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## Uncomplicated Cystitis in an Adult Male Following Influenza B Virus Infection

Authors' Contribution:  
Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

ADEF 1 **Robert J. Allen**  
EF 1 **Marios Koutsakos**  
DE 2 **Aeron C. Hurt**  
E 1 **Katherine Kedzierska**

1 Department of Microbiology and Immunology, University of Melbourne, at The Peter Doherty Institute for Infection and Immunity, Melbourne, VIC, Australia  
2 World Health Organisation (WHO) Collaborating Centre for Reference and Research on Influenza, at The Peter Doherty Institute for Infection and Immunity, Melbourne, VIC, Australia

**Corresponding Author:** Robert J. Allen, e-mail: [rjallen@student.unimelb.edu.au](mailto:rjallen@student.unimelb.edu.au)  
**Conflict of interest:** None declared

**Patient:** Male, 31  
**Final Diagnosis:** Uncomplicated cystitis  
**Symptoms:** Cough • dysuria • fever • hematuria  
**Medication:** —  
**Clinical Procedure:** —  
**Specialty:** Infectious Diseases

**Objective:** Unusual clinical course





**Background:** Influenza B viruses cause seasonal epidemics of respiratory illness, circulating concurrently with influenza A viruses. However, virological and clinical knowledge of influenza B viruses is less well advanced than for influenza A, and in particular, complications associated with influenza B infection are not as commonly reported. Complications of influenza B infection predominantly include neurological and musculoskeletal pathologies, while a review of the literature shows that bacterial infections associated with influenza B viruses often involve Gram-positive organisms, with a smaller subset featuring Gram-negative species.

**Case Report:** In this case report we highlight an uncomplicated infection of the urinary tract by *Escherichia coli* immediately following influenza B infection, in an otherwise healthy adult white male with no prior history of urinary tract infection or structural abnormalities of the renal tract.

**Conclusions:** Bacterial infections complicating influenza B infection may include organisms not commonly associated with the respiratory system, such as *Escherichia coli*. In addition, bacterial complications of influenza B infection may affect non-respiratory systems, including the genitourinary tract.

**MeSH Keywords:** Gram-Negative Bacterial Infections • Influenza B virus • Urinary Tract Infections

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## Background

Influenza A and B viruses are important human pathogens causing seasonal outbreaks of illness and resulting in significant morbidity and mortality. While a large amount of research has been conducted into influenza A viruses, less is known about influenza B, even though it is recognized as an important pathogen [1]. Infection with an influenza virus principally causes a self-limiting respiratory illness with mild to moderate systemic symptoms, although occasionally influenza virus has been shown to disseminate through cardiac, neurological, and muscular tissues [1]. The most commonly reported complications arising from influenza infection are subsequent secondary bacterial infections often resulting in pneumonia. These secondary infections have been more commonly reported following influenza A infection, but here we present a novel case of uncomplicated urinary tract infection (cystitis) in an adult male following influenza B infection.

## Case Report

A 31-year-old immunocompetent white male presented to a local hospital emergency department with a 6-day history of febrile illness. The patient reported a rapid onset and progression of symptoms, including sore throat, myalgia, arthralgia, pronounced fatigue, and fever. After 2 days of dry cough, this became productive of thick yellow sputum, approximately 200 mL/day, associated with 2 episodes of streaky hemoptysis. The patient presented to the emergency department due to ongoing symptomatology. Within the emergency department, vital signs were within normal limits (heart rate 97, blood pressure 114/77, temperature 37.1°C). Audible rhonchi were noted together with dry and erythematous oral mucous membranes, but there were no further abnormalities observed upon examination of the respiratory, cardiovascular, and gastrointestinal systems. Hematological and biochemical analyses revealed normal white cell count  $8.7 \times 10^9$  cells/L (normal 4.0–11.0) with a mild monocytosis  $1.2 \times 10^9$  cells/L (normal 0.1–0.8), while C-reactive protein was elevated at 129.9 mg/L (normal <5.0). An oropharyngeal swab was collected (6 days post-symptom onset) and following a respiratory virus multiplex polymerase chain reaction (PCR) and subsequent sequence analysis was found to contain an influenza B virus of the B/Victoria/2/87-lineage. Other viruses including influenza A, respiratory syncytial virus, rhinovirus, adenovirus, human metapneumovirus, and parainfluenza virus were not detected. Although the patient had received an inactivated 2015 trivalent influenza vaccine (Vaxigrip, Sanofi Pasteur) 6 months prior to infection, the vaccine contained a single influenza B virus (B/Phuket/3073/2013) from the B/Yamagata/166/98-lineage, which provided little or no protection from influenza B strains from the B/Victoria/2/87-lineage. The patient did not receive

any urethral instrumentation in the emergency department, or at any other time during the illness.

