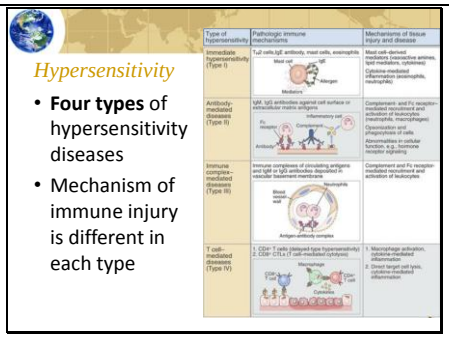
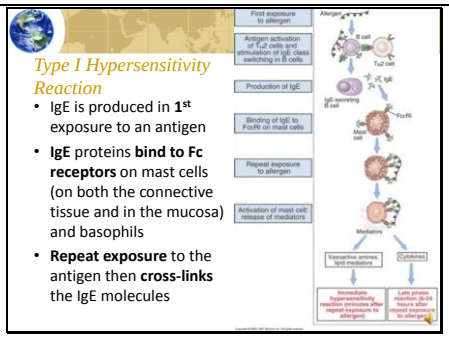
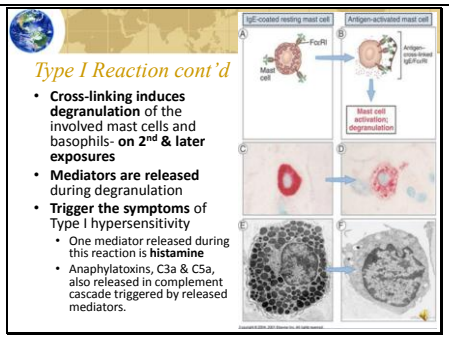
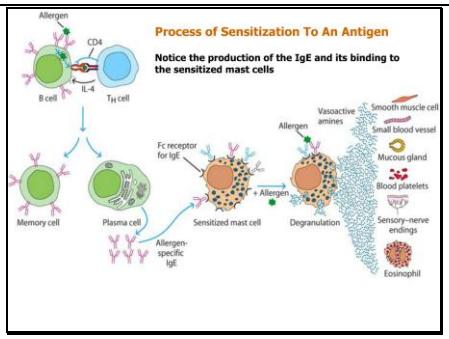
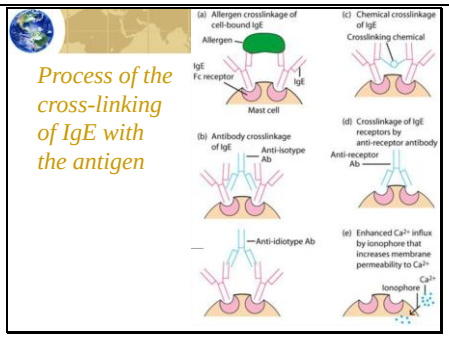
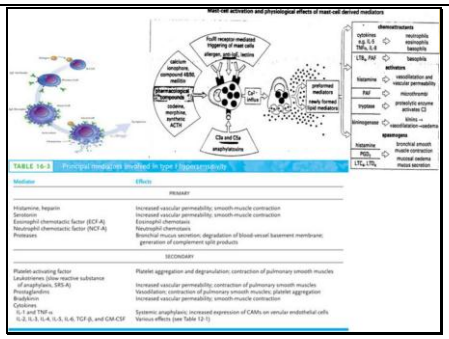
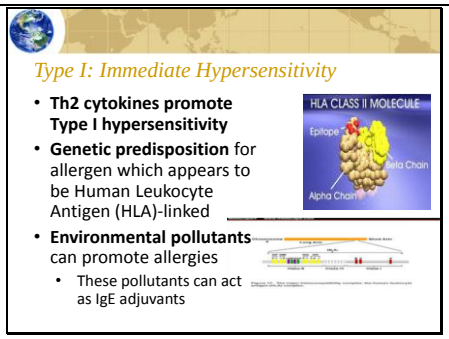
Slide 1	*Foundations of Public Health Immunology* Hypersensitivity  Type I hypersensitivity reactions can be caused by a variety of allergens	SLIDE 1 Hypersensitivity. This week's lecture will elaborate on concepts from last week- immune responses directed against self antigens. Hypersensitivity diseases are disorders primarily caused by the adaptive immune response, where tissue damage is caused by the same effector mechanisms used by the immune system to protect against microbes. Specific hypersensitivity reactions can result in different autoimmune diseases.
Slide 2	*Objectives* • Describe the hypersensitivity reaction to antigen exposure • Identify and explain the similarities and differences in the mechanism of the four types of hypersensitivity reactions • Identify selected disorders for each type of hypersensitivity reaction (selected disorders of autoimmunity) • Identify and explain the mechanisms of sepsis	SLIDE 2 Learning objectives

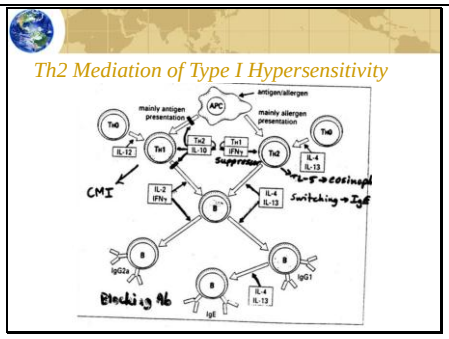
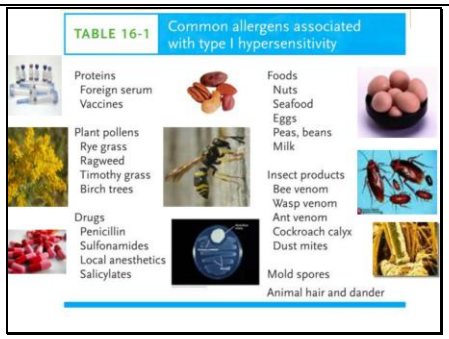
Slide 3	*Hypersensitivity*
	• Normally beneficial immune responses that occur in **an exaggerated or inappropriate form**
	  • Results in **inflammation, tissue damage** or other problems known as immunopathology
	• Hypersensitivity reaction only occur on the **second or subsequent exposure to an allergen**
	  • The host must first be sensitized to the allergen!!
		SLIDE 3 Because of tolerance, the body normally does not develop immune responses against harmless antigens. However, this system can sometimes be dysfunctional, as we discussed last week. Hypersensitivity is an exaggerated version of a normally beneficial immune response. Hypersensitivity reactions can only occur on a second or subsequent exposure to an antigen. This is a very important point!! For example, a person may be stung by a bee for the first time and not have a reaction. However, the next time that the person is stung, the person may have a severe reaction because the body had developed an immune response to the bee venom alter the first bee sting.

