BIOL 4160H Immunology

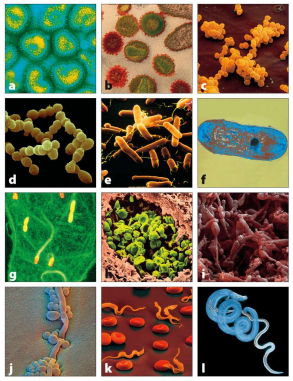


Figure 1.3 The Immune System, 4th ed. (© Garland Science 2015)

Who am I?

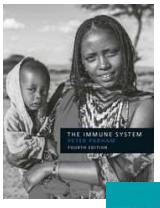
Professor: Holly Bates, PhD.
Email: hollybates@trentu.ca
Phone: 705-748-1011 x6128
Office: DNA Building, room D224

Office Hours: by drop in or appointment

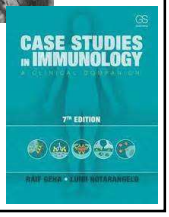
Your TA: Megan Aoki
meganarnoldussen@trentu.ca

What You Need

Required:
THE IMMUNE SYSTEM, 4TH ED.
By: Peter Parham



CASE STUDIES IN IMMUNOLOGY: A CLINICAL COMPANION, 7th Ed.
By: Raif Geha and Luigi Notarangelo



What to Expect

Lectures:
Wednesdays 3:00-4:50pm, GCS 114

Seminars (every other week) starting January 23rd:
W01: Thursdays 3:00 - 3:50 pm, SC W4
W02: Thursdays 4:00 - 4:50 pm, SC W4
W03: Fridays 9:00 - 9:50 am, SC W3
W04: Fridays 10:00 - 10:50 am, SC W3
W05: Fridays 11:00 - 11:50 am, SC W3

Lecture Schedule

(subject to change at discretion of instructor)

1. Jan 10 - Introduction; Elements of the Immune System
2. Jan 17 - Innate Immunity
3. Jan 24 - Innate Immunity
4. Jan 31 - Principles of Adaptive Immunity; Antibody Structure
5. Feb 7 - Generation of B-cell Diversity Before Antigen Exposure

- Wednesday Feb 14 - MIDTERM EXAM IN CLASS
- Wednesday Feb 21 - READING WEEK NO CLASS

6. Feb 28 - Antigen Recognition by T Lymphocytes
7. March 7 - The MHC and Development of B Lymphocytes
8. March 14 - Development of T Lymphocytes

- Note: Essay Due Monday March 19th 11:59pm

9. March 21 - T-cell Mediated Immunity
10. March 28 - B-cell Mediated Immunity
11. April 4 - Review

Course Evaluation

	Details	% Final Mark
Essay	• Vaccinations • Due: Monday March 19th, 11:59pm	15%
Seminars	• 5 seminars • Each seminar worth 5%	25%
Midterm	• Multiple Choice • Covers material from before midterm • Wednesday Feb. 14th during class	25%
Final Exam	• Focus on latter half of course • ~25% on material from first ½ of course	35%

Essay – 15% of Final Grade

DUE: MON. MARCH 19TH, 11:59PM BY SAFEASSIGN

Explain how vaccinations work and their effectiveness

Below is an outline of topics to be discussed and available marks:

1. Background on the aspects of the immune system relevant to vaccinations (**2** marks)
2. How do vaccines work? (**3** marks)
3. History of human vaccinations, focusing on vaccination rates, their effectiveness and relative safety (**2** marks)
4. Why are vaccination rates currently decreasing? Why is this an issue? (**4** marks)
5. What could / should be done about falling vaccination rates? (**2** marks)

Appropriate referencing in APA style – **1** mark;
Flow / readability – **1** marks:

TOTAL – 15 MARKS

- answer each part of the indidivudal questions

Essay – 15% of Final Grade

Format:

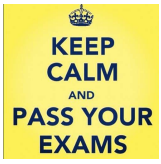
- 1500-2000 words (not including references)
- At least 10 references in APA style
- References must include:
  - Primary research articles
  - Review articles
  - Online news articles (2007-17)
- Essay format
  - Introduction, body, conclusion
  - Each paragraph has intro sentence, body, concluding sentence
- See Blackboard for more info

