**Supplementary material:**

**S1. Survey Antimicrobial Prescription.** Available via <https://www.surveymonkey.co.uk/r/RM6VMPC>

1. Which is your position?

|  |
| --- |
| * Consultant
 |
| * ST3- ST6
 |
| * ST1-ST3
 |
| * F1/F2
 |

1. What is your specialty?

|  |
| --- |
| * Internal medicine
 |
| * Family medicine
 |
| * Emergency medicine
 |
| * Intensive medicine
 |
| * Geriatrics
 |
| * Paediatrics
 |
| * General surgery
 |
| * Trauma and orthopaedic surgery
 |
| * Other clinical specialty
 |
| * Other surgical specialty
 |

1. How many years have you been practising as a doctor?

|  |
| --- |
| * <2 years
 |
| * 2 – 4 years
 |
| * >4 years
 |
| * 4 - 8 years
 |
| * > 8 years
 |

**CASE 1**

A 38 year-old female, with no relevant past medical history, presents to the Emergency department with fever, chills, left flank pain and dysuria for the last 48h. On examination, temperature of 39° C, BP 110/60 mmHg and tachycardia of 110 beats/min are noted. After assessment, the clinical picture was consistent to pyelonephritis. Two sets of blood cultures and a urine sample were taken and she is started on Co-amoxiclav 1.2g iv 8hourly.

17h later, **at 8am,**both sets of blood cultures flagged positive. The Gram stain showed gram negative rods. On reassessment the patient has no complaints, vital signs have remained within normal limits and is walking about on the ward with normal haematology and biochemistry laboratory values.

**At 4pm (same day)** the microbiological results, confirm *E.coli* bacteraemia with the following antibiotic sensitivities

**Amoxicillin** – Sensitive; **Co- amoxiclav** – Sensitive; **Gentamicin** – Sensitive; **Amikacin** – Sensitive; **Meropenem** - Sensitive; **Piperacilin/Tazobactam** – Sensitive; **Ciprofloxacin** - sensitive

Which would be your decision about antibiotic choice?

|  |
| --- |
| 1. Contact microbiology
 |
| 1. Contact consultant.
 |
| 1. Await decision at next ward round.
 |
| 1. Continue IV Co-amoxiclav.
 |
| 1. De-escalate to IV Amoxicillin.
 |
| 1. Switch to oral Co-amoxiclav.
 |
| 1. Switch to oral Amoxicillin.
 |
| 1. Add an additional antibiotic (Aminoglycosides).
 |
| 1. Escalate to Piperacilin/Tazobactam.
 |
| 1. Escalate to Meropenem.
 |

**CASE 2.**

A 65 year-old female, type 1 diabetic and chronic kidney disease two days post 5th diabetic toe amputation, spiked a temperature of 40°C and the nurse looking after her, noticed that she was disoriented and complaining of lower abdominal pain. On examination, HR 122 beats/min, BP 100/60mmHg, RR 28 breaths/min. Clinical picture was consistent with sepsis of probable urinary source. Two sets of blood cultures were drown a urine sample collected and started fluid resuscitation and given Co-amoxiclav and Amikacin.

After 17h, the following day at **12am**, both sets of blood cultures flagged positive and the gram stain showed gram-negative rods. After reassessment, the patient presents clinical improvement and Amikacin is discontinued as the patient had CKD eGFR 30ml/min. **At 11pm**, the patient develops a rapid clinical deterioration, the nurse calls for her to be reviewed and she requires further fluid therapy.

At **4am** **(next day)** microbiology contacts the clinical team, giving the results of a *K.pneumoniae* ESBL,

**Amoxicillin** – Resistant; **Co- amoxiclav** – Resistant; **Gentamicin** – Sensitive; **Amikacin** – Sensitive, **Meropenem** - Sensitive; **Piperacilin/Tazobactam** – Resistant; **Ciprofloxacin** - Resistant

Which would be your decision about antibiotic choice?

|  |
| --- |
| 1. Contact microbiology.
 |
| 1. Contact consultant.
 |
| 1. Await decision at next ward round.
 |
| 1. Continue IV Co-amoxiclav.
 |
| 1. Add a Aminoglycoside (gentamicin or amikacin) .
 |
| 1. Escalate to Piperacilin/Tazobactam.
 |
| 1. Escalate to Meropenem.
 |

**CASE 3**

A 75 year-old female nursing home resident, originally from Spain, with history of hypertension, chronic heart disease and recurrent urinary tract infections presents to the Emergency department with altered mental status and rigors. On examination, temperature of 38 °C, respiratory rate 20 breaths/min and BP 100/55mmHg. Two sets of blood cultures and a urine sample were drawn, and empirical treatment with Co-amoxiclav 1.2g iv 8 hourly and Amikacin 15mg/kg stat dose iv was started.

