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# *Dogging Sepsis*

Veterinarian Cynthia Otto:  
*Tracking Immune Response Gone Haywire*

Findings

Department of Health and Human Services  
National Institutes of Health  
National Institute of General Medical Sciences

# *Cynthia Otto Stalks Sepsis*

*Veterinarian Otto traces the cellular origins of sepsis.*



Photo: Sabina Louise Pierce

## *Sepsis*

- Is a full-body reaction to injury or illness
- Arises unpredictably
- May result from blasts of nitric oxide (NO)

*Question:*

Is NO always harmful to humans?

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# *Answer: No*

## NO is full of possibility

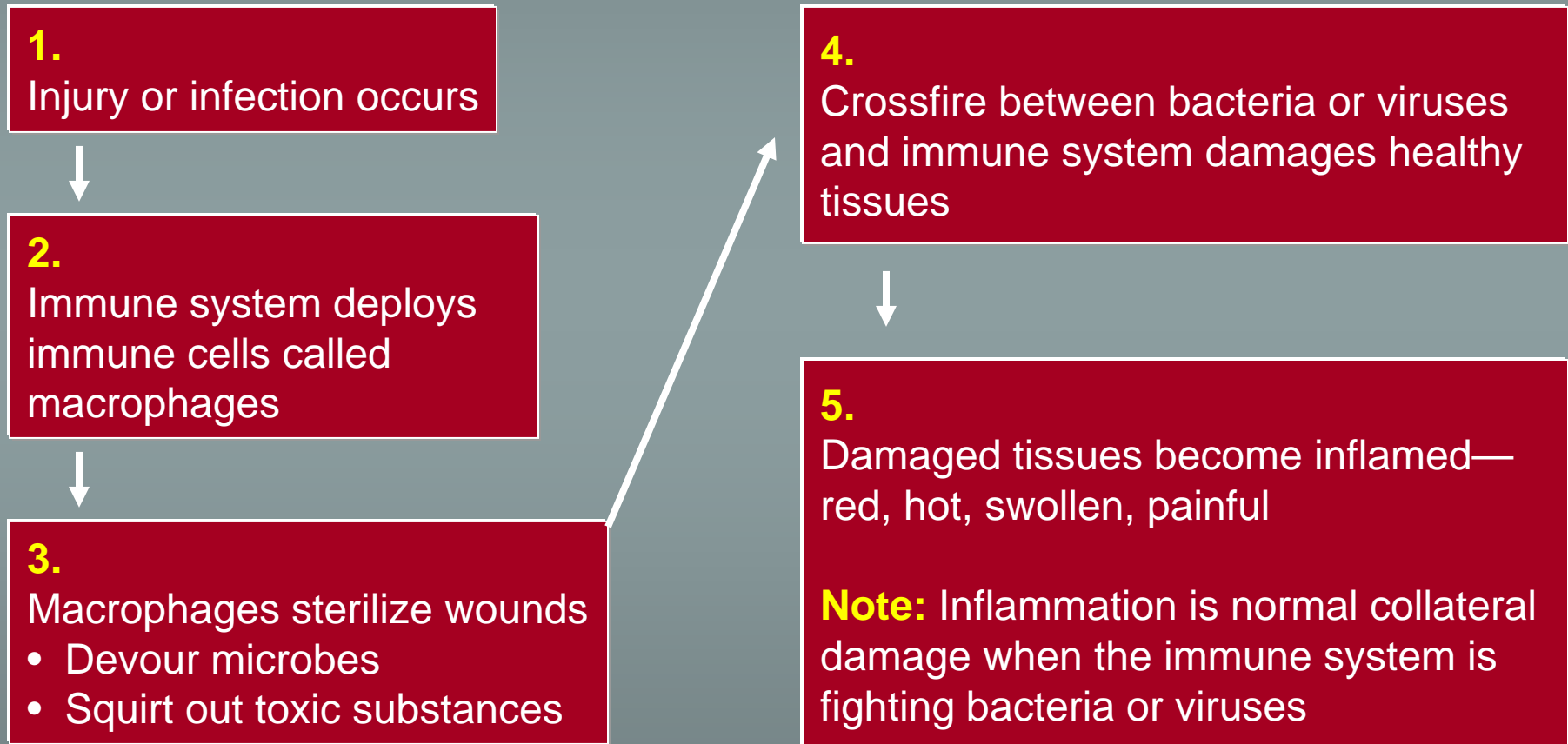
### Possible Beneficial Functions

- Helps regulate blood pressure by opening blood vessels
- Serves on the front line of defense against bacteria and other invaders

