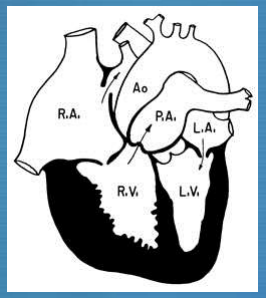
Alpha-Blocker and Angiotensin Converting Enzyme Inhibitor in the Management of Critical Pulmonary Valve Stenosis



by

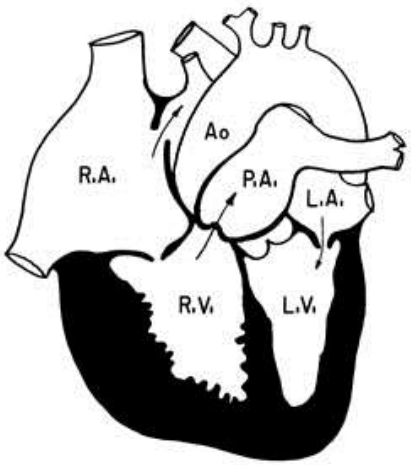
Mohammed Omar Galal, MD, PhD, MBA

KFMC, Riyadh, Saudi Arabia

Background

Outcome for crit PS / Patr IVS improved:

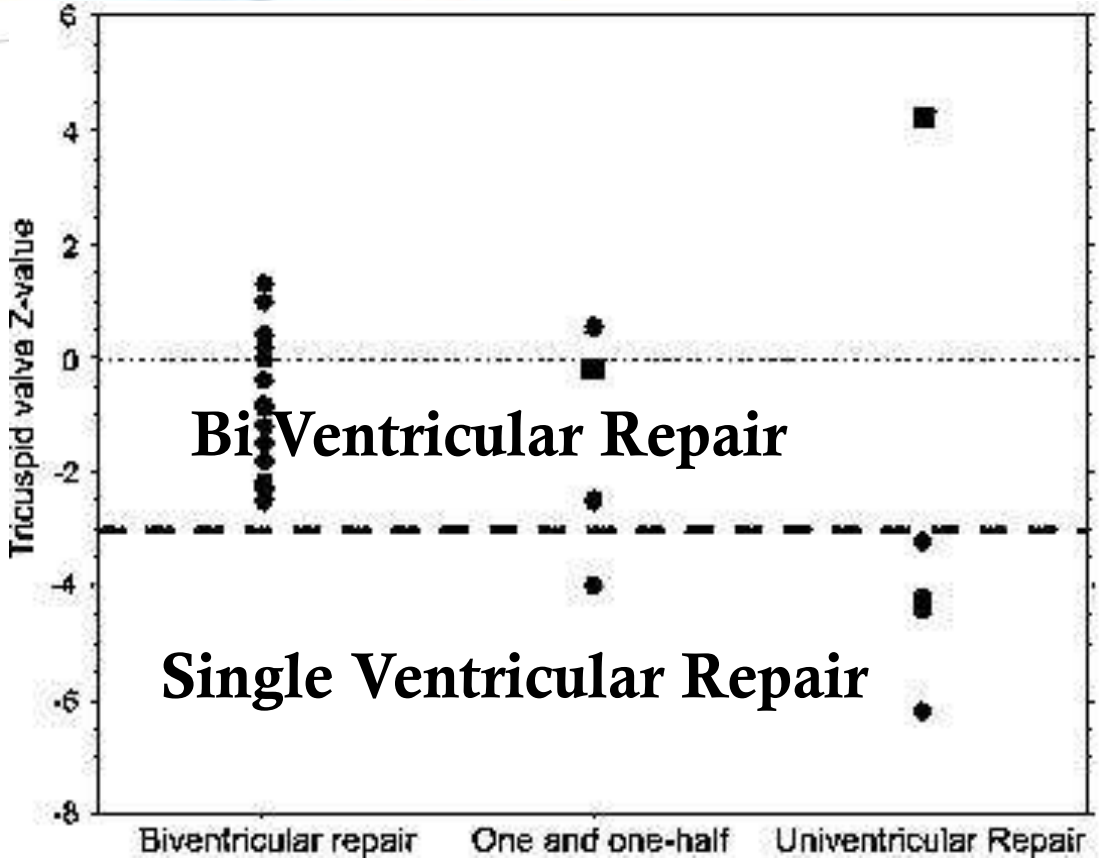
- **Introduction of PGE**
- **Decision based on TV annulus helped**
- **Improved interventional techniques**
- **Recently stent to PDA, instead BT shunt**



Decision biventricular vs single ventricular track

Limitations of biventricular repair

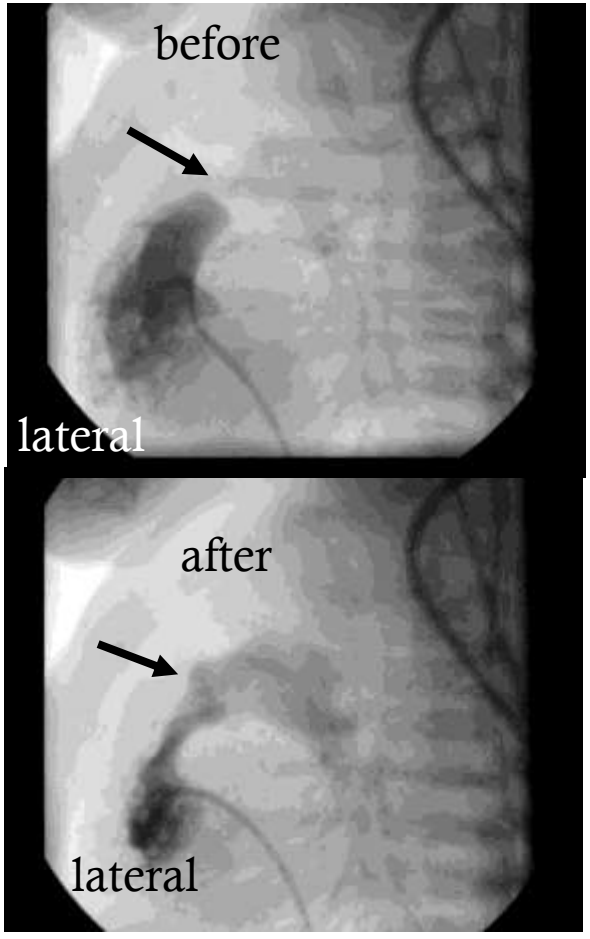
TV annulus < z value-3



Hirata Y et al. Ann Thorac Surg 2007; 84: 574

Case Report$_{1/2}$

- **2 days old, f, 2.5 kg**
- **Cyanosis since birth**
- **PGE, oxygen mask**
- **Echo: critical PV stenosis**
- **Successful balloon dilation**



Case Report$_{2/2}$

But….

- **4 days ventilated, on PGE1 + O2**
- **Consider stent PDA**

Dilemma

- **Some critical PS remain sick despite of successful intervention (ventilated, PGE, Oxygen etc.)**
- **Occasionally not clear when and whether after balloon dilation, stent/BTS of PDA needed ???**

What is generally done ?

Burkholder and Balaguru, Pediat Therapeut 2012, S5
http://dx.doi.org/10.4172/2161-0665.S5-007

Pediatrics & Therapeutics

2012

Review Article Open Access

Pulmonary Atresia with Intact Ventricular Septum: Management Options and Decision-making

Henry Burkholder* and Duraisamy Balaguru

Division of Pediatric Cardiology, University of Texas Houston Medical School, Houston, TX 77030, USA

Abstract

Pulmonary atresia with intact ventricular septum (PA-IVS) is a complex congenital heart malformation with a diverse set of anatomical and clinical findings. The incidence is 4.1 per 100,000 live births and is less than 1% of all congenital heart disease. During embryogenesis, PA-IVS is postulated to occur after development of ventricular septum which is later than the development of PA with ventricular septal defect. Every case of PA-IVS poses a considerable challenge to the pediatric cardiologist and cardiovascular surgeon. Although echocardiography is often the first line tool in cardiac imaging, cardiac catheterization is the gold standard for diagnosing PA-IVS and describing the important anatomical features that determine the plan of treatment. This article will focus on the management options and decision making from the interventional cardiologists point of view.

"If PGE cannot be discontinued…

- in 1-2 weeks, several experts advise BT shunt or stenting
- "…the ba… …eeks for the oxyge… …vels.
- "In the n… …ital or discharged home with oxygen via nasal cannula–if effective."

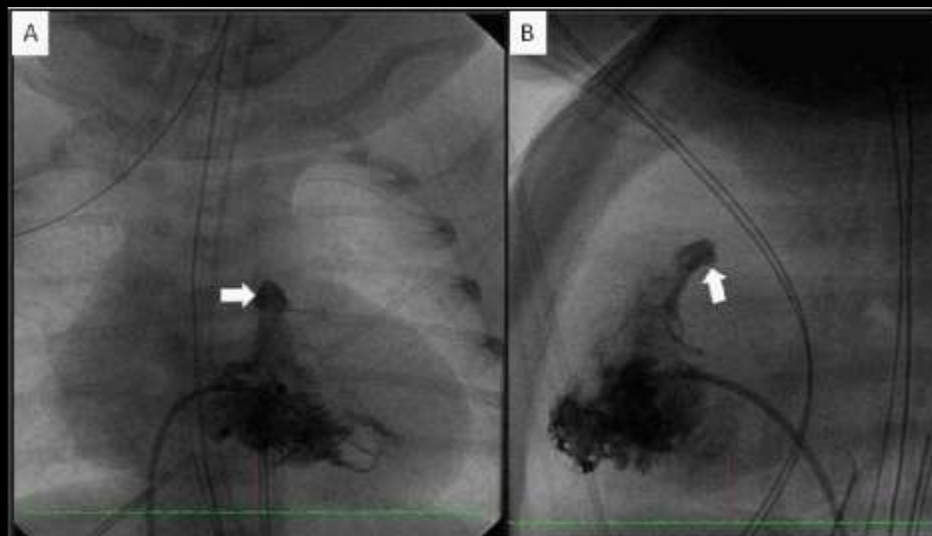
Desaturated for some time
Long Hospital Stay
PGE
Oxygen

Burkholder H et al. 2012
Pediat Therapeutics S5:1-7

Outline

- Alpha and beta receptors before and after balloon PS
- Alpha adrenoceptors in patients with poor saturation
- Assumptions why alphablocker and ACE-I work
- Some case reports
- Our experience with eight patients
- Conclusions

Alpha and beta receptors before and after balloon PS



How did it start ?
Study done in the cath lab

Question: Do beta receptors increase after balloon PS?

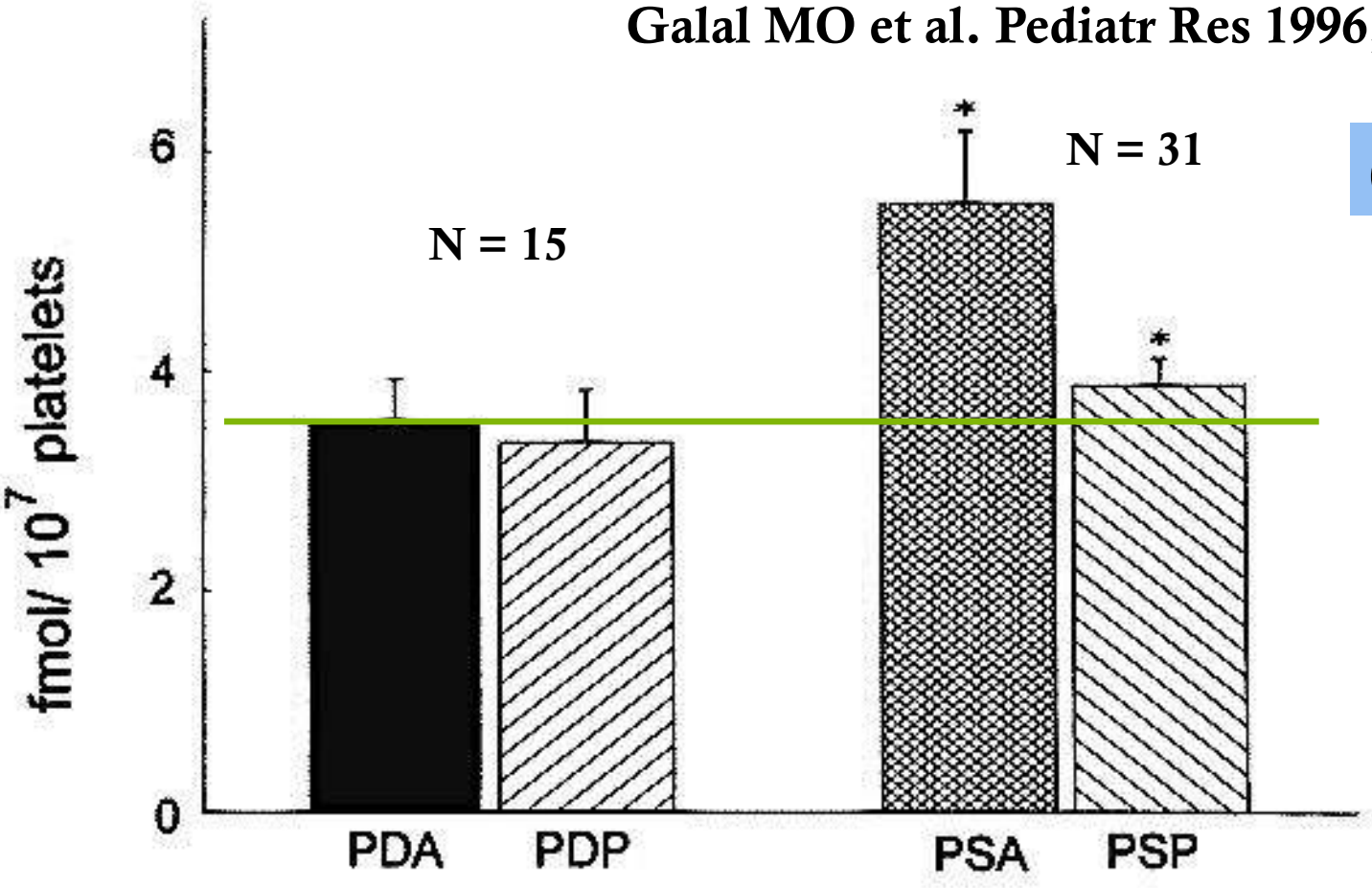
Hypothesis: Beta receptors will increase after intervention, because of stress of the procedure

Methods: 30 PS before and after balloon
(as control: 15 small PDAs)

Alpha and beta receptors from circulating cells

α-adrenoceptor density (B_{max}) in pulmonary stenosis before (*PSA*) and 10 min after (*PSP*) balloon, compared with PDA before ($n = 15$) and after (*PDP*, $n = 7$) closure.
*$p < 0.05$ pre compared with postdilatation.

Galal MO et al. Pediatr Res 1996;39:774–8.

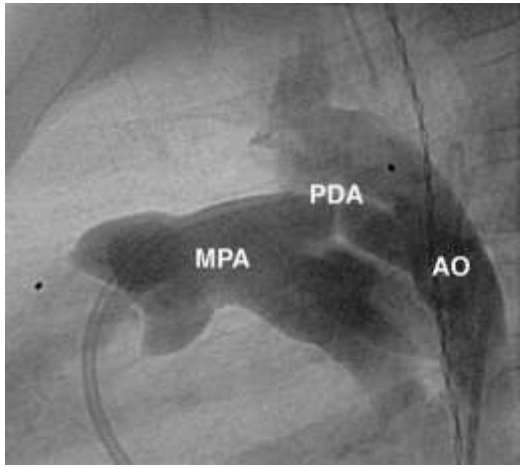


(p<0.05)

Influence of hypoxia on adrenoceptor activity in TOF

15 PDA

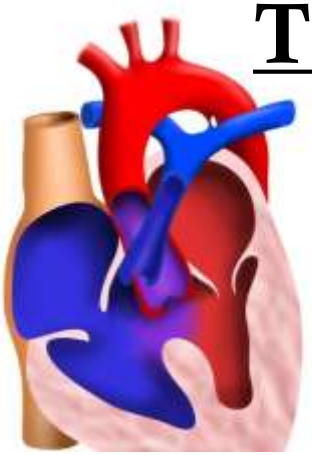
Qp/Qs< 1.5/1



29 TOF

(22 cyanotic)

7 acyanotic TOF



DZIMIRI N, Galal O
European Heart Journal, 16 (Suppl.) , 403, 1995

Influence of hypoxia on adrenoceptor activity in TOF

Results

a- adrenoceptor activity elevated by 81% ($p<0.05$) in cyanotic children (compared to PDA)

<u>Negative</u> correlation (adrenoceptor density / O2 Sat); regression coefficient (r) of -0.6

DZIMIRI N, Galal O
European Heart Journal, 16 (Suppl.) , 403, 1995

Influence of hypoxia on adrenoceptor activity in TOF

Summary of Lab study

also hypoxia leads to increase in alpha adrenoceptor activity

DZIMIRI N, Galal O
European Heart Journal, 16 (Suppl.) , 403, 1995

Indian Pediatrics

Letters to the Editor

Indian Pediatrics 2000;37: 449-450

Magnesium Sulphate for Persistent Pulmonary Hypertension in Newborns

hypoxia induces pulmonary hypertension

4. Abu-Osba YK, Rhydderch D, Balsundasam S, Galal O, Rajjal A, Halees Z, *et al*. Reduction of **hypoxia induced pulmonary hypertension** (HIPN) by MgSO4 in sheep. Pediatr Res 1990; 27: 351A.

5. Abu-Osba YK, Galal O, Manasra K, Rajjal A. Treatment of severe pulmonary hypertension of the newborn with **magnesium sulphate.** Arch Dis Child 1995; 67: 31-35.

Summary of lab and animal studies

<u>Elevated</u> alpha adrenoceptors drop after balloon dilation of PV stenosis

Hypoxia associated with elevated a-adrenoceptors

Hypoxia leads to pulmonary hypertension

Galal MO et al. Pediatr Res 1996;39:774–8.

Few years later…..

