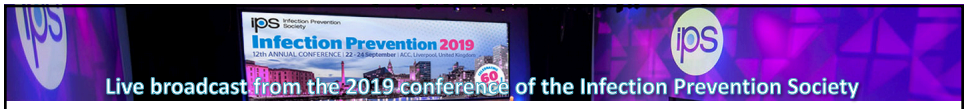


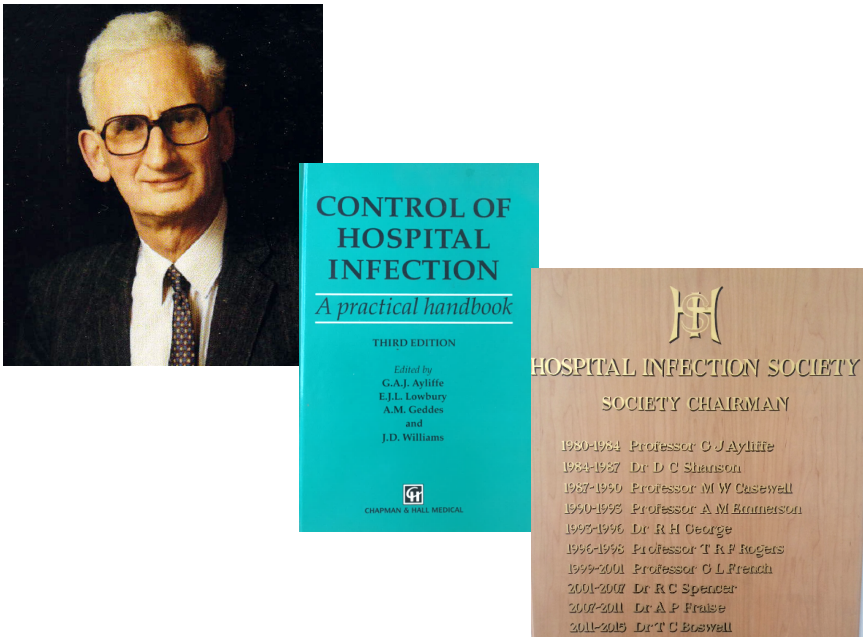
Ayliffe Lecture 2019

Pneumocystis – an important healthcare-associated infection?

Dr Tim Boswell

Consultant Medical Microbiologist & Deputy
Director of Infection Prevention and Control
Nottingham University Hospitals

www.webbertraining.com September 24, 2019



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The Graham Ayliffe Training Fellowship Award

The Graham Ayliffe Fellowship Award was established in 2013 to enable specialty trainees and infection control nurses currently working in the field of infection prevention and control (IPC) to take a one year paid leave of absence to pursue their specialist area by broadening their knowledge base and imparting that knowledge to the wider scientific and medical community.

Opportunity to work with the Journal of Hospital Infection:

For the 2019 funding round, the Graham Ayliffe Training Fellow will use 50% of their fellowship year to train as a part-time editor for the JHI (0.5 FTE). The fellow will join the Editor in Chief and other members of the JHI editorial board to develop their skills to work as an editor and to help promote the JHI. A role description is available for download and a template job plan is available on request.

Areas of special interest

In addition to the part-time editorial role, we would like the applicant to use the remainder of their Fellowship year in an innovative and novel way in order to pursue their own specialist focus within IPC. Applicants could consider working within a specialist service, developing expertise, undertaking a significant audit project, developing and implementing a guideline or performing a well defined piece of research.

- Maximum size of award: £72,000
- Duration: max 1 year
- Who: Specialty Registrars and Infection Control Nurses
- Allowances: salary, training and research
- Fellowship must be UK or Ireland based
- Availability: one award per year

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Review

Systematic review of outbreaks of *Pneumocystis jirovecii* pneumonia: evidence that *P. jirovecii* is a transmissible organism and the implications for healthcare infection control

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SUMMARY

Background: *Pneumocystis jirovecii* pneumonia (PCP) is an important cause of morbidity and mortality in immunocompromised patients. Several nosocomial outbreaks of PCP have been reported in human-immunodeficiency-virus-negative, immunocompromised patients. The primary route of *P. jirovecii* transmission has yet to be proven; however, these outbreaks of infection suggest either interhuman transmission or a common environmental source.

Aim: To identify and evaluate all published clusters and outbreaks of PCP. The main objective was to compare the epidemiology of the outbreaks, with a particular focus on the evidence for different modes of transmission.

Methods: PubMed and EMBASE were searched to identify all English-language articles describing PCP outbreaks or clusters between 1980 and March 2015. Data were extracted on the outbreak setting, features of the outbreak, application of molecular typing, results of epidemiological assessment and environmental sampling.

