NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

Pulmonary Surfactant: Alveoli's Secreted Weapon

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Part I – Setting the Scene

"I'm so proud of you," Grandma said with a wink, "carrying on the family tradition!"

Jason, who had recently finished his Bachelor of Science in Nursing degree (BSN) and was interviewing for jobs in pediatrics, looked at her with a huge smile on his face. "You know, you were my inspiration. I loved listening to the stories you used to tell me about working in the hospital. You loved what you did and that was very clear."

"Well, labor and delivery was most of the time such an exciting, happy area to work in. It was easy to love it!" Grandma replied. "Helping life come into the world, and watching new parents meet their babies for the first time was something I felt honored to do. It was a positive area of medicine to work in, even though there were sometimes complications with births that would tear at my heart. Back in the 1960s when I first started as a nurse, we didn't have a good treatment for babies that were born with hyaline membrane disease, and that was always hard to watch."

"What's hyaline membrane disease?" Jason asked "I've not heard of that one."

"It's called something else now," Grandma began. "Infant respiratory distress syndrome (IRDS), I think. But it was a big deal back then and always a worry when a baby was born prematurely. Even the president of the United States, John F. Kennedy, had a son that was born early at 34 weeks and died from it. This happened while he was in office and just a few months before Kennedy himself was assassinated. But those poor babies back then, they just couldn't breathe. The alveoli in their lungs just wouldn't expand easily. They would struggle so much to inhale, because the thin walls of the alveoli were stuck together and they just couldn't get a lot of air into them for gas exchange. And when they did, separating the walls of the air sacs from each other to let the air in would cause the alveoli to tear. When the babies exhaled, the air sacs would collapse back down, their walls would stick together again, and they would be very hard to re-inflate. Usually those babies didn't live more than a couple of days after exhausting themselves and destroying their lungs just trying to breathe, and there wasn't a lot we could do."

"That sounds awful," Jason responded. "We did learn about that condition in nursing school. I didn't recognize the first name you used, but I'm familiar with IRDS. I'm so glad we now understand what causes it and have artificial pulmonary surfactants to help with treatment for those babies that aren't making enough pulmonary surfactant on their own!"

Please note: to aid you in answering the questions below, additional resources beyond your textbook may be helpful. A list of recommended online resources is given at the end of this case. Other online resources may be used to supplement as needed.

Questions

1. Summarize everything that you've learned about infant respiratory distress syndrome (IRDS) from the paragraphs above.

2. What seems to be a risk factor for being born with IRDS?

3. What type of epithelium makes up the walls of the alveoli? Describe the cells of this tissue type and draw a picture of how they are arranged to form an alveolus.

4. Grandma described the walls of the alveoli in these babies as tearing when they separated from each other during inhalation. This happened at least partially because the tissue that makes up the alveolar walls is so thin and delicate. Why does the tissue that forms the walls of alveoli need to be so thin?

5. Explain what pulmonary surfactant is.

6. What is the name of the cells that make pulmonary surfactant and where are they located in the lungs?

Part II – Chemical Properties of Water

Babies with IRDS have immature lungs that do not produce enough pulmonary surfactant and because of that the alveolar walls stick together. This is caused simply by water! Water molecules have an attraction for other water molecules, and the lungs are a very wet environment. So there are a lot of water molecules in the alveoli.

Water (H_20) consists of two hydrogen (H) atoms bound to a single oxygen (O) atom by polar covalent bonding (Figure 1). Atoms are made up of subatomic particles including protons, electrons, and neutrons. Protons have a positive charge and are found in the centrally located atomic nucleus of the atom. Neutrons have no charge and, when present, are found in the atomic nucleus as well. Electrons are negatively charged particles that are organized into specific areas surrounding the nucleus known as atomic orbitals. Electrons can move within the orbital in which they are found, but do not normally move from one orbital into another. As you can see in Figure 1, hydrogen atoms are small and have only a single atomic orbital (which contains a single electron), while oxygen is a larger atom with two atomic orbitals.

