

## Case 2: Necrotizing Fasciitis

*Liz Zeigler's Survivor Story, National Necrotizing Fasciitis Foundation <http://www.nnff.org/>*

. . . My NF seemed to start with a little tiny blister on the heel of my right foot. In a day or two after it appeared, it started hurting and I noticed my foot swelling a bit, but I ignored it. After 3 days or so I couldn't ignore it anymore. My foot, ankle, and about halfway up to my knee were red and swollen and hot to the touch. The blister was huge and what the doctor's later called "angry looking", very large, oddly colored, with reddish-purplish streaks coming out of it extending along the side of my foot. On Monday evening I went to the ER at UCLA and was instantly told I had cellulitis and put on a penicillin IV drip. The doctor drained the blister (OUCH!!!), wrapped up my foot, and told me to unwrap it in 24 hours. I thought that was it.



**Figure 1:** cellphone photo of Liz' heel infection.

I went to work the next day and the swelling, redness and heat didn't go down, in fact they got worse, but I thought everything was fine. I even read somewhere online that cellulitis can get worse before it gets better, so I thought it was normal. When I got home that night and took the bandage off, I knew I had to get to the hospital. The blister had reformed in 24 hours, and was twice as big (about the size of a silver dollar), and had turned black and the streaks, swelling, heat were worse. I went back to the ER and when the doctor (finally) saw my foot, he instantly said I had I necrotizing infection and had to be hospitalized. They put me back on the IV drip (which stayed on for my entire hospital stay) and set about draining the blister-the most painful thing I have ever felt. They put numbing shots directly into the wound, which must have hurt more than whatever they were numbing me from feeling. It was terrible but didn't last too long.

I ended up spending eight days in the hospital. On day 1 I had surgery number 1 to cut out the dead tissue. The doctors acted very quickly and really seemed to have a plan of action and the diagnosis turned out to be right on from the start, for which I am so thankful. The first operation went well, it left a crater on the side of my right foot about the size of the blister and deep enough to see muscle (according to my dad, since I refused to look at it). The discomfort afterwards was awful though the pain was only really bad during the bandage changes twice a day. Operation 2 came on Day 8, which was a skin graft taken from my hip. This too went really well, and thankfully, I was discharged later that same day. Next came two weeks of strict bed-rest with my leg constantly elevated. I was allowed to get up only for bathroom trips. The third

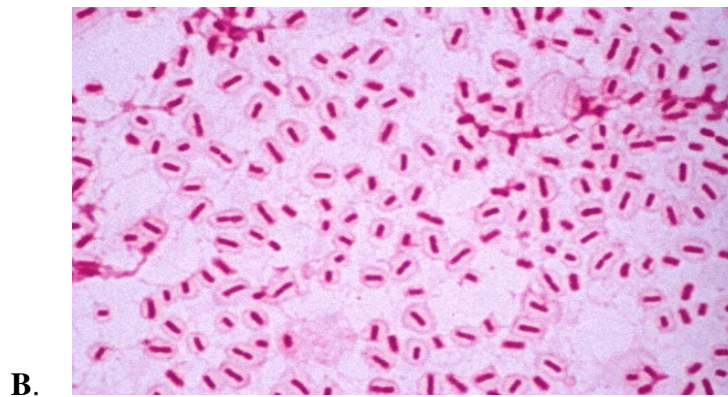
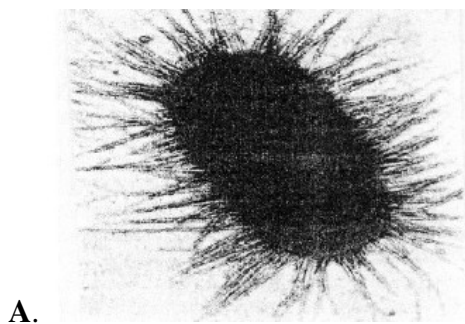
week at home was mostly bed rest, although the doctor allowed me to start getting up a bit, practice a little on the crutches, and I started with physical therapy to start rebuilding the atrophied muscles in my right leg. I am now nearing the end of this third week and am looking forward to being back at work, on my crutches, on Monday.

