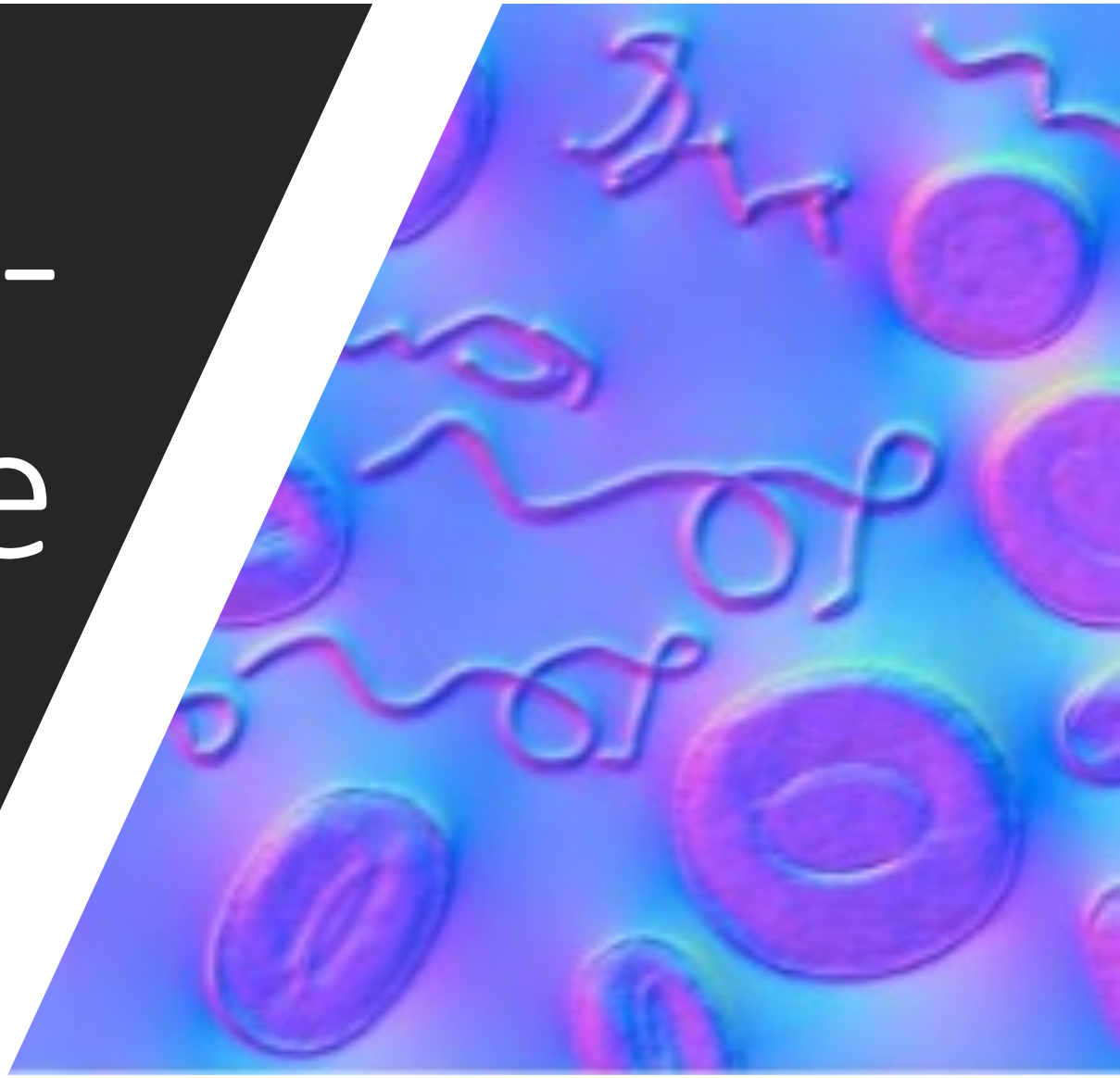
# Lyme Disease - Host Response

Catherine Gai



# Presentation Overview

- Mechanisms:
  - Host immune responses / components

  vs
  - Pathogen's evasion of the immune system

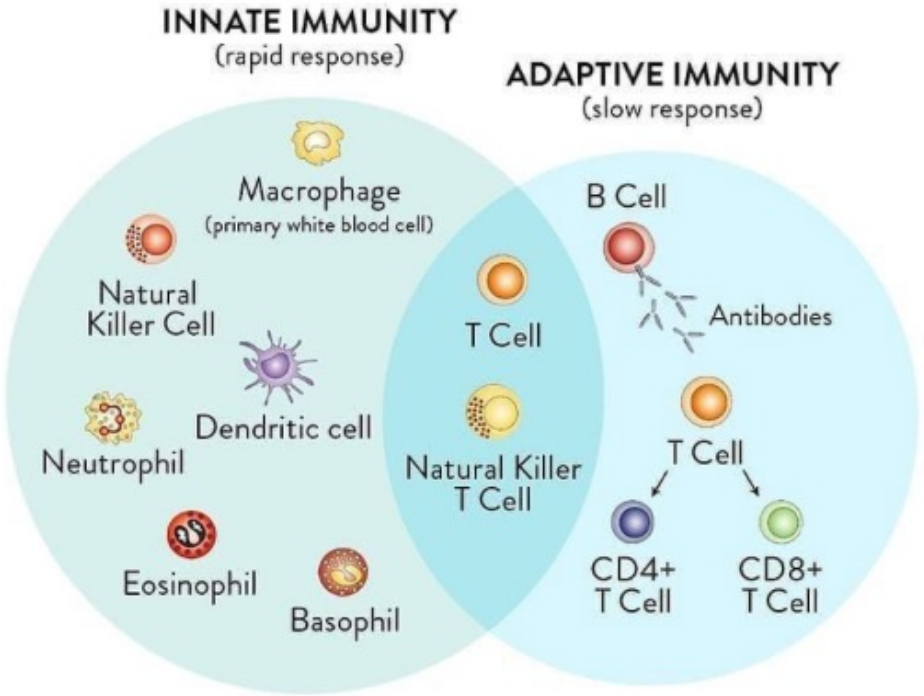
- Consequences of immune responses
  - Damages to the host

- Outcomes
  - Pathogen removal
  - Host recovery
  - Future immunity

# Host Immune Responses

VS

# Pathogen's Evasion Mechanisms

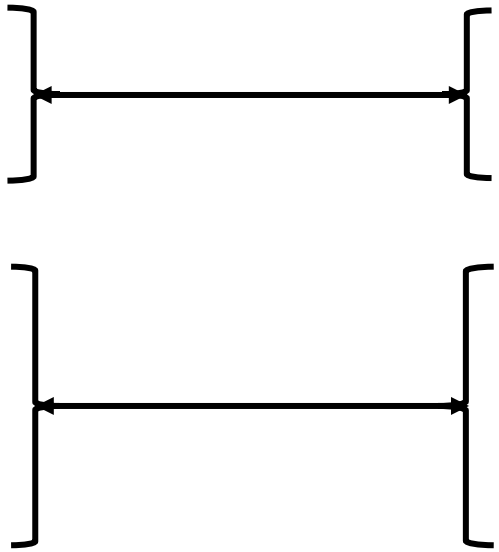


# Brief Overview

**Host**

**Immune Response**

- Innate response
  - Effector cells
  - Complement System
- Adaptive response
  - Cellular component
  - Humoral component



**Pathogen**

**Evasion of the Immune System**

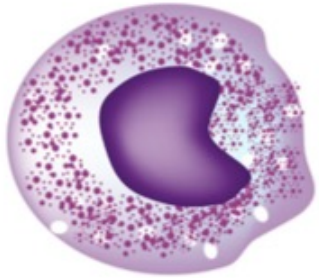
- Evading the innate response
  - Proteins from tick saliva
  - Virulence factors
- Evading the adaptive response
  - Immunosuppression
  - Colonization in tissues
  - Antigenic variation
- General mechanisms:
  - Genetic resistance
  - No iron requirement

# Innate Response vs Pathogen Evasion

**Host Innate Response**

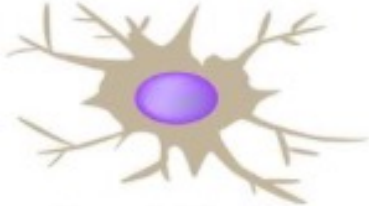
- Effector cells
  - Pathogen recognition via PRR - Phagocytosis - Antigen Presentation
    - Macrophages
    - Dendritic Cells
    - Neutrophils
    - Langerhans Cells
- Complement system / inflammatory process initiation
  - Cytokines
  - ROS
  - Antimicrobial peptides