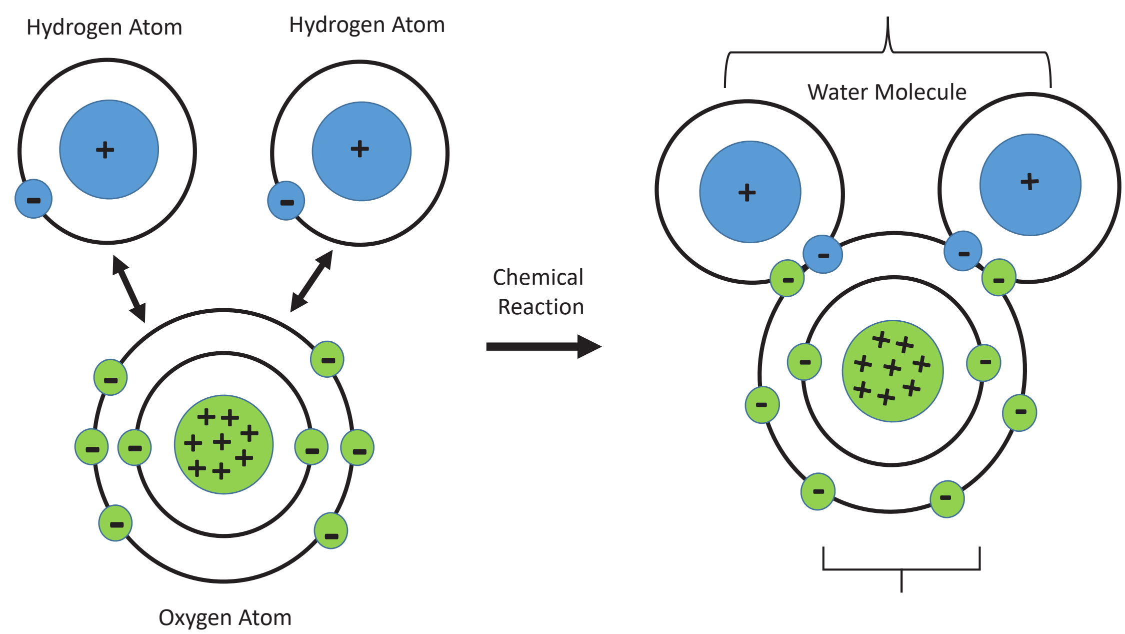

Figure 1. Polar covalent bonding leading to formation of a water molecule.

Questions

1. On the oxygen atom in Figure 1, identify and label the electrons, atomic orbitals, atomic nucleus, and protons.
2. If a single, positively-charged proton cancels out the charge on a single, negatively-charged electron (essentially a positive plus a negative = 0), would the oxygen and hydrogen atoms shown in Figure 1 have a charge? Explain your answer.

Look again at the oxygen atom above. You'll notice that there are two electrons in its first atomic orbital (the one closest to the atomic nucleus). This is because two is the maximum number of electrons that will fit in this first orbital. All of the additional electrons that oxygen has have to go into the second atomic orbital because they will not fit in the first. The second atomic orbital of an atom can hold a maximum of eight electrons before it is full.

Questions

3. Based on what you can see in Figure 1, how many electrons are in the oxygen atom's second atomic orbital? How many more does it need in this second orbital to be full?

4. Again, based on what you can see in Figure 1, how many electrons are in hydrogen's first atomic orbital? How many more electrons does a hydrogen atom need in its first orbital to be full?

5. Atoms like to exist in a state where their outermost atomic orbital is full. In the case of hydrogen, the outermost atomic orbital is the first one. With oxygen, the outermost orbital is the second. Look closely at the water molecule in Figure 1. Count up the number of electrons that are in the outermost atomic orbital of the oxygen atom and each of the hydrogen atoms. Then propose a way that each of these atoms has "filled" its outermost atomic orbital.

