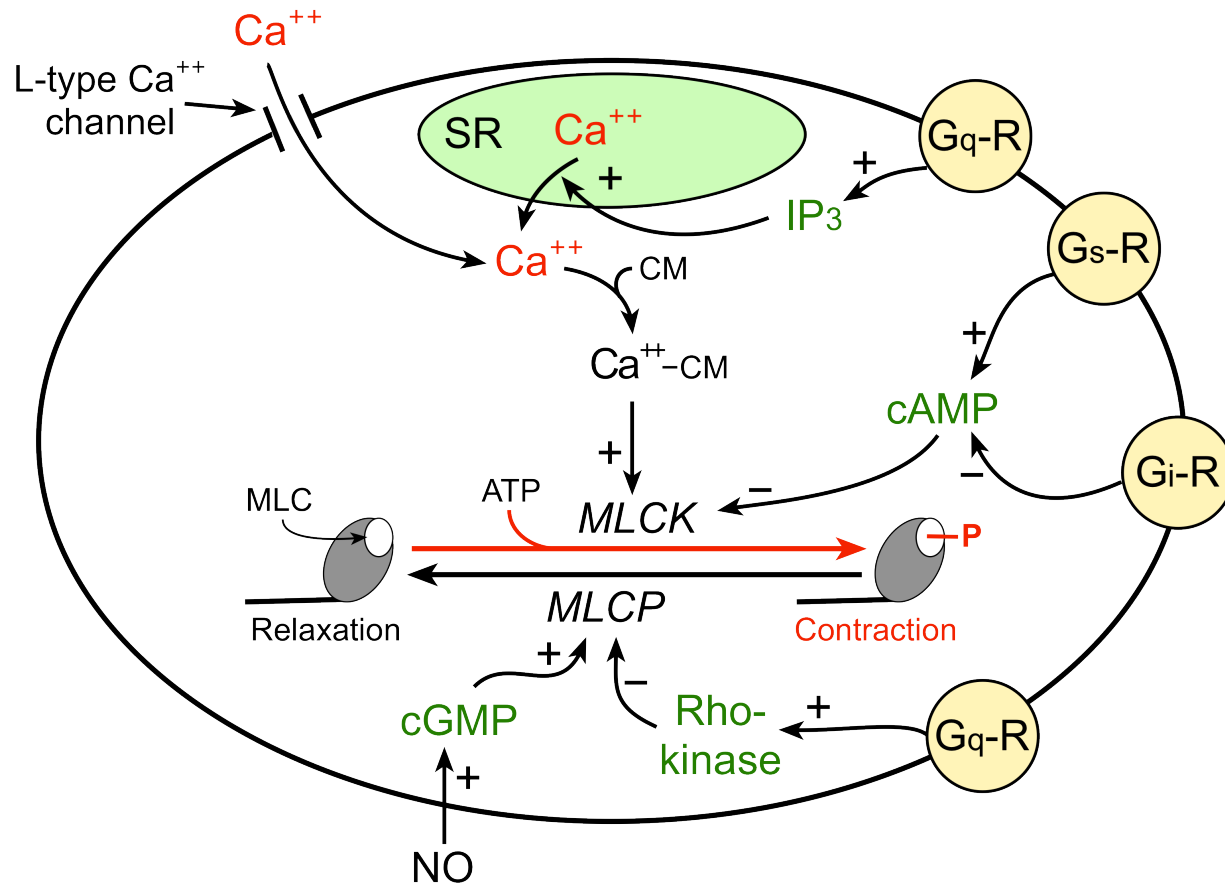
Vasodilation (arteriolar)
Venodilation (venous)



↑ cGMP:

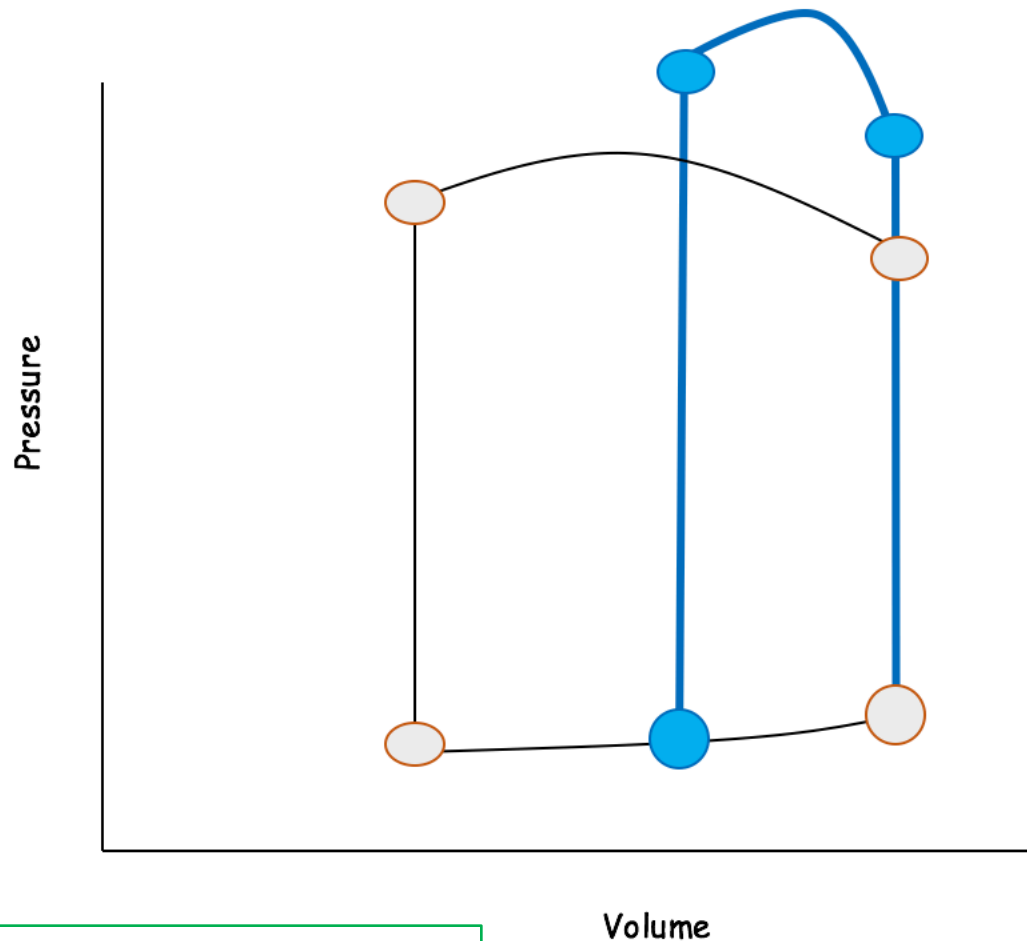
- Decreases IC $[Ca^{+2}]$
- Activates protein kinases → dephosphorylation of MLC

Malignant Hypertension: *Nitroprusside, MOA*



- ↑ cGMP:
- Decreases IC [Ca²⁺]
 - Activates protein kinases → dephosphorylation of MLC

