

## Amphibian Immunology

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## Vertebrate Immunology

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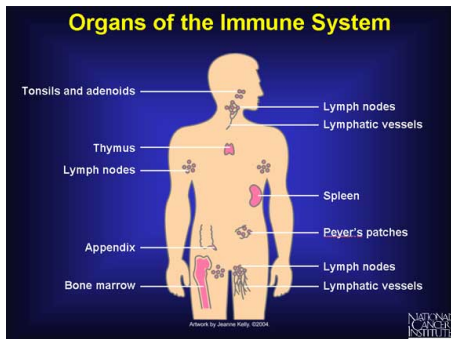
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## Lymphoid Organs



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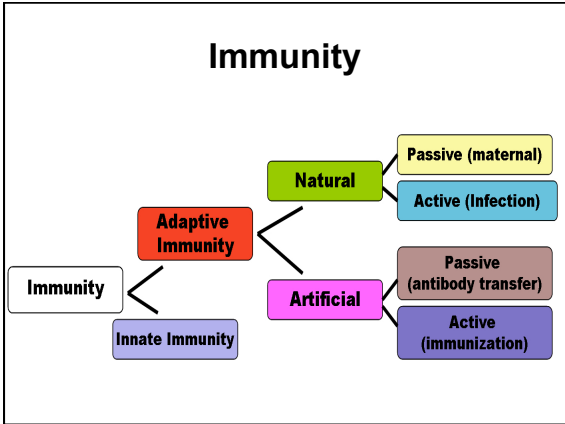
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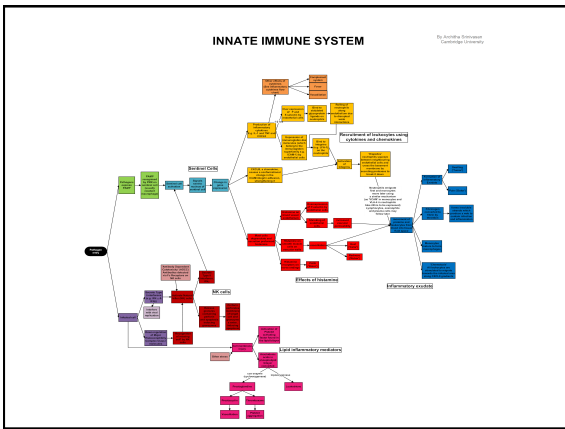
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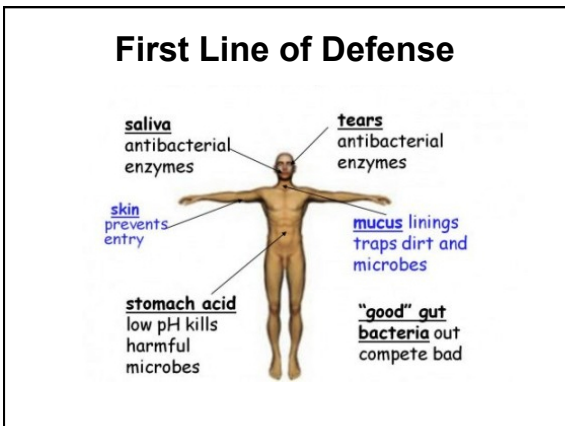
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## Innate Immunity: Terminology

- **Antigen:** something foreign or toxic to the cell or body
- **Macrophages:** "Big-eater"
  - role is to phagocytose
  - stimulate lymphocytes
  - attach foreign substances, infectious microbes, and cancer cells
- **Dendritic Cells:** Process antigen and present it to cell surface of T cells of the immune system
  - Messengers between innate and adaptive
- **Natural Killer Cells:** Cytotoxic lymphocyte
  - rapid response
  - release cytokines (signals and chemicals)

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## Innate Immunity: Terminology

- **Pattern Recognition Receptors**
  - primitive part of the immune system
  - found on host cell surface
  - recognize pathogen-associated molecular patterns
- **Pathogen-associated Molecular Patterns (PAMPs)**
  - molecules associated with groups of pathogens
  - activate immune responses
- **Antimicrobial and serum proteins**
  - potent, broad spectrum antibiotics
  - enhance immunity