Alpha blocker in two neonates

Alpha blocker in two neonates after balloon critical PS

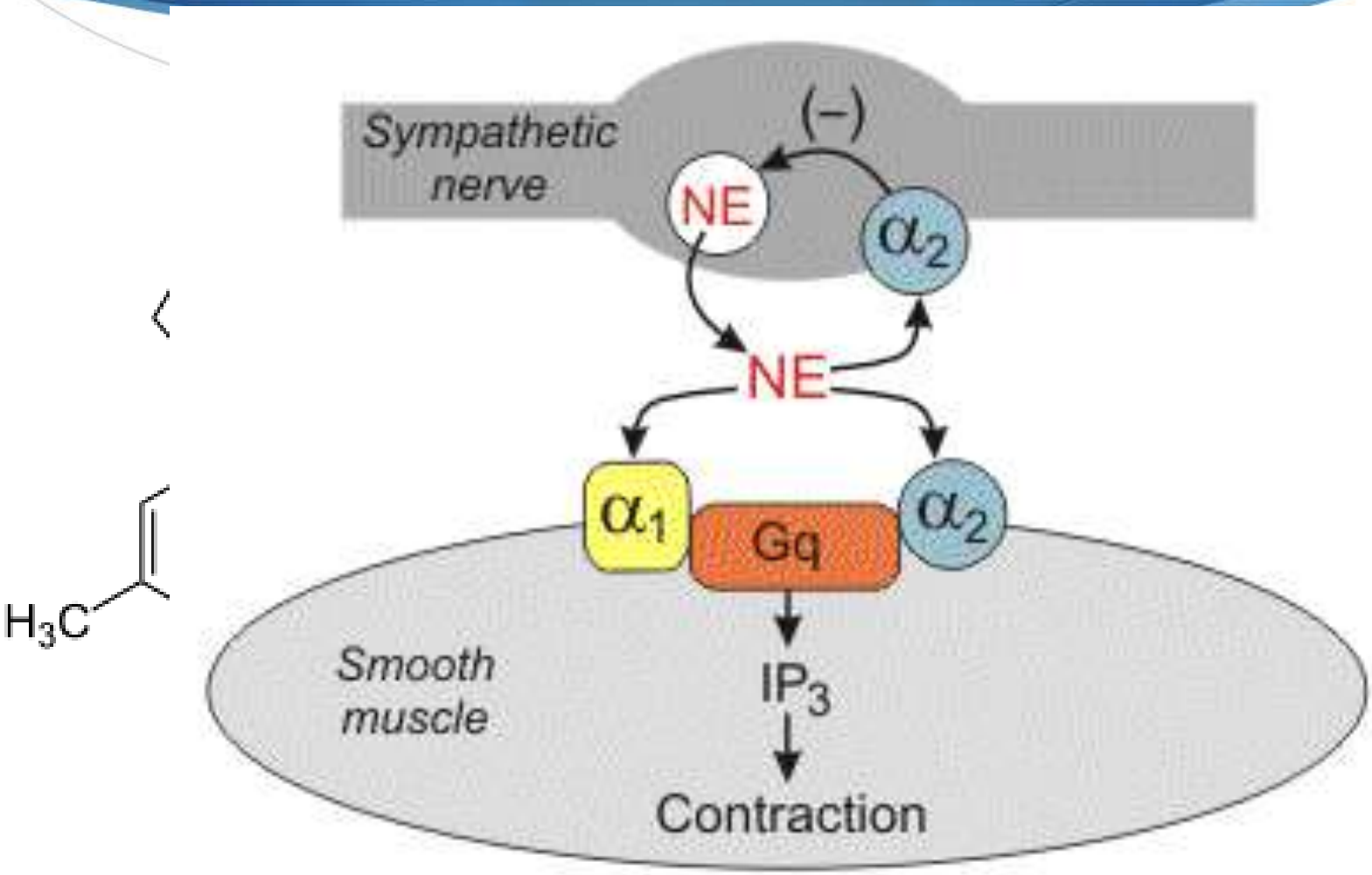
Two consecutive neonates < 2.5 kg, underwent successful balloon dilation of critical PS.

First: For 2 d suffering - adequate fluid intake and beta blockade.

Only after alpha blocker, baby normalized within hours

Second: For 1 day suffering, alpha blocker were given earlier, and baby improved

Phentolamine



Effect of alpha blocker

Stimulation of alpha adrenergic receptors on the systemic as well as the pulmonary vessels leads to vasoconstriction

Blocking of these receptors leads to vasodilation

Our Assumption[1/2]

Babies with critical PS:

combination of

1. Severe Stenosis

2. Hypoxia

= elevated alpha 2 Receptors

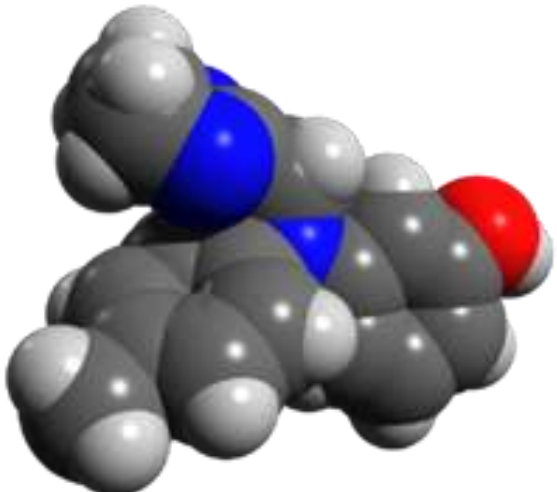
Our Assumption$^{2/2}$

In some babies, elevated alpha receptors do not drop after successful balloon dilation ??

Because of Hypoxia ?

If this is true,

alpha blockade might help !!!!

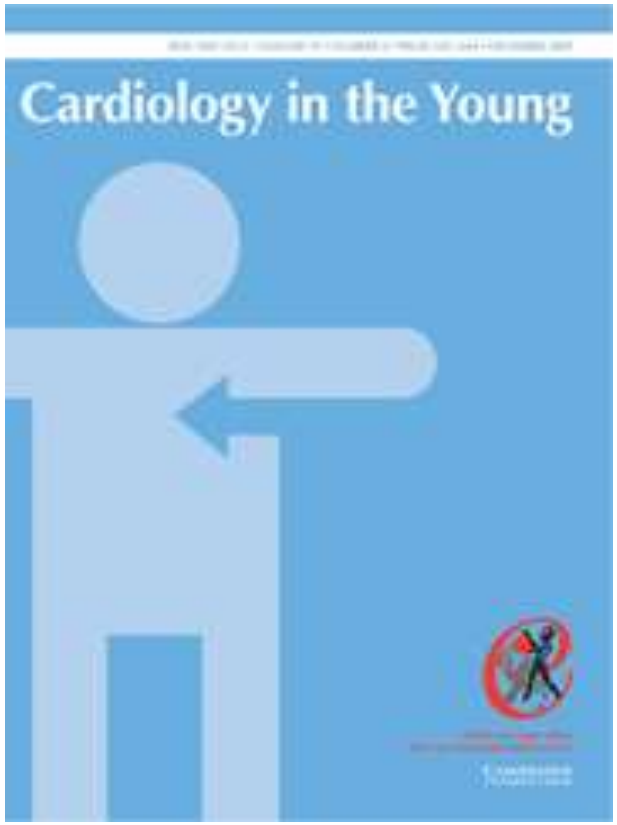


Alpha blocker in two neonates

Galal MO et al.

Phentolamine improves clinical outcome after balloon valvoplasty in neonates with severe pulmonary stenosis

Cardiol Young 1999; 9:127



Few years later…..

Alpha blocker / ACE I after balloon critical PS

Alpha blocker /ACE I after balloon critical PS

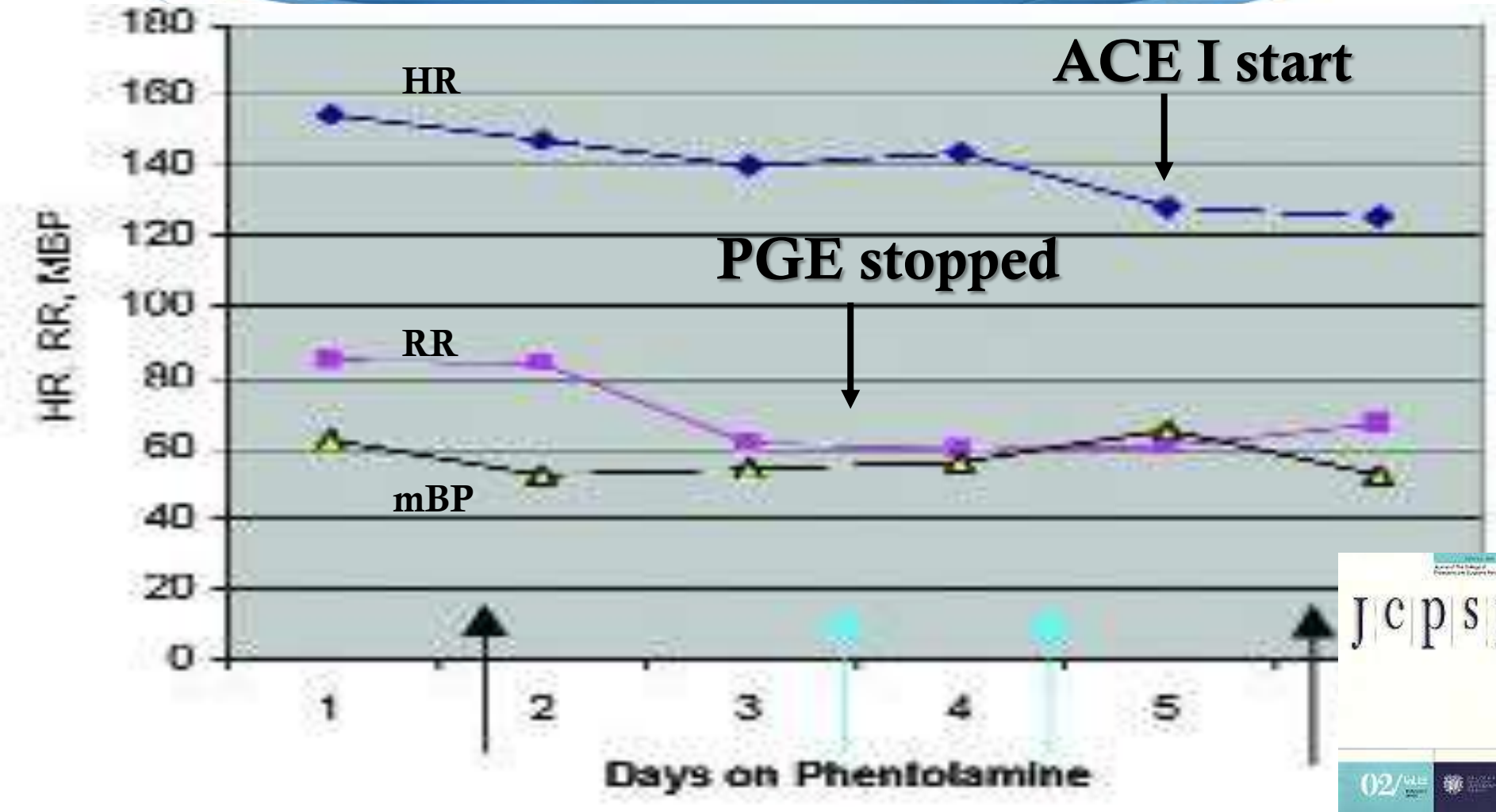
Patient kept 2 weeks on PGE, unable to decide whether BT shunt or not

Alpha blocker was given, 2 days later PGE was stopped

ACE I was added, later alpha blocker stopped

FU in clinic saturation 94 %

HR, RR and mean BP before and after Phentolamine



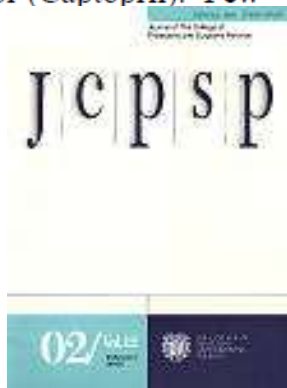
Alpha blocker, later Capoten in one neonate, **2006**

ALPHA^2 - BLOCKER HELPS TO AVOID SYSTEMIC TO PULMONARY SHUNT IN A PROSTAGLANDIN DEPENDENT INFANT WITH CRITICAL PULMONARY VALVE STENOSIS

Mohammed Omar Galal, Amin Muhammed Arfi, Jameel Al-Ata, Arif Hussain and Amjad Kouatli

ABSTRACT

A 27 days old newborn with critical pulmonary valve stenosis remained prostaglandin (PGE_1) dependent for 2 weeks after successful balloon valvuloplasty. Only the introduction of Phentolamine in his medication regimen, allowed PGE_1 to be weaned off within days of this therapy. The medication was continued for 4 days and replaced by angiotensin converting enzyme inhibitor (Captopril). Few weeks after the discharge, the patient remained clinically stable with acceptable saturation.



Galal MO et al. 2006

Recently….

Only oral ACE I after balloon critical PS

Only ACE I after balloon critical PS balloon, 2012

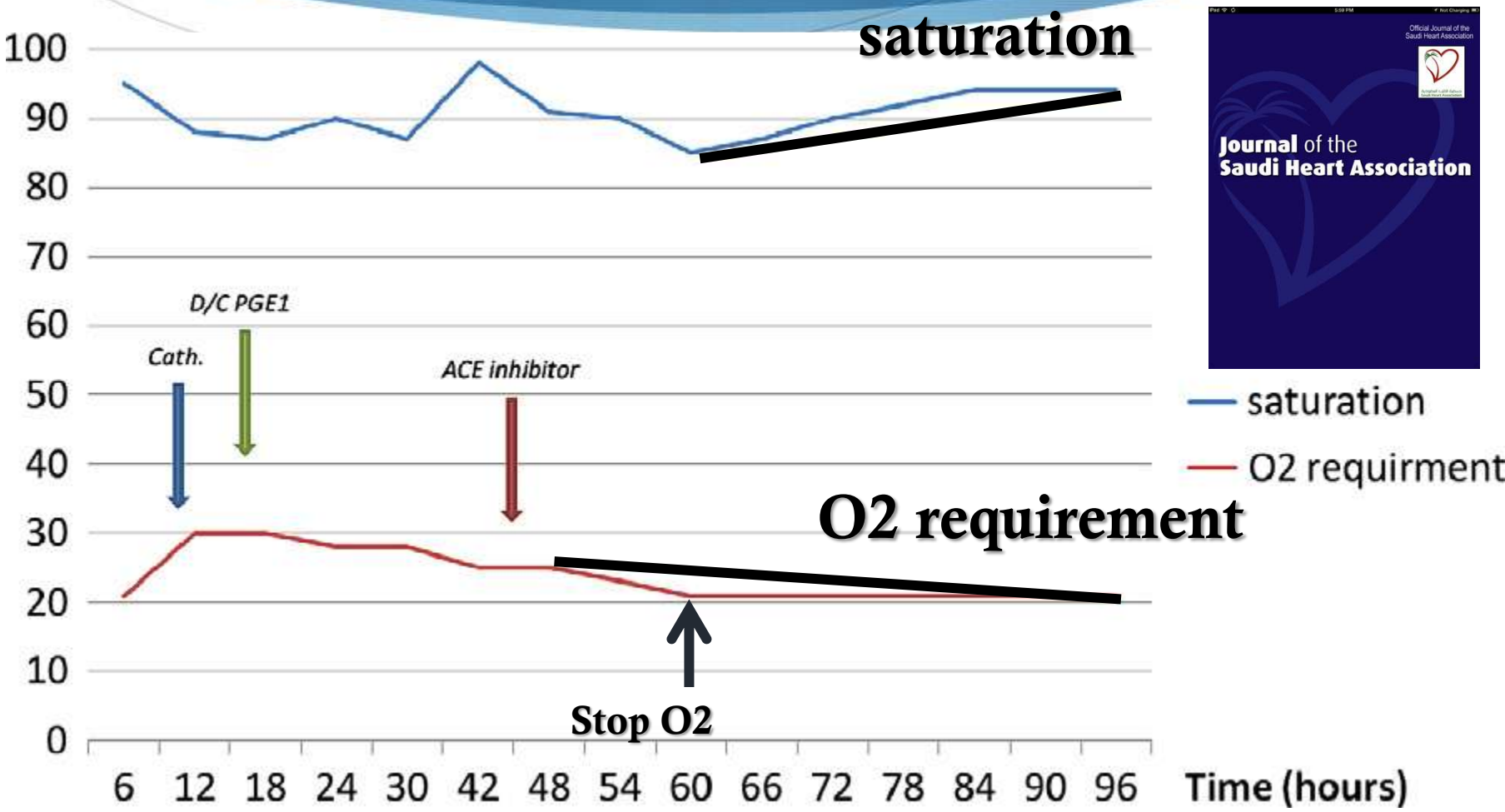
Neonate: successful BVP under elective intubation and GA

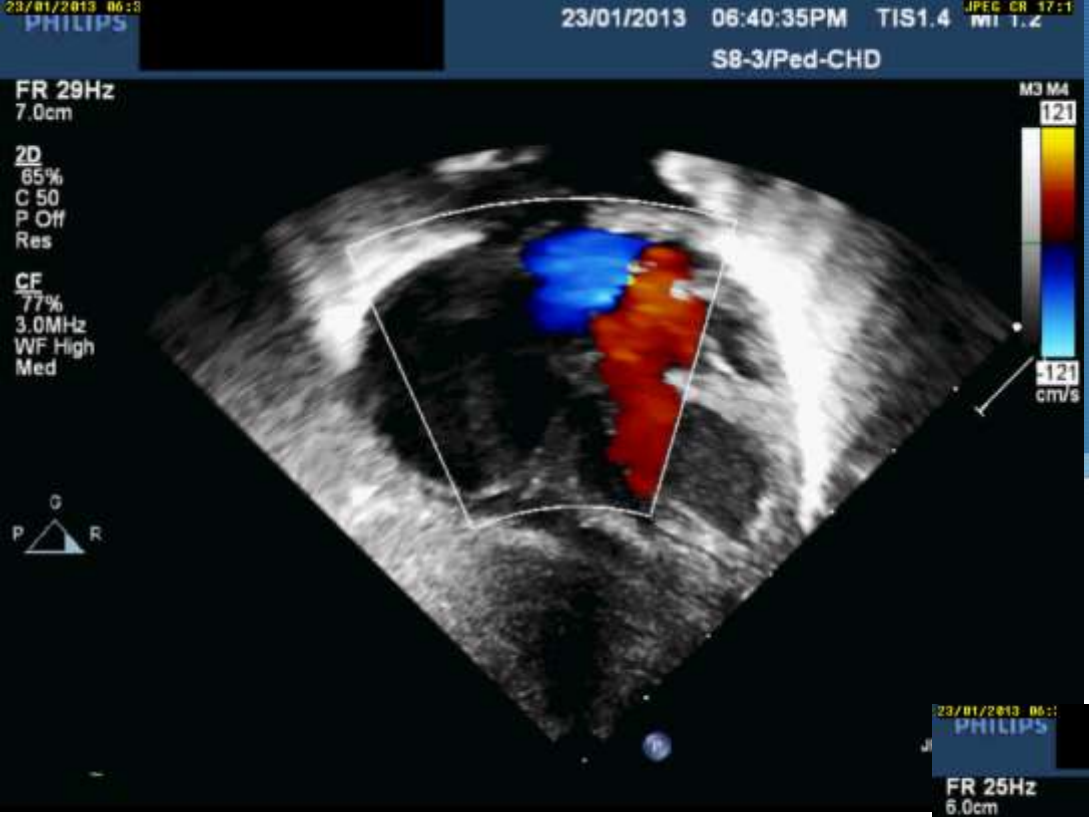
By mistake, PGE was stopped, he remained oxygen dependent

