HOST DEFENSE

SMALL GROUP PROBLEM SOLVING SESSION

ATOPY AND ALLERGY

Small Group Classrooms

LEARNING GOALS

Integrate the concepts of IgE Immunology with their clinical consequences.

BACKGROUND READING

Janeway: Same assigned reading for the *Immunology of IgE* lecture-Janeway 8th edition: 174-75; 421-23; 571-594; 600-603 **AND 718-719 & 601-603. The latter cover 2 new topics are not included in the lecture material.** Articles posted on HD website.

DEVELOPED BY

John A. Robinson, MD

Revised: 11/08/12

Before coming to class:

1. Read assigned chapters/ pages and develop answers for **ALL** the questions in the 4 clinical vignettes

During the Small Group Session:

2. Each small group (**should be 4-5 peers- please do not sort yourselves into large groups-you will learn much less**) should discuss the four case studies and decide the best solutions to the specific integrating questions associated with each case.

3. After approximately an hour of discussion by the subgroups, the facilitator will recapitulate the answers to the integrating questions by selecting a subgroup to present a synthesis of their relevant discussions to the entire group. Facilitators will select, at their discretion, a small group for the discussion of the individual cases.

4. History has shown that students who don't contribute to the Small Groups do not do well in the Course (remember that about 25-30% of the final comes from small groups!) and also have been assaulted by their fellow group members

5. At the end of the session, a master answer sheet will be posted on the Host Defense website.

INTRODUCTORY CASE TO HELP YOU MAINTAIN YOUR PERSPECTIVE ABOUT IgE IMMUNOLOGY.

ALL OF YOU SHOULD UNDERSTAND THIS VIGNETTE FIRST.

A 24 year old woman was admitted with intermittent hives (urticaria), edema and parasthesias. She was a Peace Corp employee who had been stationed in Africa doing pisciculture research. She had been previously healthy and there were no symptoms of sweats, fever or weight loss. The physical exam revealed hepatosplenomegaly and a swollen right leg. The only laboratory data of interest were a markedly elevated total white blood count with 32% eosinophils (normal: ~1%) and a concentrated blood smear that revealed the presence of Loa Loa microfilaria (a parasitic worm). An ELISA IgG test for the parasite was positive and a serum RAST was also positive.

QUESTIONS:

1. The patient had a parasitic infection transmitted by flies and endemic in central and western Africa. Predict **what cytokine(s)**, if measured in her plasma, might be elevated in this patient's blood.

2. What available laboratory data led to the conclusion you made to the question in #1.

3. Are you surprised that the antibody detected by ELISA was an **IgG?** Predict what other isotypes, if any, are elevated and may have parasite specificity.

4. Does this patient have an allergy or is she responding normally to an infection?
Faculty answer: This patient does not have an allergy in the pathologic sense of the term.

Case 1a

An older physician, surrounded by a well tended summer flower garden, is relaxing on his deck. It's hot out and he is maintaining fluid volume with diet Pepsi (actually a Dogfish Head IPA "60"). He takes a sip and feels a foreign object in his pharynx and then a sharp pain in his neck. Five minutes later he has severe abdominal cramping, diffuse itchy hives and difficulty breathing. His wife, a critical care nurse, notes his distress and treats him immediately using drugs from their home first aid kit.

Questions:

1. What happened to the doctor?

2. Describe the immunologic steps that occurred between the precipitant and the abdominal cramping and shortness of breath.

3. Are there any lab tests that could be helpful that should be done after this episode- if he survives?

4. What options does the patient have to avert this in the future?

Case 1b

A two-year old boy was tormenting his six -year old brother-actually the children of the victim in Case 1a). The older boy, in a fit of pique, smashed a homemade peanut butter sandwich into the little one's face! The two-year promptly developed a swollen eye and massive itchy swelling of the cheek on the side of the swollen eye. About 20 minutes later he began to wheeze. Unfortunately the six-year old now had a way to prevent further harassment and used it on several occasions with similar results until the two-year-old was big enough to protect himself. The younger sib, now 20, when to a Thai restaurant and had a spicy cold beef salad and chicken satay. He immediately developed severe abdominal cramping, facial flushing and vomiting.