Malignant Hypertension: *Pathophysiology*



LV Pressure-Volume Loop

Similar curve (*morphology*) with aortic stenosis

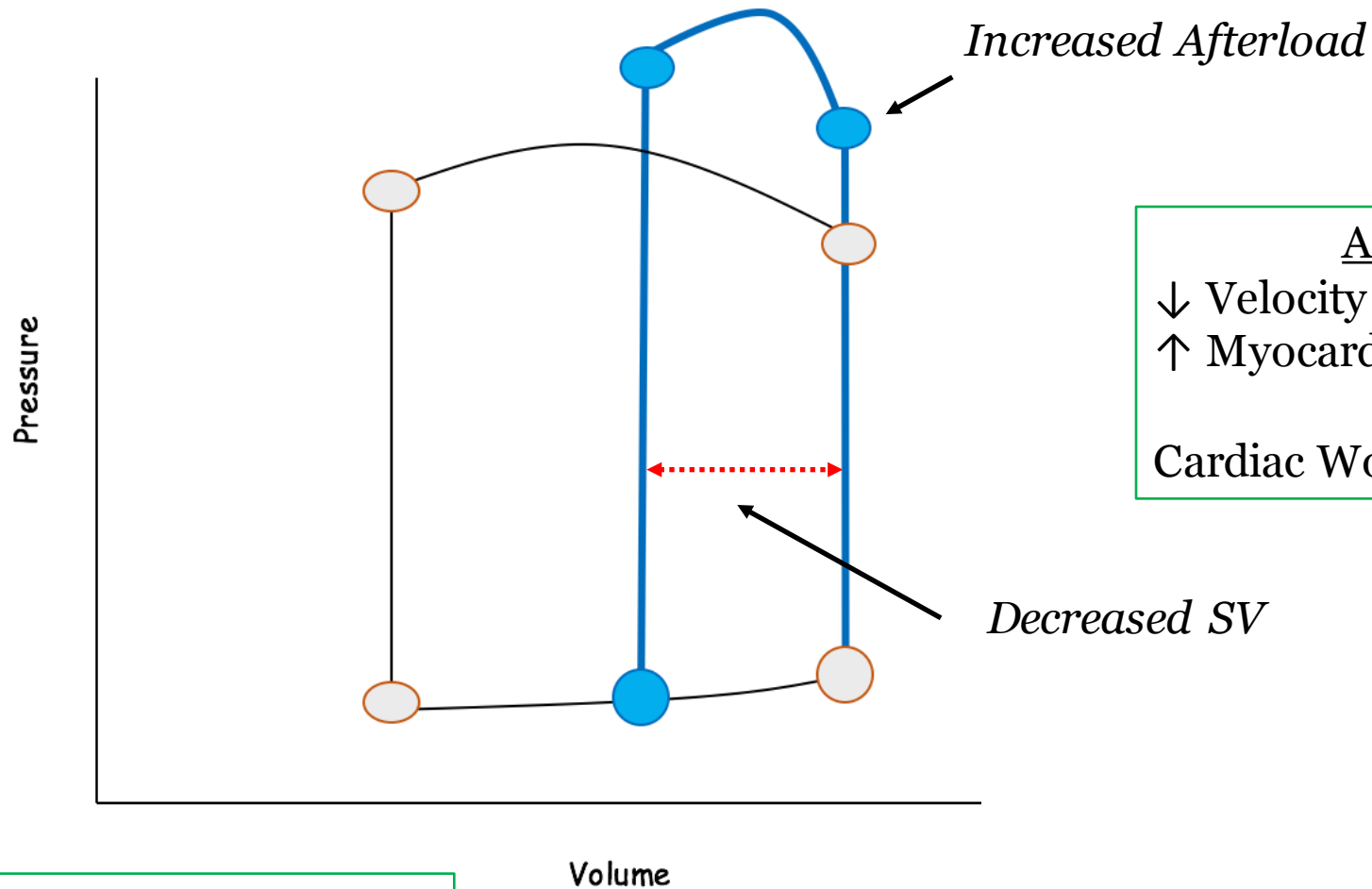
78 y.o. patient presents with syncope and a 2/6 systolic murmur at the RUSB.

His pressure volume curve is shown.

Which of following conditions will present with the same curve?

