

Protein Structure: Vampires and Vaccines

Framing analogy: Unforgettable Features

In colonial America every day was a struggle to survive. After a long, hard day of working in the family dairy, 21 year old Abraham and his father Thaddeus were in need of some recreation.



The night was foggy and cold as they made their way to the Old Mill Tavern for some well deserved pints of cider. The entire time they were walking Abraham felt a sense of dread, like they were being watched. The fog was so thick someone could have been directly in front of them and they never would have known it. Both father and son were relieved when they opened the Tavern door and found it warm and full of laughing townsfolk, the entire town was there.

Thaddeus and his son were there for not more than a minute when the door was struck by a knock so furious that it shook in its frame. All conversation in the tavern stopped abruptly as a villager opened the door to reveal a tall, bald, painfully thin man, with skin as pale as the winter frost, long yellow fingernails, visible fangs, eyes that were entirely black, and pointed ears. The bartender yelled, "What are you waiting for, don't let in the cold! Come in and join us for a drink."

For Abraham everything after that moment seemed to happen in slow motion. The pale man lunged upon his first victim, an old man sitting at the bar. He tore through the man's skin as if it were paper and bit his wolf-like fangs

into the man's throat as the remainder of the patrons looked on, frozen in horror. At first the man was screaming and flailing in an attempt to escape the creature's grasp, but within seconds, the color drained out of the old man's face. He lay lifeless in a pool of blood as the pale creature took another man down, and then another, and another until each and every person in the bar was reduced to a mutilated, lifeless corpse. Within minutes, the floor, walls and ceilings were streaked with blood and gore and an eerie quiet set in.

Thaddeus and Abraham, the lone survivors, were watching through the slats in a closet door as the creature paced around the lifeless bodies. When Thaddeus had realized the creature was

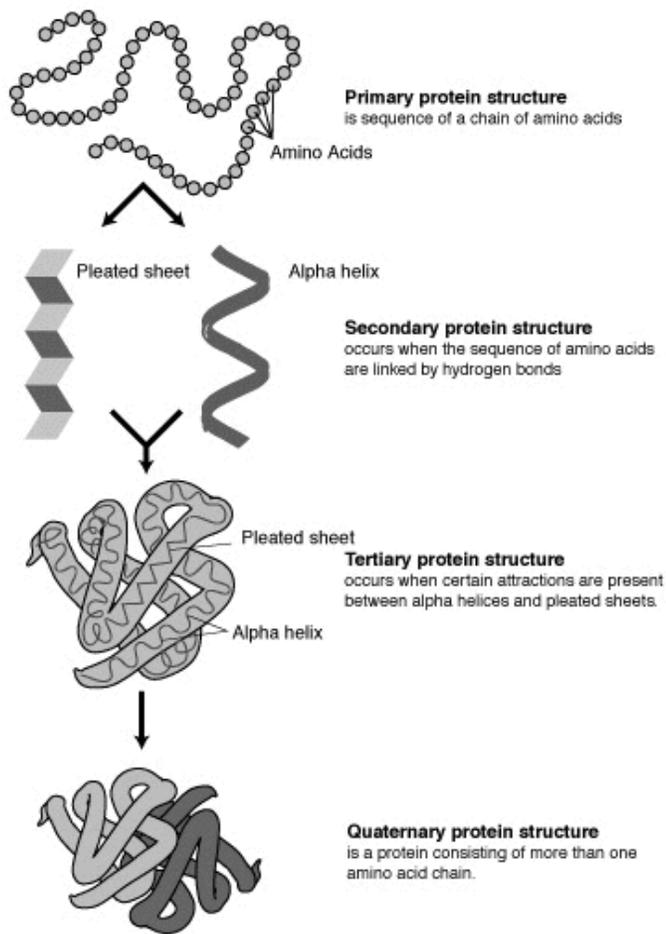
blocking the tavern door, he had cleverly pulled Abraham into the back pantry where they had been silently hiding as the pale man quenched his thirst. Thaddeus was ready with a gun and waited for the right moment to get his revenge on the creature. Just as the monster turned towards the coat closet, Thaddeus sprung out and fired a shot right into its head. But instead of relief, Abraham was horrified as the seemingly unharmed creature proceeded to suck the life out of his father. As the creature continued to feed on Thaddeus, Abraham grabbed a sharpened wooden table leg that had been broken in the struggle and plunged it into the monster's back and did not stop pushing it until it was through the creature's heart.

The dead vampire slumped to the floor but instead of relief a state of shock fell upon Abraham as he realized that the entire town had been wiped out in only a few minutes. The Creature's pale skin, claws, pointed ears, all black eyes, and fangs were forever burned into Abraham's memory. He knew that there were more creatures just like this one out there; many colonies like Roanoke had seemingly vanished before. As the lone survivor of this massacre, it would be his solemn duty to bring the vampire's corpse to every town and show people what to look for so that these monsters could be recognized and destroyed before they could kill more innocents.