Questions:

1. What was the most likely etiology of his dilemma?

2. Speculate on specific sources and contributing factors that could have precipitated his

asthma but also the skin and gastrointestinal symptoms?

3. Develop a strategy for preventing this in the future. Speculate on possible vaccine preparations that could ameliorate or prevent this reaction.

Case 1c

The uncle of the 2 boys in case 1b and the brother of the doctor in 1a is a beekeeper. When he started his business, he has several severe reactions to bee stings, but he persevered and now gets stung multiple times a week and never has a allergic reaction.

1. Can you postulate an immunologic mechanism(s) that could explain this?

Case 1d

A 6 y/o boy with leukemia, the brother of the 2 boys in case 1b, who was known to have a peanut allergy already, had an severe anaphylactic reaction during a platelet transfusion.

1. Can you postulate an immunologic mechanism(s) that could explain this?

Case 2

A seventy-two year old female from a dairy farm in Vermont has an aortic valve replaced. Unfortunately the new valve became infected with a bacterial organism that was resistant to almost all antibiotics but, strangely, remained very sensitive to penicillin G. An alert medical student notes that the patient reported having a "rash" a long time ago after receiving an antibiotic for "strep throat". The only other history that was interesting was that 2 siblings had "bad asthma" when they were in high school.
Intravenous penicillin was begun. About 10" after the infusion was started, the patient began to wheeze and then went into shock. Fortunately, a rheumatologist/allergist was making rounds nearby and realized what was happening and was then able to successfully treat the patient. Two weeks after discharge, the patient, feeling extremely fortunate to be alive, bought a "lucky" bracelet at a State fair and avowed to "never take it off". To her dismay, 3 weeks later she noted intense itching and a red, bumpy rash under the bracelet.

1. What happened in the hospital? Describe the almost fatal immunophysiology?

2. What if the patient didn't ever have a rash of any kind and had never been treated with any kind of antibiotic before? How could she have been sensitized?

3. Describe how penicillin, a very small molecule, becomes immunogenic.(Hint: Google "hapten" or go to the background reading to figure this out.)

4. Describe the unlucky immunological response caused by the lucky bracelet.

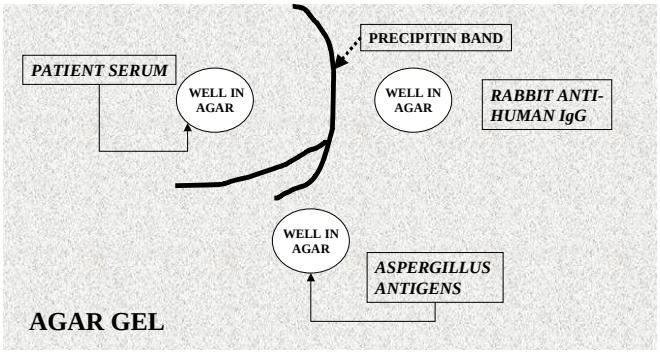
Case 3

A twenty-four year old florist developed chronic wheezing that required daily inhaler therapy and a sporadic need for high doses of oral corticosteroids to prevent severe shortness of breath. He thought there was a link between the latter episodes of severe shortness of breath and his plant repotting work assignment in the shop. A consulting pulmonologist did not feel that he had typical asthma and the patient underwent a bronchoscopy. Secretions removed at that time contained massive numbers of eosinophils and neutrophils but did not grow an organism for the first 3 or 4 days after the procedure. A complete blood count revealed an increase in the absolute number of circulating eosinophils and a very high IgE serum level. A RAST test was done for grass, mites, and aspergillus (a fungus) and found to be strongly positive for the fungus. A gel diffusion test on the patient's serum revealed strong precipitating bands between the patient's serum and fungal antigens. *The **Ouchterlony** or agar gel immunoprecipitin assay technique is a time revered immunologic assay that analyzes antigen-antibody precipitation in*

gels. Wells are punched into agar gel and antigens are placed in individual wells and antibodies-known or unknown- placed in opposing wells. The proteins are allowed to diffuse through the gel. If there is a specific antibody for the antigen diffusing towards it, a visible precipitation band will develop. ***The # of precipitin bands that form and their fusion patterns provide information on the number of specific antigens/antibody systems present and the isotype of the antibody.*** *This technique is rarely used anymore but in this particular patient illustrates an important principle. (To the astonishment of the faculty, a question about this technique was on a recent Board exam also!)*

