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The Role of NanA in Bacterial Meningitis and a Model Case Study

A thesis submitted in partial fulfillment of the requirements for the degree of Bachelor of Science in Biochemistry & Molecular Biology

by

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May, 2014
We recommend that the thesis prepared under our supervision by

Michael A. Phelan

entitled

The Role of NanA in Bacterial Meningitis and a Model Case Study

be accepted in partial fulfillment of the requirements for the degree of

Bachelor of Science, Biochemistry & Molecular Biology

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Abstract

Bacterial Meningitis is a debilitating and potentially life threatening bacterial infection of the spinal fluid and meninges of the brain. While the exact mechanism used by bacteria to pass into the otherwise isolated spinal fluid is not fully understood, it is known that NanA plays a crucial role in this process. The goal of this thesis is to describe the enzymatic function of NanA and how it relates to bacterial adhesion and transportation.

A case study of a 6 year-old child is included to demonstrate the rapid onset of symptoms in bacterial meningitis and its severity.
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Introduction

Bacterial meningitis is an infection and subsequent inflammation of the meninges surrounding the brain and spinal cord. Bacterial infections due to *Neisseria meningitidis*, *Streptococcus pneumoniae* or *Escherichia coli* (among others) can lead to a meningeal infection if the pathogens are able to cross the blood brain barrier (26). Bacterial meningitis is the cause of approximately 500 deaths per year in the United States (16) and is estimated to cause over 170,000 deaths per year globally (2). Infection that is treated can still lead to a variety of neurological complications. Because of its connection to the immune system, bacterial meningitis is particularly dangerous to infants and the very old. Although industrialized countries have seen marked decreases in infections due to the introduction of vaccines, the disease remains mostly unchecked in Third World countries (2).

Statistics

According to the CDC, in the United States, each year between 2003 and 2007 there were about 4,100 confirmed cases of bacterial meningitis including 500 deaths (16). Seeking immediate treatment after suspected infection can reduce the risk of fatality by over 15%. Due to the lethality of the disease without treatment, the World Health Organization (WHO) has introduced programs in sub-Saharan to vaccinate against group A meningococcus (also known as Nm A; the leading cause of infection in the region) (2). The meningococcus family carries the risk of causing major epidemics that, although slow to develop, can persist for decades. In one open clinic in Kenya, 2.0% of all patients
were confirmed to have bacterial meningitis with as many as 19% of the group presenting with symptoms common to the disease. (17)

In Africa, the Meningitis Vaccine Project (MVP) partnered with the WHO are estimated to have vaccinated over 20 million people between Burkina Faso, Mali, and Niger by 2010. In 2011, these countries reported the lowest recorded number of confirmed cases of Nm A bacterial meningitis on record. By 2011, an additional 22 million individuals were vaccinated in Cameroon, Chad, and Nigeria. (2)

Although vaccines for Nm A have been very successful, Group B meningococcus (Nm B) remains problematic internationally. It is estimated that Nm B has been responsible for nearly 40% of bacterial meningitis cases in North America, and up to 80% of some European countries. Unfortunately, standard vaccines cannot be developed for Nm B due to antigen mimicry of human neurological tissues by the capsular plurivalent polysaccharide surrounding the bacteria. (2)

Bacterial meningitis can be lethal in as many as 40% of cases in adults and newborns, but is significantly less dangerous in children with as low as 2% lethality. (13) Though less lethal for children, the dangers of neurological complications persist.

**Signs and Symptoms**

Symptoms of bacterial meningitis will generally present within 3-7 days after exposure to the bacteria. Often, meningitis infection will lead to the rapid onset of fever, headache and a stiff neck. As the infection becomes more severe nausea, vomiting, light sensitivity and confusion develop over the course of a few days. The disease can cause an infected individual to appear sluggish or inattentive to their surroundings. Symptoms
such as abnormal reflexes get progressively intensify as the disease progresses. Late stage symptoms include seizures and coma, which can lead to death. (16)

Positive diagnosis of non-specific meningitis looks for the presence of a Kernig’s sign. The patient lies supine with the hips and knees flexed to 90 degrees. A positive sign would show pan limiting passive extension of the knee.

