

What does *Penh* measure?

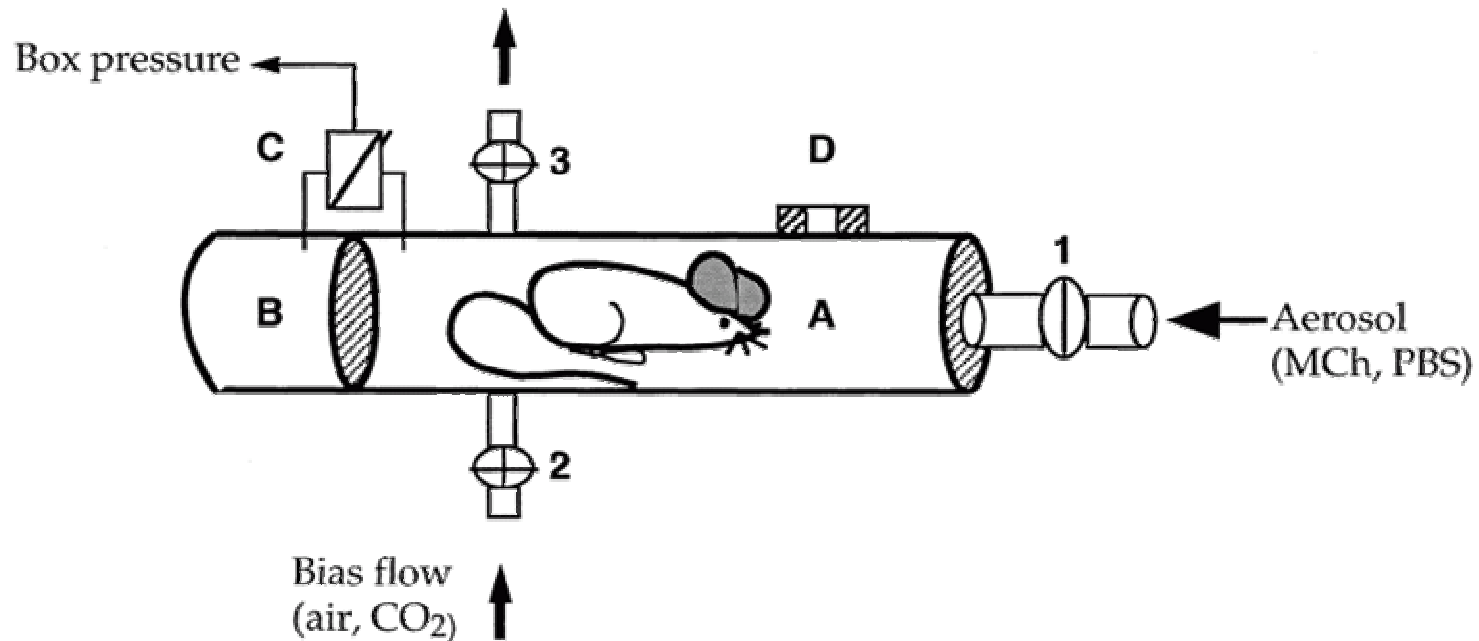
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Background:

Barometric Plethysmography

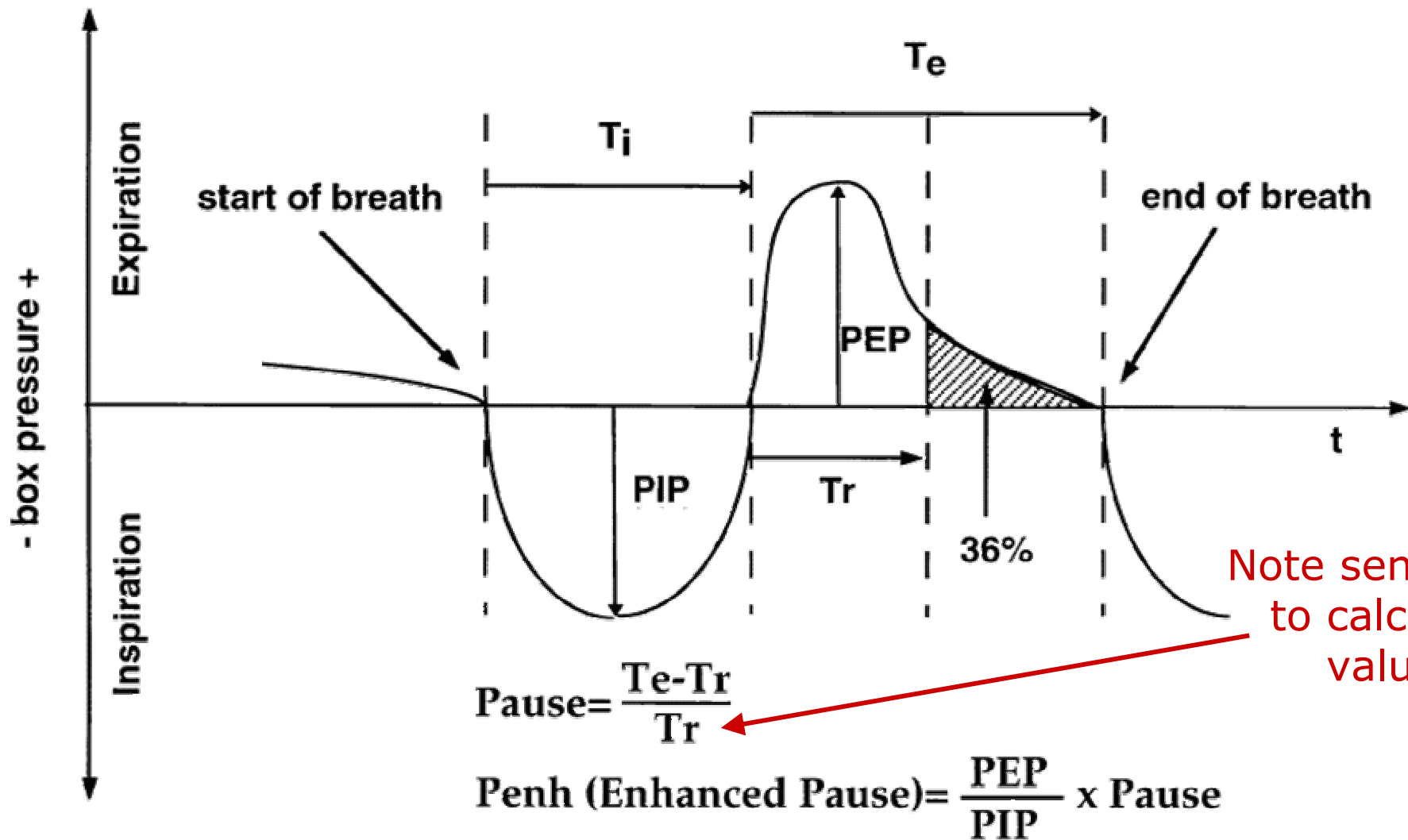


- An animal in a chamber causes breathing frequency pressure changes. Effects is from:
 - Heating and Humidification
 - Adiabatic compression
-

Background: *Penh*

- Proposed: *Hamelmann et al., 1997*
 - Heuristic parameter: *Penh*
 - BALB/c mice tested
 - Results show correlation of *Penh* vs R_{aw}
 - Advantages
 - Ease of use
 - Animal is preserved
-

Penh: definition



Issues: *Penh*

1. What does it mean?

- How does it relate to traditional parameters?
 - Why such a complicated formula?
Is it special?
-

Issues: *Penh*

2. Lack of physical support

Unfortunately:

Box pressure originates in:

- Adiabatic compression → related to P_L → Effect related to lung mechanics
- heating, humidification → related to V_T → Dominates signal (>10x)

Lundblad et al., 2002

Issues: *Penh*

3. Experimental Problems

- Reports that it doesn't *work* well in C57BL6
 - Equipment is difficult to calibrate, and results vary day to day
-

Issues: *Penh*

Species variability:

Bert P., *C.R. Soc. Biol.*, 1868

- Specific pressure change
 - large in
duck, dog, cat, guinea pig, tortoise
 - small in
rabbit, pigeon, snake, frog
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Our study: experimental evaluation of Penh

Goals:

- Compare to traditional parameters (invasive and non-invasive)
 - Test results in different strains: BALB/c and C57BL6
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Parameters calculated