Seminars – 25% of Final Grade

- 5 Seminars - 5% each
- Clinical Case Studies
  - Topic posted on Blackboard
  - Familiarize yourself with topic before seminar
  - In class quiz (2%)
  - Take home or in class questions (3%)
- **Missed seminars cannot be made up**
- For seminar related questions ask your TA (Megan)

SCHEDULE
1: January 25/26
2: February 8/9
3: March 1/2
4: March 8/9
5: March 22/23

Exams



- Midterm (25%)
  - Wed. Feb. 14 in class
  - Multiple Choice
- Final Exam (35%)
  - ¾ material after midterm, ¼ material before midterm

Course Policies

- No extensions
- No make up quizzes or assignments
  - Late assignments will be given a mark of 0
  - Exceptions may be made for valid reasons (i.e. serious illness) if acceptable documentation (i.e. a medical doctor's note) is provided to the course instructor.
- Special circumstances
- No plagiarism tolerated.
  - All assignments will be checked for plagiarism and essay will be submitted by SafeAssign.
  - Plagiarism can result in a mark of 0 for the assignment (best case) or expulsion from the university (worst case)
- Check your Trent email regularly because this is the email address that will be used to send class emails

HELP!

University Policies:

ACCESS TO INSTRUCTION:

- It is Trent University's intent to create an inclusive learning environment.
- If a student has a disability and/or health consideration and feels that he/she may need accommodations to succeed in this course, the student should contact the Student Accessibility Services (SAS)
  - Office BH Suite 132
  - 705-748-1281
  - email accessibilityservices@trentu.ca

Questions?

Elements of the Immune System

Chapter 1

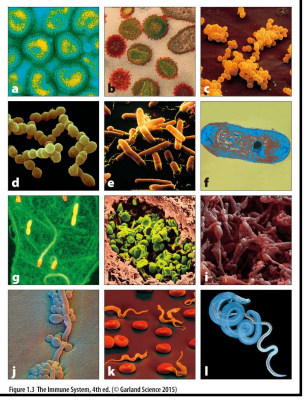


Figure 1.3 The Immune System, 4th ed. (© Garland Science 2015)

What is Immunology?

The study of the physiological mechanisms that humans and other animals use to defend their bodies from invasion by pathogens

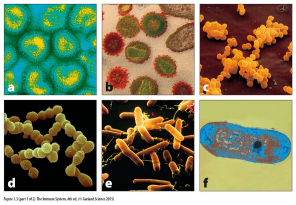


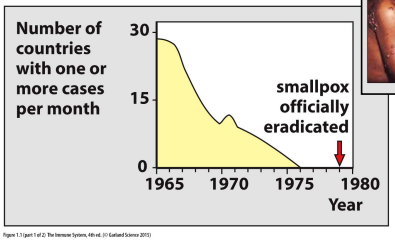
Fig. 1.3

Pathogen= microorganism that can cause disease

- microorganism can all become pathogenic under the right circumstances
-

Vaccination

Severe disease prevented by prior exposure to the infectious agent in a form that cannot cause disease



http://ed.ted.com/lessons/how-we-conquered-the-deadly-smallpox-virus-simona-zompi

Fig. 1.1

- Due to prior exposure to the infectious agent the body can mount an immune response and remembers the response when faced with the actual disease
- Variolation vs vaccination
  - Variolation= the buddhist nun
  - Vaccination= Edward Jenner

Commensal microorganisms inhabit healthy human bodies

- >1000 different microbial species live in the healthy adult human gut
  - 10 lbs (4.5 kg) of body weight
- Commensal: eat at the same table
- Symbiotic Roles:
  1. Process digested food
  2. Make vitamins
  3. Prevent colonization by pathogenic microorganisms
     - Competition
     - Secretion of antibacterial proteins (*E. coli* - colicins)

- commensal--> receive all their nutrients from the food you consume
E.coli colicins- helps prevents other pathogenic micro organisms from developing in the gut