During the acute phase of illness, the patient was administered the maximum recommended daily allowances of simple analgesics (paracetamol and ibuprofen) and decongestants (containing chlorpheniramine maleate, codeine phosphate, and pseudoephedrine hydrochloride) with little to no improvement in symptoms. Anaesthetic throat spray containing amylnmetacresol, dichlorobenzyl alcohol, and lignocaine provided temporary relief for pharyngitis, while codeine linctus provided relief of nocturnal dry cough. At the emergency department, the patient received 1L of 0.9% normal saline (NaCl) intravenously and was discharged. Systemic symptoms began to resolve after a further 3 days, and the patient returned to work at day 10 after symptom onset.

However, 6 days later (day 16 after symptom onset) the patient experienced a mild fever, progressing within the following 24 hours to include dysuria, urinary frequency, and hematuria. The hematuria lasted approximately 8 hours, with the passing of clots and blood-stained urine at 15-minute intervals, accompanied by back pain. The patient attended a local general practitioner, where a urine dipstick was positive for erythrocytes and leucocytes, although macro-hematuria had ceased by this time. As the back pain had been present since the initial phase of the respiratory illness, and onset associated with coughing paroxysms, pyelonephritis was considered unlikely. A diagnosis of uncomplicated urinary tract infection was made and a 7-day course of oral trimethoprim 300 mg daily commenced in accordance with national Therapeutic Guidelines. The urine specimen was not tested for influenza RNA by PCR. The patient had no prior history of urinary tract infections, either in adulthood or childhood. Persistent dysuria and urinary frequency lasted a further 3 days after commencement of oral antibiotics, but without further episodes of hematuria. The patient was followed up at 6 months after presentation and no further complications or ongoing symptoms relating to either the respiratory or urinary tract infections were reported.

## Investigations

- Urine dipstick: pH 6, Protein +, Glucose NIL, Ketones NIL, Blood TRACE, Urobilinogen TRACE, Bilirubin NIL, Specific gravity 1.024 (normal 1.005–1.030);
- Urine microscopy: Leucocytes  $245 \times 10^6$  cells/L (normal <10), Erythrocytes  $4 \times 10^6$  cells/L (normal <12), Squamous Epithelial cells  $3 \times 10^6$  cells/L;
- Urine culture: *Escherichia coli*  $>100 \times 10^6$  cfu/L;
- Urine culture sensitivities: Trimethoprim sensitive;
- Renal tract ultrasound: Both kidneys were of normal size. No evidence of parenchymal abnormality or hydronephrosis on

either side. No bladder abnormality seen but a small 17.5 mL residual volume was noted following micturition.

## Discussion

Complications of influenza virus infection typically occur in the very young, elderly, pregnant, immunocompromised, and those with cardiovascular comorbidities, and are less commonly seen in otherwise healthy adults. Pneumonia is the most common complication of seasonal influenza A infection in adults, and is categorized either as primary viral pneumonia or secondary bacterial pneumonia, cases of which account for approximately one-quarter of influenza-associated deaths [2]. Influenza B infections are typically limited to the upper respiratory tract, but can be exacerbated by severe systemic complications that may be fatal even in previously healthy individuals. Of the various neurological complications that have been reported, febrile seizures are among the most common [3]. Cardiovascular complications most typically involve myocarditis, which can be fatal even in otherwise healthy patients [4]. Musculoskeletal pathologies (myositis) that did not result in renal impairment have also been reported [3].

A clinical review of the microbiology of bacterial co-infection associated with severe influenza A infection identified multiple Gram-positive pathogens, which most commonly included *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Streptococcus pyogenes* [5]. While bacterial co-infections associated with influenza B infection have been reported less frequently, the same opportunistic pathogens have been observed [6,7]. Co-infection with Gram-negative organisms, including *Haemophilus influenzae* and *Pseudomonas* species, are less common [5], while *E. coli* co-infections are rare. A fatal case of influenza A infection in a previously healthy adult male was associated with *E. coli* cultured from pulmonary abscesses, although any causal relationship was complicated by the additional identification of *S. aureus* and Herpes simplex virus in this patient [8]. More recently, a case series reported 6 hemodialysis patients with pandemic influenza (pdmH1N1) complicated by nosocomial *E. coli* pneumonia [9].