- 1) *Malignant HTN*
- 2) Dilated CM
- 3) Restrictive CM
- 4) Aortic insufficiency

Malignant Hypertension: *Pathophysiology*



Afterload derivatives:
↓ Velocity of sarcomere shortening
↑ Myocardial oxygen demand

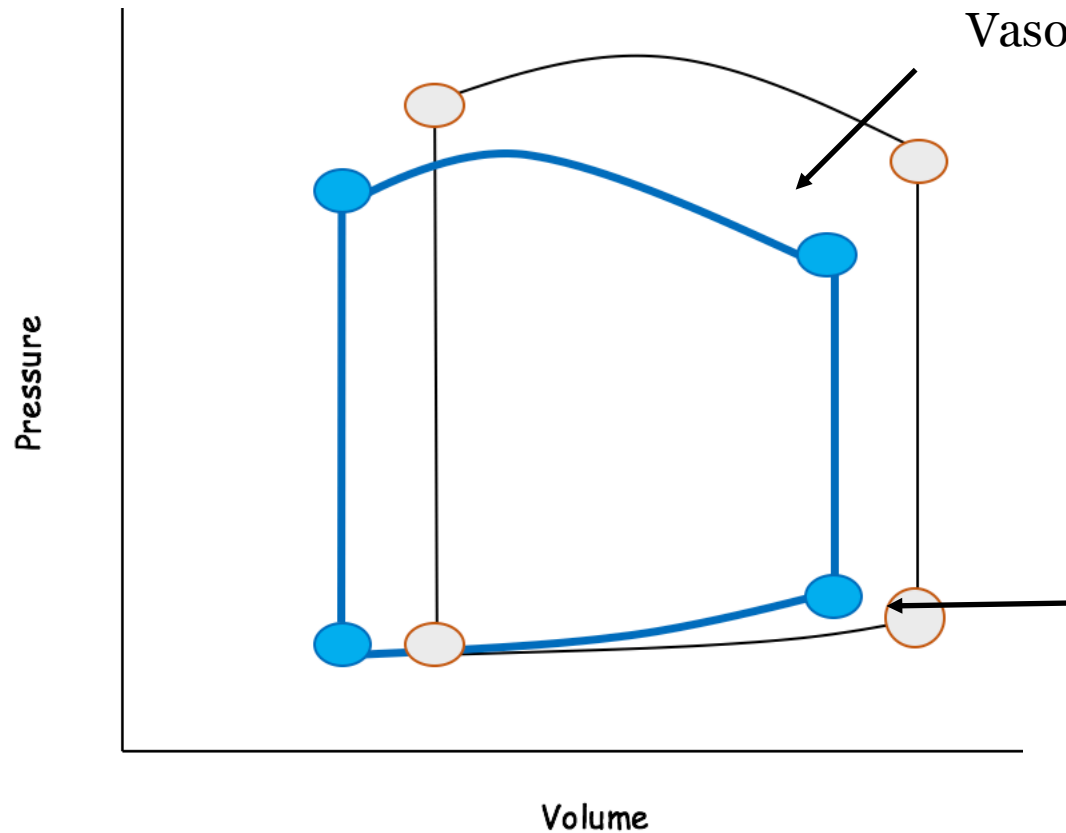
$$\text{Cardiac Work} = (\text{SV} \times \text{HR}) \times \text{MAP}$$