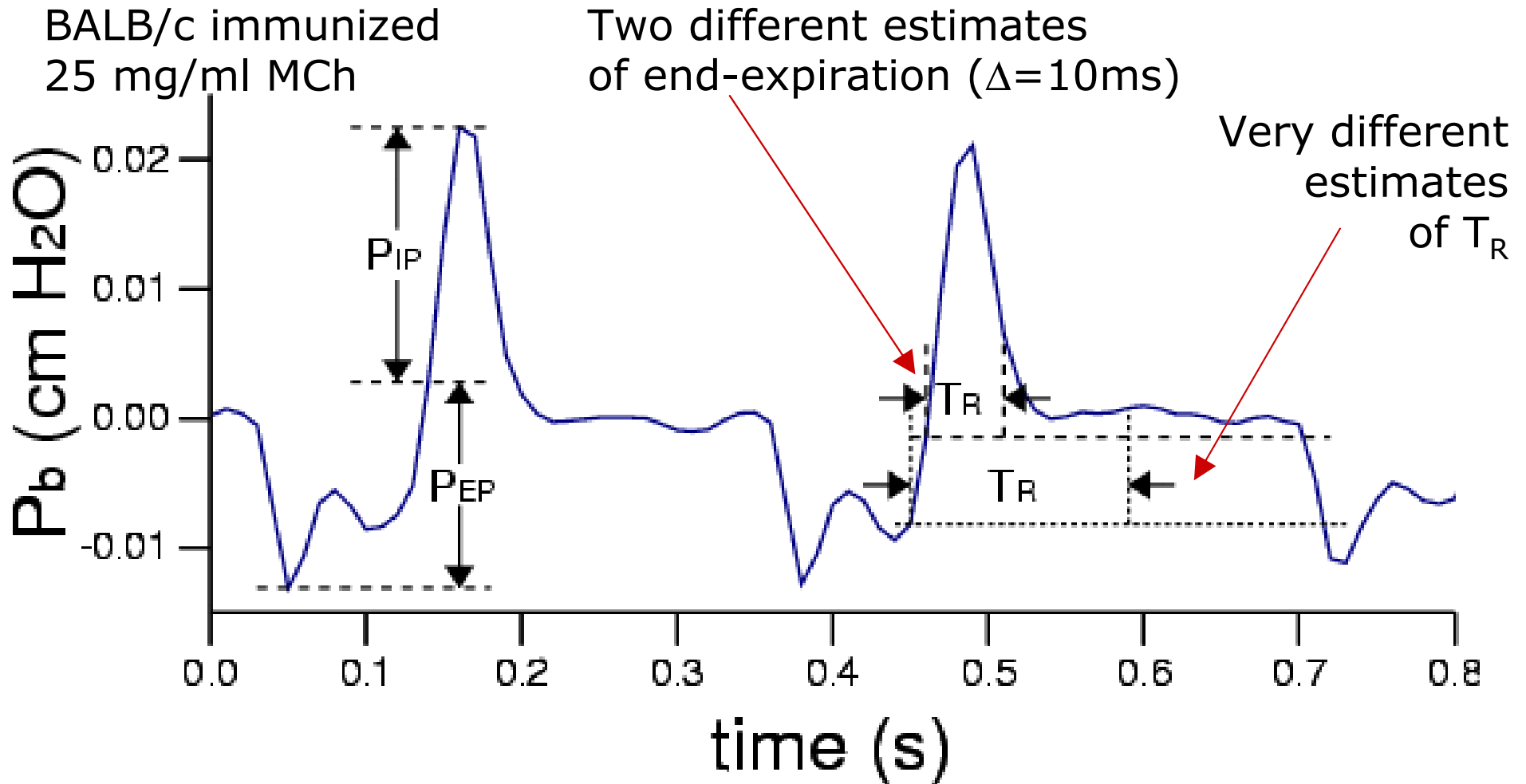
Plethysmography parameters

T_I T_E T_{Tot} T_I/T_{Tot} T_R
 P_I P_E P_{IF} P_{EF} V_T
Pause $Penh$ V_T/T_I V_T/T_{Tot} V_T/T_E