After 12h, at **4am** in the night, one set of blood cultures flagged positive. On reassessment, the patient deteriorated clinically, subsequently, the ST3 on the ward makes the decision to escalate treatment to Meropenem iv.

At **6am** (same day) microbiological results, confirm *Proteus mirabilis* with the following sensitivities:-

**Amoxicillin –** Sensitive; **Co- amoxiclav** – Sensitive; **Gentamicin –** Sensitive; **Amikacin** – Sensitive; **Meropenem** - Sensitive; **Piperacilin/Tazobactam** – Sensitive; **Ciprofloxacin** - Sensitive

Which decision would you make in this particular case?

|  |
| --- |
| 1. Contact microbiology
 |
| 1. Contact consultant.
 |
| 1. Await decision at next ward round.
 |
| 1. Continue IV Meropenem.
 |
| 1. De-escalate to IV Piper-Tazobactam.
 |
| 1. De-escalate to IV Co-amoxiclav.
 |
| 1. De-escalate to IV Amoxicillin.
 |
| 1. Add a Aminoglycoside (gentamicin or amikacin) .
 |

**CASE 4**

A 77-year-old male, with previous history of biliary surgery was admitted to the hospital with malaise and high temperature. On examination she had T 38.5 °C, BP 100/60 mmHg, HR 115 b/min and respirator rate of 25 breaths per minute. Clinical picture consistent with a cholangitis, CT-scan excludes abscess or any other postoperative complications. Two sets of blood cultures were drawn and empirical treatment with Co-amoxiclav 1.2g iv 8hourly and Amikacin 15mg/kg iv was started, and the patient initially recovered.

After 15h, at **11pm** in the night, blood cultures flagged positive. At **4pm (next day)** microbiology contacts the clinical team on the ward, giving the results of *E.coli* ESBL wth the following sensitivities.

**Amoxicillin** – Resistant; **Co- amoxiclav** – Resistant; **Gentamicin** – Sensitive; **Amikacin** – Sensitive; **Meropenem** - Sensitive; **Piperacilin/Tazobactam** – Resistant; **Ciprofloxacin** - Resistant

On reassessment, the patient presents remarkable clinical improvement, vital signs on normal limits and laboratory analysis improved.

Which would be your decision about antibiotic choice?

|  |
| --- |
| 1. Contact microbiology.
 |
| 1. Contact consultant.
 |
| 1. Await decision at next ward round.
 |
| 1. Continue IV Co-amoxiclav and Amikacin.
 |
| 1. De-escalate to IV Co-amoxiclav monotherapy.
 |
| 1. Escalate to Piperacilin/Tazobactam.
 |
| 1. Escalate to Meropenem
 |

**S2. Expert Survey.** Available via <https://www.surveymonkey.co.uk/r/BQ6C8MD>

**CASE 1.**

A 38 year-old female, with no relevant past medical history, presents to the Emergency department with fever, chills, left flank pain and dysuria for the last 48h. On examination, temperature of 39° C, BP 110/60 mmHg and tachycardia of 110 beats/min are noted. After assessment, the clinical picture was consistent to pyelonephritis. Two sets of blood cultures and a urine sample were taken and she is started on Co-amoxiclav 1.2g iv 8hourly.

17h later, **at 8am,**both sets of blood cultures flagged positive. The Gram stain showed gram negative rods. On reassessment the patient has no complaints, vital signs have remained within normal limits and is walking about on the ward with normal haematology and biochemistry laboratory values.

**At 4pm (same day)** the microbiological results, confirm *E.coli* bacteraemia with the following antibiotic sensitivities

**Amoxicillin** – Sensitive; **Co- amoxiclav** – Sensitive; **Gentamicin** – Sensitive; **Amikacin** – Sensitive; **Meropenem** - Sensitive; **Piperacilin/Tazobactam** – Sensitive; **Ciprofloxacin** - sensitive

which answers you consider **“optimal”** based on clinical details and *in vitro* susceptibility results?

