What do I know about antibiotics?

Will Cairns
ANZSPM Update
June 2013
Mr J.T. - 90 year old NH resident in low-level care

- Day 1 - presented to ED with # humerus
  - Not for surgery and offered a bed in distant hospital pending HN high-level placement – family decided he should go back to NH

- Day 4 - re-presented with a temp., “cognitive decline”, and not coping in low-level care area of NH
  - Urosepsis and # humerus
  - Early dementia
  - Chronic renal failure
  - Multiple other morbidities – AS, anaemia, double incontinence
  - 14 different medications – each with a sound therapeutic rationale
My career with antibiotics

• General Practice
  – Oral antibiotics – for the most part
  – Some antibiotic resistant organisms
  – Most people got better anyway
  – Funny bugs in the tropics
    • Tropical ear, melioidosis, vibrio in coral cuts (biofilms), leptospirosis
    • Scrub typhus, worms, dengue, Ross River virus, Q fever, malaria, histoplasmosis
  – STIs
    – Significant proportion of day-to-day work

• Infections generally get treated when possible

• Attempts to resist inappropriate use

• Many scripts per week – about 94 per 100 population per year in 1998-1999 (BEACH study) – perhaps more than 10% of consultations - ? My practice??

• UK range of 4% to 8% of visits
13 year transition to palliative medicine – 1987 to 2000

• Evolving expectations
  – Much less emphasis on life prolongation when curative treatment had failed
  – Little or no assisted ventilation in MND
  – Early chemotherapy – seldom more than first line
• When no further treatment options less effort at life prolongation – “nothing more we can do” – not a bad statement in limited context
• Development of need to keep people alive so that they can receive next line of treatment
• Growing use of life-prolonging agents
• Expectation in community that life can be prolonged
• Guilt of not trying everything
13 years full-time palliative medicine, so far – mostly in hospital

• Widespread use of antibiotics in hospitals
• Perhaps 100% of haematology inpatients
  – A wall of chemicals to keep the bug world at bay while immune system recovers
• 30-40% of hospital patients are prescribed antibiotics, up to 50% of which are inappropriate (fact sheet from The Society of Hospital Pharmacists of Australia, 2012)
• Antibiotic use/allocation has been weighted towards individual benefit rather overall community benefit
• Antibiotic resistance - evolution in action
• Concept of antibiotic stewardship
SUMMARY

The results obtained in 25 cases of bone and joint tuberculosis with sinuses treated by local installation of streptomycin are described and compared with the results of intramuscular injection.

A continuous bacteriostatic blood-level is not essential for a satisfactory clinical result.

An important advantage of local installation is that it is painless; it also seems to be more effective than intramuscular injection.

I wish to thank Mr. L. A. Kay for many helpful suggestions, and Dr. F. E. T. Scott for performing all the laboratory investigations.

REFERENCES


PENICILLIN-RESISTANT STAPHYLOCOCCUS INFECTION IN RELATION TO LENGTH OF STAY IN HOSPITAL

H. J. F. CAIRNS G. A. C. SUMMERS

B.M. Oxid B.Sc., M.B. Edin.

From the Department of Bacteriology, the Radcliffe Infirmary, Oxford

Barber et al. (1949) and others have reported an increasing preponderance of penicillin-resistant strains among the pyogenic staphylococci isolated from infections arising in hospital. By carrier surveys and phage-typing, these have been related to penicillin-resistant strains among the doctors and nurses.

We have tried to ascertain how closely infection with penicillin-resistant strains is related to the length of time spent in hospital. The strains investigated were coagulase-positive as tested by the tube method, and for present purposes we divide them broadly into sensitive and resistant categories according to their reaction on a penicillin agar plate (Fleming 1945), containing one unit of penicillin per ml. of agar in the gutter. This reaction provides a clear-cut division. In the rare cases where more than one strain was isolated from the same specimen, the most resistant strain was selected for the analysis.

