Adult Critical Care Empirical Antimicrobial Therapy Policy - September 2017

- All antimicrobial prescriptions must include the indication and stop / review date in both the medical notes AND on the paper drug chart OR in Cerner Millennium Medications Summary.

- Empirical antibiotics should be stopped after 48hrs UNLESS there is clear clinical AND / OR microbiological evidence to continue treatment. PLEASE refer to and use the Adult Critical Care Antimicrobial Decision Support Tool.

- There have been increasingly frequent isolates of carbapenem resistant G-ve organisms in long stay ICU patients at St George’s (all 3 units). PLEASE limit the use of carbapenems whenever possible.

- All doses are IV unless otherwise stated. Switch to an enteral route at the earliest opportunity. Criteria for switching are:
  - Temperature less than 38°C for 48 hours
  - Enteral food / fluids tolerated, with no evidence of impaired motility
  - Patient is clinically stable with improving clinical parameters such as SOFA score & CRP
  - Not treating infections that require high antibiotic tissue concentration such as endocarditis, meningitis, necrotising fascitis, mediastinitis, brain abscess etc.

- Patients who step down from ICU on antibiotics should have the intended duration of treatment recorded in their ICU episode summary AND on the paper drug chart OR in Cerner Millennium Medications Summary.

- Optimal dosing of antibiotics in critically ill patients remains an area of active research, with under dosing and drug toxicity being real concerns. For a review of this topic see [1]. As a starting point see diagram below. In order to optimise some beta-lactam antibiotic therapy we give a rapid loading dose followed by extended or continuous infusions. Please refer to the drug specific notes below.

  - High dose dexamethasone in suspected bacterial meningitis is controversial. To be effective it HAS TO BE given BEFORE (or with) the first dose of antibiotics. After this time point, the negative effects probably outweigh any benefit. Retrospective analysis of the limited data on which this recommendation is based suggests that the patients that probably benefit are those with a high CSF bacterial load, with Strep. pneumoniae and H. influenzae BUT NOT N. meningitidis. Contra-indications include: pre-treatment with parenteral antibiotics; recent brain injury (including neurosurgery +/- CSF shunt); AND septic shock. The recommended dose is 8mg, 6 hourly for 4 days. Please discuss the use of dexamethasone with an ICU consultant BEFORE giving [2].