Neurological Complications

Because of the damage it causes to the brain and spinal cord, bacterial meningitis can have a varied array of damaging complications. These complications can fall under four categories: physical, communicative, cognitive and behavioral/emotional. Physically, motor control problems can lead to paralysis of limbs, abnormal muscle tone or even ataxia. This continues into sensory loss such as visual or hearing impairment. In extreme cases, damage from infection and swelling can even induce chronic seizures. Clearly, motor loss can lead to speech impediments, but damage to non-motor centers of the brain such a speech or comprehension could damage an individual’s communication beyond what could be considered physical damage. (23)

Damage to the frontal lobe can also cause changes in cognitive and behavioral function. Cognitive impairment affects memory, attention, perception, judgment, problem-solving, and safety awareness. These functions are crucially important for an adult to be self-sustaining and can permanently alter an affected individual’s quality of life. These problems also extend into the behavior of the individual. Mood and emotional instability, aggression, low motivation, sexual inappropriateness and even psychosis are well-documented outcomes of neurological damage. Ultimately, the impact of meningitis
is not limited to the death toll. Although a person can be cured of infection, the longer lasting effects may permanently disable survivors. (23) With its prevalence in Third World countries lacking support systems for disabled citizens, the total societal damage of meningitis may be too complex to measure. (2)

Treatment

Bacterial meningitis is normally treated with broad-spectrum antibiotics. Although more targeted antibiotics could be used for treatment, the fast onset of the disease and high mortality rate precludes the use of cultures for the determination of a specific treatment. Corticosteroids are also admitted through IV to reduce inflammation and swelling to reduce the chance of complication. (15) The vomiting and fever from the infection can lead to dehydration that needs to be replenished with IV saline. Gram stains should be taken of the blood to determine the exact cause of infection so that specific antibiotics can be introduced. (11)

Summary of Paper

While the first chapter was a general overview of bacterial meningitis, the second chapter will discuss the mechanism used by bacteria to cross the blood-brain barrier and cause a larger infection in the meninges. The second chapter focuses most specifically on the role of sialic acid and NanA protein in bacterial binding, signaling and replication before and after entrance past the blood-brain barrier.

Sialic acid is a product of anaerobic metabolism in humans and bacteria. In humans it is formed into a glycolipid complex that is a key component of mucus
excretions and mucus membranes (22). In bacteria, sialic acid serves as a type of energy storage as it can be digested by NanA protein into mannose and pyruvate. These products will signal replication of bacteria that can lead to an increasingly dangerous infection in humans. (20)

NanA protein is present in many bacteria associated with meningitis. Its structure allows it to be positioned in membranes and therefore on the surfaces of bacteria. NanA’s active site exists in a hollow beta-sheet barrel that allows its products to exit on the opposite side of the molecule (25). Because sialic acid exists in large complexes in human mucus, NanA digests sialic acid and pushes the products away from the active site, ready for the next molecule in the chain. This mechanism is central to the bacteria binding to the surface of mucus membranes. (9)
The Role *NanA* in Bacterial Meningitis

As discussed in the first chapter, bacterial meningitis is caused by a handful of meningitis inducing pathogens, however, the presence of an infection is not an absolute indicator that meningitis will develop. *Streptococcus pneumoniae*, for example, while being a leading cause of meningitis (thousands of US cases per year), is the cause of up to 175,000 cases of pneumonia per year in the United States. (19) Although meningitis could be considered more dangerous in the long term than pneumonia, they are both potentially lethal illnesses. Clearly the immune system has developed mechanisms, between biochemical responses and epithelial barriers that help to prevent these relatively common pathogens from becoming serious threats. This chapter will focus on the mechanism of the bacteria that allows it to cross the blood brain barrier.

*Bacteria/Blood-Brain Barrier Contact*

Bacteria have the chance to contact the blood-brain barrier (BBB) through one of two ways, either through direct contact through the nasal cavity or skin or through the bloodstream (9). The bacteria can most common place of entrance is the dura mater past the arachnoid mater and into the subarachnoid space where the cerebrospinal fluid is contained and the bacterial infection spreads. The dura mater then arachnoid mater followed by the pia mater makes up the meninges and is the source of inflammation that causes dangerous complications. (1)
**Infection binding to Blood Brain Barrier**

The blood-brain barrier has both physical and chemical characteristics to prevent bacterial breach. In order for bacteria to penetrate these defenses, a series of biochemical event need to take place. The highest probability that the infection will pass into the meninges is achieved if constant contact between the BBB and the bacteria exist. (9)

