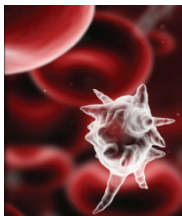




# Sepsis Supplement

November 2015

## Introduction



The total number of patients developing sepsis within the UK every year is now over 100,000. Approximately 37,000 of these patients will die, with survivors suffering long term physical and psychological problems, resulting in significantly reduced quality of life.

The awareness and understanding of sepsis is poor by both healthcare professionals and the public<sup>1</sup>. Old fashioned and incorrect terms such as blood poisoning and septicaemia are still commonly used<sup>2</sup>. These terms refer to the invasion of bacteria into the blood stream and imply the infection is limited to the blood, whereas sepsis is a systemic condition that can be caused by bacteria, rarely viruses and fungi. A recent clinical audit undertaken by the Clinical Audit and Research Unit (CARU), found that only 69% of clinicians could define sepsis and only 23% could identify the three stages of sepsis.

## Why bother with sepsis?

Sepsis is one of the biggest killers and is responsible for more deaths annually than myocardial infarction, stroke, chronic obstructive pulmonary disease (COPD) or lung cancer (Figure 1)<sup>3</sup>. Sepsis, unlike many of the other big killers, is not age or gender specific and can affect anyone, at any time<sup>2</sup>. However there are groups of patients who are more susceptible. Sepsis may begin with minor infections that over time develop into widespread illness and subsequent organ dysfunction. The delayed commencement of interventions due to poor identification drives the high mortality<sup>4</sup>.

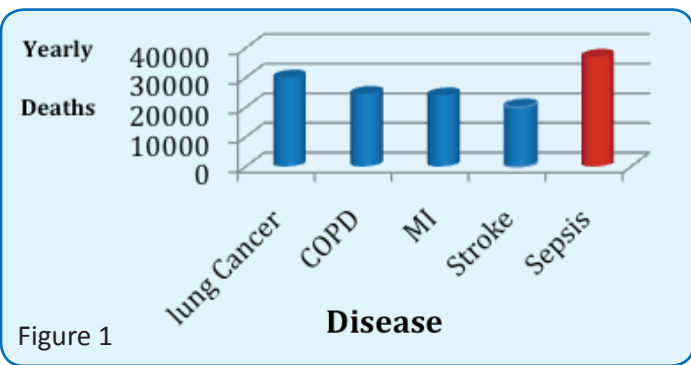


Figure 1

Ambulance clinicians may be one of the first healthcare professionals to see septic patients, despite this the current UK Ambulance Services Clinical Practice Guidelines (2013) are not consistent with the international sepsis consensus definitions and guidelines<sup>5</sup>. New guidelines for the treatment and management of sepsis are currently being constructed and will be included in future guideline updates.

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## Defining Sepsis

Sepsis is defined as a systemic inflammatory response to an infection and involves three distinct stages:

1. **Uncomplicated simple sepsis (often referred to as sepsis)** - Suspected or known infection, in the presence of Systemic Inflammatory Response Syndrome;
2. **Severe sepsis** – sepsis with any sign of organ dysfunction, and
3. **Septic shock** - Continued evidence of severe sepsis (organ dysfunction) despite adequate fluid resuscitation.

### SIRS is defined as two or more of the following:

Temperature < 36°C or > 38.3°C

Heart rate > 90 beats per minute

Respiration rate > 20 breaths per minute

Blood Glucose level > 7.7mmol/l  
(If no diabetes mellitus)

An acutely altered mental state

White cell count < 4 or >12 x 10<sup>9</sup>/l (if known)

*Box 1: Systemic Inflammatory Response Syndrome criteria in Adults.*

## Recognising Sepsis

The definitions of sepsis rely on the recognition of Systemic Inflammatory Response Syndrome (SIRS) and the identification or suspicion of an infection. SIRS is a host response to an infection that triggers a complicated, variable and prolonged cascade of events. This response involves pro-inflammatory and anti-inflammatory mechanisms that contribute to clearance of infection and recovery of tissue but also causes organ injury and secondary infections<sup>6</sup>. It is this widespread complex response that gives rise to the varying symptoms seen in SIRS such as, tachycardia, tachypnoea, hyperglycaemia and pyrexia. SIRS is deemed to be present if a patient has two or more of the criteria set out in *Box 1*.