Of 417 inpatients from whom strains of Staphylococcus pyogenes were obtained, 326 had records showing how long they had been in hospital before the organism was isolated, and (in the case of the 130 who were receiving systemic penicillin) the duration of penicillin treatment before its isolation. These 326 patients were divided into the following groups:

1. Infections arising in hospital.
2. Open infections, present on admission and susceptible to cross-infection.
3. Closed abscesses, present on admission.
4. Cases where the infecting role of the staphylococcus was doubtful.
5. Cases where no infection was present (e.g., routine nasal swabs).

<table>
<thead>
<tr>
<th>Group of patients</th>
<th>Total strains</th>
<th>% resistant</th>
<th>x²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Closed infections</td>
<td>79</td>
<td>19</td>
<td>11.00</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Open infections</td>
<td>103</td>
<td>43</td>
<td>0.13</td>
<td>0.72</td>
</tr>
<tr>
<td>Possible infections</td>
<td>27</td>
<td>46</td>
<td>1.71</td>
<td>0.19</td>
</tr>
<tr>
<td>Uninfected</td>
<td>78</td>
<td>61</td>
<td>2.98</td>
<td>0.08</td>
</tr>
<tr>
<td>Hospital infections</td>
<td>58</td>
<td>78</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>326</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For the table as a whole, x² = 31.77, p = <0.001.

These five groups show conspicuous differences in the proportion of penicillin-resistant strains isolated (table I). The high incidence of resistance in infections arising in hospital is well recognized (Barber and Roszwołowska-Dowzenko 1948). The difference between the closed and open infections which were present on admission to hospital is interesting, however, because similar proportions of the two groups had had penicillin therapy of comparable duration. Either poor access of penicillin or the absence of cross-infection could account for the significantly smaller number of resistant strains isolated from the closed group. Support for the latter explanation is gained from further study of the open infections. These were made up as follows:

- Infected fingers, hands, etc.: 23
- Skin infections: 19
- Otitis media: 15
- Otitis externa: 4
- Wound infections (not arising in hospital): 7
- Cutaneous ulcers: 7
- Treating abscesses: 6
- Animal and sinus infections: 8
- Transplantations: 3
- Total: 163

Table II shows that, with increasing time in hospital, the proportion of resistant strains rose, so that after the first week in hospital these open cases were almost indistinguishable, in respect of penicillin resistance, from infections arising in hospital (68% and 76% providing resistant strains, respectively). That this effect is not due to treatment with penicillin is shown in table III, where the correlation is seen to be with the time spent in hospital rather than with the presence or absence of previous penicillin therapy.

CONCLUSIONS

Our results seem to show that, in staphylococcal infections treated with penicillin, resistant strains would rarely emerge if cross-infection were avoided. They also show how rapidly this cross-infection occurs in hospital.

We hope to publish separately the section of this work dealing with the outpatients, who made up the balance of 1000 cases studied.

We wish to thank Mr. R. L. Vloet, D.P.H., for constant encouragement at all stages of the work, and Mr. J. D. Finney for advice on the treatment of some of the data.

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<table>
<thead>
<tr>
<th>Time in</th>
<th>Total Strains</th>
<th>% Resistant</th>
<th>chi-squared</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>hospital</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-1 day</td>
<td>51</td>
<td>25</td>
<td>5.42</td>
<td>0.02</td>
</tr>
<tr>
<td>2-7 days</td>
<td>27</td>
<td>52</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 + days</td>
<td>25</td>
<td>68</td>
<td>1.41</td>
<td>0.23</td>
</tr>
</tbody>
</table>

For the table as a whole, chi-squared = 13.63, P = 0.001.

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- Skin infections . . . . . . . . . . . . . . . 19
- Otitis media . . . . . . . . . . . . . . . . . 15
- Otitis externa . . . . . . . . . . . . . . . . 3

CONCLUSIONS
So what about palliative care?