Abraham continued his crusade until every town in colonial America had seen the features of the vampire. After that any time a vampire tried to enter a building it was quickly recognized and killed. Soon the vampire population dwindled and as the centuries passed no one ever believed that they had been real at all

Scientific Explanation:

Most readers could probably predict what was going to happen in this story as soon as the vampire was invited into the bar. No one would ever invite a vampire into their home because as soon as they saw it they would immediately recognize pale skin, pointy ears, long claws, all black eyes, and fangs as the physical characteristics of a vampire. These features are what you use to distinguish a vampire from other humans and can be considered vampire "epitopes". Epitopes are distinctive structural features that the immune system uses to recognize targets that it wants to destroy (antigens and immunogens). If the target has an epitope that the immune system recognizes as foreign then the immune system will do everything in its power to annihilate that target. The immune system has a "shoot first, ask questions later, then shoot again to make sure it is dead" philosophy. **The majority of antigens are proteins. The structural features of a protein like the specific arrangements of the alpha helices and beta sheets (secondary structures) as well as the folding of the protein (tertiary structures) are what make up the epitopes in most antigens. The sequence of amino acids that a protein is made of (primary structure) does not usually contribute to epitopes in living systems because most functional proteins are folded*. Epitopes generated from folded structures are known as conformational epitopes.** When Abraham carted the vampire's corpse from town to town he helped villagers recognize the features of a vampire so that they could be killed before they became a problem. He was effectively providing a sort of "vampire vaccine" that immunized the town from future vampire attacks. The purpose of a vaccine is to show epitopes of a dead disease causing agent to the immune system so that when the live entity is encountered it can be recognized and eliminated before it causes problems.



You can develop immunity through being previously infected by something but that is definitely learning the hard way. Despite the needle that is usually involved, vaccines are significantly less painful than the actual disease they protect against. I can guarantee that Abraham would never forget the face of another vampire again but his whole town had to be slaughtered in front of him in order to give him that memory. Likewise, a few minutes after Abraham's whole town had been massacred, if a stranger had walked into that blood soaked bar and told Abraham what vampires looked like and to watch out for them, it would not have done the town any good either. Vaccines deliver the epitopes of disease causing agents to the immune system for the purpose of preventing disease by allowing the body to recognize and destroy these agents before they cause trouble. A vaccine that is delivered while you are actively sick with the disease you are trying to prevent is typically useless. The development of a

vaccine is an arduous and expensive process and diseases that vaccines are developed against have caused blood baths that would rival any vampire. Vaccines are one of the most successful preventative disease strategies of our era. Evidence of this can be seen with diseases like Polio.....



Story: Polio

Jimmy Nikolai is a 10th grade student interviewing his grandmother for a history class report on life in America when she was growing up in the 1930's.

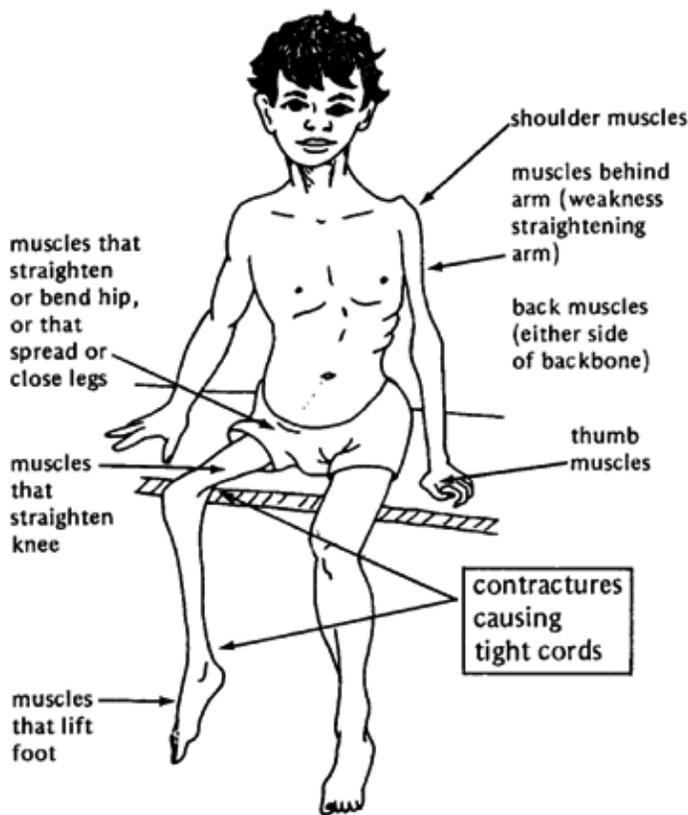
Jimmy: *What is your most significant memory growing up?*