As we did not want to give baby i.v. alpha blocker,

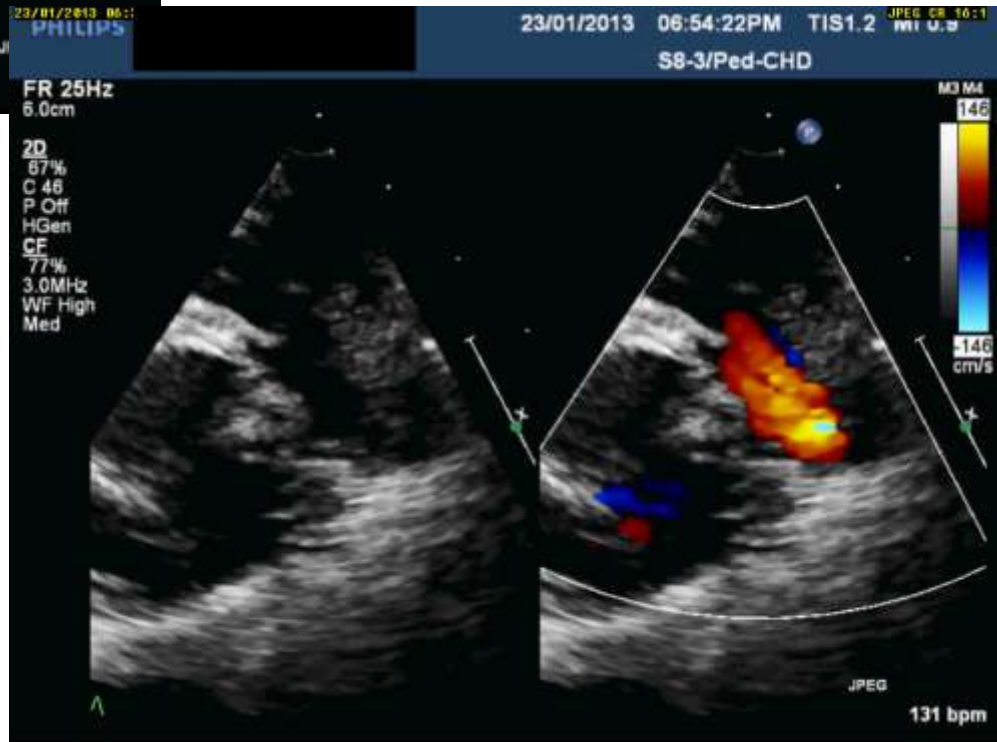
Capoten was added, and in the afternoon, oxygen supply was stopped

Only ACE I after balloon critical PS 2012

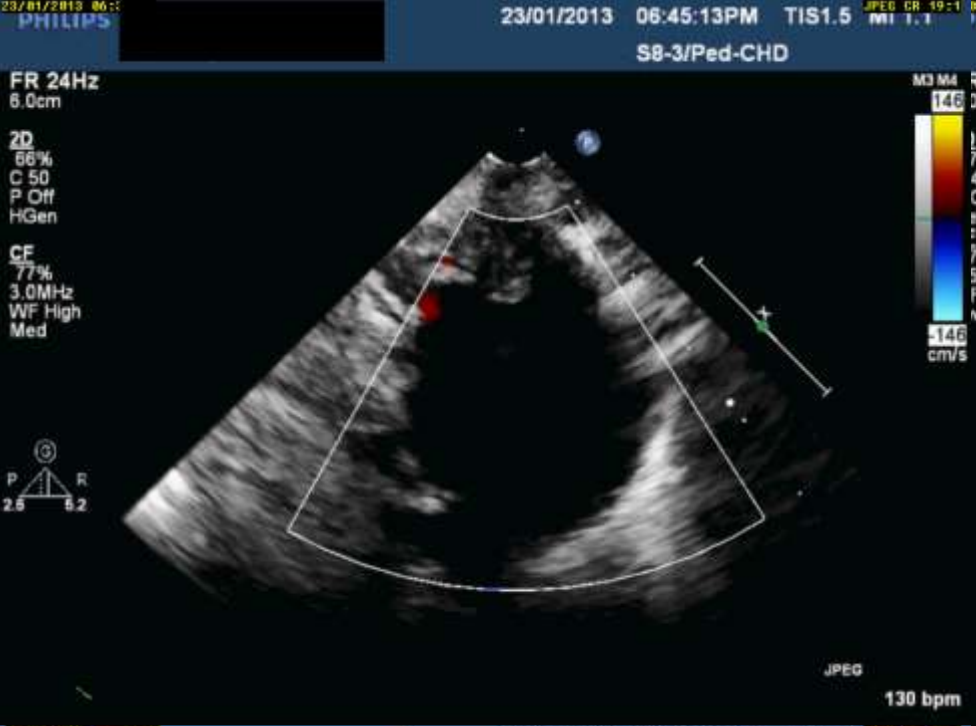




Moderate PDA



Dilated RA, septum deviated towards LA.
R to L shunt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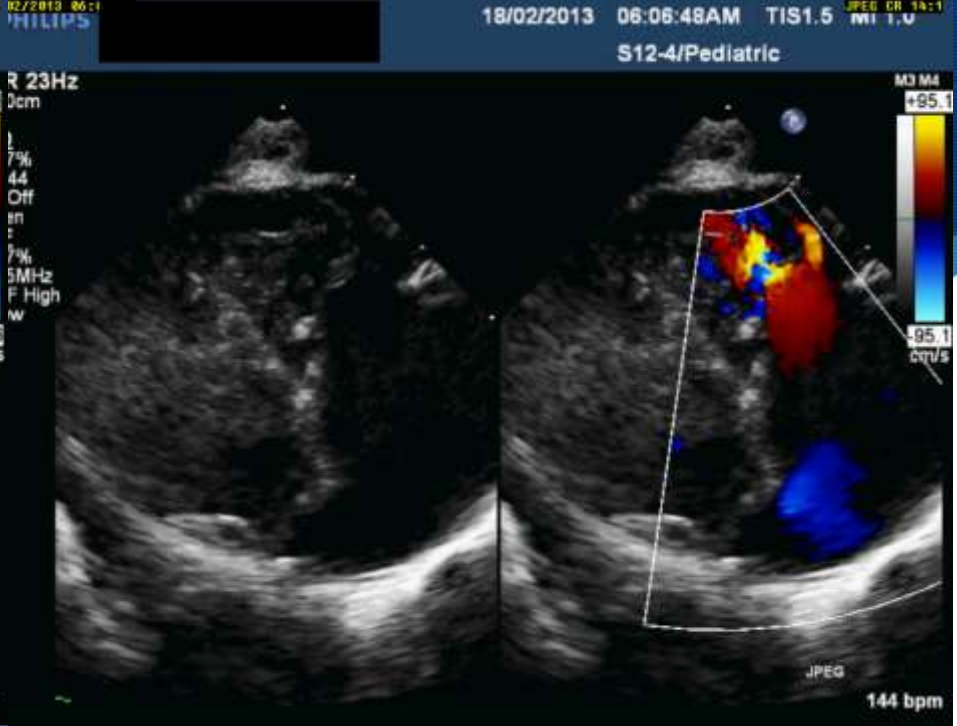
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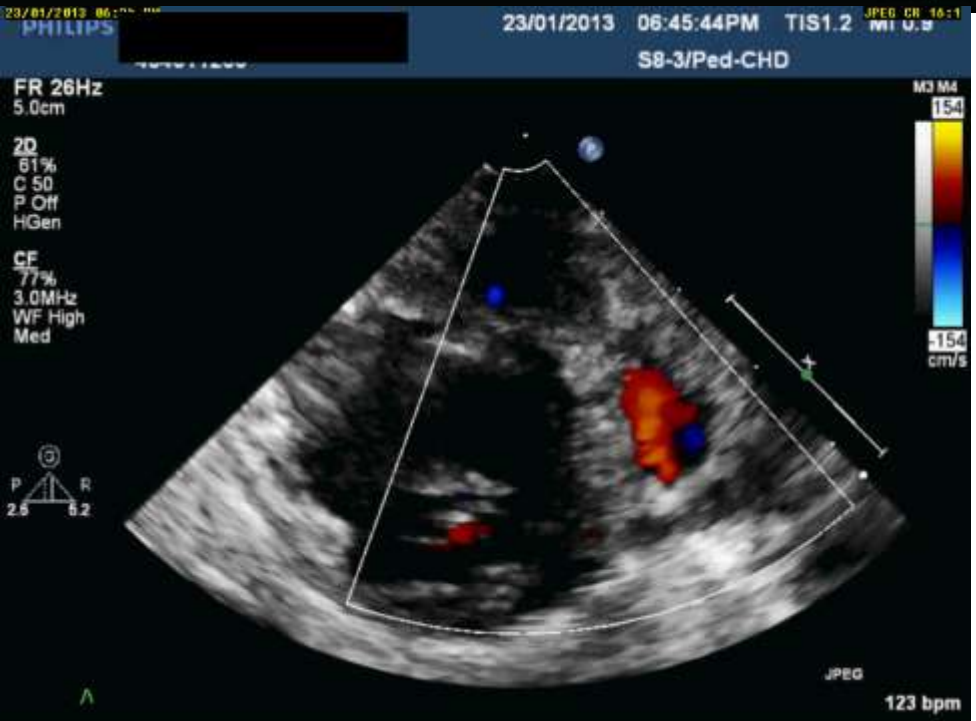
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Theoretical background behind using ACE-I

Effect of ACE-I

1/3

Angiotensin II - vasoconstriction peripheral & pulmonary vasculature

ACE-I blocks conversion of angiotensin I to angiotensin II

= lowers arteriolar resistance, increases venous capacity
Lowers resistance in pulmonary vasculature

Further effect of ACE-I

2/3

Increases bradykinin [agonist of Nitric oxide synthase (NOS)]

Increases nitric oxide (NO)

=

more vasodilation of pulmonary vascularity

Further effect of ACE-I

3/3

It facilitates forward flow into the lung as well as reduction of afterload

Through vasodilation, CO is increased and hence perfusion and overall oxygenation improved

Theory behind this Management[1/2]

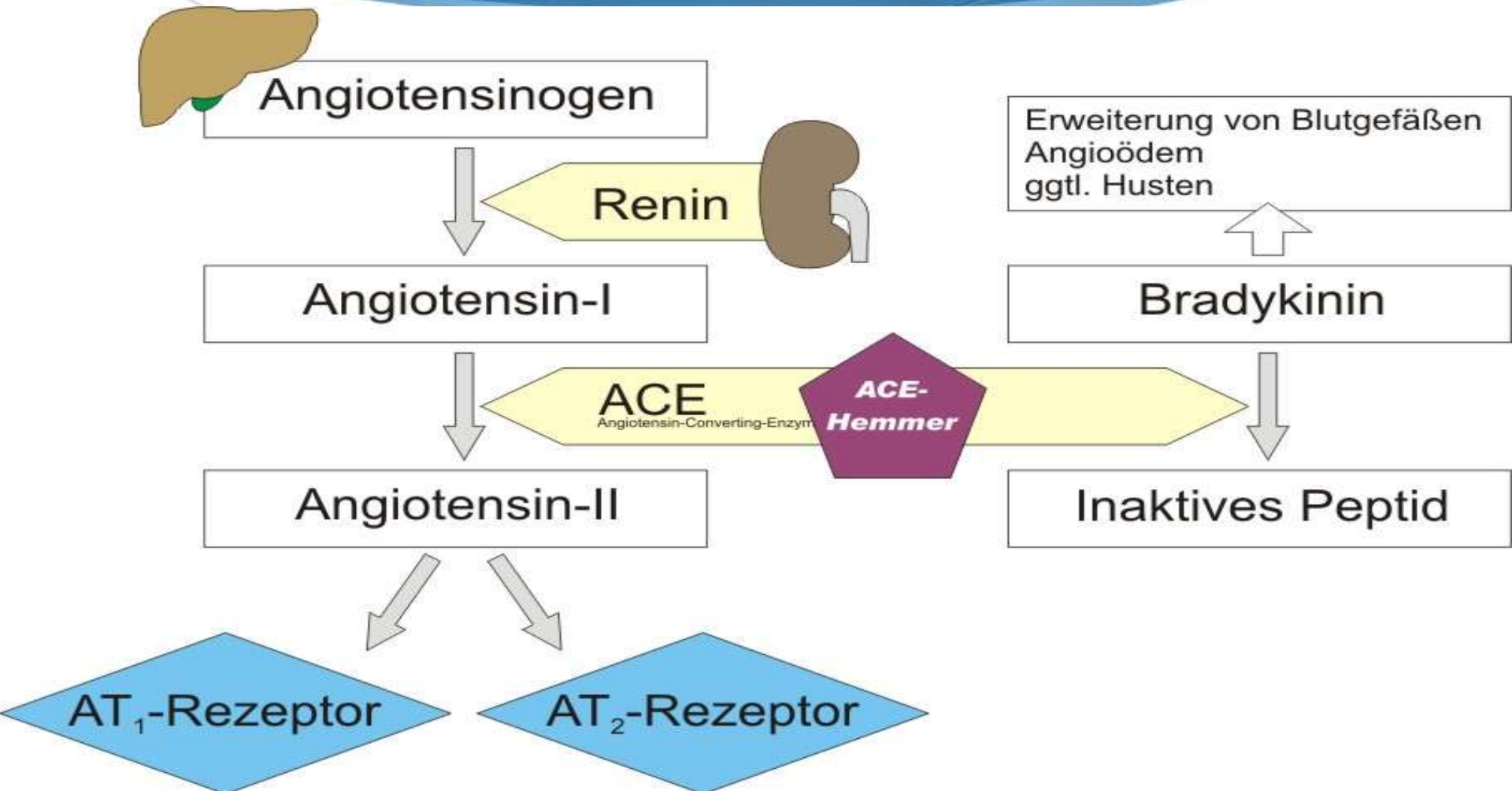
NO modulates cardiac function by abbreviating the systolic contraction thus enhancing diastolic relaxation

- Combination of blocking alpha2 adrenoceptors and ACE-I improves compliance of RV
- Improvement of RV inflow
- Decreasing R - L shunt at atrial level
- Increasing RV stroke volume

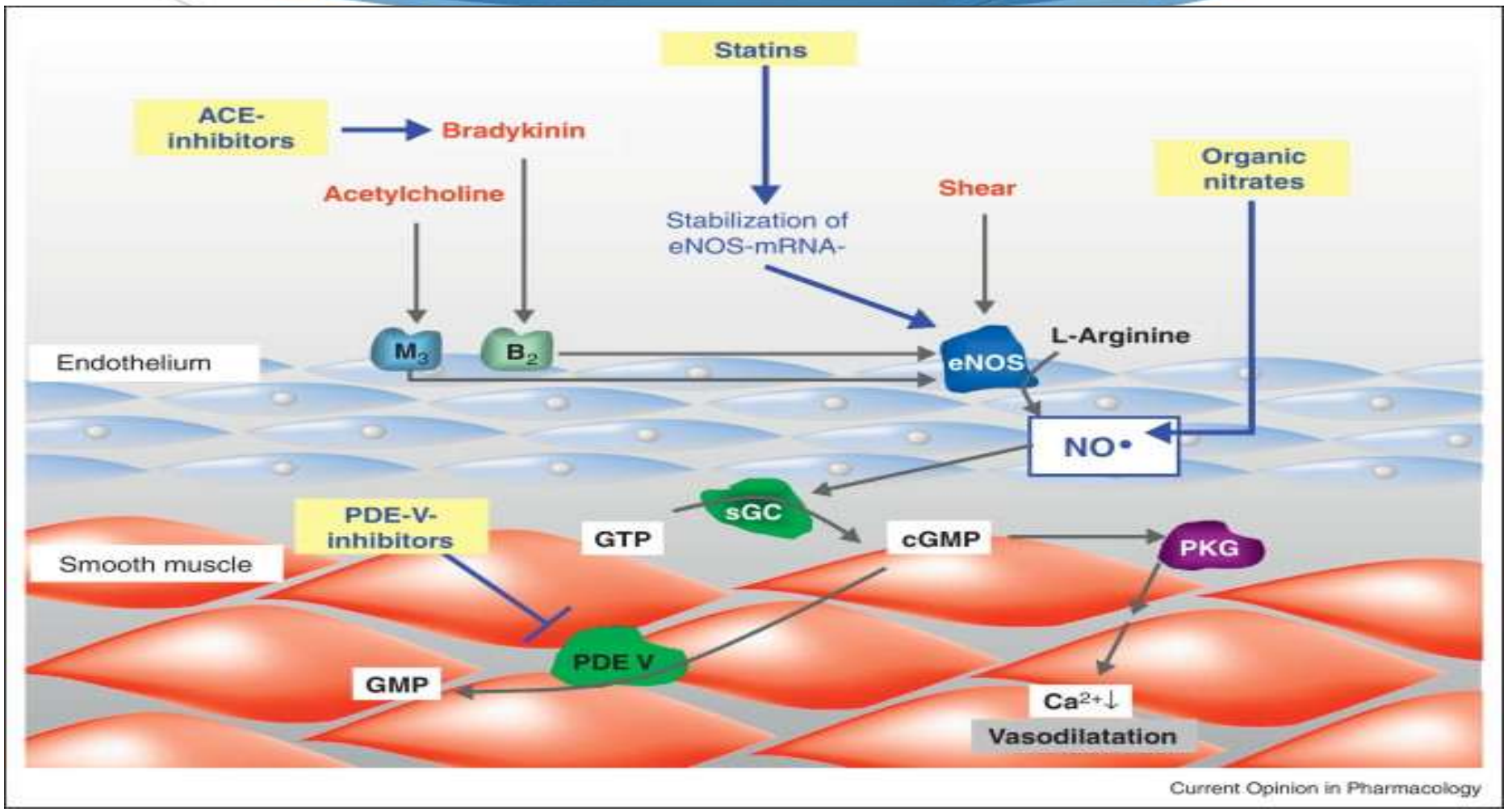
Theory behind this Management$^{2/2}$

All this adds to the noticed increase of oxygenation in our patients

Renin-Angiotensin-Aldosteron-System (RAAS)



Bradykinin, ACE, Nitric Oxide



Our experience with 8 patients treated with this regimen

Demographics

Median age: 3 days

Median weight: 2.5 kg

8 with critical PS

2 almost pulmonary atresia, IVS

Clinical Data

All babies on PGE

2 babies ventilated

O2 Sat: 84 %

Echo studies

All babies with PDA

ASD/ PFO with right to left shunt

Mean peak gradient 75 mmHg

Cath Data

All babies had successful balloon dilation

..but…

Remained oxygen dependent

Post Balloon Management

7/8 babies improved on this management

The one baby had significant infundibular stenosis

Conclusions 1/2

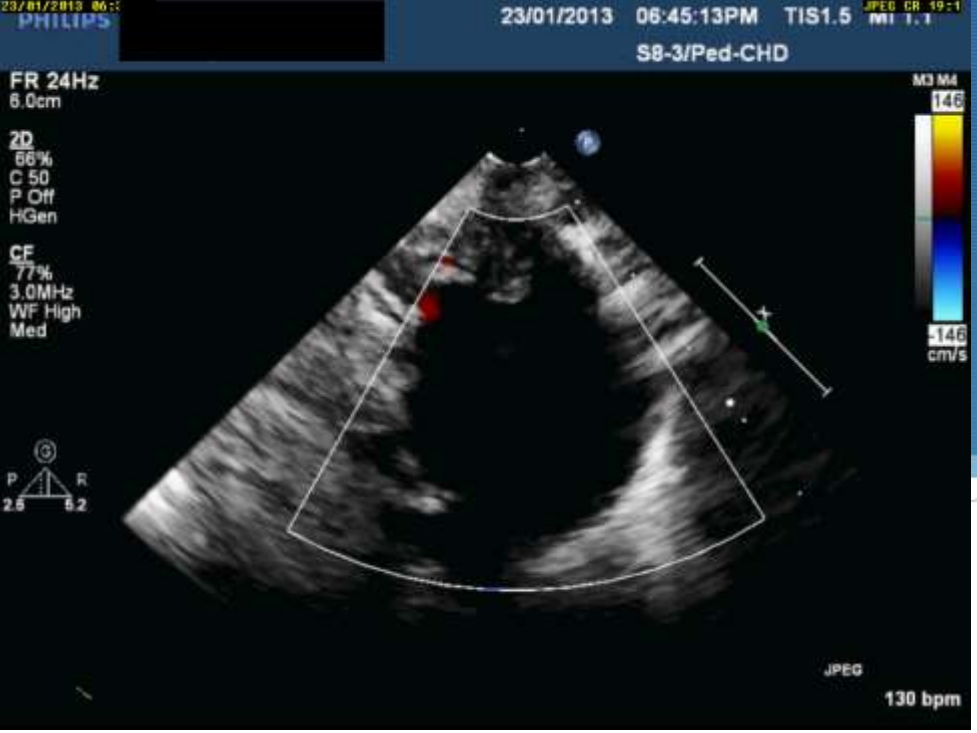
- Elevated alpha adrenoceptors drop after PVS balloon
- In critical PVS alpha receptors remain elevated
- Could be due to associated hypoxia
- + poor RV compliance