Agar Gel Immunoprecipitin assay

(SEE NOTES FOR TECHNIQUE)



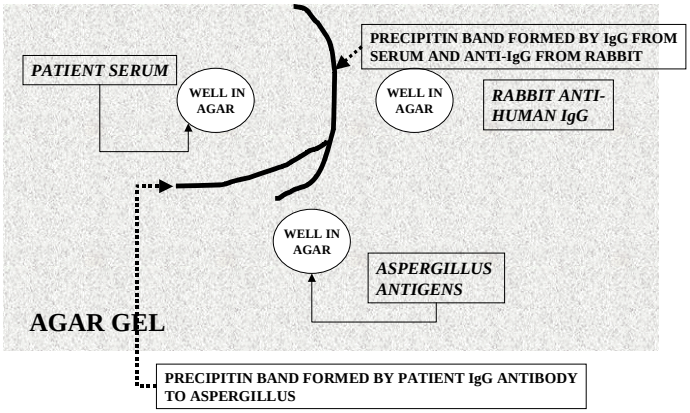
Questions:

1. Interpret the RAST findings and speculate on at least one probable etiology of his pulmonary disease. What would you predict grew in the laboratory over the next 7-10 days from the pulmonary secretions obtained by bronchoscopy?

2. The gel diffusion test appears to have detected an antibody isotype that does not correlate with his clinical presentation: What is going on here? Review the first vignette in this small group for the solution.

Agar Gel Immunoprecipitin assay

(SEE NOTES FOR TECHNIQUE)



3. Two distinct immunological reactions are occurring in the patient's lung. Describe the immunological reactions that recruit eosinophils and neutrophils from the bone marrow and culminate in their infiltration into bronchial secretions.

4. Why do corticosteroids have an efficacious effect in this type of syndrome? Reason to points in the immune response where they (steroids) could be acting. If you could design a drug that would increase the expression of transcription factors like the FoxP3 family, would it be reasonable to try them in patients with asthma?

Case 4

Three unrelated stories…or are they??

a. Crohn disease and ulcerative colitis are debilitating, chronic inflammatory diseases of the bowel. The epidemiology of these diseases is interesting in that they occur almost exclusively in industrialized societies. This observation is reminiscent of the markedly increased incidence of allergy in the western world.

b. Many children in Africa are infected with intestinal parasites, usually worms. There is a low rate of asthma in African children from the more underdeveloped countries. There have been several UN campaigns to rid the children of gut parasites. These campaigns activated the "law of unintended consequences"

c. Totally germ free mice are very susceptible to inflammatory bowel disease and asthma. If their gut microflora is restored they were no longer susceptible to the development of either disease.

Case 4a: A patient had the misfortune of having severe asthma and Crohn's disease. He had failed all forms of anti-inflammatory and immunosuppressive therapy. He was fed live whipworm ova harvested from pathogen free pigs every thirty days for 6 months. The patient went into a clinical remission of the inflammatory bowel disease. Amazingly, he also did not have another attack of asthma for over 2 years.

A second patient had severe ulcerative colitis and infected himself with whipworms (relatively innocuous worm). The disease went into remission.

Questions:

1. Predict what type of cell response is mediating inflammation in the gut in these 2 inflammatory bowel diseases. Also postulate what cytokines and T cell subsets might be found that usually aren't found in the gut

2. Predict what the live worms did and explain how it happened.

3. You should be able to predict what happened to some of the African children in case 4b!

4. You might be able to predict several immune cell types and cytokines that would be present in the lungs of germ free mice with asthma and how those cell types and cytokines might change after letting them graze on the floor at O'Hare airport, Terminal 3.The answer lies in the innate immunity lecture and Dr. Knight's lecture on microbiota and the immune response

Ref: Olszak et al. Microbial Exposure during early life has persistent effects on NKT function. Science. . 336;489. 2012