The bacteria (as anaerobic organisms) produce various chemical products, which include pyruvate and mannose. This mannose has an acetyl amine group added onto it to give ManNAc. ManNAc reacts with a pyruvate molecule through an aldolase to produce sialic acid (22). Sialic acid is structurally similar to neuraminic acid with an acetyl group added to the amine (it is also known as N-Acetylneuraminic acid, Neu5Ac or NANA). Neu5Ac is a key component in glycolipids on cell surfaces, particularly in neuronal membranes in the brain. Its glycolipid association makes it a fundamental component of mucus secreted by the body in order to reduce infection (sialic acid was named after saliva). (20)

Many bacteria associated with meningitis contain a sialic acid cleaving protein called neuraminidase, generally referred to as NanA that breaks down sialic acid as it comes into contact with it (25). The mucosal membranes also known as biofilms become consumed by the NanA protein as it catalytically hydrolases the sialic acid. The glycolipids and oligosaccharides in the mucus contain sialic acid in long chains associated in alpha (2,3), (2,6), or (2,8)-glycosidic linkage chains. As the NanA cleaves the linkages, it releases sialic acid products (mannose and pyruvate) bacterial cells anaerobic glycolysis. (22)
Because the bacteria can use the NanA protein to generate fuel, they have the highest rate of cellular mitosis and replication. Therefore, the highly sensitive and vulnerable regions of the body that have mucus as a protective barrier have their defenses backfire and become a weakness. From a biological population perspective, there are 10 times as many bacterial cells as human cells on a person at any given time. These bacteria are generally harmless and exist in many places in the body. The mucus membranes would have significantly lower bacterial population due to their antimicrobial natures and therefore have the least amount of competition to any bacteria capable of binding to them. (20)

Although NanA sounds effective at bypassing the mucosal barriers that protect the blood-brain barrier, the production of sialic acid is not its only function in that nature. Because the sialic acid exists in long chains, as the NanA protein breaks one glycosidic linkage, it is likely another similar linkage will be presented almost immediately in a chain-like fashion (4). With the bacteria having potentially thousands of free roaming NanA protein units, it has thousands of tiny binding sites that constantly pull the cell membrane closer. (22) The nature of mucosal membranes is to constantly regenerate the mucus as it is consumed, but this simply gives more binding regions for the bacteria to hold. (9)

Ultimately, NanA protein not only allows the bacteria to survive in antimicrobial mucosal conditions, but actually constantly binds the to both the bacterial cell and the source of the sialic acid chains. Figures 2 through 4 demonstrate how sialic acid and NanA work in together to allow bacteria to pass the blood brain barrier.
Passing through the Blood-Brain Barrier

With the exterior defense of the BBB neutralized, the bacteria comes into direct contact with the endothelial cells that are the structural components of the dura mater. As this event is occurring, the bacterial cells continue to divide and multiply on the surface of eukaryotic cells. As stated in the above section, the bacteria themselves can consume ManNAc and pyruvate to produce their own sialic acid. This allows the cells to form binding complexes that are not as permanent as adherence junctions in eukaryotic cells and are free flowing. (9) The cells then start to produce their own biofilms as they bind to one another. The much smaller bacterial cells quickly outnumber the cells composing the dura mater. As the dura mater cells undergo endocytosis to absorb nutrients, the bacteria can slip into or between these cells and onto the arachnoid mater. They then repeat the process a second time to reach the subarachnoid space containing the CSF. (11)

Structure of NanA

NanA is a 470 amino acid protein. The primary active site of the protein is a beta sheet barrel surrounded by additional amino acid chains. The protein also has a bulbous group of amino acids that lies to the side of the sheet. This bulbous extension is primarily non-polar but does not interact with sialic acid during the NanA reaction (8). Sialic acid binds with NanA in the front of the beta barrel (seen in figure 5) in such a way as so the products can be “excreted” behind the barrel in a transport protein-esque manner. Figure 8 demonstrates that the functional amino acids in NanA are Aspartic Acid 357, Isoleucine 427, Phenylalanine 428, Leucine 561, and Tyrosine 680. (8)
The fact that those 5 proteins are involved in the reaction may be crucial to NanA mechanism. As the beta sheet barrel closes, sialic acid is cleaved into mannose and pyruvate. Isoleucine is shown in figure 8 on the light blue chain next to sialic acid, although Phenylalanine is not shown (due to visual overlap) its position is one residue closer to the front than that of Isoleucine. The conformational change that forces the reaction forward also positions the Phenylalanine closer to the sialic acid molecule (8). This appears to serve the role of forcing the newly formed products away from the binding site of the molecule. Because the motion is from forwards to backwards, the pyruvate and mannose molecules are pushed further into the hollow center of the barrel (4).