The second part of the recognition of sepsis and probably the most important is identifying or suspecting the presence of an infection. The key to identifying or suspecting an infection is undertaking a thorough Review of Systems (ROS), as signs and/or symptoms of infection might not always be obvious<sup>2</sup>. A ROS is a *brief* structured review of body systems which may not have been discussed in the history of presenting complaint.

The ROS helps identify signs and/or symptoms that the patient may be experiencing or has experienced. The recent clinical audit by CARU found that only 44% of patients had an adequate ROS undertaken, which will have significantly contributed to the low level of sepsis identification in the LAS. *Box 2* shows an example check list of what should be described for each body system.

## Review of Systems

The review of systems should cover the following areas:

- **General**
  - > Fatigue, weight, appetite, fever and general health
- **Neurological**
  - > Headaches, dizziness, fits/faints/funny turns, vision problems, new confusion
  - > Signs of meningitis or encephalitis (neck stiffness/photophobia)
- **Cardiovascular**
  - > Chest pain, SOB, SOBOE, palpitations
- **Respiratory**
  - > Chest pain, SOB, SOBOE, cough, sputum, haemoptysis, increased respiratory rate or effort, pleuritic pain
- **Gastrointestinal**
  - > Nausea, vomiting, abdominal pain/distension, urinary and bowel habits, diarrhoea, constipation
- **Genito-urinary**
  - > UTI symptoms, urinary habits, abdominal, flank and back pain
- **Musculoskeletal**
  - > Pain, swelling, stiffness, mobility, hot painful joint, non-weight bearing
- **Skin**
  - > Purpuric rash, cellulitis, diabetic foot and ulcers, burns
- **Other**
  - > Dental problems, foreign travel, exposure to other unwell contacts

This is not an exhaustive list and clinical judgement should be used when considering whether a sign or symptom of an infection is present.

*Box 2: Review of Systems process and common signs & symptoms of an infection*

## Severe sepsis and septic shock

Although patients with uncomplicated simple sepsis will require referral to an alternative care pathway (ACP) or attendance at the Emergency Department (ED), they often don't require aggressive treatment and management. If the uncomplicated simple sepsis progresses, resulting in organ dysfunction (see Box 3), this is suggestive of severe sepsis and should be managed appropriately. If the patient continues to deteriorate despite this treatment, they may have developed septic shock.

**Severe sepsis** is defined as sepsis with any sign of organ dysfunction, which can include any one or more of the following:

- Systolic blood pressure < 90mmHg or a decreased systolic > 40 mmHg from their norm
- Oxygen saturations < 91%
- Lactate > 2mmol/l
- New onset of confusion
- Decreased urine output



### Red flag sepsis

In addition to the standard signs of organ dysfunction used in the definition of sepsis, the UK Sepsis Trust has recently introduced the concept of red flag sepsis. This introduces additional aspects to indicate that a patient is likely to be suffering from severe sepsis and requires aggressive treatment. Presence of one or more of the red flags can be suggestive of severe sepsis.

**Respiratory rate > 25 breaths per minute**

**Heart rate > 130 beats per minute**

**Oxygen saturations < 91%**

**Systolic blood pressure < 90mmHg**

**Responds only to voice, pain or is unresponsive**

Septic shock is defined as continued evidence of severe sepsis (organ dysfunction) despite adequate fluid resuscitation.

Respiratory rate is a very sensitive marker of serious illness. Accurate recording is essential.

*Box 3: Definitions of severe sepsis and septic shock<sup>7</sup> in adults*

## How should we treat sepsis ?

Patients with simple uncomplicated sepsis may require further examinations and tests, such as blood tests, urinalysis or a chest X-ray. Any patient, irrespective of age, who is SIRS positive and has evidence of infection, should not be discharged on scene without onward referral to an ACP.