Slide 4	 *Hypersensitivity* • **Four types** of hypersensitivity diseases • Mechanism of immune injury is different in each type	SLIDE 4 There are 4 different types of hypersensitivity diseases, each with distinct mechanisms of action. Carefully review the diagram to see the mechanism and cells involved in tissue damage for each type.
Slide 5	*Characteristics of Hypersensitivity* Comparison of Hypersensitivity Types Table Source: http://pathmicro.med.sc.edu/ghaffar/hyper00.htm	SLIDE 5 This table on characteristics of hypersensitivity types provides an excellent summary for this week's material. Note the mechanisms, time frames, and examples of autoimmune diseases for each hypersensitivity reaction.

Slide
 	
6
	Type I: Immediate Hypersensitivity
	• Also know as:
	  • Allergy
	  • Atopy
	  • Anaphylaxis
	  • Most severe form of Type I reaction
	• Examples of Type I reactions
	  • Asthma
	  • Hay fever
	  • Some food and drug allergies
	Normal appearance
	Severe allergic reaction (anaphylaxis)
		SLIDE 6 Type I Hypersensitivity is more commonly known as allergies or atopy (atopic individuals). The most severe forms are known as anaphylaxis Note the mechanisms and manifestations for each hypersensitivity reaction in the table.

Slide 7		SLIDE 7 The start of Type I Hypersensitivity _ Alter initial exposure to an antigen, IgE is produced against the antigen. Note that IgE is being produced rather than IgM!! These IgE antibodies bind strongly to the Fc receptors on mast cells and basophils. Mast cells and basophils are found throughout the body; and, if these cells become bound by IgE produced against an antigen, it is possible for a systemic reaction to occur with a repeat exposure to the antigen.
Slide 8		SLIDE 8 With repeated exposures to the antigen, the bound IgE antibodies cross-link and induce mast cell and basophil degranulation. Consider that this antigen might be pollen!!! Can pollen infect your cells??? No, pollen can't infect your cells; but, it can induce this immune reaction. Alter the mast cell and basophil degranulation, mediators are released that induce the allergic response. Even the complement system can release C3a and C5a which can lead to a further systemic response.
Slide 9		SLIDE 9 Note the production of IgE alter initial exposure to the antigen (allergen). The allergen is the antigen that induces the allergic reaction.

Slide 10	 	SLIDE 10 This slide illustrates the IgE cross-linking that occurs with repeated exposure to an allergen.
Slide 11		SLIDE 11 Note the cytokines involved in the induction of an allergic reaction and the numerous mediators involved in an allergic reactions. With the triggering and degranulation of the mast cell, there are numerous mediators released.
Slide 12	 	SLIDE 12 The development of allergies appears to be linked to the HLA genes; and, environmental factors can promote allergies. It's important to note that Th2 cytokines promote Type I Hypersensitivity. Think back to Block Four and the role of the CD4+ Th2 cells in immunity.

Slide 13		SLIDE 13 Note the role of the Th2 cells in Type I Hypersensitivity, as they stimulate further cell-mediated immunity, more IgE production, and recruitment of eosinophils that “accidentally” causes tissue damage to self.
Slide 14		SLIDE 14 Note some of the most common allergens, including foods pollens, and drugs.
Slide 15		SLIDE 15 Allergies can be diagnosed by the Skin Prick Test. Small amounts of the suspected allergens are introduced into the skin. lf the person is allergic to the tested antigen, swelling and redness (wheal & flare) will occur at the site. This should only be done under medical supervision because anaphylaxis can occur if the person is severely allergic to the antigen. The immediate reaction usually starts within 10 minutes, peaks within 30 minutes, and resolves alter 1 to 2 hours. Desensitization therapy can be used to generate tolerance to an allergen. This therapy adds larger amounts of an allergen to an allergic individual, with the hope that the person will develop tolerance to the antigen. These therapies may be needed for up to 5 years to complete desensitization.

Slide
 	
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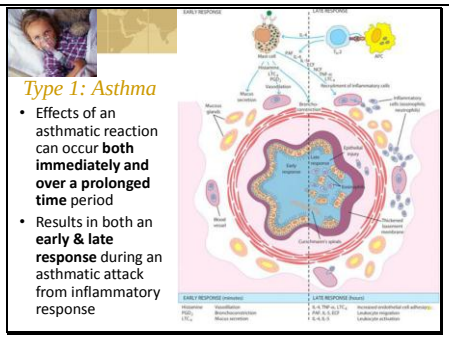
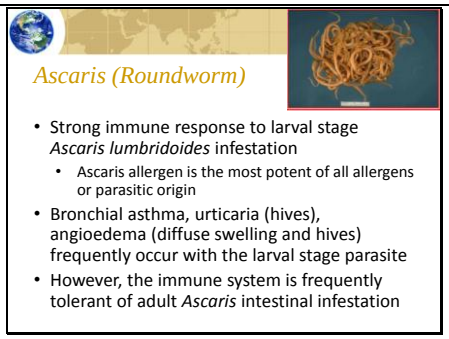
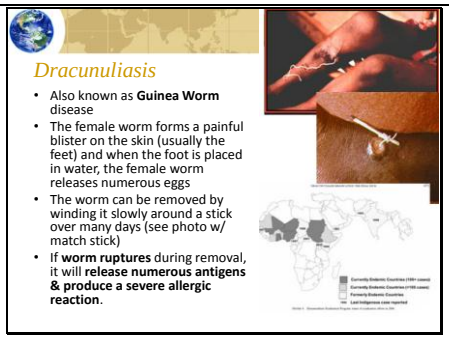
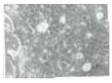
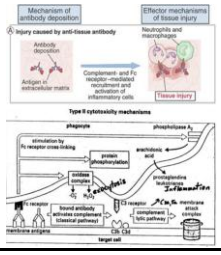
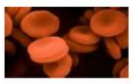
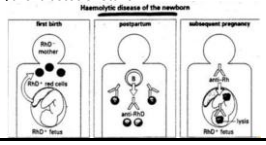
	Type I: Latex Allergy
	• Occurs when the immune system reacts to proteins in natural rubber latex
	• An estimated 1 – 6% of general population has been sensitized to latex
	  • **5 – 10% of healthcare workers are sensitized!**
	  • Should **substitute synthetic gloves** for latex
	• Products that commonly cause reactions included gloves, balloons & condoms
	• May also react to rubber bands, erasers, rubber parts of toys, pacifiers, etc.
		SLIDE 16 It has not been clearly shown why some people develop allergies while others do not. However, some people are at greater risk of developing a latex allergy: Person with a food allergy, especially to certain foods. Avocados, bananas, chestnuts, kiwis and passion fruits have some of the same allergens found in latex, and you are likely allergic to both latex & these foods. Person with family history of allergies, as your body is more likely to respond to allergens. Children with spina bifida, the risk of latex allergy is highest in these children, as they are often exposed to latex products from early and frequent health care. Nearly 50% of all children with spina bifida are allergic to latex. Dental and health care workers, lf you work in the dental or health care Held, your chances of developing an allergy are higher. lf you develop a latex allergy, you should try substituting synthetic (vinyl or nitrile) gloves for latex gloves, although they are more expensive. Avoid areas where powdered gloves are used frequently, as you may inhale latex particles and trigger allergic reactions. In addition, latex condoms can also cause serious reactions in people allergic to latex. Natural skin condoms may be used to prevent pregnancy, but they offer no protection against STDs like HIV. It is preferred that people with latex allergies use synthetic rubber condoms as they prevent both pregnancy & STDs.