Figure 7 also shows the highly non-polar nature of the external beta sheets. There are no water molecules present on any of the nine amino acid chains that form the side of the barrel that does not have the non-polar bulbous group. This presents an overall picture of a plane of non-polar molecules that exist on the external surface of the protein. This plane is perpendicular to the direction of the beta sheet barrel “tunnel.” (8)

The NanA protein is built in such a way that the beta sheet barrel is capable of being embedded in a cell’s bilipid membrane in such a way that a reaction with sialic acid external to the cell can occur while the products of the reaction are forced into the cell. This action not only provides additional energy for the cell in its products but also allows the sialic acid chain to continually present a new molecule for reaction (12). As a bacterial cell continually consumes sialic acid at its surface and releases it into its cytosol, the protein moves closer and closer to the source of the sialic acid. (20)
As hundreds or even thousands of these protein molecules work in unison, there is always a constant site of binding and pulling that allows the cell to bind to whatever is emitting the sialic acid. In the human body, this source is the blood-brain barrier. NanA, therefore, is the molecule of key importance in a bacteria binding to and drawing itself closer, and eventually into, the cells that are intended to protect the CSF, meninges and brain. (9)

**Immunological Response and Inflammation of the Meninges**

While all of the processes above are occurring, the immune system becomes activated. As peptides from a foreign antigen are recognized, the immune system begins its adaptive immune response to fight the pathogen. The adaptive immune response, however, is not instantaneous, and may take between a few hours to a few days to fully engage. During this time, if the body lacks the innate immunity to recognize the bacteria, the bacteria can seize the opportunity to jump into the meninges. Eventually, the adaptive immune system will engage and begin to release a series of cytokines that induce an inflammatory response. The inflammation increases temperature to fight the bacteria and improve blood flow to the regions to increase the number of T-Cells able to fight the infection (13). While this action is crucial to fighting an infection in most parts of the body, the sensitivity of the nervous system to heat and pressure makes it a particularly dangerous place to have an inflammatory response (18). This response puts pressure on the brain and the nervous system and begins to cause damage (23). Although the immune response has begun to combat the infection, the bacteria can still persist for up to a few days. During this time they can spread even further and become attached to the sialic acid
sources associated with neuronal membranes on the brain (as shown above) (4). This continually increases the range of the bacteria and increases the range of the inflammatory response, particularly around the brain and on the pia mater directly in contact with the brain.

The process that allows for bacterial meningitis to occur speaks towards the shortcomings of an immune system that is generally extremely effective. The presence of NanA protein in bacteria would not necessarily indicate it is only used for attachment to mucosal surfaces. Although speculation on its evolutionary basis would require significantly more research, sialic acids role in many biological processes describes NanA’s multitude of uses. The adaptive immune system constantly balances between under and over reaction. This balance creates a gap of time required to identify and attack pathogens as they appear. The mucus membranes of the blood-brain barrier serve to buy time and protect the most sensitive and vital areas of the human body. NanA and its role in bacterial meningitis exploits a vulnerability used to cover another vulnerability.
Diagrams:

Figures 1-4 self-generated in open-source program *Paintbrush*

Figures 5-8 generated with *Protein Workshop* run through *Java* from pdb.org (#8)

**Figure 1: Legend for Figures 2-4**

![Legend for Figures 2-4](image)
Figure 2

First Step
Initial Binding of Bacterial Cells

BBB (Dura Mater)
Figure 3

SECOND STEP
Mass Binding and Bacterial Replication
(Passing Through BBB)

Bacterial Endocytosis

SA glycoprotein/lipid containing vesicles

Endoplasmic Reticulum

SA vesicles combining with human membrane (exocytosis)

Direct bi-lipid bi-lipid membrane contact

Bacterial Exocytosis

CSF

ZOOM
THIRD STEP
Entering CSF and Meningeal Inflammation

Sub-arachnoid space
Arachnoid Mater
Immunologically mediated Inflammatory response

Chemokines released To control bacteria Population induce inflammation.