Invasive parameters

R_L C_L

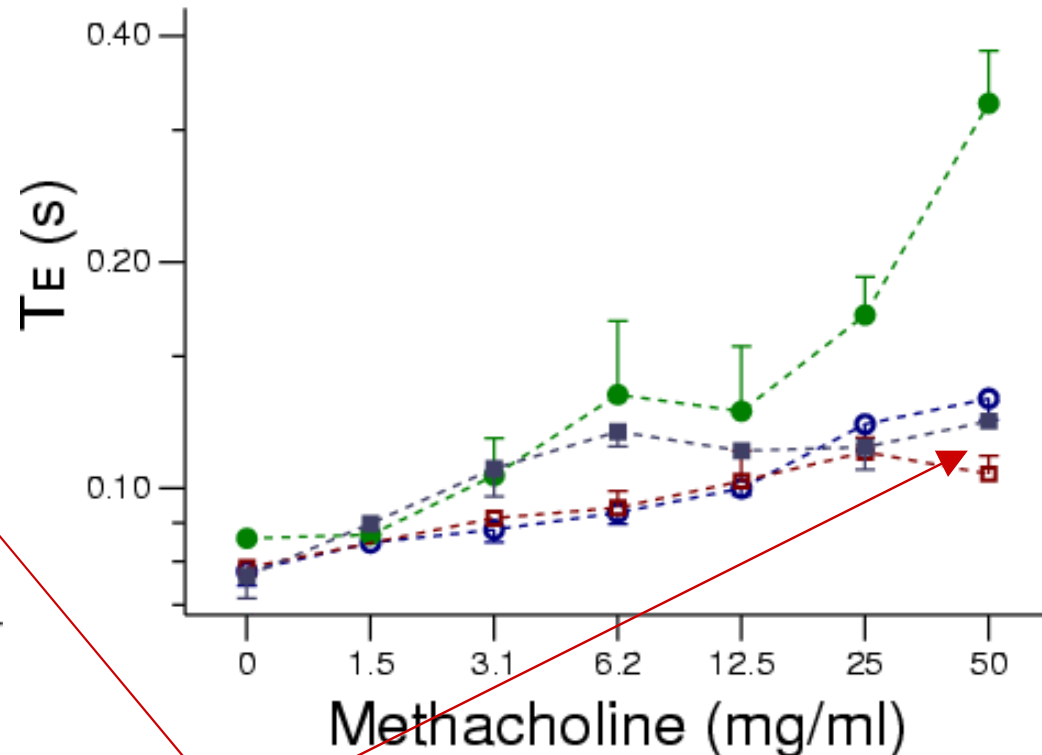
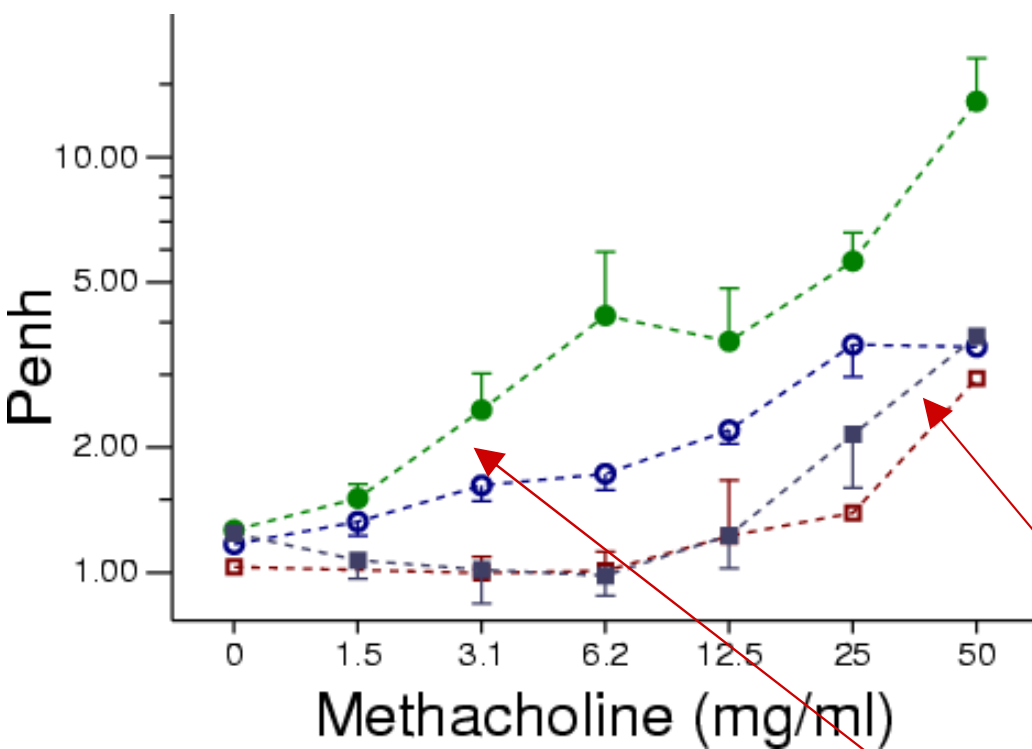
Box pressure