Sharing electrons (as seen in Figure 1) is one way that atoms join together to form molecules. However, in the case of a water molecule, the electrons are not shared equally between the hydrogen and the oxygen. Rather, the oxygen atom (which is larger and has more protons) exerts a stronger "pull" on all of the negatively-charged electrons, and thus the electrons that oxygen "shares" with hydrogen are more often found in the orbital around the oxygen atom. In addition, the hydrogen electrons that are "shared" are also more often found in the orbital around oxygen than in the hydrogen orbitals. This sets up a situation where there is now (usually) ten electrons and only eight protons on the oxygen side of the water molecule, and (usually) two protons and zero electrons on the hydrogen side of the molecule. This makes the water molecule oppositely charged on its two ends.

Questions

6. Notice that the water molecule in Figure 1 has brackets { } on the top and bottom. Using the brackets, label the end of the water molecule that will usually have a positive charge with + and the end of the water molecule that will usually have a negative charge with –.

7. If you've ever played with magnets, you may have noticed that one end of the magnet will attract metal and other magnets, and the opposite end will repel these items. Study Figure 2 for a moment, and then describe in a sentence or two what determines whether or not magnets attract each other or repel each other.

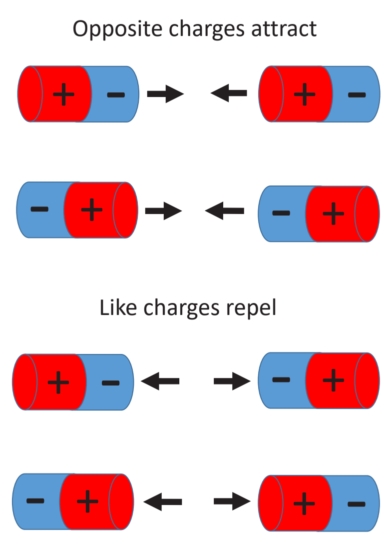

Figure 2. Magnetic interaction.

Much like a magnet, water has a positive end and a negative end, and the oppositely charged ends attract each other. Because of this attraction of water molecules to other water molecules (Figure 3), cohesion occurs. Simply put, water molecules tend to "stick" together. Water also has the property of adhesion; it tends to stick to things that aren't water as well. Imagine taking two pieces of paper and neatly stacking them on top of each other. They should be pretty easy to separate. But if you were to get the papers wet, suddenly they will stick to each other and become difficult to pull apart. If the paper is really thin and really wet, it may even tear when you try to separate the two pieces. This is because the water molecules adhere to each piece of paper, and then the attraction between the water molecules on the two sheets of paper binds the papers together (Figure 4). A similar phenomenon is at play in the lungs where very thin, wet membranes are in close contact with each other! Smaller alveoli have a diameter of about 0.2 mm, which is about the same as the thickness of two average pieces of copy paper stacked on top of each other. The simple squamous epithelium that makes up the wall of an alveolus is even thinner than the thickness of an average sheet of copy paper!

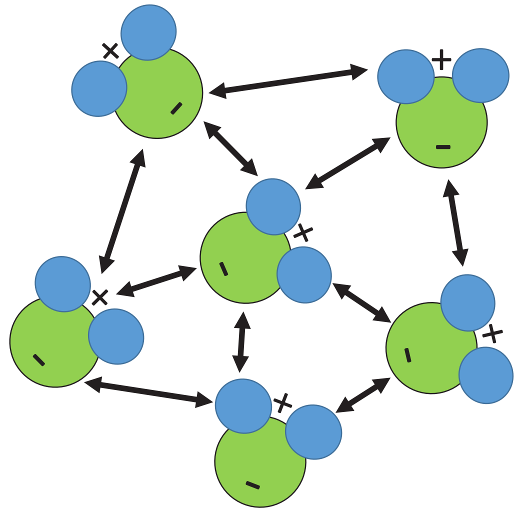

Figure 3. Attraction between the oppositely charged ends of water molecules.