Same mechanisms as Step 2 (dura mater) to Pass arachnoid mater

Induced sub-dural space

Bacterial Endocytosis

Pia Mater inflammation puts pressure on the brain. Causes damage.

Past Arachnoid Mater, infection spreads throughout CSF

Subarachnoid Space (Contains CSF, Source of Meningeal Infection)

Increased osmotic and mechanical pressure causes damage

Sialic Acid mucosal Membrane present on pia mater surface

Brain/Spinal Cord

Dura Mater

CSF

Pia Mater
Figure 5: *Streptococcus Pneumoniae NanA Structure with Sialic Acid Complex: Front view with Sialic Acid as Ball and Stick Model*

![Figure 5](image1.png)

Figure 6: *Streptococcus Pneumoniae NanA Structure with Sialic Acid Complex: Back view with Sialic Acid as Space Filling Model*

![Figure 6](image2.png)
Figure 7: *Streptococcus Pneumoniae NanA Structure with Sialic Acid Complex: Side View with H2O molecules shown (red dots). Non-polar beta-sheet region demonstrates lack of H2O molecules in (front of diagram) that would be associated with membrane placement.*
Figure 8: *Streptococcus Pneumoniae NanA Structure with Sialic Acid Complex: Sialic Acid as Space Filling Model and interacting amino acids as Ball and Stick*
Case Study

Patient: Justin Young

Age: 6

Chief Complaint

The mother brings in the child after the rapid onset of a high fever. The mother also states that the child began complaining of a headache as the fever intensified. The child appears somewhat confused and lethargic.

History of Present Illness

The mother claims that the child was in good health just the day before and began to develop a fever before other symptoms appeared. The child has had bouts of vomiting and persistent nausea. The mother describes the headaches as “more like migraines,” in that the child is sensitive to light.

Past Medical History

Justin has been relatively health most of his life. His mother states that he has an occasional cold but never a fever this high. The child had a broken arm when he was younger, but has had no trauma recently.

Justin had a slightly complex birth and was delivered via Caesarean Section. His checkups were normal and he has maintained a healthy height and weight consistently.
**Family History**

Justin’s eldest brother Jeffrey (age 8) had an allergic reaction to the DTaP vaccination when he was 18 months old. For this reason, Justin’s mother chose to forgo immunizations for the other children. Justin’s family has a history of hypertension, heart disease and diabetes, but not cancer. Justin’s father was diagnosed with epilepsy as a child, but has it well controlled with medication.

**Social History**

Justin attends a local, public kindergarten. He is in a class with 27 other children and regularly interacts with more during recess/playtime. He takes bagged lunches to school everyday but according to his teacher, Ms. Cakemuncher, has been known to share. He plays T-ball in a little league group and attends cub scouts with his older brother. He is very adventurous and usually runs and plays outside a lot (though this obviously isn’t the case today). According to Justin, he currently has a girlfriend, though both are deathly afraid of cooties.

**Allergies/Medications**

Justin has a severe peanut allergy and mild lactose intolerance. He has never received penicillin but his father reports having an allergic reaction in the past. Justin sometimes develops allergies to grasses and pollens, though it has never been severe enough to warrant anything other than Children’s Benadryl. As noted in family history, his brother had a severe allergic reaction to DTaP that resulted in a seizure. It was assumed (by his mother) that Justin would have a similar response. Mrs. Young gives
Justin no medication but will occasionally give him PediaSure drinks to supplement his vitamin and nutrient intake.

**Review of Symptoms/Physical Exam**

**General**

The child overall appears quite sick. Justin has a high fever by touch, is not responding to questions and is barely moving at all, though appears at least minimally conscious. Any attempt to sit the child up causes him to wince with pain. Small purple/red dots are spread evenly throughout his arms and legs, though they are barely noticeable.

**Neurological**

Confusion is the most obvious symptom neurologically. It is doubtful that Justin knows where he is. He was complaining of a severe headache before his mother brought him in, and this appears to be confirmed by pain associated with movement of his head. He has correct reflex responses but sensitivity to touch cannot be measured, as he will not respond to stimuli. Sporadic twitching is noticed on the limbs but it is mild. The twitch will last 2-3 seconds and then stop.

