ROYAL COLLEGE of PHYSICIANS of EDINBURGH

Evening Medical Update: Fever
Tuesday 19 November 2019

Sepsis 3.0: an update on diagnosis and management – Dr Robert Docking

Is this "sepsis"? Patient with urinary frequency, fever, and new confusion; otherwise clinically well and stable. NB - *This was a real patient, with heated discussion amongst the clinical team*.
I would argue that suspicion of infection and evidence of organ dysfunction in the setting of confusion would suggest the presence of sepsis.

Are there any good tools for spotting sepsis in the pre-hospital setting? qSOFA has been suggested.
Limited evidence for prehospital screening – most studies have sued SIRS (excluding WCC values) with a few more recently including blood pressure and new confusion. qSOFA performs reasonably as a screening tool but lacks sensitivity.

With Sepsis 3.0, the diagnosis seems to be even more difficult to make, requiring an intensivist to diagnose. What is the best screening and diagnostic tool?
I don't think that you need an intensivist to make the diagnosis! NEWS/physiological scoring tools are reasonable, but I don't like the idea that high NEWS = Sepsis: high NEWS = sick patient, but you need to have a wide diagnostic consideration. Septic shock probably is an important diagnosis to make – hypotensive patients with evidence of systemic hypo perfusion need escalation of care quickly if appropriate.

Are we right to treat sepsis as one disease? Or is there evidence that sepsis from different sources should be managed differently?
Yes and no. Fundamentals of sepsis management are similar regardless of cause, but we should be aware of the important of source control for appropriate patients – I think relying on antibiotics in patients with shock/organ dysfunction who have surgical option is dangerous – thinking of severe soft tissue infections/intra-abdominal sepsis – the role of interventional radiology hopefully has led to more interventionist approach in some cases.

Isn't there a test being researched to look for clot microstructure, which is significantly altered through the various stages of sepsis?
Yes – there is a biomarker that looks at the fractal function of clots – clot does seem far less structurally integral in patients with worsening sepsis. This may reflect the disorder of pro- an anticoagulant factors that was a trigger previously for the use of activated protein C.

Does septic shock and its effect on brain dysfunction have long-term impacts on mental health and poor sleep/wake cycle (post-inflammatory phase)?
Certainly critical illness has long-lasting effects on both physical and psychological health – sleep, mood, cognition all shown to have negative changes in the co called "post ICU syndrome" and similar seen in non ISU patients with sepsis.

Any role for procalcitonin in the prognostication of sepsis?
To my reading – no. PCT has been used by some sites for limiting duration of antibiotic therapy especially in "inflammatory" states like burns and pancreatitis. ADAPT-SEPSIS currently investigating use of PCT versus CRP for antibiotic usage.

Is there a role for Lipid Therapy?
Not to my knowledge.

Should we use steroids in patients with sepsis and pneumonia? Should we use steroids for ARDS?
First question – yes. I think there is enough evidence that steroids reduce treatment failure and need for escalation in pneumonia as per Cochrane review. In ARDS – not so sure – I think it depends on why you have ARDS – have seen florid pneumonitis with ventilator failure massively improve with steroids, but I don't think widespread use of steroids in ARDS is backed with evidence.

Regarding beta-blocker usage, is this not counterproductive with its effect on blood pressure? And doesn't beta-blockade block Noradrenaline's desired effect in septic shock?
The patients who may benefit from beta blockade are those who have a massive adrenergic/tachycardic/high stress response. The beta-blocker (highly selective B1 blockers) aims to reduce HR and therefore improve time for filling, coronary blood flow and cardiac function – as well as the potential immunological benefits of beta blockade. RCTs ongoing!

Are sepsis scores at risk of replacing clinical judgement?
Yes, completely. I don't think the "give Tazocin, ask questions later" approach has much going for it.

What do you think about peripheral short-term noradrenaline?
Completely safe if Venflon in a decent vein. Would support anyone using it.

Should you use lactate to guide fluid resuscitation?
I don't think so. The generation and metabolism of lactate is complex, and in sepsis probably reflects adrenergic tone rather than "tissue death". I don't think there's great evidence for its use, as shown by ANDROMEDA-SHOCK. Lactate has a role for identifying unwell patients, and patients who have lactate that falls do better than those who don't (as a population) but I don't think this is causative correlation.

Is there a definitive correlation between the use of Vitamin C, Thiamine and Hydrocortisone when compared to simple Antibiotic regimens?
No – hence proper large scale RCTs ongoing. We have endlessly looked for magic bullets in sepsis – I'd worry this is another one.

Would you increase steroids in patients on methotrexate for rheumatoid arthritis?
If they were septic? I'd probably replace their MTX with steroids and if on long-term steroids I'd increase the dosage.

Is there any simple tool for diagnosis and management of sepsis that can be used on the acute medical unit (AMU) or in the emergency department (ED)?
No. At present I'd use NEWS and look for red flag symptoms as per UK Sepsis Trust – but remember that high NEWS doesn't equal sepsis, it equals unwell patients that need a considered diagnosis made.

Neutropenic Sepsis – Dr Monica Szabo

Does neutropenic sepsis cause kidney failure?
Not directly. Combination of pyrexia and potentially dehydration as patient feeling too unwell to drink accompanied by other chemotherapy-induced toxicities (e.g. Diarrhoea, nausea and vomiting) may lead to this.

Why would blood cultures usually be negative in neutropenic sepsis?
They are often negative and this may be because we start antibiotics early when patient comes in feeling unwell without actual bacteraemia.