Antibiotics disrupt the natural ecology of the colon

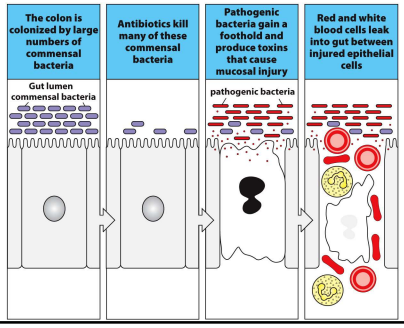


Fig. 1.2

- antibiotics kill the majority of the commensal bacteria
  - Allowing pathogenic bacteria, as well as other bacterias, to colonize in the gut
    - ie. C. Dephicile
- the release of the toxins causes leak eagle in the gut allowing injured cells to move throughout

Pathogens

- Infectious organisms that cause disease
  - Can be opportunistic

1. Bacteria
2. Virus
3. Fungi
4. Parasite

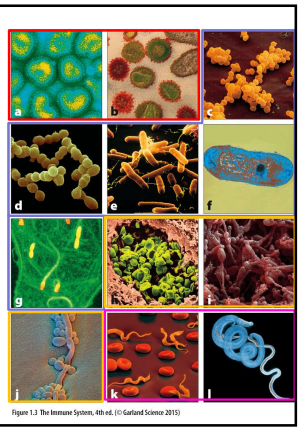
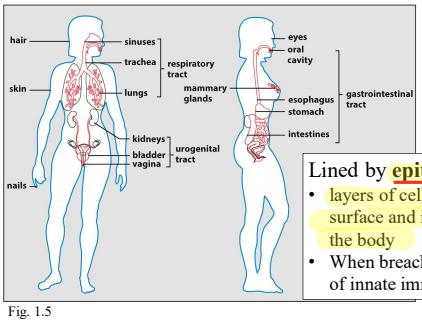


Figure 1.3 The Immune System, 4th ed. (© Garland Science 2015)

The skin and mucosal surfaces form barriers against infection



Lined by **epithelium**:

- layers of cells that line outer surface and inner cavities of the body
- When breached → activation of innate immune response

Fig. 1.5

- Skin and nails= the strongest barriers against infection
- Mucosal = second barriers

Question 1

One reason that pathogenic microorganisms have an advantage in the host they infect is because they _____.

a. Have previously been encountered through natural exposure
b. Have previously been encountered through vaccination
c. Strengthen the host's immune response
d. Reproduce and evolve more rapidly than the host can eliminate them

- Able to proliferate and change (evolve)
  - Ie. why the vaccines for the flu do not work from one year to the next
-

INNATE AND ADAPTIVE IMMUNITY

2 main categories of immunity
- Innate= immunity you are born with
- Adaptive= acquire throughout your lifetime through exposure to various microbes

Principal characteristics of innate and adaptive immunity

Recognition mechanisms of innate immunity	Recognition mechanisms of adaptive immunity
Rapid response (hours)	Slow response (days to weeks)
Fixed	Variable
Limited number of specificities	Numerous highly selective specificities
Constant during response	Improve during response

Common effector mechanisms for the destruction of pathogens

Figure 1.8 The Immune System, 4th ed. (© Garland Science 2015)

Fig. 1.8

Innate:
- fixed means will remain the same throughout lifetime

Adaptive:
- variable because it grows over time
- Highly selective--> able to identify specifics proteins of the pathogen
- Able to identify the specific pathogens and this improves with time

Innate immunity consists of two parts

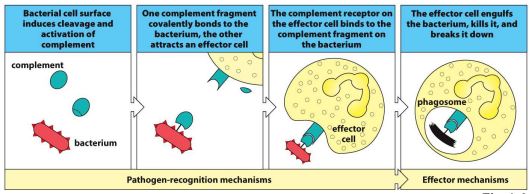


Fig. 1.6

1. Pathogen recognition:
   - Soluble proteins and cell surface receptors
   - Bind to pathogen and its products or to human cells and serum proteins that become altered in presence of pathogen
2. Recruitment of destructive effector mechanisms:
   - Effector cells engulf bacteria, kill virus-infected cells, or attack protozoan parasites

1. Soluble proteins= complement
   A. Bind to the pathogen and allow other immune cells to identify the pathogen as foreign
2. Effector cells are able to engulf the pathogenic cells due to the recruitment by the complement bound cells