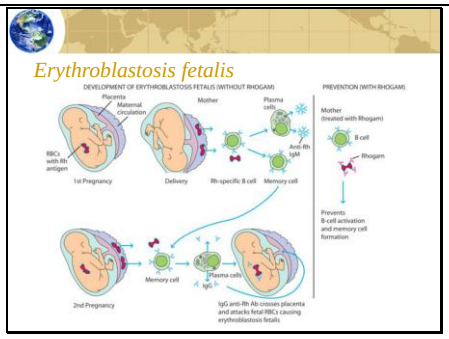
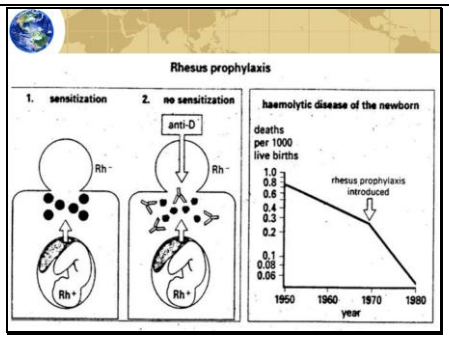
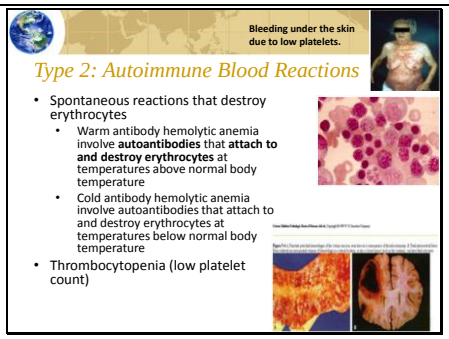
Slide 17	 *Type 1: Asthma* • Effects of an asthmatic reaction can occur **both immediately and over a prolonged time** period • Results in both an **early & late response** during an asthmatic attack from inflammatory response	SLIDE 17 Asthma is an excellent example of Type I Hypersensitivity. Note the inflammatory mediators being released in the bronchi during an asthmatic reaction. Due to the mediators released during an asthmatic attack (early response), the symptoms may return hours later (late response) even though the allergen is no longer present. Late responses have eosinophils & neutrophils recruited through cytokine release & trigger inflammation, causing epithelial injury etc.

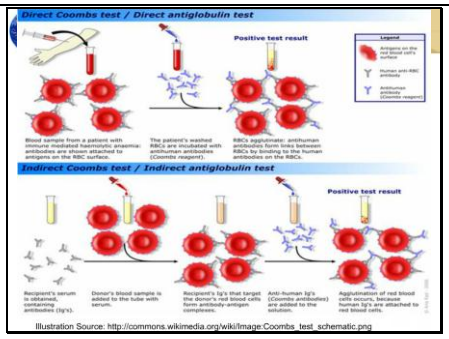
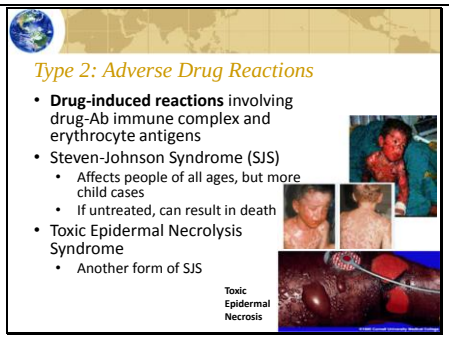
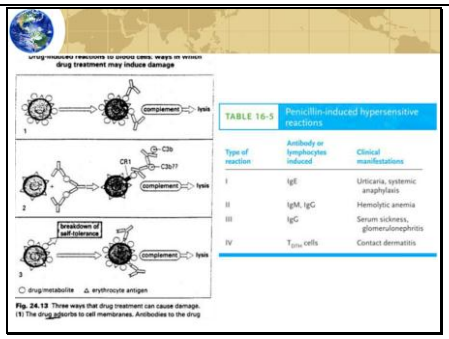
Slide 18		SLIDE 18 The body can produce a strong allergic response against Ascaris larva; however, the adult Ascaris can induce immune tolerance.
Slide 19		SLIDE 19 Guinea worm disease has been known since antiquity, and the fiery serpent in exodus is believed to be Dracunculiasis. Guinea worm disease can also produce severe allergic reactions. If the female worm ruptures as it is being removed, antigens can be released that can cause anaphylaxis.