Langerhans cell



Macrophage

Neutrophil



Dendritic cell

[5-10,14]

# Innate Response vs Pathogen Evasion

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    - Neutrophils
    - Langerhans Cells
- Complement system / inflammatory process initiation
  - Cytokines
  - ROS
  - Antimicrobial peptides

**Pathogen Evasion**

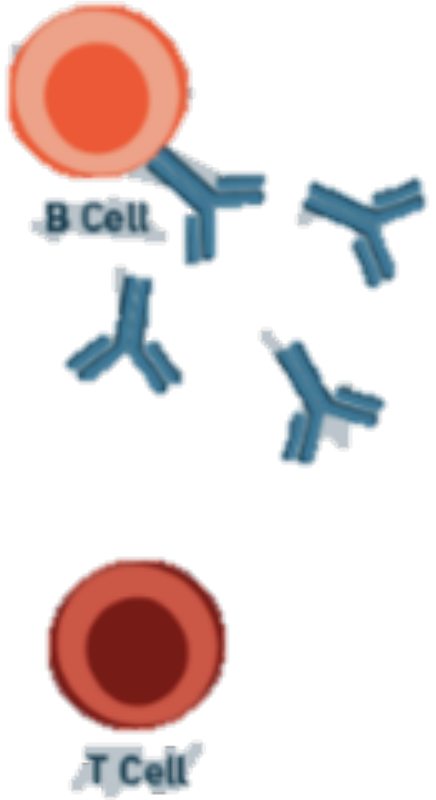
- Proteins from tick saliva
  - Interferes with complement system to avoid opsonization/phagocytosis – Salp 15
  - Upregulates anti-inflammatory IL-10
- Virulence factors
  - Inhibits the complement system via:
    - Direct binding - OspC
    - Proteolysis activity inhibition – BBK32
    - Recruitment of regulators to downregulate C4b – P43

[1-3,6-8,11,12]

# Adaptive Response vs Pathogen Evasion

**Host Adaptive Response**

- Cellular component
  - T cells are activated by antigen presenting cells, and differentiate into:
    - CD4 Tfh - aids germinal center formation, which is critical for B cell class switching and memory B cell formation
    - CD4 TH1 / CD4 TH17- make IFN-γ
    - CD8 cytotoxic T cells
- Humoral component
  - Circulating antibodies (IgM and IgG) that neutralize pathogen




[28,30,31]

# Adaptive Response vs Pathogen Evasion

## Host Adaptive Response

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## Pathogen Evasion

- Immunosuppression
  - Exploit IFN pathway – inhibit T-lymphocyte function
  - Inhibit germinal center formation – inhibit B-lymphocyte function
- Colonization in tissues
  - Breakdown connective tissue – BBK32
    - Entry into extracellular matrix – shielded from circulating antibodies
- Antigenic variation
  - Recombination of genes at the Vls locus to evade antibody response

[3,17,18]

