

Observations on sepsis and COVID-19 disease



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REFERENCES

- Alhazzani W, Möller MH, Arabi YM et al (2020) Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19) *Intensive Care Med* 46(5):854–87
- Daniels R (2018) Sepsis: the silent killer that claims around 44,000 lives every year in the UK. *Wounds UK* 14(1):94–5
- Hui Li, Liang L, Zhang D et al (2020) SARS-CoV-2 and viral sepsis: observations and hypotheses. *Lancet* 395:1517–20
- Richardson S, Hirsch JS, Narasimhan M et al (2020) Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA* doi:10.1001/jama.2020.6775
- Rogers LC, Armstrong DG, Capotorto J et al (2020) Wound Center without walls: the new model of providing care during the COVID-19. *Pandemic Wounds WND* 20200420-1
- Tang N, Li D, Wang X (2020) Abnormal coagulation parameters are associated with poor prognosis with coronavirus pneumonia. *J Thromb Haemostasis* 18(4):844–7
- White R, Jeffery S, Elstone A, Cutting K (2015) Sepsis and chronic wounds: the extent of the issue and what we should be aware of. *Wounds UK* 11(4):16–22
- White R, Witts S (2016) Sepsis and chronic wounds: What do you know? What should you know? *Wounds UK* 12(4):48–51
- Zhou F, Yu T, Du R, et al (2020) Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 395(10229):1054–62

COVID-19 disease has raised some clinically important issues of pathophysiology. Amongst these is the association with sepsis. Awareness about sepsis, and its association with chronic wounds, has increased considerably amongst healthcare professionals in recent years, to the degree that the condition should not go unrecognised through want of education (White and Witts, 2015; White et al, 2016, Daniels, 2018). Now that we are in the throes of a COVID-19 pandemic, with high rates of morbidity and mortality, an important link with sepsis has been reported (Alhazzani et al, 2020; Hui et al, 2020). What is happening to bring this about and, what does it mean for healthcare professionals?

Firstly, the recognition of the clinical development of this complication. Sepsis is a non-specific response to infection manifested by an exaggerated host immune response (a 'cytokine storm') which can often lead to death. Another feature is disseminated intravascular coagulation (DIC), especially in small blood vessels. DIC has already been noted in COVID-19 patients' lungs and kidneys and presents a real threat for organ failure (Tang et al, 2020).

For patients post sepsis, in good general health with no re-infections or immunity problems, the impact of COVID-19 is likely to be same as in the majority of the population — in other words, a relatively mild illness. However, for those defined on medical grounds as being extremely vulnerable and are at very high risk of severe illness from COVID-19, there is evidence that this infection can lead to sepsis (see also <https://sepsistrust.org/>).

From information presently available on clinical cases of COVID-19 (Richardson et al, 2020), it appears that a percentage of COVID-19 infections can result in organ failure, meaning that some patients develop kidney failure, or shock, rather than solely respiratory failure.

It is vital to be aware of any deterioration in a patient's condition. If they develop any of the following symptoms in the context of infection, urgent medical help needs to be sought: **Slurred**

speech or confusion; extreme shivering or muscle pain; passing no urine (in a day), severe breathlessness; skin mottled or discoloured.

Breathlessness, cough and fever are common in people with COVID-19. Seek help based on severe breathlessness, particularly at rest; or breathing very rapidly (more than 22 breaths a minute); or when you notice cyanosis of the lips, fingers or toes.

A recent report from China on the clinical course of COVID-19 showed that of 191 patients studied in Wuhan, 137 recovered and were discharged and 54 died in hospital (Zhou et al, 2020). The major comorbidities of hypertension, diabetes and heart disease, combined with age, increased mortality. Death was attributed, in part, to multiple organ failure marked by a key sepsis biomarker, D-dimer, being raised. This identifies a high molecular weight fibrin, an agent associated with microcirculatory failure, and multi-organ failure. Clinically, this manifested at day ten of the onset of disease symptoms. Antibody levels showed that total immunoglobulin G (IgG) was raised in a way similar to that seen in bacterial-mediated sepsis. This immunoglobulin is linked to chronic infection and reflects a humoral response in the host.

Pathogens that induce an adaptive immune response are relevant in the infection process and may be identified by measuring IgG subgroups in the blood. The humoral response to antigenic or inflammatory challenges, such as infection, vaccination or trauma, has been proposed to comprise the polyclonal activation of memory B cells of unrelated specificity. The levels of IgG being driven by the increasing infection and, in the case of the pathogen in COVID-19 disease, SARS-CoV-2, may or may not be strain specific.

Always be alert to the development of sepsis in patients suffering infection. Links with sepsis in patients with burns, surgical, traumatic and chronic wounds are well established (Roger et al, 2020) and every clinician should be aware of its potential for increased morbidity and mortality.

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