### Possible Harmful Functions

- Kills cells
- Inflames tissue
- Causes dangerous dip in blood pressure

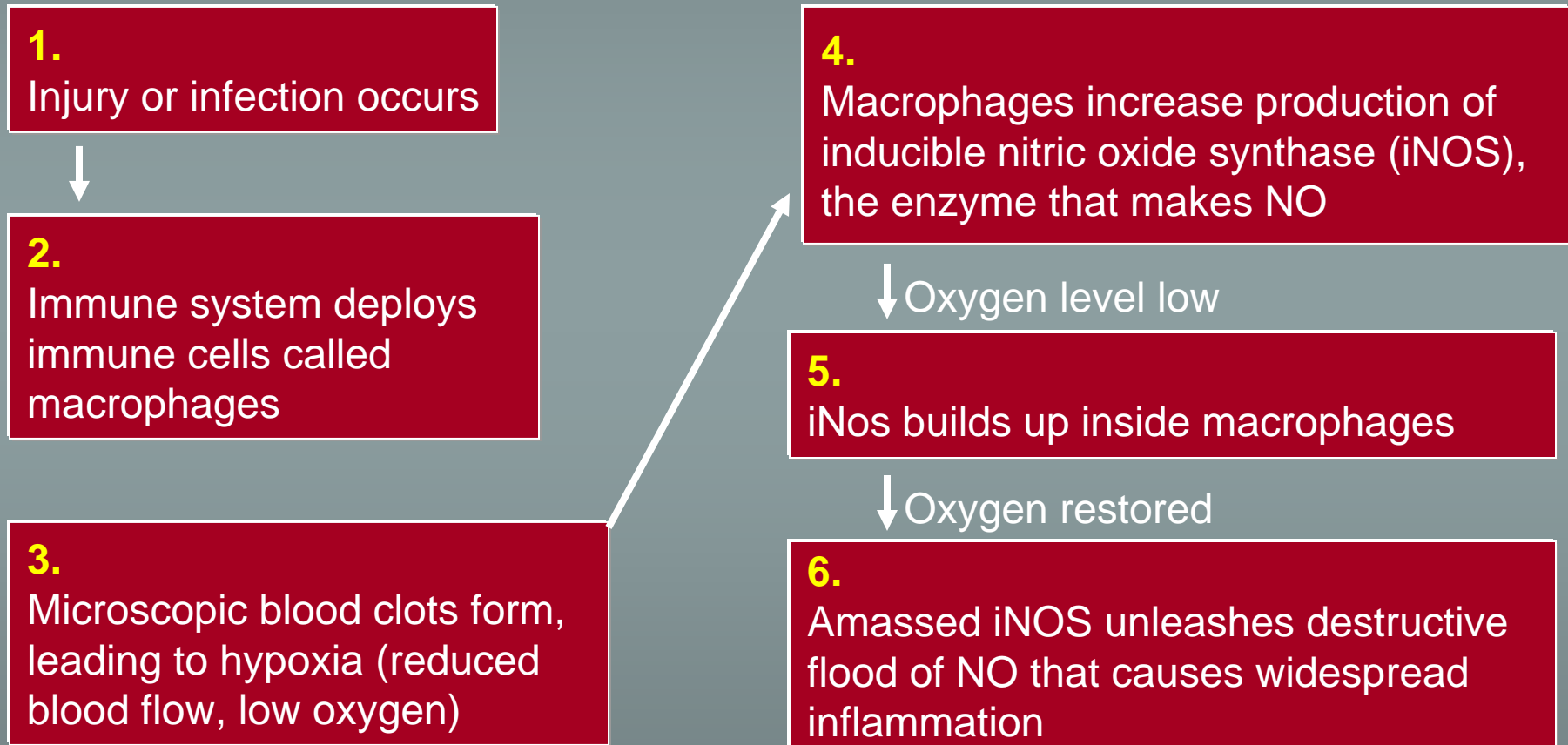
# Normal Immune Response



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# Haywire Immune Response: NO Way Out Hypothesis



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# Garage Gadget Tests Hypothesis

- FCCC system
  - Controls and measures the amount of oxygen that passes over cells
- Testing the link between hypoxia and NO production
  - FCCC delivers normal, low, or fluctuating levels of oxygen to cells
  - Researchers measure NO and iNOS levels in the cells
  - Results suggest intermittent hypoxia can cause inflammation

