## Teaching Notes

### By *Sharon Cisneros*

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**BIO 121-Biology I**

Department: Biology

Level: **Lower Undergraduate**

Course type: **Lab + Lecture**

Students: **Majors + Non-majors**

Number of Students: 35 per class

**Module Information**

Original Module Name: Nicholas’ Story

Link to Original: <http://dx.doi.org/10.25334/H82J-3C28>

Modified Module Name: **Sickle Cell Anemia using Nicholas’ Story (to be used after discussing Genetics module in textbook)**

Modification Learning Goals:

* **To understand what Sickle Cell Anemia is and what population it affects?**
* **To understand what the hemoglobin molecule is, what it is made up of, where the sickle cell mutation occurs in the gene, how it affects people who have this gene,**
* **To learn about what types of medications are used to treat people who have the disease**

**Teaching Notes**

*(Think about what you would like to read about this activity if you came back to it in 2 years)*

Suggestions for this section (not all required, and extras always welcome):

* What did you change and why?

**The majority of my students are recent graduates from high school. Most of them do not have a strong understanding of the molecular level of a cell, namely proteins, and how the structure of a protein dictates the function of that protein. Besides this, dealing with former high school students and their temperaments is also a challenge (talking in class, laughing, disrupting class, etc.)**

**My goal in this exercise was not to cover the minute details of covalent, non-covalent interactions, hydrophobic residues, intermolecular forces, etc., but rather present a clear, yet simplified version of what sickle cell anemia is and expose them to the molecular structure of a hemoglobin, rather than talk about salt bridges, carboxyl terminus groups, or prosthetic groups, etc. Showing them the 3-D structure of the molecule and being able to manipulate and move the structure around was important for their understanding. Being able to see the effect of changing an amino acid was also important. The many parts of the case were more than I would’ve been able to cover in one lab period. The boxes were great, but too much for me to talk about, so I needed to present this more as a lecture, rather than an in-depth case study that students would be able to work on in groups. I used this case study as a template for me to further discuss this disease.**

Here is how I ran the case in my class:

1. I started out with YouTube video included in the original case and followed that by another YouTube video titled “[Living with and managing Sickle Cell disease](https://www.youtube.com/watch?v=J7QaadNmQOc).”
2. Following this students watched a TedEd video “[Sickle Cell Disease: How this disease changes the shape of your cells](https://www.youtube.com/watch?v=hRnrIpUMyZQ)”
3. I then introduced students to the four levels of protein structure using my own slides.
4. I showed students pictures of hemoglobin structure and point out that they are
   * made up of 4 heme groups surrounded by the globin proteins
   * the heme contains iron, gives a red color,
   * globin proteins are made of 2 types of polypeptide chains
5. Then I described that people from certain countries in the world have a higher incidences of sickle cell disease. Besides sub-Saharan Africa, these include South America, the Caribbean, Central America, Saudi Arabia, India, Turkey, Greece, Italy.
6. Then I described what sickle cell anemia is:
   * red blood cell (RBC) disorder,
   * hemoglobin molecules become sticky in low oxygen concentrations
   * RBC becomes sickle-shaped (SS),
   * cells die prematurely, constant shortage,
   * SS RBCs clog flow in blood vessels, cause pain and infection, acute chest syndrome and stroke,
   * only cure for sickle cell anemia till now has been bone marrow transplant and stem cell transplant
7. I then described some common types of sickle cell disease (see <https://sicklecellspeaks.com/understanding-sickle-cell/types-of-sickle-cell/>)
   * HbSS: This is the most severe form, both parents have the sickle cell gene – the individual produces only HbS and leads to sickle cell anemia
   * HbSC- This is the second most common type where one parent has a sickle gene and one parent has hemoglobin C (carrier). This could lead to a HbSS or a milder form of sickle cell disease.
   * HbS Beta Thalassemia-one parent has the sickle gene, one parent has beta-thalassemia gene, there are 2 types of beta (0 and +) 0 thalassemia is severe form of sickle cell disease, + thalassemia is milder form
   * Sickle Cell **trait**- HbAS one parent has the sickle gene, one parent has a normal gene, usually no signs of disease and live a normal life, but can pass the trait on to children
8. Following this I discussed the genetics of Sickle Cell disease
   * Hemoglobin is a protein molecule in red blood cells that carries oxygen from lungs to tissues and returns CO2 from tissues back to lungs
   * There are 280 million hemoglobin molecules in each red blood cell
   * Each hemoglobin is made up of 4 proteins (globulin chains that are connected together) each globulin subunit has 2 alpha and 2 betas, encoded by alpha and beta genes
9. Visualization of Hemoglobin:
   * I showed a picture of all amino acids and pointed out to students that sickle cell disease is caused by a point mutation in the beta-globin gene. The mutation changes a glutamic acid to a valine.
   * This gene (beta globin) is located on chromosome 11 – so that is where the mutation happens.
   * I showed a picture of hemoglobin with 4 globin chains and 4 heme groups
   * I showed a picture of normal hemoglobin that has glutamate and then showed the mutated hemoglobin molecule - instead of glutamic acid there is valine at position 6 in the beta globin protein.
   * We reviewed the hemoglobin structures in the virtual exhibit at Online MacroMolecular Museum (earth.callutheran.edu)
10. We also talked about drugs that are used to treat sickle cell disease:
    * Hydroxyurea –
      + Since the fetus has different oxygen requirements than an adult, fetal hemoglobin has 2 gamma-globin polypeptide chains instead of 2 adult beta-globin chains
      + After birth genes that code for gamma-globin switch off and beta-globin genes switch on,
      + This drug reactivates the production of fetal globin chains
      + Used since 1983, patients using this experience less painful crises, but it can be toxic and increase risk of leukemia
      + In 1992 a treatment plan for SCD used alternating hydroxyurea with erythropoietin (a hormone made by the kidney to promote RBSs by bone marrow) doses.
    * Voxelotor (Oxbryta) was approved in 2019
      + The active ingredient in oxbryta is a small molecule that binds to hemoglobin and increases the protein’s infinity for oxygen
      + It is approved for 12 years and older individuals,
    * Gene therapy – currently this is being tested in 12 clinical trials, I give a link to the location of information, https://sicklecellanemianews.com/gene-therapy/https://www.cbsnews.com/news/could-gene-therapy-cure-sickle-cell-anemia-60-minutes/
11. Sickle cell disease and malaria
    * I talked about researchers in 2011 in Portugal injecting sickle cell hemoglobin into the blood of normal mice before infecting them with malaria,
    * They found the sickle cell Hb could guard against malaria because mice did not get the disease.
    * Perhaps this is because humans with sickle cell disease have misshaped red blood cells that constantly breakdown and detoxify. This is probably a hostile environment for the plasmodium parasite.
    * Also sickle cells have membranes that become porous and leak nutrients that parasite needs to survive so they are eventually eliminated
12. Assessment: 8 discussion questions used as a lab (20 points)
    * 1. What causes sickle cell disease?
    * 2. Describe symptoms of sickle cell anemia?
    * 3. What is hemoglobin, where is it present in our body, why is it important for us?
    * 4. Describe structure of hemoglobin (how many chains, what types, why is iron necessary for blood)?
    * 5. How does sickle hemoglobin differ from hemoglobin, where is the mutation, what amino acid is affected?
    * 6. What is a pain crisis in the context of sickle cell anemia, what type of pain does a person experience?
    * 7. How does sickle cell protect against malaria?
    * 8. What are some current medications being used to treat sickle cell anemia?
13. I show another video called “sickle cell has many phases” <https://www.cdc.gov/ncbddd/sicklecell/materials/video.html?s_cid=ncbddd_sc_mfgn_cdc_sm_2019_12&#sc-general>