Grandmother: *The polio outbreak was pretty scary. I don't think I will ever forget it. The disease affected children even some that were your age. We all knew the signs of Polio*

but there was no way to stop it. It affected every generation of children I had ever known so in some ways it was almost like some kind of curse. First kids would develop a headache, a fever, and some muscle aches. It wasn't different from the flu but a few days after they got better things would get bad very fast. The paralysis would set in, the muscles would become weak and their limbs would hang motionless like a doll's would. Other times it would cause the muscles to contract and spasm against the victim's will causing horrible pain. The contractions were so hard they would deform the bone. Sometimes it was the arms or the legs, other times it was the face. Several of the kids that I knew who had the paralysis eventually recovered but not all of them were so lucky. Many children lost the ability to walk altogether or were permanently deformed. A few like old Mr. Martin across the street never regained the strength in their limbs, it is why he limps. Other kids lost strength in the muscles that allowed them to breathe, these kids had to be kept alive with machines that breathed for them or they just died from suffocation. A few of the children who recovered from polio in childhood ended up having reactivation 30-40 years later and developed muscle weakness and paralysis again. I guess this is something that kids your age will never have to worry about though.

Jimmy: All that I know about Polio is that it is an old disease. Mom never said anything about Polio. You would think that if it was so bad and so scary I would have heard something from her.

MUSCLES COMMONLY WEAKENED BY POLIO



Grandmother: Your mother was born in the 1960's after Dr. Salk developed the Polio Vaccine. She was given the vaccine and so were you. Your bodies recognized the virus as soon as it tried to sneak into them and it was eliminated before it could cause trouble. No one gets Polio anymore, it doesn't inspire the fear that it used to but whenever I hear of someone getting a fever and muscle aches I always wonder if the paralysis will set in.

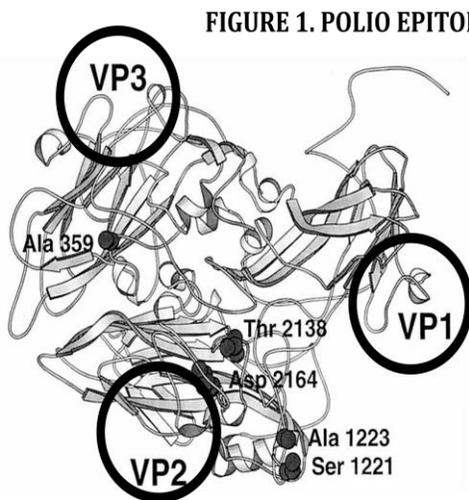
Scientific Explanation:

Polio is a really scary disease caused by a virus (poliovirus). For generations it killed and crippled many children. Polio enters the body through the digestive system after it contaminates something you eat, after that it infects the nervous system and destroys parts of it, mostly in the spinal cord. You don't have to know much about medicine to know that

nerve damage is a bad thing. Nerves are responsible for controlling the muscles in your body,

so if they are destroyed or damaged then you are going to lose that control which results in the paralysis. Of those infected by Polio, 95% develop no symptoms but the 5% that do get affected suffer significantly so in older generations almost everyone knew someone that was affected by it. It used to be a real scourge up until the 1950s when the vaccine was developed by Jonas Salk's research group. Several years later Albert Sabin's research group developed the oral Polio vaccine. The vaccine was first tested in the 1950s and was used widely in the 1960s and beyond.

The vaccine introduced "dead" poliovirus particles into the body and let the immune system see the unique epitopes of the poliovirus. These epitopes consisted of the folding pattern and the configurations of the alpha helices and beta sheets. After the polio vaccine



was administered to Jimmy and his mother their bodies knew what structural features to look for and as a result the virus was eliminated long before it could cause disease. In the era of Jimmy's grandmother, people had to encounter the virus and survive it in order to get immunity which is why so many were affected by the paralysis. Fortunately, since the vaccine was developed the disease has been virtually eradicated and in Jimmy's generation it is almost unheard of.

Polio has "fecal-oral" transmission which means that contaminated fecal matter gets on the hands of the soon to be infected. As soon as the fecal contaminated hands touch something that goes in an individual's mouth, like food, the virus has the chance to infect again.

Increased hand washing and sanitation can reduce the spread of Polio considerably. Fecal-oral spread can be as simple as someone not washing their hands after going to the bathroom, touching an apple in the lunch line and not picking it up, some unlucky person picks up that apple and eats it and then the polio virus gets inside of them. Many diseases have fecal-oral spread so frequent hand washing is essential in general. Vaccination and improved sanitation have almost completely eliminated Polio across the globe. As far as it is known, the poliovirus only survives in humans so if no humans can get it then the disease can be wiped out entirely.

Take home message: In living systems the configurations of secondary(alpha helices, beta sheets), tertiary(folding pattern) are key protein recognition points for the immune system and are the basis for the success of vaccination.

*Primary structure is the basis for protein recognition in laboratory tests like the Western Blot because in these procedures the protein is completely unfolded(denatured) and as a result are known as linear epitopes. Without folding the primary structure is exposed and capable of being recognized otherwise parts of it end up getting hidden in the body of the protein.

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