The innate immune response causes inflammation at the site of infection

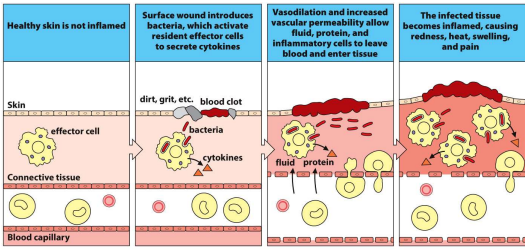


Fig. 1.7

Characteristics: Heat, Pain, Redness, Swelling

- secretion of the cyctokines begins the signalling between the inflammatory cells and elicits the cascade of immune response
- Increased blood flow in the area allows for the necessary cells to be brought to the site of infection
- Fluid movement causes swelling

If the innate immune response is insufficient, the **adaptive immune response** is added

- Organized around an ongoing infection and adapts to the nuances of the infecting pathogen
- Dependent on **lymphocytes**

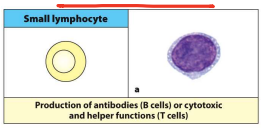


Fig. 1.11

- Innate immune response is where the immune response begins
- Adaptive immune is more powerful and specific to the pathogen
- Lymphocytes= related to adaptive immune response
  - B cells= antibody or inducing
  - T-cell= targeted cells

Selection of lymphocytes by a pathogen

- Recognize pathogens using cell surface receptors of one molecular type
  - Billions of versions!
- Clonal selection
- Clonal expansion

} Slow

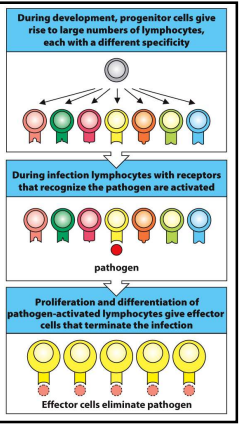


Fig. 1.9

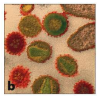
Primary Immune Response

- lymphocuyte undergoes clonal selection
  - To select for the specific cell
  - Then undergoes clonal expansion
    - Increase in the cell size

Some lymphocytes persist in body and provide immunological memory

- Memory cells:
  - Allow subsequent encounters with same pathogen to elicit a stronger response

= Acquired immunity



Examples:

- Measles virus –protection for decades
- Influenza virus – changes yearly by adapting to acquired immunity

- Secondary immune response = acquired immunity
  - Second time exposed to the pathogen results in a stronger immune response to protect the individual

Value of having both innate and adaptive immunity

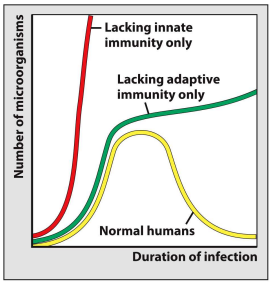


Fig. 1.10

- Vaccinations: must induce both the innate and adaptive immune response!
- normal individual follows normal bell shaped curve
- lack innate immunity--> number of micro organisms increases dramatically and no immune response can occur
- Lack adaptive immunity--> still able to mount some immune response because you still have the innate immune response
  - Require the innate immune response to imitate the adaptive immune response

Immune system cells all derive from hematopoietic stem cells

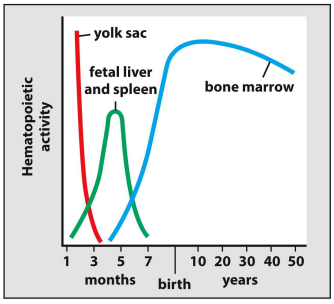


Fig. 1.12

Hematopoietic = stem cells that can become any type of blood cell

Immune system cells all derive from hematopoietic stem cells

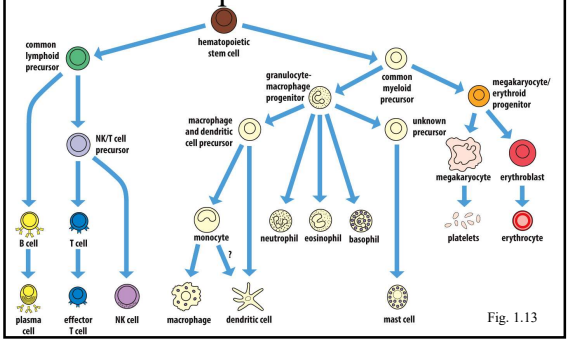


Fig. 1.13

Erythroid lineage= red blood cell production or platelet production
Myeloid lineage= granuloctyes--> good at destroying pathogens
Lymphoid lineage= lymphocyte --> adaptive immune response
B and T cells

