Electronic Supplement

Appendix A

Paediatric physician scenarios

CASE 1

A 7 year old girl with cystic fibrosis presents with her first exacerbation in 2 years. There is no improvement in her symptoms after 4 weeks of oral amoxicillin/clavulanic acid and increased chest physiotherapy. Her FEV_1 is down from 105% to 90% predicted. Her sputum culture result is reported as "mixed oral flora". She has not been able to expectorate before and therefore has no previous sputum culture result. *H. influenzae* was cultured from a previous throat swab. Her IgE levels are undetectable. She is unwell and hospitalised for intensive treatment.

CASE 2

A 12 year old boy with cystic fibrosis known to be colonised with *Pseudomonas aeruginosa* has had a wet cough for the past 5 weeks. His cough has not improved in spite of being prescribed tobramycin nebulisations 300mg BD x 4 weeks. Now there are new crepitations audible over his right lower lobe. His FEV_1% predicted is reduced from 85 to 74. His IgE levels are undetectable. He has a recent oral glucose tolerance test which was normal. Six months previously he responded well to IV piperacillin/tazobactam and IV tobramycin during a pulmonary exacerbation. Now he is admitted to hospital for intensive treatment of a pulmonary exacerbation.

CASE 3

A 15 year old boy with cystic fibrosis is known to be colonised with *Staphylococcus aureus*. He has a low grade wet cough at baseline i.e. when not experiencing a pulmonary exacerbation. He presents now with an increase in wet cough, shortness of breath, lethargy and reduced appetite. His FEV_1%predicted is down from 65 to 50. His IgE levels are 100kU/L (stable). A recent oral glucose tolerance test was normal. Three months previously during hospitalisation for a pulmonary exacerbation, he responded well to IV cefepime and IV tobramycin. Sputum MCS: moderate growth of Staph aureus sensitive to flucloxacillin. He is now admitted for intensive treatment of a pulmonary exacerbation.

Adult physician scenarios

CASE 1

A 22 year old woman with cystic fibrosis has not attended clinic for 6 months. Today she presents with shortness of breath, increased chest tightness, lethargy and weight loss of 2.0kg since last seen. Her regular prescribed medications include nebulised hypertonic saline but she admits being completely non-adherent over the past 6 weeks. She has no regular airway clearance or exercise regimen. She is not on any inhaled antibiotics. On examination, there are new crackles audible over her right middle lobe and lingula regions which are new. Her FEV_1 is 1.6L (60% predicted), which is lower than her baseline of 2.3L (85% predicted). Sputum microbiology now and 6 months ago show only mixed oral flora. She is admitted to hospital for treatment of a pulmonary exacerbation.

CASE 2

A 34 year old man with cystic fibrosis presents with his first episode of haemoptysis with 20ml of fresh blood on 2 occasions over the past 2 days. He is chronically infected with *Pseudomonas aeruginosa* (multi-resistant). He has a history of recurrent ABPA which was treated successfully 2 years ago. His IgE level (8 months ago) was 300ku/l (with a previous peak of 2000kU/l during an ABPA related exacerbation). He has CF-related diabetes. His usual medications include azithromycin 250mg daily and 6% hypertonic saline once daily but he has not been using this over the last 2 days. He is usually on cyclical inhaled dry powder tobramycin and nebulised colistin on a month on/month off basis which was stopped 2 days ago due to haemoptysis. On examination, his respiratory rate is 24/min. There are new crepitations audible over the left lower lobe. His FEV_1 is stable at 1.7L (50% predicted). *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia* are cultured from sputum collected 2 days ago. He is admitted to hospital for treatment of a pulmonary exacerbation.

CASE 3

A 25 year old woman with cystic fibrosis presents with increased productive cough for the past month. She has moderate lung disease (baseline FEV1: 1.9L [63% predicted]) and chronic *P. aeruginosa* infection. She was reviewed 2 weeks ago and her FEV_1 was 1.5L (50% predicted) at the time. *P. aeruginosa* and flucloxacillin susceptible *Staphylococcus aureus* were cultured from a sputum sample collected 2 weeks ago. Her maintenance medications include azithromycin 250mg daily. She uses nebulised 6% hypertonic saline daily. Upon review today, her symptoms have not improved despite 2 weeks treatment with oral ciprofloxacin and inhaled tobramycin. Her FEV_1 has remained unchanged at 1.5L. She is admitted to hospital for treatment of a pulmonary exacerbation.

Appendix B - Survey

Demographic Questions:

1. What state or territory do you practice in? (For Australian physicians)
a. ACT
b. NSW
c. NT
d. QLD
e. SA
f. TAS
g. VIC
h. WA

1. What country and region do you practice in? (For NZ physicians)
[Enter text]

2. How many years' experience managing CF patients do you have (inc. pre-fellowship)?
a. <5
b. 5-9
c. 10+

3. Do you mostly treat children or adults?
a. Children
b. Adults

The following questions were provided after each case scenario.