Findings: Thirty outbreaks described in 29 articles were identified. Twenty-five (83%) of these outbreaks were described in patients who had undergone solid organ transplantation, primarily renal transplantation. All studies described a defined cohort of patients who shared some nosocomial facilities, including both inpatient and outpatient areas. Genotyping was undertaken in 16 (47%) studies. Cases with an identical genotype were demonstrated in all these studies.

Conclusions: The findings of this review raise a number of concerns regarding the public health and infection control implications of infection with PCP. The evidence presented for nosocomial acquisition and possible person-to-person transmission of infection suggests the need for formal infection control policies.

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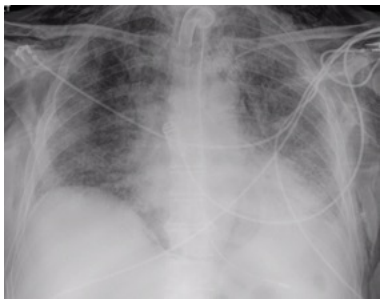
What do we know about Pneumocystis?

- *P.jirovecii (*previously *P.carinii)*
- Fungal infection (previously thought to be protozoan)
- Outbreaks 1st reported in 1950's
  - Malnourished children in orphanages
- Came to prominence in 1980's
  - HIV epidemic
- Increasingly recognised cause of pneumonia in non-HIV immunosuppressed patients



Latent vs de novo Infection

Latency

- Traditional view: infection resulted from reactivation of latent colonisation
- High prevalence of seropositivity in healthy children /adult blood donors

De Novo

- No residual organisms detected on autopsy studies of lungs in immunocompetent people
- Mice previously infected with PCP did not reactivate the infection when immunosuppressed
- Clustering of specific genotypes according to place of residence not birth
- Outbreaks involving a single identical strain of *P. jirovecii*

What did we learn from the systematic review of PCP outbreaks?

Parameter	Figures
Number of outbreaks	30
Location	70% in Europe
Patient cohort	90% adult patients 83% solid organ transplants
Median number of patients	12.5
Median outbreak duration	9 months
Epidemiological assessment (transmission map)	77% of studies
Genotyping	47% of studies
Precipitating factors	No or suboptimal PCP prophylaxis No isolation policies
Outbreak Control Measures	Outbreaks universally terminated by blanket PCP prophylaxis

Summary of Nottingham PCP outbreaks

	Adult renal transplant	Adult oncology
Year	2015	2016-17
Number of patients	11	22
Number of deaths	4	7
Transmission map	Renal outpatient clinics	Oncology outpatient clinic, in-patient transmission, other
Genotyping	Identical strain	Not done
Case-control study	Rate of attendance and number of clinic overlaps	Rate of attendance and number of clinic overlaps
Control measures	Chemoprophylaxis, masks in clinic, patient isolation	Chemoprophylaxis, masks in clinic, patient isolation

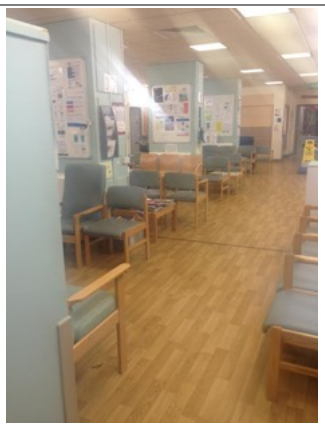
Renal transplant outbreak: case-control study

		Cases (10)	Controls (44)	Odds Ratio	95% Confidence Interval	P value
Rate of clinic attendance	Low rate	1	28	13.52	1.53 - 119.43	0.019
	High rate	9	16			

		Cases (10)	Controls (44)	Odds Ratio	95% Confidence Interval	P value
Binary overlap		9	19	12.01	1.33 – 109.77	0.027
Dose related overlap	1 overlap	1	16	1.59	0.09 – 28.3	P value for trend = 0.001
	2 or more overlaps	8	3	71.88	5.62 – 919.45	