# Immune Response vs Pathogen Evasion

**Host Immune Response**

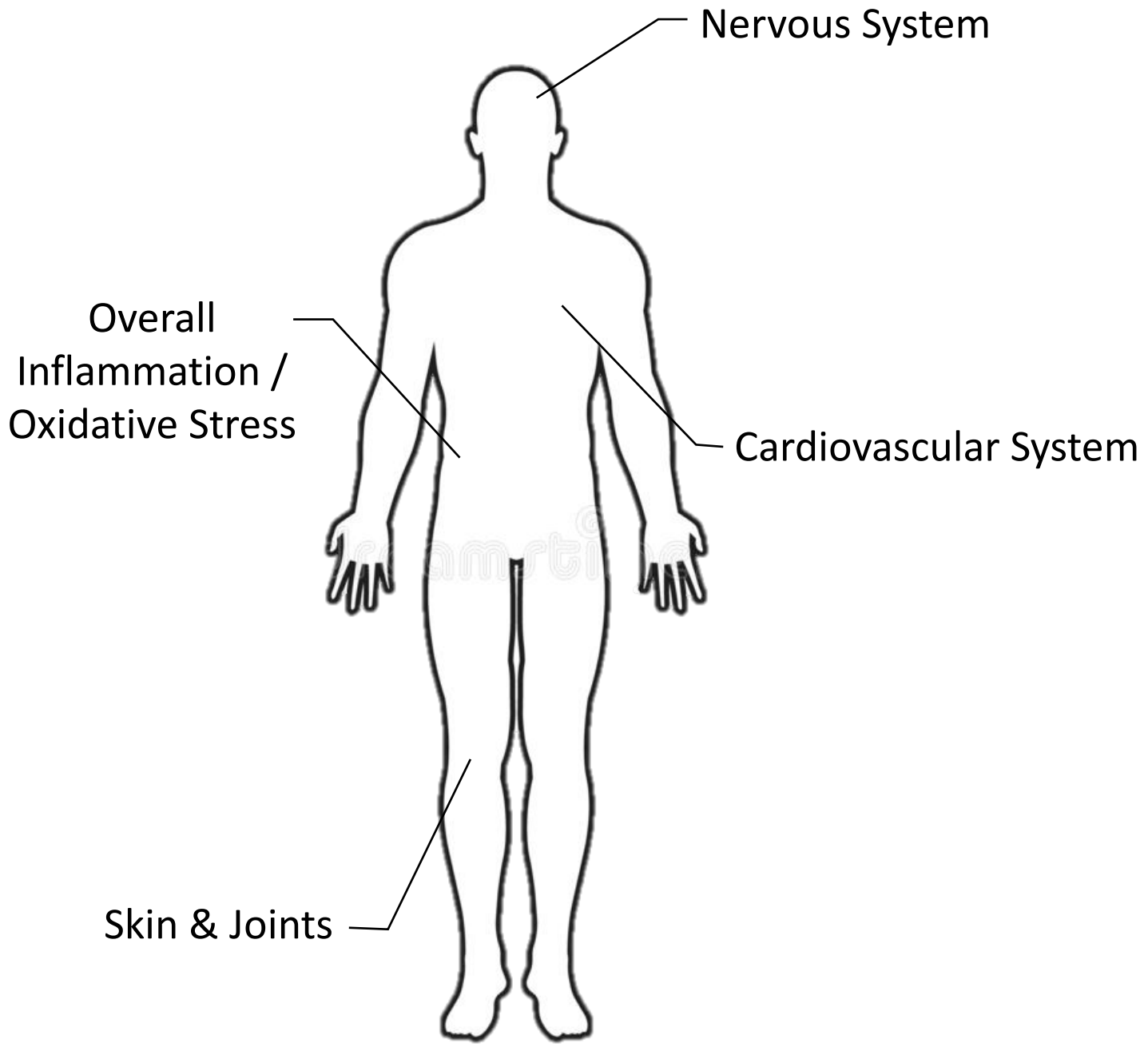
- Innate response
  - Effector cells
  - Complement System
- Adaptive response
  - Cellular component
  - Humoral component

**Pathogen Evasion**

- Genetic resistance
  - Resistance to ROS and RNS in 66 genes coding for proteins such as:
    - DNA repair enzyme
    - Transport protein
- No iron requirement
  - Resistance to lactoferrin, an antimicrobial protein

[2,7-10]

# Consequence of Immune Response: Damages to Host

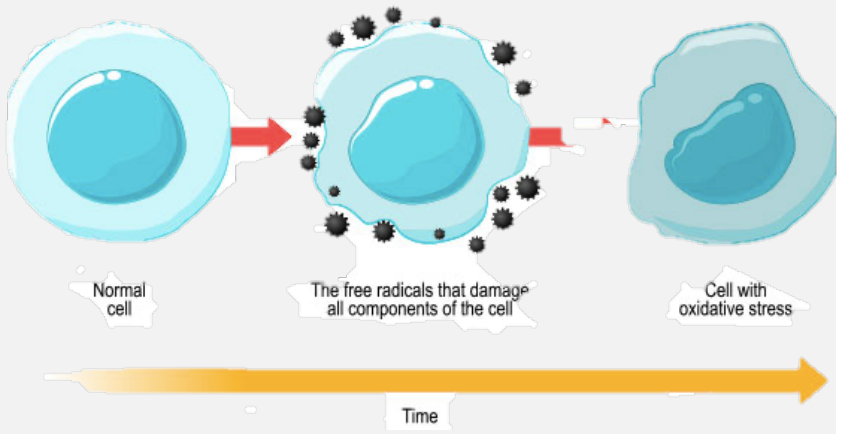


Chronic Inflammation:

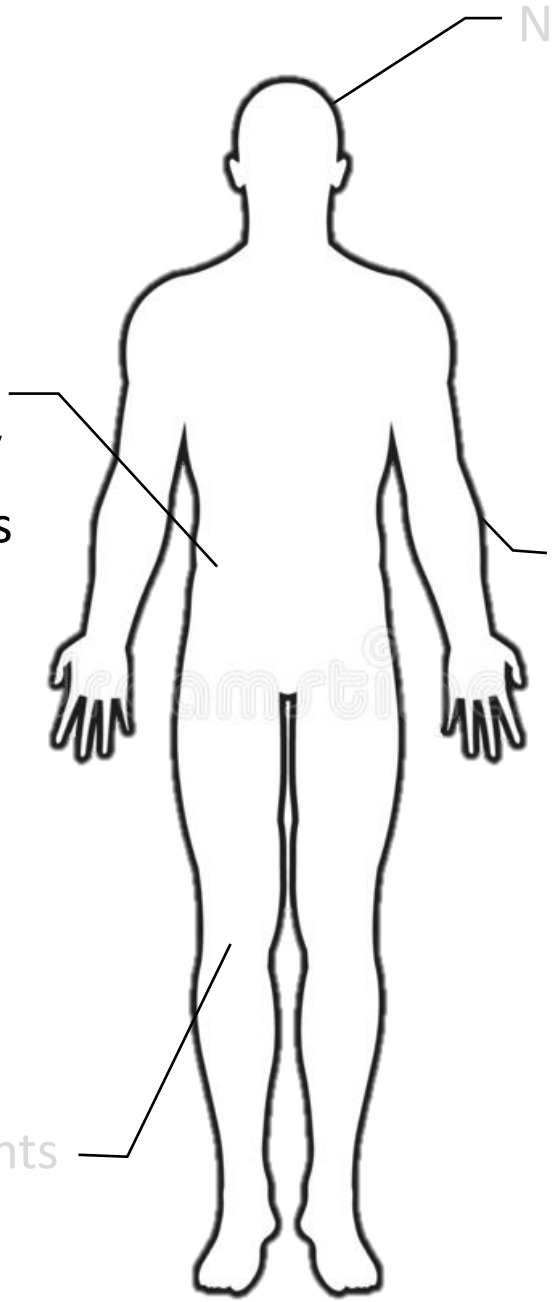
- Damages of host tissue due to increased chemokines, blood vessel permeability, and blood flow to the site of inflammation
- Risks of hypoferremia and anemia due to prolonged exposure to IL-6

Oxidative Stress

- Damages to host cell DNA / protein due to Reactive Oxygen Species made by infected endothelium cells and increased chemokines




