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Re: Case 1:17-vv-00221-UNJ Document 37 Filed 09/18/19

Dear Mr. Shoemaker,

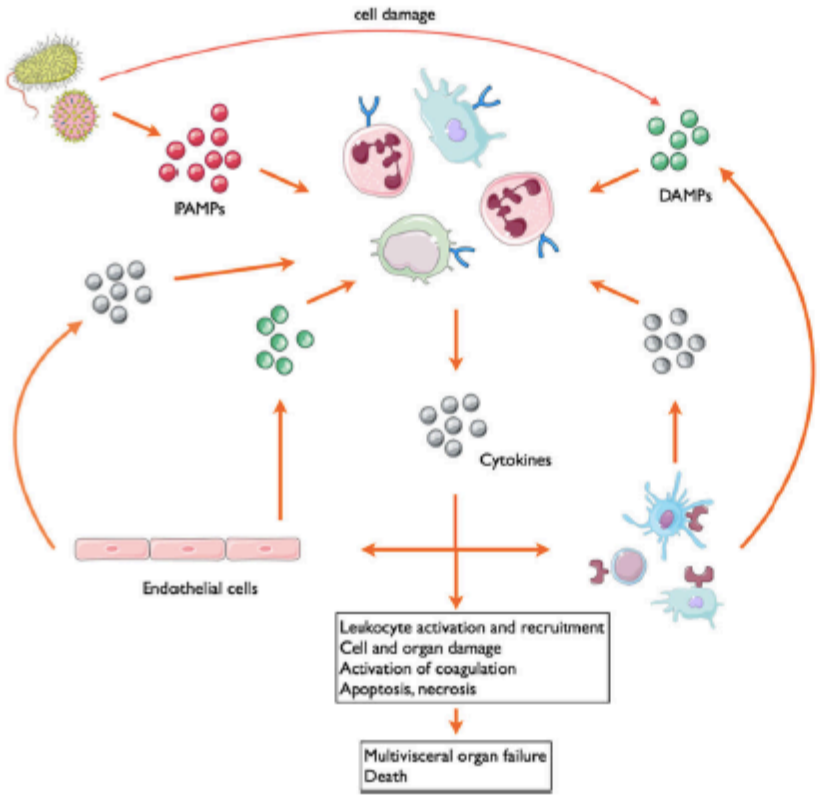
This report and the attached references will support with substantial evidence support our theory of causation by addressing each of Special Master Oler's **questions**:

1. What evidence exists in the record that Mr. Chilazi had high levels of proinflammatory cytokines either before or after his October 20, 2015 flu vaccination?

A1a) Mr. Chilazi was diagnosed and treated for sepsis. Sepsis is a severe clinical syndrome related to the host response to infection or vaccination. By design a vaccination is intended to mimic the infectious process such that the host responds quickly and has a memory of an infection. The severity of infections is due to an activation cascade that will lead to an *autoamplifying* cytokine production: the cytokine storm (Chousterman et al).

The 2017 Chousterman review elegantly and with great detail describes the cytokine cascade originally called cytokine storm. The following description of that autoamplifying cascade is a quote from that paper which is depicted schematically in Figure 1(reproduced and quoted below)

Pathogen-associated molecular patterns (PAMPS) and damage/danger-associated molecular patterns (DAMPS)bind to pattern recognition receptors on particular immune cells in the pathogenesis of sepsis. The activated immune cells induce an acute inflammatory response, which is mainly driven by not only pro-inflammatory cytokines but also anti-inflammatory cytokines that regulate the inflammatory response. An excess of pro-inflammatory cytokines can lead to endothelial injury and systemic inflammatory response syndrome.



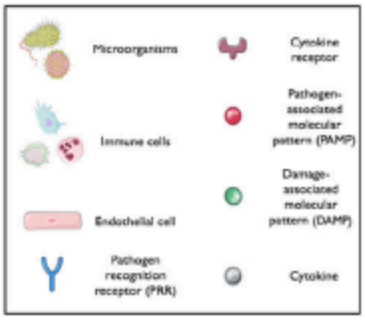


Fig. 1 Cytokine cascade during sepsis

In 2003, the cytokine storm was first associated with reaction to influenza. Appreciating that the global effects of infection are mostly due to the host response was not appreciated until the early 1990s when the consensus definition of sepsis was “systemic response to infection which is characterized by widespread inflammation”.