Conclusions 2/2

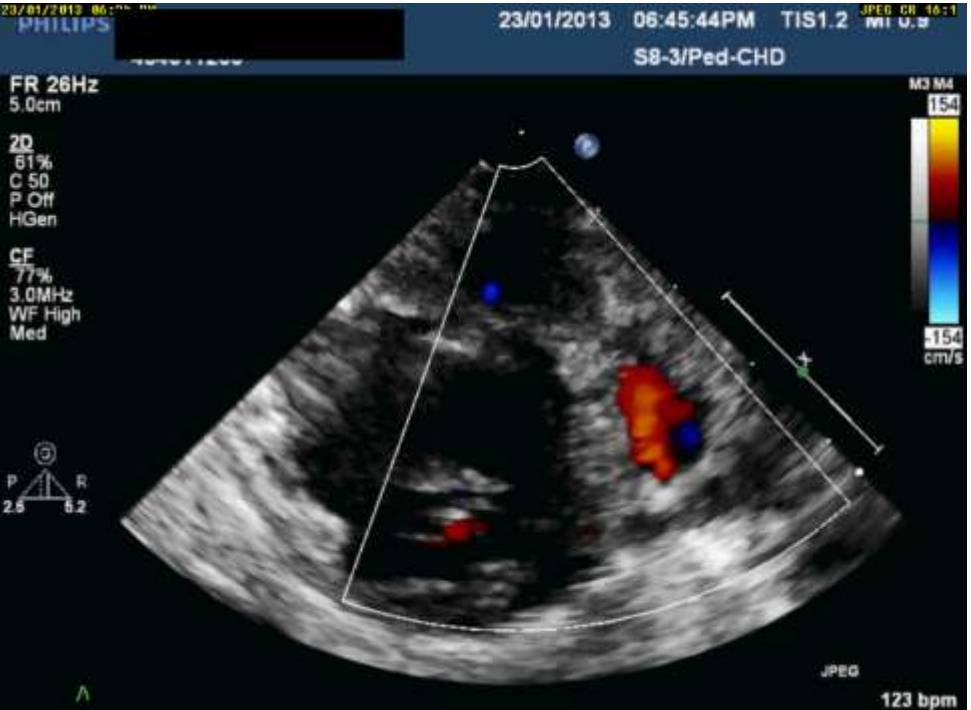
- Alpha blocker - ACE-I lead to vasodilation of systemic and pulmonary vasculature
- Additionally, they may improve RV compliance, increasing inflow to RV and reducing R-L shunt across PFO
- Both drugs were effective in the management of 7/8 newborn with critical pulmonary valve stenosis

Take home message

- Through vasodilation and improved RV compliance
- Using Phenotolamine/ACE I may shorten the need for ventilator/oxygen/PGE dependency
- Save baby from further surgical or catheter intervention
- Reduces need for ICU, hospital stay and healthcare cost

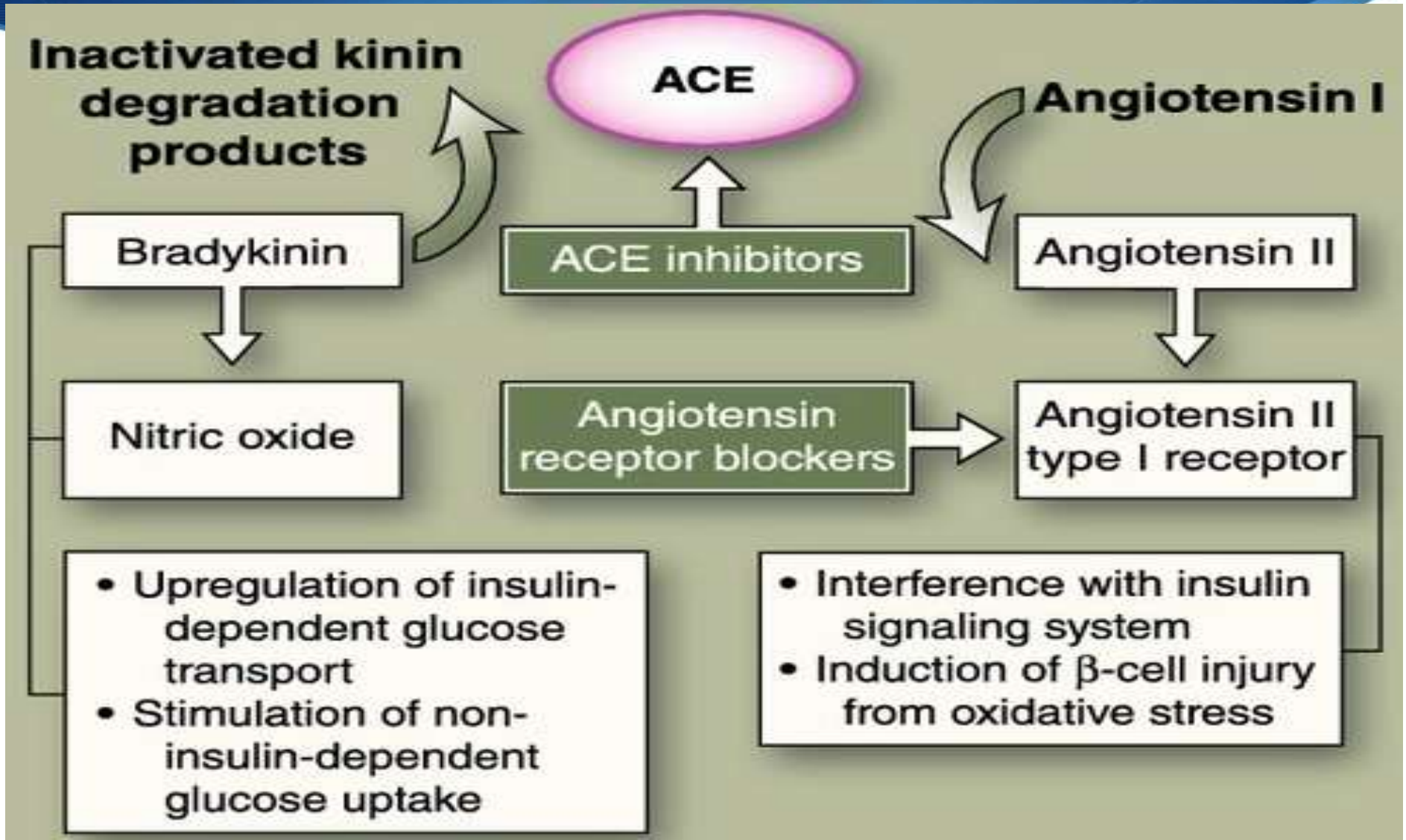


Severe TR



Thickened doming PV

Bradykinin, ACE, Nitric Oxide



First phento, later capoten

after phentolamine, improved,

2 days later, ACE I, was given

few days later discharged

2nd baby, capoten

3 days old, f

after intervention

for > 5 days Sat < 80 %

ACE I (0.15 mg/kg/day),

improved within 24 hours

3rd baby alpha blocker

7 days old, m

BVP, still PGE dependent

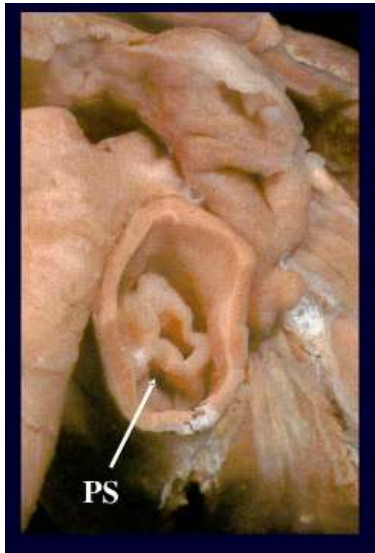
Phentolamine (5 mcgs/kg/min)
given for 48 hour, improved

1 baby capoten,
2 babies phento - later
capoten, 2013

Case Report$_{1/2}$

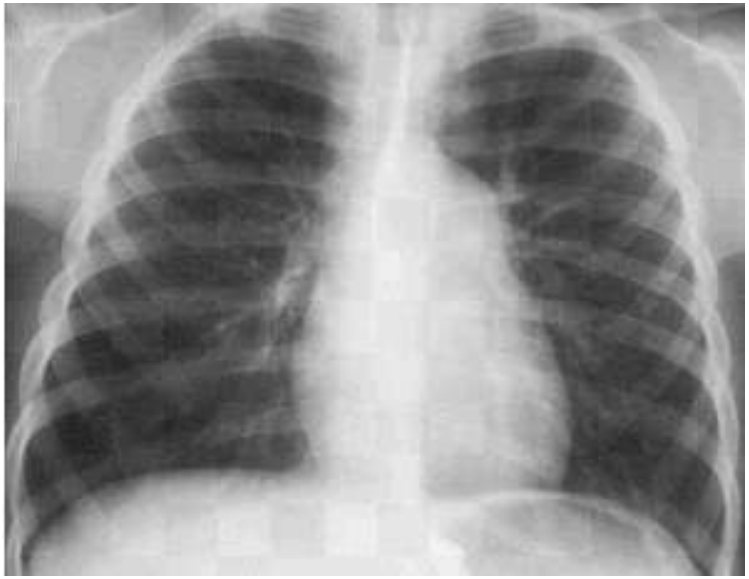
- **2 days old, f, 2.5 kg**
- **Cyanosis since birth**
- **PGE, oxygen mask**
- **Echo: critical PV stenosis**
- **Cardiac catheterization**
- **Elective intubation, arterial line**

Echo and angio



Case Report$_{2/2}$

- **4 days ventilated, on PGE**
- **Poor femoral pulse, heparin**
- **Consider stent PDA**
- **Multiple atelectasis**



First phento, then capoten

after phentolamine, improved,

2 days later, ACE I, was given

3 days later discharged

2nd baby capoten

The 2nd baby, was given ACE I and improved within 24 hours

For few days it was debated whether he needs PDA stent

3rd baby alpha blocker

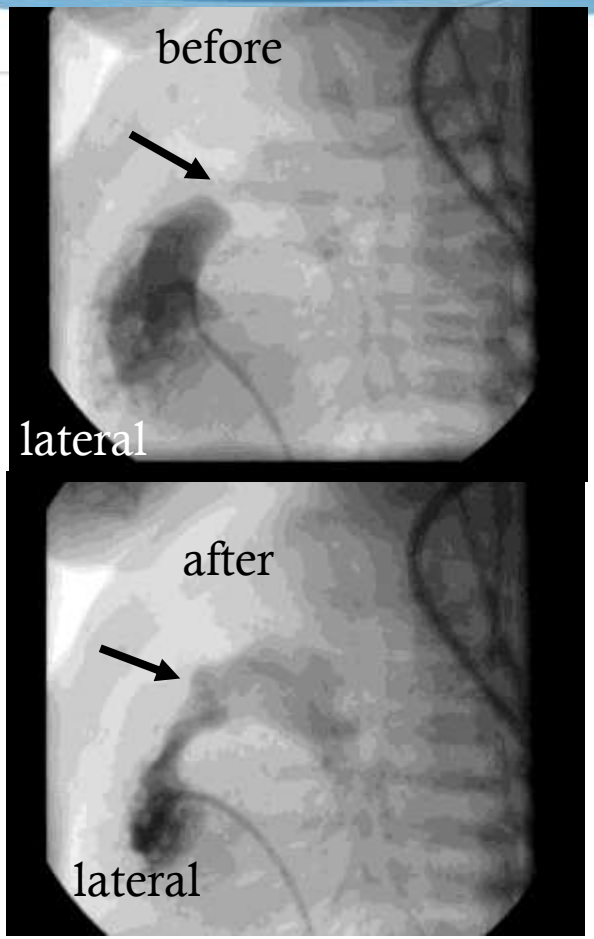
The 3rd baby, was given phentolamine and improved within 48 hours

1 baby capoten,
2 babies phento - later
capoten, 2013

Case Report 1/2

- 2 days old, f, 2.5 kg
- Cyanosis since birth
- PGE, oxygen mask
- Echo: critical PV stenosis
- Cardiac catheterization
- Elective intubation, arterial line

Balloon dilation of critical PS



Case Report$_{2/2}$

- **4 days ventilated, on PGE**
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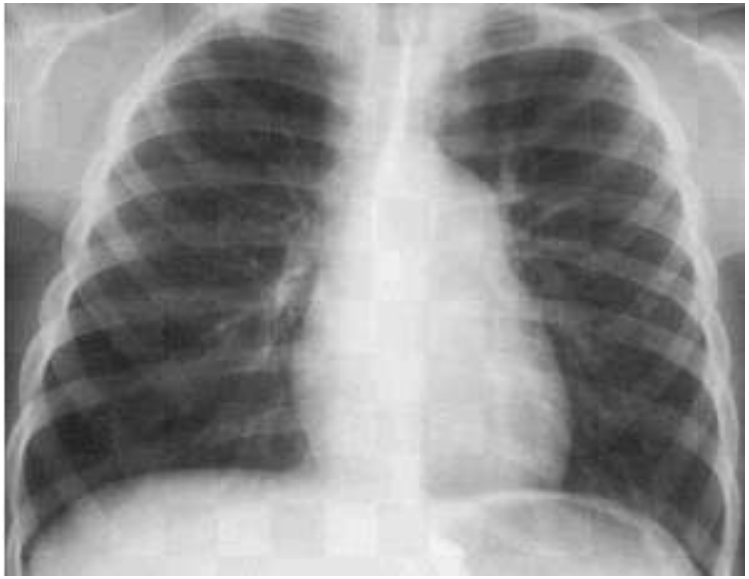


Sympathetic activity in children undergoing balloon valvuloplasty of pulmonary stenosis.

Galal MO et al. 1996; 39:774

How did it start ?
Study done in the cath lab

Question: Do beta receptors increase after balloon PS?

Hypothesis: Beta receptors will increase after intervention, because of stress of the procedure

Methods: 30 PS before and after balloon
(as control: 15 small PDAs)

Alpha and beta receptors from circulating cells

Hemodynamic data before and 10 min after balloon dilatation of pulmonary stenosis

n= 31

	Predilatation	Postdilatation	*p* values
Heart rate (beats/min)	116.6 ± 6.5	107.8 ± 5.6	0.03*
SDAP (mm Hg)	107.0 ± 2.3	107.8 ± 3.1	0.61
DDAP (mm Hg)	62.5 ± 1.9	59.7 ± 1.9	0.46
MDAP (mm Hg)	75.9 ± 2.3	82.8 ± 7.5	0.35
SPP (mm Hg)	21.9 ± 0.9	25.8 ± 2.0	0.045*
DPP (mm Hg)	13.3 ± 0.7	12.6 ± 0.7	0.42
MPP (mm Hg)	16.0 ± 0.6	16.3 ± 0.9	0.63
RVSP (mm Hg)	110.1 ± 6.3	62.6 ± 6.8	0.0000002**
RVDP (mm Hg)	13.1 ± 1.3	9.8 ± 0.9	0.024*
SYSG (mm Hg)	89.2 ± 7.3	32.5 ± 6.6	0.000001**

Galal MO et al. Pediatr Res 1996;39:774–8.

Plasma catecholamines and cAMP before and 10 min after balloon of pulmonary stenosis, compared with those of 15 PDA controls

n= 15 **n= 31**

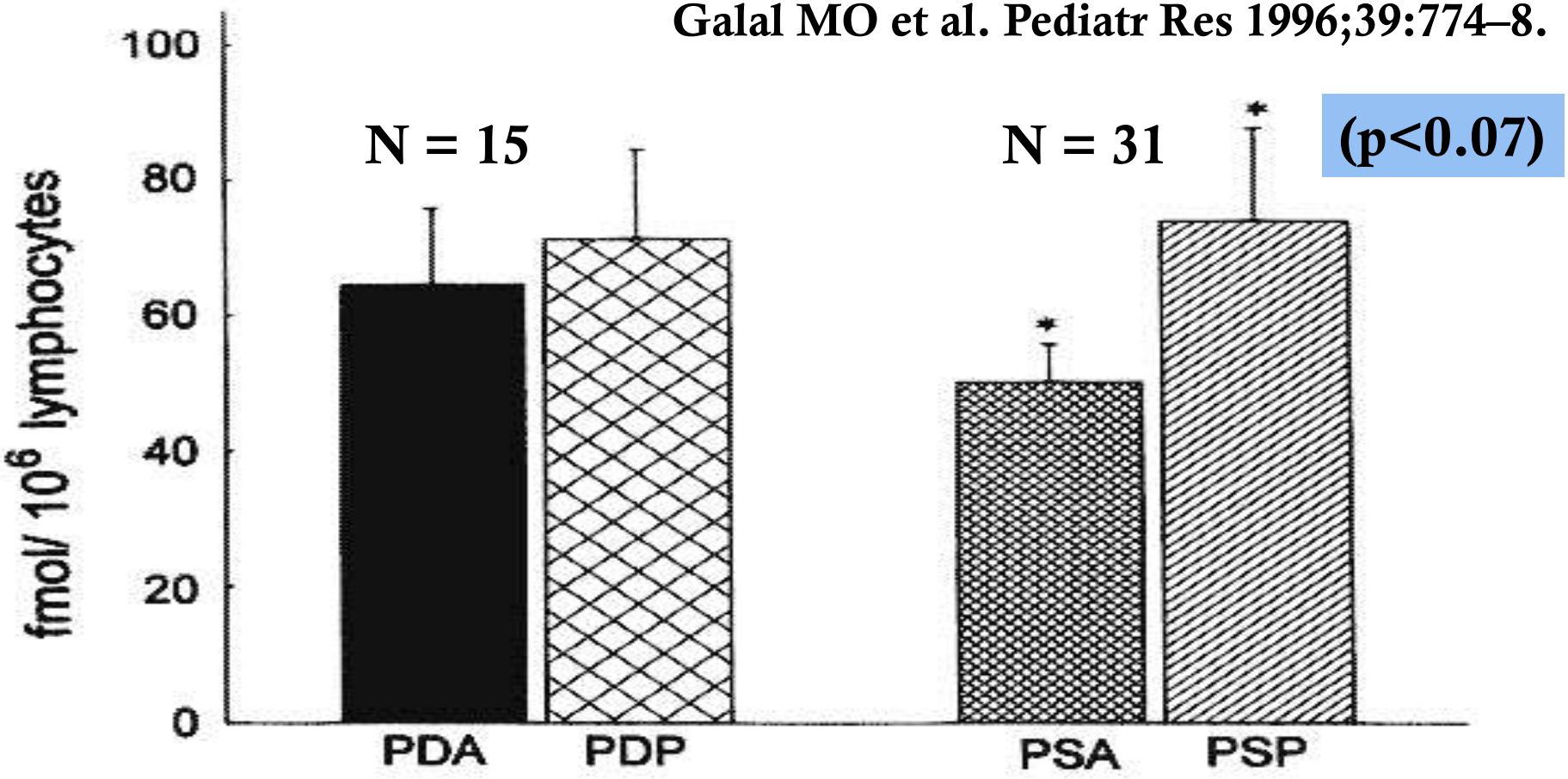
Assay	PDA	Predilatation	Postdilatation
Norepinephrine	558.5 ± 104.5	543.5 ± 56.8	546.2 ± 88.8
Epinephrine	266.3 ± 63.1	282.0 ± 42.6	461.6 ± 85*
Dopamine	103.6 ± 14.4	186.4 ± 19.5*	175.9 ± 17.3*
cAMP	15.5 ± 1.6	21.2 ± 1.4	19.1 ± 2.0

Values are given as mean ± s.e.m. Concentration are ρg/ml of plasma.
* $p < 0.05$ compared with PDA group.