  - Corticosteroids in severe pneumonia remains controversial. The best evidence suggests such therapy is safe but of NO BENEFIT [3].
<table>
<thead>
<tr>
<th>Indication</th>
<th>1st line</th>
<th>If reliable Hx of TRUE penicillin allergy (see notes for definition)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community acquired pneumonia</td>
<td>Co-amoxiclav 1.2g 8hrly + Clarithromycin 500mg 12hrly</td>
<td>Levofloxacin 500mg daily</td>
</tr>
<tr>
<td>Hospital acquired pneumonia</td>
<td>Co-amoxiclav 1.2g 8hrly + Amikacin 15mg/kg daily (if shocked)</td>
<td>Levofloxacin 500mg daily + Amikacin 15mg/kg daily (if shocked)</td>
</tr>
<tr>
<td>Ventilator associated pneumonia (VAP)</td>
<td>Pip/tazo 4.5g load then 13.5g over 24hrs + Amikacin 15mg/kg daily (if shocked)</td>
<td>Meropenem 1g load then 3g over 24hrs + Amikacin 15mg/kg daily (if shocked)</td>
</tr>
<tr>
<td>VAP if MRSA colonised</td>
<td>Pip/tazo 4.5g load then 13.5g over 24hrs + Vancomycin 500mg-3g/24hr + Rifampicin 600mg 12hrly</td>
<td>Meropenem 1g load then 3g over 24hrs + Vancomycin 500mg-3g/24hr + Rifampicin 600mg 12hrly</td>
</tr>
<tr>
<td>Aspiration pneumonitis Consider NO antibiotics</td>
<td>Co-amoxiclav 1.2g 8hrly</td>
<td>Levofloxacin 500mg daily + Metronidazole 500mg 8hrly</td>
</tr>
<tr>
<td>Intra-abdominal sepsis</td>
<td>Co-amoxiclav 1.2g 8hrly + Amikacin 15mg/kg daily</td>
<td>Meropenem 1g load then 3g over 24hrs + Amikacin 15mg/kg daily</td>
</tr>
<tr>
<td>Necrotising pancreatitis</td>
<td>Meropenem 1g load then 3g over 24hrs</td>
<td></td>
</tr>
<tr>
<td>Polytrauma: with ONLY open / contaminated wounds. [Until wound closure/cover or for 72 hours whichever comes first]</td>
<td>Co-amoxiclav 1.2g 8hrly + Amikacin 15mg/kg daily (if shocked) + CONSIDER Tetanus prophylaxis</td>
<td>Cefuroxime 1.5g 8hrly + Amikacin 15mg/kg daily (if shocked) + CONSIDER Tetanus prophylaxis</td>
</tr>
<tr>
<td>Polytrauma: wounds &amp; intra-abdominal trauma</td>
<td>Co-amoxiclav 1.2g 8hrly + Amikacin 15mg/kg daily + CONSIDER Tetanus prophylaxis</td>
<td>Meropenem 1g load then 3g over 24hrs + CONSIDER Tetanus prophylaxis</td>
</tr>
<tr>
<td>Isolated penetrating cranio-cerebral injury</td>
<td>Flucloxacillin 2g 6hrly</td>
<td>Cefuroxime 1.5g then 750mg 8hrly + Metronidazole 500mg 8hrly</td>
</tr>
<tr>
<td>Skin / Soft tissue Infections</td>
<td>Meropenem 2g load then 6g over 24hrs + Clindamycin 1.2g 6hrly + Amikacin 15mg/kg daily + Metronidazole 500mg 8hrly</td>
<td></td>
</tr>
<tr>
<td>Necrotising soft tissue infection</td>
<td>Pip/tazo 4.5g load then 13.5g over 24hrs + Amikacin 15mg/kg daily</td>
<td>Meropenem 1g load then 3g over 24hrs + Amikacin 15mg/kg daily</td>
</tr>
<tr>
<td>Neutropenic infections</td>
<td>Pip/tazo 4.5g load then 13.5g over 24hrs + Amikacin 15mg/kg daily</td>
<td>Meropenem 1g load then 3g over 24hrs + Amikacin 15mg/kg daily</td>
</tr>
<tr>
<td>Community acquired meningitis / meningo-encephalitis. Consider dexamethasone (see earlier section)</td>
<td>Ceftriaxone 4g od + Aciclovir 10mg/kg 8hrly (if viral encephalitis suspected) + Amoxicillin 2g 4hrly (if immunosuppressed OR &gt;55 years old, to cover Listeria)</td>
<td>Meropenem 2g load then 6g over 24hrs + Aciclovir 10mg/kg 8hrly (if viral encephalitis suspected)</td>
</tr>
<tr>
<td>Ventriculitis +/- EVD / post neurosurgery</td>
<td>Intrathecal Vancomycin 10mg od (or 500mg-3g/24hr IV if no device) + Meropenem 2g load then 6g over 24hrs</td>
<td></td>
</tr>
<tr>
<td>Vascular line associated infection Remove / change lines</td>
<td>ONLY if severely unwell</td>
<td>Vancomycin 500mg-3g/24hr + Amikacin 15mg/kg daily</td>
</tr>
<tr>
<td>Urinary tract sepsis</td>
<td>Co-amoxiclav 1.2g 8hrly + Amikacin 15mg/kg x1</td>
<td>Meropenem 1g load then 3g over 24hrs + Amikacin 15mg/kg x1</td>
</tr>
<tr>
<td>Suspected Clostridium difficile associated diarrhoea</td>
<td>PO/NG Vancomycin 125mg 6hrly. If patient has ileus +/- large gastric aspirates (consistently &gt;400mls over 4 hours) then GIVE IV metronidazole 500mg 8hrly</td>
<td></td>
</tr>
<tr>
<td>Toxin positive Clostridium difficile associated diarrhoea</td>
<td>PO/NG Fidaxomicin 200mg 12hrly. If patient has ileus +/- large gastric aspirates (consistently &gt;400mls over 4 hours) then GIVE IV metronidazole 500mg 8hrly</td>
<td></td>
</tr>
</tbody>
</table>

Key: Pip/tazo = piperacillin/tazobactam
### Drug specific notes

#### Beta-lactam antibiotics

*Beta-lactam antibiotics exhibit time dependent bacterial killing. Maintaining free beta-lactam levels above the minimum inhibitory concentration (MIC) for a percentage of the dosing interval (40% for carbapenems, 50% for penicillins), will ensure a near maximal bactericidal effect. There is increasing evidence to suggest that administering beta-lactams as a prolonged or continuous infusion produces a drug concentration in excess of the MIC for a longer period that standard intermittent dosing which may achieve improved outcomes in critically ill patients. For more information see [4, 5]. For the time being we are only applying these principals to Piperacillin/tazobactam or Meropenem, NOT Co-amoxiclav, Flucloxacillin, Amoxicillin, Cephalosporins or Ertapenem.*