A1b) Endothelial injury (vasculature), can proliferate to generate pro-inflammatory cytokines such as IL-6, IL-8 and MCP-1. This indicates that endothelial cell injury might play a role in forming the cytokine network composed of IL-6, IL-8 and MCP-1(CCL2 throughout the acute phase of sepsis. Also, the augmentation of IL-6, IL-8 and MCP-1 could proliferate the inflammation by endothelial cells as a positive feedback system. Among these cytokine levels, the level of IL-6 increased most strikingly over the acute phase (Fig. 1A Matsumoto et al 2018). Mr. Chilazi’s clinical symptoms noted by the home health care nurse on October 21 2015 of extreme shivering and malaise is the classic clinical presentation of acute sepsis mediated by a pro-inflammatory network of cytokines. EX ?” patient is sluggish, laying on bed with general weakness noted.” ..’No temp noted with occasional dizziness. Shivering, weakness, is evidence pro-inflammatory cytokine response driven by IL1B. Fever presents later.

A1c) The third piece of evidence is that Mr. Chilazi was diagnosed and treated for Clostridium Difficile Infection (CDI) (Sun et al). Diarrhea is evidence of CDI infection. Antibiotic exposure is the most significant risk factor for refractory and or recurrent CDI. Ex 8 p1 6/19/2015. Ex 8 p4-5 May 28, June 5 2015 ‘ZC is on antibiotics (Ciprofloxicin: a fluoroquinolone and known mitochondrial toxin) and has

Diarrhea. This is recurrent/refractory CDI and occasional diarrhea suggests CDI is involved in pathogenesis, which supports the involvement of proinflammatory cytokines.

A1d) A fourth piece of evidence is that Mr Chilazi was being treated for Atrial Fibrullation which is now recognized as an inflammatory disease driven in part by proinflammatory cytokines MCP-1/CCL2 (Al-Zaiti, Baylis, Guo & Hu). We will elaborate under question 2.

2. What evidence exists in the record that Mr. Chilazi suffered from myocarditis?

A2a) The medical dictionary defines myocarditis as "an inflammatory disease of the heart muscle (myocardium) that can result from a variety of causes. While most cases are produced by viral infection, an inflammation of the heart muscle may also be instigated by toxins, drugs and hypersensitive immune reactions.

Clinical evidence of myocarditis may include changes in eyesight, severe or persistent muscle or joint pains, severe muscle weakness, low red blood cells (anemia), irregular heart beat (Atrial fibrillation), fatigue.

From the medical records, we quoted that Mr. Chilazi had a UTI, high WBC, significantly low RBC in April May and June of 2015 (Ex 08 P1, 4-5 respectively) all of which are causes of myocarditis.

A2b) Mr. Chilazi was being (successfully) treated for Atrial fibrillation for several years. Atrial fibrillation is now recognized to be an acute and or chronic inflammatory disease. That is Atrial fibrillation is evidence of Myocarditis (Al-Zaiti, Baylis, Guo & Hu).

3. Dr. Rose states, "[a]lthough diarrhea is referred to from time-to-time in Mr. Chilazi's medical records, nothing indicates overwhelming C. difficile proliferation with extensive inflammation and continued cytokine release." Do you agree or disagree with this statement? Please provide citations to the medical records supporting your position.