* Resources Please add any slides, websites, reviews etc. that you used to prepare for this class/case. <https://www.cdc.gov/ncbddd/sicklecell/index.html>
* <https://sicklecellanemianews.com/gene-therapy/>
* earth.callutheran.edu/Academic\_Programs/Departments/BioDev/omm/jsmolnew/hemo/hemoglobina.html#II.
* <http://www.understandinganimalresearch.org.uk/>
* Developed by Molecular CaseNet, 2019-2020-Nicholas’ Story *Authors*: Shuchismita Dutta\* (Rutgers University, NJ), Kimberley Cortes (Kennesaw State University, GA), Henry Jakubowski (College of St. Benedict, St. John's University, MN), Melanie Lenahan (Raritan Valley Community College, NJ), David Marcey (California Lutherian University, CA), Patricia Marsteller (Emory University, GA), and Cassidy Terrell (University of Minnesota, Rocester MN)
* Lessons Adapted from: Sickle Cell Anemia: A Case Study Approach to Teaching High School Genetics, Developed by Jeanne Ting Chowning, BioLab in partnership with the GENETICS Project (October 2000)

How did the activity go?

* What went well and why? **The lesson went really well. The students were definitely interested and engaged, despite the Zoom meeting format. That in itself was a challenge. Students did ask me questions afterwards, which was promising. Also, most students finished and handed in the 8 questions as a lab immediately after the class was finished. It was an easy 20 points and why not do the exercise and get the points. I felt good presenting this topic because I learned a lot from this exercise. I did include 2 questions on the final exam about sickle cell.**
* What went wrong and why? **I didn’t realize that it would take me almost 2 hours to present this. The many videos took some time, but I felt it was necessary in order to keep my students interested, rather than tune out. I would not have changed or deleted the videos because sometimes students need to hear someone different rather than their professor.**

What was the prep like?

* How much time went into prep? **I spent at least 2 to 3 hours looking for slides and looking for short and to the point videos of sickle cell. It was important that they understand that sickle cell is not an African American disease. Most of my students are Hispanic and African American and I wanted them to understand this disease should not be a type of stigma or be embarrassed or ashamed of. This is a disease that they do not have control over getting, since it is genetic, but rather, having knowledge about how to deal with this disease should they have it, is the most important thing.**
* Did you have to do any prep (i.e. grow cultures, grow seeds, order supplies) ahead of implementation? no

Would you do this activity again? **I would definitely do this activity again**

* What would you change in the future? **I would perhaps rearrange some slides or condense some slides that may seem repetitive, but I am happy with the information that was disseminated.**
* What do you wish you’d known before you ran the activity? **The after-class activity, which served as a lab, was straightforward and was not confusing, so students could easily finish the task without incident.**
* Is there anything else you would like to make note of? **no**
* How does this activity fit in your overall course curriculum? **I struggled with time constraints with this activity, because this introductory course requires that I complete as many as 14-15 chapters in the 16 week semester. My class runs for almost 3 hours, but having a student’s FULL attention span is quite difficult to sustain. I chose to delete the last chapter of the text, which was biotechnology, in order to present this case. I felt that this topic was something that students can relate to.**
* In what ways, if any, did you modify your teaching practice with this activity? **For professors that teach biochemistry and molecular biology, this case study was probably very easy, but for my class that had no previous knowledge of protein structure, I needed to take it slow and make it easy to understand, while being interesting. I realize that showing them a 3-D structure of the hemoglobin molecule might have been out of their comfort zone, I did finish my lecture with the hope that students might continue this discussion on sickle cell and protein structure in other classes.**