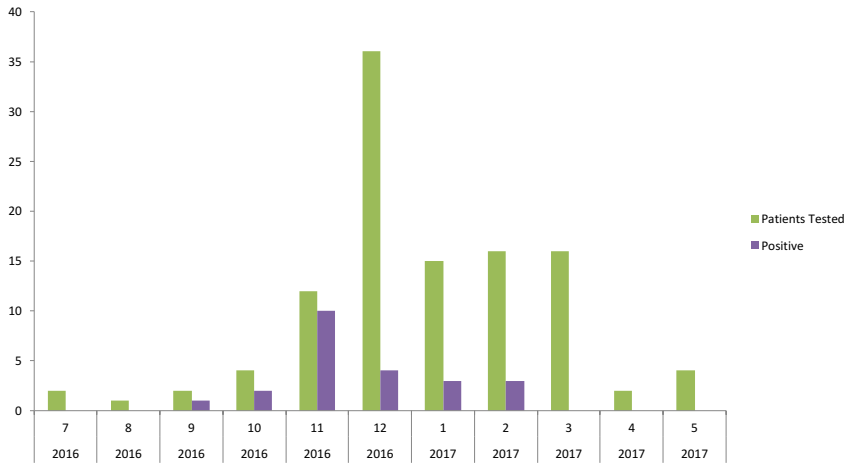
Environmental investigations

Ventilation Assessment

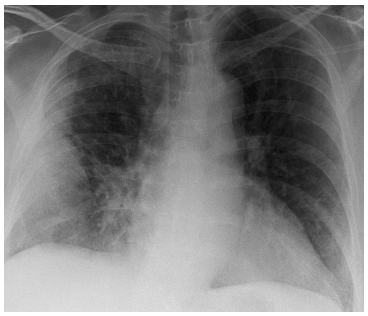


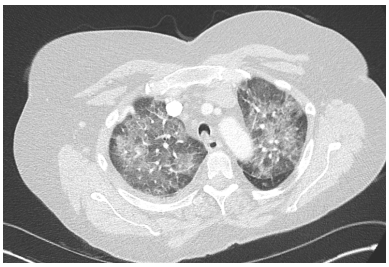
Air-Sampling

PCP outbreak curve: adult oncology



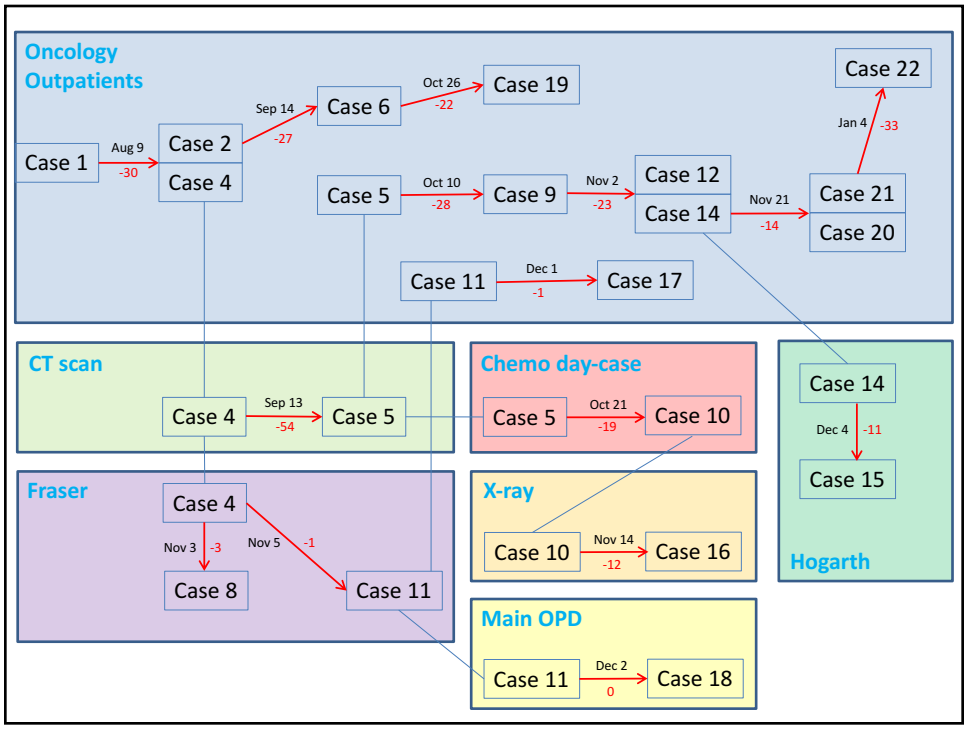
Spectrum of disease

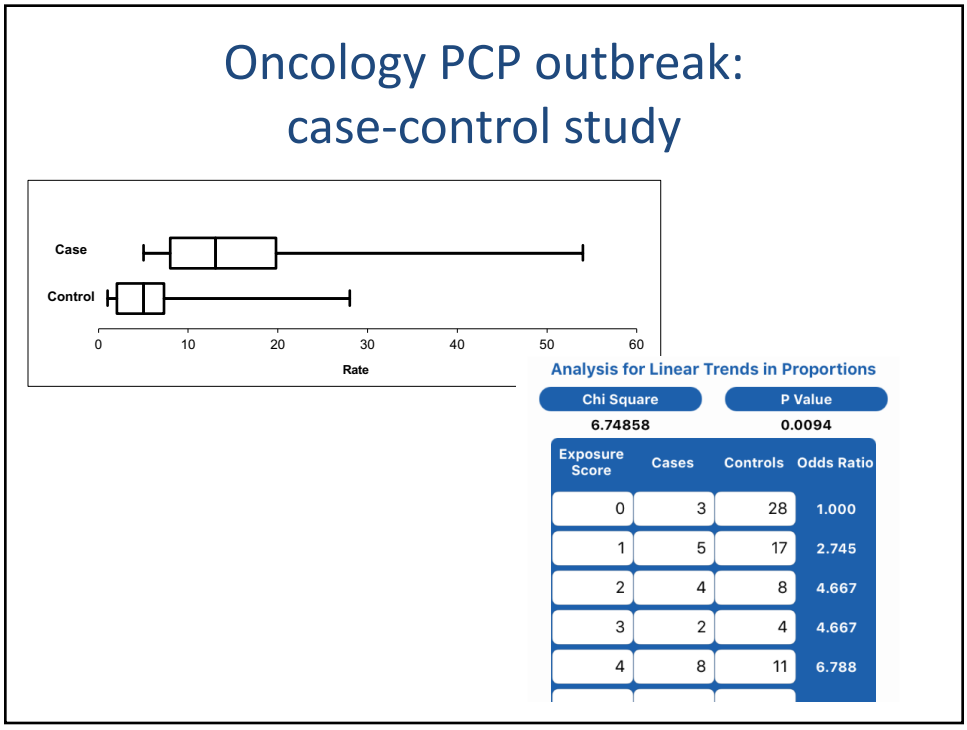




Case:control study

	Cases n=22	Controls n=68	
Male v female	8 v 14	37 v 31	p=0.21
Median age (range)	59.5 (39-78)	60 (27-85)	
Lymphopenic	17 (77%)	24 (35%)	p=0.001
Steroids	12 (55%)	20 (29%)	p=0.042
Cancer type			
Breast	9	20	
Lung	6	8	
Testicular	1	6	
Colorectal	0	6	
Oesophageal	0	5	
Prostate	0	5	


Oncology Outpatients
Case 1
Aug 9
-30
Case 2
Case 4
Sep 14
-27
Case 6
Oct 26
-22
Case 19
Case 5
Oct 10
-28
Case 9
Nov 2
-23
Case 12
Case 14
Nov 21
-14
Case 21
Case 20
Jan 4
-33
Case 22
Case 11
Dec 1
-1
Case 17
CT scan
Case 4
Sep 13
-54
Case 5
Chemo day-case
Case 5
Oct 21
-19
Case 10
Case 14
Dec 4
-11
Case 15
Hogarth
Fraser
Case 4
Nov 3
-3
Case 8
Nov 5
-1
Case 11
X-ray
Case 10
Nov 14
-12
Case 16
Main OPD
Case 11
Dec 2
0
Case 18


Oncology PCP outbreak:
case-control study
Case
Control
0
10
20
30
40
50
60
Rate
Analysis for Linear Trends in Proportions
Chi Square
6.74858
P Value
0.0094
Exposure Score
Cases
Controls
Odds Ratio
0
3
28
1.000
1
5
17
2.745
2
4
8
4.667
3
2
4
4.667
4
8
11
6.788

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Conclusions: The findings of this review raise a number of concerns regarding the public health and infection control implications of infection with PCP. The evidence presented for nosocomial acquisition and possible person-to-person transmission of infection suggests the need for formal infection control policies.

Current Guidance

Organisation (reference)	Year of Publication	Guidance
IDSA	2014	Note the existence of outbreaks but state that data insufficient to support isolation of patients with PCP from others at risk