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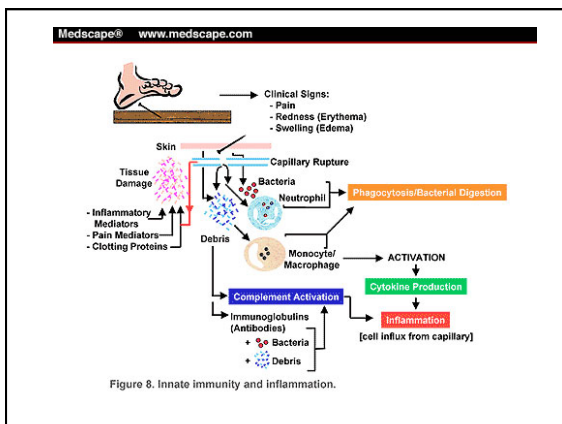
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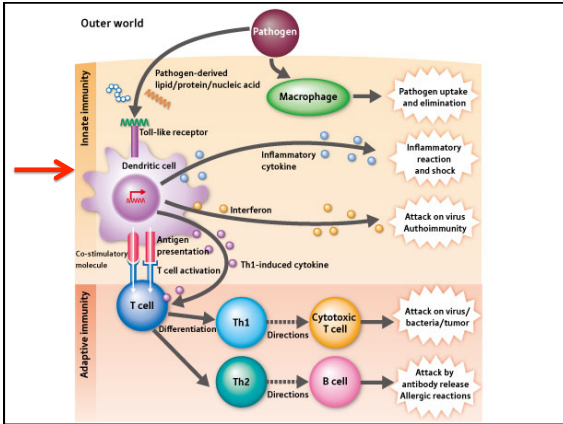
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### Innate Immunity Summary

- **Non-specific** defense mechanisms
- Immediately or within hours of antigen appearance
- Physical barriers, chemicals in the blood, immune system cells
- Activated by chemical properties of the antigen (PAMPs)

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### Adaptive Immunity

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### Adaptive Immunity: Terminology

- T cells (mature in Thymus)
  - T<sub>C</sub>
  - T<sub>H1</sub>
  - T<sub>H2</sub>
- Major Histocompatibility Complex Proteins (Found on Host Cells)
- Antigen presenting cell
- B cells (produced in the bone marrow)
- Antibody

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### T cells

- Type of lymphocyte
- Matures in the thymus
- **CD4 T cells**-Helper T cells
  - T<sub>H1</sub>: promote macrophage activation and cytotoxic T cell proliferation
  - T<sub>H2</sub>: Evoke strong antibody response
- **CD8 T cells**-Cytotoxic T cells
  - kills infected/dysfunctional cells

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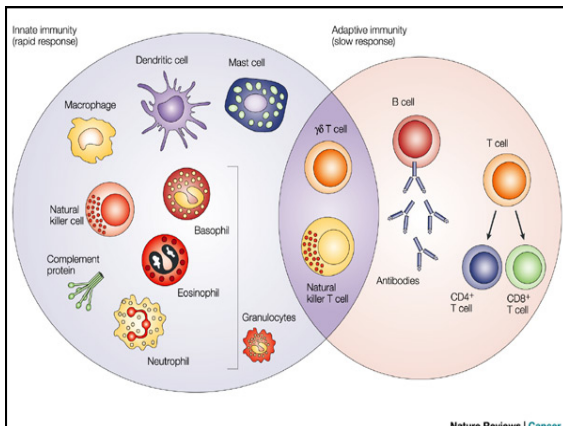
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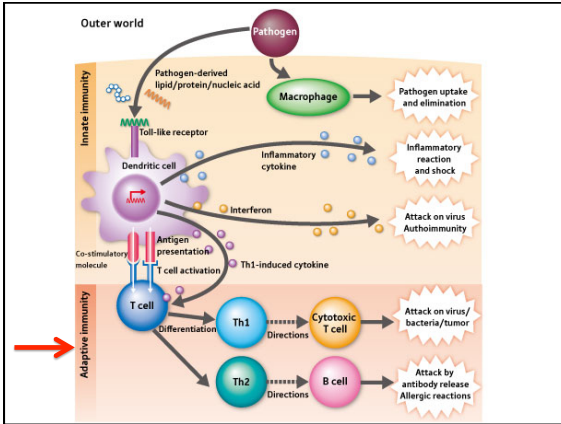
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### Major Histocompatibility Complex

- Series of genes that code for cell surface proteins controlling the adaptive immune response.
- Class I MHC contains three genes; proteins from these genes are expressed on almost all cells.
- Class II MHC genes contain 3 genes whose proteins are expressed on antigen-presenting macrophages, dendritic cells and B cells.