Parameters versus R_L

		BALB/c	C57BL6
	Pause	0.802	0.290
"Best" in BALB/c	Penh	0.809	0.288
	T_I	0.714	0.418
"Best" overall	T_E	0.745	0.703
	T_I/T_{Tot}	-0.283	-0.191
	P_{IP}	0.165	-0.385
Correlation coefficient (r)	P_{EP}	0.720	-0.038
	T_R	0.097	0.211
$r > 0.36$ is Significant at $p < .01$	V_T	0.671	-0.069
	V_T/T_E	-0.460	-0.397

Penh vs. T_E ("best" correlators in BALB/c)



BALB/c control —○—
BALB/c immun —●—
C57BL6 control —□—
C57BL6 immun —■—

Neither parameter distinguishes
C57BL6 treatment groups
Penh can distinguish BALB/c
Treatment groups at low dose

Discussion: *Penh* is

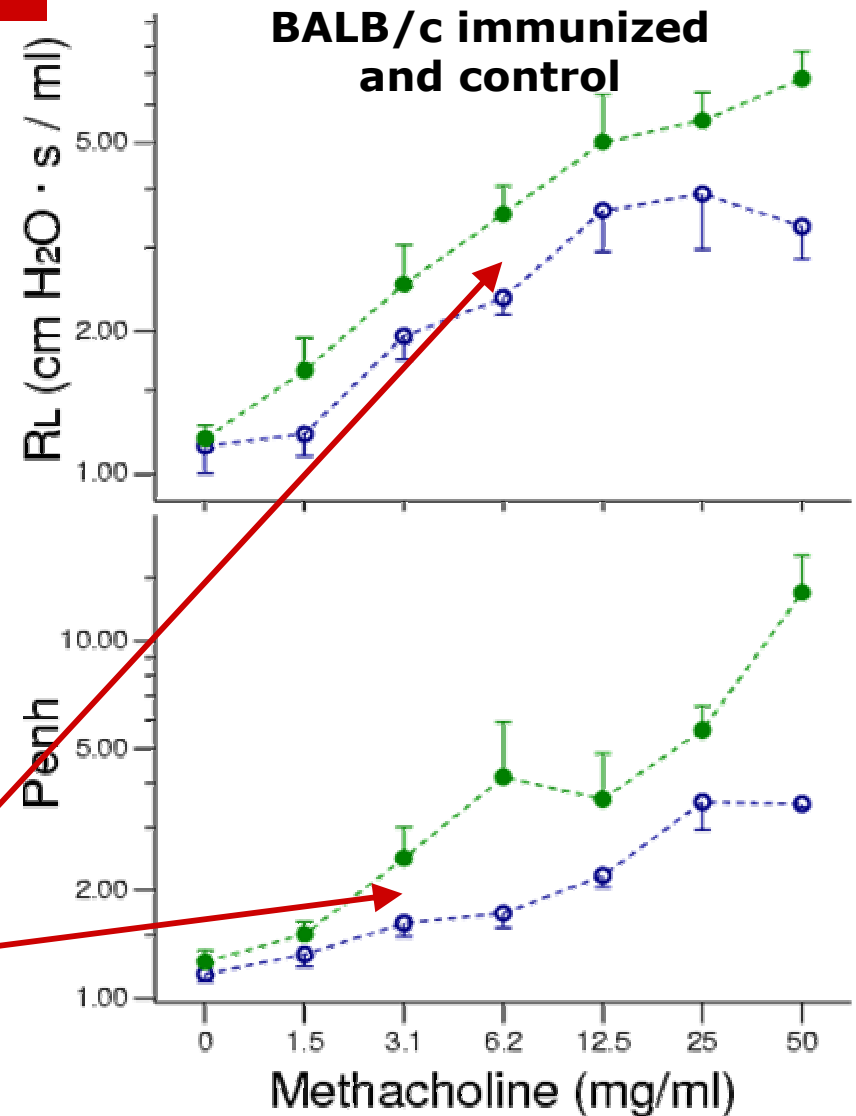
- Theoretically insensitive
 - Not “special”
 - no better than respiratory timing
 - Strain sensitive
 - no correlation in C57BL6
 - Numerically unstable
 - Sensitive to T_R calculation.
-

What is *penh* measuring?