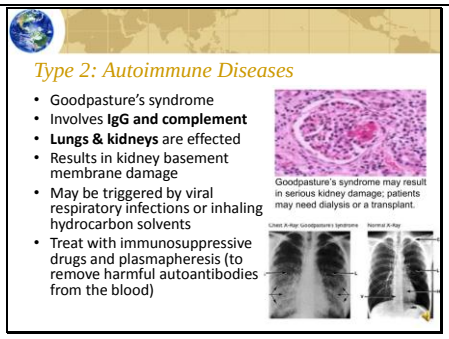
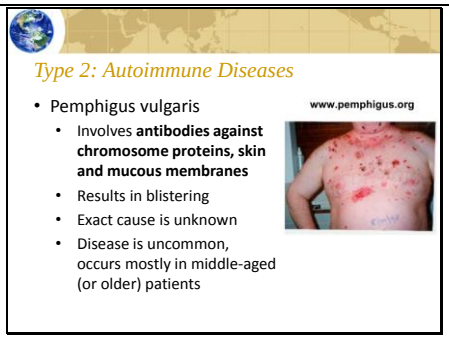
Slide 20	*Type 2: Cytotoxic Hypersensitivity*
	• With Type 2 reactions, the **reaction is against an antigen located on a cell surface**
	  • The antigen being attacked is an integral part of the cell!!
	• **IgM and IgG antibodies** bind to the cell surface or tissue antigens in conjunction **with complement activation**
	• The **complement activation** results in:
	  • Chemotaxis
	  • Inflammation
	  • Opsonization
	  • Cellular activation
	 
		SLIDE 20 In Type II Hypersensitivity the reaction is against self-antigens located on a body cell. IgM and IgG antibodies (in conjunction with complement) attack this self-antigen

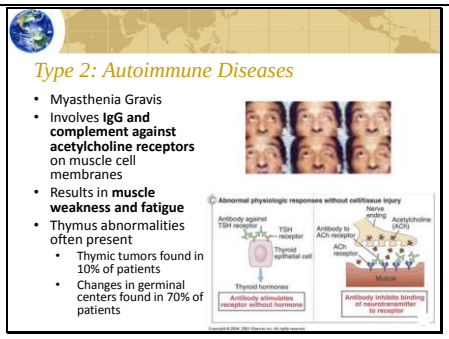
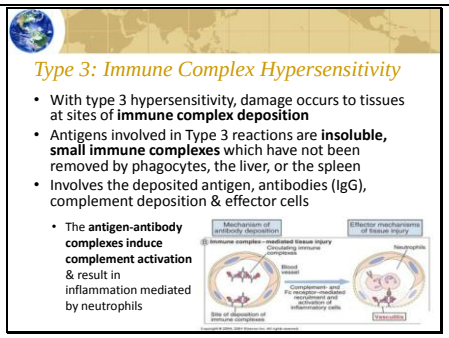
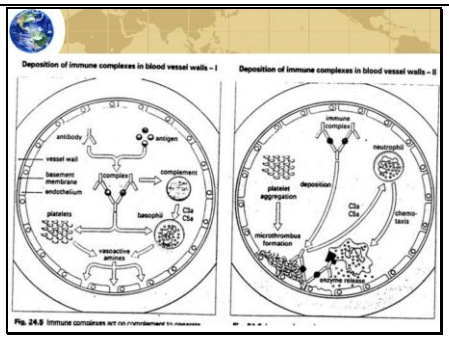
Slide 21	*Type 2 Mediated Immunopathology* 	SLIDE 21 Note the mechanism of Type II Hypersensitivity, as complement binding to Fc receptors on neutrophils and macrophages recruits these cells to destroy the self antigen. Watch the 3 mechanisms of Type II cytotoxicity in the animations provided.

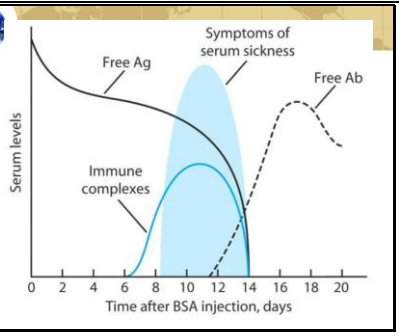
Slide 22	*Type 2: Blood Immunopathologies*
	• Blood transfusion reactions
	• Hemolytic Disease of the Newborn
	  • RhD factor
	  • Reaction involves IgG
	  • Also called erythorblastosis fetalis
	 
	 
		SLIDE 22 There are also other antigens found on red blood cells that can induce immune reactions besides the ABO antigens; however, these reactions are usually not as severe as those that will develop with mismatching of the ABO system. The RhD (Rhesus) factor is another antigen found on red blood cells. These antigens are important in a disease called hemolytic diseases of the newborn. With the first pregnancy, a RhD- mother will develop antibodies against the erythrocytes of a RhD+ fetus. The first infant will be born without problems. However, with each subsequent pregnancy with a RhD+ fetus, the mothers immune system will produce increasing amounts of antibodies that will destroy the fetal erythrocytes resulting in anemia and eventually fetal death. With each succeeding pregnancy, the effects will become more severe and increasingly fatal to the fetus. Note: A fetus with RhD- blood (like the mother) will not be affected by the antibodies