Q: Which primary (backbone) antibiotic would be preferred?
IV ceftazidime
IV ceftriaxone
IV ciprofloxacin
IV piperacillin/tazobactam
IV flucloxacillin
IV cefepime
Other (please specify)

Q: Which secondary (adjuvant) antibiotic would you prescribe?
None
IV tobramycin
IV colistin
IV gentamicin
IV amikacin
Inhaled tobramycin
Inhaled colistin
IV ciprofloxacin
Oral ciprofloxacin
Other (please specify)

Q: What is your main reason for this selection? (you may select one option below)
Professional opinion/ clinical experience
Hospital or department policy
Advice from colleagues
Availability of medication
Concern for side effects
Clinical familiarity with treatment
Other (please enter your reason below)

Q: Would you prescribe a third antibiotic?
No
Yes (please specify which antibiotic)

Q: Would you prescribe chest physiotherapy?
No
Yes, daily
Yes, BD
Yes, TDS

Q: Would you prescribe dornase alfa?
Yes
No

Q: Would you prescribe inhaled hypertonic saline?
Yes
No

Q: Would you prescribe oral prednisolone for several days?
Yes
No

Q: Would you change any aspects of treatment if the patient had no response or little response to treatment after one week?
No
Yes (please explain below)

The following questions were provided at the end of the 3 case studies:
Q: Do you consider any of the following options unacceptable?
IV ceftazidime
IV ceftriaxone
IV ciprofloxacin
IV piperacillin/tazobactam
IV flucloxacillin
IV cefepime
IV tobramycin
IV colistin
IV gentamicin
IV amikacin
Inhaled tobramycin
Inhaled colistin
Oral ciprofloxacin

Yes
No

Q: If Yes, which antibiotic/s? (you may select more than one answer)
1) IV ceftazidime
2) IV ceftriaxone
3) IV ciprofloxacin
4) IV piperacillin/tazobactam
5) IV flucloxacillin
6) IV cefepime
7) IV tobramycin
8) IV colistin
9) IV gentamicin
10) IV amikacin
11) Inhaled tobramycin
12) Inhaled colistin
13) Oral ciprofloxacin

Q: Why are these unacceptable?
[Enter text]

Appendix C: Responses for unacceptable antibiotic options

"IV cipro has no advantage over oral due to excellent absorption and bioavailability in those with a functional gut. IV amikacin is only used for NTM due to renal and ototoxicity. IV genta is never used due to renal toxicity. IV colistin must be used with extreme caution in adults with severe lung disease due to respiratory muscle weakness. Inhaled Ab must be used with caution in acutely unwell adults with severe lung disease."

"[IV ciprofloxacin] Oral route as good"

"Ciprofloxacin has good oral bioavailability. Would use IV tobramycin over gentamicin"

"[Oral ciprofloxacin is] Reserved for home treatment"

"Give ciprofloxacin orally and colistin inhaled"

"[IV ciprofloxacin] oral should give same effect"

"We use tobramycin routinely and have not used gentamicin for many years. We use Ciprofloxacin orally only"

"Cipro - reserve for oral treatment."

"Ceftriaxone other better options IV Cipro oral preps as gold absorption gentamicin no role these days as more toxicity than IV tobra"

"Ceftriaxone offers no pseudomonal cover and no advantage above other 3rd generation cephalosporins such as ceftazidime. Oral cipro has same bioavailability as IV. IV colistin has adverse effects."

"No possible to answer this [sic] questions. All are possibly acceptable, but their use is defined by the infecting bacteria"

"[IV gentamicin is] Not as effective as tobramycin"

"[IV gentamicin has] Better (daily dosing), more specific aminoglycoside alternative, i.e. iv Tobramycin"

"[IV gentamicin] ototoxicity"

"Increased renal impairment risk with gentamycin"

"[IV gentamicin] toxicity"

"Gentamicin has more side effects compared with tobramycin especially renal and no advantages apart from possibly price so we would never use it. Ceftriaxone does not cover basic CF pathogens well- the Staph cover is not great and there is no Pseudomonas cover.

"oral fluclox sufficient if eating OK. Don't use IV colistin - too toxic; ceftriaxone not very active against PsA"

"[IV ciprofloxacin & IV gentamicin] Likely resistance"

"I save colistin for Steno. I would not use amikacin due to high potential for toxicity and concern about using a single anti-Mycobacterial agent in case of as yet unrecognised NTM infection. I save cipro for Pseudomonas and would avoid using it first line for Staph in case of as yet unrecognised Pseudomonas infection."

"[IV colistin] side effects"

"Not so much unacceptable - I didn't know IV Ciprofloxacin or colistin was available or necessary"

"I have used all of these antibiotics when clinically indicated - I picked amikacin as I only reserve that for abscessus cases and it wouldn't let me leave it blank"

"We don't use inhaled medications in hospital"

"[IV ceftazidime, IV ceftriaxone, IV cefepime, IV gentamicin, IV amikacin have] poor cover"

"…All of the antibiotics may have a scenario in which they might be used depending on context and microbiology. I personally have no experience with IV colistin."

"[IV ceftazidime, IV cefepime] Using drugs from same class"

"Cipro limited role in hospitalised PWCF; I haven't found IV amikacin to be well tolerated and in the scenarios given wouldn't use."

"[IV colistin] good penetrance PO"

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