Hyperemia

Hyperemic Stimuli

Why ?
How ?
FAQ !

Bernard De Bruyne, MD, PhD
Cardiovascular Center Aalst
OLV-Clinic Aalst, Belgium

ETP, Sophia Antipolis, April 2013
Why?

1. General concept of stress test (as opposed to “rest test”)
2. Standardized measurements (as opposed to “moving target”)
3. All clinical outcome data are based on hyperemic data
Aortic Stenosis: Severe ???

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Aortic Stenosis: Severe ???
Aortic Stenosis: Severe ???

Cardiac output 3.8 L.min⁻¹
Aortic Gradient 26 mm Hg
Aortic Valve Area 0.77 cm²

Cardiac output 8.6 L.min⁻¹
Aortic Gradient 58 mm Hg
Aortic Valve Area 1.1 cm²
Oral Glucose Tolerance Test (OGTT)

75 g of sugar to be drunk within 5 minutes

Hyperemia

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Hyperemia puts the stenosis in a windtunnel
Why?

1. General concept of stress test (as opposed to “rest test”)

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The Control of Resting Myocardial Blood Flow

The balance between supply and demand depends on mechanisms which are multiple, interacting, cumulative, nonlinear.
The Control of Resting Myocardial Blood Flow

The "resting state" in biology is wishful thinking of biologists
Why?

1. General concept of stress test (as opposed to “rest test”)
2. Standardized measurements (as opposed to “moving target”)
3. All clinical outcome data are based on hyperemic data (FFR)
How?

“Keep it Simple and Standardized”

The KISS principle
Maximal Vasodilation

**Epicardial**
= Conductance
Arteries > 550 µ

**Microvasculature**
= Resistance
Arteries < 550 µ

Vasospasm

Autoregulation

Hyperemia

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Hyperemia

Maximal Vasodilation

1. Nitrates ➔ Epicardial arteries
2. Adenosine ➔ Microvasculature

- IV: 140 µg/kg/min
- IC: 100 – 200 µg in bolus
Maximal Vasodilation

1. Nitrates ➔ Epicardial arteries

2. Adenosine ➔ Microvasculature

3. Papaverine
   - inhibition of phosphodiesterase ➔ cyclic adenosine MP ↑

4. Regadenoson
   - precursor of adenosine

5. Apadenoson
   - precursor of adenosine

6. Binodenoson
   - precursor of adenosine

7. Nitroprusside
   - NO pathways direct non-selective vasodilator

8. Nicorandil
   - ↑ guanylate cyclase to increase formation of cyclic GMP

9. Dopamine
   - β₁-agonist ➔ ↑ O₂ consumption ➔ adenosine ↑

10. Exercise
    - Adren stimulation ➔ ↑ O₂ consumption ➔ Adenosine ↑

11. Coronary occlusion
    - Ischemia ➔ release of adenosine
Adenosine: Mechanisms of Action

Target organs

- Coronary arteriolar smooth muscle cells
- Renal arteries (organ level)
- Peripheral and central nervous system
- Myocardium
- Cardiac Conduction system
- Respiratory tract

Receptors (A₁, A₂A, A₂B, A₃)

- A₂A
- A₁
- A₁ A₂A
- A₃
- A₂B
- A₁

Hyperemia

ADO 40 µg bolus in Renal Artery

Half Life = 4 to 10 s

ADO 40 µg bolus in LAD

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Maximal Vasodilation

1. Nitrates ➔ Epicardial arteries

2. Adenosine ➔ Microvasculature

- IV: 140 µg/kg/min
- IC: 100 – 200 µg in bolus
Hyperemia

Specificities of IV Adenosine (140 µg/kg/min)

1. Preferred route when a pressure pull back is needed

2. Induces a brief increase in systemic pressure followed by a decrease in systemic pressure by 10-20%

3. Is almost uniformly accompanied by a burning sensation

4. Fluctuation of the $P_d/P_a$ ratio are observed in some cases

5. A-V blocks are relatively frequent, always transient
Hyperemia

Adenosine

STOP
Specificities of IC Adenosine (100-200 µg)

1. Can be used in the vast majority of lesions
2. Short half live
3. Rare AV blocks, always transient
4. Extremely reproducible: do it twice or more!
Hyperemia

INJECTING ADENOSINE
Specificities of IC Adenosine (140 µg/kg/min)

1. Can be used in the vast majority of lesions
2. Short half live
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4. Extremely reproducible: do it twice (or more!)
Hyperemia