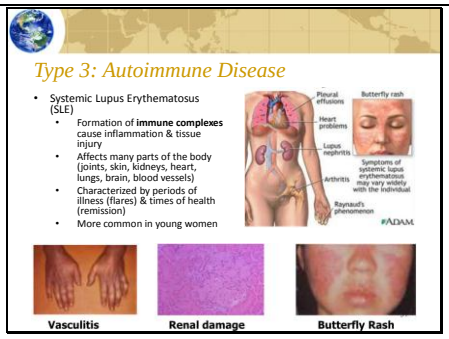
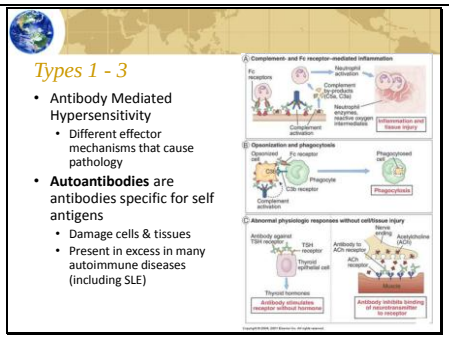
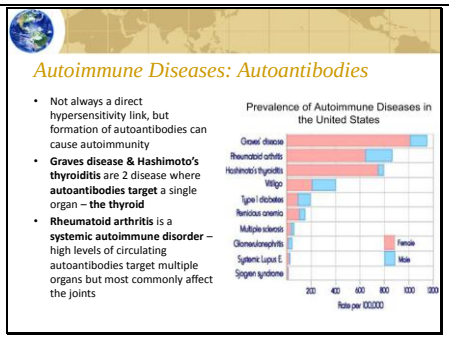
Slide 23		SLIDE 23 Note the progression of hemolytic disease of the newborn with each subsequent RhD+ infant.
Slide 24		SLIDE 24 In order to prevent the production of antibodies to the RhD+ fetus, the RhD- mother will be given Rhogam to prevent B-cell activation and memory cell formation.
Slide 25		SLIDE 25 Antibodies can develop against red blood cells and produce anemia (low red blood cell count). Body temperature can affect the reactivity of these antibodies. Warm Antibody Hemolytic Anemia is an autoimmune disorder characterized by the premature destruction of red blood cells by the body's natural defenses against invading organisms (antibodies). Normally, the red blood cells have a life span of approximately 120 days before they are removed by the spleen. In an individual affected with Warm Antibody Hemolytic Anemia, the red blood cells are destroyed prematurely and bone marrow production of new cells can no longer compensate for their loss. The severity of the anemia is determined by the time the red blood cells are allowed to survive and by the capacity of the bone marrow to continue new red blood cell production. Immune Hemolytic Anemias are subdivided by the optimal temperature at which the antibodies destroy red blood cells. As their names imply, Warm Antibody Hemolytic Anemia occurs at temperatures of 37 degrees centigrade or higher while Cold Antibody Hemolytic Anemia usually occurs at approximately 0 to 10 degrees. In addition, platelets can also be attacked in Type II Hypersensitivity. This can lead to thrombocytopenia. Without sufficient platelets, continued bleeding can occur.

Slide 26	 Illustration Source: http://commons.wikimedia.org/wiki/Image:Coombs_test_schematic.png	SLIDE 26 Coombs' tests are blood tests that identify the causes of anemia, as autoimmune responses can destroy the body's red blood cells. The Coombs' test is used to detect antibody on an individual's erythrocytes and can identify if these antibodies are directed against self. If there is antibody present on the erythrocytes, the erythrocytes will be agglutinated by anti-human antibodies. In contrast, if there is no antibody present on the erythrocytes, the erythrocytes will not be agglutinated by anti-human antibodies. If the Coombs' test is negative, the anemia is unlikely to be autoimmune.
Slide 27		SLIDE 27 Drugs (medicinal and illegal) can also produce Type II Hypersensitivity. Steven-Johnson Syndrome is a severe outcome of these drug hypersensitivities. The sensitized immune system begins to attack healthy body tissue. Toxic epidermal necrosis can also occur due to Type II Hypersensitivity. Adverse drug reactions account for nearly 150,000 deaths in the United States every year. SJS is one of the most serious adverse drug reactions that is known Almost any medication (including Ibuprofen) can cause SJS. The types of drugs most commonly associated with SJS are antibiotics, anti -inflammatory meds, and anti-convulsants.
Slide 28		SLIDE 28 Penicillin is a great example of a medication that can induce hypersensitivity reactions. Penicillin can produce all four types of hypersensitivity. However, note the different manifestations for each type of reaction. The Type II reactions to drugs can occur if the immune system reacts directly to the drug. Or, the drug may induce the immune system to react to certain antigens on a body cell. And, finally, the drug may bind to the body cell and then an immune reaction develops against the drug which results in damage to the body cell. Hypersensitivity reactions involving drugs can involve all four types of reactions.

Slide 29		SLIDE 29 Autoimmune diseases are frequently Type II Hypersensitivity. Goodpasture's Syndrome is an example. In Goodpasture's Syndrome, IgG and complement attack the kidney resulting in damage to the kidney basement membrane. Goodpasture's syndrome is a rare disease that affects the lungs and kidneys. A combination of factors is associated with this disease, including the presence of an inherited component and exposure to certain chemicals. Goodpasture's syndrome can be treated with immunosuppressive drugs and a process called plasmapheresis (the blood plasma is cleaned) to remove the harmful antibodies from the blood. The syndrome may occur for variable time periods, from a few weeks to several years. Generally, this disease does not lead to permanent lung damage, but kidney damage may be long-lasting. lf the person develops kidney failure, then dialysis or kidney transplantation may be necessary.
Slide 30		SLIDE 30 Pemphigus is another Type II autoimmune disease. Antibodies are produced against chromosomal proteins, skin, and mucous membranes which results in blistering. Sores and blisters almost always begin in the mouth. Auto-antibodies attack the “glue," which holds skin cells together, called desmogleins, and the skin can tear easily in this disease.

Slide 31		SLIDE 31 Myasthenia gravis is another example of Type II autoimmunity. IgG and complement attack acetylcholine receptors on muscle cell membranes resulting in muscular weakness and fatigue. Note the antibodies attacking the acetylcholine receptors in the illustration. The prevalence of MG in the United States is estimated between 35,000 to 60,000 cases. Women used to have the disease more often than men, developing the disease in their 20s to 30s, whereas men develop it later alter they tum 50 (but they are catching up to women in case numbers).
Slide 32		SLIDE 32 It is the deposition of immune complexes onto tissue surfaces that results in Type III Hypersensitivity. The body attacks these immune complexes but ends up also attacking healthy body tissue. These immune complexes contain small and insoluble antigens that were NOT removed by the phagocytes, liver, or spleen.
Slide 33		SLIDE 33 Note the deposition the immune complexes onto the blood vessel wall and the subsequent immune reactions. This concept is further illustrated in the Type III Immune Complex animation.