|  |  |  |
| --- | --- | --- |
|  | **Optimal** | **Sub-optimal** |
| 1. Contact microbiology
 |  |  |
| 1. Contact consultant.
 |  |  |
| 1. Await decision at next ward round.
 |  |  |
| 1. Continue IV Co-amoxiclav.
 |  |  |
| 1. De-escalate to IV Amoxicillin.
 |  |  |
| 1. Switch to oral Co-amoxiclav.
 |  |  |
| 1. Switch to oral Amoxicillin.
 |  |  |
| 1. Add an additional antibiotic (Aminoglycosides).
 |  |  |
| 1. Escalate to Piperacilin/Tazobactam.
 |  |  |
| 1. Escalate to Meropenem.
 |  |  |

**CASE 2**

A 65 year-old female, type 1 diabetic and chronic kidney disease two days post 5th diabetic toe amputation, spiked a temperature of 40°C and the nurse looking after her, noticed that she was disoriented and complaining of lower abdominal pain. On examination, HR 122 beats/min, BP 100/60mmHg, RR 28 breaths/min. Clinical picture was consistent with sepsis of probable urinary source. Two sets of blood cultures were drown a urine sample collected and started fluid resuscitation and given Co-amoxiclav and Amikacin.

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At **4am** **(next day)** microbiology contacts the clinical team, giving the results of a *K.pneumoniae* ESBL,

**Amoxicillin** – Resistant; **Co- amoxiclav** – Resistant; **Gentamicin** – Sensitive; **Amikacin** – Sensitive, **Meropenem** - Sensitive; **Piperacilin/Tazobactam** – Resistant; **Ciprofloxacin** - Resistant

which answers you consider **“optimal”** based on clinical details and *in vitro* susceptibility results?

|  |  |  |
| --- | --- | --- |
|  | **Optimal** | **Sub-optimal** |
| 1. Contact microbiology
 |  |  |
| 1. Contact consultant.
 |  |  |
| 1. Await decision at next ward round.
 |  |  |
| 1. Continue IV Co-amoxiclav.
 |  |  |
| 1. Add a Aminoglycoside (gentamicin or amikacin) .
 |  |  |
| 1. Escalate to Piperacilin/Tazobactam.
 |  |  |
| 1. Escalate to Meropenem.
 |  |  |

**CASE 3**

A 75 year-old female nursing home resident, originally from Spain, with history of hypertension, chronic heart disease and recurrent urinary tract infections presents to the Emergency department with altered mental status and rigors. On examination, temperature of 38 °C, respiratory rate 20 breaths/min and BP 100/55mmHg. Two sets of blood cultures and a urine sample were drawn, and empirical treatment with Co-amoxiclav 1.2g iv 8 hourly and Amikacin 15mg/kg stat dose iv was started.

After 12h, at **4am** in the night, one set of blood cultures flagged positive. On reassessment, the patient deteriorated clinically, subsequently, the ST3 on the ward makes the decision to escalate treatment to Meropenem iv.

At **6am** (same day) microbiological results, confirm *Proteus mirabilis* with the following sensitivities:-

**Amoxicillin –** Sensitive; **Co- amoxiclav** – Sensitive; **Gentamicin –** Sensitive; **Amikacin** – Sensitive; **Meropenem** - Sensitive; **Piperacilin/Tazobactam** – Sensitive; **Ciprofloxacin** – Sensitive

which answers you consider **“optimal”** based on clinical details and *in vitro* susceptibility results?

|  |  |  |
| --- | --- | --- |
|  | **Optimal** | **Sub-optimal** |
| 1. Contact microbiology
 |  |  |
| 1. Contact consultant.
 |  |  |
| 1. Await decision at next ward round.
 |  |  |
| 1. Continue IV Meropenem.
 |  |  |
| 1. De-escalate to IV Piper-Tazobactam.
 |  |  |
| 1. De-escalate to IV Co-amoxiclav.
 |  |  |
| 1. De-escalate to IV Amoxicillin.
 |  |  |
| 1. Add an Aminoglycoside (gentamicin or amikacin) .
 |  |  |

**CASE 4**

A 77-year-old male, with previous history of biliary surgery was admitted to the hospital with malaise and high temperature. On examination she had T 38.5 °C, BP 100/60 mmHg, HR 115 b/min and respirator rate of 25 breaths per minute. Clinical picture consistent with a cholangitis, CT-scan excludes abscess or any other postoperative complications. Two sets of blood cultures were drawn and empirical treatment with Co-amoxiclav 1.2g iv 8hourly and Amikacin 15mg/kg iv was started, and the patient initially recovered.

After 15h, at **11pm** in the night, blood cultures flagged positive. At **4pm (next day)** microbiology contacts the clinical team on the ward, giving the results of *E.coli* ESBL wth the following sensitivities.