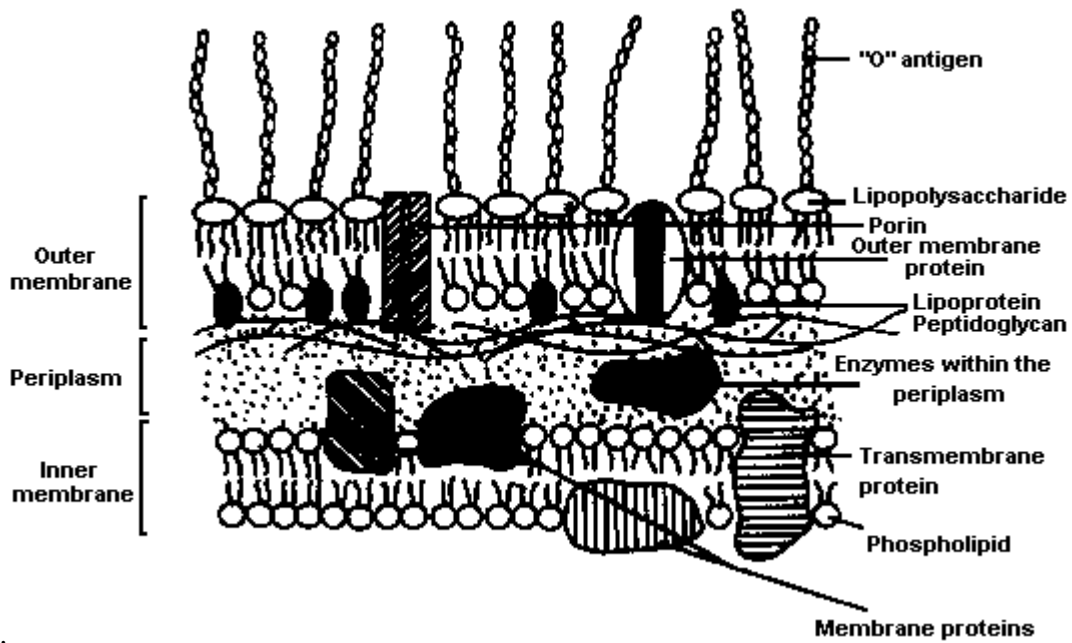
I really did not know anything about NF until I got home. I heard the diagnosis in the hospital but did not realize that it is life-threatening. I am so glad that UCLA is right around the corner from me. I really believe the treatment there is what kept my NF from becoming as serious as many other stories I have seen. Other than a scar or two, I am looking forward to getting myself back to 100% soon. . .



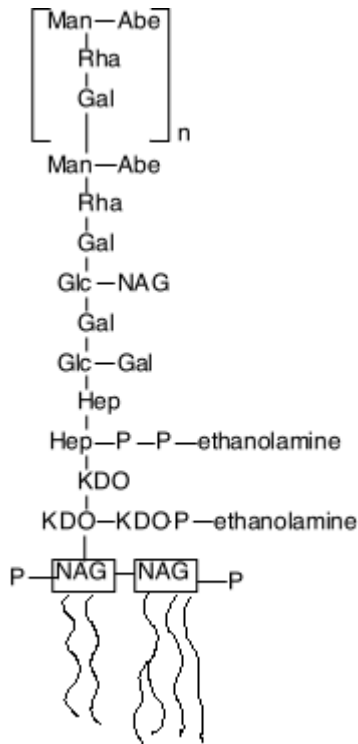
Necrotizing fasciitis (NF) is a severe soft tissue infection that can be caused by several bacteria, the best known being "flesh eating" *Streptococcus pyogenes*. Several other bacteria cause NF, including Gram positive *Staphylococcus aureus* and other *Streptococcus* spp. and Gram negative *Klebsiella pneumoniae*, *Escherichia coli*, *Vibrio* spp., *Aeromonas* spp., and *Pseudomonas aeruginosa*. Mixed infections are common. In addition to local pain and swelling, patients often have flu-like symptoms including malaise, fever, nausea, diarrhea, and confusion. Often tissue must be surgically removed to block the rapid spread of the bacteria and their toxins. If not diagnosed and treated rapidly, NF can necessitate amputation or be fatal.