Hematopoietic stem cells can commit to: 1. Erythroid Lineage

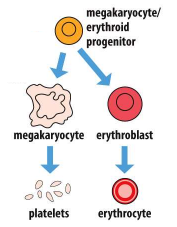


Fig. 1.13

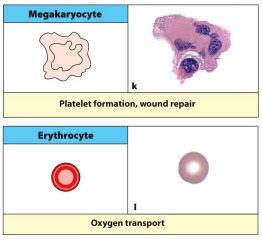


Fig. 1.11

Megakaryocyte= cells with multiple nuclei

Hematopoietic stem cells can commit to: 2. Myeloid Lineage

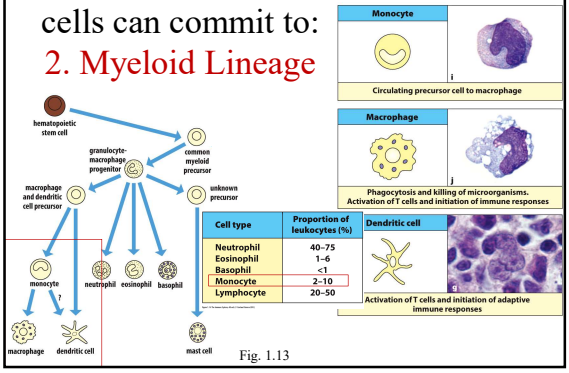


Fig. 1.13

Macrophage= resident effector cell
Monocyte = precursor to macrophage
travels through the blood and stops where their is an infection and become activated and stay put
Dendritic cell= resident cells able to sample the environment and in the case of infection can take the pathogen to the lymph node to beginthe adaptive immune response following activation of the innate

Macrophages respond to pathogens by using different receptors to stimulate phagocytosis and cytokine secretion

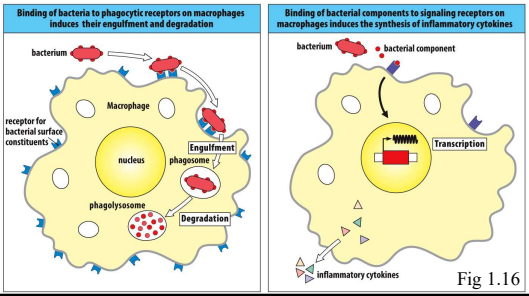


Fig 1.16

Hematopoietic stem cells can commit to: 2. Myeloid Lineage

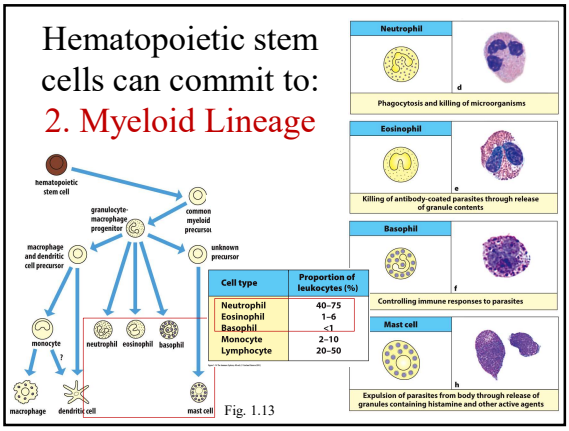


Fig. 1.13

- granuloctyes are quite prolific in the cells
  - Most important are the neutrophils (40-75%)
    - Short lived that phagocytosis and when hey die become puss because they had already attacked the pathogenic ...