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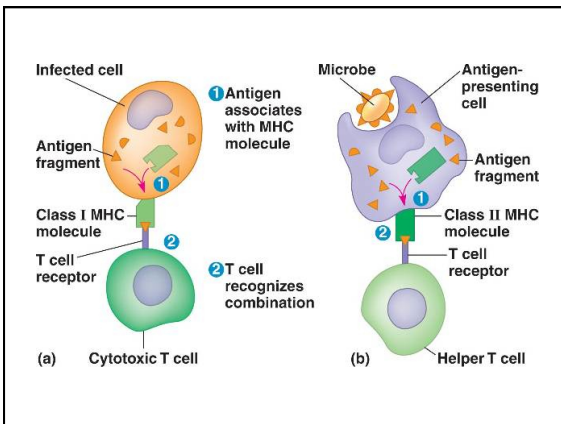
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## Antigen Presenting Cell (APCs)

- Cell that displays foreign antigens complexed with MHCs on their surfaces (called antigen presentation)
- T cells recognize using their T-cell receptors (TCRs).
- Most cells in the body can present antigen to CD8<sup>+</sup> (cytotoxic) T cells via MHC class I molecules and act as APCs
- Term is often limited to specialized cells (macrophages, dendritic cells and B cells) that generally express MHC class I and II and stimulate CD4<sup>+</sup> (Helper) and CD8<sup>+</sup> (cytotoxic) T cells

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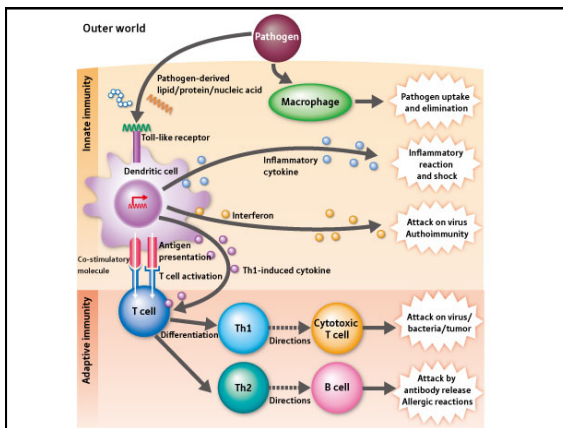
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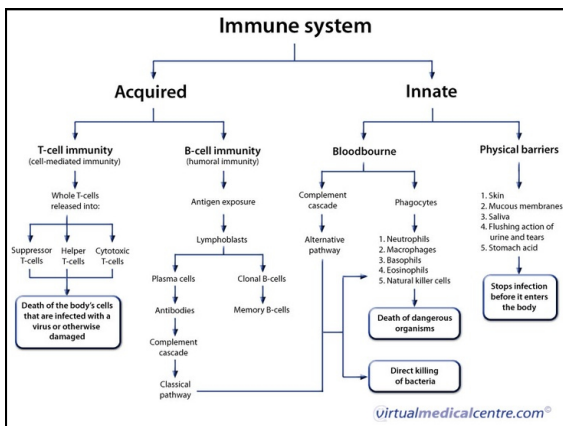
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### B cells

- Formed in the bone marrow
- Has B cell receptor protein that allows B cell binding to specific antigen
- Makes antibodies
- Develops into memory cells

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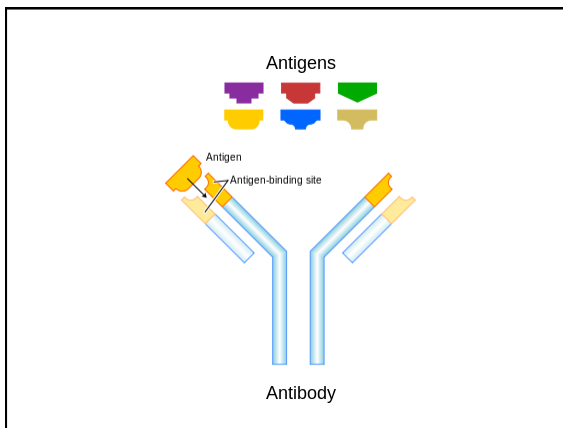
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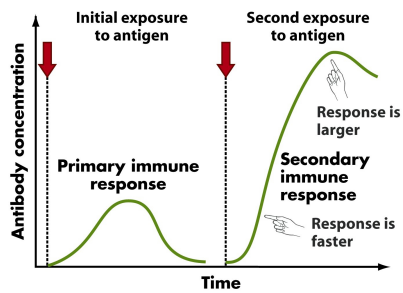
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### Memory



