Journal of Hospital Infection 96 (2017) 151–156

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevierhealth.com/journals/jhin

# Investigation of outbreaks of *Pneumocystis jirovecii* pneumonia in two Scottish renal units

T. Inkster [a,d,*], S. Dodd [a], R. Gunson [b], L. Imrie [a,c], E. Spalding [d], S. Packer [a], C. Deighan [a], C. Daly [a], J. Coia [a], T. Imtiaz [d], C. McGuffie [d], R. Wilson [d], A.M. Bal [d]

[a] *Incident Management Team, Western Infirmary, Glasgow, UK*
[b] *Department of Virology, Glasgow Royal Infirmary, Glasgow, UK*
[c] *Health Protection Scotland eField Epidemiology Service, Public Health England, UK*
[d] *Incident Management Team, University Hospital Crosshouse, Kilmarnock, UK*

ARTICLE INFO

*Article history:*
Received 5 August 2016
Accepted 2 November 2016
Available online 18 November 2016

*Keywords:*
*Pneumocystis jirovecii*
*P. jirovecii* pneumonia (PCP)
Renal transplant
Outbreak

SUMMARY

*Pneumocystis jirovecii* is recognized as an opportunistic pathogen. In recent years, human-to-human transmission of *P. jirovecii* has been demonstrated. However, outbreaks of *P. jirovecii* infections are not well defined because the epidemiological setting that facilitates transmission is not fully understood. This article describes two outbreaks of *P. jirovecii* pneumonia (PCP) in renal transplant patients in the West of Scotland. In total, 25 patients in two geographically contiguous locations were affected. Allele B was identified as the dominant type, along with allele A3. It was not possible to determine the exact reason for clustering of cases, although the outpatient clinic setting featured in one of the outbreaks. The outbreaks ceased with the use of trimethoprim-sulphamethoxazole prophylaxis; the target populations that received prophylaxis were different in the two outbreaks. Infection control teams should be alert to the possibility of outbreaks of PCP.


## Introduction

*Pneumocystis jirovecii* was first described in guinea pig and rat lungs in 1909.[1] The organism, which is ubiquitous in the environment, was initially classified as a parasite, and was subsequently reclassified as a fungus in 1988. *P. jirovecii* is a well-described pathogen in patients with human immunodeficiency virus (HIV), and was a leading cause of morbidity and mortality in this group in the 1980s. However, in more recent years, it has declined in patients with HIV but emerged in other immunosuppressed patient groups, particularly the renal transplant population. Factors that may have contributed to this increase include increasing immunosuppression, an increase in the prevalent transplant population, greater awareness with improved diagnostics, enhanced transmission between susceptible hosts, and variations in prophylaxis protocols.[2]

The epidemiology of *P. jirovecii* infection is not fully understood. In one study, most individuals were found to be exposed in early childhood, with >80% of children having detectable antibodies by four years of age.[1] Potential modes of transmission of the organism are re-activation of latent carriage, environmental exposure or interhuman transmission, as evidenced by typing of cases during recent clusters.[2] Most cases of *P. jirovecii* pneumonia (PCP) are now believed to be a result of recent acquisition.[3]

* Corresponding author. Address: Department of Microbiology, Queen Elizabeth University Hospital, Glasgow G51TF, UK.
*E-mail address:* Teresa.Inkster@nhs.net (T. Inkster).

http://dx.doi.org/10.1016/j.jhin.2016.11.005

In the absence of prophylaxis, PCP occurs in approximately 3.8% of renal transplant recipients; the risk is four times higher in the first year post transplant, with a mortality rate of up to 49%.[4] The European Renal Association recommends prophylaxis for PCP for at least four months post transplant.[5] The UK Renal Association states that all patients should receive three to six months of trimethoprim-sulphamethoxazole (TMP-SMX) 480 mg daily.[6]

This article describes two outbreaks of PCP amongst renal transplant and non-transplant renal patients receiving immunosuppression in two renal units in hospitals in the West of Scotland from October 2012 to May 2015, along with measures taken to limit transmission. Twenty-five patients across two health boards in the region developed PCP during this period.