Galal MO et al. Pediatr Res 1996;39:774–8.

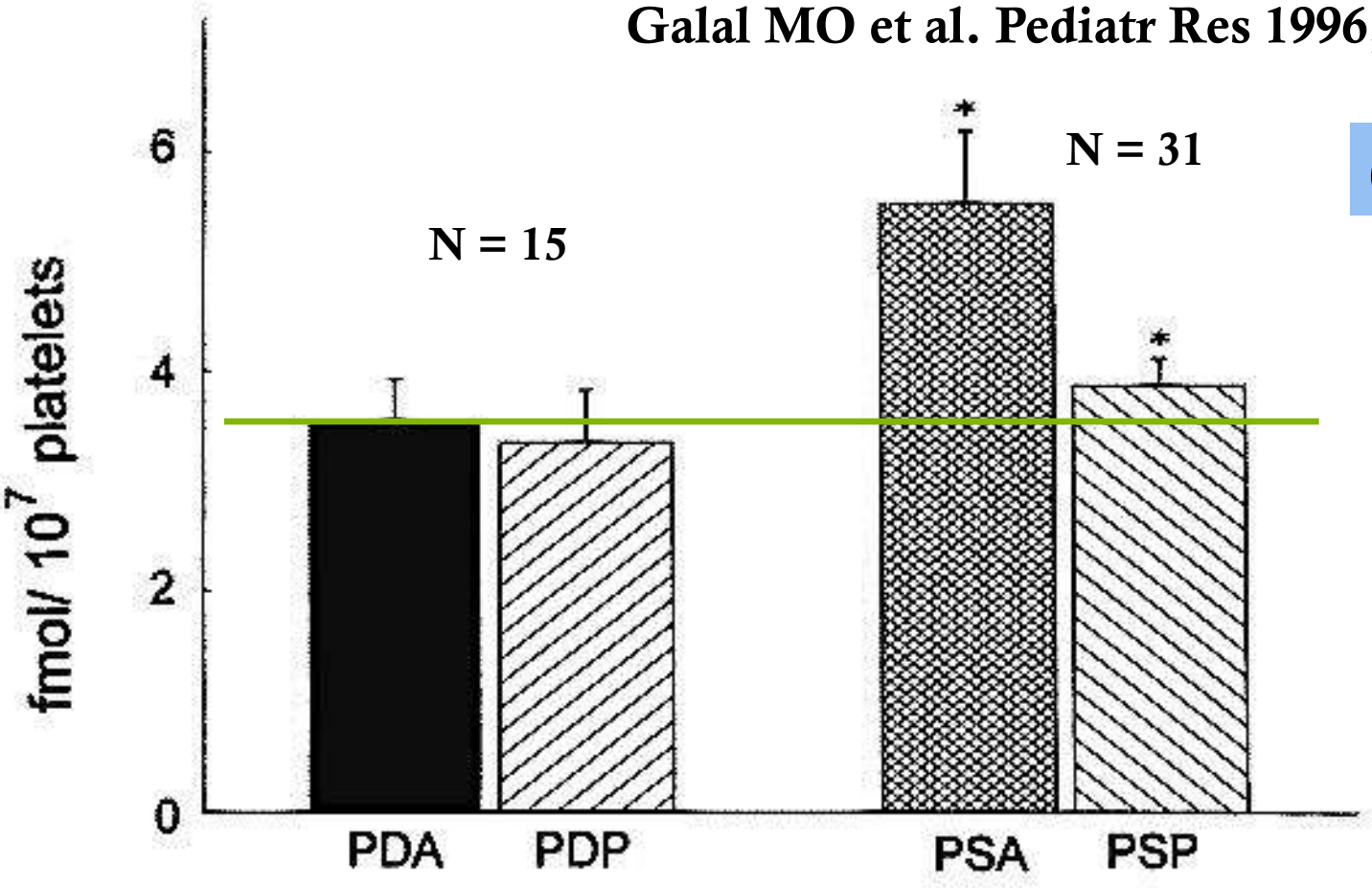
β-adrenoceptor density (B_{max}) in pulmonary stenosis before (*PSA*) and 10 min after (*PSP*) balloon valvuloplasty, compared with PDA before ($n = 15$) and after(*PDP*, $n = 7$) closure.
*$p < 0.07$ pre- compared with postdilatation.

Galal MO et al. Pediatr Res 1996;39:774–8.



α-adrenoceptor density (B_{max}) in pulmonary stenosis before (*PSA*) and 10 min after (*PSP*) balloon, compared with PDA before ($n = 15$) and after (*PDP*, $n = 7$) closure.
*$p < 0.05$ pre compared with postdilatation.

Galal MO et al. Pediatr Res 1996;39:774–8.

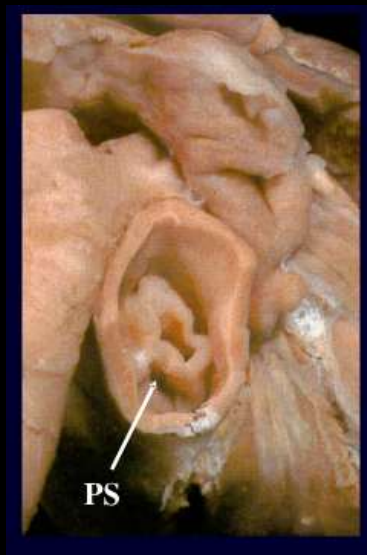


(p<0.05)

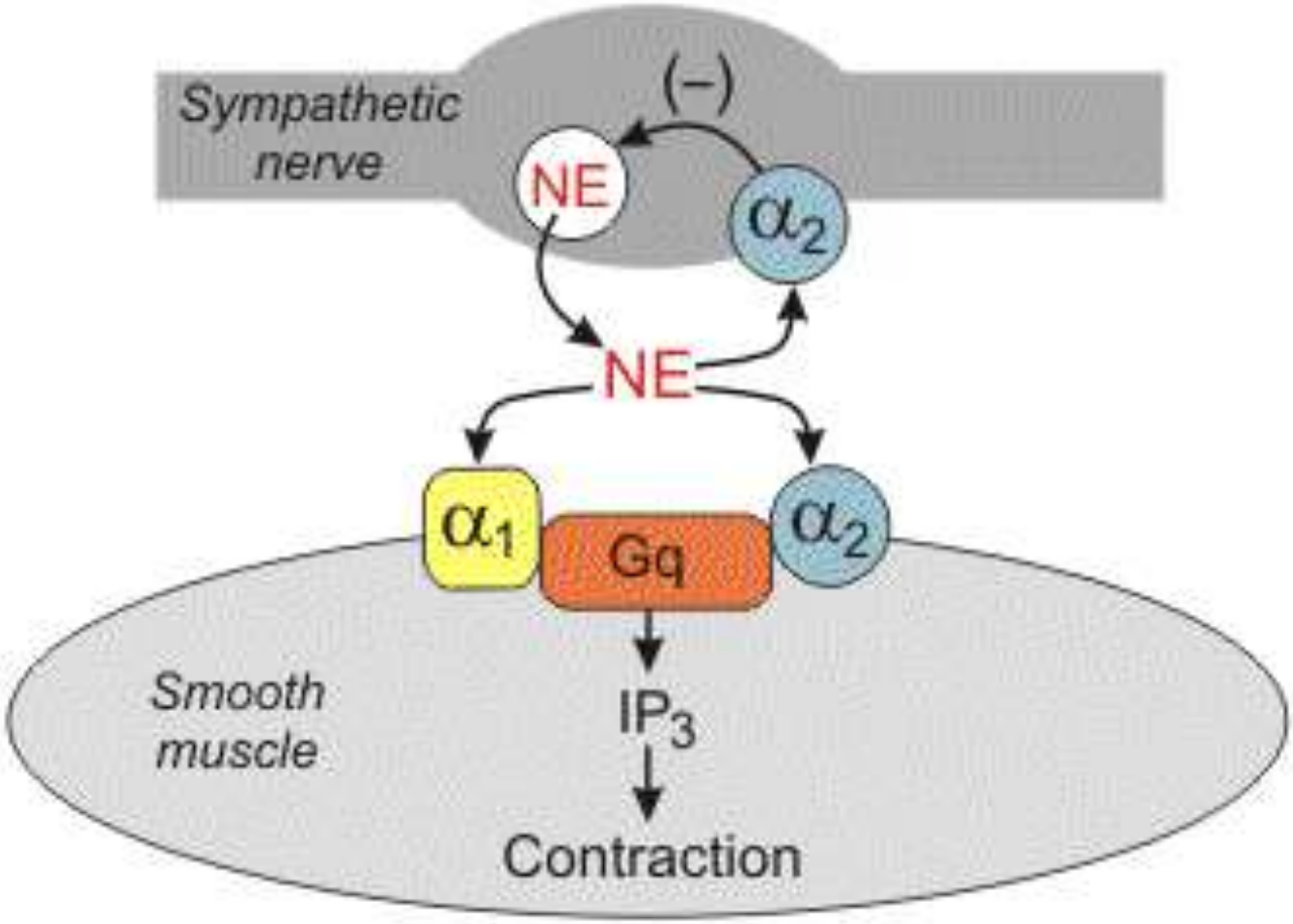
Sympathetic activity in children undergoing balloon valvuloplasty of pulmonary stenosis.

Galal MO et al. 1996; 39:774

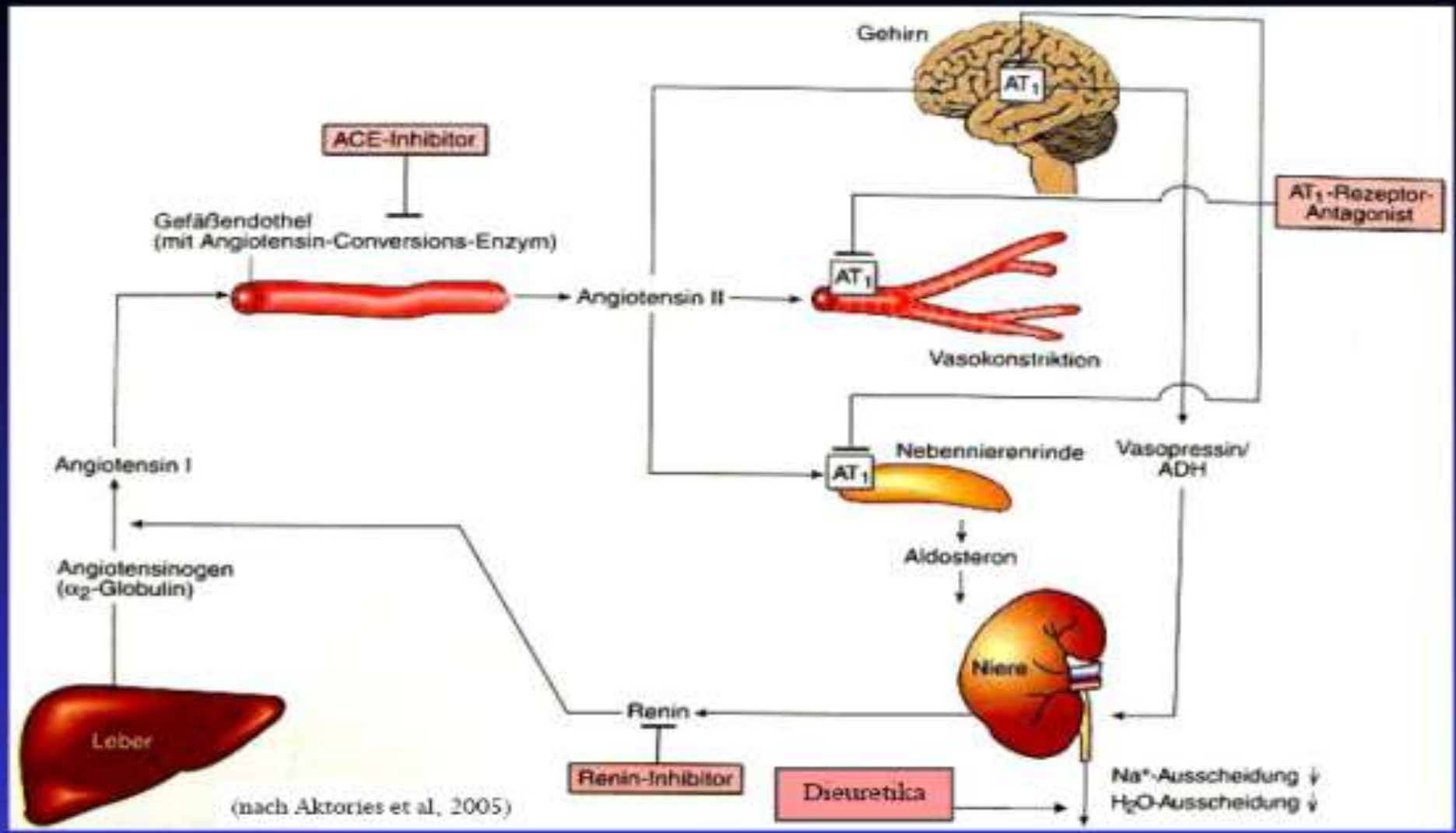
More theory supporting our management



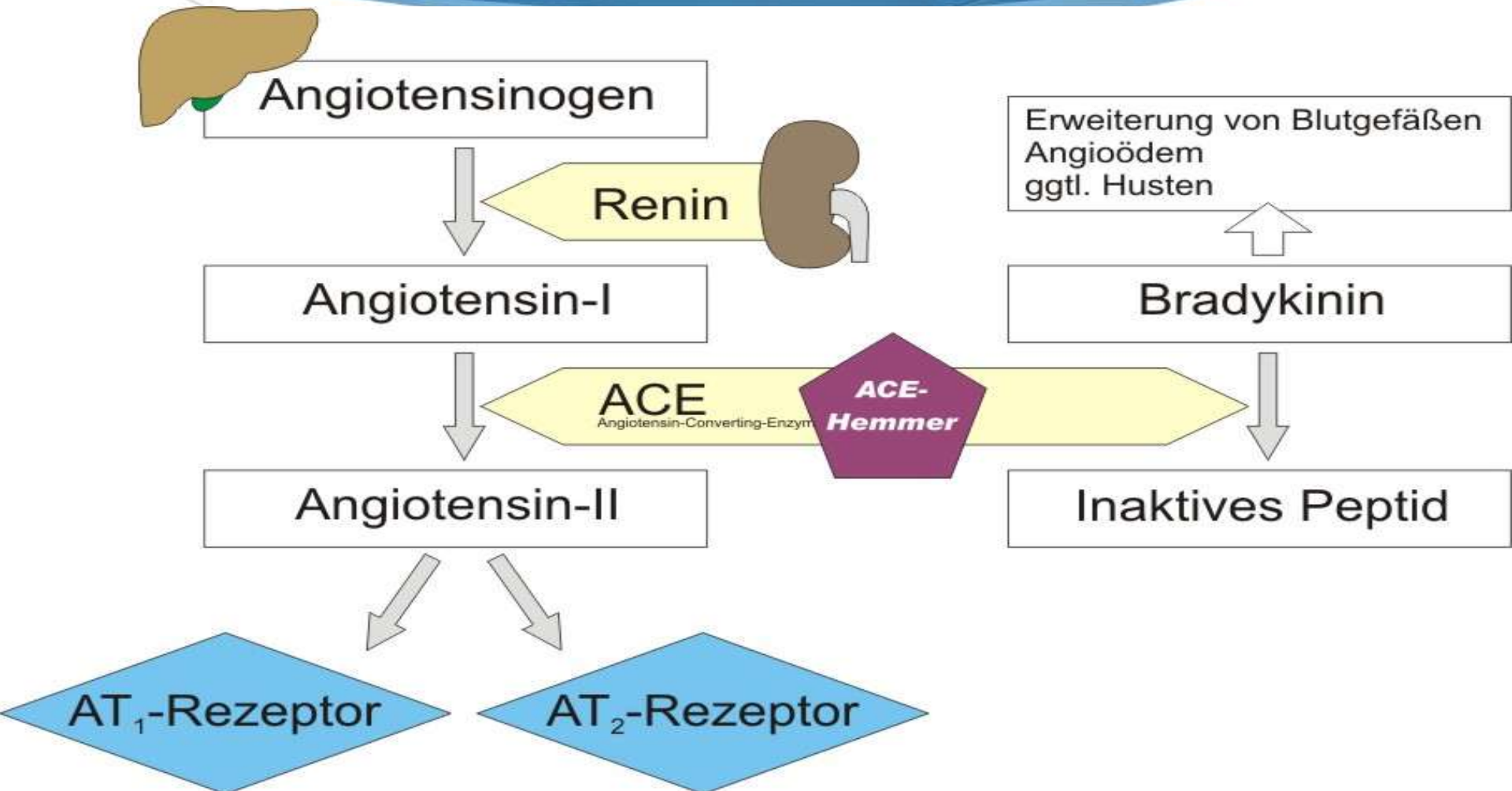
Alpha-adrenoceptors



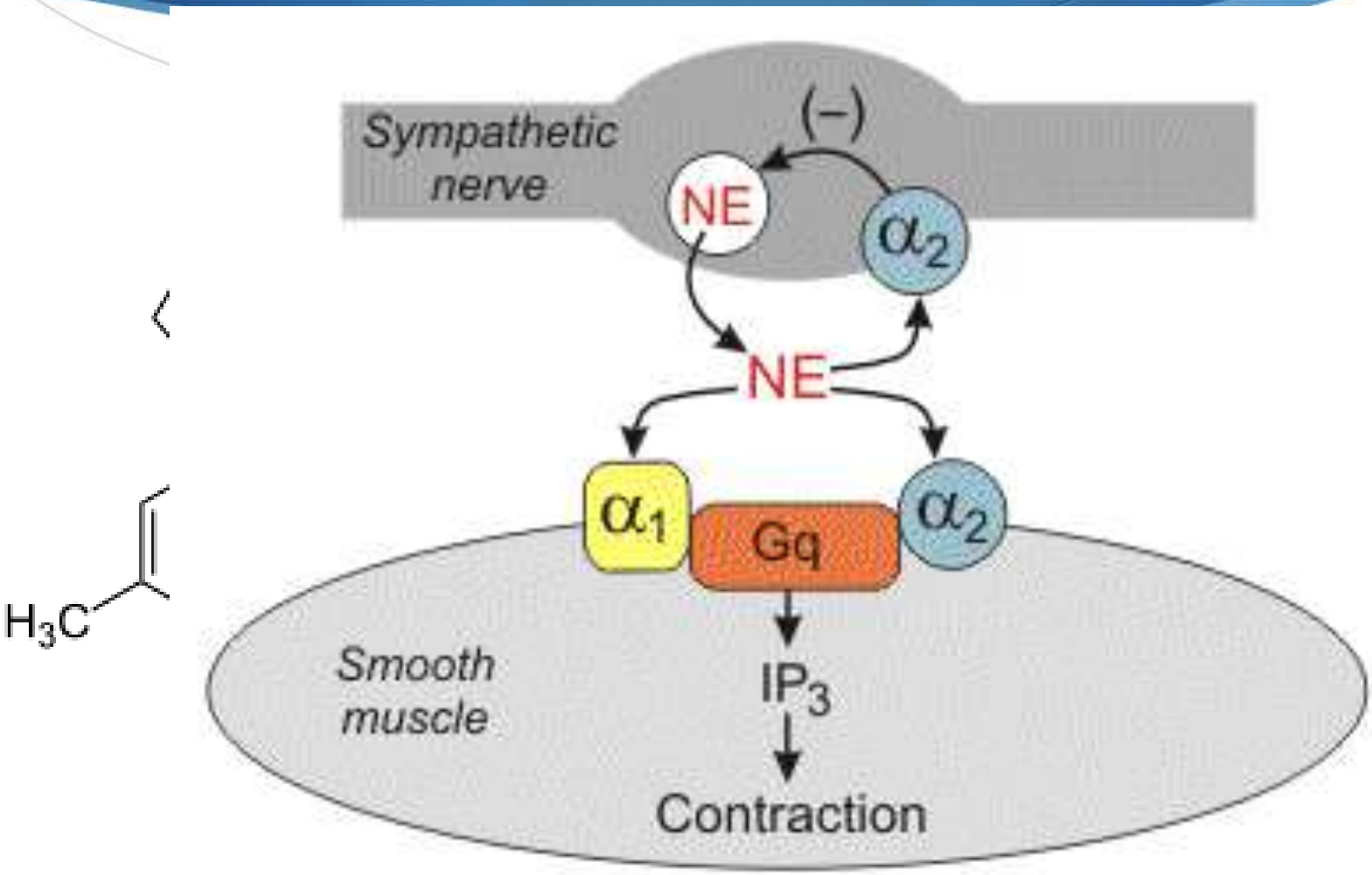
Renin-Angiotensin-Aldosteron-System (RAAS)