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### Active Immune Response Summary

- **Antigen specific** immune response
- More complex than innate
- Antigen must first be processed and recognized
- Once recognized, specific cells attack specific antigen
- Also includes memory

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### Tolerance

- Ability to discriminate self versus non-self
  - prevents over reactivity to environmental stimuli (allergens, normal microbes, etc)
  - Important for fetus, organ transplants, skin grafts

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### Amphibian Immunity

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### Xenopus



- Connecting taxon that links ancient vertebrates and mammals
- Comparative model of choice for immunological studies
- Little is known of other amphibians

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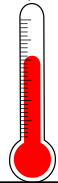
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### Great Model



Southern Leopard Frog Eggs



Adult



A  
B  
C

*x. tropicalis*      *X. laevis*

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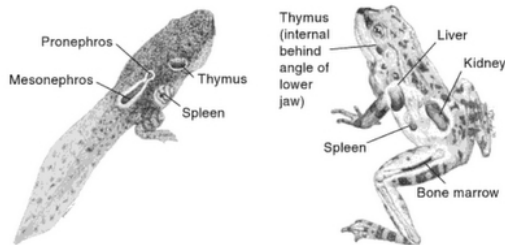
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### Differences between developmental stages



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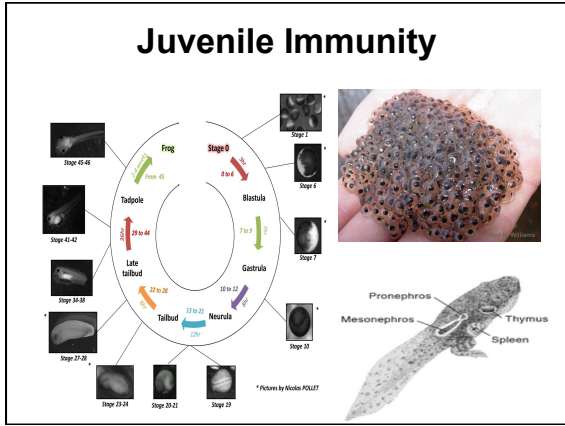
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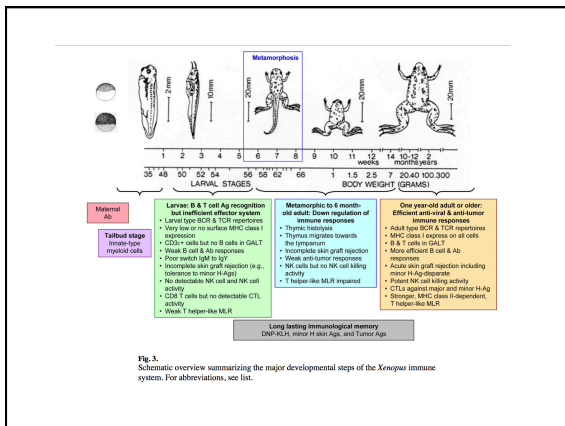
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Summary of the Main Developmental Steps of the *Xenopus* Immune System

Devel. stages (days)	Liver	Thymus	Spleen	GALT
40 (d3)		Thymic epithelium buds from 2nd visceral pouch	Absent	Few scattered CD3 <sup>+</sup> Expressing leukocytes
46 (d4)	Lymphopoiesis in peripheral layer, Ig Gland anlage, TCRB, RAG, AID	Epithelium, no precursors	Spleen anlage, mesenchymal thickening in the mesogastrium	No B cells
47 (d4-5)	Lymphopoiesis, and B cell development in absence of Ag	Colonization by lymphopoietic precursors from post-MB (<100 cells)	Blood cells (No lymphopoiesis)	
48 (d6-7)		Cortex anastomosis, full TCRB mRNA, CD3 <sup>+</sup> CD8 <sup>+</sup> Thymic class II <sup>+</sup> epithelial cells		
49 (d10-13)	IgL rearrangements	Fine CTX <sup>+</sup> thymocyte, more CD8 <sup>+</sup>	Spleen B cells (~200) and 1 <sup>st</sup> detect Ab responses	
50 (d15)		Ongoing thymocyte differentiation (2x10 <sup>6</sup> cells)		
56 (d30)		Ongoing thymocyte differentiation (9x10 <sup>6</sup> cells)	Detectable T cell responses	
58 (d44)		Max. size of the thymus (1-2x10 <sup>6</sup> cells)	Max. larval T cell response (1 x 10 <sup>6</sup> cells)	
Adult (>d60)	Adult-type leukocytes	Thymus moves near thymus New adult-type thymocyte differentiation	Adult T cell responses (1-2 x 10 <sup>6</sup> cells)	
Adult (> 1 yr)		Thymus progressively filled by fat tissues	(1-2 x 10 <sup>6</sup> cells)	Many IgM <sup>+</sup> and IgX <sup>+</sup> B cells, as well as T cells (CD8 <sup>+</sup> and CD8 <sup>-</sup> )