- Audit of current practice – April/May 2013
- Literature
- Discussion
Audit

• 57 consecutive palliative care inpatients discharged from PCC in April/May 2013
  – Average age 70
  – Male 36, Female 21
  – Died 31, Discharged 26

• Antimicrobials - 27 had some form of Abs
  – Antifungals – 14, of these, 11 had no other Abs
  – Topical metronidazole - 2
  – Oral antibiotics – 4, of whom 3 were discharged
  – Parenteral antibiotics – 11, of whom 10 died – the other one had two doses only
  – No parenteral Abs started in PCC – most stopped before or on transfer to PC
Literature review

• Limited literature
• Does it help guide our practice?
“This survey demonstrates that in specific circumstances a beneficial role exists for the use of parenteral antibiotics in a palliative care setting. The establishment of appropriate guidelines is recommended.” (913 pts of which 41 had Abs)

“Mixed evidence of benefit from antibiotics in dementia”

“According to the study, antibiotic treatment (in demented patients) was associated with longer survival after suspected pneumonia episodes compared to no treatment. Comfort, however, was highest among those not treated with antibiotics and was progressively lower as the aggressiveness of care increased (i.e., those taking either intravenous or intramuscular antibiotics were in greater discomfort).”

Commentary on
Givens, J. in Archives of Internal Medicine, July 12 2010
Study of 3884 patients dying in hospice care in USA

“Conclusion
In this nationally representative sample, 27% of hospice patients received an antibiotic during the last seven days of life, most without a documented infectious diagnosis. Further research is needed to elucidate the role of antibiotics in this patient population to maintain palliative care goals while reducing unnecessary antibiotic use.”

Albrecht J S et al, A Nationwide Analysis of Antibiotic Use in Hospice Care in the Final Week of Life, Journal of Pain and Symptom Management
published online 14 January 2013
Conclusion

• Not a large quantity of research
• Tends to suggest need for more research
• Literature that describes practice does not really help us to decide which patients to treat with antibiotics
• So how do we decide?
“Simple consultation reduces the use of antibiotics in patients in ICU who have advanced cancer”

How to approach decision making?

• Advance Care Planning – what are the patient and their family hoping to achieve?
• What is achievable? Futility!
• Does the patient have an infection that could be treated?
• Benefit vs. burden
• Open discussion with patient/decision maker
• Clarity about goals and end-points
If decision is made that antibiotic treatment might be desirable

• What is the best antibiotic and route of delivery?
  – However, for some infections the answer may cause us to go back up the decision-making tree if the options are found to be too burdensome

• If in doubt we consult with ID team – therapeutics changes fast in fields outside our core business
J.T. continued

• Family holding EPOA did not wish for life-prolonging measures
  – ARP prepared by ED RMO
• Admitted to medical ward for comfort measures only
• Slowly improved for a few days – took some fluid orally
• No particular issues apart from ongoing pain from arm
• Referred to pall care but no complex issues and managed by medical team
• Family equivocating over the decision of the EPOA, but more about letting go
• Blood cultures grew E. coli
JT continued

- Transferred to PCC under medical team with palliative medicine support
- Family remained slightly ambivalent
- Slow decline over several days
- Symptomatic Rx with standard measures
- Died on Day 14 post #
- Cause of death
  - 1. Urosepsis
  - 2. CKD (with anaemia) and severe aortic stenosis
So what is our role?

• To exercise the art of palliative medicine
• To bring our knowledge and experience, and our willingness and ability to talk openly about inevitable death, to help people make wise decisions about therapeutic options
• And when there is no choice, no technology of life prolongation, to state it openly and continue to provide care
• The answer posed in the title?
• No more than most, apart from how to help decide when to use them at the end of life
The Road Not Taken - Robert Frost

Two roads diverged in a yellow wood,
And sorry I could not travel both
And be one traveller, long I stood
And looked down one as far as I could
To where it bent in the undergrowth;

Then took the other, as just as fair,
And having perhaps the better claim
Because it was grassy and wanted wear,
Though as for that the passing there
Had worn them really about the same,

And both that morning equally lay
In leaves no step had trodden black.
Oh, I kept the first for another day!
Yet knowing how way leads on to way
I doubted if I should ever come back.

I shall be telling this with a sigh
Somewhere ages and ages hence:
Two roads diverged in a wood, and I,
I took the one less travelled by,
And that has made all the difference.