LV Pressure-Volume Loop



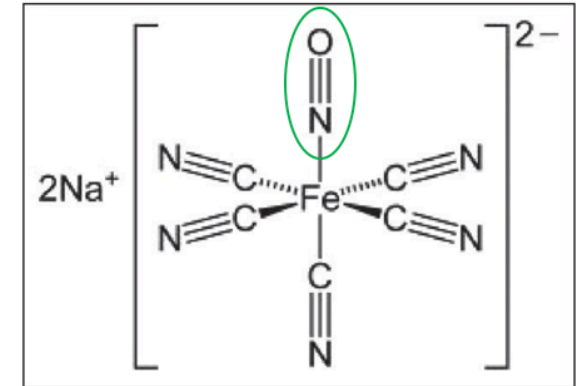
Gateway Curve

Malignant Hypertension: *Nitroprusside*



Vasodilation: ↓ Afterload

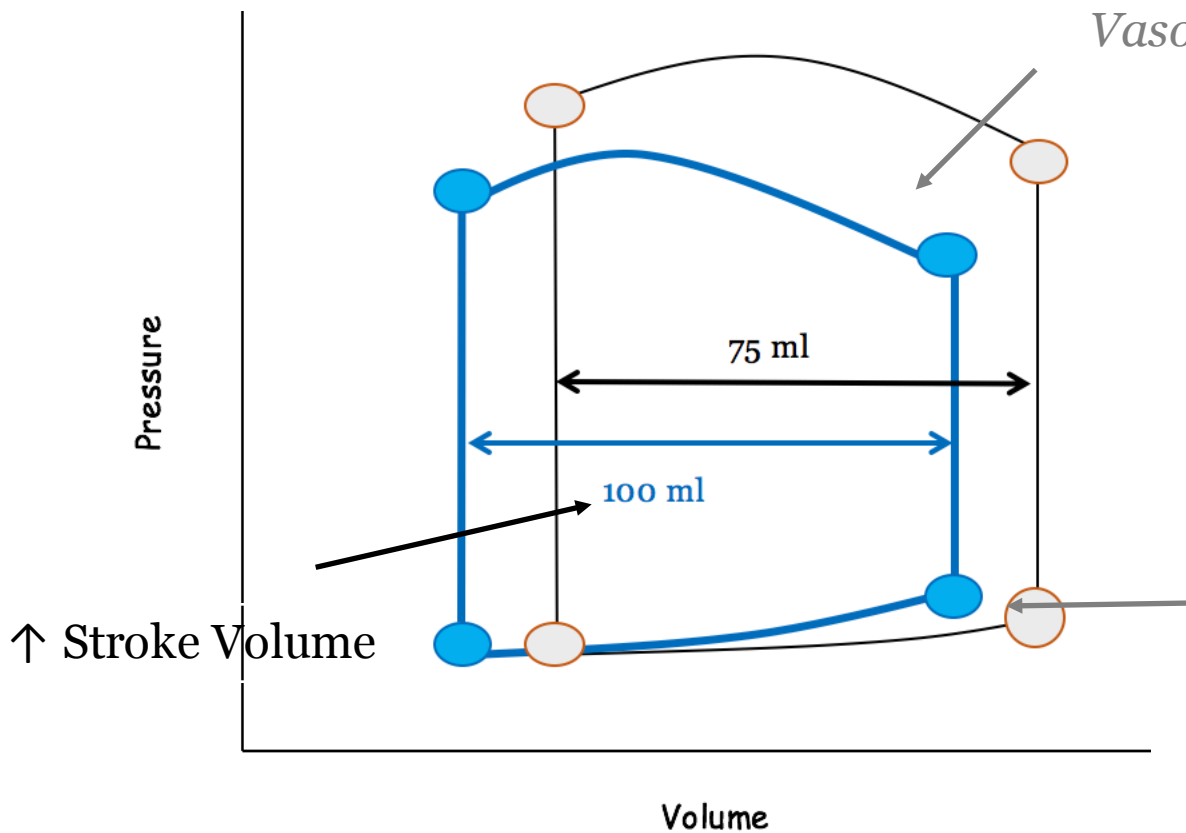
Venodilation: ↓ Preload (EDV)



Nitric oxide: vascular smooth mm relaxation

Vasodilation (arteriolar)
Venodilation (venous)