Neutrophils are stored in the bone marrow and move to sites of infection

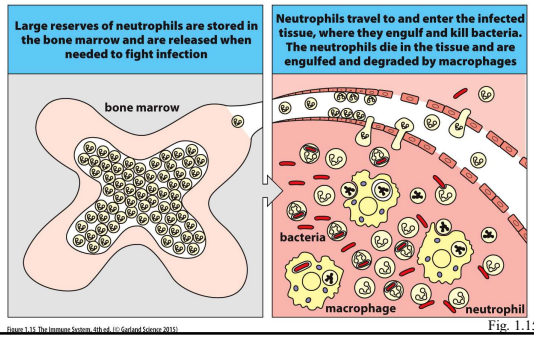
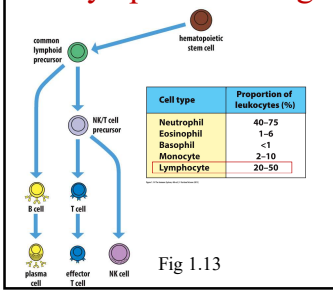


Fig. 1.15

Hematopoietic stem cells can commit to:

3. Lymphoid Lineage



Cell type	Proportion of leukocytes (%)
Neutrophil	40–75
Eosinophil	1–6
Basophil	<1
Monocyte	2–10
Lymphocyte	20–50

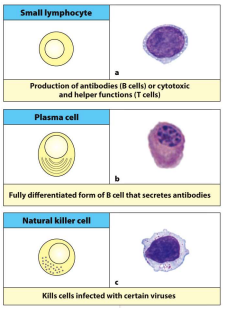
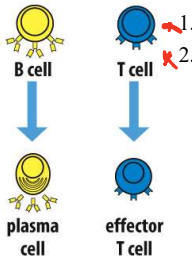


Fig 1.13

- produce the B and T cells and natural killer cells (NBK cells)
-

On encountering their specific antigen, B cells and T cells differentiate into effector cells



1. Plasma Cell → antibodies
2. Effector T cell:
   - Cytotoxic T cell
     - Kill cells infected with viruses or with certain bacteria that live inside human cells (similar to NK cells)
   - Helper T cell
     - Secrete cytokines
       - activate other cells of immune system
     - Subset (Regulatory T cells) control activities of other T cells

Fig 1.13

B cell--> plasma cell = secretion of antibodies
T cell--> effector T cell = cytotoxic or helper
- Cytotoxic are important for killing the infected human cells and destroying them
- Helper secrete cytokines and regulating and coordinating the immune response

Immunoglobulins (Ig's) and T-cell receptors are the lymphocyte receptors of adaptive immunity

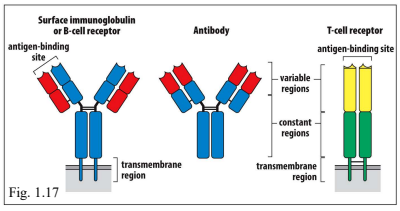


Fig. 1.17

- cell-surface and/or soluble
- Variable region contains antigen binding site(s)

- **Antigen**: Structure on macromolecule, virus, or cell that is recognized and bound by an Ig or T-cell receptor

B cell--> will release from the plasma membrane
T cell--> will remain bound to the plasma membrane
- both are comprised of two regions : Variable and Constant regions of the antibodies

Antibodies bind to pathogens and cause their inactivation or destruction

- Humoral immunity:
  - Immunity due to antibodies
  - Act through:
    - Neutralization
    - Opsonization:
      - coating of pathogen by antibody to facilitate phagocytosis

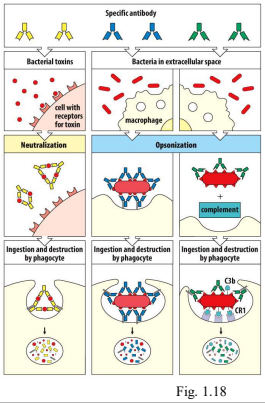
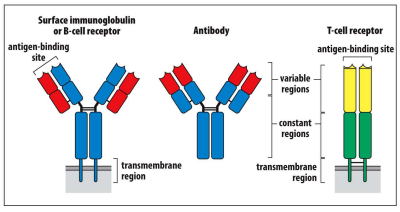


Fig. 1.18

- Humoral= body fluids
  - Humoral immunity= immunity due to antibodies

2 ways the antibodies work
- neutralization - antibodies bind directly to the bacterial toxins
- Opsonization - cover the pathogen with antibodies to flag it for destruction
  - can also work together with the complement proteins

The adaptive immune response to one pathogen provides no immunity to another



- Gene splicing and modification generates unique antigen binding sites
- each cell expresses one type of receptor

- i.e. antibodies against measles infection bind measles virus but provide no immunity against influenza virus

