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Does Inflammation Play a Role in the Development of Chronic Lung Disease?

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BRONCHOPULMONARY DYSPLASIA (BPD)

- ~7000 new cases each year in the US
- 10-15% will die in the first year
- Usually in premature infants suffering RDS
- Affects 40-70% of infants less than 1000 gm
- Annual cost ~US\$ 2.4 billion
- Multifactorial pathogenesis

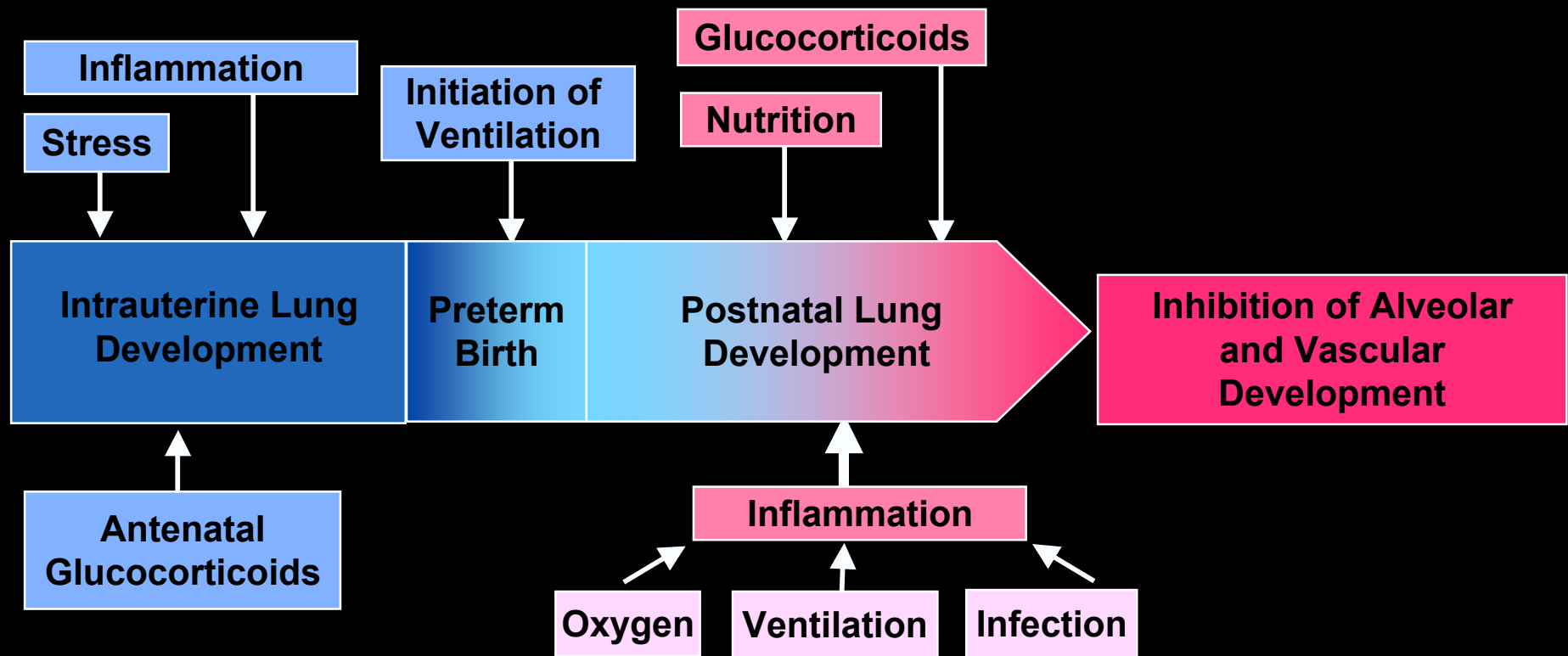
PATHOGENESIS OF BPD

- Genetic predisposition
- Immature lung structure
- Surfactant deficiency
- Barotrauma/Volutrauma
- Fluids/PDA
- Inflammation
- Infection
- Free radical damage
- Antioxidant deficiency
- Nutritional deficiencies

Mostly studied in rodent models of hyperoxia and large animal models of preterm birth and ventilation (sheep, baboon)