Overall Inflammation / Oxidative Stress



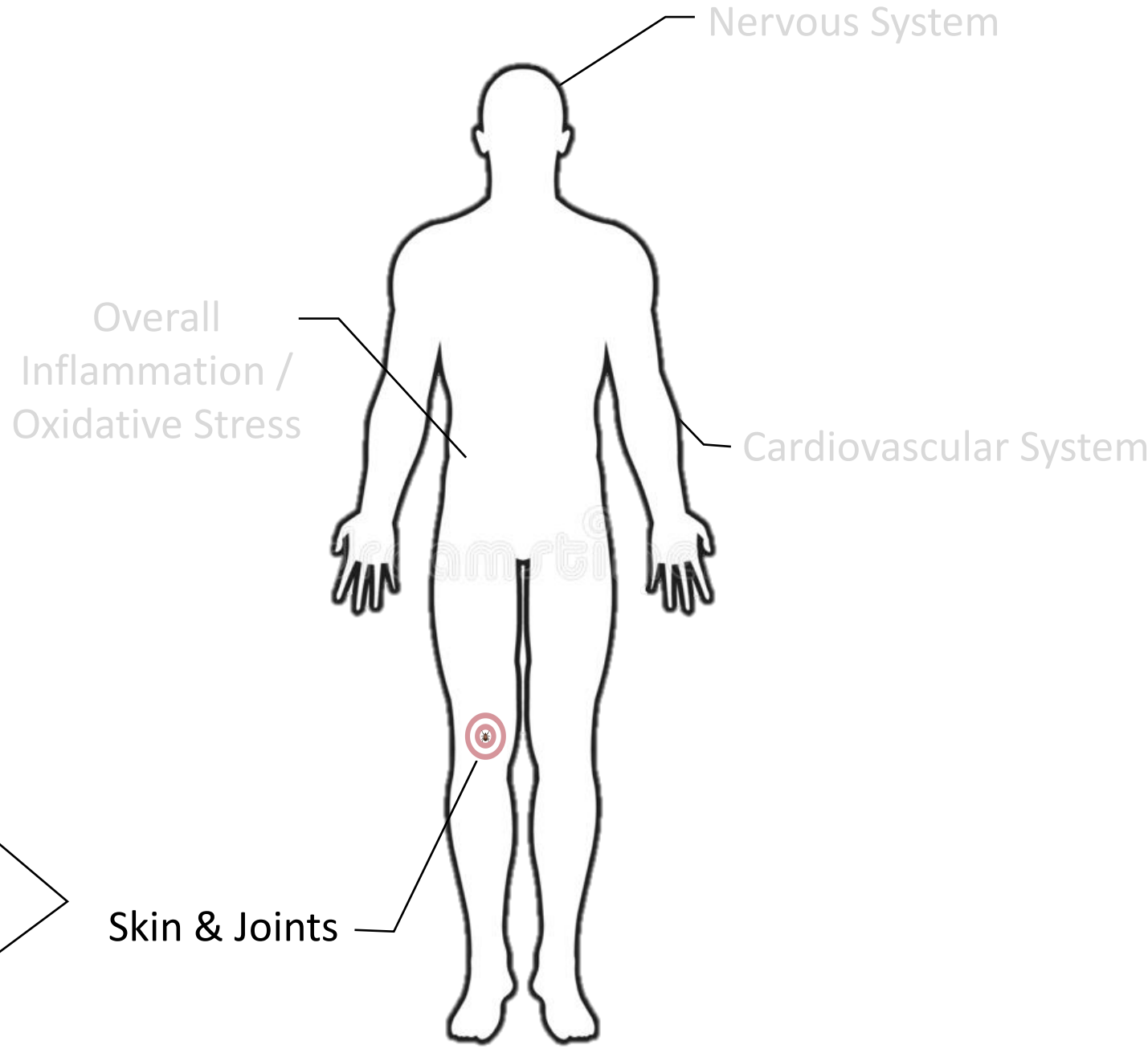

[5,6]

Skin

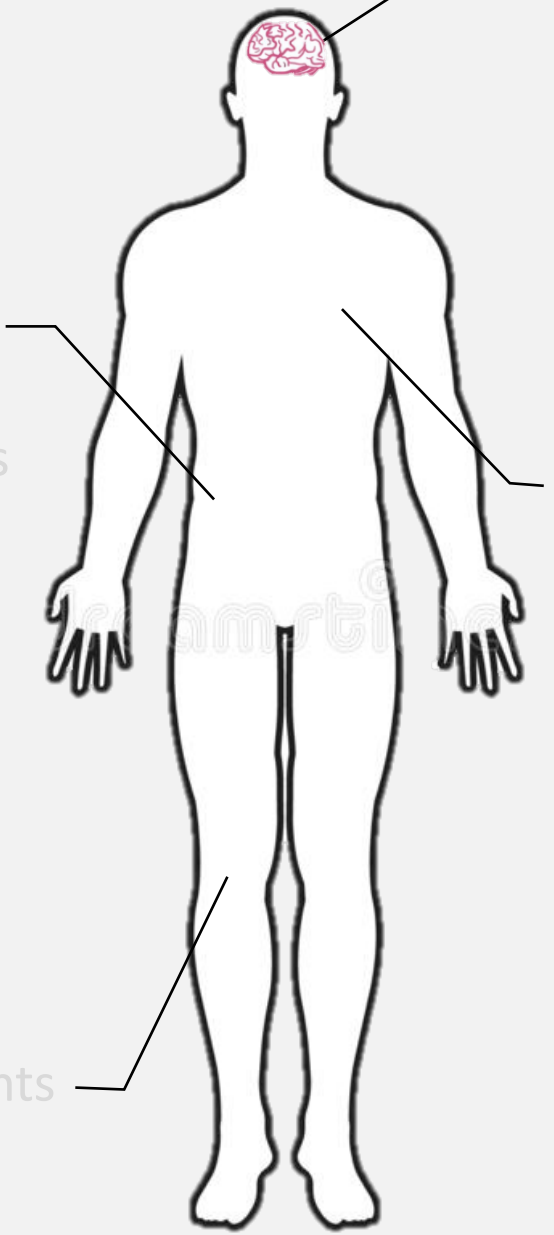
- Spotted / migrating rash due to increased blood flow to surrounding tissues and the recruitment of macrophages

