Sheakley M, Conran P, Moore M, LaVille A. !!TBL!! Inflammation and blood clotting case for first year medical students -- team based learning format. MedEdPORTAL; Available from: http://www.aamc.org/mededportal ID=3175
I. Title: Inflammation and blood clotting case for first year medical students – TBL format

II. Purpose: By the conclusion of this TBL module, students will be able to associate the underlying mechanisms responsible for inflammation, identify histological sections of inflamed tissue, and discuss the underlying cellular mechanisms responsible for inflammation. In addition, students will be able to discuss the process of blood clotting, including the factors involved in the intrinsic and extrinsic coagulation cascades. Finally, students will be able to describe and distinguish between the clinical tests used for diagnosis of clotting disorders.

III. The Learning Objectives:
   a. Learn to work in small groups effectively to solve a clinical problem.
   b. Identify the signs and symptoms of inflammation.
   c. Distinguish histological sections of inflamed tissue and specific cell types within the tissue.
   d. Associate the underlying cellular mechanisms responsible for inflammation.
   e. Describe the process of blood clotting, including the factors involved in the intrinsic and extrinsic coagulation cascades.
   f. Distinguish and select between the clinical tests used for diagnosis of clotting disorders.

Advanced Preparation Assignment: This TBL module was designed to be used fairly early in the first year of medical school when students have completed histology, cell biology, and basic biochemistry courses. It is intended to assess and overall understanding of inflammation and blood clotting. The materials for this module can be found in:
   • Principles of Medical Biochemistry, Meisenberg and Simmons, Mosby; 1998: 534-544

IV. Readiness Assurance Questions: (IRAT and GRAT)

1) Which is the only leukocyte that, after entering the connective tissue from the bloodstream, can re-enter the bloodstream?

*) lymphocyte
B) neutrophil
C) monocyte
D) basophil
E) eosinophil

2) The leucocyte that contains the major basic protein is the

A) neutrophil
*) eosinophil
C) monocyte
D) lymphocyte
E) basophil
Inflammation and Blood Clotting Case for First Year Medical Students – instructors version - TBL
Authors: Moore, LaVille, Conran and Sheakley

3) What laboratory analysis would be most appropriate in a patient who you suspected took regular doses of aspirin daily?

A) Activated partial thromboplastin time
B) Bleeding time
C) Prothrombin time test
D) Plasma antithrombin levels
E) Plasma levels of factor X

4) After a traffic accident, a 34-year-old lady was admitted to the intensive care unit for treatment. On the second day of admission a blood sample was taken and sent to the laboratory for biochemical analyses. He liver function and renal function test were normal. The following findings would be consistent with:

Albumin 30 g/L (normal 35 – 45 g/L)
C-reactive protein 68mg/L (normal < 10 mg/L)
Plasma immunoglobulin levels normal

A) Acute nutritional deficiency
B) Chronic infection
C) Acute phase response to injury
D) Nephrotic syndrome
E) Liver cirrhosis

5) Which of the following compounds is an inhibitor of platelet aggregation?

A) Thromboxane A2
B) Adenosine diphosphate (ADP)
C) Aspirin
D) Thrombin
E) Prostaglandin

6) Which of the factors in the intrinsic pathway is responsible for the cleaving and activation of factor X of the common clotting pathway?

A) Antihemophilia factor A
B) Hageman Factor
C) Factor Va
D) Christmas factor
E) Stuart-Prower factor

7) A clinical complication in a patient with a hypoalbuminemia is

A) renal failure
B) acute infections
C) edema
D) pulmonary emphysema
E) hepatic dysfunction
8) Which of the following increases dramatically in an acute phase response?