- normally the adaptive immune response is only protective against one variable and not the other
-

Question 2

Which of the following pairs is mismatched?

a. T-cell activation: cell division and differentiation
b. Effector B cell: plasma cell
c. Plasma cell: antibody secretion
d. Helper T cell: kills pathogen-infected cells

Most lymphocytes are present in specialized lymphoid tissues

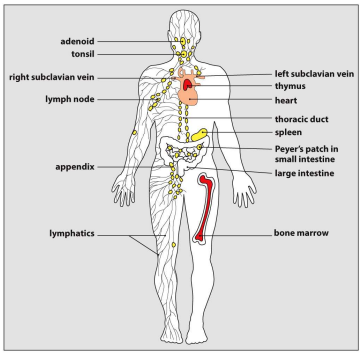
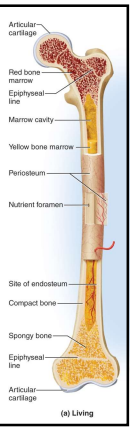


Fig 1.19

Bone marrow a nd thymus= primary lymphoid tissue
Yellow= secondary lymphoid tissue

Functional Types of Lymphoid Tissues



- **Primary** (central) lymphoid tissues:
  - Where lymphocytes develop and mature to the stage at which they can respond to an antigen
    - Bone marrow
    - Thymus
- **Secondary** (peripheral) lymphoid tissues:
  - Where mature lymphocytes become stimulated to respond to invading pathogens
    - All other sites (i.e. lymph nodes, tonsils)

Lymphatics collect plasma that leaks out of blood vessels

- Return fluid called lymph to blood
  - One-way valves
  - Flow driven by body movements
- Lymph Nodes:
  - At junctions of lymphatic vessels

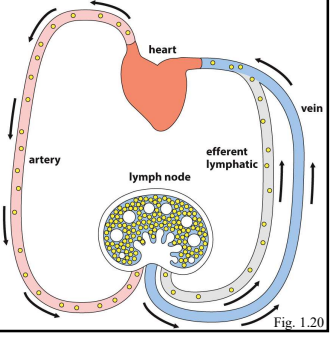


Fig. 1.20

- lymphocytes collect in the lymph nodes to see if there is a pathogen that they recognize in order to mount the immune response
  - If yes, they stay put in the lymph node
  - If no, they leave in the efferent lymphatic vessel and move on to the next lymph node

Circulating lymphocytes meet lymph-borne pathogens in draining lymph nodes

- Mature B and T cells move through blood and lymph
  - From blood, cell enters lymph nodes
  - If activated by pathogen, it remains
  - If not activated, returned to blood

= lymphocyte recirculation

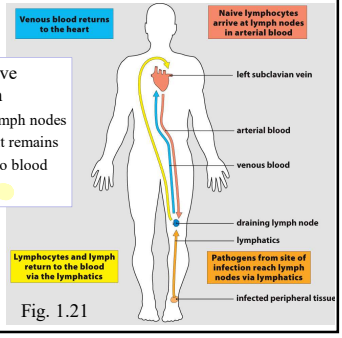


Fig. 1.21

The lymph node is where blood-borne lymphocytes respond to lymph-borne pathogens

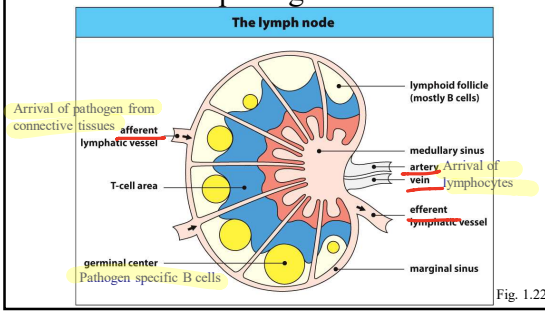


Fig. 1.22

Activation of adaptive immune response in a draining lymph node

1. Pathogens, pathogen components, and dendritic cells carrying pathogens and molecules derived from them arrive in afferent lymph draining site of infection
2. Free pathogens and debris removed by macrophages
3. Dendritic cells become resident in lymph node and move to T-cell areas
   - Stimulate division and differentiation of pathogen specific small lymphocytes into effector lymphocytes
4. Some helper T cells and cytotoxic T cells leave in efferent lymph and travel to infected tissue. Other helper T cells remain in lymph node and stimulate division and differentiation of B cells into plasma cells
5. Plasma cells move to medulla where secrete antibodies → site of infection by lymph then blood