*Klebsiella pneumoniae* is a Gram negative rod-shaped bacterium. *K. pneumoniae* is an important cause of nosocomial infections, including pneumonia, urinary tract infections, septicemia, and cellulitis. *K. pneumoniae* has **fimbriae** with which it attaches to host cells. Clinical isolates also usually have a **capsule** (extracellular polysaccharide layer, EPS), which aids with attachment to host tissue and blocks complement and phagocyte binding. At least 77 K (capsule) **serotypes** have been discovered.





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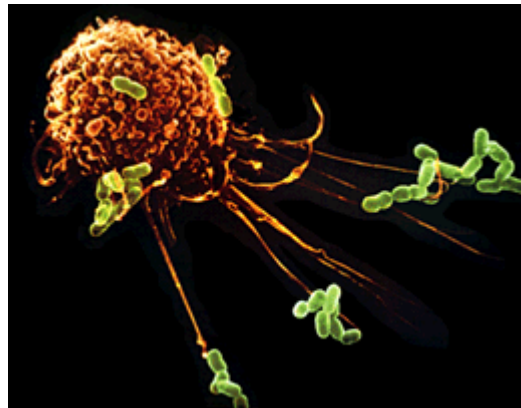


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**Figure 2:** A, electron micrograph of *K. pneumoniae* showing fimbriae. B, capsule stain of *K. pneumoniae*. C, diagram showing structure of Gram negative bacterial cell wall. D, structure of Lipopolysaccharide (LPS)

**Lipopolysaccharide (LPS or endotoxin)** is another important virulence factor for *K. pneumoniae*. The chemical structure of LPS is shown above; it is a major component of the outer membrane of Gram negative bacteria. LPS activates complement and causes the deposition of C3b onto the LPS, far enough away from the outer lipid membrane that the membrane attack complex of complement cannot form and the bacterium cannot be lysed.