Malignant Hypertension: *Nitroprusside*

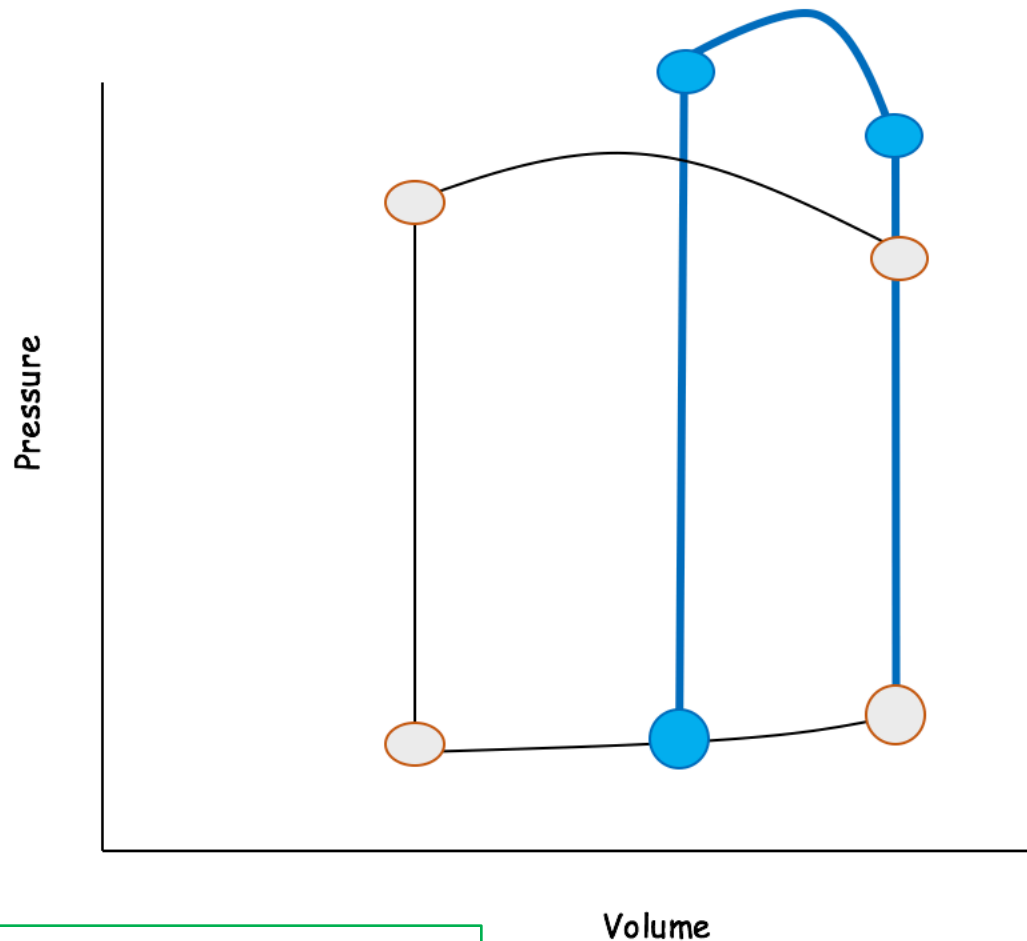


Vasodilation: ↓ Afterload



Venodilation: ↓ Preload (EDV)

Malignant Hypertension: *Nitroprusside, AE*



LV Pressure-Volume Loop

Patient presents with the pressure volume curve shown. He is started on a medication but 5 days later is *confused and develops a seizure*. Which of the following medications did he receive?