**HEENT**

The neck appears to be much more stiff that would be expected on a barely conscious individual. His pupils were reactive, though he turns away from light in an apparent sensitivity. His left tympanic membrane is red and inflamed and he pulls away when the otoscope is inserted. His nose and throat do not show any inflammation. His fever feels quite high, it is measured at 103 °F.
Muscular

Severe muscle weakness is evident. The child is unable to stand or even sit up. His limbs offer no resistance when dropped and he cannot push or pull when asked to do so. The weakness is bilateral. There is the occasional spontaneous movement of the arms of legs that seems like twitches, though they are sporadic.

Pulmonary

His breathing sounds unobstructed, though perhaps slightly shallow. There is no crackling sound and no fluid sound in the lungs. There seems to be equal and even breathing on each side.

Cardiovascular

Justin’s heart rate is slightly low and not particularly strong. There are no odd sounds and no murmurs present. The rate is regular with a standard rhythm.

Abdominal

There are no masses or obstructions/rigidity upon touch of the abdominal walls.

Bowel sounds are no
## Labs

### CBC

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<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Units</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>17,000</td>
<td>cells/µL</td>
<td>5,000-14,000</td>
</tr>
<tr>
<td>RBC</td>
<td>50</td>
<td>10^6 cells/</td>
<td>3.8-4.8</td>
</tr>
<tr>
<td>Platelets</td>
<td>240</td>
<td></td>
<td>150-440</td>
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<tr>
<td>Hemoglobin</td>
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<td></td>
<td>11.2-14.1</td>
</tr>
<tr>
<td>Hematocrit %</td>
<td>50</td>
<td></td>
<td>31-41</td>
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<tr>
<td>MCV</td>
<td>100</td>
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<td>68-85</td>
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<td>MCHC</td>
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<tr>
<td>MCH</td>
<td>2.24</td>
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<td>24-30</td>
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### Metabolic

<table>
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<th>Test</th>
<th>Result</th>
<th>Units</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>3.4</td>
<td>g/dL</td>
<td>3.9-5.0</td>
</tr>
<tr>
<td>Alkaline Phosphate</td>
<td>50</td>
<td>IU/L</td>
<td>44-147</td>
</tr>
<tr>
<td>ALT</td>
<td>15</td>
<td>IU/L</td>
<td>8-37</td>
</tr>
<tr>
<td>AST</td>
<td>14</td>
<td>IU/L</td>
<td>10-34</td>
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<tr>
<td>BUN</td>
<td>6</td>
<td>mg/dL</td>
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<tr>
<td>Calcium</td>
<td>7.5</td>
<td>mg/dL</td>
<td>8.5-10.9</td>
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<tr>
<td>Chloride</td>
<td>57</td>
<td>mmol/L</td>
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<tr>
<td>CO2</td>
<td>24</td>
<td>mmol/L</td>
<td>20-29</td>
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<td>Creatinine</td>
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<tr>
<td>Potassium</td>
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<td>mEq/L</td>
<td>3.7-5.2</td>
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<td>Sodium</td>
<td>96</td>
<td>mEq/L</td>
<td>136-144</td>
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<tr>
<td>Bilirubin</td>
<td>0.6</td>
<td>mg/dL</td>
<td>0.2-1.9</td>
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<tr>
<td>Protein</td>
<td>5.4</td>
<td>g/dL</td>
<td>6.3-7.9</td>
</tr>
</tbody>
</table>

Imaging

Figure 9: Lumbar puncture culture in blood broth

Reference: C Source: http://textbookofbacteriology.net/S.pneumoniae.html
MRI results (Figures 10 and 11)

Diagnosis and Treatment

Justin was diagnosed with bacterial meningitis from Streptococcus pneumoniae. This was based on positive result from Gram Stain, increased CSF pressure, high WBC count in the CSF and labs consistent with bacterial meningitis. After Justin’s mother is told of the diagnosis an IV with broad-spectrum antibiotics is administered with steroids to reduce inflammation along with significant quantities of isotonic saline to combat dehydration. Justin remains in the hospital until it has been confirmed that the infection is sufficiently eliminated and his vital signs and general physical appearance improve, approximately one to two weeks.

Follow-up

Justin is taken to his GP one week after being released and his vital signs are confirmed to be normal. Special attention is given to neurological signs. Justin also visits a pediatric neurologist to look for any damage from complications as well as an ENT to check for hearing loss. Justin shows no signs of damage from complications and has no fever or elevated WBCs in his new blood work, so a second lumbar puncture is not ordered.
Introduction and Role of NanA References


Case Study References