*) C-reactive protein  
B) Transferrin  
C) Albumin  
D) Thyroid binding globulin  
E) Immunoglobulins

V. Group Application Exercise: case with 5 questions

A mother brings her three-year-old son into the emergency room of a local hospital. The boy is crying hysterically. The mother says that earlier that day the boy was playing in the back yard with his older sisters. He had gone over to pick a rose off of a rosebush when he suddenly started screaming and crying. There is a region of swelling and redness on his arm and the doctor who examines him says that it looks like the boy was stung by a bee. The doctor says that the boy does not appear to be having an allergic reaction to the sting, and he releases him without any treatment. The mother asks why her son's arm is swollen and the Dr. says it is because of fluid accumulation.

1)  What is the mechanism of fluid accumulation seen around the bee sting in the picture above?

A) Decrease in blood osmotic pressure  
*) Increase in blood hydrostatic pressure  
C) Increase in water absorption by proteoglycans  
D) Increase in Na\(^{+}\) concentration in the extracellular fluid

Explanation of correct answer: the bee sting initiated an inflammatory response which resulted in vasodilation around the area of injury. The vasodilation increased blood flow to the region, thus increasing local blood hydrostatic pressure. The increase in blood hydrostatic pressure, along with the increased permeability of the capillaries (due to histamine production by mast cells…see answer explanation for question #3 for details) caused an increase in filtration of fluid to the interstitial space, leading to fluid accumulation around the site of the bee sting.
2) If the inflamed area on the boy's arm were biopsied, the histological section would look similar to the image below. What kind of cell is indicated by the arrows in the image below?

A) Lymphocyte  
B) Fibroblast  
C) Macrophage  
D) Neutrophil  
*) Mast cell

Mast Cells from Wikipedia
Page Version ID: 220391038

Explanation of correct answer: Mast cells are normal constituents of connective tissues and lamina propria of mucous membranes. They are abundant at sites of inflammation (as shown here) where they play a central role in immediate allergic reactions. They can be recognized by their large abundant granules.

3) What role does the cell illustrated above play in the swelling around a bee sting?

A) It secretes a factor that stimulates the release of C reactive factor from liver  
*) It secretes histamine  
C) It secretes IgE  
D) It secretes Hageman factor

Explanation of correct answer: Histamine receptors are found (among other places) on smooth muscle cells encircling blood vessels. When histamine is secreted by mast cells and binds to these receptors, it triggers vasodilation by causing the smooth muscle cells around blood vessels to relax. Histamine also binds to histamine receptors on endothelial cells, transiently loosening their tight junctions. This causes gaps to open up between endothelial cells resulting in increased permeability of capillaries and venules.

Several days later, the mother brings the boy to see his regular pediatrician. The boy has been scratching the insect bite (even though she has told him repeatedly not to) and it has been bleeding on and off. She noticed that it seemed to take an unusually long time for the boy's blood to clot and she had noticed this with him before. She told the doctor she was concerned about a possible infection of the bee sting and also about her son's slow blood clotting.

4) How would you determine if the boy's slow clotting time was due to a clotting factor defect or a platelet defect?

A) Measure bleeding time  
B) Measure activated partial thromboplastin time (APTT)  
C) Measure hematocrit  
D) Measure haptoglobin  
*) A and B
Explanation of correct answer: Measuring the bleeding time gives information on platelet function and disorders while APTT gives information on the clotting factors of the intrinsic pathway. In this way you lead them towards a clotting factor defect and not a platelet defect.

5) If you found that the boy had an abnormal measure activated partial thromboplastin time (APTT), what would you measure next?

A) Factor VIII concentration
B) Factor VII concentration
C) Factor X concentration
D) fibrinogen concentration
E) Fletcher factor

Explanation of correct answer: Because he has a slow clotting time it means that one of the factors is deficient and the most common here would be factor VIII. So we measure this factor first to try to find the deficiency.

6) If the diagnostic test for Factor VIII concentration revealed normal levels, and the bleeding time was 11.5 minutes (normal bleeding time is 2-8 minutes), which of the following proteins would you investigate next?