- Administer the FIRST dose of Piperacillin/tazobactam or Meropenem as a LOADING DOSE, which should be prescribed as a 'STAT' dose.
- Patients who HAVE already received a dose or doses of Piperacillin/tazobactam or Meropenem in the last 8 hours do NOT require a loading dose and can be started on the continuous / prolonged infusion immediately.
- Start the continuous Piperacillin/tazobactam or Meropenem infusion immediately after the administration of the loading dose.
- After the first 48 hours of therapy, the dose prescribed of Piperacillin/tazobactam and Meropenem will depend on the calculated creatinine clearance (cCrCl), which should be calculated according to the following formula:
  \[
  c\text{CrCl} = \frac{(140 - \text{age}) \times \text{weight (kg)} \times 1.23 {\text{ (male) or 1.04 (female)}}}{\text{serum Cr}}
  \]
  - Patients with a cCrCl GREATER than 20ml/min should continue their infusions at the same rate as the first 48 hours.
  - Patients with a cCrCl LESS than or equal to 20ml/min should have a dose reduction.
  - Patients receiving continuous renal replacement therapy (haemofiltration or haemodiafiltration) should continue their infusions at the same rate as the first 48 hours.
- Full details of the protocol can be found [HERE](#).

#### Aminoglycosides

*Aminoglycoside dosing should be based on body weight (BW). For safety and simplicity USE ideal BW. However, in very underweight patients CONSIDER dose reduction to actual BW. In very overweight patients CONSIDER increasing the dose to adjusted BW, where:
  \[
  \text{adjusted BW} = \text{ideal BW} + (0.4 \times (\text{actual BW} - \text{ideal BW}))
  \]
For more information goto [http://clincalc.com/aminoglycoside/](http://clincalc.com/aminoglycoside/)

**Note** - PLEASE use the Urban-Craig formulas for extended dosing - SELECT this in the advanced settings

- **1st line, empirical aminoglycoside (unless use restricted due to supply line problems)**
  - Give first dose STAT, 15mg/kg whatever the renal function. (Maximum dose 1500mg)
  - Thereafter, chart for 12 noon administration and GIVE when blood levels taken @~6am are <5mg/ml.
  - For empirical cover when changing a colonised urinary catheter, **GIVE** 250mg x 1

#### Amikacin

- Give first dose STAT, 5mg/kg whatever the renal function. (Maximum dose 400mg)
- Thereafter, chart for 12 noon administration when blood levels taken @~6am are <1mg/ml.

#### Gentamicin

- Load with 1g (≤65kg) or 1.5g (>65kg) over 2 hours then start continuous infusion at 500mg-3g/24hours depending upon renal function.
- Measure blood levels daily and titrate dose to achieve 20-25mg/ml
- For full protocol see [http://www.gicu.sgul.ac.uk/resources-for-current-staff/supplementary-inpatient-prescription-charts/Variable%20Rate%20Intravenous%20Insulin%20Infusion.pdf/view](http://www.gicu.sgul.ac.uk/resources-for-current-staff/supplementary-inpatient-prescription-charts/Variable%20Rate%20Intravenous%20Insulin%20Infusion.pdf/view)

#### Vancomycin

- Load with 9 million units then 3 million units 8 hourly IV
- 2 million units nebulised for colonised patients. Use nebulised & systemic therapy for severe pneumonia

#### Colistin

- Load with 9 million units then 3 million units 8 hourly IV
- 2 million units nebulised for colonised patients. Use nebulised & systemic therapy for severe pneumonia
**Fungal infections – suspected or proven**

| Invasive Candidiasis and / or Candidaemia | • *IF* invasive candidiasis or candidaemia are suspected, PLEASE complete the [risk score](#) AND send serum for beta-glucan assay  
Empirical therapy until species +/- sensitivities established:  
• Caspofungin 70mg IV od. If <80kg reduce to 50mg IV od **AFTER THE FIRST DOSE**  
For all other proven or suspected fungal infections refer to Microguide (website or App) & / or seek micro advice |