THE NEW BPD

Jobe: Pediatr Res 46(6):641-643, 1999



Modified from S. Guttentag

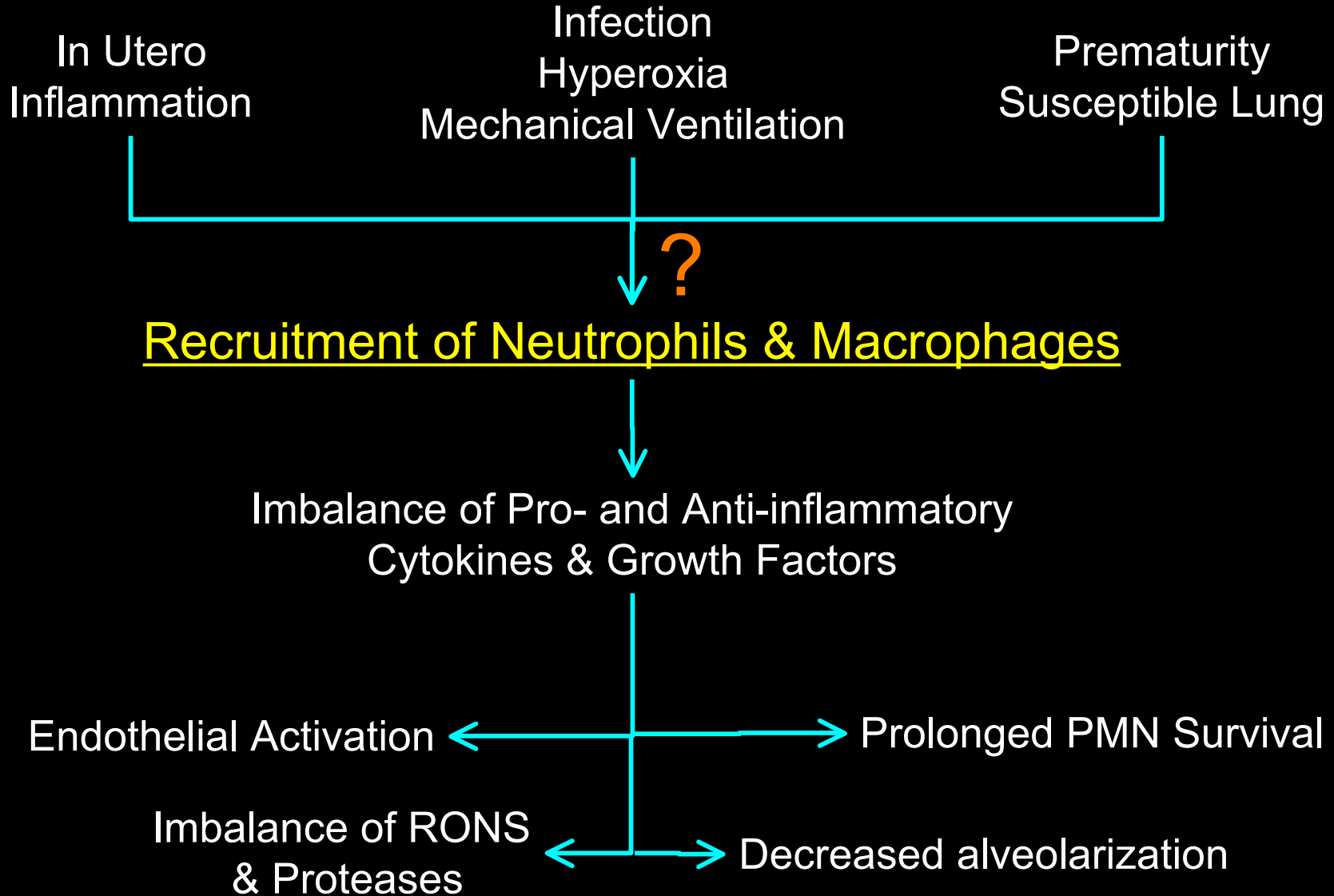
THE TISSUE RESPONSE TO INJURY

- **Acute lung injury**
 - cell damage
 - platelet adherence and degranulation
 - local release of growth factors
- **Inflammation**
 - Recruitment of neutrophils and macrophages
 - Further elaboration of pro-fibrotic growth factors
- **Granulation Tissue**
 - Fibroblast recruitment
 - Angiogenesis
 - Early ECM changes (fibronectin, hyaluronan)
- **Chronic ECM Modulation**
 - Collagen