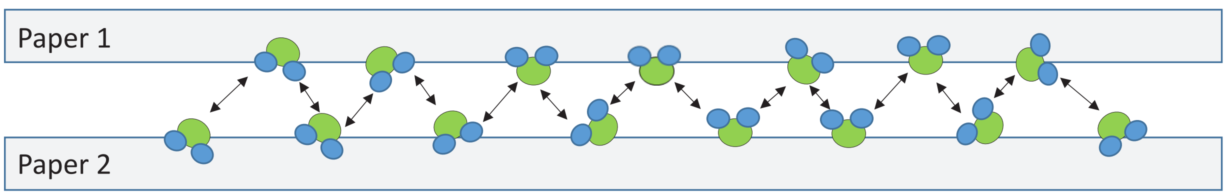

Figure 4. Representation of two wet pieces of paper stacked on top of each other with attractive forces between water molecules.

Questions

8. Based on what you've read above define "cohesion" and "adhesion" as they relate to water molecules, label Figure 4 to show where adhesion is occurring and where cohesion is occurring along the two wet pieces of paper.
9. Remember that the lungs are a very wet environment. In the picture of an alveolus that you drew previously (Part I, Question 3), add in several water molecules adhering all around the inner wall. Then explain how cohesion between those water molecules would lead to the very thin walls of the tiny alveoli tending to stick together.
10. Summarize what you've learned so far to describe how adhesion and cohesion could lead to alveoli tearing in the lungs of premature babies as described by Grandma in her conversation with Jason.

Part III – Pulmonary Surfactant to the Rescue!

Healthy, fully-developed lungs produce sufficient amounts of pulmonary surfactant to prevent water molecules from attracting each other through cohesion. This keeps alveoli inflated, preventing their walls from sticking together following exhalation and tearing during attempts to inhale. Pulmonary surfactant is composed primarily of a chemical known as DPPC (dipalmitoylphophatidylcholine), which is a large, complex molecule made up of over 100 atoms bound together. Because it is so big, DPPC is often just represented in a cartoonish way that approximates its physical structure (Figure 5). A portion of DPPC (the "head") is charged like water, but the molecule has two long "tails" that are not charged. Because the heads of DPPC are charged, they are attracted to the opposite charges on water molecules. The tails are not charged, so they have no attraction to water.

