**MED3ATB**

**Sepsis worksheet**

**Instructions**

Fill out the following worksheet while working through the *Sepsis* lesson on LMS. You must write all answers in your own words (paraphrase). Do not plagiarise from the text or videos provided!

Bring your worksheet to the workshop. You will be tested on your knowledge of this module in the weekly quiz.

1. In the context of polymicrobial sepsis, inflammation is a necessary evil. Discuss (4-5 sentences) **5 Marks**

## Sepsis occurs as a result of the immune system’s excessive reactivity through the overproduction of pro- inflammatory cytokines in response to pathogens in the blood. As the overproduction of cytokines can cause serious tissue damage, anti- inflammatory mediators are produced by the host to limit this effect. The anti-inflammatory response results in the apoptosis of the immune cells and consequently leads to lymphopenia and immune suppression. Although reducing inflammation could prevent tissue damage, excessive reduction of inflammation could impair the ability of the immune system to defend against pathogens. Polymicrobial sepsis is responsible for approximately 85 % of deaths where secondary opportunistic infections such as pseudomonas and hepatitis B are able to invade the host due to reduced inflammatory response. Hence why inflammation is a necessary evil; necessary for defense against invading pathogens, and evil as in excessive levels it can lead to septic shock.

1. In the last 25 years, about 100 clinical trials for treating sepsis have failed. Discuss the reason for this high rate of failure. **5 Marks**

The failure in clinical trials for treating sepsis in the last 25 years is as a result of attempts to block the inflammatory pathway involved in sepsis. Pro inflammatory cytokine overproduction results in a cytokine storm which leads to septic shock. Although the overproduction of these cytokines can result in sepsis, the production of adequate amounts of cytokines is absolutely essential for the recruitment of adaptive immune cells to fight and clear the infection. Thus attempts to block components in the inflammatory pathway that prevent cytokine production have failed in the past. An example of this was the blocking of the TLR 4 receptor on the innate immune cells by a LPS analogue drug. Selective targeting of certain cytokines by antibody based drugs, such as antibody against the cytokine TNF alpha have also shown to fail as treatments as multiple cytokines are involved in the inflammatory pathway during sepsis.

1. Explain the mouse model for studying sepsis. **3 Marks**

Cecal ligation and puncture (CLP) is the mouse model used for inducing polymicrobial sepsis in mice that closely relates to the human sepsis characteristics and progression. In this model the cecum is punctured to allow for the leakage of the intestinal contents in the peritoneal cavity. As the fecal matter contains gram negative bacteria, the LPS on the bacterial cell wall is specifically recognized by TLR 4 on the host’s innate immune cells giving rise to sepsis.