**Larval Immunology**

- Competent Innate Immune System
- Weak Adaptive Immune System
  - Small amount of T cells and B cells in larvae
  - NK cells only right before metamorphosis

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**Immune Remodeling During Metamorphosis**

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**What is going on during Metamorphosis?**

- Tadpoles are free-living so must be protected against potential pathogens
- During metamorphosis, they acquire adult specific molecules
- Must show tolerance to new self molecules
- T cell function becomes impaired
- Express different antibody repertoire
- Lessening of skin graft tolerance
- The appearance of MHC class I antigens
- Persistence of immunological memory

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## Adult Immunology

- Immune system becomes complete 2-3 weeks after metamorphosis
- Strong Innate and adaptive immune responses
  - Antimicrobial peptides
  - NK cells
  - Complement
- Adaptive Immune system similar to other mammals
  - Except B cells differentiate mostly in the liver and spleen (instead of bone marrow)

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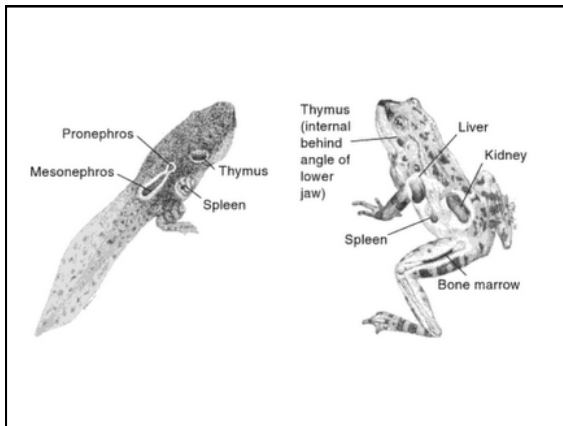
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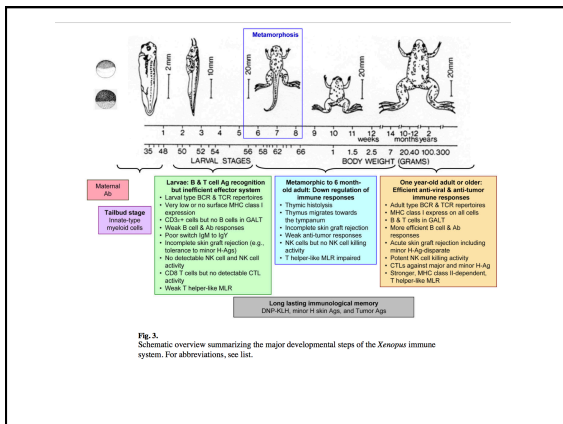


Fig. 3. Schematic overview summarizing the major developmental steps of the *Xenopus* immune system. For abbreviations, see list.

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**Temperature and Immune Status**

- Helminth clearance is slower at 15°C than 25°C
- Skin grafts are rejected faster at 27°C than at 21°C
- These and other data suggest selective inhibitory effect of low temperature on T-cell function

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**Other modulators of immune response**

- Temperature
- UV
- pH
- Predators
- Man-made modulators
- Psychosocial factors
- Xenobiotics

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**Susceptibility of amphibians to infectious diseases**

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**Review of what you just learned**

- First defenses of pathogens through the skin and digestive tract are anti-microbial peptides
- Pathogens are killed by chemical cascades (complement) and/or macrophages
- Adaptive immune response requires time to activate in the presence of antigen
  - highly specific
  - generation of memory cells

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**Increases in Susceptibility not simply due to poor immunity**

- Exposure to new, highly virulent pathogens
- New pathogens are immunosuppressive
- Pathogen "bloom"
- Stress response
- Environmental contaminants

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