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*Penicillin “allergy”*
- Many claims of penicillin “allergy” turn out to be spurious. Approximately 10% of patients report a history of penicillin allergy. However, up to 90% of these individuals are able to tolerate penicillin and are designated as having “penicillin allergy” unnecessarily [6, 7].
- Penicillins are potent bacteriocidal antibiotics and are often the best therapy, hence should be used whenever possible. Use of broad-spectrum antibiotics in patients designated as being “penicillin allergic” is associated with higher costs, increased antibiotic resistance, and may compromise optimal medical care [6, 7].
- “TRUE” penicillin allergies may be clinically sub divided into:
  - o Anaphylaxis:
    - **Timing** = <1 hour following exposure,  
    - **Clinical features** = diffuse erythema / urticaria / angioedema & / OR laryngeal oedema & / OR bronchospasm & / OR hypotension
  - o Three syndromes of non-immediate reactions with systemic involvement:
    - Drug reaction with eosinophilia and systemic symptoms (DRESS). Onset usually 2–6 weeks after first drug exposure or within 3 days of second exposure.  
    - Toxic epidermal necrolysis or Stevens–Johnson syndrome. Onset usually 7–14 days after first drug exposure or within 3 days of second.  
    - Acute generalised exanthematosus pustulosis (AGEP). Onset usually 3–5 days after first drug exposure.
  - o Non-immediate reactions without systemic involvement: Onset usually 6–10 days after first drug exposure or within 3 days of second exposure. 2 patterns, widespread red macules or papules (exanthem-like) **AND** Fixed drug eruption (localised inflamed skin). Should be confirmed by skin biopsy.
- If there is a reliable history of anaphylaxis **DO NOT GIVE ANY** beta lactam antibiotic and discuss empirical therapy with the on call microbiologist.
- If there is a reliable history of a serious non-immediate reaction to a specific antibiotic then **DO NOT GIVE IT** and discuss empirical therapy with the on call microbiologist.
- If there is an unreliable history suggestive of anaphylaxis, perform intradermal testing before administering the first dose of 1st line therapy as follows:  
  **Intradermal test for anaphylactic reactions to penicillins**  
  Inject 0.02mL intradermally of 0.9%NaCl and standard antibiotic solution into the volar surface of the forearm using an orange needle. The margins of the wheals induced by the injections should be marked with a ball point pen. An intradermal test is positive if the average wheal diameter 15 minutes after injection is >2 mm larger than the initial wheal size and also is >2 mm larger than the negative controls. Otherwise, the tests are negative For more information see [8] and [http://www.gicu.sgul.ac.uk/resources-for-current-staff/allergy-and-anaphylaxis](http://www.gicu.sgul.ac.uk/resources-for-current-staff/allergy-and-anaphylaxis)  
- If the skin test is positive, use the **TRUE penicillin allergy** column advice.  
- If the skin test is negative **OR** if the history is of **ANY OTHER** reaction, **GIVE** first line therapy.

**IVIg**
- Is indicated in SOME cases of the following rare conditions.
  - Severe invasive group A streptococcal disease (necrotising fasciitis)
  - Staphylococcal toxic shock syndrome
  - Necrotising (PVL-associated) staphylococcal sepsis / pneumonia / soft-tissue infection
- This is a time critical intervention. To be of benefit it should be commenced within 6 hours of disease onset.
  - Give 1g/kg daily for 48 hours.
  - **IT MUST NOT BE USED without ICU AND micro consultant approval.** Contact the on-call pharmacist to obtain supplies.

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Tetanus prevention

Tetanus-prone wounds include:
- Visibly contaminated wounds or burns that require surgical intervention that is delayed for more than six hours
- Wounds or burns that show a significant degree of devitalised tissue or a puncture-type injury, particularly where there has been contact with soil or manure
- Wounds containing foreign bodies
- Compound fractures
- Wounds or burns in patients who have systemic sepsis.

<table>
<thead>
<tr>
<th>Immunisation status</th>
<th>Clean wound</th>
<th>Tetanus-prone wound</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vaccine</td>
<td>HaTI</td>
</tr>
<tr>
<td>Fully immunised, i.e. has received a total of five doses of vaccine at appropriate intervals</td>
<td>None required</td>
<td>Only if high risk</td>
</tr>
<tr>
<td>Primary immunisation complete, boosters incomplete but up to date</td>
<td>None required</td>
<td>Only if high risk</td>
</tr>
<tr>
<td>Primary immunisation incomplete or boosters not up to date</td>
<td>Give</td>
<td>One dose</td>
</tr>
<tr>
<td>Not immunised or immunisation status not known or uncertain</td>
<td>Give</td>
<td>One dose</td>
</tr>
</tbody>
</table>

HaTI = human tetanus immunoglobulin
One dose = 250iu IM or 500iu IM if >24hrs have elapsed since injury / heavy contamination / contaminated burns

References