Slide 34	*Factors Contributing to Deposition of Immune Complexes* • Complement deficiencies • Low affinity antibodies • Antibody isotype • Ineffective phagocytois • Abnormal carbohydrate on antibody molecules • Size of immune complex and the antibody isotype • Increased vascular permeability (due to vasoactive amines) • High blood pressure and turbulence (for example in the glomerular capillaries of the kidneys) • Affinity of the antigen for specific tissues	SLIDE 34 There are several factors that contribute to the deposition of these immune complexes.
Slide 35	*Type 3 Hypersensitivity* exudate • Three General Groups: • **Persistent infection** involving microbial antigens and the kidneys • Autoimmune disease against **self antigen** • Damage can occur to the kidneys, joints, & arteries etc. • **Extrinsic** antigens • Inhaled antigen – (mold) lung • Serum Sickness • Arthus Reaction Serum Sickness Arthus Reaction	SLIDE 35 There are three general groups of Type III reactions: (1) persistent microbial infections, (2) autoimmunity, and (3) extrinsic antigens
Slide 36		SLIDE 36 Serum sickness is an example of a Type III reaction. Serum sickness used to occur more frequently when animals (for example, horses) were used to produce antibodies against diseases and then these antibodies were given passively to humans. Notice when the symptoms of serum sickness are occurring.

Slide 37		SLIDE 37 Lupus is another example of Type III Hypersensitivity. The “Butterfly Rash" can develop on the faces of persons affected by lupus. Common symptoms include vasculitis, renal damage, and the characteristic “butterfly rash". Systemic lupus erythematosus (SLE) is a chronic disease with many manifestations. SLE can develop at all ages, but is more common in young women and can run in families. Lupus is a very complex disease, and it is believed that environmental factors with genetic susceptibility influence disease progression. Over time, immune complexes build up in the body and result in inflammation and tissue damage to important organs.
Slide 38		SLIDE 38 The first 3 types of hypersensitivity that we have discussed are antibody mediated. All of the damage caused by these types are from antibodies attaching to self antigens & causing immune cells to enter the picture and attack “self". All people have low titers of autoantibodies, but people with autoimmune diseases have elevated levels.
Slide 39		SLIDE 39 These autoantibodies may not always be associated with specific hypersensitivity mechanisms of tissue damage. However, they are also important contributors to autoimmune diseases, as they can be generated to specific self antigens and attack specific organs, such as the thyroid (in Graves disease) or the joints (in rheumatoid arthritis).

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	Autoantibody Tests
	• Antinuclear antibody (ANA): may be found in autoimmune disorders [especially lupus, scleroderma, Sjorgren's syndrome, polymyositis, certain types of chronic active hepatitis]
	• Anti-DNA antibody: may be present in lupus
	  • Titers will decrease when treatment is successful
	  • **Usually not found in other autoimmune diseases**
	• Antiphospholipid antibody: may be found in lupus and certain other conditions
	  • Associated with miscarriages and clots
	• Rheumatoid factor: often found in blood and joint synovial fluid in rheumatoid arthritis patients
		SLIDE 40 Antinuclear antibodies (ANAs) are detectable in the blood and are unusual antibodies, in that they can bind to certain structures within the nucleus of the cells. ANAs are found in patients whose immune system may be predisposed to cause inflammation against self tissues, and indicate the possible presence of autoimmunity. It is a sensitive screening test used to detect autoimmune diseases, although approximately 5% of the general population has low titers of the ANAs in their blood. Titers of 1:80 or higher may indicate autoimmune disease. This has been especially proven for SLE patients, as 95% of these patients have positive ANA test results.

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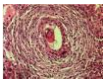
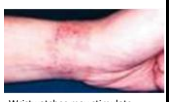
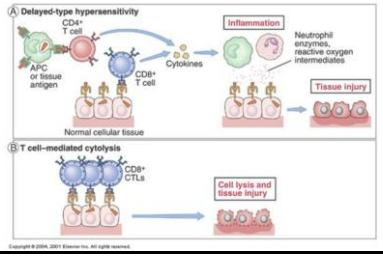
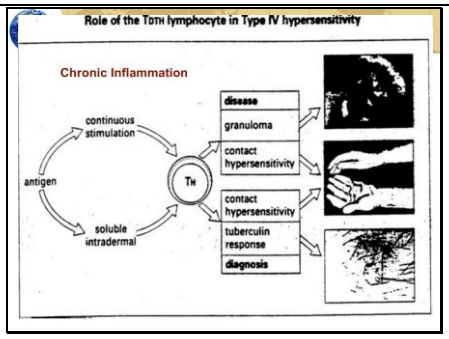
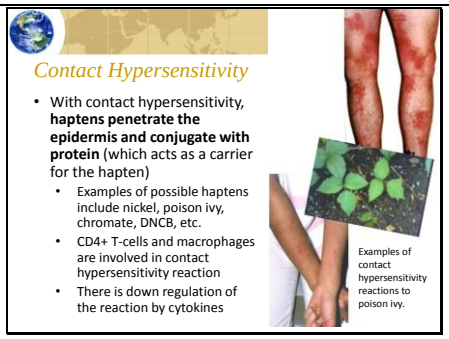
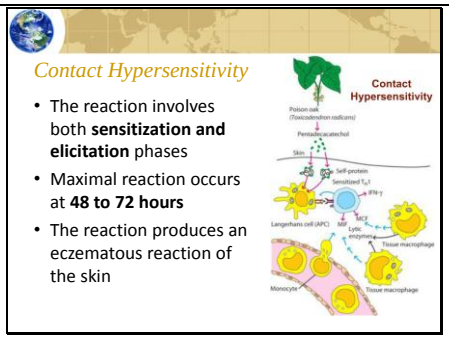
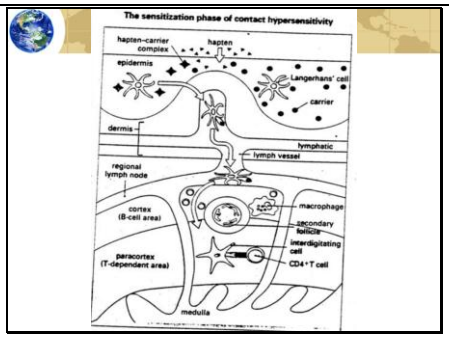
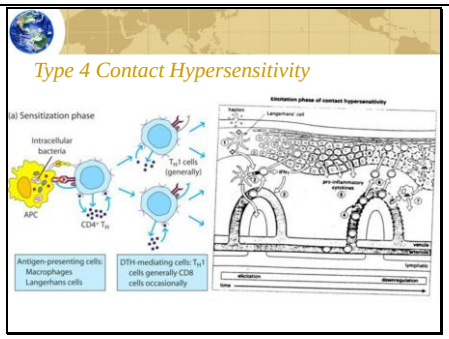
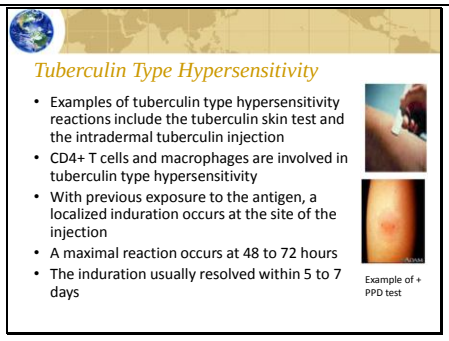
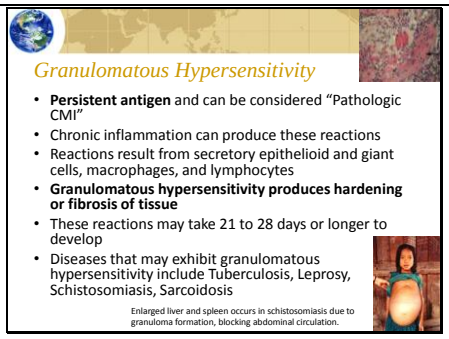
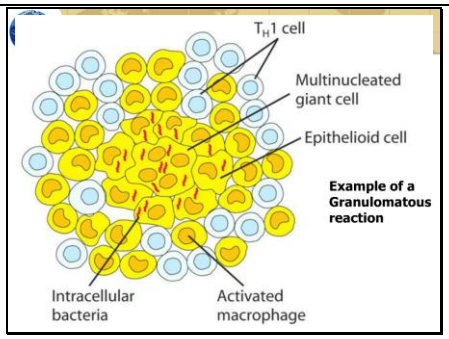
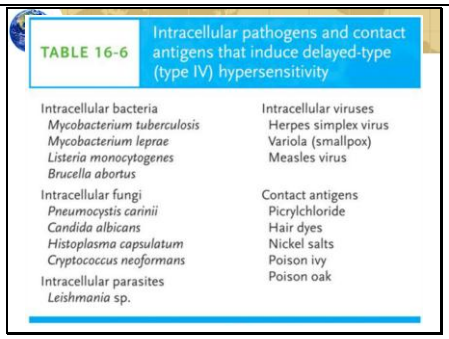
	Type 4: Delayed Hypersensitivity
	• Type 4 reactions are regulated by **cell-mediated** reactions
	• Type 4 reactions usually **take longer than 12 hours to develop** due to mediation via T-cells
	• Protective immunity does not always occur with Type 4 reactions
	• Three varieties of Type IV Hypersensitivity:
	  • Contact hypersensitivity
	  • Tuberculin type hypersensitivity
	  • Granulomatous hypersensitivity
	 