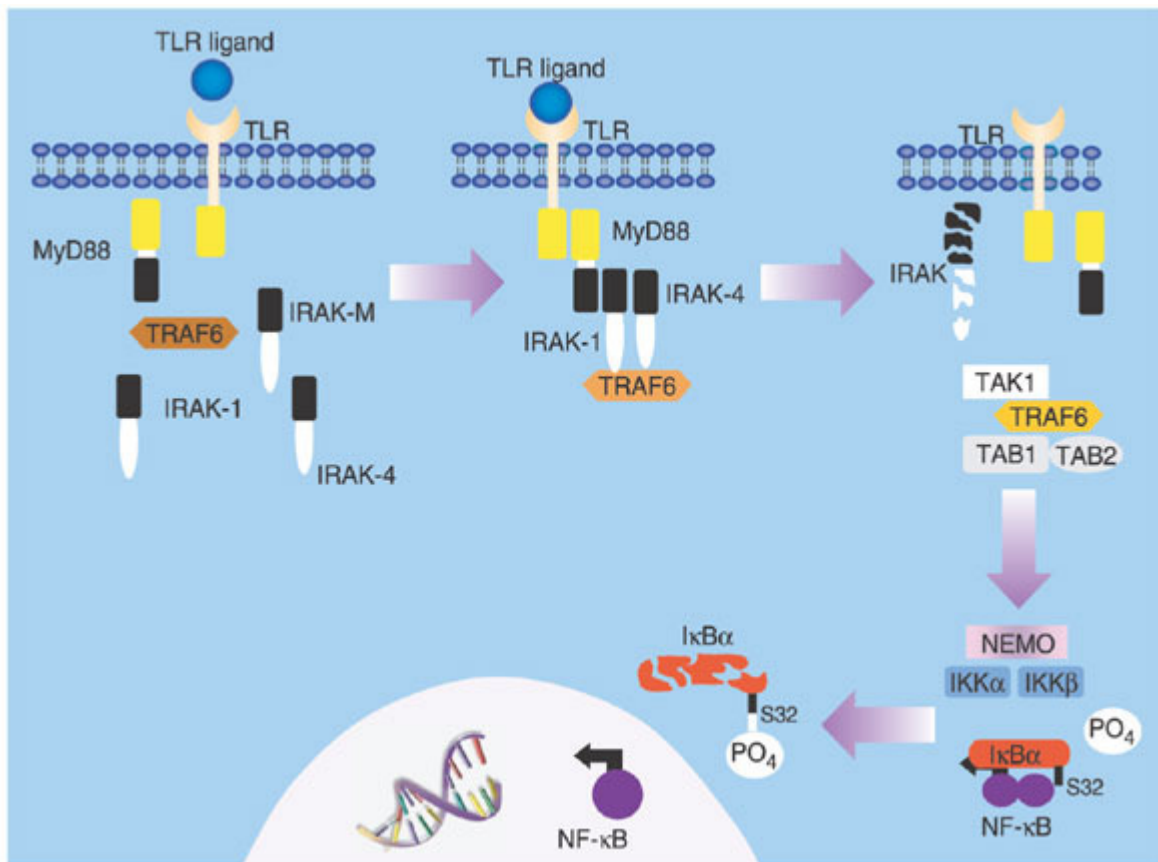
**Questions:**



1. From the information above, how does *K pneumoniae* damage the host? What immune responses will be protective?
2. What immune cells are at the infection site (in the tissues) when the pathogen enters? Which ones need to come into the infection site and how do they know to enter the tissues at the correct location? Discuss the role of adhesion molecules on leukocyte migration.
3. Macrophages must bind the pathogen in order to engulf it. Below is a list of receptors found in macrophages. Provide the ligands for each of the receptors, and b) Which of the receptors below could bind to *K. pneumoniae*?

<b>Macrophage Receptors</b>	<b>Ligands</b>
mannose receptor	
glucan receptor	
CD14	
scavenger receptors	
<b>Cell-surface TLR</b>	
TLR-1/TLR-2	
TLR-2/TLR-6	
TLR-4/TLR-4	
TLR-5	
<b>Endosomal TLR</b>	
TLR-3	
TLR-7	
TLR-8	
TLR-9	

4. Binding of ligand to TLR initiate a cascade of cytoplasmic events that include protein-protein binding and phosphorylation. The end result of these events is synthesis of mRNA for **inflammatory cytokines**. List the inflammatory cytokines produced by macrophages and what the functions of each are.



5. What is **inflammation**? What are the four signs/symptoms and what causes them? What is the purpose of inflammation?

6. What is **complement**? In what three ways is complement activation initiated and what are the three functions of complement? How is complement prevented from lysing host cells?

7. What are **acute phase proteins** and how do they enhance innate immunity?

8. What are the roles of interferons  $\alpha$  and  $\beta$  and Natural Killer cells in innate immunity? Are they important in a *K. pneumoniae* infection?

9. List as bullets with brief descriptions and in approximate chronological order the steps in the innate response to a bacterial infection. Include both the cells and the

molecules that are involved in the response to the bacteria and what each does. Include virulence factors that allow the bacterium to evade the immune system and what each does.

**Example:**

- Bacteria penetrate the skin through the punctures and enter the deeper layers of tissue.
- Bacteria begin to replicate at the site of infection.
- At the site of infection, . . .

Case adapted and Modified from Dr. Janet Deckert at the University of Arizona. Her email is [jdeckert@u.arizona.edu](mailto:jdeckert@u.arizona.edu) and her website is [webMic419 Home](#)

**Supplementary Materials:**

Tutorials: [Innate Immunity](#), [Complement](#), [Cytokines](#), [Infectious Disease](#), [Immunity Rules](#), [Antigen](#)

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