Our hypothesis:
control of breathing

1. Penh separates treatment groups at concentration levels where there is no difference in mechanics.

First significant dose level



Is Penh measuring *control of breathing?*

2. Part of the breathing pattern response to agonists is due to reflex

- Dogs (*Phillipson, JAP, 1974*)
 - Sheep (*Wagner et al., JAP, 1999*)
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Is Penh measuring *control of breathing?*

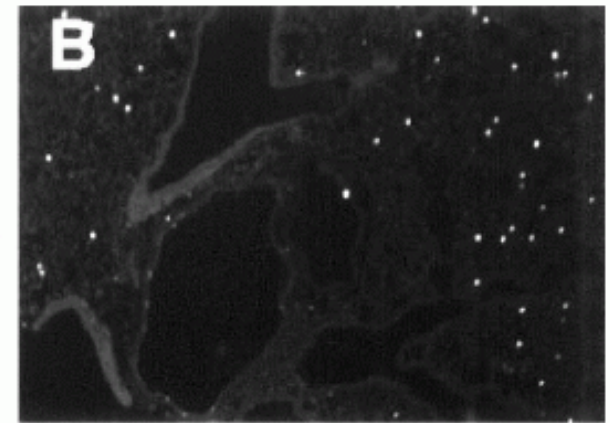
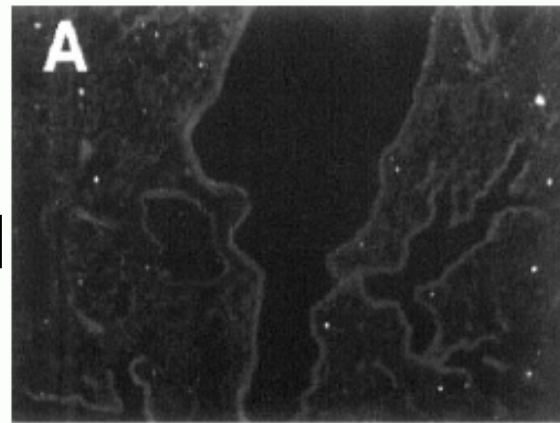
3. Relative performances correspond to known differences between strains
- BALB/c => longer, larger breaths
 - This is adaptive for an *airway* response
 - C57BL6 => change flow, small decrease in V_T
 - This is adaptive for a *tissue* response
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Strain differences

Non-treated

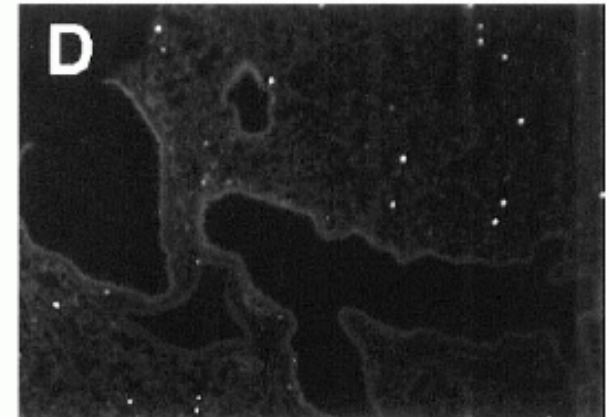
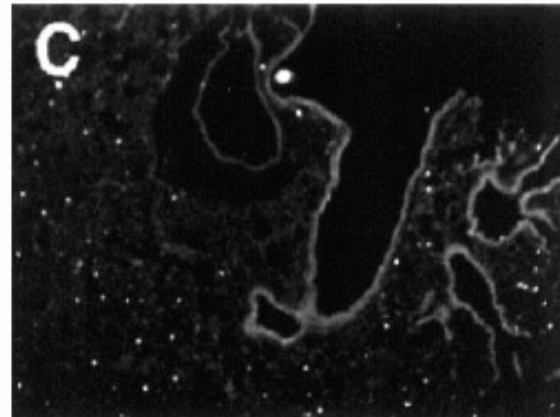
C57BL6

BALB/c



Localization of eosinophils in lung tissue.

sensitized



Takeda *et al.*,
Am. J. Physiol.,
281: L394-L402

sensitized and challenged