	Granuloma formation around a schistosome egg (center) destroys the liver tissue.
	 
	Wristwatches may stimulate contact hypersensitivity reactions.
		SLIDE 41 Type IV reactions are mediated by T-cells and not by Bcells/antibodies!! Because of this, Type IV reactions take longer to occur than the other types of hypersensitivity. Consequently, even though there is an immune response occurring during Type IV reactions, it is not an effective immune response!! There are three varieties of Type IV hypersensitivity: (1) Contact, (2) Tuberculin, and (3) Granulomatous.

Slide 42	*T Cell Mediated Hypersensitivity*  	SLIDE 42 Type IV reactions normally involve chronic inflammation and are mediated by CD4+ T cells that recruit CD8+ T cells, neutrophils, and eosinophils that cause tissue injury.

Slide 43		SLIDE 43 Type IV reactions are mediated by T cells to cause chronic inflammation and different responses as shown by this diagram.
Slide 44		SLIDE 44 Contact hypersensitivity occurs when a hapten enters the skin and attaches to a body protein. A Type IV reaction may then be produced against this conjugated hapten. This reaction is then mediated by CD4+ T -cells and macrophages.
Slide 45		SLIDE 45 An eczematous reaction may occur at the site of contact with re- exposure to the hapten. The reaction is usually greatest 48 hours to 72 hours after re-exposure to the hapten. Note the mechanism of contact hypersensitivity after exposure to poison oak.

Slide 46		SLIDE 46 Follow the process of sensitization during contact hypersensitivity.
Slide 47		SLIDE 47 Contact sensitivity involves both a sensitization phase and an elicitation phase. Note that CD4+ Th1 cells are normally involved in these reactions.
Slide 48		SLIDE 48 The tuberculin type hypersensitivity reaction is medically important. During tuberculin skin tests, small amounts of the tuberculin antigen are injected intradermally to determine if a person has been previously exposed to tuberculosis. An induration will appear at the site within 48 to 72 hours if the person has been previously exposed to TB. An induration does not indicate if the person is infected with TB rather only that the person has been exposed to TB at sometime in their lifetime.

Slide 49		SLIDE 49 Granulomatous hypersensitivity develops against persistent antigens and is considered pathologic. Examples of granulomatous hypersensitivity include TB, leprosy, schistosomiasis, and sarcoidosis. Granulomatous hypersensitivity results from secretory epithelioid and giant cells, macrophages, and lymphocytes. The cells produce tissue fibrosis around the persistent antigens to form granulomas. Formation of granulomas in an organ can significantly impair that organ's function- for example, tuberculosis granulomas in the lungs affect respiration, and schistosome granulomas in the liver that impair portal flow.
Slide 50		SLIDE 50 Note the example of a granulomatous reaction, and how these cells form a mass around the bacteria to try to wall it off & protect the rest of the body. Unfortunately, these granulomas can cause significant damage to the tissues surrounding the antigen.
Slide 51		SLIDE 51 There are a variety of antigens that can induce Type IV Hypersensitivity. Avoid them if you can!!

Slide 52	*Summary of Delayed Hypersensitivity Reactions* **Type** / **Reaction Time** / **Clinical** / **Histology** / **Antigen** Contact / 48-72 hrs / Eczema / Lymphocytes macrophages edema / Epidermal nickel poison ivy Tuberculin / 48-72 hrs / Local Induration / Lymphocytes macrophages monocytes / Intradermal tuberculin Granuloma / 21-28 days / Hardened skin & lung / Fibrosis Epithelioid Giant Cells Macrophage / Persistent Ag or Ag/Ab complexes	SLIDE 52 Compare the 3 different types of delayed hypersensitivity. Note the time difference between contact & tuberculin hypersensitivity vs. the granulomatous reaction.