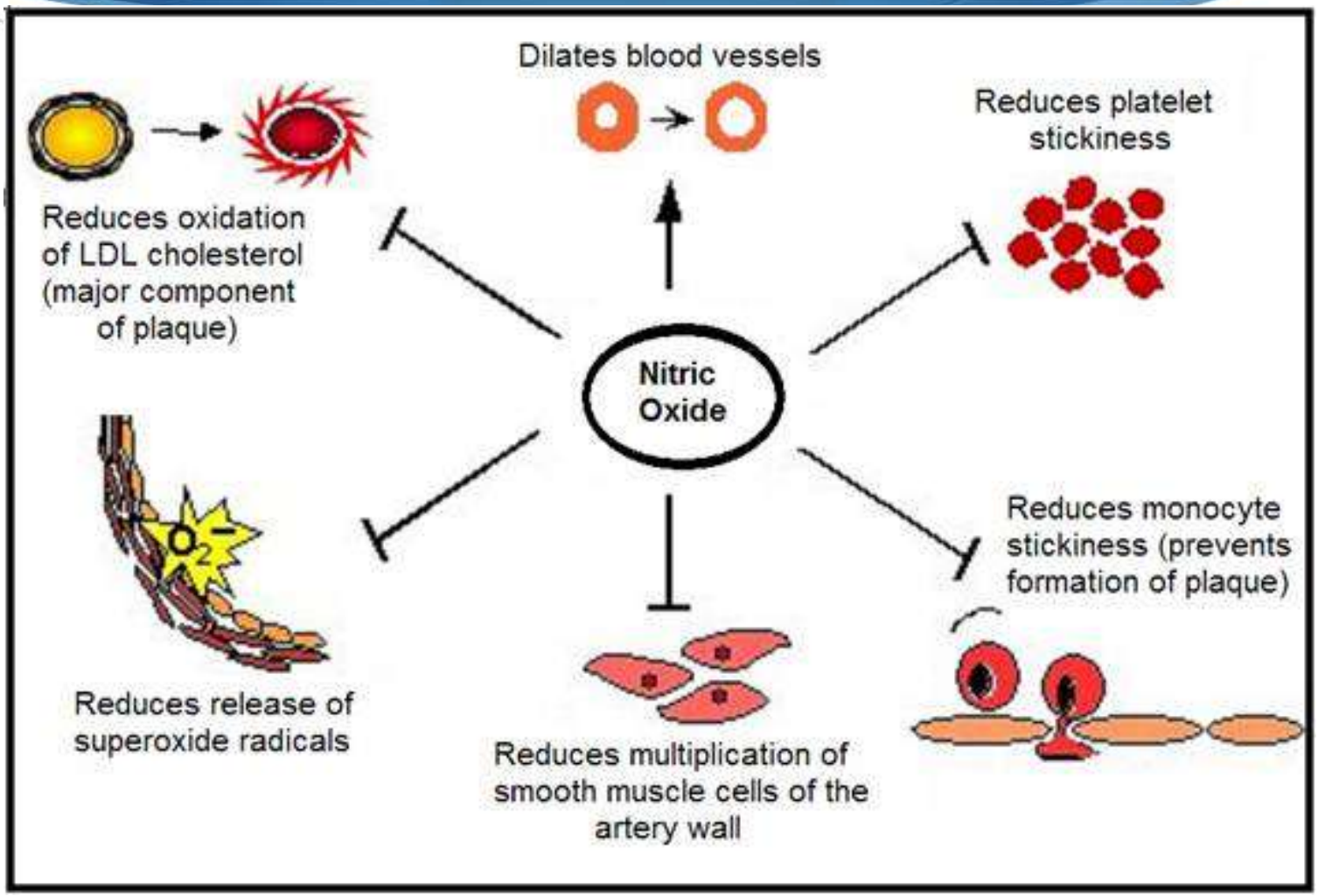
Renin-Angiotensin-Aldosteron-System (RAAS)



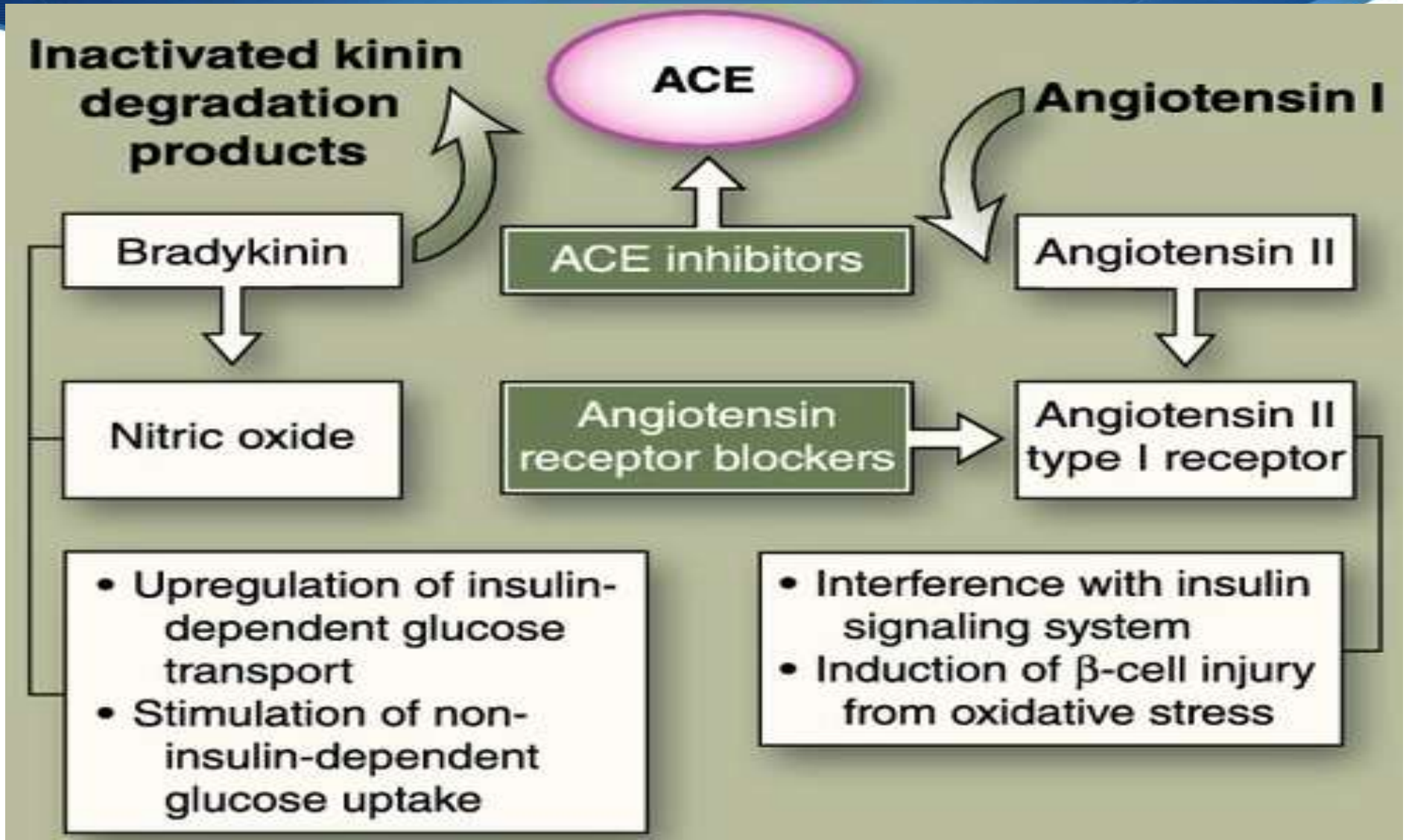
Phentolamine



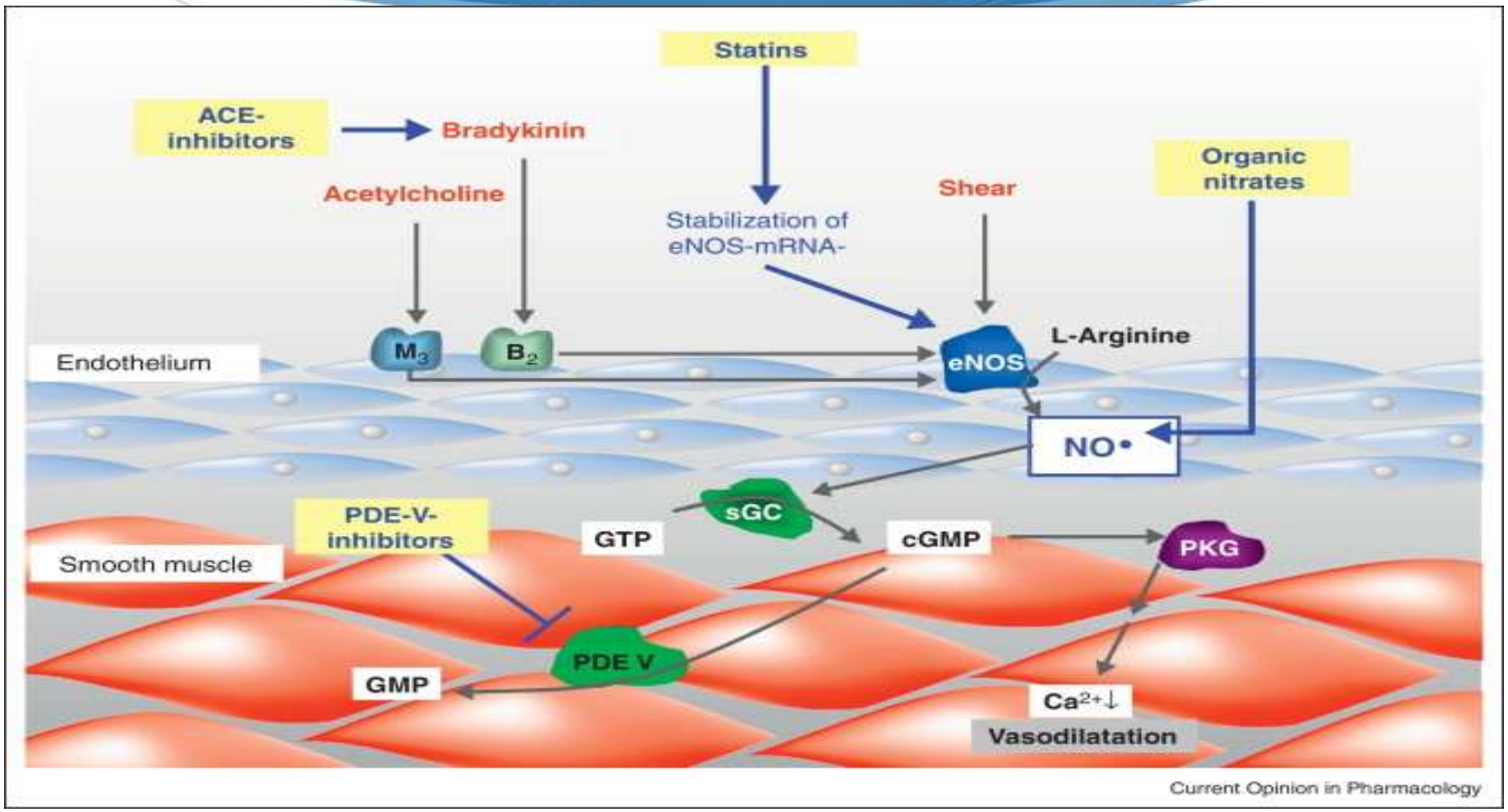
Nitric Oxide



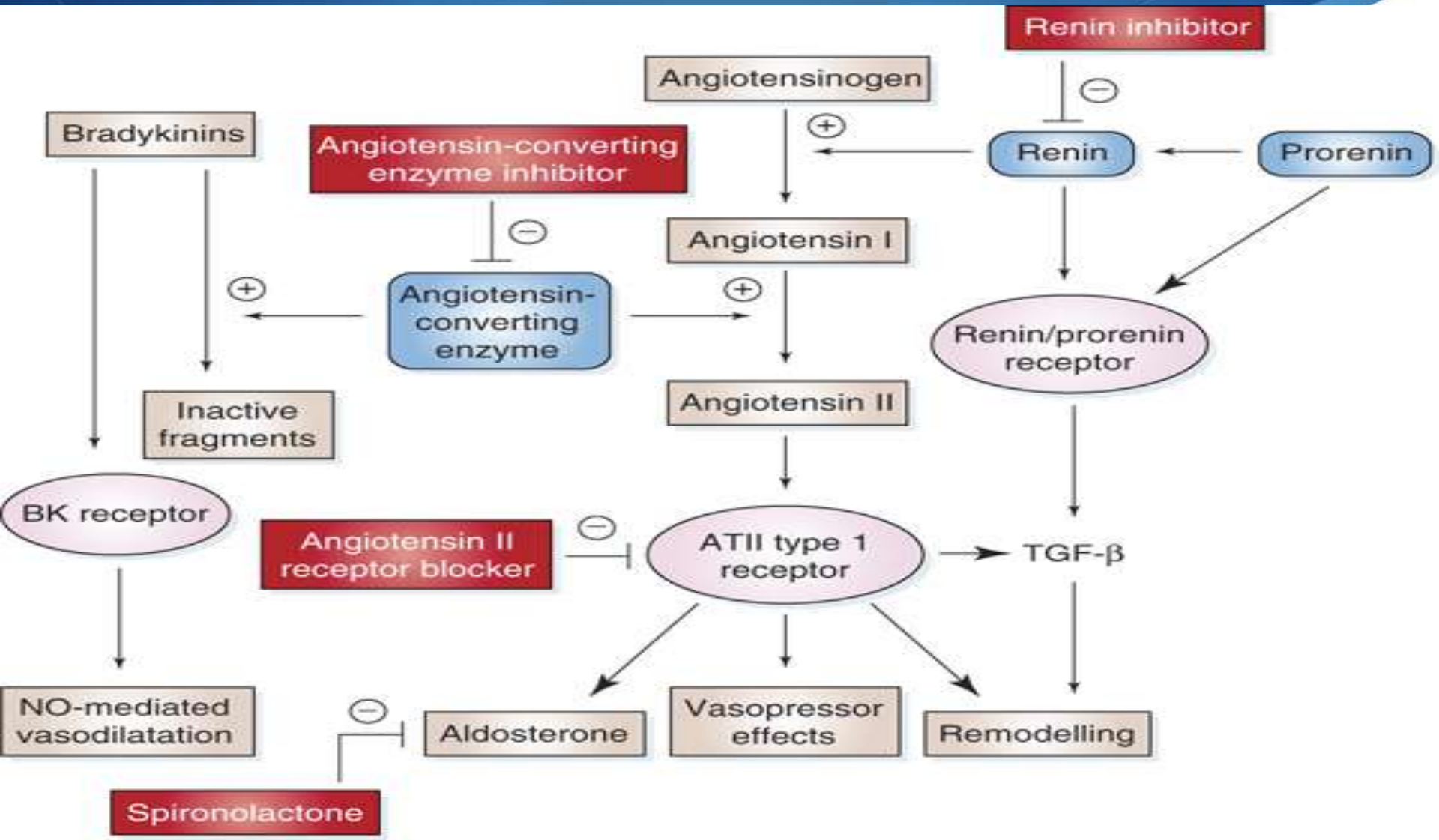
Bradykinin, ACE, Nitric Oxide



Bradykinin, ACE, Nitric Oxide



Bradykinin, ACE, Nitric Oxide



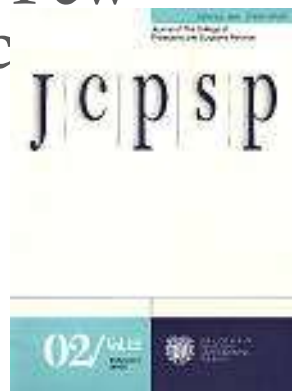
RAAS

- Das Renin-Angiotensin-Aldosteron-System ist das Ziel verschiedener Medikamente, die meist der Behandlung des hohen Blutdruckes dienen:
- Direkte Hemmer des Enzyms Renin. Als erster Arzneistoff wurde Aliskiren im März 2007 in den USA und im August 2007 in Europa zugelassen.
- Hemmer des Angiotensin-konvertierenden Enzyms (ACE-Hemmer) verhindern die Bildung von Angiotensin II.
- Alternativ kann die Wirkung des Angiotensin II an seinem Wirkungsort, nämlich am Angiotensin-Rezeptor blockiert werden (Angiotensin-Rezeptor-Blocker oder AT1-Antagonisten).
- Auch die Wirkung der sekundär freigesetzten Hormone (ADH und Aldosteron) kann pharmakologisch beeinflusst werden (zum Beispiel: Aldosteronantagonisten).