EARLY BIOMARKERS ASSOCIATED WITH BPD

- Cytokines
 - IL-1 β , IL-6, TNF- α , TGF- β 1
 - IL-8
 - LTB4, PAF
 - PAF acetylhydrolase
 - PAF (plasma)
 - C5a
- Chemokines
 - sICAM, sE-Selectin
- Lipid Mediators
 - PMNs, Macs
 - Elastase/Protease Inhibitor
 - Laminin, Fibronectin
- Complement
- Adhesion molecules
- Inflammatory cells
- Proteolytic Enzymes
- Extracellular Matrix

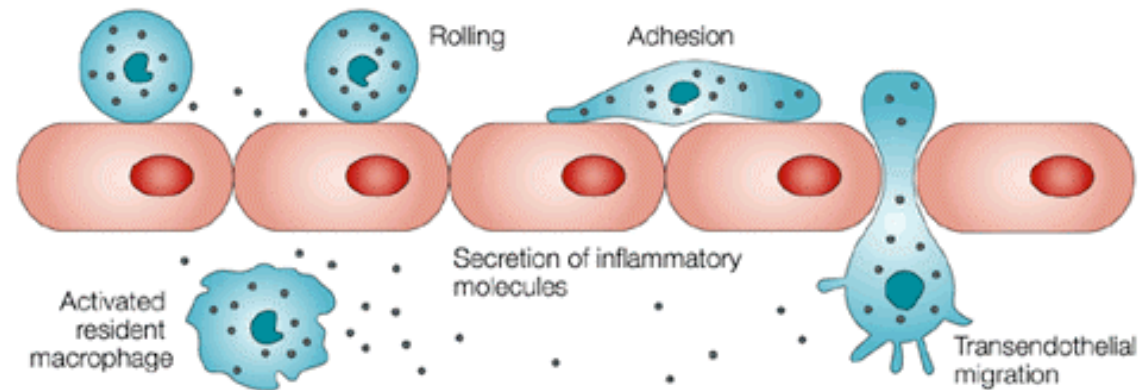
Modified from: Bose, Dammann and Laughon, 2008



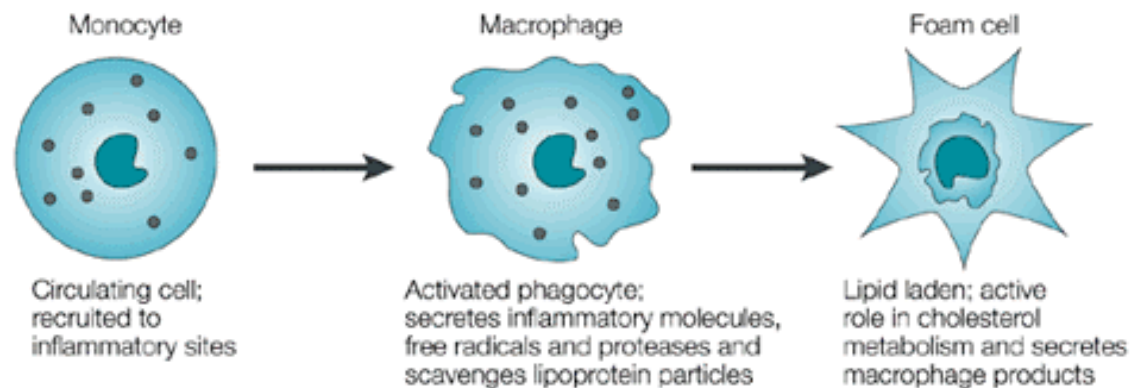
Modified from: Ryan, Ahmed, Lakshminrushima, 2008

Recruitment of Inflammatory Cells

b Monocyte adhesion and transendothelial migration



c Monocyte differentiation to macrophage and lipid-laden foam cell



Summary

- Inflammation is important in the lung response to injury
- Identification of the earliest changes that promote inflammation after injury will reveal targets for novel therapeutics

Thank you

Questions?