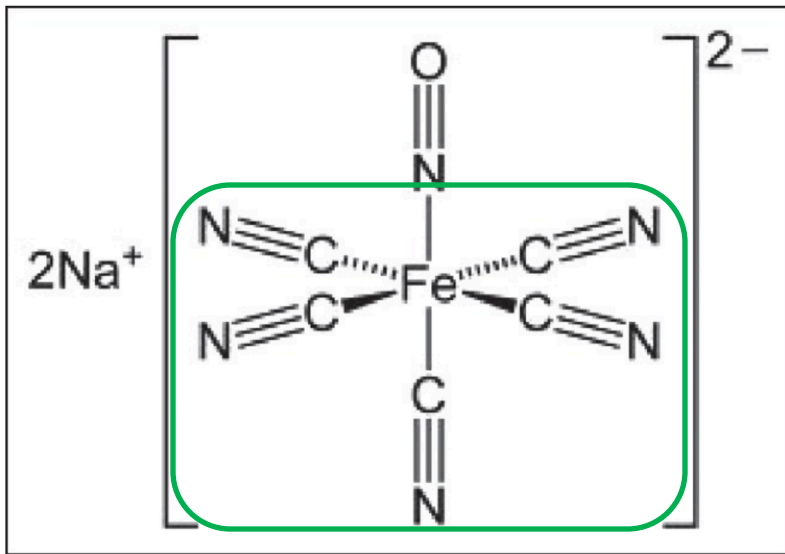
Nitroprusside

Labetalol

Fenoldopam

Nicardipine

Hydralazine



Nitroprusside \Rightarrow Cyanide



Bitter almond



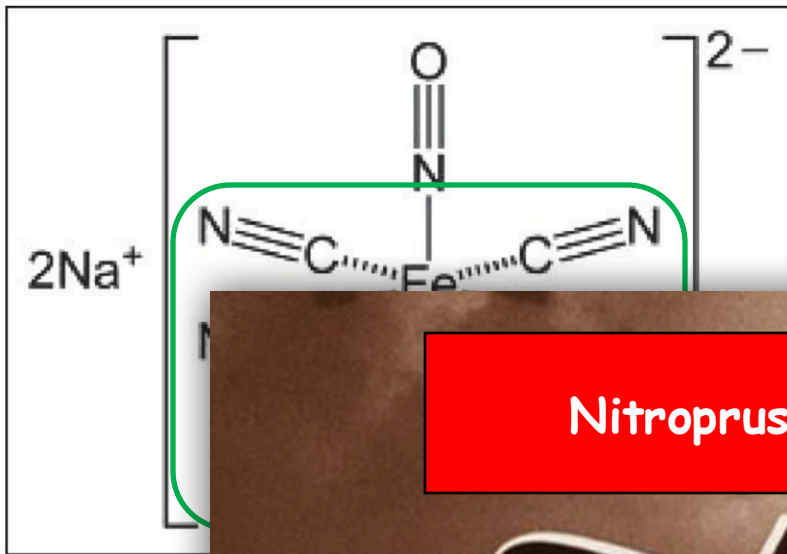
\uparrow Cyanide: lactic acidosis
(uncouples oxidative phosphorylation)

A-V O₂ difference: narrow

Rx:

Thiosulfate (sulfur donor) - detoxifies

Binds { *Hydroxocobalamin (cobalt)*
Amyl nitrate \rightarrow metHgb (ferric)