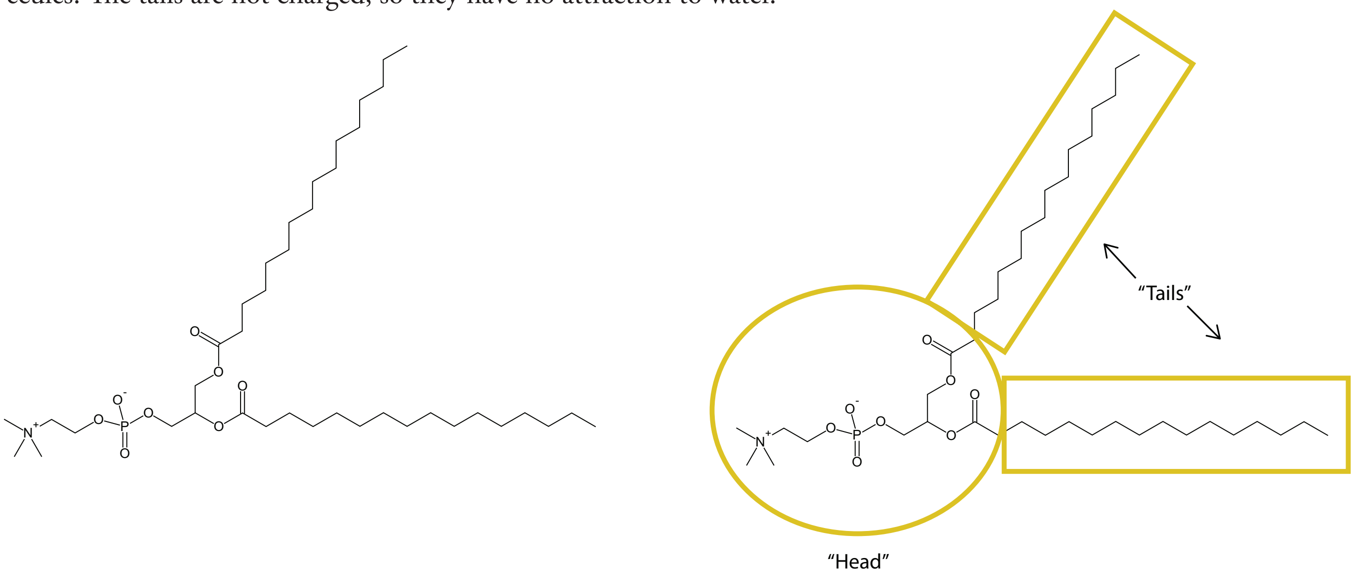

Figure 5. Skeletal structure of DPPC (left); on the right, the "head" and "tails" are indicated.

Questions

1. Examine the DPPC molecule shown in Figure 5, then fill-in-the-blanks. The ___________ (head/tail) portion of DPPC is attracted to water because it is charged. The positive charge in the head area of DPPC will be attracted to the ___________ (positive/negative) charge on a water molecule, and the negative charge in the head area of DPPC will be attracted to the __________ (positive/negative) charge on a water molecule. The ___________ (head/tail) portion of DPPC is *not* attracted to water because it is *not* charged.

2. Based on what you've determined in the question above, which of the drawings below (Figure 6) represents the most likely way that DPPC would orient itself when interacting with water, (A) or (B)? Be sure to explain your answer.

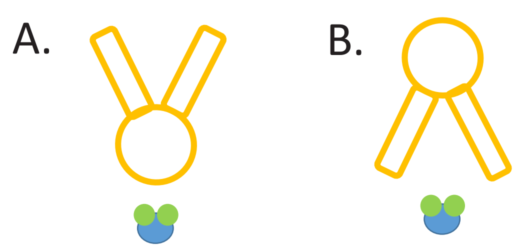

Figure 6. Options for Question 2.

3. Add a DPPC molecule interacting with each water molecule you put in your alveolus drawing from Part I, Question 3. Be sure to orient the DPPC so that the heads and tails are facing the correct direction based on how this molecule interacts with water.

4. Use what you've learned to discuss how DPPC helps to prevent alveolar walls from sticking together.

5. In his conversation with Grandma, Jason mentioned how grateful he was that we now have artificial pulmonary surfactants to help with treatment for IRDS. Do some research on treatment of this disease, and summarize your findings.

Online Resources

- Medical definition of hyaline membrane disease. MedicineNet. <https://www.medicinenet.com/script/main/art.asp?articlekey=10677>
- Adhesion and cohesion of water. U.S. Geological Survey. <https://www.usgs.gov/special-topic/water-science-school/science/adhesion-and-cohesion-water?qt-science_center_objects=0#qt-science_center_objects>
- Alveoli. Kenhub. <https://www.kenhub.com/en/library/anatomy/alveoli>
- 1,2-Dipalmitoylphosphatidylcholine. PubChem, National Center for Biotechnology Information. <https://pubchem.ncbi.nlm.nih.gov/compound/1_2-Dipalmitoylphosphatidylcholine>
- Infant respiratory distress syndrome (hyaline membrane disease). Boston Children's Hospital. <http://www.childrenshospital.org/conditions-and-treatments/conditions/i/infant-respiratory-distress-syndrome-hyaline-membrane-disease>
- Antenatal corticosteroid therapy for fetal maturation. Committee Opinion Number 713, American College of Obstetricians and Gynecologists. <https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2017/08/antenatal-corticosteroid-therapy-for-fetal-maturation>

All online resources accessible as of July 12, 2021.