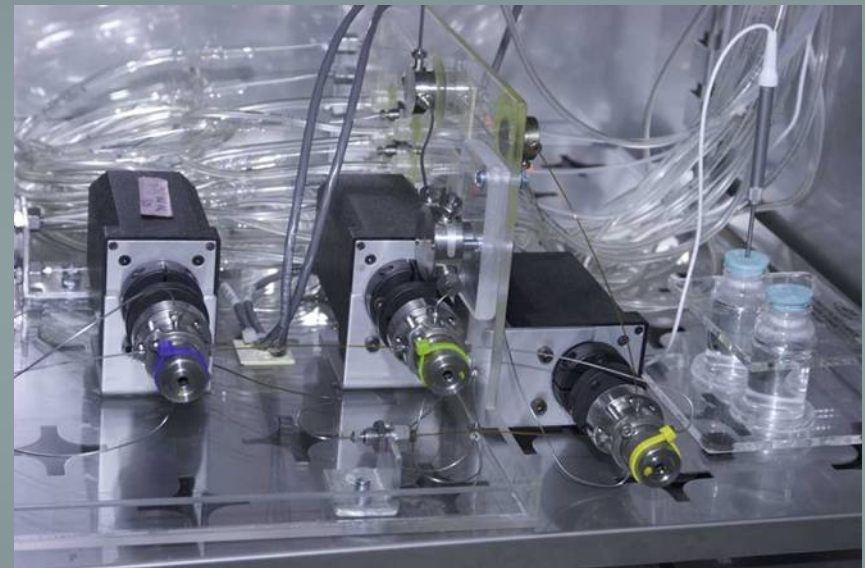


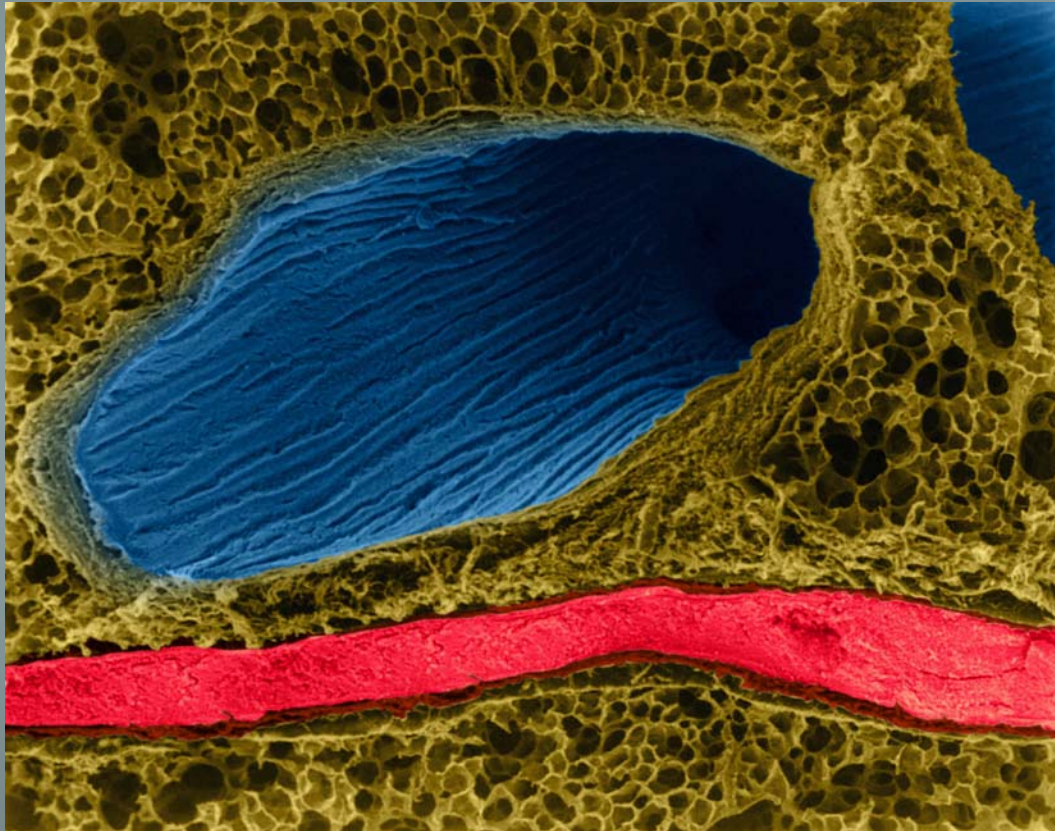
Photo: Alisa Zapp Machalek

Forced-convection cell-culture system  
(FCCC)

## Findings

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# Take a Breath



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When you breathe, oxygen travels

- Through branched passageways in your lungs (blue)
- Through alveoli (yellow)
- Into blood vessels (red)

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# *Battle to Breathe*

- Inhaled air fills alveoli in the lungs
- Injury or infection can rip, stretch, or irritate the delicate membrane around alveoli
- Flooded alveoli buckle under pressure



**What do alveoli do with the oxygen you breathe?**



**How does lung damage begin?**



**What happens when alveoli fill with watery fluid?**

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# *Animal Models for Human Conditions*



Photo: Chris Gregerson

*Patient in intensive care unit on a ventilator*

**Otto used anesthetized rabbits to study how ventilators affect alveoli in the collapsed lungs of humans**

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# Findings: Otto's Rabbit Experiment

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1. Oxygen levels fluctuated wildly in the ventilated, anesthetized rabbit.
2. The alveoli snapped open and closed with each pump of the ventilator.
3. The breathing machine could not maintain the inflated, semi-full structure typical of alveoli in healthy animals or people.
4. The continual stress of expanding and deflating alveoli appears to wear them out.
5. Ventilators may damage lungs by eroding their cellular fabric.

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# *Research Applications*

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How might Otto's research of hypoxia and ventilator-associated lung damage be applied to the care of patients who suffer trauma or severe infection?

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