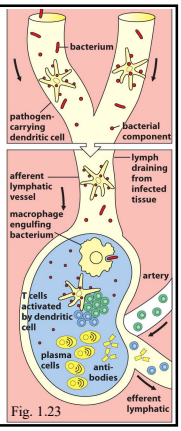


Fig. 1.23

- the dendritic cells, once in the lymph node, activate the T cells and initiate immune response

Question 3

Which of the following best describes the movement of a T cell through a lymph node?

a. It enters via efferent lymphatics and exits via the bloodstream.
b. It enters via the bloodstream and exits via efferent lymphatics.
c. It enters via the bloodstream and exits via the bloodstream.
d. It enters via the bloodstream and exits via afferent lymphatics

The spleen provides adaptive immunity to blood infections

- Pathogens can also enter blood
  - i.e. insects or when lymph nodes fail
- Red pulp:
  - removes damaged and senescent red blood cells
- White pulp:
  - Lymphocyte responses to blood-borne pathogens

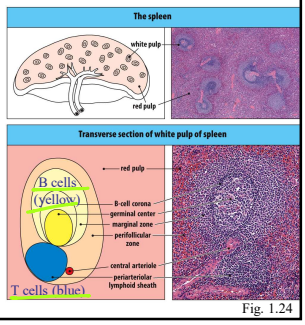


Fig. 1.24

- Important because the spleen is important for fighting blood borne infections
-

Asplenia – born without a spleen

- Mutation in gene for ribosomal protein SA
- Inheriting a single copy sufficient to cause asplenia
- Susceptible to infections (i.e. *Streptococcus pneumoniae* or *Haemophilus influenzae*)
  - Require immunization

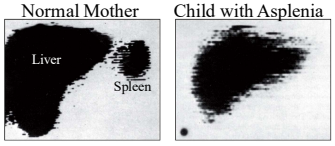


Fig. 1.25 – Scintillation scans of abdomen after iv injection of radioactive colloidal gold

Something to think about…

When a person's spleen becomes damaged from traumatic injury, it is often removed surgically to prevent life-threatening blood loss

- Children:
  - vulnerable to bacterial infections like asplenic children
- Adults:
  - consequences usually slight

Why?

- because children have not developed the adaptive immunity the adult has
  - Adults have the immunological memory

Most secondary lymphoid tissue is associated with the mucosa

- Gut = GALT
  - includes tonsils, adenoids, appendix, and Peyer's patches (small intestine)
- Bronchial = BALT
- Pathogens enter by direct transport by M cells epithelium
- Activated lymphocytes can move outwards to epithelium to perform effector actions

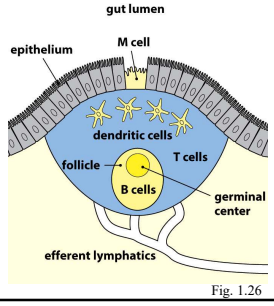


Fig. 1.26

Question 4

The _____ is (are) the lymphoid organ(s) that filter(s) the blood.

a. Spleen
b. Tonsils
c. Peyer's patches
d. Appendix

Question 5

Which of the following pairs is mismatched?

a. Megakaryocyte: formation of platelets
b. Plasma cell: mediation of phagocytosis and killing of microorganisms in the plasma
c. Dendritic Cell: Activation of adaptive immune responses
d. Natural Killer Cell: Develops from a common lymphoid progenitor

Lecture Summary

- To restrict nature, size, and location of microbial infestation, animals have evolved immune defenses
- Immune system starts with innate immunity:
  - Fast, fixed in mode of action, and effective at stopping most infections at an early stage
  - Phagocytes engulf and kill pathogens (neutrophils, macrophages)
  - Cytotoxic cells kill virus-infected cells (basophils, eosinophils, mast cells)
- Adaptive immunity brought into play when innate immunity fails to stop infection
  - Improved pathogen recognition
  - B and T lymphocytes
  - Provides long lasting protective immunity against a pathogen

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