A) Prothrombin
B) Fibrinogen
C) Antithrombin III
D) von Willebrands factor
E) Tissue factor III

Explanation of correct answer: The combination of a slow bleeding time and a normal factor VIII concentration would suggest a platelet adhesion problem, which would point to von Willebrands disease. So, von Willebrands factor should be tested next.

VI. Context: This case is one of three used for the Progressive Academic Education (PAcE) Program, an independent study program for first year medical students, at Ross University School of Medicine.

VII. Facilitation Schema: (Explanation of the Team Based Learning (TBL) format)
This case was written to be used in a Team-Based Learning (TBL) format. TBL cases utilize a specific written format and method of facilitating to produce very effective small group and class discussion. Michaelsen, Parmalee, McMahon and Levine describe in detail this theory and method in the book “Team-Based Learning for Health Professions Education”. You can also learn more about TBL at http://www.ou.edu/pii/teamlearning/.

In short, TBL cases should be written to utilize the “Four S’s” in order to foster team work and group discussion. These are: (1) the students should be working on a problem that is significant or relevant to them and/or their course of study (2) all students in the class should be working on the same problem or assignment, (3) students should be required to make a specific choice, and (4) group should all simultaneously report their choices.
1. If the case/problem is not perceived as significant or relevant, students will think they are being asked to do “busywork” and will put forth just enough effort required to get a decent grade.

2. It is important that all groups are working on the same problem because this enables a discussion both within group and between groups. If each of the groups is working on a different problem, then there is no common ground for discussion between groups.

3. The assignment should be written so students have to make a specific choice (i.e. put a multiple choice question at the end of the assignment). If students are asked an open-ended question at the end of the assignment, they make come up with one or two answers then end their discussion. If faced with a choice between five to seven possibilities, they have to discuss each possibility fully in order to accept it or reject it. Thus, more discussion is elicited when students are asked to make a specific choice. The choices should be written rather vaguely to stimulate discussion, with one best choice but other possible correct choices.

4. After group discussion, the group should be instructed to report their answer choice simultaneously. I do this by giving each group an envelope that contains 5 colored note cards lettered A, B, C, D, or E. The groups are asked to raise the note card which corresponds to their answer choice on the count of three. This allows the facilitator to immediately assess the overall performance of the class, and prevents groups from choosing their answer based on what other groups think. It also requires each group to commit to one answer choice and be ready to defend it.

This session requires approximately 80-90 minutes to complete in the TBL format. When students arrive to the class/session, they should sit in their assigned groups and the quizzes should be distributed. The students should be given approximately 15 minutes to complete the IRAT and 15-20 minutes to complete the GRAT, then allow 20 minutes for whole class discussion following the GRAT.

Next, the clinical application case should be distributed and the groups should discuss the case within their groups and answer the questions. Initially the groups should be allowed 15 minutes for this group discussion, then if more time is required, you can add an additional 5-10 minutes as needed. This discussion period should be closed-book, and no outside resources (internet, handouts, journals, etc.) should be used during the discussion or to answer the questions. After the discussion is finished, the students should simultaneously report their answer for the first question when you instruct them to do so. To facilitate simultaneous reporting, it is useful to hand out colored note cards that have the answer choices (A, B, C, D, E) written on them. Then you can ask the groups to raise the note card which corresponds to their answer choice on the count of three. This allows immediate assessment of the class responses, and makes it easy to facilitate whole class discussion based on which answers the students chose. After the first question is discussed, proceed to the remaining questions in the same format. Allow 15-20 minutes for whole class discussion of all of the questions.

**IX. Our experience with this module:**
We have used this case one time thus far in a class of 70 students who were divided into eleven groups. We found that the first three questions were fairly straight forward and
most groups got the answers correct. There was more discussion about questions 4 and 5 as these are the more clinically relevant questions, and the students are not used to analyzing diagnostic tests at this point in their medical education. In our experience, the instructors of this case should be prepared to discuss specific blood clotting disorders and the different diagnostic tests used to differentiate between them.