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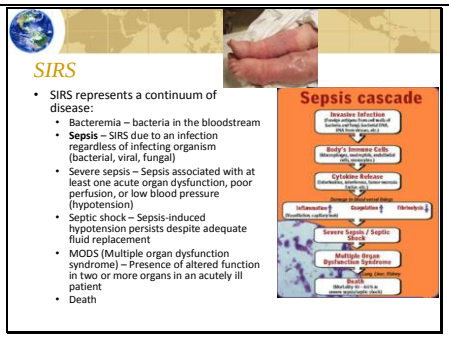
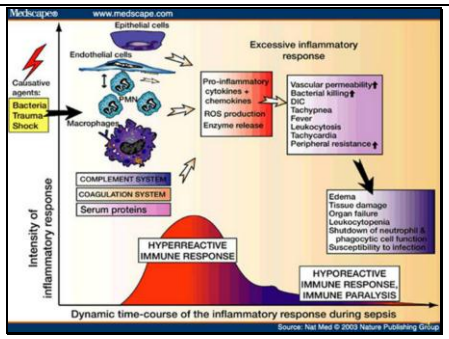
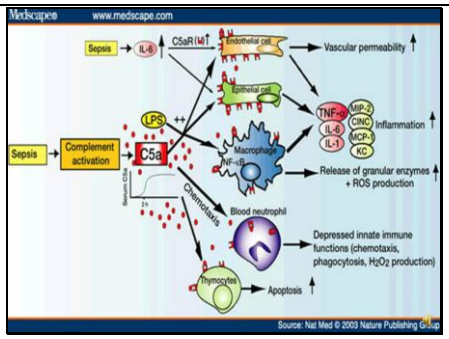
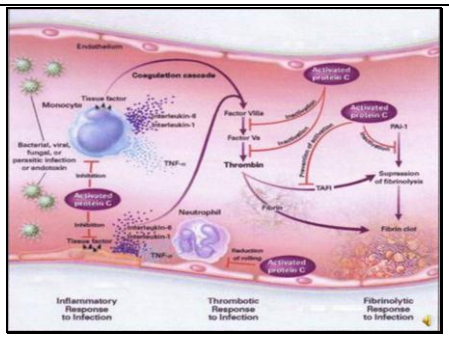
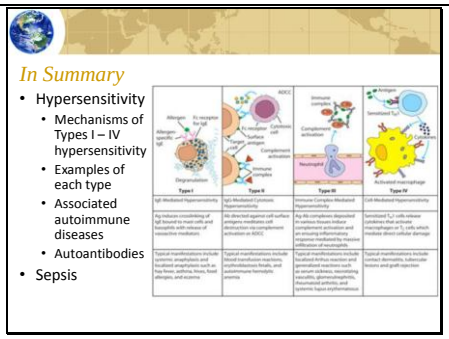
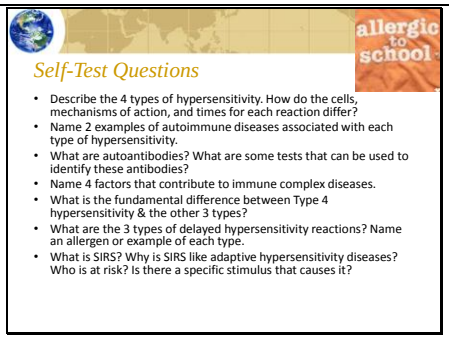
	Innate Hypersensitivity: Systemic Inflammatory Response Syndrome (SIRS)
	• Effects of a systemic activation of the innate immune response without regard to the cause
	  • The body produces an exaggerated response to the stimulus
	• Everyone is potentially at risk for SIRS
	  • However, certain individuals are at greater risk including critically ill patients and immunocompromised patients
	  • Factors contributing to increased mortality from sepsis
	  • underlying disease
	  • older age
		SLIDE 53 Systemic Inflammatory Response Syndrome (SIRS) is an exaggerated systemic activation of the innate immune response without regard to the stimulus. The stimulus may be infection; but, it may also be a bum, trauma, or other disease. Everyone is potentially at risk for SIRS; however, those with concurrent disease and increasing age are at higher risk. There are criteria for the diagnosis of SIRS, despite different stimuli such as infection, bums, pancreatitis, and trauma. However, the outcome is the same, the production of an exaggerated inflammatory response that overwhelms the homeostatic balance and produces severe organ damage and possible death in the individual. Criteria for SIRS include: Temperature greater than 100.4"F or less than 96.8"F Heart rate greater than 90 beats/min [Normal heart rate is 60 to 100 beats/min] Tachypnea (a respiratory rate greater than 20 breaths/min) or hyperventilation (PaCO2 < 32 mm Hg) White blood cell count greater than 12,000 cells/mm3, less than 4,000 cells/mm3, or the presence of greater than 10% immature neutrophils

Slide 54		SLIDE 54 SIRS is actually a continuum of disease from mild to severe. Note the progression of sepsis from initial infection until death.
Slide 55		SLIDE 55 During the inflammatory response of SIRS, there is a hyperactive immune response followed by a hyporeactive immune response (as the immune components are used up and not replaced sufficiently). Alter the hyperreactive response has occurred, there are insufficient immune components for a healthy immune response.
Slide 56		SLIDE 56 Note the effect of C5a during SIRS. C5a stimulates several other cell types to release potent cytokines that can lead to a severe septic reaction, as their effects trigger a strong inflammatory response.

Slide 57		SLIDE 57 Notice that there are three responses to infection (etc.): Inflammation, Thrombosis (clot formation), and Fibrinolysis (breakdown of clots). In sepsis, these responses become over reactive and poorly controlled thus resulting in systemic organ damage and the potential for disseminated intravascular coagulation (DIC).
Slide 58		SLIDE 58 What you need to know . . .
Slide 59		SLIDE 59 Self test questions for hypersensitivity. Is everyone allergic to school at this point in the semester? It is almost over & you have made it this far! I'm sure you will always have a special sensitivity to Immunology after we are done, but hopefully you won't break out in hives at the mere mention of the subject in the future!!