### The sepsis six (to be delivered within one hour):

- 1 **Deliver high-flow oxygen**
- 2 **Take blood cultures**
- 3 **Administer intravenous antibiotics**
- 4 **Start intravenous fluid resuscitation**
- 5 **Measure lactate**
- 6 **Measure urine output**

### Box 4: The Sepsis Six

For severe sepsis and septic shock pre-hospital clinicians have a vital role to play. In addition to recognising these patients, it is important to start the initial phase of treatment. This initial phase of treatment involves a simple set of interventions that have been shown to significantly reduce mortality in sepsis<sup>1</sup>. This is known as the Sepsis Six (Box 4) and should be delivered within the first hour of recognition. Currently not all of these interventions can be performed by Ambulance Clinicians, but it is important to know what they are and why they are performed. By commencing the interventions we can perform early on and by undertaking rapid transport to hospital we can help reduce the mortality of sepsis. Non-paramedic crews should not delay transfer to hospital by waiting for a paramedic to come to scene.

### ■ Deliver high-flow oxygen

Severely septic patients are in a state of high oxygen demand, this is due to a reduction in oxygen delivery to the vital organs caused by a reduction in oxygen content in the blood and by reduced cardiac output ( $O_2$  Delivery =  $O_2$  content of the blood x Cardiac output). Increasing the fraction of oxygen in the inspired air increases the amount of oxygen in the alveoli and subsequently increases the amount of oxygen dissolved in the blood<sup>2</sup>.

All patients with severe sepsis or septic shock should initially be given high-flow oxygen at 15 litres via a non-rebreather mask. Once the patient is stable the oxygen should be titrated to maintain the oxygen saturations at 94-98%. If oxygen saturations are not available,

high-flow oxygen at 15 litres should be continued until saturations can be measured<sup>2</sup>. The recent clinical audit found that only 14% of severely septic patients were given the appropriate dose of oxygen. Reassuringly, 90% of respondents indicated that severely septic patients should receive high flow oxygen.

Patients with COPD are at high risk of developing sepsis. They will most likely present early on with simple sepsis and should be managed appropriately following standard COPD guidelines. In the event that they present with severe sepsis/septic shock, they should be treated following the severe sepsis guidelines including high flow oxygen therapy.

### ■ Blood cultures

Taking blood cultures is not routinely performed in the pre-hospital phase by Paramedics but will likely be one of the first tasks undertaken on arrival at the ED to identify the causative agent involved in the sepsis. Some trials around sepsis management, such as in the Isle of Wight have examined pre-hospital blood taking, with trial results awaiting publication. Blood cultures need to be taken before the administration of any antibiotics so as to not affect the cultures when being grown<sup>3</sup>. This does not apply in the context of suspected meningococcal septicaemia, where benzylpenicillin should be given without delay if indicated. The LAS currently has no plans to undertake pre-hospital blood sampling.

### ■ Intravenous antibiotics

Research has demonstrated that for every hour delay in giving antibiotics in sepsis there is a 7.6% increase in mortality<sup>1</sup>. Patients will often be given a broad spectrum antibiotic initially, until blood tests can confirm the causative agent. Hospitals will often have their own local antibiotic policies depending on the source of the infection, e.g. Lower Respiratory Tract Infection, Urinary Tract Infection<sup>8</sup>. Due to the short transfer times and the varying microbial polices within NHS London Trusts, pre-hospital antibiotic administration for sepsis is not currently indicated in London. Benzylpenicillin should continue to be administered in suspected meningococcal septicaemia.

### ■ Start intravenous fluid resuscitation

One of the most significant problems in severe sepsis is end-organ dysfunction which is primarily caused by a lack of blood supply. This lack of blood supply is often caused by relative hypovolaemia (normal volume in a vasodilated state) and/or absolute hypovolaemia (reduced volume)<sup>2</sup>.

Relative hypovolaemia is caused by a normal volume in an increased space. This is caused by the disease process of sepsis where there is dysfunction of the vascular endothelium causing wide spread vasodilation<sup>2</sup>.