**Amoxicillin** – Resistant; **Co- amoxiclav** – Resistant; **Gentamicin** – Sensitive; **Amikacin** – Sensitive; **Meropenem** - Sensitive; **Piperacilin/Tazobactam** – Resistant; **Ciprofloxacin** - Resistant

On reassessment, the patient presents remarkable clinical improvement, vital signs on normal limits and laboratory analysis improved.

which answers you consider **“optimal”** based on clinical details and *in vitro* susceptibility results?

|  |  |  |
| --- | --- | --- |
|  | **Optimal** | **Sub-optimal** |
| 1. Contact microbiology
 |  |  |
| 1. Contact consultant.
 |  |  |
| 1. Await decision at next ward round.
 |  |  |
| 1. Continue IV Co-amoxiclav and Amikacin.
 |  |  |
| 1. De-escalate to IV Co-amoxiclav monotherapy.
 |  |  |
| 1. Escalate to Piperacilin/Tazobactam.
 |  |  |
| 1. Escalate to Meropenem.
 |  |  |

**Table 5. Spectrum of antibiotic activity rank classification. The** betalactam and non-betalactam options were ranked from 1 (narrowest spectrum) to 5 (broadest spectrum) and provided to all participants in the Expert survey. For each case, the surveyed experts had to choose what was the microbiologically optimal antibiotic choice using the narrowest spectrum of action. The optimal answer was then agreed using Delphi survey methodology (See text).

|  |  |  |
| --- | --- | --- |
| **Rank** | **Betalactam antibiotics** | **Non-belactam antibiotics** |
| **1** | Penicillin Amoxicillin | TrimethoprimNitrofurantoin |
| **2** | Amoxicillin-clavulanateCephalexin | CotrimoxazoleDoxyciclineMacrolides |
| **3** | CefotaximeCefiximeCefuroximeCeftriaxoneCeftazidimeCefepime | CiprofloxacinLevofloxacinGentamicin |
| **4** | Piperacillin-Tazobactam | AmikacinTobramycinAztreonamFosfomycin |
| **5** | ErtapenemMeropenemImipenemDoripenemCeftolozane/TazobactamCeftazidime/ Avibactam | Colistin |

**Table 6**. **Expert consensus on the microbiologically optimal antibiotic choice/s.** A given category was considered to be an optimal antibiotic choice if >75% of the experts surveyed agreed.

|  |  |  |
| --- | --- | --- |
|  | N=15 | Score |
| Case 1which answers you consider **“optimal”** based on clinical details and *in vitro* susceptibility results?* Contact microbiology
* Contact consultant.
* Await decision at next ward round.
* Continue IV Co-amoxiclav.
* **De-escalate to IV Amoxicillin.**
* **Switch to oral Co-amoxiclav.**
* **Switch to oral Amoxicillin.**
* Add an additional antibiotic (Aminoglycosides).
* Escalate to Piperacillin/Tazobactam.
* Escalate to Meropenem.

Case 2which answers you consider **“optimal”** based on clinical details and *in vitro* susceptibility results?* Contact microbiology.
* Contact consultant.
* Await decision at next ward round.
* Continue IV Co-amoxiclav.
* **Add a Aminoglycoside (gentamicin or amikacin) .**
* Escalate to Piperacillin/Tazobactam.
* **Escalate to Meropenem.**

Case 3which answers you consider **“optimal”** based on clinical details and *in vitro* susceptibility results?* Contact microbiology.
* Contact consultant.
* Await decision at next ward round.
* Continue IV Meropenem.
* **De-escalate to IV Piper-Tazobactam.**
* **De-escalate to IV Co-amoxiclav.**
* **De-escalate to IV Amoxicillin.**
* Add a Aminoglycoside (gentamicin or amikacin) .

Case 4which answers you consider **“optimal”** based on clinical details and *in vitro* susceptibility results?* Contact microbiology.
* Contact consultant.
* Await decision at next ward round.
* Continue IV Co-amoxiclav and Amikacin.
* De-escalate to IV Co-amoxiclav monotherapy.
* Escalate to Piperacillin/Tazobactam.
* **Escalate to Meropenem**
 | 0/150/151/151/1514/1513/1514/150/150/150/150/150/150/153/1512/151/1513/150/150/150/151/1512/1515/1512/150/150/150/150/150/150/152/1514/15 | ≤75%≤75%≤75%≤75%**>75%****>75%****>75%**≤75%≤75%≤75%≤75%≤75%≤75%≤75%**>75%**≤75%**>75%**≤75%≤75%≤75%≤75%**>75%****>75%****>75%**≤75%≤75%≤75%≤75%≤75%≤75%≤75%**>75%** |