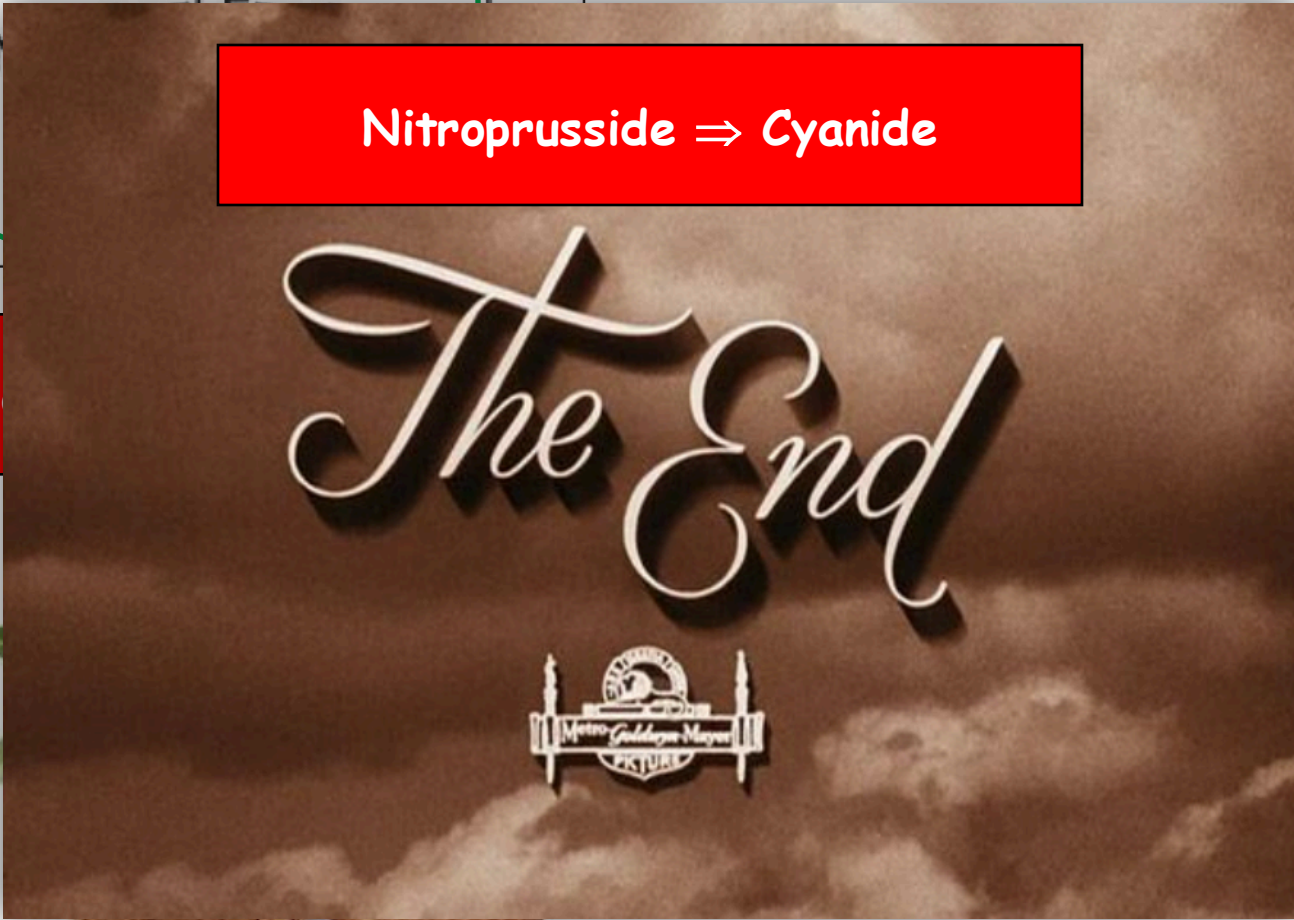


Nitroprusside ⇒ Cyanide

Nitr



Bitter almond

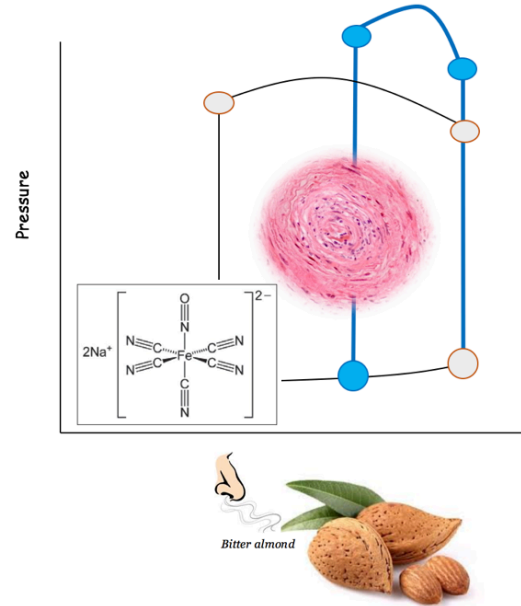


tic acidosis
phosphorylation)
nce: narrow
onor) - detoxifies
min (cobalt)
netHgb (ferric)

Malignant HTN: *Take Homes*

- Diagnosis: Severe HTN associated with Target Organ Damage
 - *Key associations*: dissection, systemic sclerosis, HELLP syndrome
- Pathology: fibrinoid necrosis/hyperplastic arteriolitis
- Pathophysiology: LV pressure volume curve/ \uparrow afterload
- Pharmacology: Nitroprusside and related derivatives
 - MOA, AE/toxicology
 - LV pressure volume curve

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