BHIVA	2011	State evidence for nosocomial infection exists but is limited. No guidance regarding infection control / isolation.
NHMRC (Australia)	2010	State that Transmission route is uncertain. Recommend standard precautions.
CDC	2007	Advise avoidance of placement with PCP in the same room as an immunocompromised patient

Local approach: PCP infection prevention and control

- *P.jirovecii* designated an ALERT organism
- PCP an ALERT condition
- Patients with confirmed/suspected pneumocystis ISOLATED (respiratory precautions)
- Pneumocystis surveillance
  - 2 linked cases ? Outbreak
- High risk outpatient areas: renal transplant, clinical haematology, oncology
  - Use of masks for patients with cough, cold, coryza, URTI
- Review of PCP chemoprohylaxis

Local approach: PCP infection prevention and control (2)

- Contact tracing: renal transplant
- Assume patients may be infectious for up to 90 days prior to diagnosis
  - Review of potential other transplant patients in contact
- Short course co-trimoxazole (960mg bd for 2 weeks) offered to these at risk contacts

Summary

- *P.jirovecii* is an airborne transmissible pathogen
  - Capable of causing significant morbidity and mortality
  - Capable of causing large HCAI outbreaks
  - Numerous outbreaks have been described
- Patients appear to be infectious for several weeks prior to diagnosis
- Transmission often takes place in out-patient or day-case facilities
- Important to consider PCP as an ALERT condition
  - Surveillance important to detect potential clustering
- IPC guidelines are needed
- Lots of opportunity for further study and investigation…

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Dr Tim Boswell, Nottingham University Hospitals
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