FFR = 0.53

FFR = 0.53

FFR = 0.54

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Tips and Tricks

1. IV: either central or large venous access
2. IC: keep the injection as short as possible
3. Be consistent, teach the nursing staff, the techs, ...
4. Pay attention to the quality of the recording of the tracings:
   "record every tracing as if you have to present this case at the opening session of the AHA"
Hyperemia

Tips and Tricks
Tips and Tricks
Hyperemia

Tips and Tricks

0.79

0.78

(92) Pa mean

(73) Pd mean

0.79

FFR

38.56

CUPSOR

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Hyperemia

Pa mean: 79
Pd mean: 67
FFR: 0.84
CURSOR: 38.42
Hyperemia

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Conclusive Remarks

1. Hyperemia is mandatory to “interrogate” a lesions properly

2. Can be obtained very easily, safely, cheaply, ...

3. Provided it is standardized in each laboratory
FAQ

✓ When $P_d/P_a$ at rest $> 0.90$, do we have to induce hyperemia?
✓ When $P_d/P_a$ at rest $< 0.80$, do we have to induce hyperemia?
✓ Useful to increase the dose of IV ado $> 140 \, \mu g/kg/min$?
✓ Useful to increase the dose of IC ado $> 200 \, \mu g$ (bolus)?
✓ Is the burning sensation related to ischemia?
✓ Are some patients resistant to Adenosine?
✓ Can Papaverine be used instead of Adenosine?
✓ Is hyperemia expensive?
✓ What to do with radial procedures?
✓ Interference with some medications?
✓ Is adenosine contraindicated in patients with lung disease?
FAQ

When $P_d/P_a$ at rest > 0.90, do we have to induce hyperemia?

YES

$P_d/P_a = 0.96$

$FFR = 0.62$
FAQ

When Pd/Pa at rest < 0.80, do we have to induce hyperemia?
When \( P_d/P_a \) at rest < 0.80, do we have to induce hyperemia?

\[ P_d/P_a = 0.56 \quad \text{FFR} = 0.42 \]
FAQ

Useful to increase the dose of IV ado > 140 µg/kg/min?

NO
Hyperemia

Increasing the dose above 140 µg/kg/min decreases systematic BP and increases the thoracic pain.
FAQ

Useful to increase the dose of IC ado > 200 µg (bolus) ?

720 µg decreases $P_d/P_a$ a bit further w/o any decrease in BP, any increase in HR and no heart blocks ????

De Luca et al JACC Interv 2011
FAQ

Is the burning sensation related to ischemia?

NO

Adenosine is an algesic substance which stimulates the same nerves than those responsible for angina ... which is also due to the local release of adenosine during ischemia.

Sylven C. Cardiovasc Drugs Ther 1993;7:745
FAQ

Are some patients resistant to Adenosine?

NO,

Resistance to exogenous Adenosine does not exist.
FAQ

Can Papaverine be used instead of Adenosine?
Papaverine IC
16 mg IC in LCA  12 mg IC in RCA
Papaverine IC

16 mg IC in LCA  12 mg IC in RCA
Hyperemia

Papaverine IC

16 mg IC in LCA  12 mg IC in RCA
Hyperemia

Papaverine IC

16 mg IC in LCA  12 mg IC in RCA
Is hyperemia expensive?

... NOT REALLY:

0.12 € / bolus of 100 µg IC;  0.24 € / bolus of 200 µg

1.34 € / syringe needed for approx 15 minutes of IV administration
FAQ

What to do with radial procedures?

IC BOLUS

IV adenosine INFUSION

IV Regadenosone BOLUS
FAQ

Some medications interfere with Adenosine

Beta-blockers
Alpha-blockers
Caffeine
Ticagrelor
ACE-inhibitors
Effect of Caffeine on FFR

Before Caffeine

After Caffeine

0.76

0.75

Hyperemia

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Aqel RA et al Am J Cardiol. 2004
Beta-Adrenergic Blockade and Myocardial Flow

Changes in Myocardial Blood Flow

- Carvedilol
- Metoprolol

Rest
Hypermia


Hyperemia

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Effect of α-Blockers on Diameter and FFR

PHENTOLAMINE

URAPIDIL

SALINE

MLD (mm)

Pre Post

Pre Post

Pre Post

FFR

p=0.03

p=0.0001

p=NS

E. Barbato et al EHJ 2004

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FAQ

Is adenosine contraindicated in all patients with lung disease?

NO

1. Adenosine is strictly contraindicated in asthma

2. Adenosine is NOT contraindicated in COPD