Joints – Lyme Arthritis

- Swelling / pain in the knee, shoulder, ankle, elbow, wrist, etc., due to cytokine/ complement accumulation in the synovial fluid




[3, 18, 20-24]




Central Nervous System:

- Without treatment:
  - Classic Triad:
    - Lymphocytic meningitis
    - Radiculoneuritis
    - Cranial neuritis
  - Signs & Symptoms:
    - Slower thinking
    - Difficulty concentrating
    - Bell's palsy (episodes of facial muscle weakness or paralysis)
    - Headache
    - Numbness in limbs

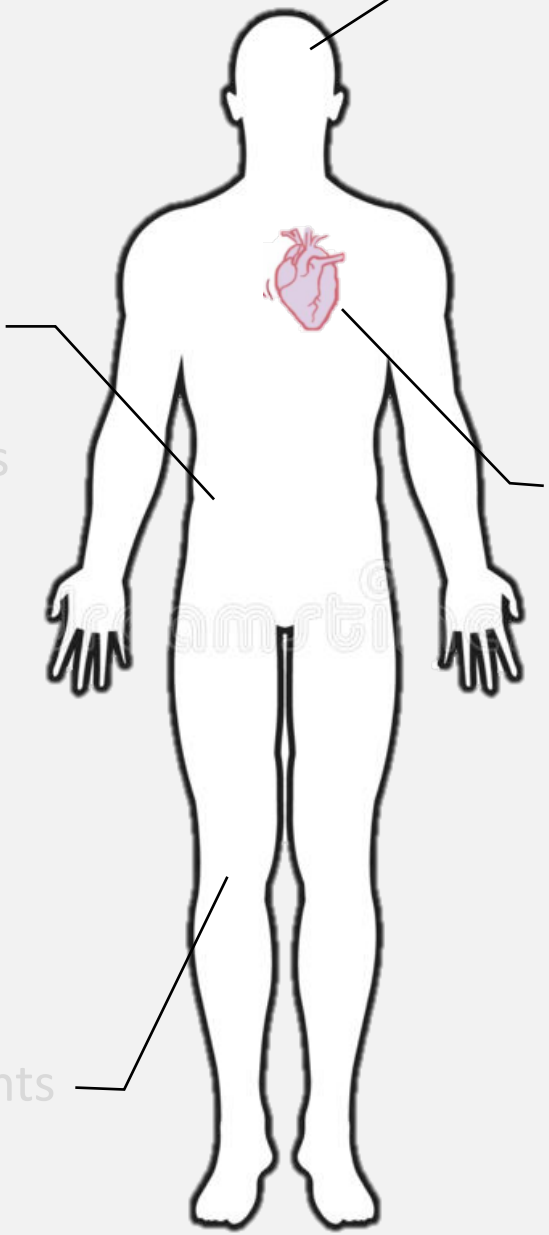
Central & Peripheral Nervous System:

- Lyme Neuroborreliosis

[7,8,13,14]

Nervous System

Overall Inflammation / Oxidative Stress



Cardiovascular System

Skin & Joints

Lyme Carditis:

- Inflammation of cardiac tissue due to pathogen infiltration
  - Disruption of normal cardiac electrical signaling and contraction coordination
- Signs & Symptoms:
  - Chest pain
  - Shortness of breath
  - Palpitation

[1,2,3,5,6]

# Outcome & Immunity

Bacteria clearance & Patient recovery

- With proper antibiotics (Doxycycline) treatment:
  - Complete B. burgdorferi clearance
  - Complete patient recovery within 2-4 weeks in the majority of cases
  - In rare situations, patients develop Post-Lyme Disease Syndrome, a condition that lasts 6+ months post-treatment:
    - Signs & Symptoms:
      - Arthritis
      - Cognitive dysfunction
      - Fatigue
    - Pathogenesis is unclear

Future immunity

- Strain-specific immunity in most cases
  - However, it is not guaranteed, due to:
    - B. burgdorferi antigenic variations
    - Lack of memory B cell formation, as a result of host's inability to form sustained germinal centers

[1,2,5,10]

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