## Methods

### *Setting*

The outbreaks took place in two regional nephrology units within acute hospital settings in the West of Scotland. The renal unit at Western Infirmary, Glasgow has 61 beds across three wards comprising of four-bedded and single rooms. Transplant clinics are situated at several hospitals across the city. The renal service at University Hospital Crosshouse is based at the John Lynch dialysis unit and in two inpatient wards. At University Hospital Crosshouse, there are two separate clinics for renal transplant and non-transplant patients, but they share a common waiting area. All patients at University Hospital Crosshouse are transplanted at Glasgow renal transplant unit and receive follow-up at the Glasgow unit for up to one year following transplantation.

### *Time course*

The outbreak at Western Infirmary lasted from October 2012 until May 2013. This was followed by an outbreak at University Hospital Crosshouse between November 2014 and May 2015.

### *Case definition*

The case definition was any renal transplant patient with a respiratory illness consistent with PCP and detectable *P. jirovecii* in sputum, throat swab or bronchoalveolar lavage by polymerase chain reaction (PCR).

### *Existing prophylaxis and immunosuppressant protocols*

At both units, all renal transplant patients receive prophylaxis for PCP with TMP-SMX for three months post transplant. There are no situations whereby prophylaxis for PCP would normally be re-instated after that. The standard immunosuppressive regime is prednisolone, tacrolimus and mycophenolate mofetil.

### *Identification and typing methods*

PCR was used to identify PCP. The West of Scotland Specialist Virology Centre (WoSSVC) undertook multi-locus sequence typing (MLST) for typing the strains. The internal transcribed spacer (ITS)-1 sequence is located on the nuclear ribosomal ribonucleic acid (rRNA) operon between the genes of 18S rRNA and 5.8S rRNA, and shows a high level of polymorphism that has been used for genetic typing applications. The amount of polymorphism at the mt26s rRNA locus is substantially less than that reported for ITS; nevertheless, the variation observed in this second locus has helped address a number of important epidemiological questions.

Respiratory samples positive for *P. jirovecii* were extracted using the Easymag Nucleisens (Biomerieux- Marcy-l'Étoile, France) extraction platform. Genotyping of *P. jirovecii*-positive specimens was performed using the MLST method described previously.[7] However, based on previous outbreak investigations in both Belfast and Liverpool, the WoSSVC chose to sequence the ITS and the mt26sRNA regions alone as these regions were most sensitive and discriminatory.[8,9] The ITS and mt26sRNA regions were amplified by nested PCR using Roche Expand High Fidelity Roche Master Mix (Roche-Basel, Switzerland) using the reaction and cycling conditions and primer concentrations as described in the protocol. Following electrophoresis on a 1.2% gel, the relevant-sized DNA amplicons (ITS1 204 bp, mt26S 347 bp) were purified using QIAquick Gel Extraction Kit (Qiagen-Hilden, Germany) and eluted in 50 μL of AE buffer (Qiagen- Hilden, Germany). Purified products were sequenced on a ABI3130XL capillary sequencer (ABI - Carlsbad, California, USA) using the Big Dyes v3.1 sequencing kit (ABI - Carlsbad, California, USA). Sequence analysis was performed with SeqMan Version 5.08 (DNASTAR). The obtained sequences were compared with *P. jirovecii* reference gene sequences for each gene (Accession No. U07220 for ITS1, M58605 for mt26S) and alleles were determined. Of the 25 isolates, one was not available for typing.

## Results

### *Description of incident and cases*

#### *Western Infirmary, Glasgow*

In February 2013, the infection control team was alerted to three concurrent PCP infections amongst renal transplant patients. A lookback exercise was performed and this identified eight renal patients diagnosed with PCP between October 2012 and February 2013. Data from the WoSSVC that performed PCR testing confirmed that there had been no PCP-positive renal transplant patients in 2010, and there had only been one case in 2011. The finding of eight positive results was therefore deemed to represent a significant increase in this patient population. Importantly, there had been no change in PCP testing methods during this time, and no increase in the number of samples being sent which may have indicated raised awareness. Subsequently during the course of the investigation and from February to May 2013, a further six cases of PCP were identified, taking the total number of cases in this incident to 14.

All patients had a history of renal transplantation and had received immunosuppression with prednisolone, tacrolimus and mycophenolate mofetil. In addition, all had received the recommended prophylaxis for PCP with TMP-SMX. None remained on TMP-SMX prophylaxis at the time of infection. No patients had significant bacteriology results at the same time as the PCP diagnosis. The interval from transplant to positive result ranged from eight months to 15 years. Only two patients had acquired PCP within one year of renal transplant. Seven