Absolute hypovolaemia can be caused by either a reduction in circulating volume or the circulating volume



is no longer in the vascular system. A reduction in the circulating volume can be caused by a loss of fluid from the body, due to a lack fluid uptake, vomiting, diarrhoea, increased sweating etc. Volume loss can also be caused by metabolic/vascular processes such as increased ventilation, coagulopathy etc. Volume loss may also occur as fluid can leak out into surrounding tissues through the damaged endothelium<sup>2</sup>.

Absolute hypovolaemia negatively affects the stroke volume of the heart, which has a negative effect on the cardiac output. The equation below demonstrates why there is an increase in heart rate in sepsis. This increase is a response to maintain cardiac output in the hypovolaemic state caused by sepsis<sup>2</sup> (Cardiac output = Stroke volume x Heart rate).

The primary reason to start fluid therapy is to correct the relative and absolute hypovolaemia, which should normalise the blood pressure and heart rate. IV fluid therapy should follow current guidelines. **Severely septic patients should be given 1000ml of sodium chloride 0.9% over 30 minutes, which can be repeated once.** In this instance it is not necessary to follow the process of administering a 250ml bolus and reassessing. Fluid therapy can be commenced irrespective of projected journey time. Severely septic patients are time critical and on scene time should be kept to a minimum. When giving fluids, caution should always be given to patients with heart failure<sup>5</sup>. The recent clinical audit found that only 17% of severely septic patients were started on fluid therapy.

### ■ Serum lactate

Lactate is not routinely measured in the pre-hospital phase by Paramedics, although the Scottish Ambulance Service, NEAS and EEAST have undertaken trials of pre-hospital lactate testing with mixed results. Lactate measurement is a useful part of in-hospital management of sepsis but further research is required to determine its validity in the pre-hospital phase.

In a normal healthy individual, the body metabolises glucose to produce energy via the anaerobic process of glycolysis. The end product of this process is pyruvate that under normal conditions is then metabolised aerobically to produce further energy. In the low oxygen state of severe sepsis there is not enough oxygen to allow this process. Therefore, the pyruvate is converted anaerobically to lactate to enable further energy production. Therefore, increased lactate levels are an indication of local or systemic ischaemia<sup>2</sup>.

## ■ Urine output

Measurement of urine output is crucial, as it is an indication of kidney function, which is an important indicator for tissue perfusion and is more reliable than blood pressure. In hospital, patients will be catheterised and urine levels will be closely monitored. As this is not routinely performed in the pre-hospital phase it is vitally important that patients are questioned about their urinary habits. If a patient has had a reduction in urinary volume or frequency in the previous days, this will be an important finding and must be documented and passed on in hand over<sup>2</sup>. Always consider the significance of dry pads in people with incontinence and ask about volume in catheterised patients.



## ■ Why is this so important?

A recent clinical audit undertaken by CARU, found that overall recognition and management of sepsis was poor. Crews only identified 26 out of 200 septic patients; less than half of patients received an adequate review of systems and worryingly only 8 of the 70 severely septic patients were managed appropriately.

When attending to a patient with abnormal vital signs, ask yourself, is this patient positive for SIRS? If so, could the SIRS be caused by an infection? Undertake a thorough assessment and review of systems. Remember, patients can and have died from sepsis caused by a sore throat!

If the patient is septic; is there any evidence of organ dysfunction or red flag sepsis? If so, remember the following:

- High flow O<sub>2</sub> via a non-rebreather mask
- Start 1 litre fluid resuscitation as per guidelines
- Ask about urinary habits
- Pre-alert to the nearest ED, stating SEVERE SEPSIS
- Please use severe sepsis PRF code 105
- Count the respiratory rate

Pre-hospital clinicians can make a significant impact on the mortality and morbidity of sepsis patients. Early recognition will save lives!

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# Sepsis FAQ's (November 2015)

## Are we using the UK Sepsis Trust screening tool?

The UK Sepsis Trust screening tool has been made available to staff attending CSR courses and via conferences and other educational events. An LAS specific tool is currently being printed and this will supersede any other versions when released.

## Are GP's and Hospitals using tools and screening?

Yes NHS England have released a Commissioning for Quality and Innovation for sepsis for all patients who present to emergency departments and other wards/units that directly admit emergencies with severe sepsis, Red Flag Sepsis or Septic Shock.