Alpha blocker /ACE I after balloon critical PS 2006

A 27 days old newborn with critical pulmonary valve stenosis remained prostaglandin (PGE1) dependent for 2 weeks after successful balloon valvuloplasty. Only the introduction of Phentolamine in his medication regimen, allowed PGE1 to be weaned off within days of this therapy.

The medication was continued for 4 days and replaced by angiotensin converting enzyme inhibitor (Captopril). Few weeks after the discharge, the patient remained clinic stable with acceptable saturation.



Alpha adreonoceptors

Stimulating alpha adrenergic receptors on the peripheral vessels as well as in pulmonary vessels leads to vasoconstriction. The blocking of these receptors with phentolamine leads to vasodilation. Also angiotensin II leads to vasoconstriction of the peripheral as well as the pulmonary vascularity. ACE-I blocks the conversion of angiotensin I to angiotensin II. This does not only lower arteriolar resistance and increases venous capacity, but also can lower the resistance in the pulmonary vasculature. In the rat model ACE inhibitor decreases pulmonary arterial pressure through preservation of endothelial nitric oxide synthase. [5] It has been also shown that ACE-I increases bradykinin, an agonist of Nitric oxide synthase (NOS). Nitric oxide is a well known vasodilator of the pulmonary vascularity [6].

[5] Kanno S et al Circulation 2001;104:945–50

[6] Wittstein IS et al. JACC 2001;38:429–35.

Alpha adrenoceptors

By facilitating forward flow into the lung as well as reducing the afterload, through vasodilation, cardiac output is increased and hence perfusion and overall oxygenation improved. The other effect of nitric oxide (NO) is to modulate cardiac function by abbreviating the systolic contraction = enhancement of diastolic relaxation, which was seen in patients with severe pressure-overload hypertrophy. Additionally, NO exerts a decrease in left ventricular end-diastolic pressure without affecting left ventricular systolic pump function [7]. If this mechanism is also effective in the right ventricle, this would facilitate right ventricular inflow and would add to the noticed improvement of oxygenation in our patient.

All the different reports of alpha blocker as well as ACE-I could explain their beneficial actions and potential important role in the management of patients with critical pulmonary stenosis described by us.

[6] Wittstein IS et al. JACC 2001;38:429–35.

[7] Jiang Z et al. Circulation 1999;99:2396–401.

Renin-Angiotensin-Aldosteron-System (RAAS)

Therapeutic Uses

Alpha-blockers, especially α_1-adrenoceptor antagonists, are useful in the treatment of primary hypertension, although their use is not as widespread as other antihypertensive drugs. The non-selective antagonists are usually reserve for use in hypertensive emergencies caused by a pheochromocytoma. This hypertensive condition, which is most commonly caused by an adrenal gland tumor that secretes large amounts of catecholamines, can be managed by non-selective alpha-blockers (in conjunction with beta-blockade to blunt the reflex tachycardia) until the tumor can be surgically removed.

Specific Drugs

Newer alpha-blockers used in treating hypertension are relatively selective α_1-adrenoceptor antagonists (e.g., **prazosin**, **terazosin, doxazosin, trimazosin**), whereas some older drugs are non-selective antagonists (e.g., **phentolamine**, **phenoxybenzamine**). (Go to www.rxlist.com for specific drug information)

Renin-Angiotensin-Aldosteron-System (RAAS)

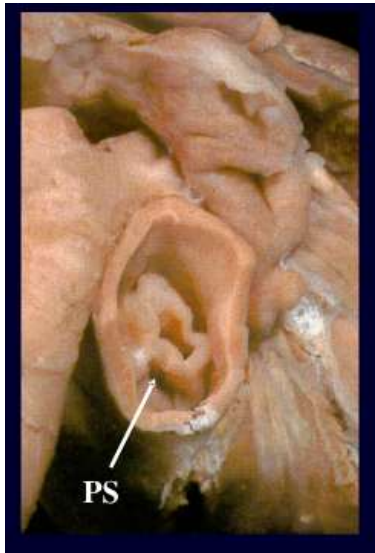
Vascular smooth muscle has two primary types of alpha-adrenoceptors: alpha$_1$ (α_1) and alpha$_2$ (α_2). The α_1-adrenoceptors are located on the vascular smooth muscle. In contrast, α_2-adrenoceptors are located on the sympathetic nerve terminals as well as on vascular smooth muscle. Smooth muscle (postjunctional) α_1 and α_2-adrenoceptors are linked to Gq-proteins, which activate smooth muscle contraction through the IP_3 signal transduction pathway. Prejunctional α_2-adrenoceptors located on the sympathetic nerve terminals serve as a negative feedback control mechanism for norepinephrine release.

α_1-adrenoceptor antagonists cause vasodilation by blocking the binding of norepinephrine to the smooth muscle receptors. Non-selective α_1 and α_2-adrenoceptor antagonists block postjunctional α_1 and α_2-adrenoceptors, which causes vasodilation; however, the blocking of prejunctional α_2-adrenoceptors leads to increased release of norepinephrine, which attenuates the effectiveness of the α_1 and

Case Report$_{1/2}$

- 13 days old, m, 2.7 kg (434011266)
- Cyanosis since birth
- PGE, oxygen mask
- Echo: critical PV stenosis, grad 130 mmHg, PFO right to left, PDA, TV annulus normal

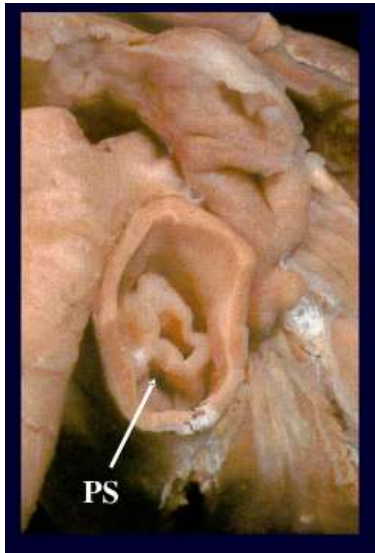
Echo and angio



Case Report 1/2

- Cardiac catheterization 26 Jan 2013 (434011266)
- Elective intubation, arterial line
- 4 Febr Echo
- PV gradient 14 mmHg, mod PI, PFO bidirectional.

Echo and angio



Only ACE I in 1 neonate **2012**

Angiotensin converting enzyme inhibitor as an additive treatment after successful balloon dilation of a critical pulmonary valve stenosis

M.O. Galal [a,b,*], A.M. Alzahrani [a], M.E. Elhoury [a]

[a] Prince Salman Heart Center, King Fahad Medical City, Riyadh; [b] University Children's Hospital in Essen

[a] Saudi Arabia; [b] Germany

A 2 days old, 2.7 kg heavy baby boy with critical pulmonary stenosis, underwent successful balloon dilation. After the uneventful procedure, he remained oxygen dependent. The baby was given oral angiotensin converting enzyme inhibitor (ACE inhibitor), instead of an infusion of alpha blocker.

Within few hours, in the afternoon of the same day after administration of ACE Inhibitor, the baby could be weaned off oxygen, maintaining on room air, oxygen saturation between 87% and 92%. At follow-up, two months later, his saturation was 99% on room air.

We believe that some neonates with critical pulmonary valve stenosis who remain oxygen dependent despite successful balloon dilation, could benefit from such management.

Influence of hypoxia on adrenoceptor activity in children with tetralogy of Fallot

N. Dzimiri[1], O. Galal[2], A. Moorji[1], A. A. Almotrefi[3]. [1]*Biological and Medical Research Dept.*, [2]*Cardiovascular Diseases Dept., King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia,* [3]*Dept. of Pharmacology, King Saud University, Riyadh, Saudi Arabia.*

We investigated the platelet α-adrenoceptor and lymphocyte β-adrenoceptor activities in 29 children with tetralogy of Fallot (22 cyanotic, 7 acyanotic) and compared them with those of 15 children having patent ductus arteriosus (PDA) with pulmonary to systemic flow ratio of <1.5. Adrenoceptor activity was estimated by ligand binding methods. The PDA patients exhibited a B_{max} of 3.38±0.41 *f*mol per 10^6 platelets and K_d of 2.72±0.52 nM. Compared to the PDA group, the α-adrenoceptor activity was elevated by 81% ($p < 0.05$) in cyanotic children, but was not significantly altered in acyanotic children. The correlation of the α-adrenoceptor density and oxygen saturation gave a regression coefficient (r) of -0.6. Their binding affinity (K_d) to [^{3}H]-yohimbine was increased by 57%. The β-adrenoceptor density of the PDA group was 5.01±0.97 *f*mol mg^{-1} protein and the K_d was 82.3±13.4 pM. Neither the β-adrenoceptor density nor their binding affinity towards [^{125}I]iodocyanopindolol was significantly changed. The results suggest that hypoxia exerts a significant influence on α-adrenoceptor activity, while it does not appear to affect β-adrenoceptor activity.

How do alpha blocker and ACE-I work ?

- Alpha receptors lead to vasoconstriction
- Alpha-blocker leads to vasodilation
- AGT II leads to vasoconstriction,
- ACE-I blocks AGT I – AGT II

  blocking it, leads to vasodilation

August 20-24, 1995
AMSTERDAM - THE NETHERLANDS

Influence of hypoxia on adrenoceptor activity in children with tetralogy of Fallot

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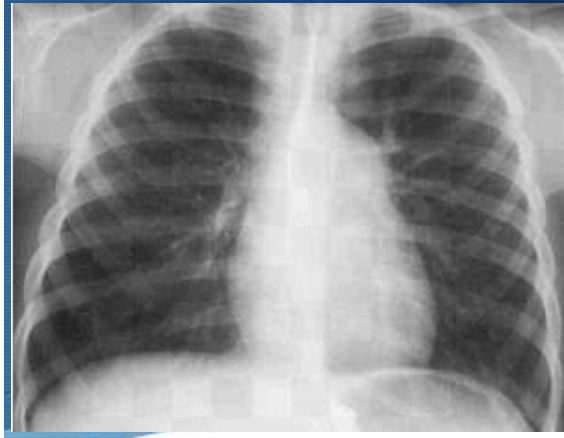

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N.DZIMIRI, O.GALAL, A.MOORJI and A.A. ALMOTREFI
Influence of hypoxia on adrenoceptor activity in children with tetralogy of Fallot. European Heart Journal, 16 (Suppl.) , 403, 1995

Alpha and beta receptors before and after balloon PS

- Galal O, Dzimiri N, Bakr S, Moorji A, Almotrefi AA.
- Sympathetic activity in children undergoing balloon
- valvuloplasty of pulmonary stenosis.
- Pediatr Res 1996;39:774–8.

Sympathetic activity in children undergoing balloon valvuloplasty of pulmonary stenosis.

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Pediatr Res. 1996 May;39(5):774-8.

Sympathetic activity in children undergoing balloon valvuloplasty of pulmonary stenosis.

Galal O, Dzimiri N, Moorji A, Bakr S, Almotrefi AA.

Department of Cardiovascular Diseases, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia.

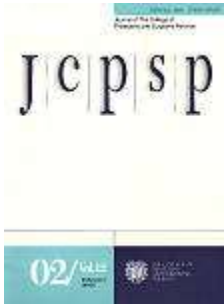
Abstract

We studied the influence of balloon valvuloplasty on alpha- and beta-adrenoceptor densities, plasma catecholamine, and cAMP levels in children and infants with pulmonary stenosis before and 10 min after balloon dilatation, employing as controls children undergoing transcatheter occlusion of patent ductus arteriosus (PDA) with Qp/Qs ratio < 1.5. In the PDA group, the alpha-adrenoceptor density (Bmax) was 3.75 +/- 0.72 fmol/10(7) cells (n = 15) before occlusion and remained unchanged at 3.35 +/- 0.47 fmol 10 min thereafter. In the pulmonary stenosis patients (n = 31), the receptor density was 59% higher ($p < 0.05$) before, and decreased to PDA levels 10 min after, the procedure. The control beta-adrenoceptor density was 64.8 +/- 11.0 fmol/10(6) cells before, and 71.2 +/- 13.2 fmol 10 min after, occlusion. In the study group, the density was 23% lower ($p < 0.07$) and increased to the PDA levels 10 min after the dilatation. Compared with the PDA, pre- and postdilatation plasma norepinephrine levels were not significantly changed; epinephrine was slightly elevated before, but increased by 73% after, dilatation; dopamine was 80% ($p < 0.05$); and cAMP was 37% higher before, and remained elevated at 70 and 23% above the PDA values after, the procedure. Accordingly, alpha-adrenoceptor density is significantly elevated in children with pulmonary stenosis and decreases significantly immediately after balloon valvuloplasty. On the other hand, beta-adrenoceptor density is attenuated and increases toward normal levels after the procedure. The immediate reversal of the receptor levels after balloon valvuloplasty suggests that this procedure exerts acute effects on the sympathetic functional level in this disease.

PMID: 8726227 [PubMed - indexed for MEDLINE]

Alpha blocker, later Capoten in one neonate **2006**

- J Coll Physicians Surg Pak. 2006 Dec;16(12):780-2.
- **Alpha(2)-blocker helps to avoid systemic to pulmonary shunt in a prostaglandin dependent infant with critical pulmonary valve stenosis.**
- Galal MO, Arfi AM, Ata JA, Hussain A, Kouatli A.



Pulmonary Atresia and Intact Ventricular Septum

1. Definition

Congenital malformation in which pulmonary valve is atretic, coexisting with variable degrees of RV & TV hypoplasia

2. Historical Note

Hunter : 1st case report in 1783

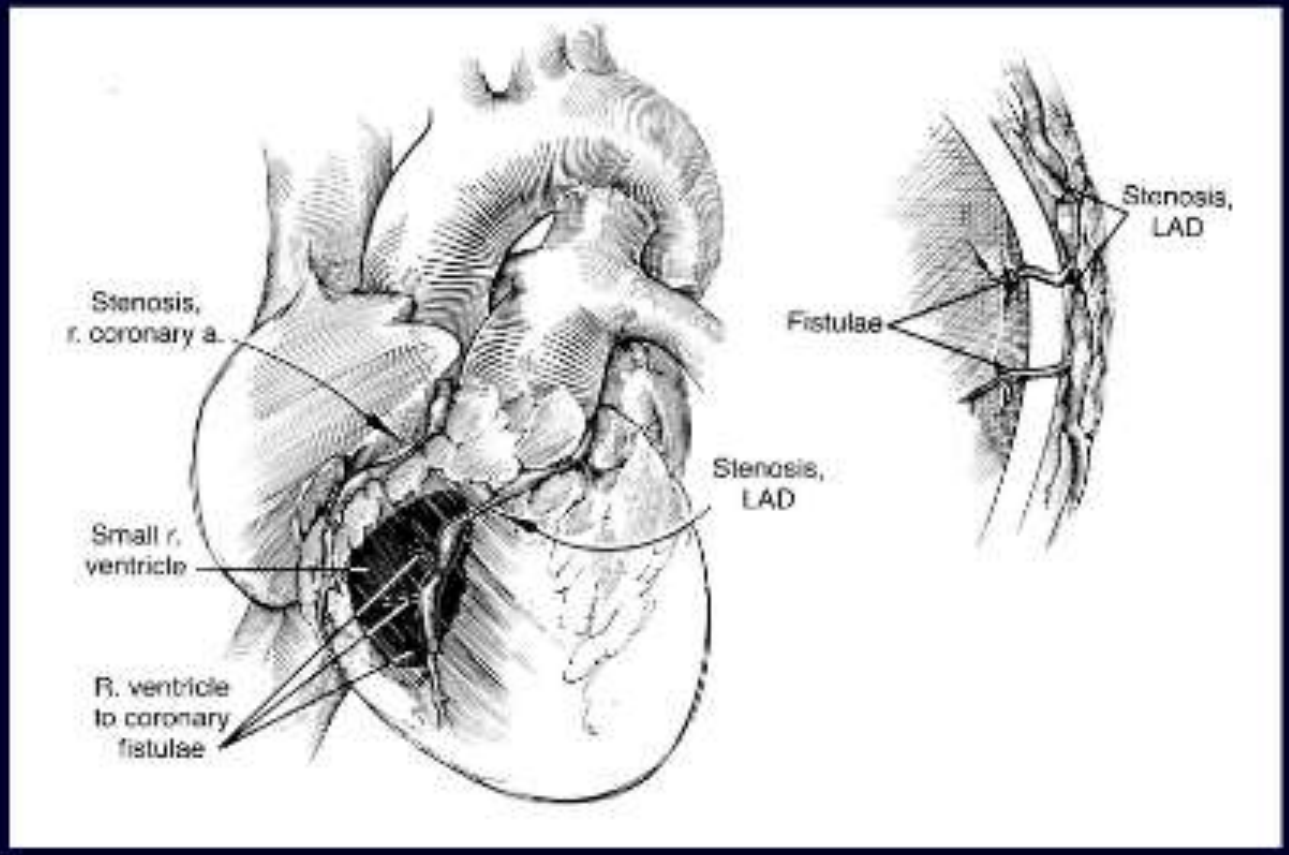
Peacock : Collected 7 patients report in 1839

Grant : Coronary sinusoid & fistula recognized in 1926

Davignon : Suggest systemic-pulmonary artery shunt in 1961

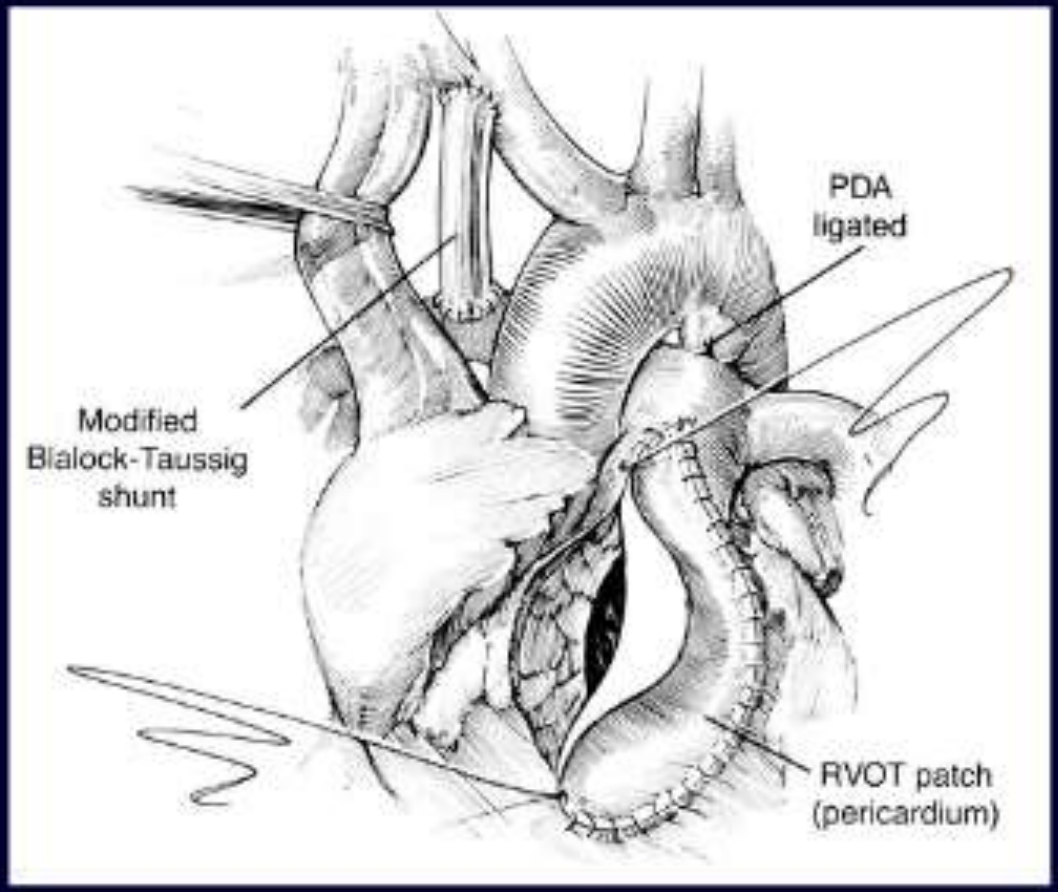
Bowman : Shunt and RV outflow operation in 1971