Hematuria describes the presence of red blood cells in the urine, which may originate from proximal urinary tract structures such as the kidneys to more distal genitourinary tissues, requiring clinicians to consider both renal and genitourinary pathologies. There are multiple reports of influenza B infection resulting in acute renal failure as a consequence of myositis and rhabdomyolysis, occurring in both males and females, and in both pediatric [10,11] and adult patients [12]. Acute renal injury associated with influenza B virus most likely occurs as a result of myoglobinemia, marked elevation of serum creatine kinase, and acute tubular necrosis. While ultimately resulting

in end-organ renal pathology, these reports highlight an initiating infection and/or inflammation of skeletal muscle, rather than direct injury to the renal or genitourinary systems. Nevertheless, direct infection of renal tissue has been documented in a case report of renal transplant from a donor positive for influenza B [13]. Biopsy of the kidney at transplantation was positive for influenza B virus by reverse transcription polymerase chain reaction (RT-PCR), although this did not result in systemic transmission of infection to the organ recipient, and there was no detectable virus on repeat biopsy at day 14 post-transplant.

Tabbutt et al. [11] describe a case of influenza B associated myocarditis and myositis requiring extracorporeal membrane oxygenation and hemodialysis in a 4-year-old girl. The patient initially presented with lethargy and dehydration, and was started on antibiotics for urinary bacteriuria (*E. coli* <25,000 cfu on urine culture) prior to deterioration and diagnosis of influenza B virus by nasopharyngeal swab. It is not fully clear if the presence of *E. coli* in the urine culture was responsible for the child's clinical condition, or if bacteriuria occurred as a result of influenza B infection, as these matters were not the focus of the report. Nonetheless, to the best of our knowledge, this is the only other case of influenza B infection describing a possible association with urinary tract infection.

In general, bacterial infections of the renal system are less common in males compared with females, and tend to occur in pediatric and geriatric cohorts, in the immunocompromised, in patients with spinal cord injury, and following procedures involving instrumentation of the bladder or renal tract surgery [14,15]. As such, the annual incidence of uncomplicated cystitis in a healthy adult male is given as 5 infections per 10,000 men, compared with 0.5 infections per person/year in women [16,17]. Indeed, as a result of the low incidence of urinary tract infections in adult males, patients are sometimes investigated with renal tract ultrasound for the detection of structural abnormalities, but this is rarely performed for female patients with uncomplicated cystitis.

This case report represents an unusual complication following influenza B infection. A healthy adult male, with no prior history of urinary tract infection, and no structural abnormality of the renal tract, developed dysuria, frequency, and hematuria 9 days after resolution of most respiratory symptoms. This time period is consistent with cases of secondary bacterial pneumonia associated with influenza A infection, where the subsequent bacterial infection can occur up to 11 days following the initial viral illnesses [5]. The mechanism that underpins the development of uncomplicated cystitis, or indeed of any systemic complication, following influenza B infection remains unclear. Possibilities include direct infection of genitourinary epithelium by influenza B virus and weakening of

local innate defences, elaboration of a hypercytokinemia state resulting in immunopathology, and/or dissemination of infected leucocytes from the site of respiratory infection to distant tissues. It is known that initial infection of respiratory epithelium with influenza A virus increases bacterial colonization, growth, and adherence to respiratory mucosa [2,18,19]. In this case, it is possible that infection with influenza B virus weakened the innate defences of the genitourinary mucosa, facilitating the urinary tract infection with *E. coli*.

## Conclusions

We highlighted an unusual case of uncomplicated *E. coli* cystitis that was temporally associated with influenza B infection in an otherwise healthy adult male. This case should be considered in context alongside other bacterial complications of influenza infection, which more typically involve Gram-positive pathogens. In conclusion, primary care and emergency department clinicians should be alert to the possibility of complications associated with influenza B virus infection, including

Gram-negative bacteria and conditions that affect non-respiratory systems.

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## Conflicts of interest

There are no conflicts of interest to declare.

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