A stage 2 patient safety alert was disseminated to all NHS Trusts in September 2014, summarised below.

'This stage 2 alert has been issued to continue to raise awareness of sepsis and to signpost clinicians in the ambulance service, primary and community services and secondary care to a set of resources developed by the UK Sepsis Trust, and others, to support the prompt recognition and initiation of treatments for all patients suspected of having sepsis. These resources include the Sepsis six, a care bundle whose use is associated with significant numbers of lives saved and reduced length of hospital stays'

**NICE guidelines for treatment and management of sepsis are due for publication in July 2016.**

## Why does sepsis happen?

The condition is caused by the way the body responds to microorganisms such as bacteria entering the body. The infection could start anywhere or be localised. When someone has sepsis the immune system triggers some reactions including widespread inflammation, swelling and blood clotting. Blood supply to vital organs such as the brain, heart and kidneys is reduced. If not recognised and treated quickly, sepsis can eventually lead to multiple organ failure and death.

## Who is at risk of getting severe sepsis?

It is unknown why the body responds in this way and often people who get sepsis are in good health without long term illness. Some factors increase the risk of severe sepsis:

- Extremes of age
- Diabetes
- Long-term steroids or drugs to treat cancer (chemotherapy)
- Anti-rejection drugs after an organ transplant

- Illnesses that affect the immune system
- Having an infection or a complication after an operation
- Pregnancy / very recent childbirth

## Is sepsis always severe?

Most cases of sepsis are caused by common bacteria. Sometimes the body responds abnormally to these infections causing sepsis. Many people can have simple sepsis. However some patients develop severe sepsis, which means they become seriously ill and need hospital treatment straight away.



## Is everyone with a fever or elevated temperature septic?

No, sepsis can present with vague and non-specific symptoms and may not become obvious until organs begin to fail. This requires a high index of suspicion for sepsis to spot the subtle signs. Septic patients can become hypothermic and once their temperature drops below 36.0 degrees centigrade mortality in a normal environment increases significantly.

## What is the Sepsis Six?

The Sepsis Six is a care bundle for in hospital management and should be delivered as quickly as possible and always within one hour of recognition. Some elements of the sepsis six can be carried out in the pre-hospital phase, such as intravenous fluid administration and oxygen therapy.

## What elements of the Sepsis Six do we currently carry out in the LAS.

**High Flow O<sub>2</sub>** as per JRCALC and British Thoracic Society guidelines.

**Fluid Therapy** as below:

Current intravenous fluid administration in severe sepsis follows national clinical practice guidelines. In contrast with other approaches to fluid administration, the initial dose is 1 litre of normal saline where fluids are indicated. Repeat doses after 30 minutes may be required, however in the LAS setting the expectation would be that a time critical patient of this nature would already be in an ED.

## Will we be getting Lactate testing kits?

Elevated lactate is one of the markers used in hospital in the Sepsis Six. In hospital they usually use arterial blood whereas the pre hospital kits use venous blood. There are no plans to purchase lactate meters at present, due to proximity to Emergency Departments. Some trusts have gone ahead with lactate testing and this is the subject of current research so evidence relating to pre hospital lactate is emerging. Elevated lactate gives a good indication of tissue perfusion prior to some of the physiological changes becoming apparent.

## Paracetamol administration

Paracetamol should be administered on a case-by-case basis in accordance with AACE guidance. It is not mandatory to administer paracetamol to all patients with fever, although it would seem reasonable to consider paracetamol in cases where the patient is uncomfortable or in pain as a result of fever. However, routine administration in the absence of these features is not required.

Research is currently on-going to investigate the influence of paracetamol on outcomes in sepsis. It is not clear that attempting to reduce fever through the administration of paracetamol improves outcomes, and there is some evidence that it may be harmful.

## Why is reduced urine output significant, and how do we measure this?

Reduced urine output is significant; it provides a window on the circulation. It is measured in sepsis for in hospital management often with a catheter in situ. In the early stages of sepsis urine output is key. For pre-hospital management we cannot measure this so noting a reduction of urine output provides a useful indicator to the presence of sepsis.