RV-Coronary Artery Fistula



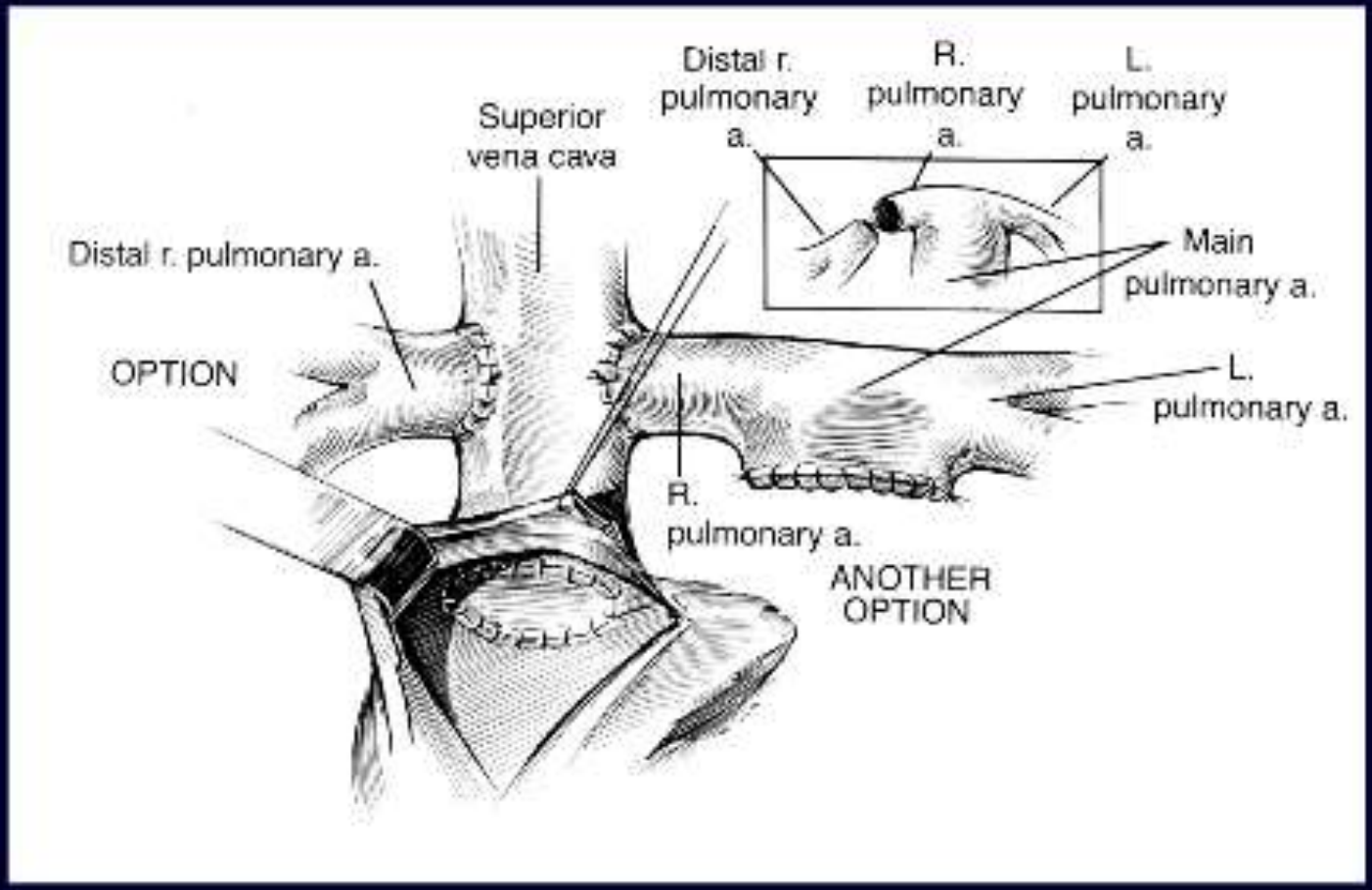
Operation for PA+IVS

Concomitant placement of patch & shunt

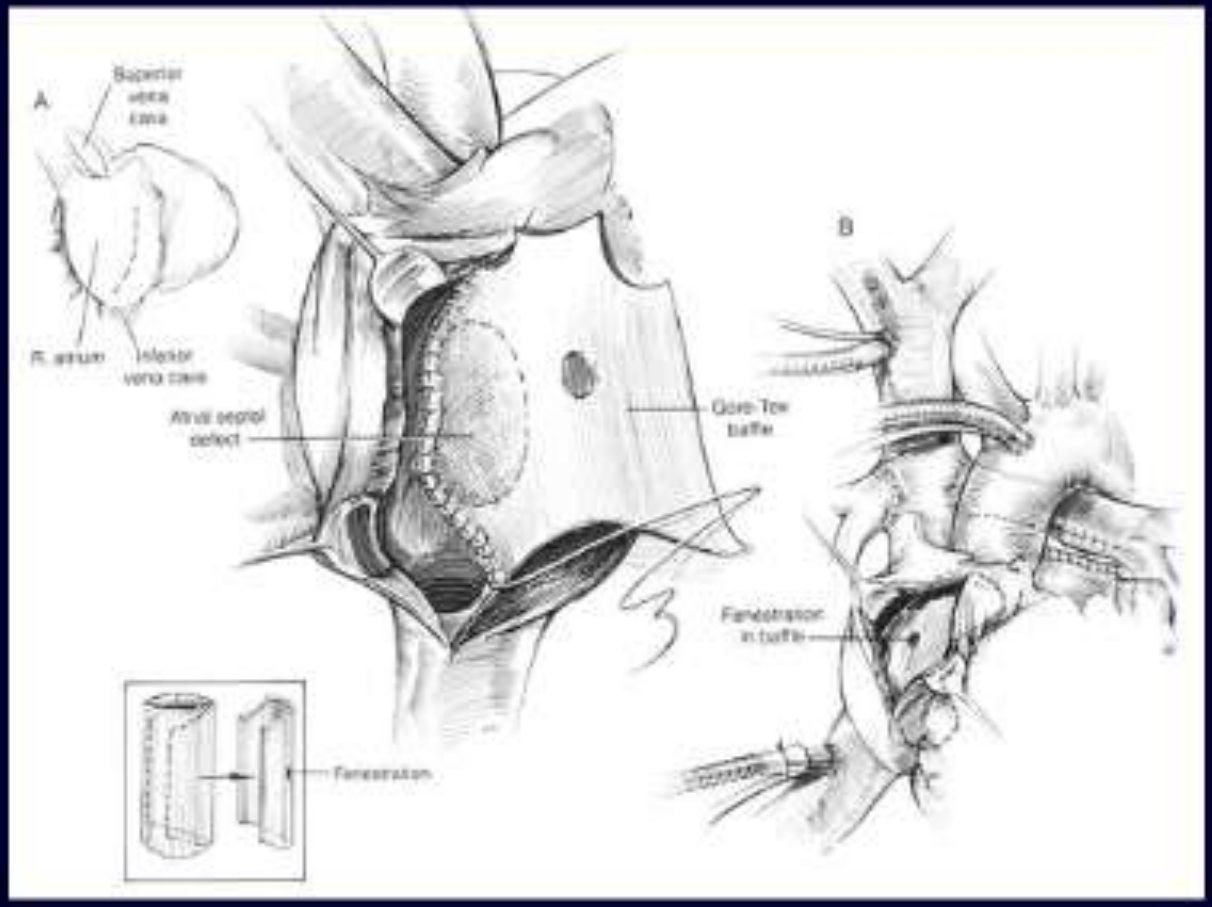


PA + IVS – Hemi Fontan

Alternative Method



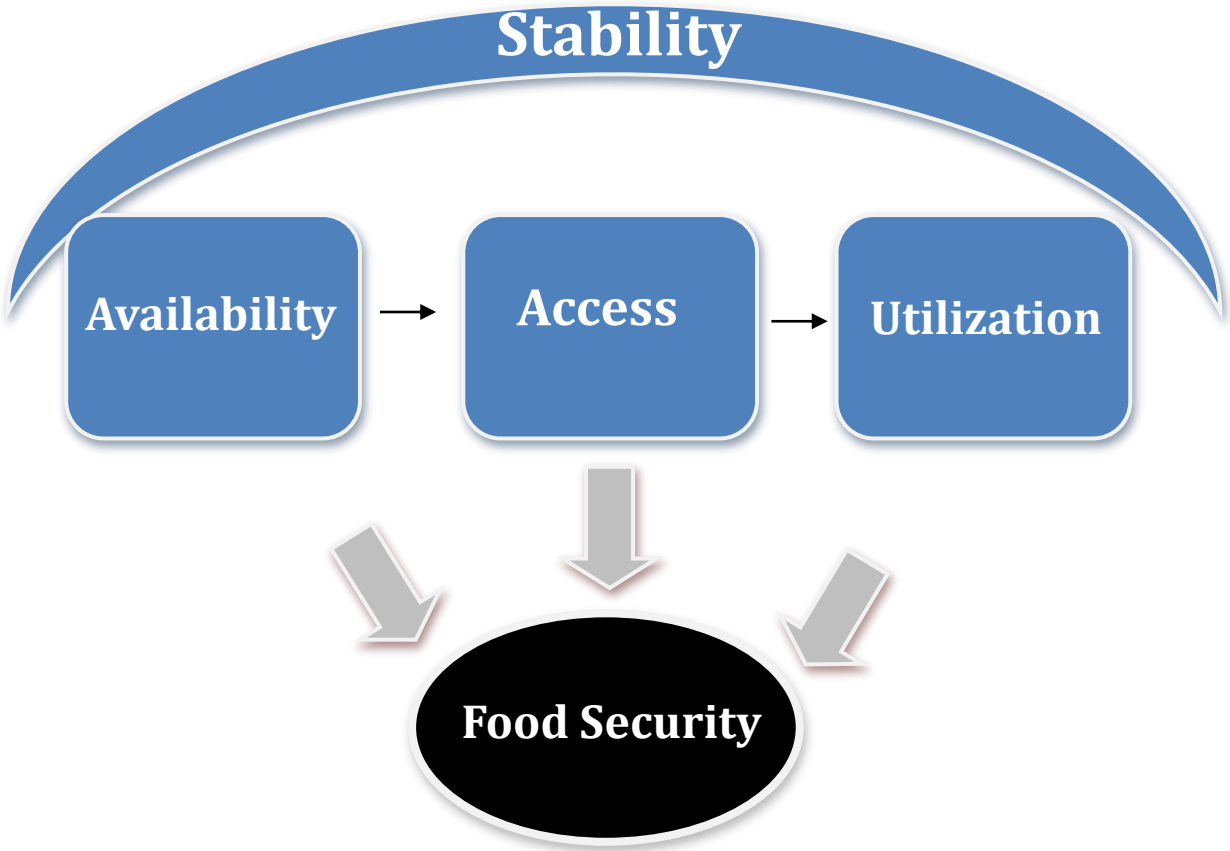
Lateral Tunnel with Fenestration



Valvar PS ; Operative View

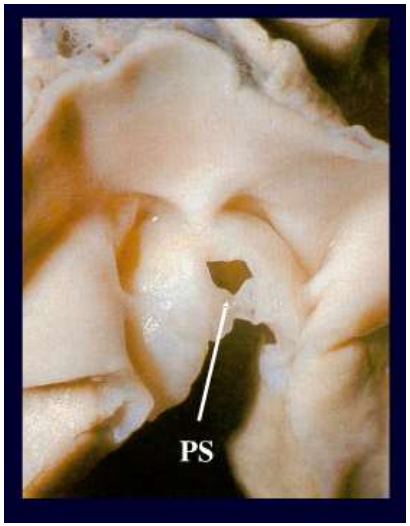
(Dysplastic leaflets with commissural fusion)

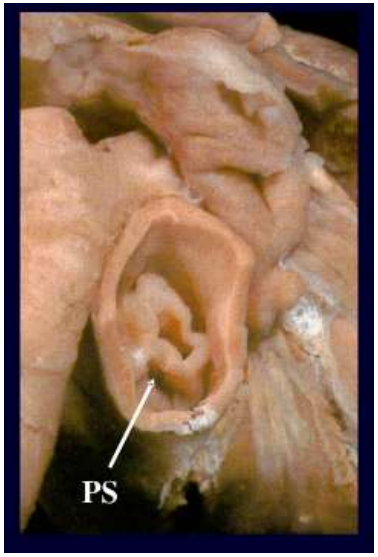
Defining Food Security



From Bench to Bedside

From lab to cath lab





Latin America

- General positive economic development
- High food *availability*
- Malnutrition at 15.4% among youth
- High inequality in food *access*
- Low food *utilization*

Latin America

- Who suffers the most?

The Indigenous **Women** **Rural Inhabitants**

Guatemala

- Population of 13 million
- Indigenous population of 5.4 million
- Equal split between urban and rural
- Chronic malnutrition at 43%
- Percent of people in poverty 51%
- Over half of children are underweight

Guatemala's Indigenous

- Primarily Mayan heritage
- Spanish arrival in the 1500s
- Mass death from disease
- Marginalized by the government

Guatemalan History

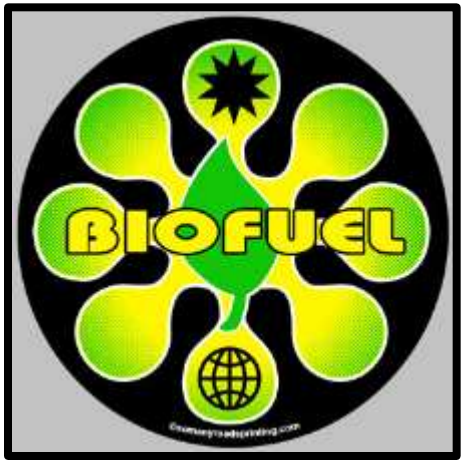
Civil war

- The Guatemalan Civil War ran from 1960 – 1996
- Death of hundreds of thousands of people
- Instable governments
- Migration to the USA

Guatemalan Current Events

Globalization

- Opening to world markets influences food prices
- International demand changes food production



Guatemalan Current Events

Climate Variability

- Droughts and floods destroy over 30% of crops

Dealing with Food Insecurity

- Migration to the city
- Migration to the USA
- Involvement in non-agricultural work
- Eating less and eating differently

Government Projects

El Pacto Hambre Cero

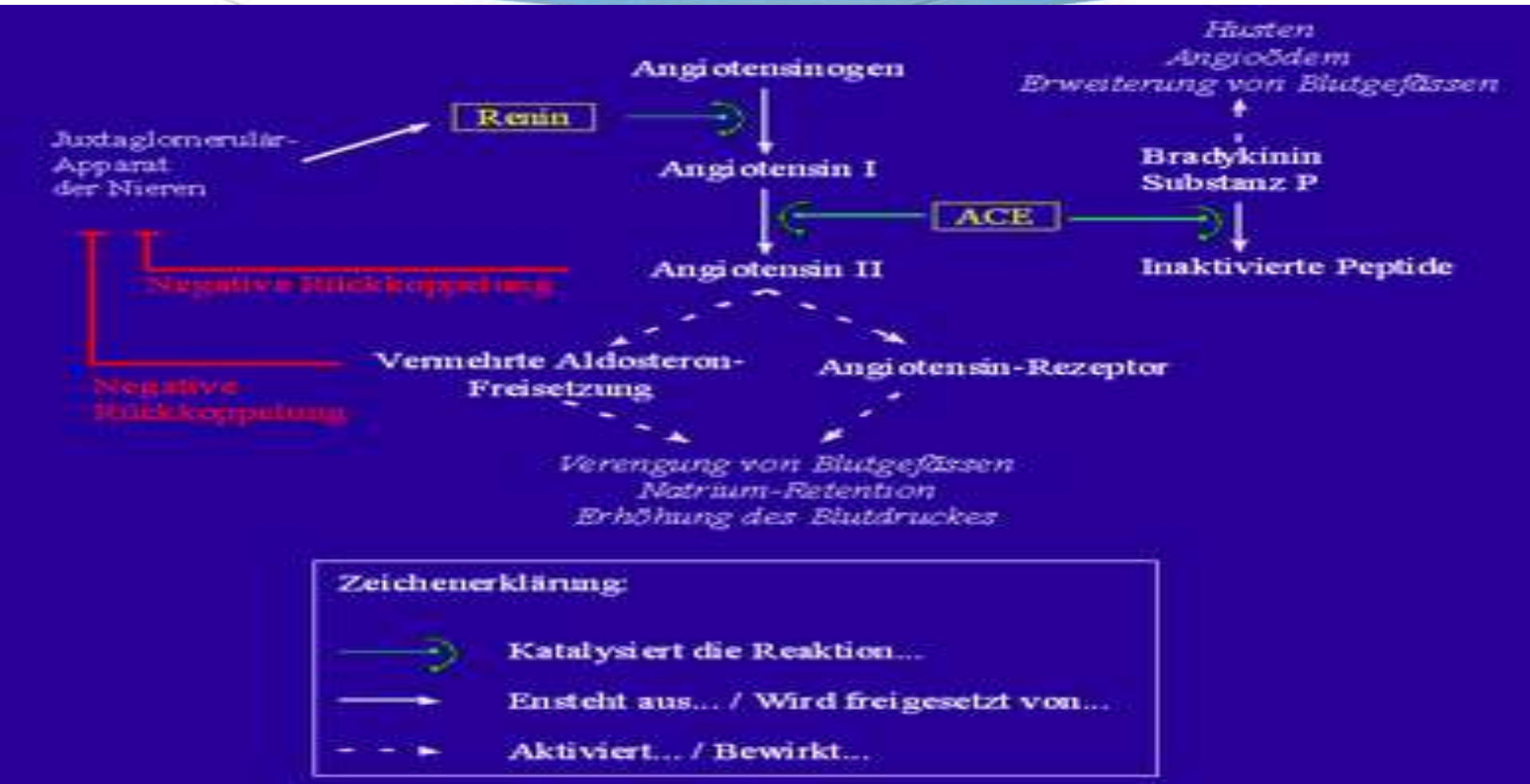
- US commits 200 million dollars
- Aimed to benefit 166 municipalities
- Support drought resistant strains
- Focused on the youth

PACTO
HAMBRE CERO
GUATEMALA

Review

- Guatemala has high food insecurity
- The indigenous populations suffer from lack of access, availability and utilization
- Many difficulties are connected with international interactions

Renin-Angiotensin-Aldosteron-System (RAAS)



Thank you for your attention

I would like to thank:

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