We strongly disagree with this statement which in Dr. Rose's report follows the statement "Dr. "C. difficile colitis is a medical emergency that must be promptly treated. We did not state C Difficile Colitis nor did the medical records. Mr. Chilazi was treated for C. Difficile Infection (CDI) not C.Difficile Colitis. Systemic inflammation is caused by recurrent or refractory CDI. In their 2015 Review Sun and Hirota write "The clinical manifestation of CDI is highly variable from asymptomatic carriage to mild self-limiting diarrhea to the more severe pseudomembranous colitis. Furthermore, in extreme cases, colonic inflammation, tissue damage can lead to toxic megacolon. (Toxic megacolon~= C Difficile Colitis). Similarly, systemic inflammation is not necessarily "extensive inflammation ". The inflammation was controlled by antibiotics but ciprofloxicin is a powerful mitochondrial toxin and changes both the microbiome and the cytokine profile as we discussed in our original report. The recurring diarrhea is evidence of the continued dysregulation and cytokine release, which is depicted in Figure 1 of Sun and Hirota's review and reproduced below:

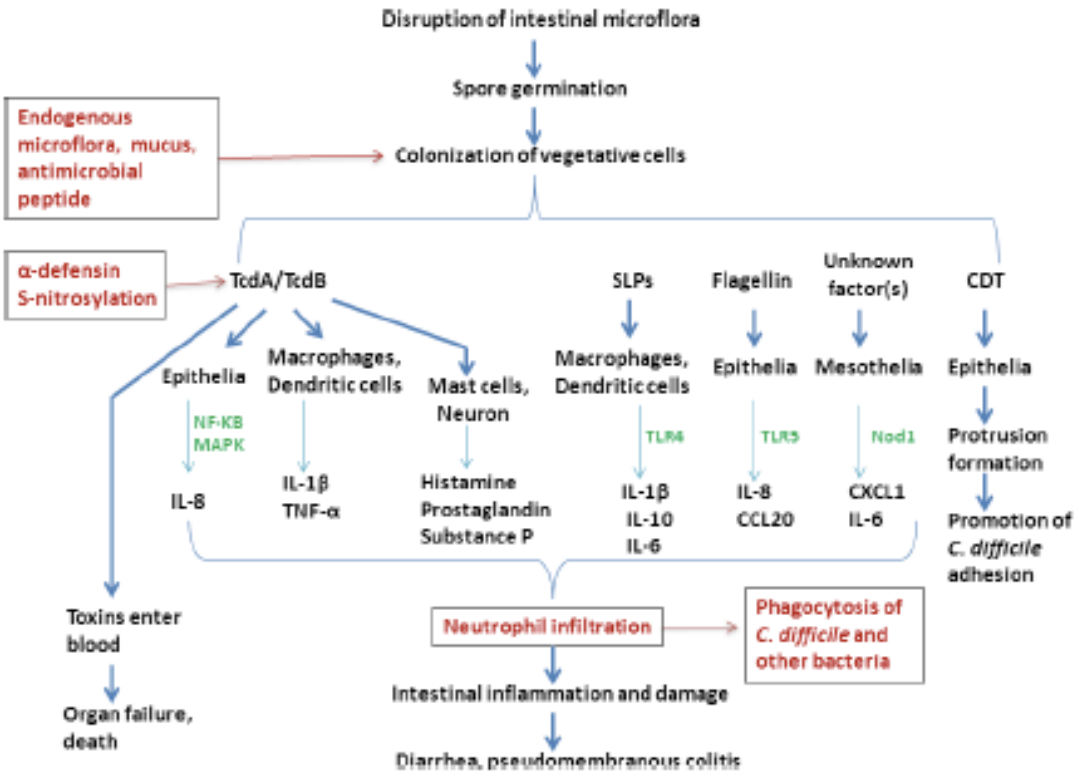
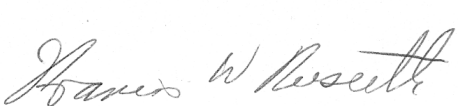


Figure 1. CDI pathogenesis/Host-pathogen interactions – outlining the innate signaling pathways activated by *C. difficile*

Note that Mr. Chilazi tested positive for high neutrophils, and Alkaline Phosphatase (Exh 07 p4, 5) which support ongoing systemic inflammation which can cause tissue injury and promote tissue injury. Ex 7 p5 also clear shows the persistence of CDI with positive expression of C. Difficile Tox A & B and GDH antigen.

It remains our opinion to a reasonable degree of scientific and medical certainty that the influenza vaccine (Fluvirin) Mr. Chilazi received on October 20, 2015 caused his cardiac arrest and death.

Sincerely,

Judy A Mikovits, PhD and Francis W. Ruscetti, PhD

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