Tazocin is used in neutropenic sepsis and it is known to cause neutropenia. Is it safe?
The rate at which it can cause neutropenia is actually far lower than its benefit. Yes, we believe it is safe option.

Are certain cancers more likely to lead to neutropenic sepsis?
We are always more concerned about this in patients with risk for bone marrow insufficiency e.g. in the elderly or in patients with folic acid deficiency and bone marrow infiltration of their cancer. Usually it is the type of chemotherapy that is the risk and not the cancer, however, some cancer types require some of these more bone marrow toxic drugs.

Do you always give GCSF in neutropenic sepsis?
No, we would usually only give if the patient is either very unwell, requiring an intervention or with a neutrophil count of less than 0.1.

Would we discuss with oncology or haematology regarding GCSF?
I would discuss with the department who is looking after the patient so for haematological malignancies with haematology else with oncology.

When would you recommend GCSF in neutropenic sepsis?
If the patient is either very unwell, requiring an intervention or with neutrophil count of less than 0.1

Are there any groups of patients who shouldn't have GCSF when tested for Neutropenic sepsis?
Patients who are not deteriorating on antibiotics, requiring an intervention. Else also consider GCSF if neutrophils less than 0.1.

Can G-CSF in neutropenic sepsis lead to reversal of the benefits of preceding immunotherapy?
There is no evidence of this to date.

Is the MASCC score appropriate for all neutropenic sepsis or just those with cancer?
As I don't have much experience of neutropenic sepsis in any other patient entity I would say for cancer patients only.

Low risk neutropenia for ambulatory care - any thoughts/opinion?
If the patient is low risk then ambulatory care is appropriate with worsening advice. The local acute oncology team should call back the following day to review.

What criteria do some oncologists use to try and salvage a line growing gram negative bacilli (GNBs) given the high mortality associated with GNBs?
A short trial with specific antibiotics such as combination treatment using vancomycin (but check with your local microbiology department) is reasonably. If the patient deteriorates on this or has no evident improvement over the next 4-5 days despite negative cultures, then the line should be removed.

Is there any need to continue antibiotics if neutropenia is resolved and cultures are negative and no infective source is found?
We usually recommend continuation of antibiotics for 5 days.

For those working in rural areas without easy access to specialist oncology input what would be your key advice?
Start IV antibiotics on suspicion and if confirmed continue for at least 48 hours before switching to oral antibiotics or other IV antibiotics. Only escalate antibiotics if the patient deteriorates.

What is the rationale for adding Gentamicin with Tazocin?
This is only in the haemodynamically and acutely unwell patient to cover a broader spectrum.

If neutropenic but no signs of infection, would you consider antibiotics?
Not usually unless an obvious potential risk e.g. a damaged tooth

If it is treated on suspicion - how do you avoid over-diagnosing?
I assume this question is directed at over use of antibiotics. The recommendation is to treat on the assumption so one dose which can be stopped if bloods come back with a normal neutrophil count.

What's your views on neutropenia with count less than 1?
That is our cut off for neutropenia. If definitely asymptomatic and incidental finding no need for treatment else treat.

How do you manage neutropenic fever?
Neutropenic fever is really a subtype of neutropenic sepsis so I would treat in the same fashion – IV antibiotics on suspicion and pending on patients risk assessment score.

Our oncologists have suggested against using paracetamol in neutropenic sepsis. What is the evidence for this?
Paracetamol masks temperatures but if a patient is an inpatient, then overall clinical assessment can give a good indication of whether the patient is responding to treatment. I would usually only give paracetamol as PRN rather than regular to view temperature trend for response assessment too.

Among putting the patient on a third antibiotic and adding antifungal after 48 hours of not responding to two antibiotics, which one should come first?
That is a difficult question to answer as the likelihood of fungal or viral infections needs to be evaluated on the individual case. I would discuss these patients with the local microbiology department who usually give excellent advice.

Would a patient not require basic infection screen (CXR, cultures etc.) if neutropenic? Some patients may be compromised enough to elicit a fever response.
I would always do cultures, but if a patient remains completely asymptomatic from respiratory symptoms – and maybe even have an obvious source of infection i.e. cellulitis – then an x-ray is just excess exposure to radiation. And an oncology patient usually has a lot of that already.

Should we do viral and fungal screening on admission to all patients with suspected neutropenic sepsis (like CMV EBV BDG)?
Yes, to viral swabs, as quite commonly positive, fungal swabs really only if history of prolonged or frequent neutropenia.

Would you do a viral nasal swab for all presentations of neutropenic sepsis?
Yes

Does pembrolizumab cause neutropenic sepsis?
Yes

Can we safely discharge asymptomatic patient with neutrophils count as low as 0.1?
That is a difficult call to make and I would feel nervous about that as there is usually a reason why this patient has come in the first place. I would tend to keep the patient in for monitoring as often symptoms will arise within a few hours and repeat bloods the following day as the counts might be recovering.

Is there a figure for the case fatality rate from neutropenia sepsis?
Reported mortality rate for untreated neutropenic sepsis ranges from 2% - 21%

- Prognosis is worst in patients with proven bacteraemia:
    - Mortality rate of 18% in Gram-negative
    - Mortality rate of 5% in Gram-positive

Is there any role of Antifungal treatment for neutropenic sepsis?
Yes, if a fungal infection is suspected or likely e.g. in patients with prolonged or recurring episodes of neutropenia

Do cultures ever change the management of neutropenic sepsis?
Yes as switch to specific antibiotics – even oral antibiotics – possible and helps to avoid resistance.

Does CRP have any role in prognosis?
Not directly but it helps assess response but also can raise the suspicion of fungal infections which might have a worse prognosis.