## Sepsis v CVA

A member of staff attended a patient who had slurred speech, slight pyrexia (elderly patient) and a possible UTI. She had a history of stroke and a lot of risk factors. The family stated this is how she presented last time when she had her stroke. Sepsis can present with slurred speech, what would the advice be that if you had to choose between the two go with sepsis i.e. local A&E or HASU? There were no other neurological signs that could differentiate.

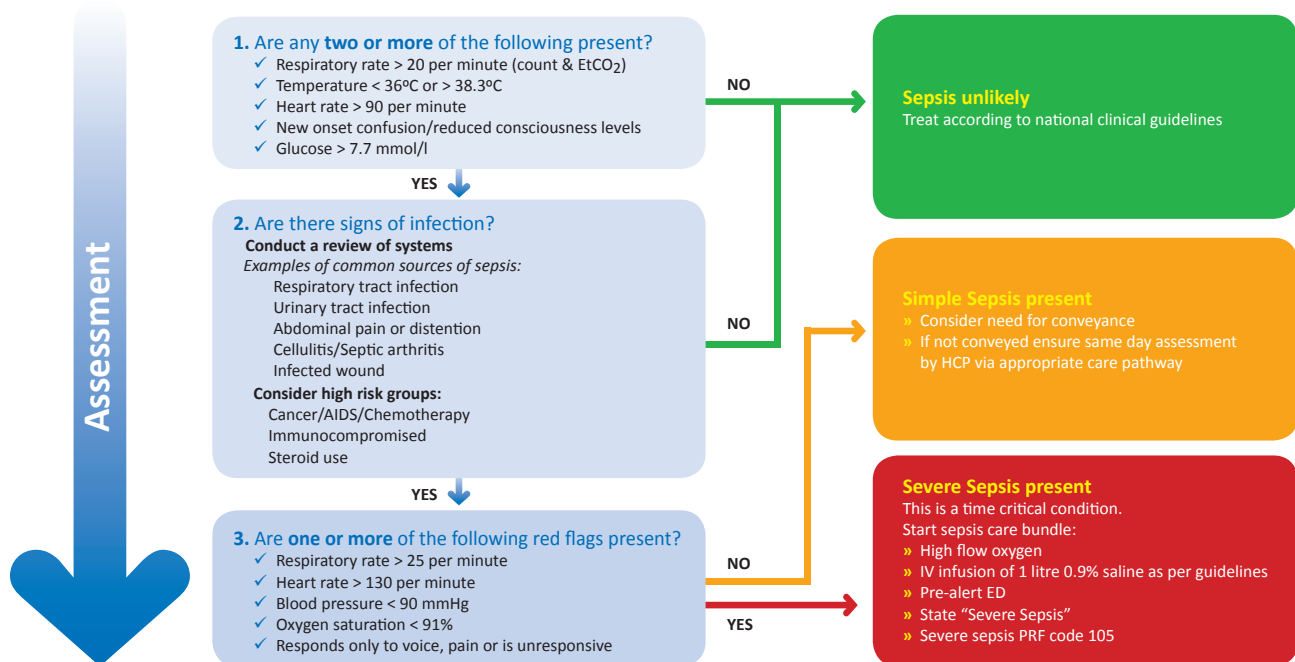
Stroke symptoms like slurred speech, confusion should be acute onset. If they are acute onset in the circumstances described and the family are stating that this is how the patient was when they last had a stroke, a stroke unit attached to an ED would be able to treat both conditions. If the patient goes to a non-HASU ED and then is found to have had a stroke the delay would likely be highly detrimental.

## Look out for the LAS Adult Sepsis Screening Tool due out soon



London Ambulance Service **NHS**  
NHS Trust

### Adult Sepsis Screening Tool



\*\* RASH \*\* Meningococcal disease should continue to be managed according to specific guidance

## Case studies

### Simple Uncomplicated Sepsis

**Call details:** Crew called to a 47 year old female at home, call given as 'uncontrollable shaking with neck pain'. On arrival the crew find the patient sat in a chair complaining of lower central abdominal pain.

**PC** – Abdominal pain

**HPC** – Patient complaining of 2 day history of abdominal pain, worsening this morning. The patient's mother has called, concerned about the shaking.

**PM/SHx** – Asthma: Has never been admitted for asthma and rarely has symptoms.

**DHx** – Salbutamol, fluticasone/salmeterol, Occasional OTC drugs, paracetamol, ibuprofen, as required. No recreational drugs. NKDA

**S/FHx** – Full time mother, lives in four bedroom townhouse with husband, 2 children and mother. Has never smoked and drinks alcohol 3-4 times a week.

**O/E** – Patient is fully alert, able to talk in full sentences and does not appear short of breath. RR 20, SpO<sub>2</sub> 98%, HR 102R, BP 124/72, good colour with CRT <2s, BM 6.8, Temp 38.9°C, pain score 3/10, GCS 15.

#### ROS

**NS** – Occasional self-limiting headache over the last 2 days

**CVS** – No CP, No SOB/SOBOE

**RS** – No SOB/SOBOE, No cough

**GIS** – Lower central abdominal pain

**GUS** – Increased frequency of urination with some slight pain. Urine appears slightly darker and foul smelling. No risk of pregnancy

**MSK** - NAD

**Plan** – The patient is SIRS positive, with a heart rate above 90 and a temperature above 38.3°C. There is a suspicion of a urinary tract infection, due to the abdominal pain and dysuria. With no evidence of organ dysfunction the crew suspect simple sepsis. The crew advise the patient she needs to be seen by another healthcare professional today, for a urine dip and likely antibiotics. They advise that they can take her to the local UCC or they can refer her to her GP. She would prefer to be seen by her own GP. The crew contact the surgery and arrange an appointment for the patient later that day. The crew advise her to stay well hydrated and she can self-administer 1g of oral paracetamol every 4 hours to settle the abdominal pain. The crew advise the patient to call 999 again if her condition deteriorates.

### Severe Sepsis

**Call details:** Crew called to a 77 year old male in a care home, call given as 'DIB not alert'. On arrival the crew find the patient lying in bed, breathing deeply with a reduced LOC.

**PC** - Unresponsive

**HPC** – The care staff state the patient has been unwell for a few days with a cough and was seen by the GP yesterday evening and was prescribed antibiotics for a possible chest infection. He has not started the antibiotics yet as these are due to be delivered today.

**PM/SHx** – From care notes: right sided stroke in 2011, HTN, AF

**DHx** – From care notes: warfarin, simvastatin, digoxin, ramipril, bendroflumethiazide, amlodipine. NKDA

**S/FHx** – Patient has been resident at the care home for six weeks

**O/E** – Patient is only responsive to pain and is breathing heavily and rapidly. RR 30, SpO<sub>2</sub> 90%, HR 119R, BP 75/44, pale colour with CRT >2s, BM 9.8, Temp 39.4°C, GCS 10 (E3, V3, M4)

#### ROS

**NS** –The patient has a significantly reduced GCS as they are normally well communicative

**CVS** – Patient had complained of chest pain prior to the GP visit

**RS** – Prior to GP visit, patient had 3 day history of SOB and cough with yellow/green sputum

**GIS** – Nothing in care notes

**GUS** – Care staff state that the patient's catheter bag appears to be draining less than normal and the urine was dark, when it was emptied this morning

**MSK** – Unable to ascertain

**Plan** - The patient is SIRS positive with a RR greater than 20, HR greater than 90, elevated BM (with no evidence of DM) and temperature above 38.3°C. There is also evidence of an infection due to the respiratory and urinary symptoms; this suggests the patient is septic. The patient is also showing signs of severe sepsis, indicating they are time critical and require rapid transport to hospital. The patient is placed on high flow oxygen and removed to the ambulance. A pre-alert is placed to the nearest ED, providing the vital signs and stating 'severe sepsis'. IV cannulation is undertaken en route and 1L fluid resuscitation is started. The Paramedic considers administering IV paracetamol but decided that fluid therapy was the priority for this time critical patient and does not give paracetamol. The crew record PRF illness code 105: severe sepsis.